Aswan University Medical Journal, volume 5 / No.3/ September 2025 (1-12) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Validity of Platelet Mass Index in Platelet Transfusion in Management of Neonatal Thrombocytopenia

Ashraf A. Meabed[1], Entesar Awn Allah Gaber Barsi[1*], Hanan Mohammed abd el moneim[1], Magda F Gabri[1], Khalid IA Elsayh[2].

1- Pediatrics Department, Faculty of Medicine, Aswan University

2- Pediatrics Department, Faculty of Medicine, Assuit University

ABSTRACT

Keyword: : NT, NICU, PMI Guideline, PC Guideline.

*** Corresponding author**: Entesar Awn Allah Gaber Barsi

Mobile: +201065035578

E-mail: entesarawny2016@gmail.com

Background: Platelets serve as the primary defense mechanism against hemorrhage. Neonatal thrombocytopenia is a common hemostatic abnormality among newborns in the neonatal intensive care unit (NICU), and using prophylactic platelet transfusion resulted in a higher rate of death or significant bleeding. **Objectives:** This study aimed to compare the outcome of using Platelet Mass Index (PMI) versus Platelet Count (PC) guidelines in prophylactic platelet transfusion. **Methodology:** This single-blinded, randomized controlled trial was conducted on 140 neonates with a <100,000/ml platelet count admitted to the NICU. **Results:** A significantly higher percentage of patients needed platelet transfusion in the PC guideline group vs. the PMI guideline group (77.1% vs 17.1%). Further, there was a statistically significantly higher percentage of hemorrhage, pulmonary hemorrhage, and mortality in the PC group vs. the PMI group (24.3% vs 10%, p=0.025, 17.1% vs 5.7%, p=0.034v 22.9% vs 10%, p-value=0.040, respectively). **Conclusion:** This study demonstrated that transfusion strategies based on PMI guidelines resulted in higher post-transfusion platelet counts compared to the PC approach. Also, significant improvements in clinical outcomes were observed in the PMI group, including lower bleeding rates, intracranial hemorrhage, and mortality.

INTRODUCTION

Platelets act as the main defense against hemorrhage brought on by both microvascular and macrovascular injuries by adhering and aggregating to maintain endothelial integrity. If your platelet count (PC) is less than 150 × 10^9/L, you have thrombocytopenia **(1)**.

A common hemostatic abnormality among newborns in the Neonatal Intensive Care Unit (NICU) is neonatal thrombocytopenia (NT), which rises in proportion with prematurity. Numerous immunologic and non-immunologic factors have been found to contribute to NT **(2)**.

There was a higher risk of death or significant bleeding when prophylactic platelet transfusion was used based on a platelet-count threshold of 50,000 as opposed to 25,000 **(3)**. Platelet transfusion rates in the NICU may be decreased by using criteria based on the platelet mass index (PMI), but more information from prospective studies is needed **(4)**.

The primary objective of this study was to assess the efficacy of utilizing PMI criteria as a predictive tool to optimize the administration of prophylactic platelet transfusions in neonates with NT admitted to the NICU at Aswan University Hospital (AUH).

PATIENTS AND METHODS

This single-blinded Randomized Controlled Clinical Trial (RCT) was conducted on 140 neonates with NT, admitted to the NICU at AUH from April 2022 to October 2023. The sample size was calculated using Stata 16. The alpha error = 0.05, power 80%, and the reduction of prophylactic blood transfusion from 92% to 73% **(5)**. The minimum required sample was 124 participants. To compensate for attrition and drop-outs, the sample was raised by 20% to 140 (i.e., 70 per group).

Cases admitted to NICU with NT with a <100,000/ml PLT count were included. On the other hand, those with significant congenital anomalies, hydrops fetalis, family history of thrombocyte diseases, or coagulation disorders were excluded. The patients were grouped according to the onset of thrombocytopenia. Thrombocytopenia before 72 h was defined as early-onset thrombocytopenia and after 72 h as late-onset thrombocytopenia(4).

Randomization:

Random numbers were generated at the computer center. Eligible cases were randomly assigned into two equal groups: Group I, which included 70 neonates with platelet transfusion according to the PLT count-based guideline, and Group II, which included 70 neonates with platelet transfusion according to the PMI-based guideline. Allocation was contained in opaque, sequentially numbered, sealed envelopes.

PMI is determined by multiplying platelet count by mean platelet volume (MPV), and the recommendation for transfusion based on PMI is as follows: PMI is < 800 in pre/postoperative patients, < 400 in unstable patients, and < 160 in stable patients (4).

Procedure

All cases underwent entire history taking, clinical examination, and complete blood count (CBC). The number of PLT transfusions in both groups was recorded.

Clinical conditions of patients were classified into stable patients, unstable patients and immediate pre or postoperative patients.

Stable patients: premature (heart rate: 120-170 beats/minute, blood pressure: 55-75/35-45 mm Hg, respiratory rate: 40-70 breaths/minute). Full-term (heart rate: 100-150 beats/minute, blood pressure:65 -85/45-55 mm Hg, respiratory rate: 35-55 breaths/minute).

Unstable patients (neonates<1500 g birth weight in the first week of life or patients with heart rate or blood pressure or respiratory rate below the expected level for age and need resuscitation including mechanical ventilators or receiving continuous vasopressors) **(6)**.

The PLTs were extracted from whole blood donations, which underwent leucofiltration. After matching, they were given in a dosage of 10–20 milliliters per kilogram of body weight.

PLT counts and MPVs were determined using a Sysmex Xn 1000 Hematology Analyzer and a Mindray Hematology Analyzer BC-5150. Venous blood sample (3ml) anticoagulated with ethylene diamine tetra acetic acid (EDTA).

Morbidity and mortality in both groups were recorded. Morbidity included infections, birth asphyxia, prematurity, low birth weight, necrotizing enterocolitis and hyperbilirubinemia. In addition, hemorrhages (pulmonary, gastrointestinal and mucocutaneous) in both groups were evaluated.

Major hemorrhage is defined as a hemorrhage requiring prompt, sustained nursing intervention (e.g., pulmonary hemorrhage requiring repeated endotracheal tube suctioning) or medical evaluation/intervention (e.g., red blood cell transfusion within 24 h).

Statistical analysis

Data analysis was undertaken using IBM-SPSS version 26 **(7)**. Categorical data were presented as frequencies and percentages. Numerical data were checked for normality by the Shapiro-Walk test and presented as mean and standard deviation (SD) or median and range according to their distribution. The Independent Sample T-test/Mann-Whitney U test was used to compare the mean/median difference between the two groups as appropriate. A Paired Sample T-test/Wilcoxon Sign test was used to compare the mean/median within the group before vs. after transfusion. The chi-square test/Fisher's exact test was used to compare proportions between groups as convenient. The level of significance was considered at p-value < 0.05.

Ethical considerations

The institutional Ethics and Research Review Board (IRB) of the Faculty of Medicine at Aswan University approved the study's methodology. The newborn enrolled in this study signed a written informed consent before the trial execution. Our team adhered to the World Medical Association Declaration of Helsinki (1964), which discusses the ethical conduct of research involving humans and/or animals. The study was not based on any incentives or rewards for the participants or their caregivers and abided by the Helsinki Declaration (8) guidelines and the STROBE guidelines for observational studies **(9)**.

RESULTS

Table 1 shows the baseline characteristics of the studied cohort. The mean gestational age was 34.9 ± 2.9 weeks, ranging from 26 to 40 weeks. The mean weight was 2061.6 ± 766.4 grams and ranged from 800 to 4200 grams. 57.1% were males, and 42.9% were females.

Table 1: Demographic data of studied neonates with thrombocytopenia.

Variables	**Total (n=140)**	
Gestational age (weeks)	Mean ± SD (range)	34.94 ± 2.9 (26 - 40)
Weight (gm)	Mean ± SD (range)	2061.57 ± 766.4 (800 - 4200)
Sex	N	%
Males	80	57.1
Females	60	42.9

Table 2 compares the demographic and clinical data of the studied groups. Both groups were matched for age (p=0.074), weight (p=0.108), and sex (p=0.495). Likewise, non-significant differences regarding neonatal and maternal risk factors were observed between the two studied groups.

Table 2: Baseline Demographic and Clinical Data Differences Between Groups

Variables	PC guideline (n=70)	PMI guideline (n=70)	P-Value
Gestational age (weeks)			
Mean ± SD	34.50 ± 2.9	35.37 ± 2.8	0.074*
(range)	(26 - 40)	(30 - 40)	
Weight (gm)			
Mean ± SD	1956 ± 709.2	2167.14 ± 829.9	0.108*
(range)	(800 - 3500)	(900 - 4200)	
Sex			
Males	42 (60.0%)	38 (54.3%)	0.495**
Females	28 (40.0%)	32 (45.7%)	
Neonatal risk factors			
Respiratory distress syndrome	36 (51.4%)	47 (67.1%)	0.058**
Prematurity	39 (55.7%)	34 (48.6%)	0.398**
Sepsis	34 (48.6%)	26 (37.1%)	0.172**
Hyperbilirubinemia	13 (18.6%)	16 (22.9%)	0.532**
Blood incompatibility	8 (11.4%)	5 (7.1%)	0.562**
Premature rupture of membrane	13 (18.6%)	15 (21.4%)	0.673**
Necrotizing enterocolitis	12 (17.1%)	12 (17.1%)	0.999**
Intrauterine growth restriction	8 (11.4%)	11 (15.7%)	0.459**
Maternal risk factors			
Pre-eclampsia	10 (14.3%)	17 (24.3%)	0.134**
38467Diabetes mellites	3 (4.3%)	6 (8.6%)	0.493***
Hepatitis B, C	3 (4.3%)	1 (1.4%)	0.620***
ITP	1 (1.4%)	2 (2.9%)	0.999***
SLE	2 (2.9%)	1 (1.4%)	0.999***
COVID-19	1 (1.4%)	2 (2.9%)	0.999***

***Independent Sample T-test compares mean between two groups**
****Chi-square test compares proportion between groups**
***** The Fisher Exact test was used to compare proportions between groups**

Table 3 presents the comparison of thrombocytopenia characteristics between the studied groups. An insignificant difference was found regarding the onset of thrombocytopenia, day of onset, and severity of thrombocytopenia ($p>0.05$). On the other hand, a significantly ($p<0.001$) higher percentage of patients needed platelet transfusion in the PC guideline group vs. the PMI guideline group (77.1% vs 17.1%, respectively). Likewise, the median number of platelet transfusions for patients in the PC guideline group was significantly higher ($p<0.001$) than the PMI guideline group. Likely, the mean total number of transfusions was significantly higher ($p<0.001$) compared to the PMI guideline group.

Table 3: Comparison of thrombocytopenia characteristics among studied groups.

	PC guideline (n=70)	PMI guideline (n=70)	P-Value
Onset of thrombocytopenia			
Early onset	26 (37.1%)	33 (47.1%)	0.231*
Late onset	44 (62.9%)	37 (52.9%)	
Day of onset:			
Mean ± SD	3.97 ± 2.5	4.14 ± 3.4	0.856**
Median (range)	4.00 (1 - 13)	4.00 (1 - 20)	
Severity of thrombocytopenia			
Moderate (50,000-100,000)	33 (47.1%)	41 (58.6%)	0.176*
Server (Less than 50,000)	37 (52.9%)	29 (41.4%)	
Patients need platelets transfusion			
Not needing a platelet transfusion	16 (22.9%)	58 (82.9%)	**<0.001***
Need platelet transfusion	54 (77.1%)	12 (17.1%)	
Number of platelets transfusions for patient			
Mean ± SD	1.33 ± 1.3	0.24 ± 0.6	**<0.001****
Median (range)	1.00 (0 - 7)	0.00 (0 - 2)	
The total number of transfusions in patients who **need platelet transfusion**			
Mean ± SD	93.22 ± 9.1	17.92 ± 1.8	**<0.001****
Median (range)	93 (77 - 97)	17 (10 - 22)	

***Chi square test was used to compare proportions between groups**

****Mann-Whitney U-test compares median between two groups**

Table 4: Effect of Transfusion on the Laboratory Findings among studied groups.

	PC guideline (n=70)	PMI guideline (n=70)	P-value*
White blood cells (×1000)			
Before transfusion	11.80 (2.3-35.0)	9.30 (1.2-68.0)	0.128
After transfusion	10.00 (3.0-36.0)	10.10 (3.9-32.8)	0.707
P-Value**	**0.021**	0.505	
Neutrophils (×1000)			
Before transfusion	6.45 (1.2-20.6)	4.90 (0.4-65.5)	0.145
After transfusion	5.00 (0.09-22.00)	5.30 (2.00-25.00)	0.144
P-Value**	**0.039**	0.872	
Lymphocytes (×1000)			
Before transfusion	3.00 (0.10-10.00)	3.15 (0.70-20.00)	0.395
After transfusion	3.25 (0.27-11.40)	3.20 (1.10-18.30)	0.419
P-Value**	0.639	0.758	
Hemoglobin (g/dl)			
Before transfusion	13.42 ± 2.2	14.17 ± 2.8	0.081
After transfusion	13.20 ± 2.2	13.64 ± 2.4	0.303
P-Value**	0.425	0.064	

	PC guideline (n=70)	PMI guideline (n=70)	P-value*
Mean corpuscular volume (Um)			
Before transfusion	93.36 ± 8.9	97.66 ± 8.5	**0.001**
After transfusion	91.47 ± 7.7	95.97 ± 7.9	**<0.001**
P-Value**	**0.017**	**0.007**	
Platelets (×1000)			
Before transfusion	48.50 (10.0-99.0)	49.00 (5.0-96.0)	0.943
After transfusion	125.00 (10.0-348.0)	162.50 (8.0-312.0)	**<0.001**
P-Value**	**<0.001**	**<0.001**	
Mean platelet volume (Fl/nl)			
Before transfusion	10.31 ± 1.4	10.49 ± 1.7	0.281
After transfusion	9.66 ± 1.1	9.44 ± 1.2	0.232
P-Value**	**<0.001**	**<0.001**	
Platelet mass index			
Before transfusion	513.60 (88.0-1138.5)	502.90 (60.0-1035.5)	0.717
After transfusion	1239.0 (80.0-3828.0)	1489.0 (96.0-2808.0)	**0.002**
P-Value**	**<0.001**	**<0.001**	
Prothrombin time (sec.)	12.11 ± 0.6	12.01 ± 0.7	0.357
Partial thromboplastin time (sec.)	34.25 ± 4.9	33.78 ± 4.5	0.549
International normalization ratio	1.09 ± 0.1	1.05 ± 0.1	0.155
C-Reactive protein	5.0 (.50-276.0)	4.75 (0.50-130.0)	0.423
For infants with hyperbilirubinemia			
Total bilirubin	22.0 (7.8-38.0)	21.75 (9.6-30.9)	0.948
Direct bilirubin	1.0 (0.30-16.60)	1.95 (0.50-8.40)	0.124
Indirect bilirubin	19.50 (6.0-34.0)	19.00 (8.6-29.9)	0.878

***Independent Sample t-test/Mann-Whitney U test compares mean/median between groups.**
****Paired Sample T test/Wilcoxon Sign test compares mean/median between groups in each group before and after transfusion**

Table 4 shows no significant difference between groups or within each group (before vs. after transfusion) regarding WBCs, neutrophils, lymphocytes, and hemoglobin. However, there was a significant reduction (p=0.039) in neutrophilic ratio within the PC guideline group. Moreover, there was a higher mean MCV among the PMI vs. PC group, and within each group, there was a significant reduction in mean MCV after transfusion.

For platelet count, there was an insignificant difference between groups before transfusion, while there was a significantly higher mean platelet count among the PMI group after transfusion vs the PC group, and within each group, there was a statistically significant increase in mean platelet count after transfusion

Regarding MPV, each group had a significant reduction after the transfusion. Also, there was a statistically significant higher PMI among the PMI group after transfusion vs. the PC group. Within each group, there was a significant rise in PMI after transfusion. Conversely, both groups were comparable concerning coagulation profile and C-reactive protein. Also, insignificant differences

were found among infants with hyperbilirubinemia regarding total, direct, and indirect bilirubin before transfusion.

Table 5 and **Fig 3** compare outcome measures among the studied groups. There was a non-significant difference between the two studied groups regarding blood culture results. For the imaging findings, there was a significantly higher percentage of positive signs for respiratory distress (RD) in chest x-rays among the PMI group vs. PC group (70% vs. 50%, p-value=0.016). However, no significant difference was delineated regarding plain erect and transcranial ultrasound. Furthermore, the PC group had a statistically significant higher percentage of hemorrhage than the PMI group (24.3% vs. 10%, p=0.025). Likewise, the PC group had a higher percentage of pulmonary hemorrhage than the PMI group (17.1% vs. 5.7%, p=0.034). Also, there was a statistically significant higher percentage of mortality in the PC group compared with the PMI group (22.9% vs. 10%, p-value=0.040) **(Fig. 3)**.

Table 5: Comparison of Outcome results among studied groups

Variables	PC guideline (n=70)	PMI guideline (n=70)	P-value*
Blood culture			
No growth	39 (55.7%)	44 (62.9%)	0.390
Gram-negative organism	27 (38.6%)	17 (24.3%)	0.069
Gram-positive organism	4 (5.7%)	9 (12.9%)	0.243
Chest X-ray			
Positive signs of RD	35 (50.0%)	49 (70.0%)	**0.016**
Plain erect			
No abnormal signs	45 (64.3%)	52 (74.3%)	0.200
Necrotizing enterocolitis	11 (15.7%)	12 (17.1%)	0.820
Intestinal obstruction	14 (20.0%)	6 (8.6%)	0.054
Transcranial ultrasound			
Hemorrhage	6 (8.6%)	2 (2.9%)	0.145
Hemorrhage	17 (24.3%)	7 (10.0%)	**0.025**
Type of hemorrhage			
Pulmonary	12 (17.1%)	4 (5.7%)	**0.034**
Intracranial hemorrhage	6 (8.6%)	2 (2.9%)	0.275
Cutaneous	2 (2.9%)	2 (2.9%)	0.999
Gastrointestinal	3 (4.3%)	0 (0.0%)	0.245
Outcome			
Alive	54 (77.1%)	63 (90.0%)	**0.040**
Dead	16 (22.9%)	7 (10.0%)	

***Chi square test was used to compare proportions between groups**

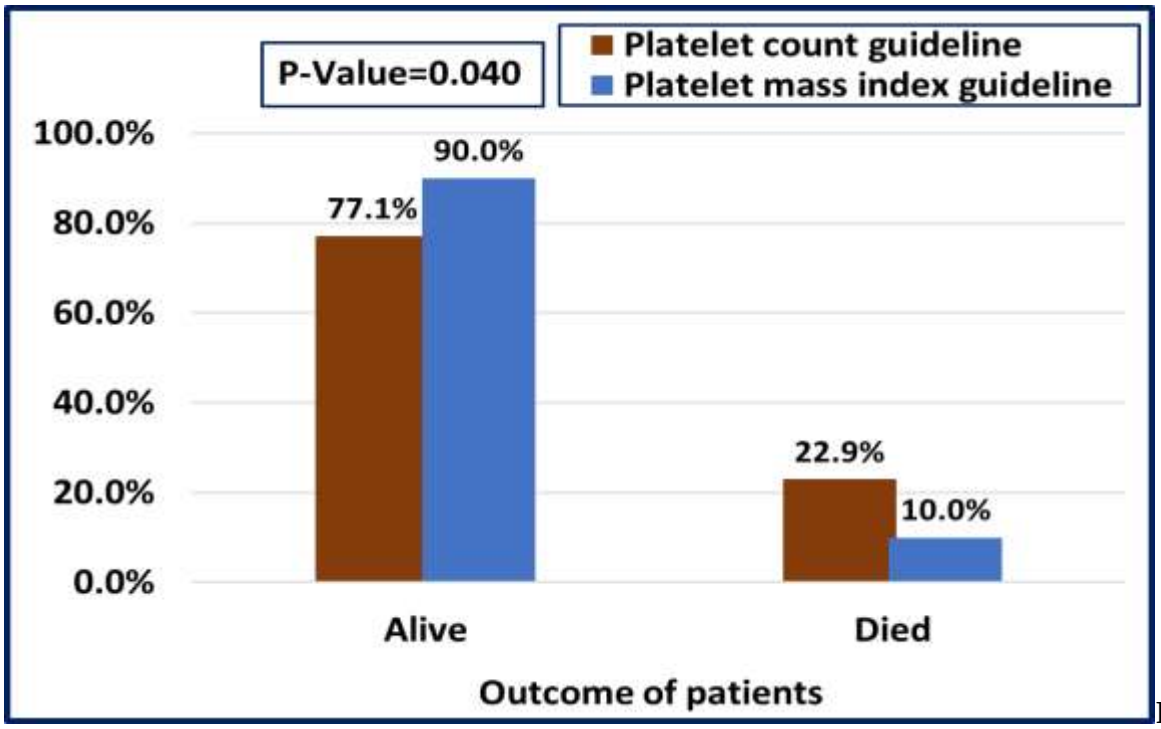

Figure 3: Comparison of outcome among studied groups

DISCUSSION

About one-fourth of neonates in NICUs have thrombocytopenia, which is defined as a platelet count below 150,000/mm^3. The incidence of thrombocytopenia rises with decreasing gestational age, and it affects about 70% of very low birth weight neonates **(11, 12)**. Despite the lack of evidence linking platelet counts to the risk of bleeding in neonates, prophylactic platelet transfusions are used in hospitalized neonates as part of clinical practice **(13)**.

Increased mortality and morbidities, including severe intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity and acute kidney injury in preterm infants, are linked to platelet transfusion **(3, 14)**. Therefore, the use of a restrictive neonatal platelet transfusion guideline is advocated to decrease potentially hazardous platelet transfusions in NICUs, while the benefits of prophylactic platelet transfusions in neonates are disputed **(15)**.

IS PMI harboring a chance that platelet transfusions in the NICU will decline? The only specific treatment for thrombocytopenia, a common issue in NICU, is platelet transfusion, which carries known risks **(16)**. There are no documented Egyptian or Arabic randomized clinical trials about the role of platelet mass index in platelet transfusion in neonatal thrombocytopenia. Hence, the current work aimed to determine if PMI guidelines would lead to decreased transfusions. This single-blinded RCT was conducted on 140 neonates with thrombocytopenia at NICU, Pediatric Department, Aswan University Hospital, Egypt.

Among the studied group, the mean gestational age was 34.9 ± 2.9 weeks, the mean weight was 2061.6 ± 766.4 grams, and 57.1% were males and 42.9% were females. Likely, a Turkish retrospective study that was conducted by Kasap et al. (4) on 395 neonates with at least one recorded platelet count < 150×109/L detected that the mean gestational age was 34.4 ± 4.5 weeks, the median weight was 2322 grams, and 56% were males and 44% were females. In a Turkish retrospective cross-sectional study conducted by **Okbay et al. (17)** on 28 neonates who received prophylactic platelet transfusion, the median gestational age and weight values of the neonates were 34.5 (26–37) weeks and 2450 (740–3100) grams, respectively. About 53.6% of them were males.

As for the comparison of demographics and risk factors between studied patients among studied groups (PC group and PMI group), both groups were matched for gestational age, weight, sex, and neonatal and maternal risk factors. Similar to our results a Turkish study that was conducted by **Yavuzcan Öztürk et al. (16)** detected that demographic characteristics and risk factors of the infants in both groups showed insignificant differences.

Furthermore, in the current study, an insignificant difference was found regarding the onset of thrombocytopenia and the severity of thrombocytopenia. However, the number of patients who needed platelet transfusion was higher in the PC group vs. the PMI group (77% vs 17%, p<0.001). Moreover, there was a significantly higher median number of platelets transfusions for the PC vs PMI group (p<0.001). This was in agreement with an American study done by **Gerday et al. (5),** the incidence of PLT transfusion was lower when the PMI guideline was used. The number of PLT transfusions administered per transfused patient was the same in both groups, but significantly fewer PLT transfusions were given for prophylaxis when the PMI guideline was used and there was no recognized increase in hemorrhagic problems. In another Turkish retrospective study done by **Kahvecioglu et al. (18)**, they found that 53% of the babies transfused according to the PC -based guidelines were transfused beyond the current guideline indications and an additional 11.5% would not be transfused if the PMI guideline was used.

On the other hand, our results disagreed with an American pilot study by **Zisk et al. (19)**, in which neonates were randomized to receive PLT transfusions based on PMI vs. PC, and no difference was found in the number of platelet transfusions received. Notably, more infants (47% vs 38%) were transfused in the group where the PMI guideline was used. A small sample of this pilot study may explain this. Moreover, **Yavuzcan Öztürk et al**. **(16)** detected no significant difference between the two studied groups regarding the mean number of platelets transfusion and the median age of transfusion.

This study observed insignificant differences between groups regarding WBC, neutrophils, or lymphocytes before and after platelet transfusion. However, there was a significant reduction in WBC and neutrophils post-transfusion in the PC group, suggesting that transfusion may influence these specific immune cell counts in this group. The lack of significant change in lymphocytes between and within groups indicates that lymphocyte levels remain relatively unaffected by platelet transfusion. This pattern could be related to the selective impact of transfusion on different immune cells, or the underlying conditions being treated.

In the current study, hemoglobin levels remained consistent, showing non-significant differences between the groups or within each group before and after transfusion. This indicates that the platelet transfusion did not significantly impact hemoglobin levels.

In contrast, MCV was significantly higher in the PMI group compared to the PC group. Additionally, MCV decreased significantly after the transfusion in both groups. This suggests that platelet transfusion may influence red blood cell size, particularly reducing MCV, which could

reflect changes in the characteristics of circulating red blood cells, possibly due to the dilution effect or shifts in red blood cell production post-transfusion. Platelet counts showed no significant differences between groups before transfusion; however, the PMI had significantly higher platelet counts after transfusion than the PC group, with both groups showing a significant increase in mean platelet counts post-transfusion.

MPV did not differ significantly between groups before or after transfusion, but there was a significant decrease in MPV within each group following transfusion, indicating a potential reduction in platelet size. Regarding PMI, there were no significant differences before transfusion, but it demonstrated significantly higher values after transfusion compared to the PC group, with both groups showing a significant increase in PMI post-transfusion, highlighting the effectiveness of transfusions in elevating both platelet counts and overall platelet mass in circulation. **Yavuzcan Öztürk et al. (16)** detected no significant difference between the two studied groups regarding platelets and platelet mass index.

As regards blood culture, there was an insignificant difference between the groups regarding blood culture results. Since infections are a significant cause of NT, this uniformity in blood culture results suggested that both groups were similarly affected by the infectious component, which did not bias the platelet response, clinical condition, or outcomes related to transfusion. It also implies that infection management strategies likely remain consistent across groups, with similar interventions for sepsis or other infection-related complications. Therefore, any differences in other clinical outcomes between the groups would be more likely attributed to factors other than infection, such as transfusion protocols or underlying clinical conditions.

Regarding imaging, the PMI group had a significantly higher percentage of positive signs for RD in chest X-rays than the PC group (70% vs. 50%, p=0.016). However, there was an insignificant difference between the groups regarding plain erect and transcranial ultrasound results. This could be explained by the fact that ARDS is associated with several clinical disorders, including direct pulmonary injury from pneumonia and aspiration and extra-pulmonary injury from sepsis, traumas, and multiple transfusions **(20)**.

As regards the comparison of outcomes, there was a statistically significant higher percentage of hemorrhage in the PC compared with the PMI group (24% vs 10%, p=0.025. Moreover, there was a statistically significant higher percentage of pulmonary hemorrhage in the PC vs PMI group (17% vs 5.7%, p=0.034), nevertheless, other types of hemorrhage did not show any significant difference. Additionally, there was a statistically significant higher percentage of mortality in the PC vs PMI group (23% vs 10%, p=0.040).

Yavuzcan Öztürk et al. **(16)** detected that there was a significant difference between the two studied groups as regards gastrointestinal bleeding (P= 0.08) while other types of hemorrhage showed non-significant between groups. Also, they reported no statistically significant difference as regards mortality. **Zisk et al. (19)** detected that no difference was found in bleeding episodes or mortality between the studied groups. Similarly, **Kahvecioglu et al. (18)** revealed that there was no recognized increase in hemorrhagic problems.

CONCLUSION

In conclusion, this study provides important insights into managing neonatal thrombocytopenia, demonstrating that transfusion strategies based on PMI guidelines resulted in significantly higher post-transfusion platelet counts than the traditional PC approach. Also, compared to the PC group,

significant improvements in clinical outcomes were observed in the PMI group, including lower bleeding rates, intracranial hemorrhage, and mortality. Overall, these findings supported using a PMI-based approach for more precise transfusion management, potentially reducing complications and improving survival rates in NT.

Study Limitations

The current study had some limitations. First, it was a single-center study, which limited its external validity (generalization). Second, possible confounding factors (presence of alloimmunization, platelet refractoriness, etc.) were not accounted for when matching between groups.

Conflict of interest: All authors declare no conflicts of interest.

Financial Disclosures: None

Acknowledgement:

The authors wish to thank the medical and administrative staff of the pediatric department at Aswan University Hospital for their consistent help and support. This work would not have been possible without the help, support, and approval of the recruited patients' caregivers.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (13-25) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Subtle Urinary Tract Infection in Type-1 Diabetic Children attending Aswan University Hospital

Mohamed B Hawary, Manal F. Mekky*, Ashraf A. Maebed, Mohamed A. Abd_el_basset

Pediatric department, faculty of Medicine, Aswan University

ABSTRACT

Keyword: T1DM, UTIs, HbA1c, ASB, DKA.

*** Corresponding author:**

Manal fawzy Mahmoud

Mobile: 01005636224

E-mail: manalfawzy101@gmail.com

Background: In Egypt, people with diabetes have four times the prevalence of Asymptomatic bacteriuria compared to the general population. It may cause pyelonephritis or cystitis. Unfortunately, it may be difficult to distinguish pyelonephritis from cystitis clinically, especially in infants and young children. This study aimed to identify the risk factors of subtle Urinary Tract Infection in Type 1 diabetic children. **Methodology:** this case-control study was conducted in the Pediatrics Department, Aswan University Hospital, on 212 children, 106 diabetic patients and 106 controls. All the studied groups carried out urinalysis or urine cultures. **Results:** the prevalence of UTI by urine analysis in our cases was 76.42% vs 16% in the controls, with a significant p value <0.001. Although urine culture was insignificant between 2 groups. Further, abnormal ultrasound findings were significantly increased in T1DM groups than in controls. **Conclusion:** T1DM group had a higher prevalence of UTI by urine analysis compared to the controls. However, urine culture results were insignificantly different between the groups, suggesting a potential discrepancy between the presence of asymptomatic bacteriuria and the development of overt UTI symptoms.

INTRODUCTION

Even with appropriate care and glycemic control, patients with type 1 diabetes may experience several diabetic sequelae **(1)**. Urinary tract infections (UTIs) are among the most common infections, and they are one of the sequelae that raise the incidence of morbidity and mortality in children with diabetes. Additionally, both asymptomatic and symptomatic bacteriuria are more common in diabetics **(2)**. This can be explained by the defective host immune factors and the inhibition of neutrophil phagocytosis and diapedesis caused by elevated serum and urine glucose levels. Furthermore, other factors that contribute to the development of diabetic UTIs include renal papillary necrosis, vesicourethral reflux, nephropathy, and urine retention in diabetic neuropathy **(3)**.

The presence of $\geq 10^5$ colony-forming units/ml of one or more bacterial species in a culture of clean-voided midstream urine taken from a patient who does not exhibit symptoms of a urinary tract infection is known as asymptomatic bacteriuria (ASB) **(4)**. The prevalence of ASB in diabetic patients in Egypt is four times higher than the general population **(5)**. Both the lower

urinary tract (i.e., cystitis) and the upper urinary tract (i.e., pyelonephritis) may be impacted by the infection. Unfortunately, based on clinical symptoms and signs, it may be difficult, if not impossible, to differentiate between cystitis and pyelonephritis, particularly in infants and young children **(6)**.

These two conditions are covered under the general heading of UTI. The high frequency, propensity for recurrence, related morbidity, and difficulties in obtaining an uncontaminated urine sample pose serious difficulties for the physician **(7)**. So, the current study aimed to identify the risk factors of subtle UTI in Type 1 diabetic children.

PATIENTS AND METHODS

This observational case-control study was conducted on diabetic children attending the pediatric endocrinology clinic at Aswan University Hospital, Egypt from May 2023 till April 2024.

The minimum required sample size was calculated using G*Power statistical package program Version 3.1.9.7 (Franz Faul, Universitat Kiel, Germany) using two population means formula using independent t-test and the following assumptions were considered: α= 95%; Power (1 - β): 99%; Effect size = 0.5; Two tail test. A total of 212 children were included in the study and divided into 2 equal groups.

Children between one and 15 years, with type-1 DM (both controlled and uncontrolled) and non-diabetic were included. On the other hand, those with symptomatic UTI at the time of the study, history of urologic disease, other autoimmune diseases, and chronic diseases were excluded.

Sampling

The recruited sample was divided into two groups:

Group-I (cases, no = 106), including children with type 1 diabetes who had regular follow-up in the pediatric endocrinology outpatient's clinic of Aswan University Hospital. All of them have asymptomatic bacteriuria with positive urinalysis or urine culture

Group-II (control, no = 106), including children matched to cases in age and sex, confirmed to be non-diabetic by measuring their fasting blood glucose. All of them have asymptomatic bacteriuria with positive urinalysis or urine culture.

Procedure

All the studied children were subjected to:

- History taking including demographic data, diabetes-focused history (age of disease onset, disease duration, presentation of diabetes, insulin therapy i.e., type of insulin, dose and frequency), history suggestive of UTI (burning micturition, change of urine color or odor, frequency or urgency), history suggestive of chronic diabetic complication (ocular and cardiovascular system (CVS) complications), and history of other medications i.e. antibiotics or any other associated disease.
- Clinical examination including anthropometric measurements (weight, height, and body mass index (BMI)), general and systemic examination.
- Laboratory investigation including complete blood count (CBC), Renal function test (serum BUN and serum creatinine), HbA1c, CRP, urine albumin/creatinine ratio (UACR) and urine analysis (via urinary catheterization). Also, in cases with infection-positive urinalysis, urine culture and pelvic-abdominal
- Full ultra-sound (US) was performed.

Statistical analysis

Data analysis was undertaken using IBM-SPSS version 26 **(8)**. Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD) and were analyzed using independent sample t-test. Quantitative non-parametric data were presented as median and interquartile range (IQR) and were analyzed using Mann Whitney U-test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the chi-square test. A two tailed p-value < 0.05 was considered significant.

Ethical considerations

All the regulations of the ethical committee of the faculty of medicine were followed. Each patient had a private file with non-disclosure policy at data presentation where all presented data don't contain any personal information specifying the identity of any of the patients. All participants' guardians were required to sign a written consent after reading the patient information sheet or having it read to them.

The World Medical Association's 1964 Declaration of Helsinki, which addresses the research ethics guidelines involving humans and/or animals, was followed **(9)**. The study adhered to the STROBE guidelines for observational studies **(10)**. Also, no incentives or rewards for the participants or their caregivers were provided.

RESULTS

A total of 212 children with asymptomatic UTIs were included for the current study, which was carried out in the Pediatrics Department of Aswan University Hospital.

As shown in **Table 1**, both groups were matched for age (p=0.067), sex (p=0.345), weight (p=0.102), height (p=0.097) and BMI (p=0.224).

Table 1: Baseline Demographic and Clinical data of the studied groups.

		Group I (n=106)	Group II (n=106)	P-value
Age (years)	• **Mean ± SD**	10.61 ± 3.24	7.99 ± 4.05	= 0.067*
	• **Range**	3 – 15	1 - 15	
Gender	• **Male**	58 (54.72%)	55 (51.89%)	= 0.345**
	• **Female**	48 (45.28%)	51 (48.11%)	
Weight (kg)	• **Mean ± SD**	33.97 ± 10.46	27.05 ± 12.21	= 0.102*
	• **Range**	13 – 55	9 - 55	
Height (cm)	• **Mean ± SD**	132.02 ± 16.93	117.16 ± 21.84	= 0.097*
	• **Range**	94 – 157	70 - 152	
BMI (kg/m^2)	• **Mean ± SD**	18.98 ± 2.33	18.72 ± 2.79	= 0.224*
	• **Range**	13.46 - 24.06	14.49 - 26.2	

***Mann-Whitney U-test compares median between two groups**
****Chi-square test compares proportion between groups**

Regarding diabetic disease related data among Group-I (Diabetic group) (n=106), the age of onset ranged between 2 and 12 years with a mean of 8.6 ± 2.2 years. Also, disease duration ranged between 0 and 6 years. About 72% (n=76) of cases had DKA, and about 28% (n=30) had hyperglycemia. Further, the mean insulin daily dose was 0.9 ± 0.2 with a range of 0.6-1.2 IU **(Table 2)**.

Table 2: Disease characteristics of the diabetic patients.

		Group I (n=106)
Age of onset (years)	**Mean ± SD**	8.64 ± 2.24
	Range	2 - 12
Duration of disease (years)	**Mean ± SD**	1.99 ± 2.03
	Range	0 - 6
Type of presentation	**DKA**	76 (71.7%)
	Hyperglycemia	30 (28.3%)
Insulin dosage (IU)	**Mean ± SD**	0.92 ± 0.2
	Range	0.6 - 1.2

Table 3 presented the comparison of laboratory findings between the studied groups. Insignificant difference was found regarding the level of Hgb (p=0.063). On the other hand, significantly (p=0.004) higher mean platelet count was found in Group-I (260.3 ± 88.9*10^9/L) compared with Group-II (255.9 ± 83.5*10^9/L). Also, Group-I had higher mean TLC (13.0 ± 4.1*10^9/L) compared with Group-II (8.8 ± 4.9*10^9/L) (p<0.001). Likely, Group-I had significantly (p<0.001) higher mean level of blood urea (55.7 ± 13.7mg/dl) than Group-II (31.9 ± 10.1mg/dl). Likewise, Group-I had higher mean serum creatinine (1.2 ± 0.2mg/dl) vs. Group-II (0.8 ± 0.3mg/dl) (p<0.001). In contrast, the median CRP was significantly (p<0.001) lower among the diabetic group (20 [12-32]) than the non-diabetic one (34 [24-60]). Consistently, the mean HbA1c level was significantly (p<0.001) higher in Group-I (10.1 ± 2.5%) than Group-II (5.1 ± 0.4%).

Table 3: Laboratory investigations Differences Between groups

	Group I (n=106)	Group II (n=106)	P value

Hb (g/dl)	**Mean ± SD**	11.46 ± 0.96	11.78 ± 1.46	0.063*
	Range	9.3 - 13.2	7 - 16	
Platelets ($x10^9$/L)	**Mean ± SD**	260.29 ± 88.77	225.96 ± 83.53	**0.004***
	Range	135 – 433	98 - 430	
TLC ($x10^9$/L)	**Mean ± SD**	13.03 ± 4.13	8.77 ± 4.99	**<0.001***
	Range	6.3 – 22	2.5 - 22	
Urea (mg/dl)	**Mean ± SD**	55.66 ± 13.75	31.97 ± 10	**<0.001***
	Range	21 – 87	18 - 55	
Creatinine (mg/dl)	**Mean ± SD**	1.15 ± 0.21	0.78 ± 0.26	**<0.001***
	Range	0.6 - 1.6	0.2 - 1.3	
CRP (mg/dl)	**Median**	20	34	**<0.001****
	IQR	12 – 32	24 - 60	
HbA1c (%)	**Mean ± SD**	10.06 ± 2.47	5.07 ± 0.39	**<0.001***
	Range	6.8 - 14.5	4.2 - 5.8	

***Independent Sample T-test compares the mean between two groups**
****Mann-Whitney U-test compare median between two groups**
Hb: hemoglobin, TLC: total leucocyte count, CRP: C-reactive protein, HbA1c: glycated hemoglobin, *: significant as P value ≤ 0.05

As shown in **Table 4 (Urine analysis parameters)**, significantly (p<0.001) higher percentage of patients with pus cell count > 5/HPF was recorded in diabetic group vs. non-diabetic group (84% vs 23.6%, respectively). For crystals, diabetics had a higher proportion of amorphous urates (33%) than non-diabetics (7.6%), while a higher proportion of uric acid and co-oxalate (56.6% and 3.8%) in non-diabetics in comparison with diabetics (51.9% and 0%) (p<0.001). Diabetic cases had significantly (p<0.001) higher frequency of positive detection of glucose (100%), ketones (100%) and casts (granular [23.6%] and hyaline [11.3%]) compared with non-diabetic cases glucose (0%), ketones (0%) and casts (granular [5.7%] and hyaline [3.8%]). Further, positive urinary leucocyte was significantly (p<0.001) among Group-I (15.1%) than Group-II (7.5%) **(Fig. 1).**

Table 4: Comparison of Urinalysis Results among studied groups.

		Group I (n=106)	**Group II (n=106)**	**P value**
pH	• **Mean ± SD**	5.86 ± 0.22	5.82 ± 0.24	0.240*
	• **Range**	4.8 – 6	4.9 – 6	
Pus cells	• **0-5**	17 (16.04%)	81 (76.42%)	**<0.001****

	• **>5**	89 (83.96%)	25 (23.58%)	
RBCs	• **0-4**	94 (88.68%)	100 (94.34%)	0.139**
	• **>4**	12 (11.32%)	6 (5.66%)	
Crystals	• **Nil**	16 (15.09%)	34 (32.08%)	**<0.001****
	• **Uric acid**	55 (51.89%)	60 (56.6%)	
	• **Urate**	35 (33.02%)	8 (7.55%)	
	• **Ca oxalate**	0 (0%)	4 (3.77%)	
Glucose	• **Positive**	106 (100%)	0 (0%)	**<0.001****
	• **Negative**	0 (0%)	106 (100%)	
Ketones	• **Positive**	106 (100%)	12 (11.32%)	**<0.001****
	• **Negative**	0 (0%)	94 (88.68%)	
Casts	• **Nil**	69 (65.09%)	96 (90.57%)	**<0.001****
	• **Granular**	25 (23.58%)	6 (5.66%)	
	• **Hyaline**	12 (11.32%)	4 (3.77%)	
Protein	• **Nil**	97 (91.51%)	100 (94.34%)	0.126**
	• +	5 (4.72%)	6 (5.66%)	
	• ++	4 (3.77%)	0 (0%)	
Nitrite	• **Nil**	106 (100%)	104 (98.11%)	0.498**
	• +	0 (0%)	2 (1.89%)	
Leucocytes	• **Nil**	52 (49.06%)	80 (75.47%)	**<0.001****
	• +	38 (35.85%)	18 (16.98%)	
	• ++	16 (15.09%)	2 (1.89%)	
	• +++	0 (0%)	4 (3.77%)	
	• ++++	0 (0%)	2 (1.89%)	

***Independent Sample t-test compare mean between two groups**
****Chi square test was used to compare proportions between groups**
RBCs: red blood cells, *: significant as P value ≤ 0.05

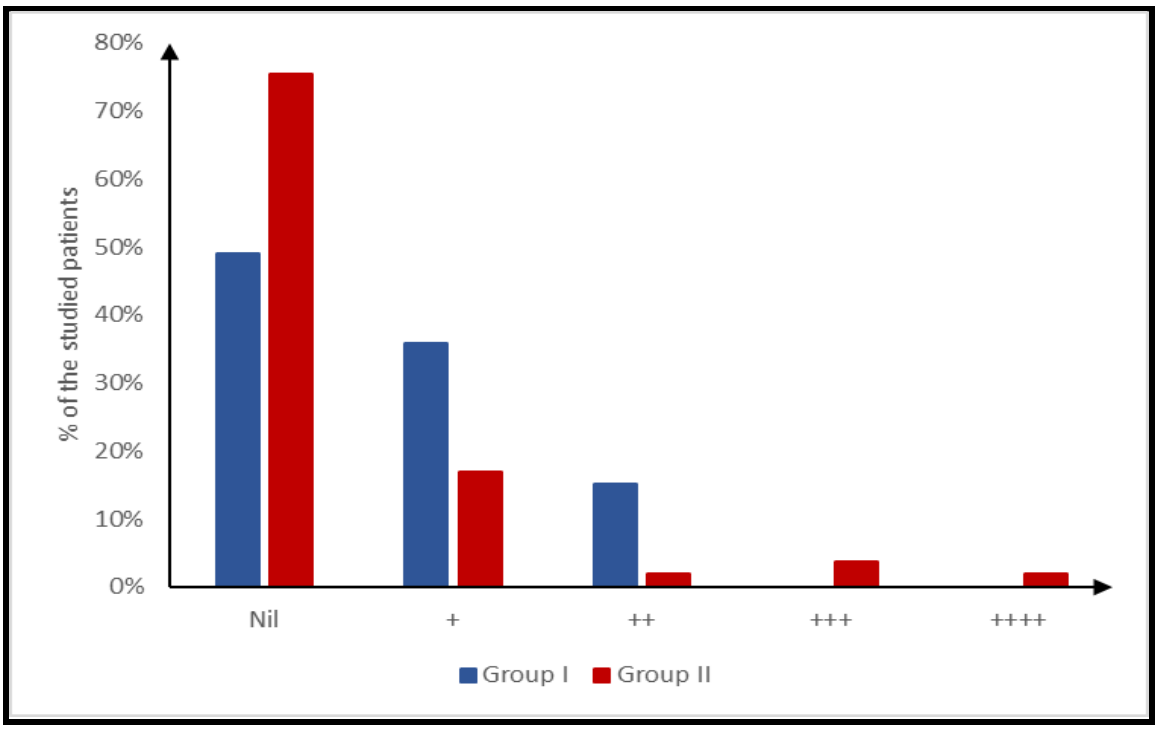

Fig. 1: Urinary Leucocytes among the studied NT cases

Regarding the urine culture results **(Fig. 2),** there was insignificantly (p=0.622) higher percentage of positive findings (E. coli) among diabetic group (9.4%, n=10) vs non-diabetic group (7.6%, n=8).

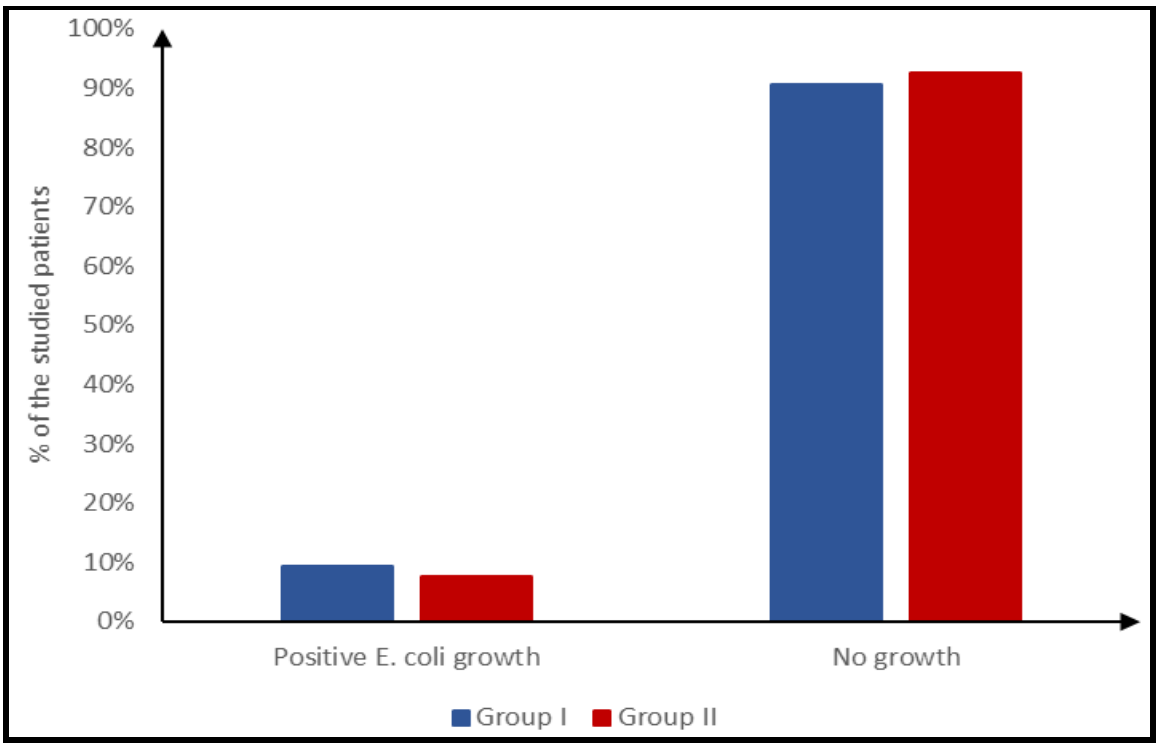

Fig. 2: Urine culture among studied cases

Furthermore, there was a significant (p<0.001) difference respecting the US findings between groups i.e., higher percentage of gaseous distention, nephropathy grades and IPF in diabetic group (28%, 4.7%, 3.8% and 1.9%) vs. non-diabetic group (0%, 3.8% and 0%). In contrast, a higher percentage of hepatomegaly and ascites in the non-diabetic group (5.7% and 1.9%) than the diabetic group (0%) **(Table 5 and Fig. 3)**.

Table 5: Difference in US findings between studied groups

	Group I (n=106)	**Group II (n=106)**	**P value**
Normal	65 (61.32%)	94 (88.68%)	**<0.001***
Gaseous distention	30 (28.3%)	0 (0%)	
Grade 1 nephropathy	5 (4.72%)	4 (3.77%)	
Grade 2 nephropathy	4 (3.77%)	0 (0%)	
Hepatosplenomegaly	0 (0%)	6 (5.66%)	
Ascites	0 (0%)	2 (1.89%)	
IPF	2 (1.89%)	0 (0%)	

***Chi square test was used to compare proportions between groups**

US: ultrasound, IPF: idiopathic pulmonary fibrosis, *: significant as P value ≤ 0.05

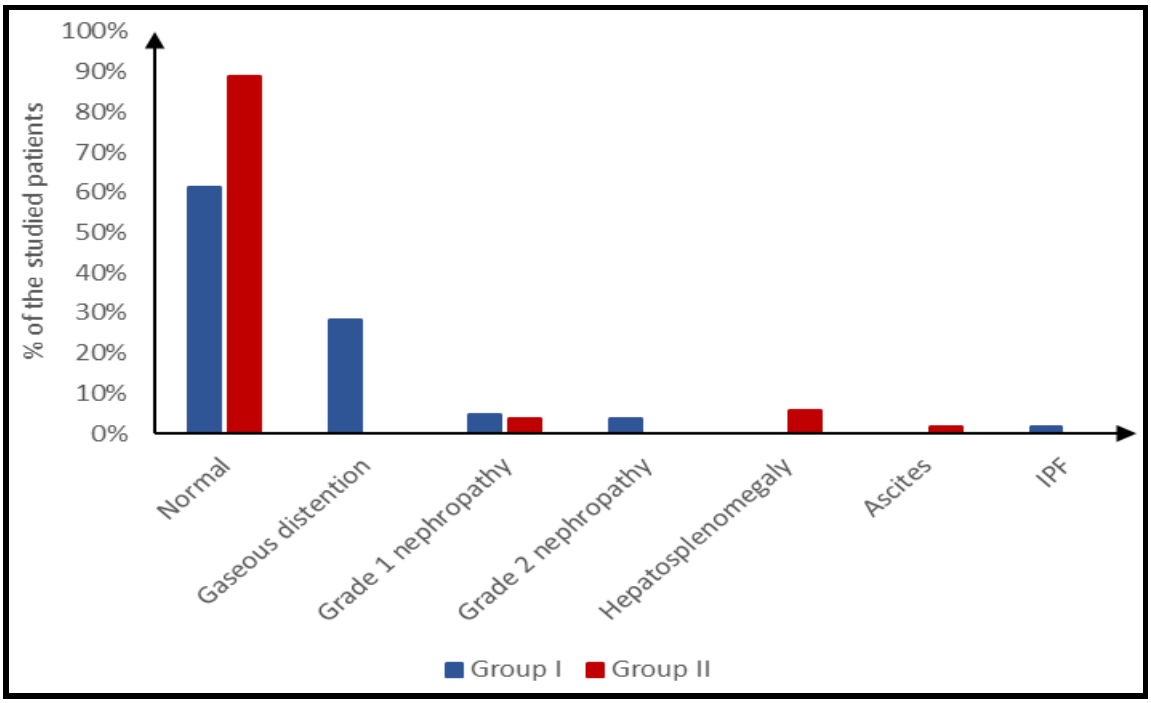

Figure 3: Comparison of US Findings among studied group

DISCUSSION

There is a lot of interest in the medical literature regarding the link between infections and DM. There is a proof that in diabetic cases, proper glycemic control enhances immune function and lowers morbidity and mortality linked to serious infections **(11)**. It's crucial to keep in mind that DM is categorized based on its etiopathogenesis. Type 2 diabetes (T2D) is the most common kind, particularly in adults, and type 1 diabetes (T1D) is the most common type, particularly in children and adolescents. Studies evaluating the incidence and prevalence of infections don't usually specify the kind of DM. T1D is caused by an autoimmune process that targets the β-cells of the pancreas, which produce and secrete insulin. This process destroys the cells, resulting in insulin insufficiency and hyperglycemia. It is mostly linked to microvascular problems (retinopathy, nephropathy, and neuropathy) **(12)**.

People with DM are more likely to get UTIs, which can have serious consequences. An impaired immune response, inadequate bladder emptying, and altered metabolic control are some of the variables that increase the risk of UTI. Escherichia coli and other enterobacteria are the most prevalent agents, just like those found in the general population. Asymptomatic bacteriuria, upper urinary tract infections (pyelonephritis), lower urinary tract infections (cystitis), and urosepsis are the most prevalent illnesses. Additionally, complications such as renal abscess, emphysematous cystitis, and renal papillary necrosis could occur **(13)**.

Our results revealed that the prevalence of UTI by urine analysis in our cases was 76.42% vs 16% in the controls, with a significant p value <0.001. Although urine culture was insignificant between 2 groups.

According to previous research, the prevalence of asymptomatic bacteriuria and UTI infections in diabetic patients varies from 11% to 68% **(14)**. This high prevalence may be related to autonomic neuropathy, which causes bladder dysfunction, inadequate bladder emptying, and urine stagnation, which creates an environment that is conducive to the growth of microorganisms.

This study's objectives were to determine the risk of asymptomatic UTIs in children with T1D and identify the risk factors for developing DKA. A total of 212 children (106 diabetic cases and 106 controls) were enrolled in this case-control study.

In the current study, the male/female ratio was 55%/45% in Group I, this was consistent with the Saudi Health Interview Survey (SHIS), which was conducted in 2013, where the male/female ratio was 15%/12% of women had diabetes. This difference was seen between the sexes **(15)**.

Similar to the findings of other studies, the characteristics of diabetic patients linked to their chance of getting UTIs were examined, and it was discovered that age and disease duration had a significant impact **(16)**. Longer duration of DM may increase the risk of diabetic chronic complications, hospitalization, and urinary tract catheterization, all of which raise the risk of urinary tract infections **(13)**.

Gorter et al. (17) reported several risk factors for recurrent urinary tract infection (rUTI) in females, including insulin treatment. Also, **Wilke et al. (18)** reported that insulin treatment was not associated with rUTI risk. Another study including 1157 Indian patients, showed a correlation between the percentage of patients with UTI and the duration of diabetes (41.8% < 10 years vs. 58.2% > 10 years) **(16)**.

Per the current study, **Desouky et al. (19)** reported that there was a significant increase in the risk of UTI among patients with diagnosed diabetes >10 years. This may be attributed to the long-term effects of diabetes like an impaired immune system and neuropathy. Long-standing diabetes may develop cystopathy, nephropathy, and renal papillary necrosis, which predispose to UTI **(20)**. In contrast, A Saudi study found that the DM duration did not influence the risk of UTI in diabetic patients **(15)**.

In our study, diabetics were insignificantly older compared with healthy controls. This was in agreement with **Al-Rubeaan et al. (14)** who did not find any relationship between age and increased risk of UTI among diabetic patients **(15)**. Contrarily, in Carrondo study, it was found that UTI rate in people aged 18 – 64 was 9%, compared with 27.5% in people over 85 years old and rate of UTI in females was higher than in males, which seems to be associated to bladder neurological malfunction, physiological bladder alterations brought on by aging or dyspnea, and female's close closeness to the anus **(21)**. Similarly, **Desouky et al. (19)** reported that the risk of UTI was associated significantly with increasing mean age.

In this study, HbA1c was significantly decreased in the healthy control group than the T1DM groups (P value < 0.001). These findings are in agreement with those in previous reports suggesting an association between elevated HbA1c levels and presence of UTIs **(22-24)**.

This contradicts the finding from a meta-analysis of 22 studies that the degree of HbA1c derangement does not necessarily impact the biological flora or play any role in UTI susceptibility **(25)**. In the same line, **Ahmed et al. (26)** in a study in Saudi Arabia reported that higher levels of HbA1c were unrelated to the patients' UTI status, either positive or negative, and had only a weak correlation. **Chiţă et al. (13**) demonstrated that glycemic control had no significant influence on the risk for UTIs in the univariate analysis, but appeared as a significant risk factor when multivariate logistic regression model was applied .

Moreover, in the current study, pus cells, glucose, ketones, casts and leucocytes were significantly increased in T1DM groups than control. Likewise, urine culture was significantly different between the studied groups.

It was reported that the main organism that causes UTI in diabetics was E. coli **(27)**. Septic bacteria causing UTI with apparent symptoms such as increased frequency of urination, dysuria, hematuria, and a painful touch, while aseptic bacteria causing UTI without obvious symptoms **(28)**. It was proposed that the risk of aseptic bacteria in people with diabetes is three times higher than in normal people. Several mechanisms were claimed to increase the UTI risk, such as diabetic nephropathy, autonomic neuropathy, immune system abnormalities, and glucosuria **(29)**. Abnormal US findings were significantly different between the studied subgroups in the current study. Consistently, a large retrospective cohort study including 179,580 subjects with T2DM, showed that both cystitis and pyelonephritis were more common in diabetic patients than control (1.34% vs. 0.9% for cystitis and 0.14% vs. 0.07% for pyelonephritis, respectively). Also, recurrence of UTI was higher in diabetics (1.6% vs. 0.6%) **(30)**.

Conclusion

In conclusion, the prevalence of UTI by urine analysis in diabetic patients was significantly higher than in the controls. Although , urine culture results were insignificantly different between the groups, suggesting a potential discrepancy between the presence of asymptomatic bacteriuria and the development of overt UTI symptoms. Further, abnormal US findings were significantly increased in T1DM groups than group II.

In recommendation, further studies with many patients should be done to support our results for a better outcome.

Acknowledgement:

The authors wish to extend gratitude to the medical and administrative staff of the pediatric departments, Aswan University Hospital, for the keen help and support. This work would not be completed without the help, support, and approval of the assigned patients and their guardians.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (26-35) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Immunohistochemical Expression of NECTIN-4 in Urothelial Carcinoma of the Urinary Bladder

Shaimaa MM Bebars[1], Rasha Mohamed Samir Sayed[1], Shimaa Ghanem Abdelaziem[*1], Eman MS Muhammed[2]

1 Pathology Department, Faculty of Medicine, Aswan University, Egypt

2 Pathology Department, Faculty of Medicine, Sohag University, Sohag, Egypt.

ABSTRACT

Keyword: Urothelial carcinoma, IHC, Nectin-4.

*** Corresponding author:**
Shimaa Ghanem Abelaziem
Mobile: 01126610189
E-mail:
Shimaaghanem555@gmail.com

Background: Urothelial bladder carcinoma is the most frequent histopathological type of urinary bladder cancer. Immunohistochemistry (IHC), as a diagnostic or prognostic method, could be helpful particularly in the differentiation among muscle invasive and non-muscle invasive urothelial carcinoma (MIUC, NMIUC) as it has completely different implication on clinical management of the patients. Nectin-4 has act as a cancer associated inducer in a number of tumor types including urothelial carcinoma (UC). **Objectives**: This study aimed to assess Nectin-4 expression in invasive and non-invasive urothelial carcinoma and its association with the available clinico-pathological parameters. **Methodology:** This retrospective cohort observational research has been performed on 60 cases of UC to detect the IHC expression of Nectin-4. **Results:** Nectin-4 showed elevated expression in UC of the urinary bladder carcinoma (78.3%). A non-significant upward association was observed between Nectin-4 expression and muscle invasive UC cases. Nectin-4 was higher expressed in larger cancers, high grade and stage UCs, but there was no significant difference. **Conclusions:** These findings suggest an important function of Nectin-4 in predicting the prognosis in UC of the urinary bladder.

INTRODUCTION:

Urothelial bladder carcinoma represents the prevalent histopathological type of bladder tumors, exhibiting peak frequency during the seventh decade of life. The ratio of squamous cell carcinoma to urothelial carcinoma has altered characterized by a decline in squamous cell carcinoma and a rise in urothelial carcinoma (1, 2). smoking is the most frequent risk factor, involved in nearly fifty percent of analyzed urothelial bladder tumors cases. Occupational exposure to aromatic amines and polycyclic aromatic hydrocarbons constitutes additional significant risk factors, whereas the influence of diet and environmental pollution remains less clear (3).

Tumor antigens are found on the surface of neoplastic cells and act as possible drug targets. One of these antigens is tumor-associated Nectin-4, a constituent of the Nectin family within the immunoglobulin superfamily (4).

The Nectin cell adhesion molecule (Nectin) family comprises Ca2+-independent immunoglobulin-like cellular adhesion molecules (nectins 1-4), which included cell adhesion

through homophilic and heterophilic interactions. The Nectin family significantly contributes to the enhancement of cellular viability and movement. Unlike the enrichment of nectins 1-3 in normal tissues, Nectin-4, a protein associated to the poliovirus receptor (pvrl-4), is predominantly elevated in embryonic and placental tissues, exhibiting significantly reduced expression in adult. It is significantly expressed and acts as a tumor-associated inducer across many types of tumors. include lung, urothelial, breast, pancreatic, colorectal, and ovarian carcinomas (5, 6).

Previous studies have revealed that Nectin-4 is widely expressed in urothelial carcinoma (4, 7), however, the relation of this expression to clinicopathological factors is not clear. This investigation aimed to analyze the IHC expression of Nectin-4 in urothelial carcinoma and to detect its association to the available clinicopathological factors related to prognosis of this tumor e.g., tumor size, type, grade, pathological (p) stage.

MATERIAL AND METHOD:

This retrospective cohort observational research has been conducted on 60 formalin-fixed paraffin embedded tissue blocks related to 60 cases of UC obtained from the archived material of Pathology Lab, Aswan University Hospitals in the period from January 2018 to December 2021.

Transurethral resection biopsy (TURB) represent 34/60 cases, while the other 26/60 were radical cystectomy which were selected as half of them (13 cases) were NMIUC and the other half (13 cases) were MIUCs.

The research has been performed following expression from the Ethical Committee of Aswan University Egypt (EC Ref NO.: Asw.Uni / 629 / 5 / 22).

Histological examination:

Tissue blocks were utilized to produce (4µm)-thick tissue slices that were hematoxylin and eosin (H&E) stained. Slides have been examined using a light microscope and the histological diagnosis, tumor grade and pathological stage was conducted in accordance with The WHO 2004/2016 classification system (8).

Immunohistochemical staining:

Four micrometer (4µm)-thick sections have been prepared and mounted on pre-labelled poly-L-lysine coated slides. Immunostaining was done as shown in the product data sheet.

Positive control: Positive control slides from tonsillar tissue were included in each staining session. **Negative controls**: Additional tissue sections were stained simultaneously, but without utilizing the main antibody.

Immunohistochemical detection and scoring of Nectin-4:

Tissue slices were analyzed histologically using a bright-field microscope. The immunoreaction was deemed positive when a brownish cytoplasmic and membranous staining has been detcted. The level of Nectin-4 expression has been assessed utilizing a semi-quantitative technique. A histological scoring technique (H-score), which is a composite measure, takes into account both the proportion of positive cells and the intensity of their staining. The ultimate score varied from 0 and 300. The samples have been categorized depending on a discriminatory threshold. Specimens with scores ranging from 0 to 14, 15 to 99, 100 to 199, in addition 200 to 300 were categorized as having negative, weak, moderate, and high positive, correspondingly (8).

Statistical analysis

The gathered data has been revised, coded, tabulated, and statistically analyzed utilizing the Statistical Package for Social Sciences (SPSS 25), utilizing appropriate analyses based on the nature of the data for each parameter.

Range and Mean ± Standard deviation (± SD) for parametric numerical data, whereas Interquartile range (IQR) and Median for non-parametric numerical data, percentage and frequency of non-numerical data.

RESULTS:

The study was conducted on 60 patients. The mean age of the studied population was 59.78 (± 10.83) years. More than half (63.3%) were males and 36.7% were females. Regarding to 34/60 of cases were smokers, 31 of them were males and only 3 were females. There were 26/60 radical cystectomy cases with tumor size ranging from 3.5cm to 6cm. Most patients had high grade lesion (58.3%). Urothelial carcinoma with squamous differentiation was found in 6/60 (10%) cases **(Table 1).**

The mean Nectin-4 expression for the studied cases was 168.15 (± 104.38) and it was ranged from 2 to 299. More than two thirds of cases 47/60 (78.3%) had positive score "> 15". Most Nectin-4 positive cases (32/47; 68.1%) had strong Nectin-4 score followed by moderate Nectin-4 expression in 10/47 (21.3%) of cases and weak Nectin-4 expression was found in the rest of cases (5/47; 10.6%) as shown in **Table (2).**

Regarding Nectin-4 H score in radical cystectomy cases (MIUC and NMIUC groups), positive score was found in 10/13 of MIUC cases and only 7/13 of NMIUC cases showed positive score.

There was a statistical insignificant variance in expression of Nectin-4 when comparing MIUC and NMIUC groups. Among positive Nectin-4 level there was a statistical insignificant variance in H score among both examined groups **(Table 3).**

There was a statistical insignificant variance in expression of Nectin-4 regarding tumor size, grade and stage **(Table 4).**

There was positive correlation between smoking and cancer grade, and between smoking and Nectin-4 expression. There was significant increase in tumor grade in smokers. There was a statistical insignificant variance in expression of Nectin-4 between smokers and non-smokers' patients (**Table 5).**

Table 1: Clinico-pathological data of the examined cases

Studied parameter	**Results**
Age • Age range	 37-87
Sex • Male • Female	 38/60 (63.3%) 22/60 (36.7%)
Smoking	34/60 (56.7%)
Histological variant • Muscle-invasive • Non-muscle invasive	 13/26 (50%) 13/26 (50%)
Tumor grade • Low grade • High grade	 25/60 (41.7%) 35/60 (58.3%)
Tumor stage • pT1	 34 (56.7%)

• pT2 • pTa	13 (21.7%) 11(18.3%)
Other histological features UCs with squamous differentiation	6/60 (10%)

Table 2: Nectin-4 (H score) in the studied cases

Nectin-4 (H score)		**Results**
H score • Mean ± SD • Median • Range		168.15 ± 104.38 216.5 (67.5 – 255.5) (2 - 299)
H score	Negative	13/60 (21.7%)
	Positive	47/60 (78.3%)
Positive H score (N= 47 "Positive cases")	Weak (15 – 99)	5/47 (10.6%)
	Moderate (100 – 199)	10/47 (21.3%)
	Strong (200 – 300)	32/47 (68.1%)

Table 3: Nectin-4 (H score) in the two studied groups

Nectin-4 (H score)		No. of cases	H&E		Test of significance	
			Muscle Invasive	Non-muscle invasive		
			N (%)	N (%)	p-Value	Sig.
H score Median			177 (17 - 238)	87 (10 - 198)	0.356(M)	NS
H score	Negative	9	3 (23.1%)	6 (46.2%)	0.411(F)	NS
	Positive	17	10 (76.9%)	7 (53.8%)		
Positive H score (N= 17)	Weak (15 – 99)	3	2 (20%)	1 (14.3%)	1.00(F)	NS
	Moderate (100 – 199)	6	3 (30%)	3 (42.9%)		
	Strong (200 – 300)	8	5 (50%)	3 (42.9%)		

(M) Mann-Whitney test of significance, (F) Fisher's Exact test of significance.

Table 4: Relation between marker expression, tumor size, grade and stage

		No. of cases	**H score**		Fisher's Exact test	
			Negative	Positive		
			N (%) Mean ± SD	N (%) Mean ± SD	p-Value	Sig.
Tumor size (Cm)			4.39 ± 0.89	4.76 ± 0.86	0.314(T)	NS
Tumor grade	Low grade	25	6 (46.2%)	19 (40.4%)	0.711(C)	NS
	High grade	35	7 (53.8%)	28 (59.6%)		
Tumor stage	PT1	34	9 (69.2%)	25 (53.2%)	0.157(F)	NS
	PT2	13	3 (23.1%)	10 (21.3%)		
	PTA	11	0 (0%)	11 (23.4%)		
	PTIS	2	1 (7.7%)	1 (2.1%)		

(T) Student-t test of significance, (C) Chi-Square test of significance, (F) Fisher's Exact test of significance.

Table 5: Relation between smoking, Nectin-4 expression & tumor grade

		Smoking		Chi-Square test	
		No	Yes		
		N (Row %)	N (Row %)	p-Value	Sig.
Tumor grade	Low grade	18 (72.0%)	7 (28.0%)	<0.001	S
	High grade	8 (22.9%)	27 (77.1%)		
H score	Negative	5 (38.5%)	8 (61.5%)	0.689	NS
	Positive	21 (44.7%)	26 (55.3%)		
H score		226.5 (70 – 256)	194 (17 – 250)	0.493	NS

NS: non significant, S: significant.

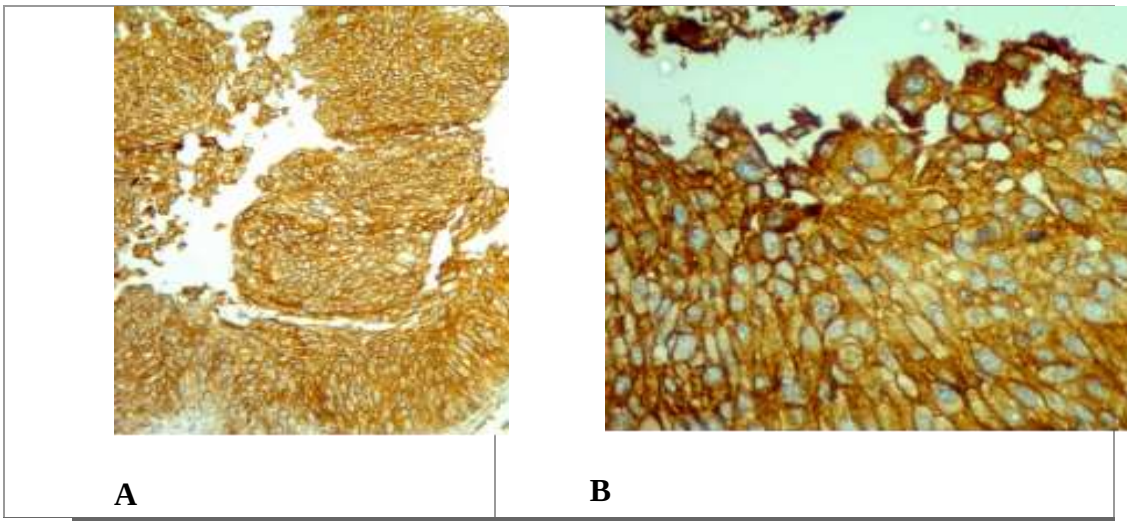

Figure 1: **A** Urothelial carcinoma showing strong Nectin-4 staining (×200)**, B** Urothelial carcinoma showing strong Nectin-4 staining (×400)**.**

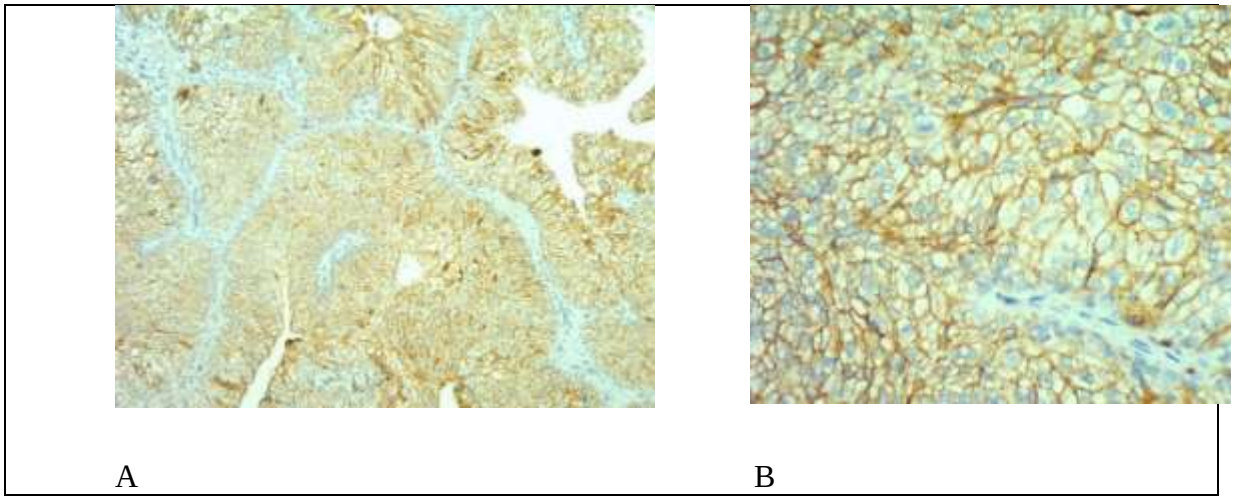

Figure 2: **A** Urothelial carcinoma showing moderate Nectin-4 staining (×200**, B** Urothelial carcinoma showing moderate Nectin-4 staining (×400)**.**

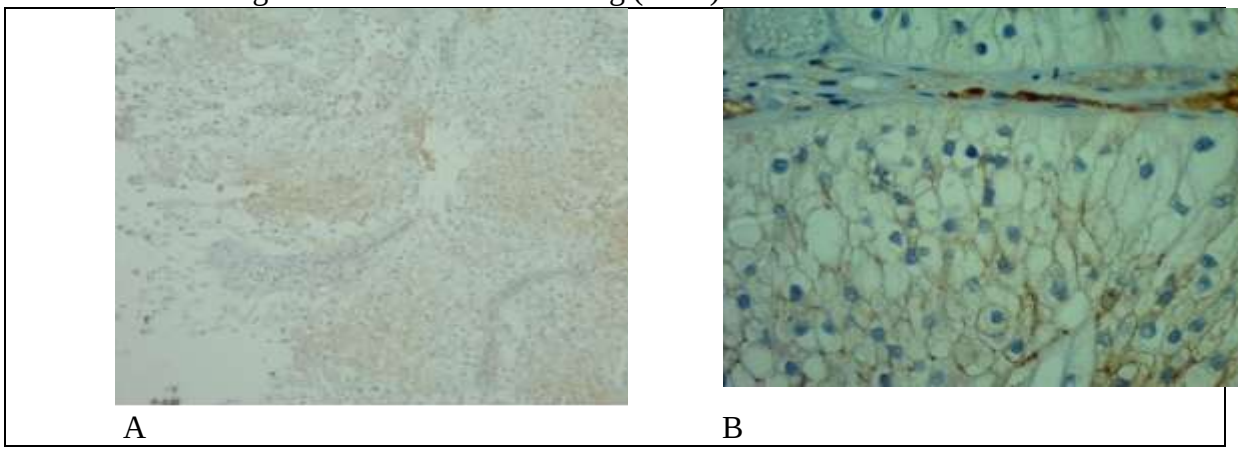

Figure 3: **A** Urothelial carcinoma showing weak Nectin-4 staining (×200)**, B** Urothelial carcinoma showing weak Nectin-4 staining (×400)**.**

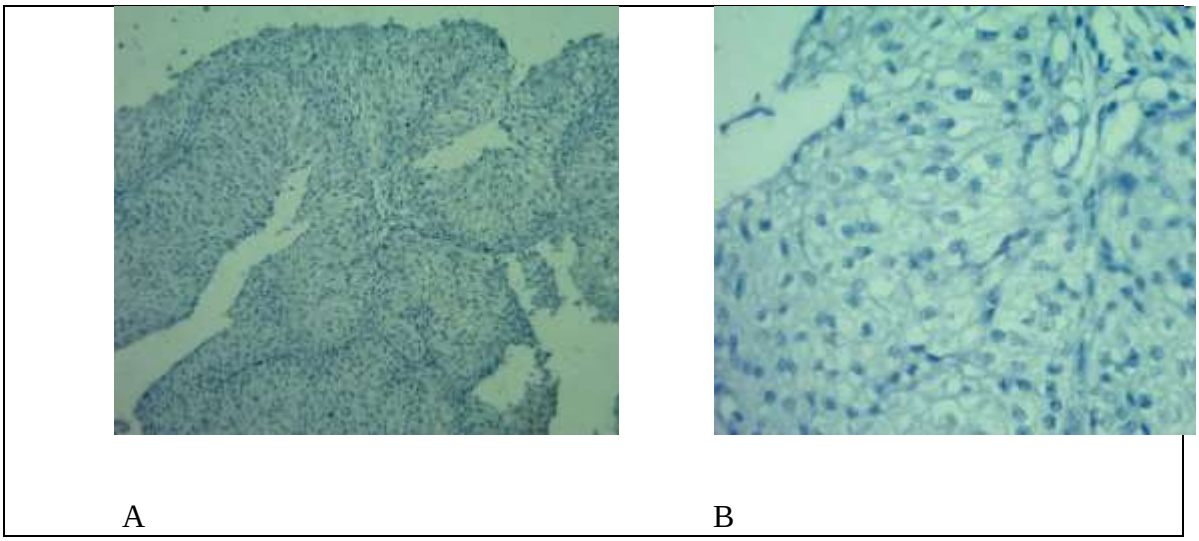

Figure 4: **A** Urothelial carcinoma showing negative Nectin-4 staining (×200)**, B** Urothelial carcinoma showing negative Nectin-4 staining (×400)**.**

Discussion

Urothelial carcinoma is an international public health problem. It ranks as the seventh most prevalent tumor globally among males and the seventeenth among females (3). Differentiation between MIUC and NMIUC by IHC could be helpful as it has completely different implication on clinical management of the patients.

In the present investigation, the age range of the examined cases was 37-87 years. The mean age of UC patients was 59.78 ± 10.83 years. 8/60 (63.3%) of cases were men and 22/60 (36.7%) were women, with male to female ratio of 1.7:1. This showed aligning with Hoffman et al's findings that the average age of UC at diagnosis was 69 years (range 42-86) and male to female ratio of bladder cancer was 3.44:1 (9). Halaseh et al found that three-quarters of bladder tumor cases happen in males (10), while Lobo et al documented that UBC is about fourfold greater in males in comparison with women in females (11).

Nectin-4 was positive in 47/60 (78.3%) and negative in 13/60 (21.7%) of cases of UC, agreeing with Challita-Eid et al's finding that 83% of bladder cancer cases showed positive Nectin-4 expression (12).

Within the 47 Nectin-4 positive cases of UC and according to H score 32/47 (68.1%) cases were strongly positive, 10/47 (21.3%) cases were moderately positive and only 5/47 (10.6%) cases were weakly positive. Rosenberg et al., found that most of his studied UC cases showed strong positive Nectin-4 expression (7).

Of the radical cystectomy cases, 17/26 showed H-score positive Nectin-4 and 9/26 showed H-score negative Nectin-4 expression. Out of the 17 positive cases, 7/17 (41%) were NMIUC.

From 26 radical cystectomy cases 13 were NMIUC cases, 7 of them (7/13, 53.8%) were Nectin-4 H-score positive. Regarding the other 13 MIUC cases, 10 of them (10/13, 77%) were Nectin-4 H-score positive. Hoffman et al., stated that 87% of NMIUC samples showed H-score positive Nectin-4 expression and 68.2% of MIUC cases showed H-score positive Nectin-4 expression (9).

Tomiyama et al., stated that 72% of NMIUC cases showed H-score positive Nectin-4 expression and only 50% of MIUC cases showed H-score positive Nectin-4 expression (13).

Regarding tumor grade, 77% of patients with high grade tumor were smokers and only 28% of patients with low grade tumors were smokers in the recent investigation. This result comes in concordance with Mohseni et al's finding that 90% of cases with high-grade tumors were smokers and only 36.1% of the cases with low-grade tumors were smokers (14).

In the current study, low grade lesions showed H-score positive Nectin-4 expression in 76% of cases, and high grade lesions showed H-score positive Nectin-4 expression in 80% of cases of UC. Tomiyama et al., stated that low grade lesions of upper tract Urothelial carcinoma (UTUC) cases showed H-score positive Nectin-4 expression in 53% of cases, and high grade lesions showed H-score positive Nectin-4 expression in 68% of cases. Both the current study and the previously mentioned study detected slightly higher H-score Nectin-4 expression in higher grades UC cases (13).Non-significant difference was found regarding the relationship between tumor stage and marker expression. H-score positive Nectin-4 expression was 100% in non-invasive papillary urothelial carcinoma (PTA), 73.5% of PT1 showed H-score positive Nectin-4 expression (papillary urothelial carcinomas invading lamina propria) and 76.9% of PT2 showed H-score positive Nectin-4 expression (muscle-invasive urothelial carcinomas). This is in accordance with Chu et al who observed lower Nectin-4 expression in pT1 compared to pT2 tumors (14).

Out of 6 UC cases with squamous differentiation, 5 cases showed H-score positive Nectin-4 expression (83.3%), 4 of them were strong positive (80%) and only one case showed H-score negative Nectin-4 expression. This is comparable with what has been stated by Hoffman et al., who observed that 70% of UC cases with squamous differentiation illustrated H-score positive Nectin-4 expression in the squamous component, 57% of them were strong positive. So the current study and previous findings indicated elevated H-score Nectin-4 expression and strong positivity in UC cases with squamous differentiation (9).

Conclusions:

There is high H-score positive Nectin-4 expression in UC of the urinary bladder. Nectin-4 is relatively increased in larger tumor size, high grade and stage UCs, but with no significant difference. These findings suggest an important function of Nectin-4 in diagnosing UCs of the urinary bladder.

Recommendations

We recommended to study Nectin-4 expression on a larger number of cases with different histological variants of UC of the urinary bladder and to make further comparative studies between Nectin-4 expression in MIUC and NMIUC.

Financial support and sponsorship: Nil

Conflict of Interest: Nil

Abbreviations: IHC; immunohistochemistry, MIUC; muscle invasive urothelial carcinoma, NMIUC; non-muscle invasive urothelial carcinoma, UC; urothelial carcinoma,

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (36-48) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Relationship between Severity of Neonatal Thrombocytopenia and Prophylactic Platelet Transfusion in NICU

Ashraf A. Meabed[1], Entesar Awn Allah Gaber Barsi[1*], Magda F Gabri[1], Khalid IA Elsayh[2], Hanan Mohammed abd el moneim[1].

[1]Pediatrics Department, Faculty of Medicine, Aswan University, Egypt

[2]Pediatrics Department, Faculty of Medicine, Assuit University, Egypt

ABSTRACT

Keyword: NT, NICU, Hemorrhage, NEC, Sepsis.

*** Corresponding author:**
Entesar Awn Allah Gaber Barsi

Mobile+201065035578

E-mail:
entesarawny2016@gmail.com

Background: Prophylactic platelet transfusion carries higher risk of complications, however, there no solid proof that a newborn's platelet count and severe bleeding are related. **Objectives:** The current study aimed to explore the association between NT severity and platelet transfusion and the possible complications based on NT severity. **Methodology:** 140 newborns hospitalized to the Neonatal Intensive Care Unit with a platelet count <100,000/ml participated in this randomized controlled experiment. **Results:** cases with severe NT had higher rates of sepsis and NEC (53% and 26%) than those with moderate NT (34% and 9.5%). Also, need for platelet transfusion was higher among severe (70%) vs moderate NT (27%) cases (p<0.001).In addition, NEC was higher in cases needed transfusions and proportion of patients with hemorrhage was higher in those needed transfusion or with hemorrhage. Likewise, the need for transfusion and cases with hemorrhage was associated with higher prevalence of mortality (33.3% and 83%) than no need (1.4% and 2.6%) (p<0.001). **Conclusion:** the current study shredded the light on the positive relationship between NT severity, need for transfusion and hemorrhage with the patients' main outcomes i.e., hemorrhage and mortality.

INTRODUCTION

Neonatal thrombocytopenia (NT) is a common hemostatic abnormality among newborn in the Neonatal Intensive Care Unit (NICU), which had positive correlation with prematurity **(1)**. Different etiologies for NT have been identified either immunologic or non-immunologic **(2)**. The following criteria were used to determine the degree of thrombocytopenia: A platelet count of 100,000 to 150,000/μL is considered mild; a platelet count of 50,000 to <100,000/μL is considered moderate; a platelet count of 30,000 to <50,000/μL is considered severe; and a platelet count of < 30,000/μL is considered very severe **(3)**.

Prophylactic platelet transfusion using 50,000/μL at threshold carries higher risk of complications i.e., death or major bleeding compared with 25,000/μL **(4**). Thus, the use of a restrictive neonatal platelet transfusion guideline is advocated to decrease potentially hazardous platelet transfusions in NICUs, while the usefulness of prophylactic platelet transfusions in neonates is disputed **(5)**. Using criteria based on the platelet mass index (PMI) may reduce platelet transfusion rates in the NICU, but more data from prospective studies is required **(6)**. Hence, severity of NT should be included to boost these guidelines.

The current study aimed to explore the association between NT severity and platelet transfusion and the possible complications based on NT severity.

PATIENTS AND METHODS

In the period from April 2022 to October 2023, 140 newborns with NT who were hospitalized to the NICU at Aswan University Hospitals participated in this single blinded Randomized Controlled Trial (RCT).

Using Stata v-16, a minimum sample of 124 neonates were required to reveal prophylactic platelet transfusion reduction of 20% (92% to 73%) with error probability of 5% and study power of 80% **(11)**. A 20% increase in the sample was applied to compensate for attrition and dropouts, hence the total sample became 140 (i.e., 70 per group).

Inclusion criteria were: NT cases who were admitted to the NICU and had a PLT count of <100,000/ml. However, those with hydrops fetalis, thrombocyte illnesses, coagulation problems, or significant congenital anomalies were excluded.

Randomization:

Automated random number generator was used for case distribution. According to eligibility, two equal groups with random assignment were created i.e., **Group-I**: consisted of 70 neonates who had platelet transfusions in accordance with the PLT count-based recommendation and **Group-II:** included 70 neonates with platelet transfusion according to PMI based guideline. Allocation was kept in sealed, opaque envelopes with sequential numbers. A Sysmex Xn 1000 Hematology Analyzer and a Mindray Hematology Analyzer BC-5150 were used to measure PLT counts and MPVs. Three milliliters of venous blood were anticoagulated using ethylene diamine tetra-acetic acid (EDTA). The following criteria were used to determine the degree of thrombocytopenia: A platelet count of 100,000 to 150,000/μL is considered mild; a platelet count of 50,000 to <100,000/μL is considered moderate; a platelet count of <50,000/μL is considered severe.

Procedure

Every case under study had routine investigation (complete blood count, or CBC), clinical examination, and detailed history taking. Clinical condition was categorized based on the amount of PLT transfusions received by subjects receiving one or more transfusions, as well as the total number of transfusions in both groups: I- ***Stable patients*** **(8)** either premature or full-term, II- ***Unstable patients*** and ***III- immediately pre or postoperative patients***. PLTs that were matched to the groups performed all of the transfusions. The PLTs were extracted from whole blood donations, which underwent leuco-filtration and were given in a dosage of 10–20 milliliters per kilogram of body weight. All transfusions were carried out using group-matched PLTs. Leuco-filtered whole blood donations were used to extract the PLTs, which were then administered at a dosage of 10–20 milliliters per kilogram of body weight.

Statistical analysis

IBM-SPSS version 26 was used to analyze the data **(9)**. Frequencies and percentages were used to display categorical data. In accordance with their distribution, numerical data were shown as mean and standard deviation (SD) or median and range after being examined for normality using the Shapiro-Walk test. Mann Whitney U test/Independent Sample T-test were used, as appropriate, to examine the difference in the mean/median between the two groups. Paired Sample T-test/Wilcoxon Sign test was used to explore the difference in mean/median within group before vs. after transfusion within each group. Chi-square test/Fisher's exact test was used to compare the difference in frequency between groups as convenient. A p-value of less than 0.05 was deemed significant.

Ethical considerations

The study's methodology was authorized by the Aswan University Faculty of Medicine's Institutional Ethics and Research Review Board (IRB). Before the trial was conducted, the neonates' caregivers signed a written informed consent form. The study adhered to STROBE standards for observational studies **(10)**, as well as Helsinki Declaration **(11)**, and was not abided with any incentives or rewards for participants or their guardians.

RESULTS

The recruited 140 neonates had gestational age of 26-40 weeks and weight of 800-4200 gm. Also, males represented about 57% of the studied cohort.

Table 1 showed the NT associated characteristics, it was found that 42% (n=59) of the sample had early-onset NT and about 58% (n=81) had late-onset NT. The median onset time was 4 (1-20) days. Also, nearly 53% had moderate NT and 47% have sever NT. Further, 47% (n=59) of the studied neonates needed platelets transfusion. Additionally, the median number of platelet transfusions per patient was 0 (0-7) and the total number of transfusions in all patients who needed transfusion was 110 Transfusions.

Table (1): Characteristics of thrombocytopenia among studied neonates

Variables	Total (n=140)	%
Onset of thrombocytopenia		
▪ Early onset	59	42.1%
▪ Late onset	81	57.9%
Onset day:		
▪ Mean ± SD	4.10 ± 2.93	
▪ Median (range)	4.0 (1.0 - 20.0)	
Severity of thrombocytopenia		
▪ Moderate (50,000-100,000)	74	52.9%
▪ Sever (Less than 50,000)	66	47.1%
Patients need platelets transfusion		

▪ Not need	74	52.9%
▪ Need	66	47.1%
Number of platelet transfusion for patient		
▪ Mean ± SD	0.79 ± 1.11	
▪ Median (range)	0.0 (0.0 - 7.0)	
Total number of transfusions in all patients need transfusion	**110 transfusions**	
Transfusion guidelines according to:		
▪ Platelet count guideline	70	50.0%
▪ Platelet mass index guideline	70	50.0%

Data expressed as Mean ± SD/median (range) or frequency (%)

As shown in figures 1 and 2, showed that 17% have post-transfusion hemorrhage namely, 11.5% pulmonary, 5.7% intracranial, 2.9% cutaneous, and 2.1% gastrointestinal. Regarding overall mortality, mortality rate was 16.4%.

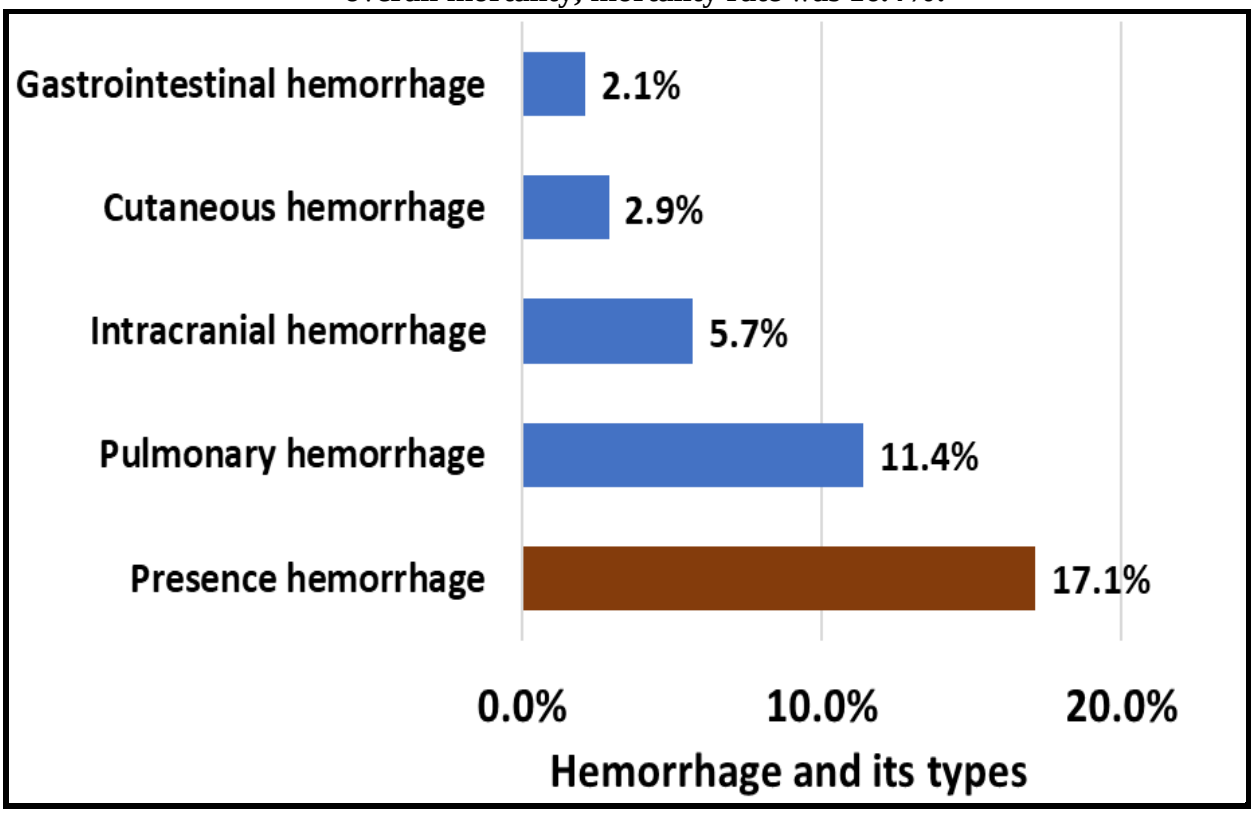

Figure (1): Hemorrhage among studied neonates with thrombocytopenia

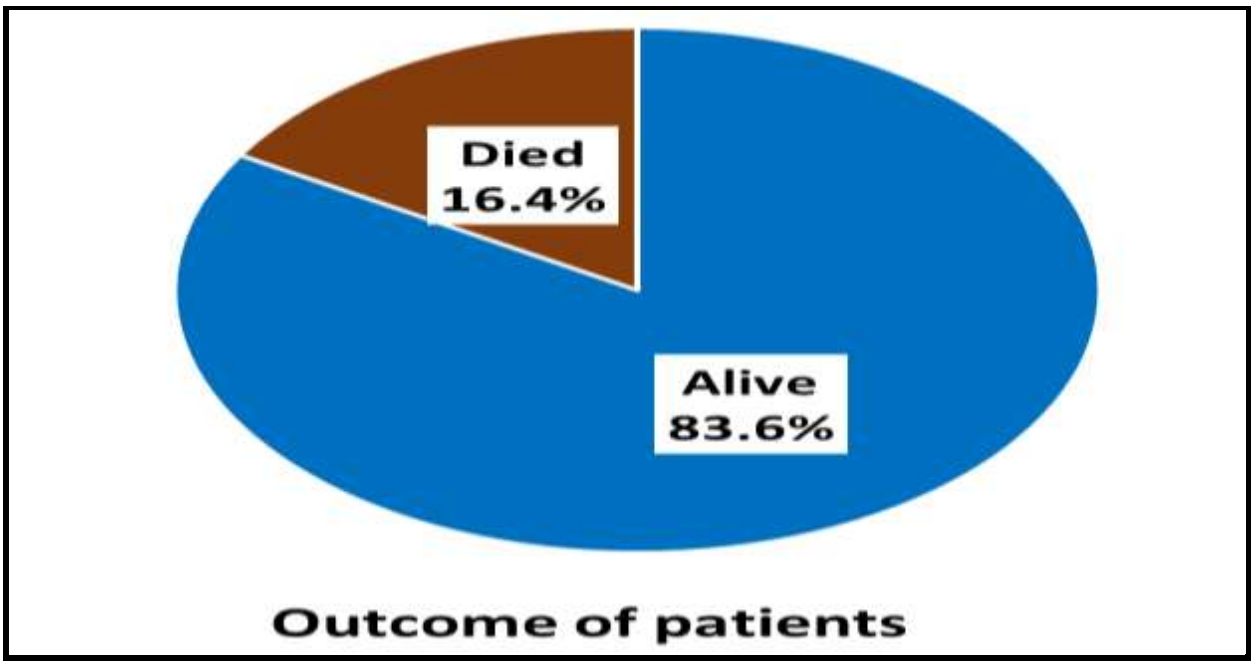

Figure (2): Outcome of studied neonates with thrombocytopenia

Table 2 illustrated relationship between patient characteristics and disease severity. For neonatal risk factors, cases with severe NT had significantly (p=0.022 and 0.011) higher rates of sepsis and NEC (53% and 26%) than those with moderate NT (34% and 9.5%). Also, need for blood transfusion was higher among severe (70%) vs moderate NT (27%) cases (p<0.001).

Table (2): Comparison of patient characteristics based on severity of thrombocytopenia

Variables	Severity of thrombocytopenia		P-Value*
	Moderate (n=74)	Sever (n=66)	
Gestational age (weeks)			
▪ Mean ± SD ▪ (range)	34.99 ± 3.1 (26 - 40)	34.88 ± 2.7 (30 - 40)	0.827
Weight (gm)			
▪ Mean ± SD ▪ (range)	2156.89 ± 770.8 (800 - 4000)	1954.7 ± 774.5 (1000 - 4200)	0.124
Gender			
▪ Males ▪ Females	41 (55.4%) 33 (44.6%)	39 (59.1%) 27 (40.9%)	0.660
Risk Factors			
Neonatal risk factors			
▪ Respiratory distress syndrome	40 (54.1%)	43 (65.2%)	0.182
▪ Prematurity	34 (45.9%)	39 (59.1%)	0.120
▪ Sepsis	25 (33.8%)	**35 (53.0%)**	**0.022**
▪ Hyperbilirubinemia	15 (20.3%)	14 (21.2%)	0.891
▪ Premature rupture of membrane	13 (17.6%)	15 (22.7%)	0.446
▪ Necrotizing enterocolitis	7 (9.5%)	**17 (25.8%)**	**0.011**
▪ Intrauterine growth restriction	12 (16.2%)	7 (10.6%)	0.333

Maternal risk factors			
▪ Pre-eclampsia	10 (13.5%)	17 (25.8%)	0.067
▪ ITP	2 (2.7%)	1 (1.5%)	0.999
▪ Blood incompatibility	6 (8.1%)	7 (10.6%)	0.611
▪ SLE	1 (1.4%)	2 (3.0%)	0.602
▪ Infant of diabetic mother	5 (6.8%)	4 (6.1%)	0.999
▪ Hepatitis B and C	3 (4.1%)	1 (1.5%)	0.622
▪ Corona virus disease	1 (1.4%)	2 (3.0%)	0.602
Patients need platelet transfusion			
▪ Not need	54 (73.0%)	20 (30.3%)	**<0.001**
▪ Need	20 (27.0%)	46 (69.7%)	
Hemorrhage	6 (8.1%)	18 (27.3%)	**0.003**
Type of hemorrhage			
▪ Pulmonary	2 (2.7%)	14 (21.2%)	**0.001**
▪ Intracranial	3 (4.1%)	5 (7.6%)	0.370
▪ Cutaneous	3 (4.1%)	1 (1.5%)	0.622
▪ Gastrointestinal	0 (0.0%)	3 (4.5%)	0.102
Outcome			
▪ Alive	69 (93.2%)	48 (72.7%)	**0.001**
▪ Dead	5 (6.8%)	18 (27.3%)	

Chi square test/Fisher Exact test compare proportion between groups
Independent Sample T test compare mean between two groups
Severity: Mild: 100,000-150,000. Moderate: 50,000- less than 100,000. Severe: less than 50,000.

there was no statistically significant difference between moderate and severe thrombocytopenia regarding gestational age, weight, gender, p value >0.05. Additionally, prevalence of hemorrhage (particularly pulmonary) was higher in severe vs moderate NT (21.2% vs 2.7%, p=0.001). Likely, mortality rate was higher in severe (27%) compared with moderate NT (6.8%) (p=0.001).

Comparison of patients' characteristics regarding the need for platelet transfusion was demonstrated in **table 3.** The mean weight was significantly lower among those needed transfusions vs those did not (1896.8 ± 739.1 vs 2208.5 ± 784.2, p=0.017). Further, NEC was higher in cases needed transfusions (24.2% vs 10.8%, p=0.035). Proportion of patients with hemorrhage was higher in those needed transfusion (particularly pulmonary [24%] and intracranial [12.4%]) in comparison with cases who did not need transfusion (pulmonary [0%] (p<0.001) and intracranial [0%] (p=0.002)). Likewise, the need for transfusion was associated with higher prevalence of mortality (33.3%) than no need (1.4) (p<0.001).

Table (3): Comparison of patient characteristics based on need for a platelet transfusion

Variables	Not need Platelet transfusion (n=74)	Need Platelet transfusion (n=66)	P-Value*
Gestational age (weeks)			
▪ Mean ± SD ▪ (range)	35.32 ±2.8 (26 - 40)	34.50 ± 2.9 (27 - 40)	0.092
Weight (gm)			
▪ Mean ± SD ▪ (range)	2208.51 ±784.2 (900 - 4200)	1896.8 ± 739.1 (800-3500)	**0.017**
Gender			
▪ Males ▪ Females	42 (56.8%) 32 (43.2%)	38 (57.6%) 28 (42.4%)	0.922
Risk Factors			
Neonatal risk factors			
▪ Respiratory distress syndrome	47 (63.5%)	36 (54.5%)	0.281
▪ Prematurity	33 (44.6%)	40 (60.6%)	0.058
▪ Sepsis	26 (35.1%)	34 (51.5%)	**0.051**
▪ Hyperbilirubinemia	20 (27.0%)	9 (13.6%)	**0.051**
▪ Premature rupture of membrane	14 (18.9%)	14 (21.2%)	0.735
▪ Necrotizing enterocolitis	8 (10.8%)	16 (24.2%)	**0.035**
▪ Intrauterine growth restriction	11 (14.9%)	8 (12.1%)	0.636
Maternal risk factors			
▪ Pre-eclampsia	15 (20.3%)	12 (18.2%)	0.755
▪ ITP	3 (4.1%)	0 (0.0%)	0.247
▪ Blood incompatibility	8 (10.8%)	5 (7.6%)	0.571
▪ SLE	2 (2.7%)	1 (1.5%)	0.999
▪ Infant of diabetic mother	6 (8.1%)	3 (4.5%)	0.500
▪ Hepatitis B, C	2 (2.7%)	2 (3.0%)	0.999
▪ Corona virus disease	2 (2.7%)	1 (1.5%)	0.999
Hemorrhage	3 (4.1%)	21 (31.8%)	**<0.001**
Type of hemorrhage			
▪ Pulmonary	0 (0.0%)	16 (24.2%)	**<0.001**
▪ Intracranial	0 (0.0%)	8 (12.1%)	**0.002**
▪ Cutaneous	4 (5.4%)	0 (0.0%)	0.122
▪ Gastrointestinal	0 (0.0%)	3 (4.5%)	0.102
Outcome			
▪ Alive ▪ Dead	73 (98.6%) 1 (1.4%)	44 (66.7%) 22 (33.3%)	**<0.001**

***Chi square test/Fisher Exact test compare proportion between groups**
Independent Sample T test compare mean between two groups

Table 4 showed the differences in patients' characteristics for occurrence of hemorrhage. There was significantly (p=0.019) lower mean weight among patients with hemorrhage than patients without hemorrhage (1724.6 ± 798.5 vs 2131.3 ± 756.6). For neonatal risk factors, there was a significantly (p=0.021) higher percentage of NEC in cases with hemorrhage vs those without (33.3% vs 13.8%). For maternal risk factors, there was a significantly (p=0.005) higher proportion of SLE among hemorrhagic cases vs non-hemorrhage (12.5% vs 0%). Regarding patient's outcome, there was significantly (p<0.001) higher mortality rate among patients with hemorrhage vs patients without hemorrhage (83% vs 2.6%).

Table (4): Comparison of patient characteristics based on occurrence of hemorrhage

Variables	No hemorrhage (n=116)	Hemorrhage (n=24)	P-Value*
Gestational age (weeks)			
▪ Mean ± SD ▪ (range)	35.12 ± 2.7 (26-40)	34.04 ± 3.7 (27-40)	0.190
Weight (gm)			
▪ Mean ± SD ▪ (range)	2131.29 ± 756.6 (900 - 4200)	1724.58 ± 798.5 (800 - 3500)	**0.019**
Gender			
▪ Males ▪ Females	69 (59.5%) 47 (40.5%)	11 (45.8%) 13 (54.2%)	0.219
Risk Factors			
Neonatal risk factors			
▪ Respiratory distress syndrome	66 (56.9%)	17 (70.8%)	0.206
▪ Prematurity	57 (49.1%)	16 (66.7%)	0.118
▪ Sepsis	47 (40.5%)	13 (54.2%)	0.219
▪ Hyperbilirubinemia	26 (22.4%)	3 (12.5%)	0.275
▪ Premature rupture of membrane	23 (19.8%)	5 (20.8%)	0.911
▪ Necrotizing enterocolitis	16 (13.8%)	8 (33.3%)	**0.021**
▪ Intrauterine growth restriction	17 (14.7%)	2 (8.3%)	0.410
Maternal risk factors			
▪ Pre-eclampsia	21 (18.1%)	6 (25.0%)	0.436
▪ ITP	2 (1.7%)	1 (4.2%)	0.434
▪ Blood incompatibility	13 (11.2%)	0 (0.0%)	0.125
▪ SLE	0 (0.0%)	3 (12.5%)	**0.005**
▪ Infant of diabetic mother	9 (7.8%)	0 (0.0%)	0.358
▪ Corona virus disease	3 (2.6%)	0 (0.0%)	0.999
Onset of thrombocytopenia			
▪ Early onset ▪ Late onset	49 (42.2%) 67 (57.8%)	10 (41.7%) 14 (58.3%)	0.959
Onset day			

▪ Mean ± SD ▪ Median (range)	4.05±2.90 4.00 (1.0-20.0)	4.12±3.15 4.00 (1.0-13.0)	0.784
Outcome			
▪ Alive ▪ Dead	113 (97.4%) 3 (2.6%)	4 (16.7%) 20 (83.3%)	**<0.001**

Data expressed as Mean ± SD or frequency (%). *Chi square test/Fisher Exact test compare proportion between groups, Independent Sample T test compare mean between two groups

Contrarily, there was no significant differences between groups regarding all other parameters.

DISCUSSION

Numerous studies have been conducted on platelet transfusion in neonates, and it is a common issue to identify strategies for reducing the incidence of platelet transfusion without raising the rates of bleeding or incorrect proof mortality **(12)**. Further testing is usually not necessary for individuals with mild NT, which is an accidental finding, if the platelet count stabilizes and improves on its own without treatment **(13)**. Similarly, babies delivered after a history or clinical indication of placental insufficiency and with moderate NT typically simply require platelet count monitoring to make sure it is temporary **(14)**. Bleeding is very common in neonates with severe NT. Neonates with very severe NT have higher incidence rate of cutaneous bleeding than those with severe NT **(15)**. Instant and short term adverse outcomes have been linked with severe NT at presentation **(16)**. In the 1st week of life, the majority of NT cases who were not transfused recovered spontaneously **(17)**. Babies with severe NT have the highest mortality rates, followed by those with mild to moderate disease and those without NT **(18)**.

This single blinded randomized controlled clinical trial was conducted on 140 neonates with NT at NICU, Pediatric department, Aswan University Hospital, Egypt. This study aimed to examine the association between NT severity disease outcomes and disease correlates. Recruited cases encompassed about 43% females and 57% males, with a mean weight of 2061.6 ± 766.4 grams and a mean gestational age of 34.9 ± 2.9 weeks.

In this study, NT had a median onset of 4 (1-20) days, with 42% experiencing early onset and 58% experiencing late onset. Similar to our results, **Zekry et al**. revealed that among newborns with NT, 84.5% had late onset **(19)**. Likely, in institution-based descriptive retrospective research conducted on 242 neonates with NT, a total of 205 (84.7%) of the neonates showed thrombocytopenia within the first 72 hours **(20)**. While, **Bolat et al**. found that out of 208 neonates with NT, 57% of the cases had early-onset **(21)**.

Numerous studies have found that infections such as late-onset sepsis, prematurity, prolonged hospitalization with intensive care interventions, the use of medications that suppress bone marrow or increase platelet destruction, and immune-mediated conditions are the main causes of the increased incidence of late-onset neonatal thrombocytopenia. Higher rates of thrombocytopenia seen in later phases of newborn care are caused by these variables, which are particularly common in critically sick neonates **(22)**.

As regard NT severity, about 53% have moderate and 47% have sever NT. This was disagreed with **Dahat et al** study who detected that the majority of neonates had moderate NT (37.4%); however, mild thrombocytopenia was seen in 32 (32%), and the rest of the neonates (31, 3%) had severe NT **(23)**. In a study by **Meena et al**., most of neonates had mild (46%), followed by moderate (35%)

and then severe NT (19%) **(24)**. The discrepancy between the current findings and other studies could be due to differences in study population characteristics, such as higher risk factors (e.g., maternal conditions like pre-eclampsia), variations in the definitions or thresholds for severity, timing of platelet count measurements, underlying causes of thrombocytopenia, or differences in sample size and study design.

Regarding platelets transfusion, about 53% did not need platelets transfusion, while 47% needed. The median number of transfusions was 0 (0-7). Total number of transfusions in all patients need transfusion was 110 Transfusions. Very small number of patients received PLT transfusions in **Kasap et al**. study as among the 395 thrombocytopenic patients, 30 (7%) received PLT transfusions. This lower rate in their NICU may be multifactorial; first, strict criteria are applied for PLT transfusions in their NICU to avoid unnecessary transfusions. In addition, our NICU includes both second level and third-level NICU patients, which may have resulted in the lower rates of severe thrombocytopenia and, consequently, PLT transfusions **(6)**. The difference in platelet transfusion rates in NT across studies can be attributed to variations in clinical guidelines, thresholds for transfusion, and institutional practices. Other factors include differences in the severity of thrombocytopenia in the study populations, underlying conditions (e.g., sepsis or NEC), and the availability of transfusion resources.

Based on NT severity, there was significantly higher percentage of sepsis and NEC among patients with severe thrombocytopenia. In line with our results, a retrospective cohort study of 422 NT cases detected that there was gradient association with Severity **(25)**. In Kasap et al. study, neonatal risk factors (sepsis, RDS, IUGR) showed positive correlation with severity) **(6)**. Likewise, it was reported that NT cases had higher proportion of need for platelets transfusion **(25)**. Consistent results for the mean number of platelet transfusions **(6-25).**

In addition, in our study there was statistically significantly higher percentage of hemorrhage particularly pulmonary among patients with severe NT, however, other types of hemorrhage were insignificant. Our result disagreed with **Von Lindern et al**. who did not find relationship between hemorrhage and NT severity. This suggests that bleeding in neonates depends on more variables than a platelet count alone **(25)**. In approximately one-third of cases, ICH was discovered before NT and this raises the question whether ICH can be explained as a cause or an effect **(26-27)**. Hemorrhage is probably due to pre-existing fragility in vessel wall structure and damaged blood vessels, amongst others by cytokines and/or a co-existing coagulopathy (**26**, **28**).

For patient's outcome, severe NT was related with higher mortality rate. In agreement, Al **Ghadeer et al**. detected that mortality rate was 5.3% in cases with mild compared to 21.8% in moderate NT and 25.7% in severe NT **(20)**. Also**, Kasap et al**. found similar results **(6)**.

Comparison of patient characteristics based on need for a platelet transfusion, there was significantly higher rate of NEC among those needing transfusions. Consistently**, Kasap et al**. detected that there was significant difference as regard sepsis and NEC between patients do not need transfusions and patients need transfusion. Likewise, they detected significant difference as regard ICH and mortality **(6)**. The current study reported similar results i.e., cases need transfusion had higher rates.

Moreover, there was significantly lower mean weight among cases with hemorrhage. In dis-concordance**, Kasap et al**. found that was no significant differences between patients with IVH and without IVH as regard gestational age, and birth weight **(6)**. As well, hemorrhagic cases had higher percentage of NEC. This could be explained by that NEC is closely related to hemorrhage in neonates with NT, as both conditions can exacerbate each other **(29)**. For maternal risk factors,

those with hemorrhage had higher proportion of mothers with SLE. Likely, **Zekry et al**. found that SLE and PIH were associated with bleeding NT **(19)**. Respecting outcome, there was significantly higher mortality rate among cases with hemorrhage. Similar results were reported by **Resch et al**., who detected that a mortality rate of 10.8% was significantly associated with bleeding signs **(30)**.

CONCLUSION

In conclusion, the current study shredded the light on the positive relationship between NT severity and patients' main outcomes i.e., hemorrhage and mortality. Also, the effect of neonatal risk factors on the need for transfusion, as well as the effect of such need on the patients' outcomes (hemorrhage and mortality). Likewise, the predictors of hemorrhage in NT cases were NEC among cases and SLE of their mothers, and higher mortality among those with hemorrhage.

Study Limitations

The current study had certain limitations. First, the study was conducted at a single center that jeopardize the external validity of the study. Second, in order to match groups, we did not assess potential confounding variables (i.e., the presence of alloimmunization or platelet refractoriness).

Conflict of interest: All authors declare that they have no conflicts of interest.

Financial Disclosures: None

Acknowledgement:

The authors would like to express their gratitude to the pediatric departments' administrative and medical staff at Aswan University Hospital for their continuous assistance and support. Without the assistance, encouragement, and consent of the caregivers of the patients who were recruited, this work would not have been possible.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (49-61) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Age and Sex Discrimination via Tibial Measurement Estimation by Computed Tomography in Aswan governorate

Aly E. Mohamed[1]*, Randa H. El-hady[2], Safaa M. George[2], Heba A. Yassa[2]

[1]Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Aswan University

[2]Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Assiut University

ABSTRACT

Keyword: Tibia, Measurement, Age, Sex, Discrimination CT scan.

***Corresponding author: Aly E. Mohamed**

Mobile: +201044322898

E-mail: sabawy75@gmail.com

Background: There are numerous applications for computerized tomography in anthropometric studies and the analysis of skeletal remains. By examining computerized models of the tibia bone, it was found to be significant indicators of sex and age and this was significant advance in forensic science. **Aim:** This study aimed to test the accuracy of age and sex identification on the basis of computed tomographic image from different tibial measurement. **Methodology:** This observational cross-sectional study was conducted in the period from September 2019 to June 2023 on 200 living Egyptian persons at Aswan governorate submitted to spiral computed tomography of the Tibia. **Results:** there was significant (<0.001) difference between male and female, age group ≤50 years and age group >50 years and between stature <165 cm and ≥165 cm according to different diameters (AB, CD and EF). Also, A-B distance was the most accurate (81.5%), C-D distance was the most sensitive (83%), and A-B distance was the most specific (93%). **Conclusion:** this study highlights that the morphological differences represented by tibial dimensions between males and females, and in respect to their corresponding age groups were highly significantly different. This study provided an equation to predict a person's height based on the length of the tibia. Therefore, the current investigation yielded outstanding findings that are applicable in a forensic anthropological setting.

INTRODUCTION

One of the main goals of forensic medical investigations is to identify unrecognized human remains. Basic information on the individual's age, gender, height, and other anthropological traits has to be gathered in order to approximate a biological profile that will allow us to confirm identity. Forensic pathologists frequently examine highly decomposed, burned, or otherwise damaged human remains **(1)**. Particularly in cases that result in significant mortality, forensic

investigators work to determine the four main components of biological identification (sex, age, ethnic origin, and stature) **(2)**.

An essential component of forensic analysis is determining an individual's age. Among the many biomarkers that can be used to identify missing persons whose remains have been located is age at death **(3)**. The most suitable techniques are determined by the age distribution and the existence or lack of skeletal features. Bethard and VanSickle (2020) state that different methods must be used when determining the age of death in a fetus, baby, child, or other immature individual than when examining an adult's skeleton **(4)**.

Making a precise sex prediction from measurements of bone fragments is the most important step in the identification process **(5)**. Skeletal remains are sensitive for sex estimation, but they cannot be used when human and skeletal remains are only partially found. In these situations, attempts are made to estimate sex or height using other body parts **(6)**. The accuracy of sex identification depends on the degree of sexual dimorphism the skeleton exhibits, but damaged or incomplete human skeletal remains are commonly used in forensic investigations **(7)**.

The ability to determine sex from these materials becomes essential when mass murderers attempt to disfigure their victims to prevent identification or when bones are mixed, burned, and broken following a natural disaster **(8, 9)**. The errors presented here are in line with earlier studies that estimated sex using measurements from the lower limbs, particularly the tibia, and frequently obtained accuracies of over 80% **(9-11)**.

Because it showed the strongest correlation with stature in earlier research on comparable populations, the tibia was chosen as the ideal skeletal component **(4, 6-9),** as well as showing a significant degree of sexual dimorphism **(12).**

There are numerous applications for computerized tomography in anthropometric studies and the analysis of skeletal remains **(13)**. Examining sexual dimorphism helps one comprehend the overall intersexual divergence of the same species and provides information about how selective forces affect each sex **(14)**. Compared to differences in standard cortical metrics of radius and tibia, age-related differences in cortical porosity as measured by HR-pQCT are more noticeable. These structural variations have greater biomechanical significance for men and women as they age, and they offer discriminating information about the effects of menopause on bone quality **(15)**.

The goal of this study was to test the accuracy of age and sex identification on the basis of computed tomographic image from different tibial measurement among a known population in Aswan.

PATIENTS AND METHODS

This observational cross-sectional study was conducted in Aswan university hospital in the period from September 2019 to June 2023. The study involved 200 living Egyptian persons (100 males & 100 females), each group was subdivided to include 50 right and 50 left tibia) in Aswan governorate submitted to spiral computed tomography of the Tibia.

Inclusion criteria were Egyptian residents in Aswan governorate without history of previous knee, ankle or tibial fracture and aged > 30 years old. On the other hand, those with fractured tibia, previous history of knee or ankle surgery, history of underlying endocrine, metabolic or nutritional disorder were excluded.

Procedure

Every individual is subjected to measurement of his/her stature in centimeters; the length, proximal and distal breadth of tibia right & left are measured by CT **(Fig. 1)**:

- Landmark A-B [A] i.e., point (A): on outer most point on lateral condyle and point (B): on outer most point on medial condyle.
- Landmark C-D [B] i.e., point (C): on outer most point on medial malleolus and point (D): on outer most point on lateral end.
- Landmark E-F [C] i.e., point (E): on upper most point and point (F): on lower most point.

Fig. 1: Normal Tibial Measurement by CT

Statistical analysis

Data analysis was undertaken using IBM-SPSS version 26 **(16)**. Categorical data were presented as frequencies and percentages. Numerical data were checked for normality by Shapiro- walk test and presented as mean and standard deviation (SD) or median and range according to their distribution. Independent Sample T-test/Mann Whitney U test was used to compare mean/median difference between the two groups as appropriate.

Linear/Logistic regression analysis was calculated to investigate the independent predictor power of measurements (Odds Ratio -OR-, 95% confidence interval -95% CI- and p-value-). ROC curve was depicted to explore the diagnostic performance/cutoff of different parameters in predicting age and sex, analyzed as area under the curve (AUC), standard error (SE) and 95% CI. Validity statistics (sensitivity, specificity, positive and negative predictive value –PPV & NPV-) were calculated. The level of significance was considered at p-value < 0.05.

Ethical considerations

Institutional Ethics and Research Review Board (IRB no. 69/6/16) of the Faculty of Medicine at Aswan University approved the study's methodology. Anonymity and confidentiality were assured. Before participation, the purpose and nature of the study as well as risks and benefits

were fully explained. An informed written consent was a taken from the cases. This work was in line with the guidelines of Helsinki Declaration **(17)** and the STROBE guidelines for observational studies **(18)**.

RESULTS

In this study, 200 Egyptian persons (lived in Aswan) were included to test the accuracy of CT-based age and sex identification from different tibial measurement.

Table 1 described the baseline data of the study population. Age ranged from 31 to 70 years with a mean of 49.6 ± 10.1 years. For sex, male/female ratio was 1:1. Regarding stature, it ranged from 155 to 183 cm with a mean of 164.8 ± 6.9 cm and accordingly; about two-thirds (n=121) had stature <165 cm and 39.5% (n=79) had stature ≥165 cm.

Table 1: Basic Characteristics of the Studied Population

	n = 200	%
Sex		
• Male	100	50.0
• Female	100	50.0
Age (years)		
• Min. - Max.	31 – 70	
• Mean ± SD	49.56 ± 10.1	
stature (cm)		
• <165 cm	121	60.5
• ≥165 cm	79	39.5
• Min. - Max.	155 – 183	
• Mean ± SD	164.81 ± 6.9	

As shown in **fig.2**, One-quarter of the studied groups were 30-40 years (23 male/27 female); 26.5% were 41-50 years (24 male/29 female); about one-third were 51-60 years (36 male/31 female); and 15% were over 60 years old (17 male/13 female). This association was insignificant (p=0.637).

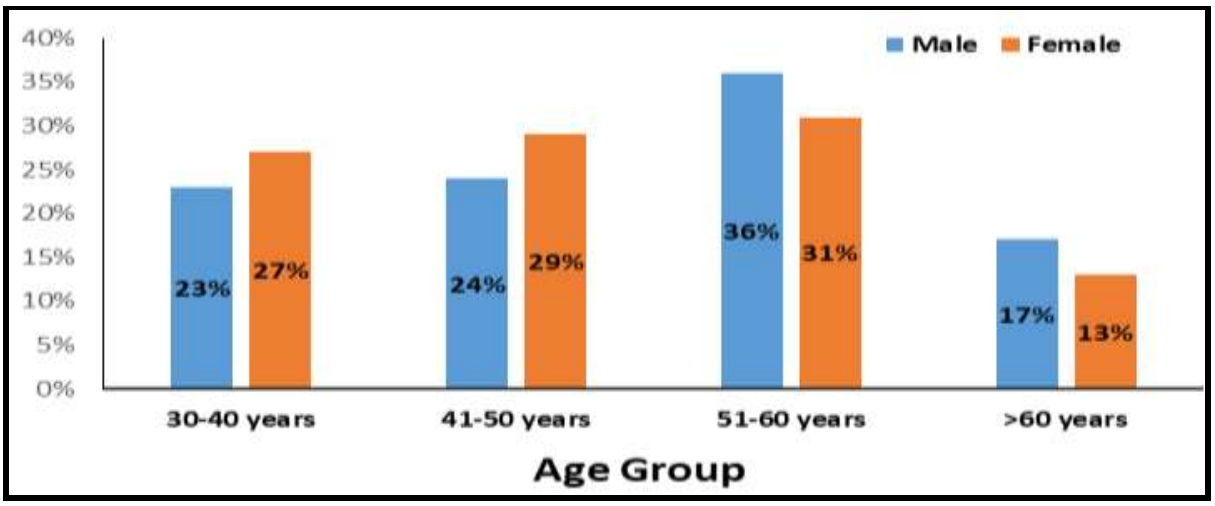

Fig. 2: Age Distribution according to Patient's Sex

Table 2 illustrated the association between sex and tibial measurements, there were statistically significant ($p < 0.001$) difference between males and females i.e., males had longer measurements (A-B: 7.3 ± 0.7, C-D: 4.8 ± 0.3 and E-F: 37.1 ± 1.8 cm) vs. females (A-B: 6.6 ± 0.2, C-D: 4.4 ± 0.2 and E-F: 35.1 ± 1.9 cm).

Table 2: Relationship between Tibial Measurements and Sex

Measurements (cm)	Total (n=200)	Male (n=100)	Female (n=100)	t-Stat.	P-value
Lateral & medial condyle (A-B)					
• **Min. - Max.**	5.6 - 8.3	5.6 - 8.3	6.2 - 7.7		
• **Mean ± SD**	6.95 ± 0.6	7.29 ± 0.7	6.61 ± 0.2	9.29	**<0.001***
Medial malleolus & lateral end of the tibia (C-D)					
• **Min.-Max.**	4.2 - 5.5	4.2 - 5.5	4.2 - 4.8		
• **Mean ± SD**	4.60 ± 0.3	4.78 ± 0.3	4.41 ± 0.2	10.21	**<0.001***
Length of the tibia (E-F)					
• **Min.-Max.**	31 - 40.1	31.5 - 40.1	31 - 37.9		
• **Mean ± SD**	36.07 ± 2.2	37.14 ± 1.8	35.01 ± 1.9	8.01	**<0.001***

***Independent Sample T test compare mean between two groups**

Table 3 presented the relationship between patient's age and tibial measurements, there were statistically significant ($p < 0.001$) difference according to age i.e., younger age group [30 - 50 years] had longer measurements (A-B: 7.1 ± 0.6, C-D: 4.7 ± 0.3 and E-F: 37.1 ± 1.8 cm) vs. older age group [50 - 70 years] (A-B: 6.8 ± 0.6, C-D: 4.5 ± 0.3 and E-F: 35.07 ± 2.1 cm).

Table 3: Relationship between Tibial Measurements and Age

Measurements (cm)	Age groups		t-Stat.	P-value
	30-50 years (n = 103)	50-70 years (n = 97)		
Lateral & medial condyle (A-B)				
• **Min.-Max.**	6.3 - 8.2	5.6 - 8.3		
• **Mean ± SD**	7.11 ± 0.6	6.78 ± 0.6	3.972	**<0.001****
Medial malleolus & lateral end of the tibia (C-D)				
• **Min.-Max.**	4.2 - 5.4	4.2 - 5.5		
• **Mean ± SD**	4.69 ± 0.3	4.5 ± 0.3	4.404	**<0.001****
Length of the tibia (E-F)				
• **Min.-Max.**	31.4 - 40.1	31 - 40		
• **Mean ± SD**	37.01 ± 1.8	35.07 ± 2.1	7.047	**<0.001****

***Independent Sample T test compare mean between two groups**

The interaction between age and sex for the tibial measurements was presented in **table 4**. For age group 30-50 years, there were statistically significant ($p < 0.001$) difference between males and females i.e., males had longer measurements (A-B: 7.7 ± 0.4, C-D: 4.9 ± 0.3 and E-F: 38.3 ± 1.3 cm) vs. females (A-B: 6.7 ± 0.3, C-D: 4.5 ± 0.2 and E-F: 35.9 ± 1.4 cm) **(Fig. 3)**.

Table 4: Relationship between Tibial Measurements and Sex stratified by Age

Measurements (cm)	Age group [30-50 years] (n=103)		t	P-value
	Male (n=47)	Female (n=56)		
Lateral & medial condyle (A-B)				
• Min.-Max.	6.4 - 8.2	6.3 - 7.7		
• Mean ± SD	7.65 ± 0.4	6.66 ± 0.3	14.458	**<0.001****

Medial malleolus & lateral end of the tibia (C-D)				
• Min.-Max.	4.4 - 5.4	4.2 - 4.8		
• Mean ± SD	4.97 ± 0.3	4.45 ± 0.2	12.741	**<0.001****
Length of the tibia (E-F)				
• Min.-Max.	34.8 - 40.1	31.4 - 37.9		
• Mean ± SD	38.33 ± 1.3	35.91 ± 1.4	9.157	**<0.001****
Measurements (cm)	**Age group [50-70 years] (n=97)** **Male (n=53)**	**Female (n=44)**	**t**	**P. value**
Lateral & medial condyle (A-B)				
• Min.-Max.	5.6 - 8.3	6.2 - 7.4		
• Mean ± SD	6.97 ± 0.7	6.55 ± 0.2	3.766	**<0.001****
Medial malleolus & lateral end of the tibia (C-D)				
• Min.-Max.	4.2 - 5.5	4.2 - 4.8		
• Mean ± SD	4.62 ± 0.3	4.35 ± 0.2	5.277	**<0.001****
Length of the tibia (E-F)				
• Min.-Max.	31.5 - 40	31 - 37.9		
• Mean ± SD	36.08 ± 1.5	33.85 ± 2.1	6.060	**<0.001****

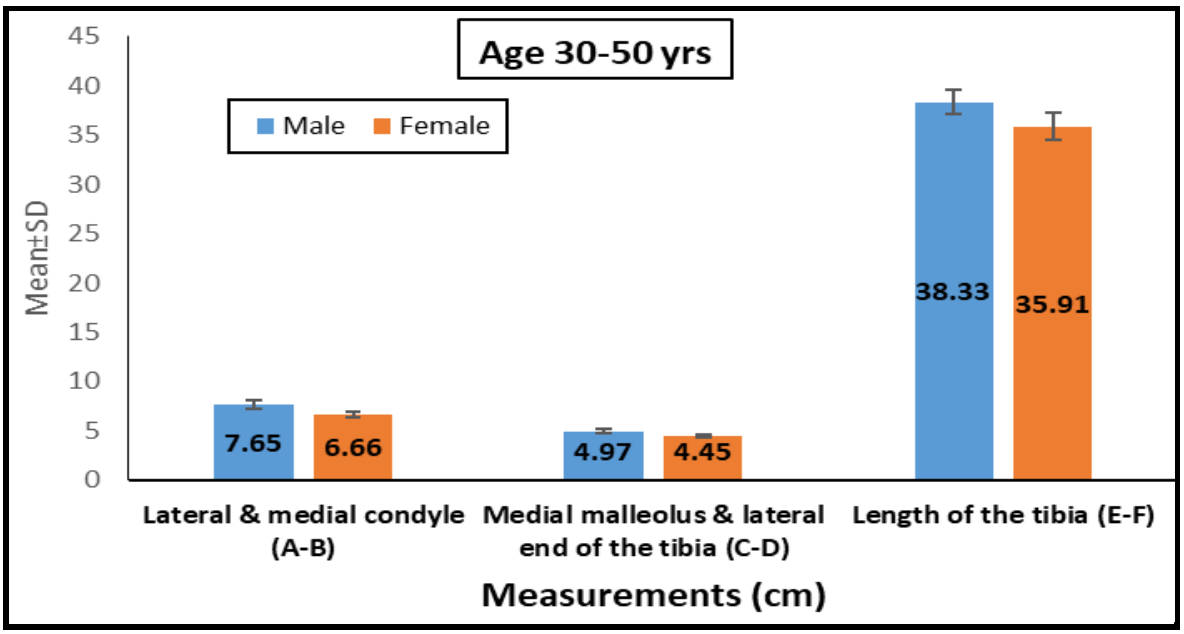

Fig. 3: Sex Distribution of Tibial Measurements Age Group [30-50 year]

For age group 50-70 years, there were statistically significant ($p < 0.001$) difference between males and females i.e., males had longer measurements (A-B: 6.9 ± 0.7, C-D: 4.6 ± 0.3 and E-F: 36.1 ± 1.5 cm) vs. females (A-B: 6.6 ± 0.2, C-D: 4.4 ± 0.2 and E-F: 33.9 ± 2.1 cm) **(Fig. 4)**.

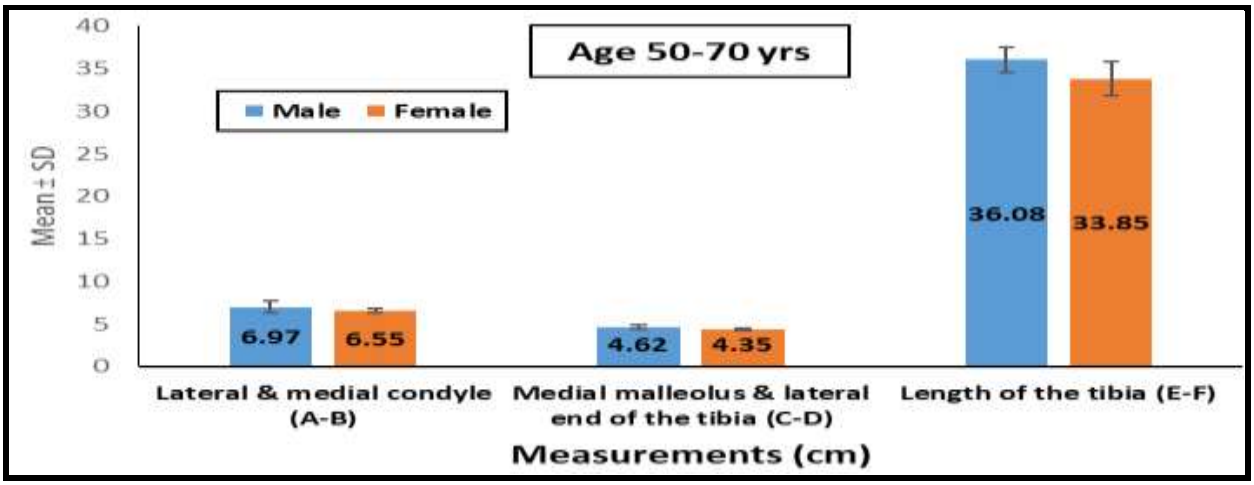

Fig. 4: Sex Distribution of Tibial Measurements Age Group [50-70 year]

As illustrated in **table 5 and Fig. 5,** the most accurate distance measurement was A-B [Lateral/medial condyle] 81.5% accuracy, followed by E-F distance [Medial malleolus & lateral end of the tibia] 76% accuracy, then C-D distance [Length of the tibia] 75% accuracy. Further, C-D distance was the most sensitive distance (83%), followed by A-B distance (70%), and then E-F distance was (63%). Also, A-B distance had the highest specificity (93%), followed by E-F distance (89%), and then C-D distance was (67%).

Table 5: Validity of Different Tibial Measurements for Sex Discrimination

	AUC	Cutoff	Sensitivity %	Specificity %	PPV	NPV	Accuracy	P-value
Lateral & medial condyle (A-B)	0.802	>6.9	70	93	90.9	75.6	81.5	**<0.001***
Medial malleolus/lateral end of the tibia (C-D)	0.828	>4.4	83	67	71.6	79.8	75	**<0.001***
Length of the tibia (E-F)	0.778	>36.6	63	89	85.1	70.6	76	**<0.001***

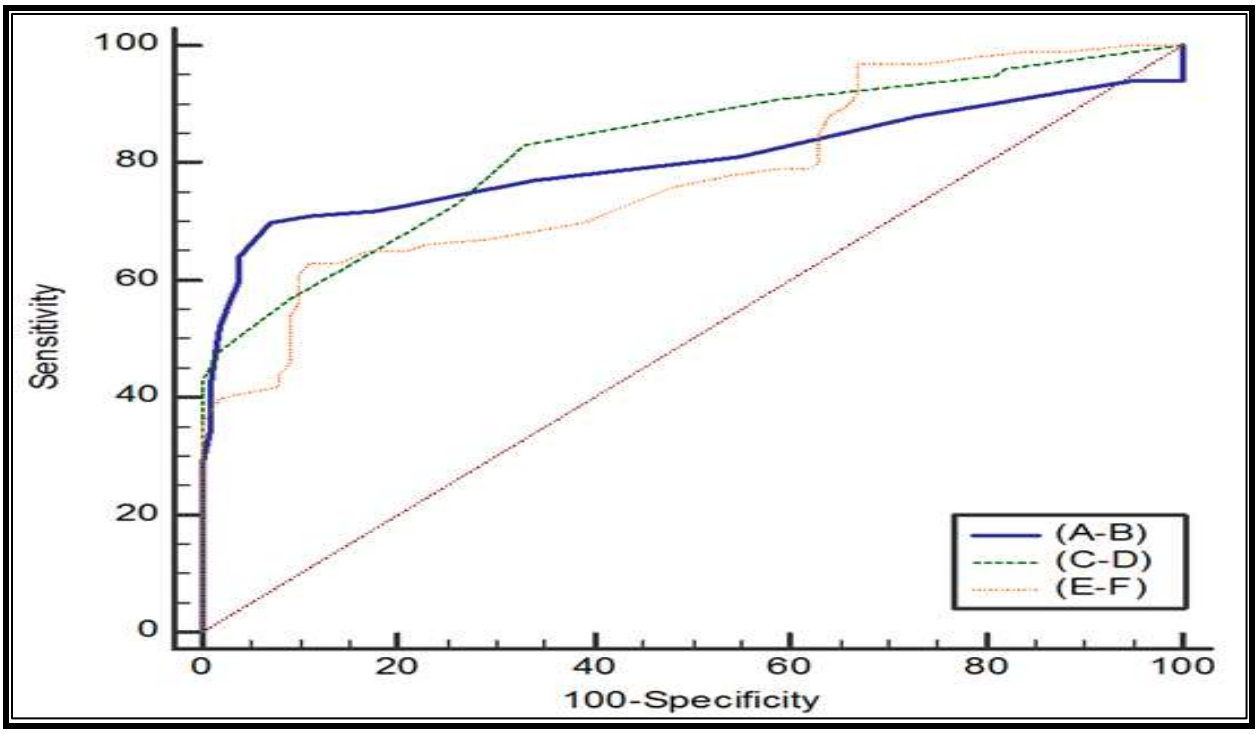

Fig. 5: ROC curve for different tibial measurements for sex discrimination

DISCUSSION

Rebuilding the biological profile—which includes determining sex, age, and stature—is crucial when unexplained skeletal remains are found **(19)**. Twenty-two percent of the body length is made up of the tibia. Because it is said to withstand erosion and retain its anatomical shape even after a lengthy period of burial, Tibia is frequently chosen by researchers **(20)**. Previous studies have demonstrated that tibial length enables more precise estimation of stature, which is why previous researchers chose it as the working material. Some research suggests that the tibia is the most accurate long bone to use when estimating stature **(21, 22)**.

The present study aimed to assess the efficacy of age and sex identification based on CT images derived from various tibial measurements among populations in Aswan. In this study, the mean age was 49.6 ± 10.1; 24% was in age group 30-40 years; 25% in 41-50 years; 37% in 50-60 years and 14% over 60 years.

In agreement, Karimi et al., (2019) investigated the morphometry of the proximal tibia in the standard resected surface of total knee arthroplasty in 132 patients, including 80 males (61%) and 52 females (39%) within the age range of 20-60 years; the mean age of the subjects was 38.26 ± 11.5 year **(23)**. Also, Diac et al., (2021) studied cases aged (22 to 91) years with a mean of 60.6 ± 16.4 **(24)**. Likely, in an Egyptian study by El-Meligy et al., (2006), the participants age was between 19 and 21 years **(25)**.

In this study, there was significant ($p<0.001$) difference between age ≤50 years and age >50 years according to different diameters (AB, CD and EF). In accordance with a study of Diac et al., (2021), there were significant differences between age and the height **(24)**. Also, López-Costas et al., (2012) examined the development of five tibial variables to assess their importance and potential for determining age and sex both during and after growth. Sexual significant

differences were observed from age 15 onward, suggesting that these variables could be useful for sex determination in individuals older than 15 years. Strong correlation coefficients were identified between the five tibial variables and age **(26)**.

In the current study, the mean length of tibia in male was 37.1 ± 1.8 cm and 35 ± 1.9 cm in females. There was significant ($p<0.001$) difference between male and female according to different diameters (AB, CD and EF). Consistently, it was discovered that Malaysian men were taller than women in Ismail et al., (2018) study **(27)**. Likewise, in Italy, Gualdi-Russo et al., (2018) revealed that the average tibia length was higher ($p<0.001$) in males (40.2 ± 2.9 cm) compared with females (37.1 ± 2.7 cm) **(28)**. Males tend to be taller than females, which causes sex differences in adult linear bone measurements **(29)**. As a result, size normalization is required for sex comparisons **(30)**. Further, it was proposed that male bones are frequently bigger and stronger than female bones. It has also been demonstrated that females have smaller tibia morphology in relation to body size **(31)**.

The mean values of tibia measurements were higher in males than females in Nanayakkara et al., (2019) study in Sri Lanka. The results of this study clearly reaffirm that tibia is sexually dimorphic **(19)**. Gardasevic. (2019) examined standing stature in both Kosovan genders in the Western Region as well as its association with tibia length, as an alternative to estimating standing height. The mean of the standing height for male was 179.71 ± 5.9 cm and tibia length were 41.4 ± 3.1 cm, while for female the standing height was 166.3 ± 5.2 cm and tibia length were 37.6 ± 2.5 cm. The sex difference between standing height and tibia length measurements was significant ($p<0.001$) **(32)**.

In this study, validity of different tibial measurements for discrimination between male and female was as follows; (A-B) distance was the most accurate while C-D distance was the most sensitive and A-B distance was the most specific (93%). These results were in line with Akhlaghi et al., 2011 study who found that sex could be distinguished using the anthropometric parameters of the tibia; the lateromedial length with 90% sensitivity and 80% specificity, the medial length with 90% sensitivity and 85% specificity, the proximal width with 85% sensitivity and 87.5% specificity, and the distal width with 67.5% sensitivity and 75% specificity **(33)**. According to the findings of Nanayakkara et al., 2019, the prediction accuracies for determining sex utilizing tibial measurements ranged from 61.9% to 80.2% in the Sri Lankan population **(19)**. Also, Kranioti et al., 2017 study confirmed the existence of sexual dimorphism of the tibia. Furthermore, the study revealed the utility of tibia as a predictor of sex in Greek Cypriots and Cretans **(34)**. Similarly, Kranioti et al., 2017 analyzed the tibia in different populations of the southern Europe such as Greece, Italy, and Spain providing standards for sex estimation in a forensic context. All measurements were significantly different between the sexes in all three populations and in the pooled sample. A discriminant function of the pooled sample for Southern Europeans resulted in about 88 % accuracy using all three variables **(9)**.

CONCLUSION AND RECOMMENDATION

In conclusion, spiral CT of the proximal epiphysis of femur using the parameters previously mentioned (AB, CD and EF) distances which was identified by three points on tibia may be useful in sex identification which may be applied in cases in semi-fleshed or charred bodies. CT might be efficiently used as an alternative method applicable in certain circumstances. Our study had been carried out among Egyptian population, and so population specific aspects of sexual

dimorphism must be taken in considerations when using this method, as there are population differences as mentioned before.

In recommendation, further consideration should be given to the comparison of ultrasonography and MRI 3D models to their physical counterpart. Other mathematical methods could be applicable in future research in the field of forensic anthropology bone fragments as well as with whole skeletons. Wide application of CT scan to be done in sex identification and in forensic practice. Further studies to compare results obtained from CT scan when used for determination of sex from bones and the results obtained from using MRI and plain X-ray.

Study Limitations

There were some limitations to the current study. Firstly, this was a single-center study which limits the study's external validity (generalization). Secondly, the possible confounding factors (presence of alloimmunization, platelet refractoriness, etc.) were not accounted for to do matching between groups.

Acknowledgement:

The authors wish to thank the medical and administrative staff of the faculty of Medicine, Aswan University Hospital for the consistent help and support. It was not possible to complete this work without the help, support, and approval of the recruited patients.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (62-67) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Role of Patient Positioning and Ultrasound Probe Selection in Erectro Spinea Plan Block.

Tarek S. Hemaida, Rehab Ahmed Kassem*, Ayman Mohammady Eldemrdash , Mohammed S. Ali, Soudy S. Hammad ,

Anesthesiology, Surgical Intensive Care and Pain Medicine Department, Faculty of Medicine, Aswan University

ABSTRACT

Keyword: ESPB, kidney surgery

***Corresponding author:**

Rehab Ahmed Kassem

Mobile: 01155620747

E-mail:
rehabk311@gmail.com

Introduction: Patients having open kidney procedures might benefit greatly from erector spinae plane block (ESPB) as a postoperative treatment. Our objective was to assess the effects of the patient's posture and the kind of US probe utilized in the ESPB. **Methods:** This retrospective study involved 60 individuals who had renal exploratory procedures. Both lateral and supine positions were used for the ESPB procedures. Since US was used for ESPB, either a linear or curved prob was used. **Results:** Regarding the block's time and simplicity of execution, there were notable variations across the four groups. There were only two recorded failures in sitting postures, compared to four in lateral positions. In addition, only six of the 13 individuals complained of pain at the injection site when they were seated. **Conclusion:** We recommend using the sitting position in ESPB with the straight US prob, and if the lateral position has been chosen, curved probe is recommended.

INTRODUCTION

Regional anesthetic techniques are commonly recommended for pain control during open nephrectomy because they improve patient satisfaction and lessen the requirement for parenteral opioids. (1)

Erector spinae plane block (ESPB) was initially reported by Forero et al. (2016) as a treatment for thoracic neuropathic pain. **(6)** It has been widely used in adults and children at different levels for a number of reasons, such as open kidney surgery, thoracic and breast surgery (T4-5), upper abdominal surgery (T7-8), and chronic shoulder discomfort (T2), even though it has only recently been documented in the literature. **(1)(5)(16)**.

ESB is a novel, user-friendly, safe, and efficient regional anesthetic technique for the management of pain after a mastectomy. ESB at T4 efficiently reduces pain and the requirement for postoperative analgesics by blocking the anterior cutaneous branches of the intercostal nerves. **(2)(22).** ESB showed pain relief in individuals with numerous unilateral rib fractures. The injection has an analgesic effect and exhibits paravertebral and cephalocaudal LA spread that extends to the intercostal nerve origin. **(9)**. Although ESP block is frequently used for chronic pain and severe postoperative pain, there are reports of it being used as a surgical anesthetic method in small operations, such as lipoma excision in the Para scapular region under ESP block at T4. **(3).**

It's still unclear how much local anesthetic (LA) should be administered precisely for ESB. Using a high volume (20–40 ml) is advised. Most commonly used are ropivacaine and bupivacaine.

The safe maximum doses for ropivacaine and buprevacaine are respectively 2 mg/kg and 3 mg/kg (maximum 300 mg). Better LA dispersion in the facial plane, deep into the muscle, would result from a higher volume.**(10).**

It may be difficult to position a patient with back injuries. Additionally, the injectate's poor dispersion may cause variations in the block's duration and intensity. Possible remedies for this include continuous infusion, the use of LA adjuvants, or catheter implantation, which allows for several injections.**(19).**

Bilateral blocks would be required for incisions that extend across the midline because ESB only provides unilateral analgesia. Not to mention the possibility of an accidental intravascular injection or systemic absorption of a significant quantity of LA administered. Aspirating often before and during LA injection helps prevent these uncommon occurrences. The patient's ideal body weight should be used to calculate the LA dose.**(19)(13)**. ESP block has several advantages over traditional neuroaxis-near techniques. First off, it is simple to use ultrasonography to visualize the erector spinae muscle, and it is easy to aim the needle at it. Because of this, the method is highly applicable. Because the key structures (principal veins, pleura, or dura) that are vulnerable to severe consequences from injury are situated distant from the blockage target, the second advantage is the minimal danger of consequences. Additionally, it is a part of multimodal analgesia, which promotes recovery after surgery.(**11)**.

Bilateral ESPB reduces the requirement for rescue analgesia and total opioid consumption while successfully managing postoperative pain for stomach surgeries, as well as incisional and ventral hernias. **(11)(19).**

The patient can execute ESPB in a variety of postures, including sitting, lateral, or prone. The patient can more easily identify landmarks and feel more comfortable while they are seated. **(18)**.

We aim to compare the effectiveness of lateral and sitting positions in patients undergoing ESPB and type of ultrasound probe selected.

PATIENTS AND METHODS

This retrospective cohort was carried out using the medical data of 60 individuals who had renal exploratory procedures performed at Aswan University Hospital. Patients with bleeding problems and block site infections were not included.

Under general anesthesia (GA), the patients underwent ESPB following the technique described by Vadera and Mistry (**20)** either in the lateral position or supine position. As ESPB was performed using US using linear or curved prob.

And the ease of performing the block measured by numerical scale from 1 to 10 [1 the easiest and 10 the most difficult], duration of the performing the block [excluding time of sterilization], failure rate and injection site pain were recorded.

Statistical analysis was done by R 4.4.2. Quantitative parametric data were presented as mean and standard deviation (SD) and were analyzed by ANOVA (F) test with post hoc test (Bonferroni). A two tailed P value < 0.05 was considered statistically significant.

RESULTS

In this retrospective cohort, we included 60 patients underwent open renal surgery under GA. Patients received ESPB either in lateral or Sitting position while using either Linear or curved prob.

Regarding to the demographic data, the mean age of the included participants was 42.25 years of them 41 were males. Table 1

Table 1: Demographic data of the participants included

	Lateral Linear	Lateral Curved	Sitting Linear	Sitting Curved
	n = 15	n = 15	n = 15	n = 15
Age	43.6 (11.1)	36.4 (10.7)	45.5 (15.2)	43.5 (12.4)
BMI	28.8 (2.3)	29.7 (3)	28.3 (2.3)	29.5 (2.8)
Sex (Male)	10 (66.7%)	9 (60.0%)	10 (66.7%)	12 (80.0%)

Regarding the ease of performing the block, we found that there were significant differences between the four groups in terms of both the ease and duration to perform the block. Table 2

Table 2: The ease of performing the block

	Lateral Linear	Lateral Curved	Sitting Linear	Sitting Curved	
	n = 15	n = 15	n = 15	n = 15	
Ease	5.1 (1.7)	4.4 (1.9)	3.3 (0.9)	6.5 (1.8)	< 0.001
Duration	16.9 (2.9)	14.1 (3.7)	10.3 (2.4)	13.1 (2.9)	< 0.001

Post-hoc analysis showed that there was significant difference between Lateral Curved Vs Sitting Curved, Lateral Linear Vs Sitting Linear and Sitting Linear Vs Sitting Curved, while the other pairwise comparison was statistically insignificant. Table 3

Table 3: Pairwise comparison of the Ease of performance

Pairwise comparison	Mean difference [95% CI]	**p-value**
Lateral Curved Vs Sitting Curved	-2.133 [-3.759, -0.507]	0.004
Lateral Curved Vs Sitting Linear	1.067 [-0.559, 2.693]	0.469
Lateral Linear Vs Lateral Curved	0.733 [-0.893, 2.359]	1
Lateral Linear Vs Sitting Curved	-1.4 [-3.026, 0.226]	0.132
Lateral Linear Vs Sitting Linear	1.8 [0.174, 3.426]	0.022
Sitting Linear Vs Sitting Curved	-3.2 [-4.826, -1.574]	0.001

Post-hoc analysis showed that there was significant difference between Lateral Curved Vs Sitting Linear, Lateral Linear Vs Sitting Curved and Lateral Linear Vs Sitting Linear, while the other pairwise comparison was statistically insignificant. Table 4

Table 4: Pairwise comparison of the duration of performance

Pairwise comparison	Mean difference [95% CI]	**p-value**
Lateral Curved Vs Sitting Curved	1.067 [-1.941, 4.074]	1
Lateral Curved Vs Sitting Linear	3.8 [0.793, 6.807]	0.006
Lateral Linear Vs Lateral Curved	2.733 [-0.274, 5.741]	0.096
Lateral Linear Vs Sitting Curved	3.8 [0.793, 6.807]	0.006
Lateral Linear Vs Sitting Linear	6.533 [3.526, 9.541]	0.001
Sitting Linear Vs Sitting Curved	-2.733 [-5.741, 0.274]	0.096

There were 4 failed cases in the lateral position, while only 2 in sitting positions. Moreover, there were 13 cases complaining from injection site pain, while only 6 cases were in sitting positions.

Table 5: Complications of the operations

	Lateral Linear	Lateral Curved	Sitting Linear	Sitting Curved
	n = 15	n = 15	n = 15	n = 15
Injection site Pain	5 (33.3%)	7 (46.7%)	3 (20.0%)	3 (20.0%)
Fail	3 (20.0%)	1 (6.7%)	0 (0.0%)	2 (13.3%)

DISCUSSION

According to the International Association for Studying Pain (IASP), pain is a stressful experience that involves sensory, emotional, cognitive, and social aspects and is associated with either existing or potential tissue damage.**(21)**.

A wide section of the cerebral cortex called the "pain matrix," which includes the thalamus, anterior cingulate cortex, and somatosensory area (S1 & S2), is activated during acute pain activation. The cerebral cortex produces affective and emotional responses, whereas the thalamus is responsible for processing sensory discrimination. This describes how a person's emotions, beliefs, genetics, and cognitive processes (such distraction or catastrophizing) may all affect how painful they feel.**(12).**

Acute postoperative pain treatment has repercussions that impact both mental and physical functionality. Postoperative pain can have a variety of effects on the respiratory system, including decreased lung capacity, tidal volume, functional residual capacity (FRC), hypertonia of the abdominal muscles, and altered diaphragm function. Furthermore, a patient's dread of discomfort may keep them from coughing or taking deep breaths, which may result in atelectasis and a buildup of secretions.**(8).**

Since kidney transplant surgery is linked to moderate to severe postoperative discomfort, effective pain management is essential. The concerns of hypotension from pain management approaches interfering with graft perfusion, concomitant coagulopathy, and/or altered pharmacokinetics and pharmacodynamics due to disease processes make choosing an analgesic strategy even more challenging. Poor pain management during surgery is associated with discharge, agitation, delirium, and a delayed recovery. Therefore, in order to promote early recovery and reduce postoperative effects, it is essential yet challenging to administer suitable postoperative analgesia.**(7)(14).**

The novel ultrasound-guided ESB technique for treating acute and persistent thoracic pain was recently presented. In the ESP block regional anesthesia technique, local anesthetic (LA) is injected between the transverse process and erector spinae muscle under ultrasound guidance to block the dorsal and ventral rami of the intercostal and abdominal nerves.**(15).**

According to a study by Sharipova et al. on kidney transplant patients, erector spinae plane block (ESPB) at T10 and T11 levels significantly lowers the pain intensity (numeric rating score) after 6, 12, 18, and 24 hours after surgery. Additionally, compared to the control group, the ESPB group used a lot less morphine within the first 24 hours (4.7 ± 6.2 mg vs. 15.9 ± 7.1 mg).**(17).**

Our study showed that there were significant differences between the four groups in terms of both the ease and duration to perform the block. Moreover, there was significant difference between Lateral Curved Vs Sitting Curved, Lateral Linear Vs Sitting Linear and Sitting Linear Vs Sitting Curved, while the other pairwise comparison was statistically insignificant. Also, there was significant difference between Lateral Curved Vs Sitting Linear, Lateral Linear Vs Sitting Curved and Lateral Linear Vs Sitting Linear, while the other pairwise comparison was statistically insignificant.

Our study showed that there were 4 failed cases in the lateral position, while only 2 in sitting positions. Moreover, there were 13 cases complaining from injection site pain, while only 6 cases were in sitting positions.

According to our knowledge, this is the first study to investigate the rule of patient position and

type of probe used in ESPB in patients undergoing renal surgeries.

CONCLUSION

In ESPB, we advise utilizing the sitting position with the linear US probe; if the lateral position has been selected, we advise using the curved probe.

Sponsors and funding sources: There are none to be declared.
Acknowledgment: There is none to be declared.
Conflict of interests: None to be declared.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (68-79) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Serum homocysteine level in Acne patients before and after oral Isotretinoin.

Doaa H.A. Mohamed [1]*, Ghada M. Abousedera [1],Abdallah M. El-Ebidi [2], Moustafa A.A. El Taieb[1]

[1] Department of Dermatology, Andrology and venereology, Faculty of Medicine, Aswan University

[2] Department of Medical Biochemistry and Molecular Biology, Faculty of Medicine, Aswan University

ABSTRACT

Keyword:Acne, Homocysteine (Hcy), Isotretinoin.

***Corresponding author:**

Doaa H.A. Mohamed

Mobile: 01119336880
E-mail:
doaafandokly @gmail.com

Background and Aim: Acne vulgaris (AV) is a chronic inflammatory skin lesion of the pilosebaceous unit. Whatever the dose of prescribed Isotretinoin (Iso), follow-up of the homocysteine (Hcy) level is beneficial for the patients to prevent hyperhomocysteinaemia and associated complications. This study is aimed at measuring the serum level of Hcy in AV cases pre- and post-treatment of oral Iso. **Methodology:** This is a cross-sectional case control study that conducted on 60 individuals, 30 patients diagnosed with acne vulgaris, and 30 age-matching healthy volunteers as control group. The chosen patients were allocated to receive 20 mg of Iso every day for three months. **Results:** There was insignificant difference in serum levels of Hcy, liver function test (LFT) (SGOT, SGPT), total cholesterol and triglycerides (TGs) between case and control groups before isotretinoin treatment. While, there was significant increase in serum level of Hcy, liver function test (SGOT, SGPT), total cholesterol and triglycerides after three months of treatment with Iso among acne cases. **Conclusion:** Serum level of Hcy increased after 3 months of Iso treatment, which could be due to liver dysfunction. So, evaluation of Hcy was useful for acne cases prior to the initiation of Iso therapy.

INTRODUCTION

Acne vulgaris (AV) is a skin lesion characterized by the development of papules, pustules, comedones, and nodules. AV cases are often associated with a bad quality of life. It occurs secondary to blockade of the hair follicles and follows the next processes: a greater than normal amount of sebum formation (influenced by androgens), extreme accumulation of keratin causing comedo formation, hair follicles' colonisation by Propionibacterium acnes (P. acnes), and the discharge of proinflammatory cytokines. In addition, androgens have a central function in AV pathogenesis from increased levels or aggravated responses [1].

In 2015, AV affects about 633 million subjects all over the world, making it the 8th most frequent disease all over the world. Acne typically manifests during adolescence, affecting about 85% of teenagers. However, teenagers can also be affected before and after puberty [2].

A lot of therapeutic modalities for AV are available, such as lifestyle modification; which include healthful life style, drugs and medical approach. In spite of the availability of several therapeutic modalities, none of them has confirmed to be optimum [3].

Oral isotretinoin has the ability to counteract the pathogenetic mechanisms that participate in AV development via its wide actions on cellular differentiation, apoptosis, inflammation, and sebaceous gland activity. It causes a marked decrease in sebum formation, affects comedogenesis, lowers surface and ductal Propionibacterium acnes, and demonstrates anti-inflammatory characteristics [4].

Together with various clinical adverse events, isotretinoin could trigger hyperlipidemia, elevated liver enzymes, and reduction of biotinidase activity, which can lead to elevation of serum homocysteine (Hcy) level, which is associated with vascular, neurological, renal, cardiac, and gastrointestinal disorders [5]. So, this work aimed to measure serum level of Hcy in AV cases pre- and post-treatment of oral Iso therapy, as well as, to correlate between serum level of Hcy and severity of acne vulgaris patients.

PATIENTS AND METHODS

The study approved by the local Ethics Committee of the Faculty of Medicine, Aswan University, Aswan, Egypt, and informed written consent was obtained from all patients. The study was conducted by Helsinki standerds as revised in 2013.

This is a clinical based cross-sectional case control study that was conducted on 60 individuals, 30 patients diagnosed with acne vulgaris as case group, and 30 age-matching healthy volunteers as control group. The selected patients were assigned to receive 0.5mg/kg/day of isotretinoin once daily with heavy meal. The treatment was continued for at least three months. All subjects selected from those attending the outpatient clinic of Dermatology, Venereology and Andrology Department, Aswan University Hospital, between December 2020 and December 2021.

Patients with history of systemic isotretinoin treatment in last 3 months, pregnant, lactating or female willing to conceive during the study period, patients with history of allergic reaction to isotretinoin, patients with history of hyperlipidemia, endocrine disorders, cardiac disorders, renal disorders, liver disorders, hematological disorders, patients with history of malignancies, patients with recent history of alcohol abuse or psychiatric illness, marked depressive manifestations, and patients not giving consent or unable to come for three months follow-up, were ruled out.

The patients were subjected to full history taking include: Personal history as name, age, sex, residence, and occupation; Present history as onset, course, duration and type of acne; Past history of any medical ailments like endocrine disorders, cardiac disorders, renal disorders, liver disorders, hematological disorders or psychiatric illness; Family history of acne or other general disorders; and drug history of any systemic or topical therapy for acne vulgaris.

Examination of patients were done and included: General examination for assessment of general condition of the patients, and dermatological evaluation of cases in order to define type of and severity of acne.

As regard biochemical investigations, two blood samples (5 cc) were acquired by venipuncture of the antecubital veins of cases and after a 12-hour fasting. One sample collected in EDTA blood to measure homocysteine, the other sample collected in Serum

separator tubes (SST) to measure Liver function test (LFT) (SGOT, SGPT), Cholesterol and Triglycerides. The blood samples were permitted to clot for half an hour at 22C prior to centrifugation for fifteen min at 1000 x g [6].

Liver function test (SGOT, SGPT), Cholesterol and TGs were measured spectrophotometrically using commercial kits. The kits were from **Diasys Company (Germany)**. SGOT and SGPT were measured by Auto Analyzer Technical RA 1000 in patient's plasma. Cholesterol was measured using the cholesterol oxidase approach (CHOD). Measurement of TGs was conducted by colorimetric enzymatic test using glycerol-3-phosaphate oxidase (GPO).

Total plasma homocysteine levels were measured according to the Biotin double antibody sandwich technology, by using Human Homocysteine (Hcy) enzyme-linked immune sorbent assay (ELISA) Kit **(Shanghai Crystal Day Biotech Co., Shanghai, China)**.

Screening for biochemical parameters was conducted pre and 3 month post-treatment of isotretinoin. These parameters included serum levels of Hcy, LFT (SGOT, SGPT), total cholesterol and triglycerides.

Statistical methods: The collected data were coded, and analyzed using the SPSS (IBM-SPSS/PC/VER 24.0) program for windows. Descriptive data: mean±SD, median, range, frequencies, percentage were measured. Chi square and Fisher Exact tests were used to compare the difference in distribution of frequencies among various groups. U test was calculated to test the median differences in continuous variables between groups and related-samples The Wilcoxon test was used to compare the median Pre- vs. Post-treatment. Multivariable logistic regression was conducted to assess the independent effect of HC on AV. ROC curve was showed the diagnostic performance of HC for diagnosis of AV. Validity statistics were also conducted. Significant difference was set at $p < 0.05$.

RESULTS

There was insignificant difference between both groups as regard age and sex (p= 141, 318) respectively. Regarding the serum level of homocysteine: the mean level was lower in acne cases (8.2 ± 3.4 mcmol/L) in comparison with controls (p=0.008), as shown in **(Table 1)**.

As regard sociodemographic characteristics of the studied acne patients, their age ranged between 16 and 29 years with a mean of 20.8 ± 3.6 years. Also, about three-quarters of cases (n=22) were females and one-quarter (n=8) was males. Moreover, the patient's weight ranged between 47 and 78 with a mean of 63.6 ± 8.8 and a median of 63.5 kilograms. For the acne severity, about 13% of cases (n=4) had mild severity, one-quarter (n=8) had moderate severity and 60% had severe disease, as shown in **(Table 2)**.

As regard the effect of treatment on the SGOT, SGPT, TG, Cholesterol and homocysteine Levels, the mean SGOT SGPT, TG, Cholesterol and homocysteine Levels was significantly (p<0.001) increased after treatment Levels was significantly (p<0.001) increased after treatment, as shown in **(Table 3)**.

As regard correlation between homocysteine level and the other parameters before and after treatment with isotretinoin among acne cases, the level of homocysteine before treatment showed negative moderate significant correlation with SGOT before and after

treatment, SGPT and TG after treatment and this was statistically significant ($p<0.05$), as shown in **(Table 4)**.

As regard the relationship between Hcy Level and disease severity in AV cases. There was non-significant association between grades of severity regarding Hcy level before treatment (p=0.844). Likewise, there was non-significant association between grades of severity regarding Hcy level after treatment (p=0.083). Moreover, plasma Hcy levels were significantly increased in the moderate and severe cases after 3-months of Iso therapy (p=0.003 and <0.001, respectively). However, non-significant elevation was found in the mild cases after 3-months of Iso therapy (p=0.055), as shown in **(Table 5)**.

Tables

Table 1: Socio-demographic Data Differences between both groups.

	Control	Case	P-value
Age in years	**23.20 ± 4.9**	**20.83 ± 3.6**	= 0.141*
Sex			
• **Male**	11 (36.7%)	8 (26.7%)	= 0.318**
• **Female**	19 (63.3%)	22 (73.3%)	
Homocysteine Level (mcmol/L)			
• **Mean±SD**	11.77 ± 9.8	8.23 ± 3.4	= 0.008*

***T-test was utilized to compare the mean differences between cases and controls**
****Chi-square test was utilized to compare the ratios among groups**

Table 2: Socio-demographic characteristics of the studied Acne Cases.

Variable	Category	n = 30
Age in years	• **Mean±SD**	20.83 ± 3.6
	• **Median(Range)**	20 (16 - 29)
Sex	• **Male**	8 (26.7%)
	• **Female**	22 (73.3%)
Weight in Kg	• **Mean±SD**	63.57 ± 8.8
	• **Median(Range)**	63.5 (47 - 78)
Acne Severity at	• **Mild**	4 (13.3%)

Baseline	• **Moderate**	8 (26.7%)
	• **Severe**	18 (60%)

Table 3: Effect of Isotretinoin on the SGOT, SGPT, TG, Cholesterol and homocysteine Levels.

Variable			**n = 30**	**P-value**
SGOT Level	**Before Treatment**	• **Mean±SD**	**20.01 ± 6.5**	**< 0.001***
		• **Median(Range)**	**19 (12 - 33)**	
	1.5 month After Treatment	• **Mean±SD**	**23.77 ± 7.1**	
		• **Median(Range)**	**21.5 (14 - 37)**	
SGPT Level	**Before Treatment**	• **Mean±SD**	**18.95 ± 5.1**	**< 0.001***
		• **Median(Range)**	**19.5 (9.5 - 27)**	
	1.5 month After Treatment	• **Mean±SD**	**24.47 ± 6.3**	
		• **Median(Range)**	**25.5 (12 - 35)**	
TG Level	**Before Treatment**	• **Mean±SD**	**73.37 ± 25.7**	**< 0.001***
		• **Median(Range)**	**67 (39 - 146)**	
	1.5 month After Treatment	• **Mean±SD**	**79.31 ± 27.3**	
		• **Median(Range)**	**71.5 (40 - 151)**	
Cholesterol Level	**Before Treatment**	• **Mean±SD**	**141.09 ± 28.5**	**< 0.001 ***
		• **Median(Range)**	**137 (89 - 192)**	
	1.5 month After Treatment	• **Mean±SD**	**156.10 ± 35.2**	
		• **Median(Range)**	**146 (101 -**	

			233)	
Homocysteine Level	**Before Treatment**	• **Mean±SD**	**8.23 ± 3.4**	**< 0.001 ***
		• **Median(Range)**	**7.4 (4.3 - 23)**	
	3 months After Treatment	• **Mean±SD**	**11.63 ± 4.4**	
		• **Median(Range)**	**11 (4.6 - 25)**	

Table 4: Correlation between Homocysteine and other Parameters before and after treatment with isotretinoin among Acne cases.

	Homocysteine BT		**Homocysteine AT**	
	rho*	**P-value****	**rho**	**P-value**
Homocysteine BT	**1**		**0.771**	**<0.001**
SGOT BT	**-0.374**	**= 0.023**	**-0.322**	**= 0.044**
SGOT AT	**-0.411**	**= 0.013**	**-0.363**	**= 0.026**
SGPT BT	-0.156	= 0.058	-0.032	= 0.867
SGPT AT	**-0.419**	**= 0.024**	-0.068	= 0.726
TG BT	-0.215	= 0.262	**-0.334**	**= 0.038**
TG AT	-0.131	= 0.499	-0.095	= 0.626
Cholesterol BT	-0.100	= 0.605	-0.107	= 0.582
Cholesterol AT	-0.032	= 0.868	-0.067	= 0.729

Table 5: Relationship between Homocysteine Level and Disease Severity in AV cases.

Variable	**Mild (1)**	**Moderate (2)**	**Severe (3)**	**P-value***
Homocysteine Level				
Before Treatment				= 0.844

• **Mean±SD**	**8.02 ± 2.3**	**7.80 ± 2.7**	**8.25 ± 3.9**	
• **Median(Range)**	**9.1 (4 – 9.5)**	**8.1 (4 - 12)**	**6.9 (5 - 23)**	
• **P-value****	1 vs. 2=0.917	1 vs. 2=0.766	1 vs. 2=0.909	
After Treatment				
• **Mean±SD**	**11.01 ± 3.7**	**14.20 ± 4.8**	**10.77 ± 4.1**	= 0.083
• **Median(Range)**	**11.6 (6 - 15)**	**14.7 (4.5 - 19)**	**10 (6 - 25)**	
• **P-value****	1 vs. 2=0.142	1 vs. 2=0.081	1 vs. 2=0.714	
P-value***	= 0.055	**= 0.003**	**< 0.001**	**< 0.017*[4]**

DISCUSSION

It has been demonstrated that Hcy values increase following the use of Iso therapy [6, 7]. Therefore, we aimed to measure the serum level of Hcy in AV cases pre- and post-treatment of oral Iso. As well, to correlate between serum levels of homocysteine and clinic-demographic data in AV cases pre- and post-treatment of oral Iso therapy.

This study conducted on 60 individual, 30 patients presented with acne, and 30 as control, at the beginning of the study we found significant difference between case and control groups as regard age and gender, as we found that, case group was younger and the majority of patients were female (the cases were 22 (73.3%) female and 8 (26.7%) male with a mean age of 20.83 ± 3.6 years).

This finding matches with Karadag et al. [6], Kamal and Polat, [7], Dursun et al. [8], Roodsari et al. [9], and Polat et al. [10], as they found female predominance with a group mean age of 21.0±2.7; 21.0 ± 6.0; 22.3 ± 4.7; 21.4 ± 3.4; 21.72 ± 3.76 years in their studies respectively.

The previous finding may be due to the fact that, AV is a common disease in adolescence with female preponderance [11]. As well Goulden et al. [12], found presence of hormonal alterations in acne female patients. Additionally, Yang et al. [13], reported that, female preponderance may be due to the fact that not all male cases with AV present and seek medical advice.

At the beginning of this study, we found insignificant difference in homocysteine level between both groups before isotretinoin treatment.

In accordance to our results, Kamal and Polat, [7], made a case-control study on 124 individuals (62 cases and 62 control), and reported that, the differences between the baseline values of homocysteine, was not statistically significant between the groups.

Moreover, Schulpis et al. [5], conducted a study on 28 cases with cystic acne, and 30 subjects as control, and they reported no statistical differences were observed in Hcy levels among studied groups before isotretinoin treatment. As well, Polat et al. [10], reported the same results. This can be explained by that, the randomization process encouraged a balance between both groups (similar groups).

On the other hand, Jiang et al. [14], made a study on 124 AV cases and 70 healthy subjects, matched regarding age and sex in which serum Hcy levels were measured. At the end of the study they found that, Hcy levels in AV cases were higher than in normal subjects. Also, Arora et al. [15], made a study on 60 females with severe AV and compared their Hcy levels with healthy subjects, and they found that, serum Hcy levels were displayed to be high in females with severe AV compared to controls. This variation between previous study and ours, might be due to alteration in sample size, type of study, different ethnic groups, additionally, Jiang et al. [14], study had limitation, as the serum Hcy level was not detected with different durations in the same subject [14]. As well, Arora et al. [15], study had limitation, as the serum Hcy level was measured in female gender only and in one type of acne.

In the present study, we demonstrated significant increase in liver enzymes (SGOT and SGPT) as well as increase in lipid profile (triglyceride and cholesterol), after isotretinoin treatment.

Our finding goes in line with, Sallam et al. [16], conducted a prospective study on 44 cases (22 cases with moderate AV and 22 cases with severe AV). Iso was initiated in a dose of 0.5, and one mg/kg/day in moderate and severe AV cases correspondingly. They found a significant elevation in lipid profile and LFT that was detected in entire patients.

This finding matches with Zane et al. (2006) [17], who studied 13772 cases with AV undergoing oral Iso treatment. The authors found increased liver enzymes (ALT and AST) and serum lipid levels [17].

In the study of Kızılyel et al. [18], they displayed that there were significant increases in TG values in cases undergoing Iso therapy. Also, Vieira et al. [19] conducted there study on a total of 130 cases managed by Iso and observed an increase in LFT, and TG levels. Additionally, Sarkar et al. [20], found that, hypertriglyceridemia and hypercholesterolemia was present in most of patients.

In addition, Leelambika and Sarkar, [21] Bershad et al, [23] have recorded that Iso increases cholesterol and TGs, comparable to the current study. The laboratory changes were noticed in the serum values throughout and following the therapeutic duration in comparison to the basal value.

Some studies suggest that, Iso raises the TG level in fifty percent and cholesterol in 30% of cases [24]. The actual etiology of the increase in lipid by Iso isn't identified. On the other hand, the retinoids typically bind to the plasma albumin and may affect certain important groups in the active site of the proteins or enzymes (during lipid metabolism) [25]. It is theorized that retinoid-albumin interaction could displace the TG from albumin, inducing its increase. Another suggested theory is that Iso affects the levels of ALT and AST, possibly by hepatic inflammatory changes [26, 27].

Although much research recorded changes in serum transaminase and lipid levels, in contrast to our findings, other studies recorded no effect. Brito et al. [28] conducted their study on 150 subjects and displayed insignificant changes in LFTs, TG, or cholesterol levels following Iso treatment. In addition, Alcalay et al, [29] conducted their study on a total of 1292 subjects and demonstrated that serum values of liver enzymes weren't increased to a degree requiring cessation of Iso therapy. Also, Baxter et al. [30] conducted their study on 30 subjects and recorded insignificant difference in TG or cholesterol levels measured at pre- or throughout treatment with Iso. Also, in the study of Kızılyel et al. [18], liver enzymes were slightly affected compared to lipid profile in cases using Iso treatment. This variation between previous studies and ours could be secondary to alteration in sample size, type of study, follow-up period, and different ethnic groups.

We demonstrated a significant increase in homocysteine (Hcy) level after three months of treatment with Iso. This result was in the same line with a lot of previous studies that displayed the impact of Iso on Hcy values.

Recently, Kim et al. [31], assessed ten studies that evaluated plasma values of Hcy during Iso therapy in acne cases, and they revealed significant increase in Hcy levels in the Iso treatment group.

Also, Sallam et al. [16], conducted a prospective study on 44 patients (22 patients with moderate AV and 22 cases with severe AV). Iso was initiated in a dosage of 0.5 mg/kg/day and 1.0 mg/kg/day in moderate and severe AV cases, correspondingly. They found a significant difference in Hcy level among all cases. In addition, Hcy serum level in the patient's group receiving a high dose of Iso (one mg/kg/d) displayed highly significant results ($p=0.001$) in contrast to the patient's group receiving a low dose of Iso (0.5 mg/kg/d) ($p=0.003$).

This matches with Yosef et al. [32], who made a study on 60 cases with moderate to severe AV. Using a chemiluminescent immunoassay, Hcy, levels were measured at baseline and after four months of Iso therapy. At the end of the study they demonstrated that, Iso-treated cases have to be followed up carefully for Hcy level, as they found that, Hcy was significantly higher after 4 months of Iso treatment compared with the baseline values.

Moreover, in a study of Kamal and Polat [7], who made a case-control study on 124 individuals (62 cases and 62 controls), they reported that Hcy levels were significantly elevated in both groups taking 0.5 and 1.0 mg/kg/day isotretinoin.

In accordance with previous results, Karadag et al. [6], made a study on 66 cases with moderate or severe AV and found that Hcy levels increased after the termination of four months of Iso therapy.

In a similar Roodsari et al. [9], had 47 cases with moderate or severe AV receiving Iso, and they reported that, Hcy level increased after treatment.

Similarly, Polat et al. [10], comprising 74 patients on Iso therapy with nodulocystic acne, and found that plasma Hcy levels increased after treatment.

As well, Schulpis et al. [5], they assessed Hcy values in 28 cases on Iso therapy for AV, and demonstrated that plasma values of Hcy, was elevated after 45^{th} day of the treatment.

The possible explanation with supporting the previous findings is that, increased Hcy values may be secondary to the drug effect on the enzyme cystathionine-beta-synthase (CBS) with no impairment of hepatic functions [7]. Furthermore, increased Hcy was linked to diminished levels of folate and vitamin B12 during Iso therapy. This indicates that Iso could be linked to deficiencies in these vitamins, complicating the recycling of Hcy [31].

On the other hand, Chanson et al. [33] conducted a study on 20 cases with acne and 20 elderly healthy male volunteers and reported that Iso therapy didn't cause significant changes in the plasma Hcy value. This variation between the previous study and ours could be due to alteration in sample size (20 patients), gender (male only), and different ethnic group (France).

In this study, we found no significant correlation between homocysteine and other biochemical parameters (SGOT, SGPT, total cholesterol and triglycerides) before and after treatment with isotretinoin among acne cases.

This goes in line with Roodsari et al. [9], as they didn't detect any association between Hcy and the plasma values of other biochemical parameters pre- and post-treatment with Iso, indicating that increased Hcy values may be secondary to the action of Iso on the enzyme CBS.

In contrast, Schulpis et al. [5], they assessed plasma Hcy values in 28 cases on Iso treatment for nodulocystic acne, and found significant association between Hcy levels, vitamins, and both ALT and AST. This variation between the previous study and ours could be secondary to change in sample size (28 patients), type of acne (nodulocystic only) and different ethnic group (Greece).

Limitations

Our cases were limited to cases living in Upper Egypt that may stress the significance of geographic and ethnic background in the clinical presentation of acne. Second, a small sample size and a relatively short period of study suggest significant differences in our findings compared with the other studies. Finally, the study design and the possibility that selection bias was introduced by including patients already attending our outpatient clinic.

RECOMMENDATIONS

We recommend that, the inclusion of a higher number of high-quality randomized controlled trials, long period of study and follow-up, and selection of different ethnic groups would be required in upcoming studies.

CONCLUSION

In conclusion, the serum level of Hcy increased after 3 months of isotretinoin treatment. Evaluation of Hcy, liver function test (SGOT, SGPT), total cholesterol, and TGs was valuable for acne cases prior to the initiation of isotretinoin treatment. Moreover, it is suggested that the increased Hcy levels in cases after 3 months with isotretinoin treatment may be due to the suppression of CBS by the drug and/or their impaired liver functions.

Funding support: None.

Conflicts of interest: None.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (80-88) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Magnitude of Extubation Failure in Mechanically Ventilated Cases at Pediatric Intensive Care Unit at Aswan University Hospital

Mohammad Bahaa El dein El Amir Hawary, , Entesar Muhammad Foad Shalapy Khaled Abd Elhay Mohammed

Pediatrics department, Faculty of Medicine, Aswan University

ABSTRACT

Keyword: Extubation Failure, Mechanically Ventilated.

***Corresponding author:**
Entesar Mohammad Foad Shalapy
Email:entesar.m.foad@gmail.com
Mobile: 01119113167

Background: Around fifty-five percent of pediatric intensive care unit (ICU) admissions necessitate mechanical ventilation (MV). The extubation and intubation of such cases are significant risks and may correlate with elevated morbidity and mortality rates. **Aim:** To assess the magnitude of extubation failure of mechanically ventilated cases admitted to pediatric ICU at Aswan University Hospital and to study different factors related to extubation failure. **Methodology:** This research has performed in the PICU of the Pediatric Department at Aswan University Hospital, over a six-month period from June 2022 to December 2022. All admitted cases in this period have been involved in the research. **Results:** This research analyzed 50 pediatric ICU cases, of which 20 (40%) experienced extubation failure. No significant differences were found in sex, age, or diagnosis. Extubation failure was significantly associated with intubation >1 week (73.91%, p<0.001), hospital stays >2 weeks (62.5%, p=0.03), absence of pre-extubation steroids (80%, p<0.001), VAP (82.35%, p<0.001), positive CRP (70.83%, p<0.001), ETT/blood culture growth (92.31%, p<0.001), severe oxygenation index (p=0.006), mechanical complications (p=0.002), cardiopulmonary arrest (p=0.006), electrolyte imbalances (p<0.001), and sedation >5 days (76.19%, p<0.001). Pre-extubation steroid use and addressing risk factors may reduce extubation failure. **Conclusion:** Extubation failure is linked to prolonged intubation, hospital stay, VAP, mechanical complications, high oxygenation index, sedation, electrolyte imbalance, and cardiopulmonary arrest; corticosteroids may help prevent it.

INTRODUCTION

Around fifty-five percent of ICU admissions need mechanical ventilation [(1)].
The intubation and extubating of these cases are significant risks and might correlate with elevated mortality and morbidity [(2)].
Multiple factors contribute to this increase, including essential ventilatory parameters and the length of MV [(3)].
Although mechanical ventilation provides advantages when appropriately indicated, its extended application may lead to airway injuries, cardiovascular instability, lung infections, and problems associated with immobility. [(4)].

Comparably, premature EXT can also be harmful due to failure and the need for reintubation are related to prolonged stay at hospital and neurological and/or cardiorespiratory impairments, which can result in prolonged disability [(5)].

The most recent edition of the Brazilian Guidelines for MV defines extubation failure as the necessity for reintubation within forty-eight hours following the removal of artificial airway. In the pediatric demographic, the failure rate is predicted to be between sixteen percent and twenty-two percent [(6)].

The determination of the optimal timing for extubation is a difficulty and is usually determined by clinical judgment, considering the case's neurological, cardiorespiratory, and hemodynamic status [(7)].

Consequently, carrying out of a well-defined extubation readiness protocol is very important [(8)].

The Pediatric Acute Respiratory Distress Syndrome: Consensus (PARDS) advises conducting daily assessments of extubation readiness in pediatric cases [(9)].

Prior to 2017, the Recommendations for Mechanical Ventilation of Critically Ill Kids from the Paediatric Mechanical Ventilation Consensus Conference lacked consistent information demonstrating that any device or test for predicting failure was greater than clinical assessment. Consequently, no procedure has been recommended for determining extubation readiness. [(10)].

Aim of work: To evaluate the incidence of extubation failure of mechanically ventilated cases admitted to pediatric intensive care unit at Aswan University Hospital To study different factors related to extubation failure.

PATIENTS AND METHODS

This prospective cohort research has been carried out in pediatric ICU, Pediatric department, Aswan University Hospital, Aswan, Egypt. over 6-month duration, from June 2022 to December 2022.: All cases admitted in this period and connected to mechanical ventilation, aged one month to fifteen years with mechanical ventilation dutation 24 hours or more were included in the study. On the other hand, patient with accidental extubation, patient undergoing tracheostomy and patient died before first extubation were excluded

procedure: ***The eligible subjects involved in this research have been exposed to the following:***

- Informed consent has been achieved from care givers of the participants before beginning, after explaining the objective of the study, the type of operation, the possibility of complications, and the potential benefits.
- Full history including: age, weight & gender, chronic or recurrent chest disease, underlying cardiac disease, underlying neuromuscular disease, renal disease, haematolgical disease, gastrointestinal disease & endocrinal disease and history of present illness, duration of pediatric intensive care unit admisson, duration of intubation, prolonged steroid adminestration, steroid adminestration before extubation, prolonged sedation, cardiopulmonary arrest during course of intubation. Features of sepsis and Ventilatory Acquired pneumonia (VAP) before and after intubation
- . Clinical examination including**:** all participants have been exposed to complete physical examination involving evaluation of the general condition and vital signs as blood pressure, heart rate, respiratory rate and Random blood Glucose, cases have been categorized into subgroups according to the primary diagnosis on admission to the pediatric intensive care unit. Respiratory cases involved those with pneumonia, asthma, bronchiolitis, and acute respiratory distress syndrome; neurologic patients included those with seizures, encephalitis, congenital myopathy, and meningitis; and cardiac patients included those with congenital heart disorder, myocarditis, and myocardiopathy. Renal patients incorporate those with acute and chronic renal

failure and other renal diseases; patients with Gastrointestinal tract diseases, Haematological diseases and endocrinal diseases.

- Investigations: ***Laboratory investigations:*** 5 millimeters was drawn from each patient once and complete blood count, Random blood glucose, Arterial blood gases, serum sodium, serum potassium, serum magnesium, serum calcium, serum phosphorus, C-reactive protein were done at first day of intubation, after 48 hours, at day of extubation and at day of reintubation, endotracheal swab culture and blood culture were done at first day of intubation, after 48 hours, at day of extubation and at day of reintubation
- Radiology: Chest X-ray was performed on all patients at first day of intubation, after 48 hours, at day of extubation and at day of reintubation.
- Evaluation of ventilatory acquired pneumonia**:** amount and type of secrtions (massive and purulant secretion indicate VAP), presence of fever (high grade fever indicate VAP) and endotracheal swab culture and blood culture (positive or negative) **(11)**..
- Calculation of oxigenation index done on the first day of intubation Oxygenation index is calculated as OI = MAP × Fio2 × 100 / Pao2, where MAP indicates mean airway pressure and Fio^2 indicates fraction of inspired oxygen**(12)**.
- The decision to extubate, after weaning protocol, involved several largely subjective evaluations: resolution or development of the underlying illness, intact respiratory drive, minimal sedation effects from medications, adequate cough reflex for secretion clearance, sufficient spontaneous gas exchange as indicated by blood gas analysis, oxygen saturation, as well as FIO2 requirements ≤0.40, negative inspiratory force below thirty centimeters water (measured with a handheld manometer), and vital capacity above ten milliliters per kilogram (assessed with a Wright spirometer). Additionally, clinical evaluations of mechanics, hemodynamic status, and respiratory rate, as well as well-compensated metabolic stability, have been carried out primarily on neuromuscular cases capable of cooperation. Steroids have been provided pre-extubation at the discretion of the attending pediatric intensivist**(13)**.
- Failed extubation is defined as a return of an endotracheal tube within forty-eight hours following an extubation attempt**(14)**. The failure extubation rate was determined by dividing the number of initial failed extubations by the total number of initial extubation trials and multiplying the result by one hundred. Reintubation has been executed at the attending intensivist's discretion. Reintubation typically occurred due to a lack of oxygen and/or ventilation, as determined by clinical evaluation of work of breathing, blood gas analysis, failure to sustain an upper airway edema, or patent airway.
- Cases on mechanical ventilation were assessed daily until one of four objectives was reached: 1) Two days of post-extubation. 2) Two days after the move to an intermediate care level within the same facility. 3) Discharge from the pediatric intensive care unit to home or transfer to another institution (inpatient rehabilitation or another pediatric intensive care unit). 4) Death. Cases who were reintubated within forty-eight hours of extubation have been evaluated as a singular mechanical ventilation event. Outcome measures were rates of failed extubation, length of hospitalization, the length of mechanical ventilation in hours, requirement for tracheostomy, and hospital death rates.

Ethical Consideration: ***Confidentiality:*** The confidentiality of all participants was fully protected possible. The study participants were identified by name in any report or publication resulting in being admitted to this study from data collected in this study.

Research statement: This investigation involved ethical problems, both substantial and procedural. Prior to the admission of participants into this trial, the objectives, nature, and associated risks have been explained to the cases. Participants must acknowledge their comprehension of the investigational nature of the research, its associated risks and benefits, their right to opt out in participation without compromising their access to appropriate healthcare at the research site, the

chosen contact for questions about the research, and that they have freely given informed consent for participation in this research.

Informed consent: The signed informed consent form was permanently incorporated into the participant's research records and has been preserved in the same manner as other records.

Time schedule

Topic	**Period(month)**
Preparatory phase	1
Design of examination sheet	1
Review of literature	2
Collection, organization, entering of data and statistical analysis	2

Data management and Statistical Analysis: Historical data has been gathered, fundamental clinical assessments have been executed, laboratory tests have been carried out, and outcome measures have been encoded, documented, and analyzed utilizing Microsoft Excel software.

The data were subsequently imported into the Statistical Package for the Social Sciences (SPSS version 20.0) for analysis. Qualitative data is represented as numbers and percentages, while quantitative data is expressed as mean ± standard deviation. The following tests have been utilized to assess significance: Pearson's correlation or Spearman's correlation for correlation analysis.

P- value: level of significance: P-value below 0.05: Significant (S). P-value above 0.05: Non-significant (NS). P-value below 0.01: Highly significant (HS).

Descriptive statistics: Standard deviation (± SD), Mean and range for parametric numerical data, while Inter-quartile range (IQR) and Median for non-parametric numerical data.

Percentage and frequency of non-numerical data.

Analytical statistics: Kruskal-Wallis test has been utilized to assess the statistical significance of the distinction of a non-parametric variable among above two study groups.

RESULTS

Table(1)): Duration of intubation in the studied cases.

Duration of intubation				**P value**
	Total number	**Extubation failure**	**Percentage%**	
Less than or equal 1wk	27	3	11.11%	P<0.001*
More than 1wk	23	17	73.91%	
total number	50	20	40%	

. * p< 0.05 is statistically significant.

Table (2): Duration of hospital stay in the studied cases.

Duration of hospital stay				
	Total number	**Extubation failure**	**Percentage %**	**studied cases**
Less than 0r equal 2wks	26	5	19.23	P=0.003*
More than 2wks	24	15	62.50	
total number	50	20	40%	

Table (3): Ventilatory acquired pneumonia(VAP) assessment of the studied cases

VAP assessment				
	Total number	**Extubation failure**	**Percentage**	**P-value**
Cases Acquired vap	17	14	82.35	P<0.001*
Cases Not acquired vap	33	6	18.18	
Total number	50	20	40%	

VAP: ventilation associated pneumonia. * p< 0.05 is statistically significant.

Table (4): Oxygenation index among the studied cases

Oxygenation index				
	Total number	**Extubation failure**	**Percentage**	**P-value**
Mild HRF OI 4-8	20	6	30.00 %	P=0.006*
Moderate HRF OI 9-16	24	8	33.33 %	
Severe HRF >16	6	6	100.00 %	
Total number	50	20	40%	

Table (5): Complication of mechanical ventilation (subglottic edema & laryngeal edema) in the studied cases

Complication of mechanical ventilation				**P value**
	Total number	**Extubation failure**	**Percentage %**	
Yes	**6**	**6**	**100**	**P=0.002***
No	**44**	**14**	**31.82**	
Total number	**50**	**20**	**40%**	

Table(6) Laboratory investigations at day of extubation in the studed cases.

Laboratory investigations at day of extubation				**P-value**
Electrolyte imbalance				
	Total number	**Extubation failure**	**Percentage**	
With electrolyte imbalance	**19**	**14**	**73.68%**	**P<0.001***
Without electrolytes imbalance	**31**	**6**	**19.35%**	
Total number	**50**	**20**	**40%**	

Table (7): Prolonged sedation among the studied cases

Prolonged sedation				**P-value**
	Total number	**Extubation failure**	**Percentage**	
Less than 5 days	29	4	13.79	P<0.001*
More than 5 days	21	16	76.19	

DISCUSSION

Our prospective cohort research aimed to assess the incidence of extubation failure in mechanically ventilated cases (n=50) admitted to PICU at Aswan University Hospital over 6 month duration, from June 2022 to December 2022 and to study different factors related to extubation failure.

We calculated the duration of intubation, which were less than or equal 1wk in 27 cases of examined cases and more than 1wk in 23 cases of examined cases. In the extubation failure group, the number of cases with intubation for more than one week was significantly higher 17 (73.91%) compared to those who were intubated for less than 1 week 3 (11.11%) there was statistically significant variance according to the duration of intubation statistically significant variance regarding the length of intubation ($p < 0.001$).

In terms of the duration of hospital stay, it were less than or equal 2wk in 26 cases of studied cases and more than 2wk in 24 cases of studied cases, respectively. In the extubation failure group, the number of cases with hospital stay for more than two weeks was significantly higher 15(62.5%) compared to those with hospital stay for less than 2 weeks 5 (19.23%)there was statistically significant difference regarding the duration of hospital stay ($p= 0.03$).

Consistent with our findings, **Heubel et al.** [15] noted that longer stays in the ICU ($p=0.000$) and hospital ($p=0.010$) correlated with a heightened an opportunity of extubation failure.

Consistent with our predictions, the primary predictors of planned extubation failure detected in a recent investigation by **Thille et al.** [16] were also recognized as risk factors for extubation failure in the current research: mechanical ventilation length exceeding one week before extubation, ineffective cough, as well as severe systolic left ventricular dysfunction.

Consistent with our findings, ***Johnston et al.*** [17] reported that extubation failure transpired in six (fifteen percent) of the 40 extubated infants. The relative age, weight, and duration of MV for the extubation-failure and extubation-success groups were as follows: age 5 (3-8) months versus 4 (4-6) months ($P = .87$), weight 4 (3-5) kilograms versus 6 (5-7) kilograms (P-value below.001), and MV days 8 (6-23) Vs 6 (5-12).

Baisch et al. [18] ensured our results and concluded that PICU cases with failed extubation have longer hospitalization.

The total number of cases with VAP were 17 of them 14 cases failed to be extubated.

In the extubation failure group, the number of cases who had ventilatory acquired pneumonia (VAP) was significantly higher 14(82.35%) compared to those who not have VAP 6 (18.18%) there was statistically significant distinction regarding VAP ($p < 0.001$). In addition, **Dries and colleagues** [19]found an increased incidence of VAP in patients who failed extubation

The oxygenation index was Mild HRF OI 4-8, moderate HRF OI 9-16, Severe HRF >16 in 20, 24, and 6 patients, correspondingly. There was statistically significant variation in the oxygenation index among the extubation failure cases ($P= 0.006$) of them 6cases show Mild HRF OI 4-8,8 cases show moderate HRF OI 9-16 and 6cases show Severe HRF >16.

Our results were in coincidence with Studies utilizing OI as a predictor of extubation failure have been initiated by ***Fontela et al.*** [20]**,** who enrolled 124 children intubated for at least 12hours and found that OI > 5, was a risk marker for extubation failure.

In the extubation failure group, cases with mechanical complications were significantly higher 6 (100%) (4 of them complicated with laryngeal edema & 2 of them complicated with subglottic edema) compared to those with no Mechanical complications14 (31.82%). there was statistically significant difference regarding mechanical complication ($p<0.002$). In agreement, ***Heubel et al. (2020)***[15] noted that the main cause attributed to extubation failure was laryngeal stridor (subglottic edema in our results) with totaling 57% of the 89 cases. He concluded that laryngeal stridor was responsible for more than half of cases of extubation failure.,

In line with our risk factors, a previous recent study in 2023 collected 318 extubation events from 246 patients. Of these, 35 (11%) events were extubation failures. The predictive factors associated

with extubation failure included a history of pneumonia before extubation and stridor after extubation ***(Saengsin et al, 2023)*** [21].

Regarding the laboratory investigations, the extubation failure cases with electrolyte imbalance 14 (73.68 %) (5 0f them suffering from hypomagnesmia, 4 of them suffering from hypophosphatemia, 2 of them suffering from hyponatremia, 2 of them suffering from hypokalemia,1 of them suffering from hypocalcemia) were significantly higher than those without electrolyte imbalance 6 (19.35%) there was statistically significant difference regarding electrolyte imbalance (p <.001).

Previous laboratory research results indicate that electrolyte imbalance is a risk factor for extubation failure. ***Alsumrain et al***. [22] verified the association among hypophosphatemia and weaning failure in cases within two medical intensive care units, concluding that hypophosphatemia correlates with failure to wean from mechanical ventilation in cases in intensive care units receiving ventilatory support.

In the extubation failure group, the number of cases with prolonged sedation for more than 5 days was significantly higher 16(76.19%) compared to those with sedation less than 5 days 4(13.79%), while in the all cases, 29 patients had more than 5 days. there was statistically significant difference regarding prolonged sedation (p <.001).

Similarly, a previous study by ***Fontela et al.*** [20] aimed to describe the incidence of extubation failure and its associated risk factors among mechanically ventilated children. ***Fontela et al.*** [20] determined that extubation failure occurred more frequently in young children who underwent intravenous sedation.

This previous findings confirm that patients who experienced intubation for more than 1 week, hospital stay for more than 1 week, prolonged sedation, mechanical complications (laryngeal edema and subglottic edema), VAP, electrolyte imbalance or cardiopulmonary arrest are in high risk of extubation failure.

CONCLUSION

Extubation failure is linked to prolonged intubation, hospital stay, VAP, mechanical complications, high oxygenation index, prolonged sedation and electrolyte imbalance.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (89-97) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Effect of Diabetes Control on the Prevalence of Subtle Urinary Tract Infection in Type-1 Diabetic Children

Mohamed B. Hawary, Manal F. Mekky, Mohamed A. Abd-el-basset, Ashraf A .Maebed

Pediatric department, faculty of Medicine ,Aswan University

ABSTRACT

Keyword: T1DM, UTIs, Glycemic Control, Controlled, Uncontrolled.

Corresponding author :

Manal fawzy Mahmoud

Mobile: 01005636224

E-mail: manalfawzy101@gmail.com

Background: It is important to highlight that opinions on how blood sugar regulation affects UTIs vary. There is much debate regarding the connection between blood sugar regulation and UTIs. This study aimed to explore the role of diabetic control among T1DM children in the occurrence of UTI. **Methodology:** this observational case_control study was carried out in the Pediatrics Department, Aswan University Hospital on 106 children (53 controlled and 53 uncontrolled T1DM). **Results:** cases with uncontrolled T1DM were younger in age and had lower BMI. Additionally, the younger age at onset was correlated with uncontrol of disease and those patients had higher prevalence of DKA. Further, the levels of CRP and HbA1c were significantly lower in controlled T1DM vs. uncontrolled T1DM group. Also, pus cells, ketones, casts and leucocytes were significantly increased in uncontrolled T1DM group than uncontrolled T1DM group. **Conclusion:** glycemic control in T1DM children with UTIs.

INTRODUCTION

Diabetes can lead to severe complications or death in children **(1)**. Diabetic patients are more prone to bacterial infections, elevated risk of hospitalization, and increased mortality related to infections. Among diabetics, the most prevalent infection is the urinary tract infection (UTI). UTIs contribute to overall medical expenses and are a primary cause of end-stage renal disease **(2)**. In 1 diabetes mellitus (T1DM), glycemic fluctuation and chronic hyperglycemia impair endothelial function through various mechanisms that contribute to the onset of different levels of diabetic microangiopathy, including retinopathy, nephropathy, and peripheral neuropathy **(3)**.

Since the advent of intensive insulin therapy protocols for managing T1DM, it is now uncommon for children and teenagers to have clinically detectable microangiopathy. Nonetheless, vascular dysfunction might show subclinical symptoms which contribute to higher rates of morbidity and mortality and are linked to poor quality of life **(4)**.

Despite extensive research, infections' function as a catalyst for the autoimmune process that results in the clinical development of T1DM, there is limited data on the risk of infections in individuals with de novo or old T1DM. There is a bidirectional relationship between infections and T1DM: inadequate glycemic management heightens the odds of infections, while for both recently diagnosed and chronic patients, infection might serve as a trigger for metabolic dysfunction, which may result in diabetic ketoacidosis **(5)**.

There were multiple reasons that caused the incidence of UTIs in diabetic patients i.e., increased glucose levels in renal parenchyma foster proliferation of microorganisms (this is a contributing factor to pyelonephritis and other renal issues, such as emphysematous pyelonephritis). Various immune system disorders, affecting humoral, cellular, and innate immunity, can contribute to the development of UTIs in individuals with diabetes. Diabetic patients with UTI exhibited reduced levels of interleukin-6 and interleukin-8 in the lower urinary tract **(6)**.

The current study aimed to explore the role of diabetic control among T1DM children in the occurrence of UTI.

PATIENTS AND METHODS

From May 2023 to April 2024, this observational case_control study was carried out on 106 children with subtle UTIs at the Pediatric Department of Aswan University Hospital in Egypt. According to G*Power software v. 3.1.9.7 (Faul, et al., 2007), the minimum required sample utilizing two population means formula with an independent t-test, the following assumptions were taken into account: $\alpha = 95\%$; Power $(1 - \beta)$: 99 percent; Effect size is equal to 0.5; Two-tailed test was 106 cases. children which further subdivided into two groups: **Group-I** (n=53): including children with controlled T1DM, **Group-II** (n=53): including children with uncontrolled T1DM. Both groups were on regular follow up at Pediatric Endocrinology outpatient's clinic.

Children aged 1 to 15 years, diagnosed with T1DM (regardless of their diabetic control status), were recruited for the current work. Conversely, those with symptomatic UTI during the study, a history of urologic disease, other autoimmune diseases, or chronic diseases were excluded.

Procedure

All eligible cases under study underwent complete history taking (demographic data, diabetes-focused history, history indicative of UTI, history suggestive of chronic diabetic complications and a record of other medications used (e.g., antibiotics). Clinical examination (anthropometric measurements, general/systemic examination. Laboratory investigation (complete blood count (CBC), Renal function test and urine analysis.

Statistical analysis

IBM-SPSS version 26 **(7)** was applied for data processing. For data summarization: Means, standard deviations, medians, inter-quartile range (IQR) and frequency was presented. Test of significances: Chi-square and Fisher Exact tests were applied to analyze the differences in frequency distributions among groups. Shapiro-Wilk test and histogram was used to test for data normality. For continuous variables with two categories; independent sample t-test analysis was be carried out to compare the means of normally distributed data, while Mann-Whitney U test was be calculated to test the median differences of the data that don't follow normal distribution. A two-tailed p-value < 0.05 indicated significance.

Ethical considerations

All ethical committee regulations from the faculty of medicine were adhered to. Each patient had a private file governed by a non-disclosure policy during data presentation, ensuring that all presented information did not reveal any personal details identifying any of the patients. Guardians of all participants had to sign a written consent after reviewing the patient information sheet or having it read to them. The research conformed to the Declaration of Helsinki regarding ethical guidelines for human and animal research (8) and followed the STROBE guidelines for observational studies (9). Additionally, no incentives or rewards were given to participants or their caregivers.

RESULTS

The current study, conducted in the pediatrics department of Aswan University Hospital, included 106 pediatric cases with T1DM.

As shown in **table 1**

Table 1: Disease characteristics of the diabetic patients.

		Group I (n=106)
Age during disease onset (years)	• **Mean ± SD**	8.64 ± 2.24
	• **Range**	2 - 12
Duration of disease (years)	• **Mean ± SD**	1.99 ± 2.03
	• **Range**	0 – 6
Type of presentation	• **DKA**	76 (71.7%)
	• **Hyperglycemia**	30 (28.3%)
Insulin dosage (IU)	• **Mean ± SD**	0.92 ± 0.2
	• **Range**	0.6 - 1.2

Table 2: Demographic data Differences Between groups

		Controlled T1DM (n=53)	Uncontrolled T1DM (n=53)	P-value
Age/years	• **Mean ± SD**	11.28 ± 2.9	9.94 ± 3.4	< **0.001***
	• **Range**	5 – 15	3 - 15	
Sex	• **Male**	28 (52.83%)	30 (56.6%)	= 0.284**
	• **Female**	25 (47.17%)	23 (43.4%)	
Weight (kg)	• **Mean ± SD**	37.66 ± 10.2	30.28 ± 9.4	< **0.001***
	• **Range**	21 – 55	13 - 52	
Height (cm)	• **Mean ± SD**	136.68 ± 14.6	127.36 ± 17.9	= 0.097**

	• **Range**	102 – 153	94 - 157	
BMI (kg/m^2)	• **Mean ± SD**	19.75 ± 2.3	18.21 ± 2.1	**= 0.041***
	• **Range**	16.52 - 24.06	13.46 - 23.49	

***Independent Sample T test was used to compare mean between the two groups**
****Chi-square test was used to compare frequency between the two groups**
T1DM: type 1 diabetes mellitus, BMI: body mass index

Table 3: Comparison of Disease characteristics among studied groups.

		Controlled (n=53)	Uncontrolled (n=53)	P-value
Age during disease onset (years)	• **Mean ± SD**	9.32 ± 1.74	7.96 ± 2.48	**< 0.001***
	• **Range**	5 - 12	2 – 11	
Disease Duration /years	• **Mean ± SD**	3.35 ± 1.07	3.69 ± 1.64	= 0.421*
	• **Range**	1 - 5	1 – 6	
Type of presentation	• **DKA**	31 (58.49%)	45 (84.91%)	**< 0.001****
	• **Hyperglycemia**	22 (41.51%)	8 (15.09%)	
Insulin dosage (IU)	• **Mean ± SD**	0.94 ± 0.2	0.9 ± 0.21	= 0.494*
	• **Range**	0.7 - 1.2	0.6 - 1.2	

***Independent Sample t-test compare mean between two groups**
****Chi square test was used to compare proportions between groups**
T1DM: type 1 diabetes mellitus, DKA: diabetic ketoacidosis

Regarding the laboratory data **(table 4),**

Table 4: Difference in Laboratory investigations between studied groups

		Controlled T1DM (n=53)	Uncontrolled T1DM (n=53)	P value
Hb (g/dl)	• **Mean ± SD**	11.54 ± 0.97	11.39 ± 0.96	= 0.147*
	• **Range**	9.3 - 13.2	9.3 - 12.5	
Platelets ($x10^9$/L)	• **Mean ± SD**	249.06 ± 69.36	271.53 ± 104.13	= 0.372*
	• **Range**	135 - 367	143 – 433	
TLC ($x10^9$/L)	• **Mean ± SD**	12.07 ± 3.22	13.99 ± 4.71	= 0.077*
	• **Range**	7.3 - 17.9	6.3 – 22	
Urea (mg/dl)	• **Mean ± SD**	53.57 ± 10.63	57.75 ± 16.13	= 0.171*
	• **Range**	36 - 75	21 - 87	
Creatinine (mg/dl)	• **Mean ± SD**	1.1 ± 0.17	1.2 ± 0.23	= 0.076*
	• **Range**	0.8 - 1.4	0.6 - 1.6	
CRP (mg/dl)	• **Median**	18	32	**<0.001****
	• **IQR**	12 - 20	11.5 - 50	
HbA1c (%)	• **Mean ± SD**	7.87 ± 0.31	12.25 ± 1.55	**<0.001***
	• **Range**	6.8 - 8.2	9.2 - 14.5	

***Independent Sample t-test compare mean between two groups**

****Mann Whitney U test compare median between two groups**

T1DM: type 1 diabetes mellitus, Hb: hemoglobin, TLC: total leucocyte count, CRP: c reactive protein, HbA1c: glycated hemoglobin, *: significant as P value ≤ 0.05, P1: P value between controlled and uncontrolled T1DM, P2: P value between controlled T1DM and group II, P3: P value between uncontrolled T1DM and group II

The differences in urinalysis findings were depicted in **table 5**.

Table 5: Difference in Urinalysis Findings between studied groups

		Controlled T1DM (n=53)	Uncontrolled T1DM (n=53)	P value
pH	• **Mean ± SD**	5.88 ± 0.24	5.83 ± 0.19	= 0.234*
	• **Range**	4.8 - 6	4.9 - 6	
Pus cells	• **0-5**	12 (22.64%)	5 (9.43%)	**= 0.046****
	• **>5**	41 (77.36%)	48 (90.57%)	
RBCs	• **0-4**	48 (90.57%)	46 (86.79%)	= 0.263**

	• **>4**	5 (9.43%)	7 (13.21%)	
Crystals	• **Nil**	14 (26.42%)	2 (3.77%)	
	• **Uric acid**	24 (45.28%)	31 (58.49%)	**= 0.005****
	• **Amorphous urate**	15 (28.3%)	20 (37.74%)	
Casts	• **Nil**	40 (75.47%)	29 (54.72%)	
	• **Granular**	11 (20.75%)	14 (26.42%)	**= 0.024****
	• **Hyaline**	2 (3.77%)	10 (18.87%)	
Protein	• **Nil**	53 (100%)	44 (83.02%)	
	• +	0 (0%)	5 (9.43%)	**= 0.007****
	• ++	0 (0%)	4 (7.55%)	
Leucocytes	• **Nil**	33 (62.26%)	19 (35.85%)	
	• +	18 (33.96%)	20 (37.74%)	
	• ++	2 (3.77%)	14 (26.42%)	**= 0.002****
	• +++	0 (0%)	0 (0%)	
	• ++++	0 (0%)	0 (0%)	

***Independent Sample t-test compare mean between two groups**
****Chi square test was used to compare proportions between groups**
T1DM: type 1 diabetes mellitus, RBCs: red blood cells, *: significant as P value ≤ 0.05, P1: P value between controlled and uncontrolled T1DM, P2: P value between controlled T1DM and group II, P3: P value between uncontrolled T1DM and group II

DISCUSSION

The connection between infections and diabetes mellitus is a topic of great interest in the medical literature. Proper glycemic control in diabetics has been shown to improve immune function and reduce morbidity and mortality from serious infections **(10)**. The β-cells of the pancreas, which make and secrete insulin, are the target of an autoimmune process that causes T1DM. Insulin deficiency and hyperglycemia are the results of this process, which kills the cells **(11)**.

UTIs are more common in people with DM and can have dangerous repercussions. UTI risk factors include a compromised immune response, insufficient bladder emptying, and altered metabolic control **(12)**. T1DM cases that have poor glycemic control are more likely to experience UTI. This association implies that factors directly related to glycemic control may affect the risk of lower UTI and are independent of other well-established predictors of UTI **(13)**.

It is important to highlight that opinions on how blood sugar regulation affects UTIs vary. There is much debate regarding the connection between blood sugar regulation and UTIs. It works well for UTIs, but in Greeling's study, blood sugar control had no effect on the presence of UTIs. **(14)**. According to Chiţă et al. 2017, when using a multivariate logistic regression model, glycemic control—which is determined by HbA1c levels—appeared as a significant risk factor for UTIs, but in univariate analysis, it had no discernible impact **(12)**. The presence of UTIs and metabolic control have not been linked in other reports **(15-16)**.

The current study aimed to determine the effect of glycemic control on the presence of UTI in children with T1DM. A total of 106 children with T1DM were recruited for in this study. Cases were

categorized into two equal groups: Group I consisted of 53 controlled T1DM patients and Group II: 53 uncontrolled T1DM patients.

In this study, cases with controlled T1DM were older than those with uncontrolled diseases. In contrast, the duration of disease was similar between the two groups. Regarding the type of presentation, a higher proportion of patients in the uncontrolled T1DM group presented with diabetic ketoacidosis and hyperglycemia compared to the controlled T1DM group.

Agreed with the current results, Janifer et al., found that age and the length of diabetes were found to have a substantial impact on **(17)**. Also, insulin medication was found to be one of the risk factors for recurrent UTIs in women, according to Gorter et al., 2010 **(18)**. Similarly, according to Wilke et al., 2015, insulin therapy did not raise the risk of recurring UTIs **(19)**. Further, the percentage of patients with UTI and the length of diabetes were correlated in another study with 1157 Indian patients (42% aged less than 10 years) **(20)**.

Likewise, we found that cases with controlled T1DM had higher mean BMI than those with uncontrolled disease. In disagreement, Al-Rubeaan et al. 2013 found no connection between diabetic patients' age and their increased risk of UTI. On the other hand, both sexes are more susceptible to UTIs as they age, but females are more susceptible than males i.e., according to the Carrondo study, the UTI rate for those between the ages of 18 and 64 was 9%, while the incidence for those over 85 was 27.5% **(16)**. According to previous studies, women experienced UTIs at a higher rate than men did. This seems to be connected to bladder neurological dysfunction, physiological bladder changes brought on by aging or dyspnea, and women's closeness to the anus **(21)**.

Furthermore, in this study, CRP and HbA1c were significantly lower in controlled than uncontrolled T1DM groups. These results are consistent with earlier studies that found a link between the occurrence of UTIs and higher CRP and HbA1c levels **(21)**. Based on Ribera et al. (2006), symptomatic UTIs in DM patients were linked to elevated inflammatory biomarkers and a HbA1c level more than 7% **(22)**.

The finding of this study was that pus cells, ketones, Casts, protein and leucocytes were significantly increased in uncontrolled T1DM group than controlled group. This was supported by the findings of different studies that claimed that inadequate glycemic control may both directly and indirectly raise the risk of UTIs having pathophysiological backing. First, increased urine glucose levels may serve as a culture medium, encourage bacterial adhesion to the urinary tract, and encourage the growth of harmful bacteria **(23-24)**. In accordance, pyuria was found to be detectable by the dipstick leukocyte esterase test (which has a sensitivity of 75% examination) or by microscopic examination (defined as ≥10 leukocytes/mm3) **(25)**. Similar results were detected in other studies that examined the relationship between glycemic control and incidence of UTIs **(26-27)**.

Conclusion and Recommendation

In conclusion, cases with uncontrolled T1DM were younger in age and had lower BMI. Additionally, younger age at onset was correlated with uncontrol of disease and those patients had higher prevalence of DKA. Further, levels of CRP and HbA1c was significantly lower in controlled T1DM vs. uncontrolled T1DM group. Also, pus cells, ketones, casts and leucocytes were significantly increased in uncontrolled T1DM group than uncontrolled T1DM group.

Acknowledgement:

The authors would like to express their appreciation to the pediatric department medical and administrative staff at Aswan University Hospital for their prompt assistance and support. Without the assistance, encouragement, and consent of the designated patients and their guardians, this work could not be finished.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (98-102) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Incidence and Risk Factors of Acute Kidney Injury In Diabetic Ketoacidosis Patients

Hala abd allah Mahmoud abd allah[1], Abdallah Mahmoud Abdallah[2], Mohamed Mohye eldin Foad[1], Hebatullah Ahmed Mohamed Soliman[1] , Weaam MohamedMohamed ali[1*]

[1]Department of Internal Medicine, Faculty of Medicine, Aswan University

[2]Department of Biochemistry, Faculty of Medicine, Aswan University

ABSTRACT

Keyword: Diabetes mellitus, acute kidney injury, Diabetic Ketoacidosis

Corresponding author :

Hebatullah Ahmed Mohamed Soliman

Mobile: 01111090961

E-mail: hebaelnaby94@gmail.com

Background: Dehydration severity varies among patients. Hypovolemia can lead to prerenal acute kidney injury (AKI), which, if severe, can progress to acute tubular necrosis. Recent DKA care guidelines recommend conservative rehydration with iso-osmotic fluids and continuous intravenous insulin to prevent renal hypoperfusion**. Goals and Objectives:** To evaluate the frequency and risk factors of AKI in DKA individuals and investigate their correlations**. Methods and Subjects:** Cross-sectional research was performed on 100 cases of DKA admitted to the Internal Medicine Department of Aswan University Hospital.
Findings: The severity of AKI and its primary causes were assessed. Only 3% had severe AKI, 19% had mild, 13% had moderate, and 65% had non-azotemic severity. The causes of AKI included: 4% with additional causes, 44% with missed medication, 34% with infection, and 18% with other diagnoses. **Conclusion:** Several variables, such as age, glucose, white blood cell counts, sulfate, pH, serum alkaline phosphatase, coma, and pre-existing chronic kidney disease, are linked to AKI in DKA. There is a correlation between AKI, particularly severe ones, and rapid progression of CKD. The early identification and prevention of AKI in individuals with DKA are essential for the preservation of renal function.

INTRODUCTION

The condition known as diabetes mellitus (DM), which is an endocrine illness, is the cause of the improper metabolism of blood glucose. As a result of this chronic disease, an individual may experience difficulties in both the short term and the long term. The condition known as DKA and hyperosmolar hyperglycemic state (HHS) are two of the problems that can arise as a consequence of diabetes (4).

Between four percent and forty percent of deaths in developing countries are attributable to hyperglycemic emergencies (5).

DKA is associated with a significant mortality and morbidity rate, making it the most serious hyperglycemic emergency in individuals with type 1 or type 2 DM (6). Ketosis (presence of ketones in blood and urine), Acidosis (venous blood pH < 7.3 or HCO3 < 15 mmol/L), as well as hyperglycemia (blood glucose > 200 mg/dl) are the three conditions that are considered to be the hallmarks of DKA, according to the guidelines issued by the International Society for Pediatric and

Adolescent Diabetes (ISPAD) in 2014. The severity of the condition is determined by the following criteria: a venous pH below 7.3 or HCO3 below 15 mmol/L is considered mild; a pH below 7.2 or HCO3 below 10 mmol/L is considered moderate; as well as a pH below 7.1 or HCO3 below 5 mmol/L is considered severe (7).

Reduced urine production (oliguria) and increased serum creatinine levels (a marker of renal excretory function) are quantifiable indicators of AKI, which is defined as an abrupt loss of kidney function that lasts no more than seven days. Reduced urine production (oliguria) and increased serum creatinine levels (a marker of renal excretory function) are quantifiable indicators of AKI, which is defined as an abrupt loss of kidney function that lasts no more than seven days. Furthermore, Kidney Disease Improving Outcomes (KDIGO) recommends that AKI be staged according to severity, as illustrated in Table 1 (8).

Table 1: Although renal injury is frequently encountered in hyperglycemic hyperosmolar state, it is not so well reported in DKA *(Zeitler et al., 2011).*

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline or ≥0.3 mg/dl (≥26.5 µmol/l) increase	<0.5 ml/kg/h for 6–12 h
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ≥12 h
3	3 times baseline or ≥4.0 mg/dl (≥353.6 µmol/l) increase or initiation of RRT or in patients <18 years a decrease in eGFR <35 ml/min/1.73 m²	<0.3 ml/kg/h for ≥24 h or anuria ≥12 h

PATIENTS AND PROCEDURES

A total of 100 DM cases with DKA who were admitted to the prior study setting over the study period (one year) were chosen to participate in this cross-sectional investigation. At Aswan University Hospital's Department of Internal Medicine, Faculty of Medicine, all of the included patients underwent investigations into arterial blood gases, serum urea and creatinine, and full blood counts.

Inclusion criteria Age: above 16, sex: both male and female, and diabetes patients with AKI and DKA.

Exclusion criteria: patients with chronic renal disease who are less than 16 or older than 60.

Methods A thorough medical history, a clinical examination, and laboratory testing were performed on each study participant.

Informed consent

A participant's informed consent form was kept in the same way as other documents and was considered a permanent part of their research records.

Statistical analysis

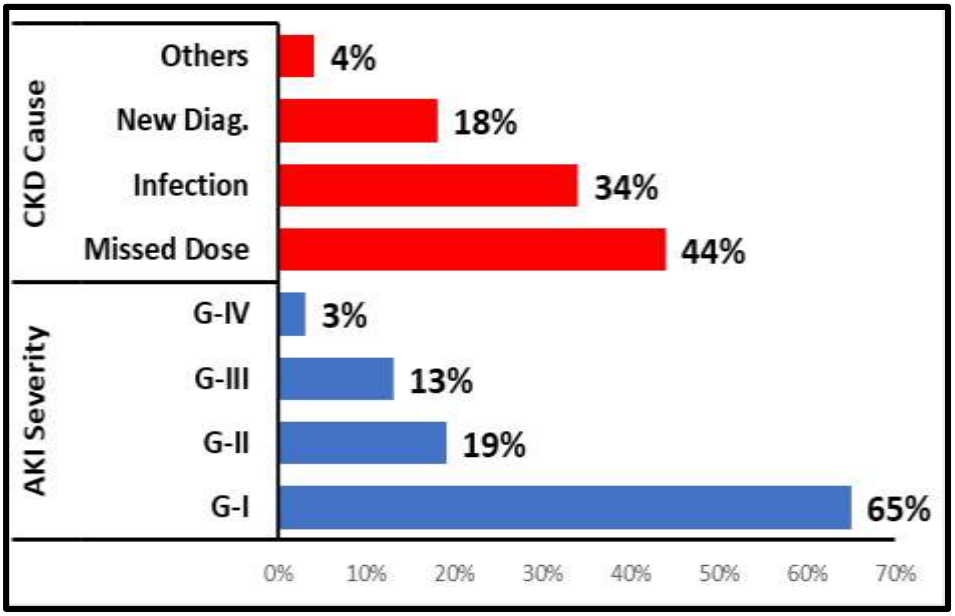
IBM-SPSS 21.0 (IBM-SPSS Inc., Chicago, IL, United States) was utilized by the researcher in order to verify, code, and analyze the data. Descriptions based on statistics: It was determined how to compute the standard deviations, means, and percentages. Evaluation of the significance test: For the purpose of determining the degree of dissimilarity in frequency distributions among the various groups, the Chi square, Fisher's exact, and Monte Carlo exact tests were utilized. For the purpose of determining whether or not there was a difference in the frequency distribution among the members of the group, the McNemar test was utilized. The Shapiro-Wilk test was employed to ascertain the normal distribution of continuous variables. Independent sample t-tests were conducted on continuous variables with two categories to ascertain the mean differences between the groups. A

one-way analysis of variance (ANOVA) was conducted to ascertain the mean differences among groups and repeated measures for continuous variables with multiple categories. The RM-ANOVA test was carried out in order to evaluate the mean differences in data that exhibited a normal distribution and contained repeated measures (between groups, within groups, and overall differences). The two research groups were compared pairwise using Bonferroni adjustments and a post-hoc test. A p value of 0.05 or less is statistically significant. Multivariate logistic regression was used to identify MR-influencing factors. The odds ratio (OR), 95% CI, and p-value were analyzed. A p-value below 0.05 was significant.

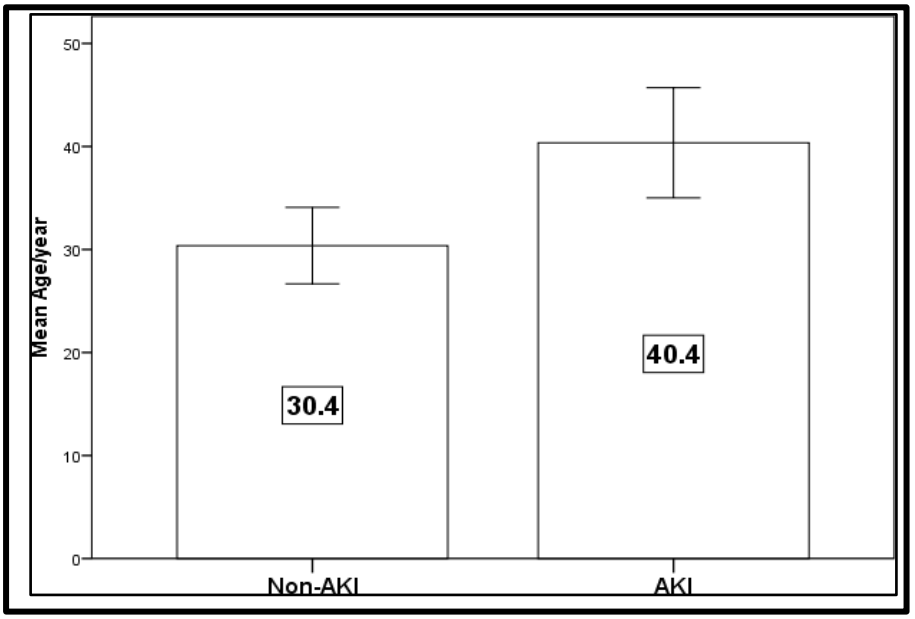
Results

The incidence of AKI in DKA was about (n= 44) 44$%.

The Grades of severity of AKI are about two- thirds (n=65) had non-azotemic severity, about one-fifth had mild (n=19), 13% (n=13)had moderate and only 3% had severe AKI.



the variances in the baseline characteristic among the examined groups. AKI cases were significantly (p=0.002) older (40.4 ± 6.1 years) than non-AKI (30.4 ± 8.4) (Fig. 6). As regard patient's sex, both groups were matched for sex (p = 0.284)



DISCUSSION:

The current research did not find a statistically significant distinction in the frequency of AKI among participants with newonset DM and those withestablished diabetes mellitus. However, the study found that all participants with grade-III AKI were newly diagnosed with diabetes mellitus. Delayed diagnosis of new-onset DM and delayed medical consultation might result in hospital admission with severe degrees of dehydration and acidosis with subsequent development of AKI, These findings confirmed the results of previous studies that reported more frequent AKI among patients with severe volume depletion. (9)

This study found that clinical markers of volume depletion at hospital admission were significantly associated with development of AKI. Participants with AKI had significantly higher pulse rate and respiratory rates and significantly lower systolic and diastolic blood pressure at hospital admission. Moreover, severe dehydration at hospital admission was significantly more frequent among participants with AKI.

The study found that disturbed conscious level was significantly more frequent among participants with AKI and that GCS at hospital admission was significantly lower in participants with AKI. Moreover, multivariate regression analyses revealed that the odds for development of AKI was increased by 2.7 times if the patient had GCS below 14 at hospital admission and that the odds for development of severe AKI was increased by 4.6 times in the patient had GCS below 14 at hospital admission. In a study on adult patients with DKA conducted by (10), Coma at admission was significantly more frequent Discussion in patients with AKI compared to participants with no AKI. Furthermore, (11) reported that GCS scores decreased below14 in 1.8% of DKA episodes in participants with no AKI and in 5.9% of DKA episodes in participants with AKI. However, these differences were not significant in multivariate analysis. Severe dehydration and volume depletion that affect the cerebral blood flow and induce disturbed conscious level are likely to affect the renal blood flow and induce AKI (11).

CONCLUSION:

AKI is a serious consequence of DKA related to age, glucose levels, sulfate levels, white blood cell (WBC) counts, pH, serum alkalinity, coma, and prior CKD. In persons with DKA, AKI and severe stages of AKI are associated with the accelerated progression of CKD and increased long-term mortality. In hospitals, the early identification and prevention of AKI are

paramount, as is the consistent monitoring aimed at safeguarding renal function in DKA cases with AKI.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (103-111) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Association between Helicobacter Pylori Infection and Nonalcoholic Fatty Liver Disease in School-Aged Children in Aswan

Magda F Gabri[1], Hanan M. Abd-El Moneim[1], Mostafa O Mohammad[1*], Ahmed M Ali[2], Mohammed Z Abu Rahma[3], Sherin A. Taha [4]

[1] Pediatrics Department, Faculty of Medicine, Aswan University.

[2]Pediatrics Department, Faculty of Medicine, Assiut University

[3] Department of gastroenterology and Tropical Medicine, Faculty of Medicine, Assiut University

[4] Pediatrics Department, Faculty of Medicine, Suez University

ABSTRACT

Keyword: Diabetes mellitus, acute kidney injury, Diabetic Ketoacidosis

Corresponding author :

Mostafa Omar Mohammad

Mobile: 01069280855E-

mail: mostafaomar040@gmail.com

Background Information: Nonalcoholic fatty liver disease (NAFLD) is one of the gastrointestinal and metabolic conditions linked to Helicobacter pylori infection. NAFLD has emerged as one of the most prevalent hepatic disorders in pediatric populations as a result of the growth in childhood obesity. **The objective** is to assess how an H. pylori infection affects liver health, particularly how it can contribute to the development of nonalcoholic fatty liver disease. **Methodology**: Ninety-five school-aged children who presented with dyspepsia at Aswan University Hospital participated in a cross-sectional study. Stool antigen testing was used to diagnose an H. pylori infection. Liver function tests and abdominal ultrasonography were used to evaluate liver health. **Results**: Of the 95 kids, 48 (50.5%) tested positive for H. pylori. According to ultrasound results, 5.3% of patients had hepatomegaly and elevated liver echogenicity, which could indicate fatty liver abnormalities. Children with H. pylori infection had significantly higher mean ages (9.07 ± 2.40 vs. 7.88 ± 2.62 years, p=0.023), hepatomegaly rates (10.4% vs. 0%, p=0.023), and epigastric pain rates (89.6% vs. 29.8%, p<0.001) than children without H. pylori infection. Gender, residence, hematemesis, vomiting, and stomach discomfort did not significantly differ from one another (p>0.05). **Conclusion**: Hepatomegaly and epigastric pain are substantially linked to H. pylori infection in children. These results underline the need for more research in this field and point to a possible involvement of H. pylori in the development of NAFLD.

INTRODUCTION

Helicobacter pylori (H. pylori) is a Gram-negative rod bacterium. associated with peptic ulcer disease, gastric cancer, and many gastrointestinal disorders. (1) It is among the most prevalent bacterial illnesses globally, affecting more than fifty percent of the population. (2) Recent data indicates a correlation between metabolic disorders, including nonalcoholic fatty liver disease (NAFLD), and H. pylori infection (3).

NAFLD is increasingly prevalent among youngsters, primarily attributed to escalating obesity rates. The incidence in Egypt was 15.7% (4). The "multiple hit" hypothesis posits that changes in gut microbiota, insulin resistance, and deregulation of hepatic lipid metabolism may facilitate the onset of NAFLD (5). H. pylori infection is recognized as a modulator of gut microbiota composition, potentially influencing the development of NAFLD. (2) Although this link has been well examined in adults, limited research exists concerning its effects on children. There is more data supporting a link between NAFLD and H. pylori (6).

This study sought to evaluate the correlation between pediatric patients' NAFLD and H. pylori infection.

PATIENTS AND METHODS

A study that is cross-sectional performed at Aswan University Hospital.
Individuals involved: The study comprised ninety-five school-aged children (4-14 years) exhibiting dyspepsia. Children with pre-existing chronic liver disease, obesity, metabolic syndrome, or diabetes mellitus were omitted.
Data Collection: Each participant received a comprehensive medical history, physical examination, stool antigen assay for H. pylori identification, liver function tests (AST, ALT, total bilirubin, total protein, serum albumin), fasting plasma glucose measurement, lipid profile analysis, and abdominal ultrasound evaluation.

The Mindray Diagnostic Ultrasound System, manufactured by Shenzhen Mindray Bio-Medical Electronics in China, used a 4.5 MHz convex probe to conduct an abdominal ultrasound examination on all subjects by a Gastroenterology and Liver Consultant with extensive experience (7). Each child's stool was collected at a rate of approximately 1 g and subsequently diluted in a 5 ml samples diluent. Eagle Biosciences, Inc., Amherst, NH, USA, provided the reagent for the Enzyme Immunoassay Test (ELISA) to investigate the H. pylori antigen in this test (8). No acid-suppressive medicines or antibiotics were ingested in the four weeks preceding the test.
Statistical Analysis: The gathered data were analyzed using IBM SPSS Statistics software (version 26). Continuous variables were presented as mean ± SD and analyzed using independent t-tests or Mann-Whitney tests where applicable. Chi-square tests have been utilized to analyze categorical variables. A p-value of less than 0.05 was used to establish statistical significance.

Ethical consent:

The Institutional Ethics Committee authorized the study protocol and Research Review Board of Aswan University's Faculty of Medicine. Prior to their children's enrollment in the experiment, each parent of a participating child furnished signed informed consent.

RESULTS

Table 1 presents the demographics of our cases: The average age of participating children was 8.48 ± 2.57 years, comprising 45.3% males and 54.7% from rural areas.

Table (1): Patients' demographic characteristics (n=95)

Variables	Frequency (Percentage %)
Gender **Male** **Female**	 43 (45.3%) 52 (54.7%)
Age (years) **Mean ± SD.** **Range**	 8.484 ± 2.5697 4-14
Age categories **4-9.50** **10-14**	 65 (68.4%) 30 (31.6%)
Residence **Urban** **Rural**	 43 (45.3%) 52 (54.7%)
Weight (kg) **Mean ± SD.** **Range**	 23.879 ± 7.8898 23 (14.50-54)
Height (cm) **Mean ± SD.** **Range**	 119.237 ± 15.3377 119 (92-160)
Body mass index (Kg/m^2) **Mean ± SD.** **Range**	 16.3492 ± 1.7937 16.1 (12.30-21.50)

Figure (1) Displays the clinical parameters of the examined patients, with epigastric soreness being the most prevalent, succeeded by vomiting and stomach pain. Five children exhibited hepatomegaly, whereas just one child presented with hematemesis. 50.5% (48) of the evaluated youngsters tested positive for H. pylori.

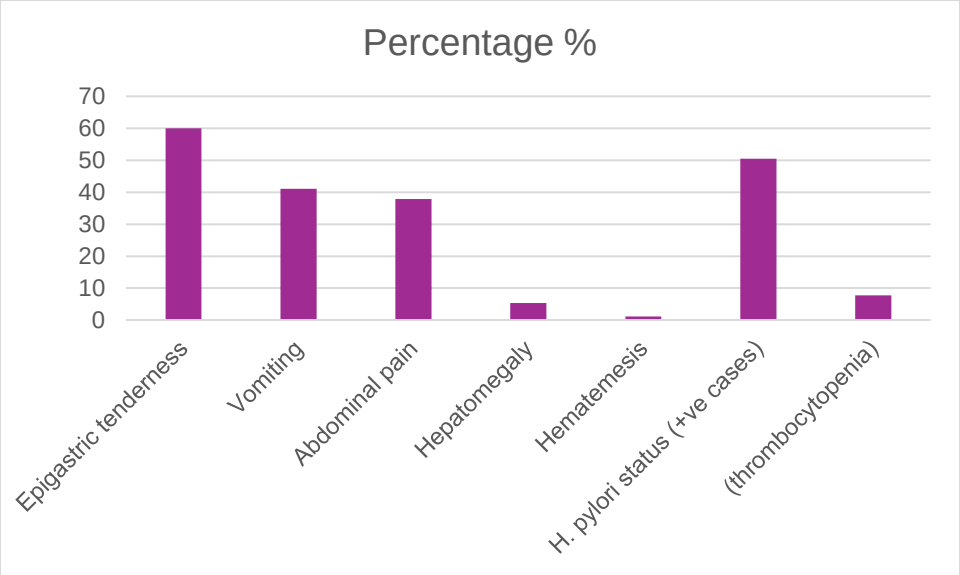

Figure (1) shows the clinical parameters of the studied cases.

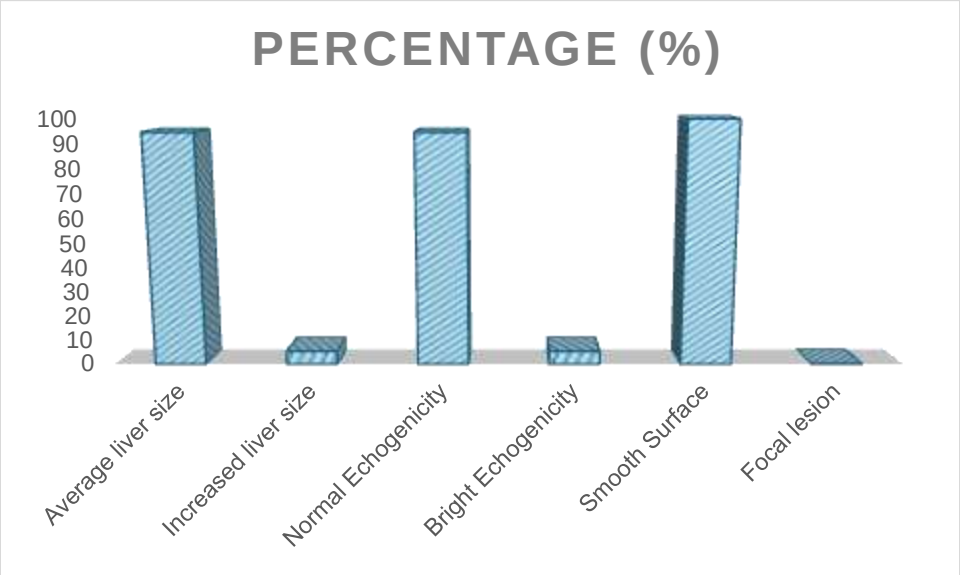

Figure (2): Abdominal ultrasound of study children

Figure 2 shows that 5.3% of cases had increased liver size and bright echogenicity, while all children had smooth liver surfaces.

Table (2): Pattern of liver function test and Liver US in H. Pylori positive and negative cases

Parameters	H. Pylori status		P value
	Positive (n=48)	Negative (n=47)	
	Mean ± SD	**Mean ± SD**	
AST (U/L)	24.50 ± 4.654	23.30 ± 5.369	0.246#
ALT (U/L)	24.31 ± 4.921	23.64 ± 4.678	0.496#

Total bilirubin (mg/dL)		0.682 ± 0.1627	0.6128 ± 0.1813	0.052#
Total protein (gm)		7.002 ± 0.4349	6.968 ± 0.3648	0.681#
Serum albumin (gm)		4.05 ± 0.3345	3.983 ± 0.6001	0.502#
		Number (%)	**Number (%)**	
Serum Albumin level	Low (<3.5 gm)	1 (2.08%)	3 (6.38%)	0.235
	Normal (3.5-5.3 gm)	47 (97.92%)	43 (91.48%)	
	High (>5.3 gm)	0 (0%)	1 (2.13%)	
Liver size (US)	Average	43 (89.6%)	47 (100%)	**0.023***
	Increased	5 (10.4%)	0 (0%)	
Echogenicity	Normal	43 (89.6%)	47 (100%)	0.023*
	Bright	5 (10.4%)	0 (0%)	

*Significant chi-square test; Student t-test; AST: Aspartate transferase; ALT: Alanine aminotransferase.

Table 2 shows that epigastric tenderness was significantly more common in H. pylori-positive children (89.6% vs. 29.8%, p<0.001). Hepatomegaly was also significantly higher in the H. pylori-positive group (10.4% vs. 0%, p=0.023). No statistically significant difference exists between H. pylori infection and liver function tests, p-value >0.05.

Table (3): Lipid profile in H. pylori infection (comparison between positive and negative cases)

Parameters		**H. Pylori status**		**P value**
		Positive (n=48) N (%)	Negative (n=47) N (%)	
Total cholesterol (mg/dL)	Normal (<170)	44 (91.7%)	47 (100%)	**0.043***
	Elevated (≥170)	4 (8.3%)	0 (0%)	
	Mean ± SD	123.47 ± 33.98	74.51 ± 10.9899	**<0.001****
Serum triglycerides (mg/dL)	Normal (<90)	37 (77.1%)	46 (97.87%)	**0.002***
	Elevated (>90)	11 (22.9%)	1 (2.13%)	
	Mean ± SD	81.92 ± 33.114	62.298 ± 11.497	**<0.001****
HDL-C (mg/dL)	Normal (>45)	29 (60.4%)	36 (76.6%)	0.090
	Elevated (<45)	19 (39.6%)	11 (23.4%)	
	Mean ± SD	48.446 ± 8.213	50.489 ± 7.0707	0.197
LDL-C (mg/dL)	Normal (<110)	45 (93.8%)	47 (100%)	0.082
	Elevated (>110)	3 (6.3%)	0 (0%)	
	Mean ± SD	70.267 ± 18.72	66.085 ± 10.034	0.178
HBA1c	**Mean ± SD**	4.988 ± 0.2647	5.015 ± 0.3252	0.651

*Significant chi-square test; **Significant student t-test; HDL-C: High-density lipoprotein; LDL-C: Low-density lipoprotein; HBA1c: Glycosylated hemoglobin.

Regarding lipid profile, H. pylori-positive cases exhibited significantly higher total cholesterol levels (8.3% vs. 0%, p=0.043) and triglycerides (22.9% vs. 2.13%, p=0.002), suggesting a potential metabolic impact of H. pylori infection.

Table (4): Relation between H. pylori status, demographic, and clinical features

Parameters		H. Pylori status		P value
		Positive (n=48)	Negative (n=47)	
		N (%)	N (%)	
Gender	Male	21 (43.8%)	22 (46.8%)	0.765
	Female	27 (56.3%)	25 (53.2%)	
Residence	Urban	21 (43.8%)	22 (46.8%)	0.765
	Rural	27 (56.3%)	25 (53.2%)	
Hepatomegaly		5 (10.4%)	0 (0%)	**0.023***
Hematemesis		1 (2.1%)	0 (0%)	0.320
Vomiting		21 (43.8%)	18 (38.3%)	0.589
Abdominal pain		19 (39.6%)	17 (36.2%)	0.732
Epigastric tenderness		43 (89.6%)	14 (29.8%)	**<0.001***
Age (years)		**Mean ± SD**	**Mean ± SD**	
		9.073 ± 2.399	7.883 ± 2.6235	**0.023****

*Significant Chi-square test, **Significant student t-test

Significant differences were observed in liver size (hepatomegaly), epigastric tenderness and age between the H. pylori-positive and negative categories (p>0.05) in Table 4.

DISCUSSION

Infection with H. Pylori was identified in 50.5% of our patients via stool antigen testing. Similar findings have been documented in Türkiye (49%) by Çınar et al. (9). In Egypt, Al-Mendalawi (10) did a study on healthy schoolchildren as Serum IgG levels against H.pylori were assessed in the governorate of Al Qulubia., which revealed a Frequency of 44%. Our finding surpassed the 15.1% observed in Taiwan (11) and the 27.4% recorded in Saudi Arabia (12). Research findings, along with information from other sources, indicate a significant variation in the prevalence of H. pylori infections globally. Tsongo et al. (13) indicated that the discrepancies in findings are likely attributable to variations in the study population, encompassing urban inhabitants, age, and health status of the subjects. Research conducted by Biernat et al. (14) and Ozbey et al. (15) has demonstrated that lower socioeconomic position, sanitary conditions, educational background, and the proportion of immigrant children from nearby cities are significant risk factors for H. pylori infection among youngsters.

Insulin resistance, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, autoimmune liver and biliary disorders, liver fibrosis, and cirrhosis have all been linked to H. pylori infection in numerous studies. (16).

Our research indicates a significant correlation between hepatic conditions in pediatric patients and H. pylori infection. Hepatomegaly and dyspepsia were more prevalent in children who were infected with

H. pylori. Although there was no apparent hepatic damage indicated by liver enzyme levels, the elevated incidence of fatty liver markers suggests that H. pylori may contribute to the onset of NAFLD.

Previous research has indicated comparable outcomes in adults, linking H. pylori to hepatic illness and metabolic dysfunction. A study by Barakat et al. (5) found H. pylori infection as an independent risk factor for NAFLD in children. Furthermore, H. pylori infection has been associated with a disruption of lipid metabolism, evidenced by a notable elevation of cholesterol and triglyceride levels in the infected individuals observed in our investigation.

A study carried out by De Giacomo et al. (17) that include a school population with a sample size of 808 individuals aged 6 to 19 years established a significant association between severe epigastric discomfort and infection with H. pylori (5.3% vs. 1.7%; OR: 3.2; p = .04). In addition, they reported that fasting discomfort (28.4% vs. 18.7%; OR: 1.7; p = .029), recurrent vomiting (24.2% vs. 14.9%; OR: 1.8; p = .025), and acid reflux (8.4% vs. 3.9%; OR: 2.2; p = .047) were all statistically correlated with H. pylori infection.

Barakat et al. (5) identified H. pylori infection as an independent predictor of NAFLD in the pediatric population (OR 95% CI 5.021 (1.105–22.815). Yan et al. (18) noted a comparable outcome in adults (95% CI 1.02–1.79, OR 1.35, p = 0.036), Sumida et al. (19) (95% CI 1.111–7.644, OR 2.915, p = 0.03), and Mostafa et al. (20) (95% CI 1.967–16.130, OR 5.632, p = 0.001).

This discovery may influence clinical procedures such as screening and management.

In contrast to our findings, a study conducted by Abo-Amer et al. (16) demonstrated that liver enzymes (AST and ALT) were statistically elevated in cases infected with H. pylori compared to those without infection. This corroborates the findings of Sumida et al. (19), who identified a considerable disparity in AST and ALT levels between groups with and without H. pylori infection. This discrepancy may be attributed to variations in the age group of the study population, sample size, and measuring methodology.

H. pylori infection is markedly correlated with increased lipid levels: 8.3% of H. pylori-positive individuals had high total cholesterol (none in the negative group, p=0.043), and 22.9% demonstrated higher triglycerides (2.13% in the negative group, p=0.002). No substantial differences were noted for HDL-C and LDL-C ($p > 0.05$). A study by Haeri et al. (21) indicated that individuals with H. pylori seropositive status exhibited markedly elevated levels of total cholesterol and triglycerides compared to those without the illness.

Furthermore, the study by Hashim et al. (22) revealed markedly elevated Triglyceride, total cholesterol, and LDL-c values in H. pylori-infected individuals relative to healthy individuals ($p < 0.001$, $p = 0.041$, and $p < 0.00$, respectively). A study by Tindberg et al. (23) done in Korea revealed that H. Pylori is linked to elevated levels of total cholesterol and LDL-c.

Although our work offers valuable insights, specific limitations must be acknowledged. The cross-sectional design inhibits the establishment of causality. Moreover, the dependence on ultrasonography for the diagnosis of NAFLD, albeit non-invasive, exhibits lower sensitivity compared to liver biopsy or MRI evaluations. Future investigations necessitate bigger sample sizes and longitudinal follow-ups to examine this association.

CONCLUSION

Children with H. pylori infection exhibited markedly elevated incidences of hepatomegaly and epigastric pain. Furthermore, H. pylori infection was associated with increased cholesterol and

triglyceride levels, indicating a possible contribution to the development of NAFLD. Further work is required to validate these results and explore potential processes behind this connection.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (112-117) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Association between Helicobacter Pylori Infection and Platelet Indices among the pediatric population in Aswan

Magda F Gabri[1], Hanan M. Abd-El Moneim[1], Mostafa O Mohammad[1*], Mousa Mohsen[1], Edress H. Zaki[2]

[1] Pediatrics Department, Faculty of Medicine, Aswan University.

[2]Pediatrics Department, Faculty of Medicine, Assiut University

ABSTRACT

Keyword: H. Pylori, platelets, children

[*] **Corresponding author**: Mostafa Omar Mohammad
Mobile: +201069280855
E-mail: mostafaomar040@gmail.com

Background: Clinical studies on adults in developed countries have linked Helicobacter pylori infection with thrombocytopenia. However, there is extremely limited study in children, particularly in developing countries.**Objectives**: To investigate the effect of H. pylori infection on platelet indices in children. **Methods:** This observational cross-sectional study included 195 children with dyspepsia recruited from the gastroenterology pediatric department of Aswan University Hospital. **Results:** Children with *H. pylori* infection had significantly lower hemoglobin levels (11.015 ± 1.109 g/dL vs. 11.553 ± 1.00 g/dL, p=0.015), reduced platelet counts (p=0.004), and higher prevalence of low MCV (64.6% vs. 25.5%, p<0.001), low MCH (20.8% vs. 2.13%, p=0.004), leucopenia (27.1% vs. 8.5%, p=0.018), and low MPV (22.9% vs. 4.3%, p=0.014) compared to *H. pylori*-negative children. **Conclusion:** *H. pylori* infection is associated with hematological alterations, including lower hemoglobin levels, reduced platelet indices, and altered red cell indices, suggesting its potential role in anemia and nutritional deficiencies.

INTRODUCTION

Helicobacter pylori is a widespread chronic infection globally. Its prevalence varies by geographic region, often persisting due to reinfection and inadequate eradication efforts. Socioeconomic factors significantly contribute to its transmission [(1)]. Beyond its well-established role in gastrointestinal disorders, *H. pylori* has been linked to conditions such as inflammatory bowel disease, gastroesophageal reflux disease, non-alcoholic fatty liver disease, and even hematological and metabolic disorders [(2)]. Infected children exhibit higher rates of anemia and stunted growth than their uninfected counterparts [(3)].

Evidence suggests a relationship between *H. pylori* and idiopathic thrombocytopenia (ITP). Although the exact mechanism remains unclear, one hypothesis involves the cytotoxin-associated gene A (CagA), which may trigger the production of cross-reactive antibodies that affect platelet function [(5)]. While studies in adults from high-income countries suggest a link, there is limited data on pediatric populations in low-income regions where *H. pylori* prevalence is high [(6)].

This study evaluates the effect of *H. pylori* infection on platelets in children presenting to Aswan University Hospital.

PATIENTS AND METHODS

This observational cross-sectional study included children aged 6-15 who were presented with dyspepsia at the gastroenterology outpatient clinic of Aswan University Hospital. A stool antigen test confirmed an H. pylori infection. Children with chronic liver disease, obesity, metabolic syndrome, or diabetes mellitus were excluded.

Comprehensive data collection included medical history, demographic details, anthropometric measurements, and systemic examination. Laboratory investigations comprised of complete blood count (CBC), fasting plasma glucose, glycosylated hemoglobin (HbA1c), and *H. pylori* stool antigen testing.

To evaluate the H. pylori antigen, approximately 1 g of stool from each child was collected in a 5 ml sample diluent using an Enzyme Immunoassay Test (ELISA) technique kit (Eagle Biosciences, Inc., Amherst, NH, USA) [(7)].

Statistical Analysis:

We used IBM SPSS version 27 to analyze the data. The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to determine normalcy. Numerical variables were presented as means and standard deviations, whereas categorical variables were displayed as frequencies and percentages. Depending on the situation, chi-square, Fisher's exact, independent t-tests, or Mann-Whitney tests were used to compare the groups. Statistical significance was defined as a p-value <0.05.

Ethical Approval: The Institutional Ethics and Research Review Board of Aswan University approved the study. Parents gave written informed consent before enrollment, adhering to the Declaration of Helsinki guidelines.

RESULTS

This study included 195 children with a mean age of 10.5 ± 2.57 years; 43.6% were male, and 50.3% resided in urban areas (table 1).

Table (1): Patients' demographic characteristics (n=195)

Variables		Frequency (Percentage %)	
Gender	Male	85 (43.6%)	
	Female	110 (56.4%)	
Age (years)	6 - 9.50	105 (53.8%)	
	10-15	90 (46.2%)	
	Mean ± SD	10.5 ± 2.5697	
Residence	Urban	98 (50.3%)	
	Rural	97 (49.8%)	
		Mean ± SD	**Median (range)**
Weight (kg)		24 ± 7.8898	23 (14.50-54)
Height (cm)		119.1 ± 15.328	119 (92-160)

Body mass index (Kg/m^2)	16.35 ± 1.8	16.1 (12.30-21.50)
H. Pylori + ve cases	102 (52.3%)	

Table 2 shows children with *H. pylori* infection had significantly lower median Height-for-Age Z-scores (p<0.001) and higher rates of stunting (25.4% vs. 6.5%, p=0.013). Additionally, *H. pylori*-positive children had lower BMI-for-Age Z-scores, with a higher prevalence of wasting (27.45% vs. 4.3%, p<0.001). No significant difference in Weight-for-Age Z-scores was observed (p>0.05).

Table (2): Impact of H. pylori infection on nutritional status

Parameters		**H. Pylori status**		**P value**
		Positive (n=102)	Negative (n=93)	
		N (%)	N (%)	
Height-for-age Z-score (HAZ)	Normal	76 (74.6%)	87 (93.5%)	**0.013***
	Stunted	26 (25.4%)	6 (6.5%)	
	Median (IQR)	-1.445 (-1.975-0.8775)	-2.23 (-2.69-(-1.78))	**<0.001****
Weight-for-age Z-score (WAZ)	Normal	53 (52%)	41 (44.1 %)	0.470
	Underweight	49 (48%)	52 (55.9 %)	
	Median (IQR)	-0.945 (-1.84- (-0.3875))	-1.030 (-1.410- (-0.68)	0.967
BMI for age Z-score	Normal	72 (70.59 %)	68 (73.1 %)	**<0.001***
	Wasted	28 (27.45%)	4 (4.3 %)	
	Overweight risk	2 (1.96 %)	21 (22.6 %)	
	Median (IQR)	0.285 (-0.965-0.46)	0.60 (0.16-1.06)	**<0.001****
Weight for height Z-score (WHZ)	**Median (IQR)**	0.325 (-0.7775-0.7125)	0.750 (0.32-1.30)	**0.005****

Table 3 shows laboratory findings indicated significant differences between *H. pylori*-positive and negative children in terms of hemoglobin levels (p=0.015), MCV (p<0.001), MCH (p=0.004), leucopenia (p=0.018), and platelet counts (p=0.004). Mean platelet volume (MPV) was also significantly lower in *H. pylori*-positive children (p=0.014).

Table (3): Laboratory findings of study children (n=195)

Parameters	**Mean ± SD**	**Median (range)**
HBA1c (%)	5.001 ± 0.2946	5 (4.50-5.70)
Complete blood count (CBC)		
WBCs (×10^3/ µL)	6.938 ± 2.2231	7 (2-12.7)
Hemoglobin (g/ dL)	11.281 ± 1.0853	11.50 (9-13.50)
MCV (FL)	75.624 ± 9.8873	77 (8.2-90)
MCH (pg.)	27.814 ± 2.7736	28 (20.1-34)
Platelets (×10^3/ µL)	209.04 ± 52.849	199 (88-420)
MPV (FL)	8.141 ± 0.7017	8 (7-10.6)

Table 4 reveals a statistically significant correlation of H. pylori infection with MCV and MCH (p = 0.004), WBC (p = 0.004). Leucopenia was found in 27.1% of H. pylori-positive patients and 8.6% of H. pylori-negative patients. Besides, platelet count was highly reduced in H. pylori-positive patients compared to H. pylori-negative patients. Finally, a significant correlation was determined for H. pylori infection and mean platelet volume (MPV), being low in 20.59% of the H. pylori infections versus 2.15% of the H. pylori negativities (p = 0.014).

Table (4): Association between H. Pylori infection and hematological parameters

Parameters		H. Pylori status		P value
		Positive (n=102)	Negative (n=93)	
		N (%)	N (%)	
Hemoglobin (gm/dL)	Anemia (<11.5)	59 (57.8%)	35 (37.6%)	0.051
	Normal (≥11.5)	43 (42.2%)	58 (62.4%)	
	Mean ± SD	11.015 ± 1.109	11.553 ± 1.00	**0.015****
MCV (FL)	Low (≤75 FL)	64 (62.7%)	24 (25.8%)	**<0.001***
	Normal (> 75 FL)	38 (37.2%)	69 (74.2%)	
	Mean ± SD	73.44 ± 6.9896	77.855 ± 11.823	**0.029****
MCH (Pg.)	Low (<25)	21 (20.6 %)	2 (2.15%)	**0.004***
	Normal (>25)	81 (79.4%)	91 (97.85 %)	
	Mean ± SD	27.423 ± 3.302	28.213 ± 2.0635	0.165
WBCs (×10^3/µL)	Leucopenia	13 (27.1%)	8 (8.6%)	**0.018***
	Normal	35 (72.9%)	85 (91.4%)	
	Mean ± SD	6.571 ± 2.4003	7.313 ± 1.9822	0.104
Platelets (×10^3/µL)	Thrombocytopenia	13 (12.7 %)	2 (2.15 %)	0.053
	Normal count	89 (87.3 %)	91 (97.85 %)	
	Mean ± SD	193.77 ± 42.22	224.64 ± 58.258	**0.004****
MPV (FL)	Low (<7.5)	21 (20.59 %)	2 (2.15 %)	**0.014***
	Normal (7.5-10)	79 (77.45%)	89 (95.7 %)	
	High (>10)	2 (1.96 %)	2 (2.15%)	
	Mean ± SD	7.84 ± 0.6153	8.449 ± 0.654	**<0.001****

DISCUSSION

Platelets play a crucial role in hemostasis and immune regulation. Previous studies indicate that *H. pylori* affect platelet count and function, potentially contributing to hematological abnormalities. In chronic ITP patients, platelet counts often improve following *H. pylori* eradication [(8)].

In this study, *H. pylori*-infected children exhibited significantly lower hemoglobin levels, platelet counts, and MPV. These findings align with prior research indicating an association between *H. pylori* and anemia, due to chronic gastritis-related blood loss and impaired iron absorption. The bacterium reduces gastric acid secretion, which may promote enteropathogen colonization, diarrhea, malabsorption, and subsequent iron deficiency anemia [(9)].

Several studies support the relationship between *H. pylori* and hematological alterations. **Bille et al.** [(10)] reported a high prevalence of microcytic hypochromic anemia in infected children. Similarly, studies from Ethiopia, Sudan [(11)], and Pakistan [(12)] found lower platelet counts among *H. pylori*-infected

individuals. However, research from the Netherlands [13] did not identify significant differences, due to variations in study populations and methodologies.

Elevated MPV levels in some *H. pylori*-infected individuals may indicate a compensatory response to platelet destruction. Increased MPV reflects young platelet production, a common response to systemic inflammation. This variability underscores the complexity of *H. pylori*-related hematological effects and the need for further investigation [14].

In the current research, H. pylori-positive cases also presented significantly lower median Height-for-Age Z-scores, BMI-for-age Z-score, and a higher prevalence of wasting ($p < 0.001$). The median Weight-for-Height Z-score was significantly lower among H. pylori-positive cases ($p = 0.005$). No significant difference between the groups was noted for Weight-for-Age Z-scores ($p > 0.05$). Early childhood growth measures have been correlated with H. pylori. There is a great heterogeneity in the findings of research looking at the impact of H. pylori infection on a child's growth. H. pylori infection has been correlated in numerous studies with a decrease in the growth of children [15, 16, 17]. Cross-sectional studies from several countries, however, show no correlation [18].

This may be explained by the fact that H. pylori decrease the production of gastric acid, which can result in an enteropathogenic infection that can cause diarrhea, nutrient malabsorption, decreased food intake because of dyspepsia, and iron-deficiency anemia [19]. However, with so many confounding variables, such as diet and socioeconomic status, it is difficult to prove that H. pylori alone cause growth impairment in children.

CONCLUSION

This study highlights a significant association between *H. pylori* infection and reduced platelet indices in children, supporting a potential role in anemia and altered hematological profiles. Further longitudinal research is warranted to establish causality and explore the underlying mechanisms.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (118-125) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Comparative Study of Induction of Labour at term by Misoprostol Vaginal Insert versus Dinoprostone Vaginal Insert

Mohamed Salah El Deen Fahmy[1], Hany Ahmed Farouk[1], Mohamed Ali Abd El Rahman Anan[1], Aly Abdel-bagy Mohamed[1], Mohamed Hamed Mekky Mohamed[1*]

[1]Department of Obstetrics & gynecology Faculty of Medicine, Aswan University

ABSTRACT

Keyword: Induction of Labour, Misoprostol Vaginal Insert, Dinoprostone Vaginal Insert, Outcome

[*] **Corresponding author**: Mohamed Hamed Mekky Mohamed
Mobile: +201032142444
E-mail: mekky.h.mohamed@gmail.com

Background: Inducing labor risks inefficient contractions (fetal hypoxia) or excessive activity (uterine rupture), often from induction agents. **Objectives:** Compare 25µg vaginal misoprostol vs. 3mg dinoprostone for term labor induction. **Methodology:** Compare 25µg vaginal misoprostol vs. 3mg dinoprostone for term labor induction. **Results:** Regarding delivery outcomes in two groups, Vaginal delivery: 80% success (A) vs. 88% (B). **CS rates**: 20% (A; 2 for failed induction, 3 for bradycardia) vs. 12% (B). **Time to deliver**: Dinoprostone faster (327 vs. 613 min; *p<0.05*). **Safety**: Comparable side effects (*p>0.05*). **Neonatal outcomes**: mean APGAR 8 (both groups); NICU admissions: 2 per group **Conclusion:** According to the results of our study, Dinoprostone gives less time and can beused safely in induction of labour.

INTRODUCTION

An essential component of obstetric practice is labor induction. It is mostly used in modern obstetrics when carrying a pregnancy to term could endanger the mother, the fetus, or both **(**1**).**

Traditionally, oxytocin infusion has been used to induce labor; however, multiple investigations have demonstrated that this method does not produce equally satisfying outcomes in cases of unfavorable cervical anatomy **(2)**.

The principal concerns related to labor induction are ineffective contractions and excessive uterine activity, which may lead to fetal hypoxia and increase the risk of complications **(3)**.

oxytocin was synthesized in the 1950s, and since then, the treatment of labor induction has been frequently employed to facilitate delivery by stimulating uterine contractions before spontaneous labor begins (**4)**.

Prostaglandins are frequently employed to induce labor in women who have a postdate pregnancy or a problematic pregnancy with conditions such as preeclampsia, diabetes mellitus, intrauterine fetal growth retardation, or fetal distress **(5)**.

An analogue of prostaglandin E1, misoprostol is approved for use in the management and prevention of peptic ulcers.For obstetric indications of inducing labor and abortion, it is commonly utilized. By

binding specifically to EP-2/EP-3 prostaglandin receptors, it functions as an efficient myometrial stimulant in the uterus of a pregnant woman **(6)**.

The US Food and Drug Administration has approved dinoprostone (prostaglandin E2) vaginal inserts for cervical ripening in women who are full term. These inserts have historically been used for cervical priming. Dinoprostone is costly, must be refrigerated, inserted into the cervix, and many patients need extra oxytocin augmentation during labor induction **(7).**

The objective of the research was to evaluate the effectiveness and safety of two methods for inducing labor at term: 25µg vaginal misoprostol and 3mg dinoprostone vaginal insertion.

PATIENTS AND METHODS

This was a randomized controlled, single blind trail conducted on 50 patients who were candidates for labor induction at term. The low-risk patients with unfavorable cervices before induction of labor were targeted at Obstetrics & Gynaecolog department, Aswan University Hospital, Egypt from march 2023 to september 2023.

Inclusion criteria: Age less than 35 years, gestational age ≥ 36weeks, Singleton pregnancy, multigravida (Para1, 2, 3), A reactive cardiotocographic trace with a Bishop score of five or lower prior to the onset of labor.

Exclusion criteria: Individuals experiencing active labor, symptoms and signs indicative of chorioamnionitis, signs of fetal distress, such as the presence of other maternal or fetal factors that contraindicate induction of labor, and meconium or a non-reassuring cardiotocographic trace. Premature rupture of the membranes 24 hours or more prior to the commencement of treatment, if the gestational age is under 36 weeks. Severe preeclampsia and a body mass index above 50.

Methods

The following were administered to the eligible subjects included in this investigation:

Full history involving: Personal, obstetric, menstrual, past, family history and history of present pregnancy**, Clinical examination including:** General examination: Vital signs, heart, chest, and lower limb examination and anthropometric evaluation included weight in kilograms (Kg) and height in centimeters (cm), **abdominal examination:** in order to evaluate the fundal level, the location and orientation of the foetus, the anticipated weight of the foetus, the foetal heart rate, and the existence of scars from prior operations such as myomectomy or cesarean sections and **vaginal examination:** in order to evaluate the cervical position, dilatation, consistency, length, and head station (using a modified version of Bishop's score, in addition to checking the state of the membranes, pelvic capacity, positioning, and presentation).

Investigations

Laboratory investigations: 5 millimeters was drawn from each patient once and blood grouping and Rh typing, CBC, urine analysis, screening of diabetes mellitus were done, **Abdominal ultrasound:** Following the transvaginal sonography (TVS) examination, a digital vaginal exam was carried out to evaluate the cervical consistency, effacement, dilation, position, and station of the presenting part. The Burnett modification was used to compute the bishop score, which was subsequently used to confirm the gestational age, fetal number, viability, presentation, position, estimated fetal weight, and grade of placental maturity **(8)** and **CTG:** Evaluation through the implementation of fetal heart rate tracing.

Enrollment & Allocation of the patients

A computer-generated random schedule was employed to designate individuals to one of the two study groups: Group (A): all patients received 25µg misoprostol inserted in the posterior

vaginal fornix by the physician in the delivery suite (given every 4hrs for a maximum of 3 doses or until active labor started) **(9)** and **Group (B):** The physician in the delivery suite inserted 3mg dinoprostone into the posterior vaginal fornix of all patients at a 6-hour interval, with a maximum of two doses or until active labor commenced **(9)**. The progression of labor was monitored. The duration of the active phase of labor and the time until delivery was recorded. Assignments were concealed by placing them in opaque, sealed envelopes that were consecutively numbered and drawn in a specific order. Before the designated treatment administration, the envelope was opened. The intervention was known to the physician, while the mothers were unaware of the preparation they received. Treatment allocation was not subject to modification. Mothers withdrew from the study after they requested an alternative treatment.

Follow up

Cardiotocography (CTG) was conducted after 120 minutes of each dose to confirm fetal wellbeing and assess uterine contractions. Patients were examined abdominally and vaginally at 4 hours intervals in the misoprostol group and at 6 hours intervals in the dinoprostone group. The next dose was administered if no uterine contractions or unfavorable cervices were found. Active labor or reaching the maximum dose of the medicine caused the dosage to be stopped. When patients' membranes were still intact when they entered the active phase of labor, they were given an AROM. Examining the vagina every four hours during active labor allowed for the evaluation of cervical dilatation, effacement, state of liquor, head station, and moulding, among other outcomes. The use of electrocardiotocography or Sonicade for continuous fetal monitoring was performed as prescribed. The women were observed using a digital adaptation of the World Health Organization partograph, which incorporates an alert line to indicate the anticipated cervical dilatation and an action line to be drawn four hours later. In the initial stage of labor, when the action line was passed, labor dystocia was detected. During the second stage of labor, labor dystocia was identified when either the latent period or the ejection phase extended more than an hour.

Outcome measures

The primary outcome measure: The interval from medication insertion to delivery, also known as the induction to delivery interval. **While secondary outcomes include Maternal outcomes:** Mode of delivery, uterine hyperstimulation, rate of occurrence of nausea &vomiting and **Pyrexia:** Defined as maternal temperature of ≥ 38C. **Fetal outcomes:** Admissions to the NICU and Apgar scores at 1-5 minutes.

Ethical Consideration

Confidentiality: All participants in this investigation were guaranteed confidentiality to the greatest extent possible. The study participants will not be identified in any report or publication that is as a result of the data collected in this research. **Research statement:** This study raised questions of ethics, both in terms of substance and methodology. All patients were informed of the study's goals, procedures, and potential dangers before they were allowed to participate. In order to participate in this study, participants must acknowledge that it is an investigational study, that there are risks and benefits associated with it, that they can withdraw from it at any time without compromising their right to adequate healthcare at the study site, that they will be able to reach someone with questions about the study, and that their participation is voluntary and informed. **Informed consent:** In the same way as her other records, the participant's signed informed consent form was a permanent component of the research records.

RESULTS

Table (1): Comparison between studied cases according to Demographic data

	Group A (n = 25)		**Group B (n = 25)**		**p-value**
Age (years)					
Range.	20 – 35		23 – 35		0.642
Mean ± SD.	28 ± 4.64		28.4 ± 3.33		
BMI					
Range.	23.7 – 31.7		23.9 – 31.8		0.642
Mean ± SD.	27.47 ± 2.49		28.05 ± 2.56		
Parity	No.	%	No.	%	
1	16	64.0	12	48.0	0.290
2	7	28.0	8	32.0	
3	0	0	3	12.0	
4	1	4.0	2	8.0	
5	1	4.0	0	0.0	
Previous abortion	No.	%	No.	%	
No	23	92.0	23	92.0	1.0
Yes	2	8.0	2	8.0	
Gestational age					
Range.	36 – 42		36 – 42		0.156
Mean ± SD.	38.8 ± 2.14		39.64 ± 1.98		
Bishop score					
Range.	1 – 4		1 – 4		0.070
Mean ± SD.	2.64 ± 1.19		2.04 ± 1.1		

The mean age was 28 years old ± 4.64, and the mean BMI was 27.47 ±2.49, all study subjects were multi para with mean gestational age of 39 weeks. (Table 1)

Table (2): Comparison between examined cases in accordance with Delivery outcomes

	Group A(n = 25)		**Group B(n = 25)**		**p-value**
	No.	%	No.	%	p
Vaginal delivery	20	80.0	22	88.0	0.157
Cesarean section:	5	20%	3	12%	0.157
Failure of induction	2	8%	2	8%	
Emergency CS due tofetal bradycardia	3	12%	1	4%	

Induction to labortime (min)					
Range.	549 – 677		250 – 447		0.003*
Mean ± SD.	613 ± 63.25		327 ± 37.14		
Labor duration(min)					
Range.	205 – 410		211 – 520		0.076
Mean ± SD.	263.24 ± 83.81		358.6 ± 127.46		
Oxytocin use	7	28.0	11	44.0	0.239
Tachysystole	10	40.0	3	12.0	0.024*
Tocolysis use	5	20.0	1	4.0	0.612

Regarding delivery outcomes in two groups, In Group A, 20 cases of successful vaginal delivery were reported, with 5 cases requiring CS. Two cases were due to induction failure and three to severe fetal bradycardia. The mean induction time was 613 minutes. In Group B, 22 cases had successful vaginal delivery, with 3 cases requiring CS. The mean induction time was 327 minutes. (Table 2)

Table (3): Comparison between examined cases in accordance with maternal complications

	Group A(n = 25)		**Group B(n = 25)**		**p**
Side effects	No.	%	No.	%	
excessive vomiting	14	56.0	15	60.0	0.772
Diarrhea	6	24.0	9	36.0	0.355
epigastria pain	14	56.0	10	40.0	0.258
Pyrexia	7	28.0	8	32.0	0.758
Delivery complications					
uterine ruptureOASIS*	0	0%	0	0%	0
Post partum hemorrhage	1	4%	1	4%	0.286
	6	24%	5	20%	0.733

* OASIS: Obstetrical anal sphincter injuries

Regarding maternal complication of study subjects, it showed vomiting was about 56% in group A and 60% in group B, also the cases with pyrexia where 7 in the first group and 8 cases in the second group, and regarding the delivery complication, there was no case of uterine rupture, only one case of OASIS in each group, also, there was 6 cases had postpartum hemorrhage in group A and 5 cases in group B, there was no significant variance between two groups concerning Side effects and delivery complications p>0.05. (Table 3)

Table (4): Comparison between examined cases in accordance with fetal outcomes

	Group A(n = 25)		**Group B(n = 25)**		**P-value**
Complications	No.	%	No.	%	P
Apgar score 5					
Range.	6 – 10		6 – 10		0.449
Mean ± SD.	8.4 ± 1.19		8.12 ± 1.39		
NICU admissions	2	8.0	2	8.0	1.0

Regarding fetal complications among the study subjects, in Group A and Group B the mean APGAR score was 8 while 2 neonates in each group required early NICU admission. There was no significant variance regarding Apgar score 5 and NICU admissions p= 0.449, 1.0 respectively. (Table 4)

DISCUSSION

The medical practice of inducing labor is an essential component of obstetrics. It is most commonly attempted in contemporary obstetrics when continuing the pregnancy could be harmful to either the mother or the fetus or both. Oxytocin infusions have been the standard method for inducing labor for many years, however a large number of studies have demonstrated that this method is unable to provide similarly satisfying results in women who have an unfavorable cervix **(10)**.

In terms of the demographic data collected from the study subjects, such as their age, gestational age, parity, BMI, physical examination, modified Bishop's score, and laboratory examinations, no significant distinction was found among the groups. The findings were comparable to those of **Maggi et al.,** who assessed the efficacy of a vaginal insert containing 200 μg of misoprostol against a vaginal insert containing ten milligrams of dinoprostone in facilitating labor induction in women with an unfavorable cervix. Participating in the trial were 220 women; 109 (49.5%) were given MVI and 111 (50.5%) were given DVI. The research displays demographic information as well as baseline characteristics. There was little difference between the two groups with regard to maternal age, BMI, method of conception, and Bishop score **(10)**.

In this study, **Ayaz et al.** aimed to evaluate the safety and effectiveness of two methods for elective induction of labor in women who had never given birth before: intravaginal misoprostol and dinoprostone. Among the 120 participants in the study, 78 (or 65%) were younger than 25 years old, while the remaining 30 were older than 25 years old. Both Groups had similar mean ages; Group A was 23 and Group B was 25. After the insertion of a single dose, 18 (30%) subjects in Group A experienced active labor, while only eight (14%) in Group B went into labor **(11)**.

In accordance with **Sire et al.,** there was no significant variance between the two groups in terms of instrumental deliveries. Cesarean delivery was significantly more prevalent in the misoprostol group ($p = 0.005$) due to abnormal fetal heart rate **(12)**.

Consistent with this investigation, there were statistically significant variations between the groups with regard to of tachysystole and induction to labor time. Our results contradict those of **Maggi et al.,** who reported no difference in the probability of surgical vaginal delivery; rather, they observed that women induced with MVI had a higher likelihood of vaginal birth compared to those induced with DVI (88% vs 74%, P = 0.007). The MVI group exhibited a significantly shorter median interval from drug administration to the onset of labor and from drug administration to delivery in comparison to the DVI group **(10)**.

Misoprostol had a significantly reduced median duration between induction and labor onset in contrast to dinoprostone (855 min vs 1740 min; P < 0.001), which is in line with the findings of **Wing et al (13)**.

Misoprostol and dinoprostone vaginal inserts were tested for inducing labor with intact membranes in a recent research by **Mlodawski et al.** Consistent with our findings, they also found that vaginal misoprostol increased the incidence of cesarean section (OR 2.71 95% CI 1.63-4.47). While misoprostol has been the subject of numerous research in recent years, very few have examined PROM as an individual case **(14)**.

Kerr et al. performed a review encompassing thirteen randomized trials that compared low-dose oral misoprostol with vaginally administered dinoprostone. The findings indicate that oral misoprostol is associated with a reduced incidence of cesarean sections compared to vaginal dinoprostone (RR 0.84, 95% CI 0.78–0.90; 13 trials, 9676 women; evidence of moderate uncertainty). However, it was found that most trials included women with both intact and ruptured membranes, complicating the conduct of meaningful analyses. Furthermore, the analysis revealed a significant imbalance among the subgroups **(15)**.

Wang et al. reported that neonatal outcomes 5, there was not a significant distinction in neonatal Apgar ratings of seven or higher at the intervals of one, five, and ten minutes. In addition, there was not a significant variation in the rates of meconium-stained fluid or neonates admitted to the NICU. Vaginal dinoprostone was associated with a significantly higher frequency of non-reassuring fetal heart rates than OMS (p = 0.04) **(16)**.

CONCLUSION

According to the results of our study, Dinoprostone gives less time and can be used safely in induction of labour

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (126-134) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Efficacy of adding Glucose Co-transporter 2 -Inhibitors in Treatment of Non-Valvular Paroxysmal Atrial Fibrillation

Ramadan G Mohamed, Naggeh M. Mahmoud, Aml M. Soliman, Esraa A. Abdelaziem

*Department of Cardiology, Faculty of Medicine, Aswan University, Egypt

ABSTRACT

Keyword: AF, SGLT2, MACE, Efficacy.

* **Corresponding author**: Esraa A. Abd-Elaziem

Mobile: +201150723777

E-mail: essraa.abozied94@gmail.com

Background: In individuals with type 2 diabetes mellitus, SGLT2 inhibitors have been demonstrated to lower blood pressure, decrease weight, improve left ventricular remodeling, and decrease hospitalization for heart failure and cardiovascular death. **Objectives:**The aim of this study was to evaluate the efficacy of SGLT2 inhibitors on the AF cardiovascular outcome. **Methodology:**This single-blinded randomized controlled trial was carried out on 60cases with non-valvular paroxysmal atrial fibrillation at the cardiology department, Aswan University Hospitals. **Results:**the change in LAD% and LAV-i% was significantly lower in group A (those who received SGLT2 inhibitors) compared to group B (those who did not receive SGLT2 inhibitors), both in absolute terms and relative terms. In the same way, LAS absolute and relative % change showed a significant improvement in the study group compared to control**.** After adjusting for all correlates, it was found that adding SGLT-2 to the standard treatment resulted in reduction of the risk of MACE by 32% (AOR= 0.678, 95% CI; 0.071 – 0.984, p=0.043) compared with those treated with the standard regimen.**Conclusion:**the addition of SGLT-2I to patients' existing guideline-directed medical therapy for non-valvular paroxysmal AF was found to be independently associated with reduction in the short-term adverse effects of the disease.

INTRODUCTION

With an estimated prevalence of about 3% in adults aged ≥20, atrial fibrillation (AF) is the most prevalent arrhythmia in the world. It is considerably more common in those with diseases including hypertension, valvular heart disease, or chronic kidney disease**(1)**.

In order to prevent glucose reabsorption, increase urine glucose excretion, and lower blood glucose levels, sodium glucose cotransporter-2 (SGLT-2) inhibitors were created to specifically inhibit these transporters, which are only present in the kidneys' proximal convoluted tubule**(2)**.Several trialshad demonstrated the cardiovascular benefits of these medications on management of AF **(3-8)**. In individuals with type 2 diabetes mellitus, SGLT2 inhibitors have been demonstrated to lower blood pressure, decrease weight, improve left ventricular remodeling, and decrease hospitalization for heart failure and cardiovascular death**(9)**.

A post-hoc analysis of the DECLARE-TIMI 58 study revealed that dapagliflozin decreased the incidence of AF and atrial flutter-related events in type 2 DM patients, irrespective of their prior history of AF or atrial flutter. This finding pertains to the direct effects of SGLT2 inhibitors on AF**(9)**.

SGLT2 inhibitors may lower atrial fibrillation and atrial flutter as well as all-cause mortality in patients with type 2 diabetes, according to a meta-analysis of 16 trials. These results imply that by decreasing and/or reversing structural and electrical remodeling, SGLT2i may have anti-arrhythmic benefits**(10)**. The direct impact of SGLT2 inhibitors on left atrial remodeling in non-valvular paroxysmal atrial fibrillation, independent of diabetic status, has not yet been investigated.
The aim of this study was to evaluate the efficacy of SGLT2 inhibitors (dapagliflozin) on LA remodeling in non-valvular paroxysmal AF and on AF cardiovascular outcome.

PATIENTS AND METHODS

This study adopted a double-blinded Randomized Controlled Clinical Trial (RCT)and was carried out on 60cases with non-valvular paroxysmal atrial fibrillation at the cardiology department, Aswan University Hospitals. Sample size was calculated using G Power software version 3.1**(11)**. The alpha error = 0.05, power 80%, and the effect size was 0.4 in the mean of echocardiographic parameters **(2)**. The minimum required sample was60cases (30 cases treated with standard regimen plus SGLT-2and 30 treated with standard regimen only as control).
Non-valvular paroxysmal AF cases aged 18-60 years with Glomerular Filtration Rate (GFR) > 45 ml/min/1.73 m2and with normal or slightly dilated left atrium were included. In contrast, those with valvular heart diseases, hugely dilated LA, GFR <45 ml/min/1.73 m2, ischemic heart disease, or with ischemic stroke were excluded.

Randomization:

Random numbers were generated at the computer center. Eligible cases were randomly assigned into two equal groups i.e., **Group-I (Study group)**: included30patients with AF were treated with rhythm control, anticoagulants based on their CHADs VASc score, plus SGLT2 inhibitors (dapagliflozin), for six months and **Group-II (Control group):** included30patients with AF were treated with rhythm control, anticoagulants based on their CHADs VASc score only. Allocation was contained in opaque, sequentially numbered sealed envelopes.

Procedure

Every visit includes a comprehensive clinical evaluation that includes heart rate, rhythm, and full cardiac examination at baseline and at 6-months, as well as demographic data, other risk factors, past or current medication treatment history, history of an AF attack, and any new complaints or indications of decompensating HF. Thyroid function, serum electrolytes, PT, PC, INR, ECG, laboratory evaluation of diabetic condition and renal functions, and any other research required given the patient's clinical circumstances

Non-invasive Imaging(Transthoracic Echocardiography was performed before treatment and at 6-months follow-up to detect the following i.e., Left atrium antero-posterior diameter in parasternal long axis view, Indexed LAV (LAV-i)**.**

Speckle tracking (STE) analysis of LA was performed to calculate LA strain (LAS)**.**

Following patient evaluation, a block randomization procedure was used to randomly assign the patients to receive medication containing dapagliflozin 10 mg once day. Patients were given one blinded tablet of the experimental drug, dapagliflozin, once daily for six months. Every month, 30 blinded dosages were administered to each participant. To monitor compliance, pill counts were conducted every three months. Both groups were followed up for 6-months to assess LA remodeling, recurrent presentation by paroxysmal AF, mortality rate and HF at hospital.

Statistical analysis: Shapiro-Wilk test and histograms were used to evaluate the normality of the data distribution. Quantitative parametric data, represented as mean and standard deviation (SD),

were evaluated using the unpaired student t-test. Quantitative non-parametric data, represented as the median and interquartile range (IQR), were assessed using the Mann Whitney test. The qualitative data, which were presented as frequency and percentage (%), were evaluated using the Chi-square test or Fisher's exact test as applicable. A p-value below 0.05 was considered statistically significant. The software utilized was SPSS version 26 (IBM Inc., Armonk, NY, USA) **(12)**.

Ethical Consideration: IRB approval was given by the Faculty of Medicine's Medical Ethic Committee at Aswan University (IRB 693/11/22). The study was prospectively registered using clinical trial.gov (NCT05993897). The study was carried out in compliance with the CONSORT checklist for research ethics**(13)**and the guidelines provided in the Helsinki Declaration**(14)**. Before the study began, each patient's informed consent was obtained, and the study's purpose and title were thoroughly stated. All collected data was kept confidential and used only for scientific research. The quality of the medical care that each research participant received was unaffected by their decision to withdraw from the study at any time.

RESULTS

Sixty cases with non-valvular paroxysmal AF participated in this RCT. They were randomly allocated into two equal groups.

As shown in **Fig. 1-3**, both groups were matched for demographic characteristics (age [p=0.694] and sex [p=0.573])**(Fig. 1)**, the main risk factors (smoking [p=0.260], DM [p=452], renal disease [1.000] and HTN [p=0.573])**(Fig. 2)** and Restoration of sinus rhythm (p=0.612).

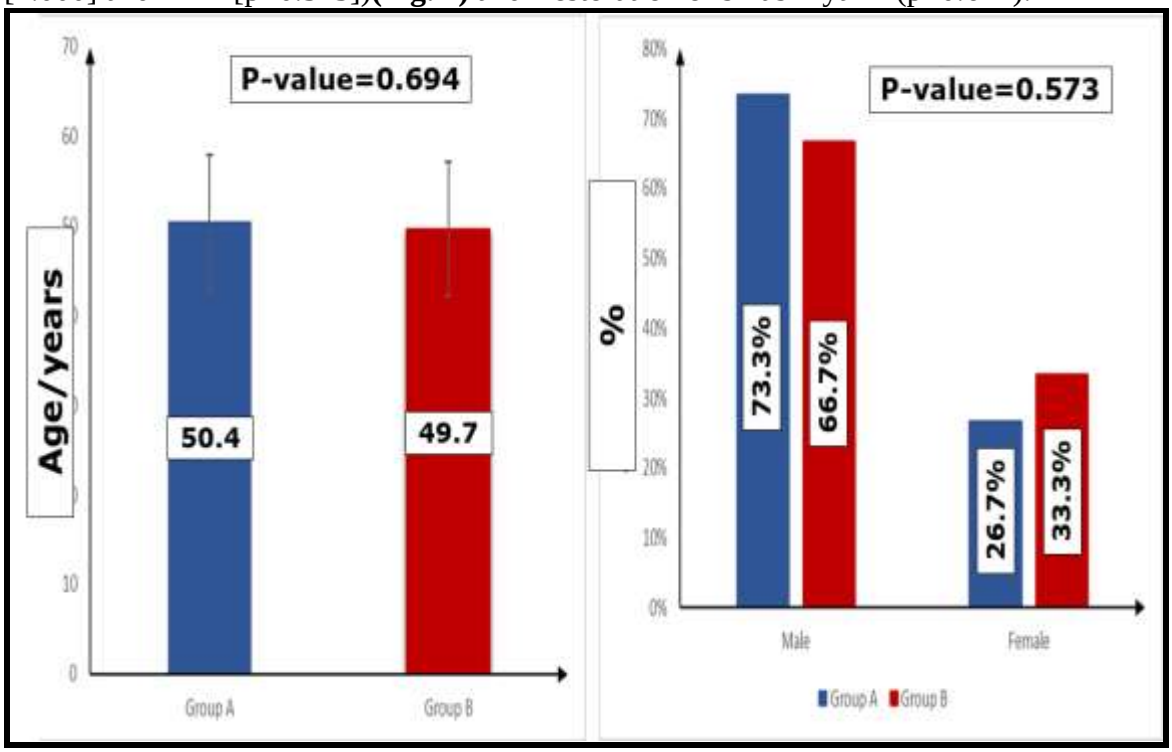

Fig. 1: Age and Sex Distribution of the studied groups

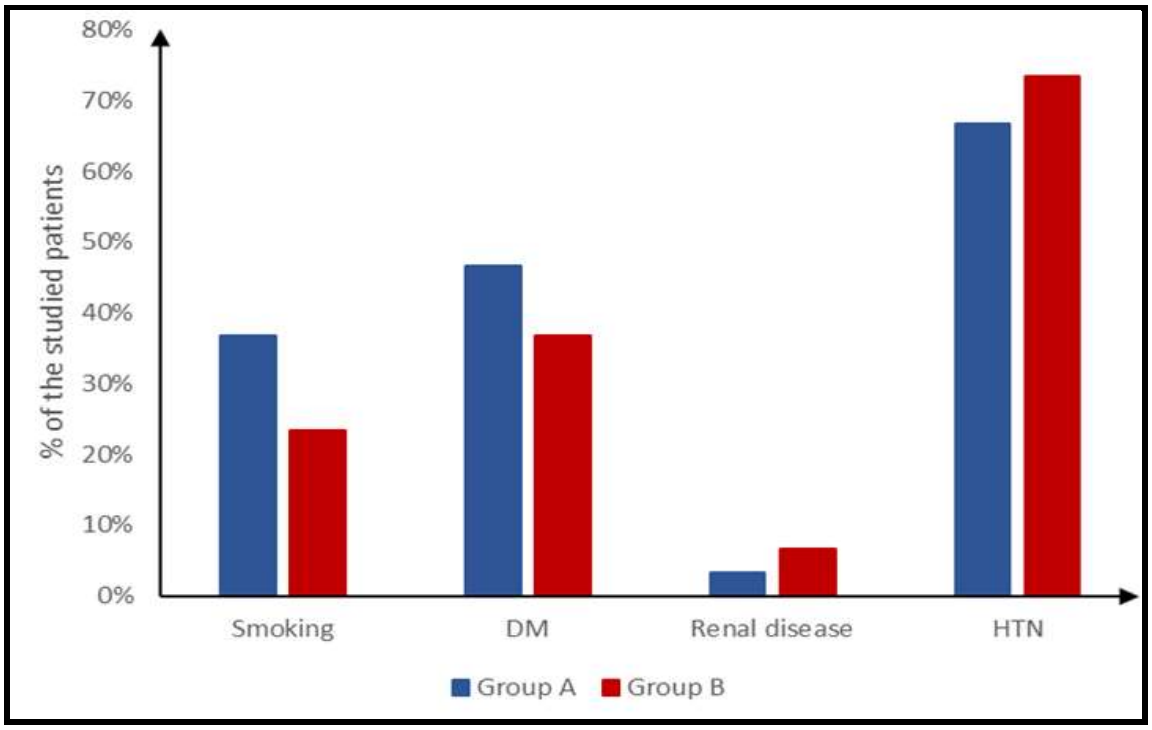

Fig. 2: Distribution of the studied groups according to Risk Factors

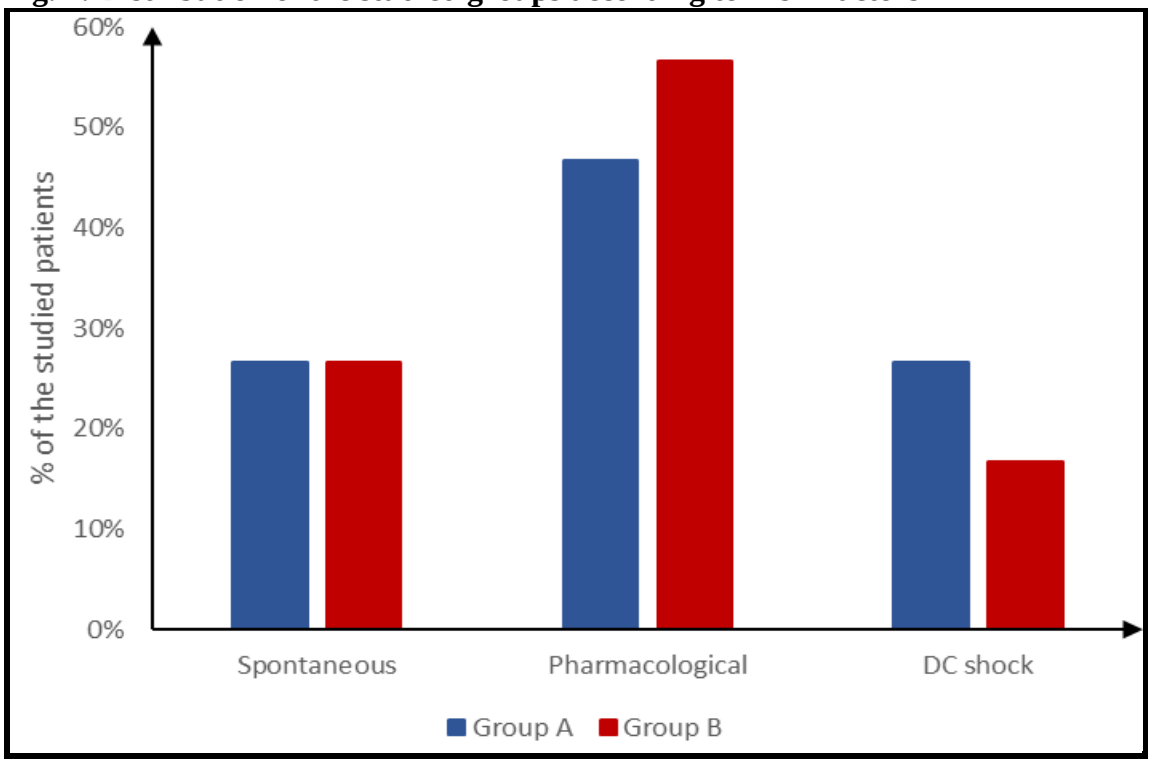

Fig. 3: Distribution of the studied groups according to Rhythm resolution

Table 1 showed the history of treatment of the studied groups. Non-significant difference was observed regarding medications (rhythm control [p=00000] and anticoagulant [p=0.821]) and

different anticoagulant therapy [p=0.638]. Contrarily, the study group had significantly (p=0.004) lower rate of recurrent AF history (90% [n=9] than control (66.7% [n=20]).

Table 1: Treatment history Differences of the studied groups

	Group A (n=30)	Group B (n=30)	P value*
Medications			
• **Rhythm control**	30 (100%)	30 (100%)	----
• **Anticoagulants**	24 (80%)	21 (70%)	= 0.821
Anti-coagulant			
• **NOACs**	21 (87.5%)	19 (90.5%)	= 0.638
• **Warfarin**	3 (12.5%)	2 (9.5%)	
Recurrent AF	9 (30%)	20 (66.7%)	**= 0.004**

***Chi-square test was used to compare Frequency between groups**

The mean values of baseline vital parameters were insignificantly different between groups i.e., HR (p=0.472), SBP (p=0.496) and DBP (p=0.418). Likewise, all basic laboratory investigations were comparable between groups (p>0.05). Parallel to that, both groups were matched for the Baseline Echocardiography findings (p>0.05).

Table 2: Treatment history Differences of the studied groups

	Group A (n=30)	Group B (n=30)	P value*
HR (beat/min)			
• **Mean ± SD**	131.97 ± 27.36	136.83 ± 24.58	= 0.472
• **Range**	76 - 159	72 - 158	
SBP (mm/hg)			
• **Mean ± SD**	123.2 ± 37.3	129.73 ± 36.64	= 0.496
• **Range**	65 - 179	68 - 176	
DBP (mm/hg)			
• **Mean ± SD**	79.1 ± 31.01	85.5 ± 29.77	= 0.418
• **Range**	46 - 132	48 - 130	

***Independent t-test was used to compare mean between groups**

HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure

As shown in **Fig.4**, The absolute and relative changes in LAD% were significantly (p<0.001) lower inthe study group compared withcontrol (relative% change: -8.8% vs. 3.5%, and absolute% change: -3.9 vs. 1.54 mm.). Likewise, there was a significant (p<0.001) decrease in the LAVI absolute and relative % change in the study group than control i.e. absolute% change: -4.04 vs 2.07 mm and relative% change: -9.7% vs 5.1%. As well, Group A, which got SGLT2 inhibitors, showed a substantial (p<0.001) improvement in the absolute and relative percentage change of the LA strain compared to group B, which did not receive SGLT2 inhibitors (relative% change was 18.7% versus -7.8% and absolute% change was 4.01 versus 0.16 mm).

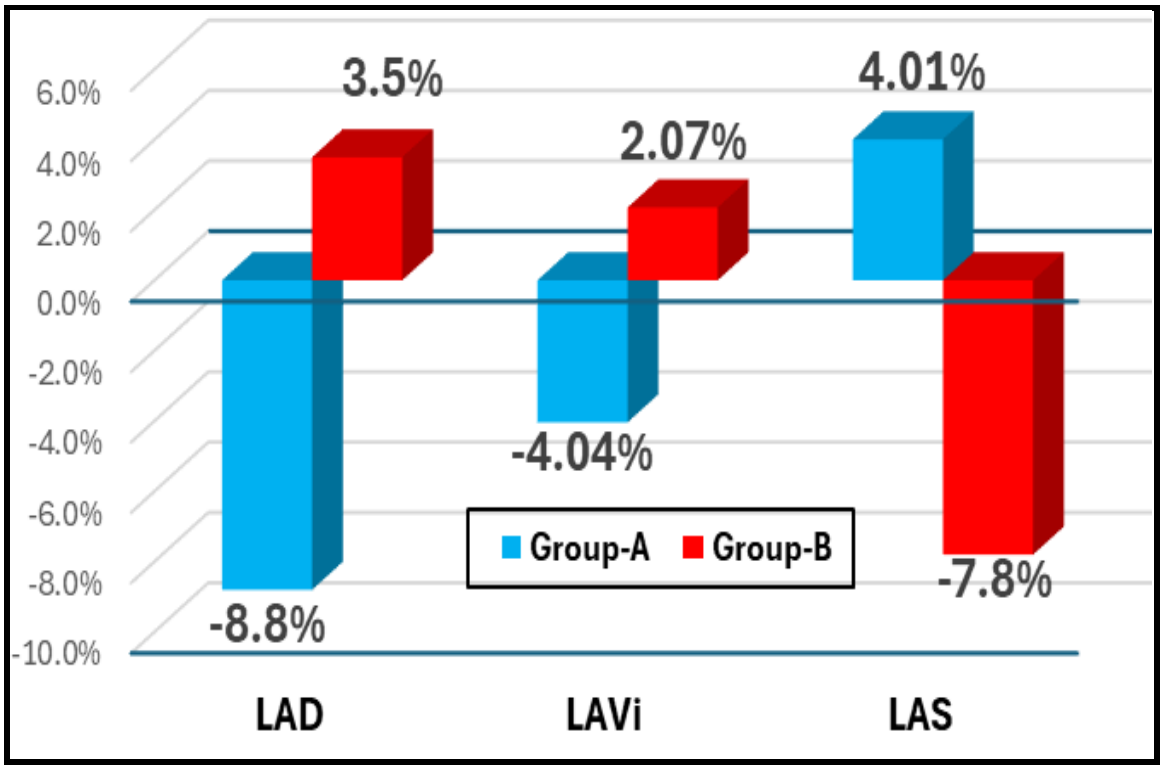

Fig.4: Percent Change in Echocardiography Parameters

The main outcome measures (total mortality, vascular mortality, heart failure hospitalization, and cerebrovascular stroke) showed insignificant difference between the two studied groups **(Fig. 5)**.

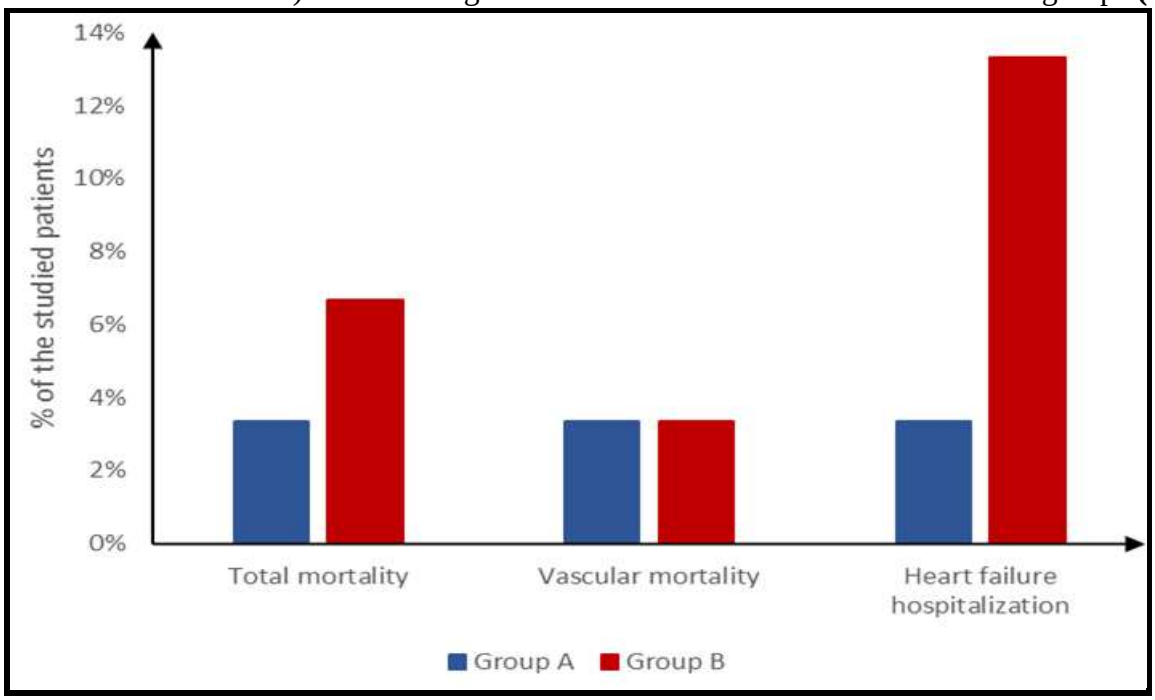

Fig.5: Outcomes of the studied groups

Table 3 showed the multivariable logistic regression model for the predictors of MACEamong the studied cohort. After adjusting for all correlates, it was found that adding SGLT-2 to the standard

treatment resulted in reduction of the risk of MACE by 32% (AOR= 0.678, 95% CI; 0.071 – 0.984, p=0.043) compared with those treated with the standard regimen.

Table 3: Predictors of MACE among the studied groups

Variable	Univariate		Multivariate	
	Unadjusted OR (95% CI)	**P-value**	**AOR (95% CI)**	**P-value**
Treatment (Study)	0.286 (0.53 – 1.549)	= 0.146	0.678 (0.071 – 0.984)	= **0.043**
Age/years	1.039 (0.927 – 1.165)	= 0.511		
Sex (Male)	1.447 (0.292 – 7.166)	= 0.651		
Hypertension	1.224 (0.188 – 7.959)	= 0.832		
DM	5.674 (0.668 – 22.260)	= 0.762	6.107 (1.044 – 9.924)	= **0.043**
Smoking	1.664 (0.811 – 14.718)	= 0.342		
Renal Disease	1.007 (0.934 – 1.084)	= 0.861		
Recurrent AF	2.906 (1.091 – 5.060)	= **0.002**	1.903 (1.011 – 6.343)	= **0.039**
LAD (post-)	1.441 (1.071 – 2.128)	= **0.008**	1.213 (1.045 – 1.408)	= **0.011**
LAV-i (post-)	2.084 (1.064 – 4.678)	= **0.016**		
LAS (post-)	1.597 (1.011 – 5.052)	= **0.027**		

AOR, Adjusted Odds Ratio; CI, Confidence Interval

DISCUSSION

The current study included 60 at Aswan University Hospitals' cardiology department who had non-valvular paroxysmal atrial fibrillation.The current study aimed to assess the effects of dapagliflozin (an SGLT2 inhibitor) on the CV outcome of AF and left atrial remodeling in non-valvular paroxysmal AF. AF is thought to be the most common persistent cardiac arrhythmia causing mortality all over the world.

In this study, demographic data, comorbidities, baseline echocardiography, and biochemistry results between the two groups in this study did not differ significantly. This was consistent with El-Saied et al., who found similar results across the groups**(15)**.

The present work showed that in the study group, there was a significant reduction in LAD and LAV-i. In contrast, the study group showed a significant improvement in LA average strain.Furthermore, the change in LAD% and LAV-i% was significantly lower in group A (those who received SGLT2 inhibitors) compared to group B (those who did not receive SGLT2 inhibitors), both in absolute terms and relative terms. In the same way, LAS absolute and relative % change showed a significant improvement in the study group compared to control. This was in agreement withEl-Saied et al.**(15)**.

In the present work, MACE parameters (total/vascular mortality, HF hospitalization, and CVS were insignificantly different between the studied groups. In line with this, a meta-analysis by Li et al. revealed consistent results **(16)**. Also, Zinman et al. conducted a study in which patients were randomly assigned to receive either a placebo or 10 mg or 25 mg of empagliflozin once daily. The findings indicated that the rates of hospitalization for heart failure, all-cause mortality, and cardiac mortality were insignificantly lower in the empagliflozin group compared to the placebo group**(3)**.

The efficacy of adding SGLT2 in the treatment of AF was shown in the multivariable model i.e., after adjusting for all factors, there was independently better results in the study group regarding the adverse outcomes (there was 32% (AOR= 0.678, 95% CI; 0.071 – 0.984, p=0.043) reduction in the

risk of MACE in cases treated with rhythm control in addition to anticoagulant according CHADs VASc score and SGLT2 inhibitors (Dapagliflozin) compared with those treated with the standard regimen.

Alongside our research, Böhm et al. found that the incidence of outcomes was lower with empagliflozin than with placebo. The frequencies of new-onset AF as determined by the electrocardiogram were low (1.6% for placebo and 2.3% for empagliflozin)**(17)**. In consistent, according to Zhao et al., 2023, AF recurred in 33 patients (23.9%) from the SGLT2i group, while in total, it occurred in 150 patients (38.7%)**(18)**.This aligned with that of Peters, 2021 in a meta-analysis discovered that the incidence of cerebrovascular events was similar across groups (RR: 1.06; 95% CI 0.85–1.32; p = 0.59) **(19)**.

This could be explained by that empagliflozin and other sodium glucose co-transporter-2 (SGLT2) inhibitors are anti-hyperglycemic medications that enhance the kidneys' excretion of glucose. In patients with T2DMat high CVrisk, empagliflozin has been demonstrated to lower CV and all-cause mortality, HF hospitalizations, and halt the course of kidney disease **(20)**. Similar outcomes have been shown with various SGLT2 inhibitors in T2 DM at high CV risk, including individuals with and without a history of heart failure, with the exception of mortality advantages. In the HF population, AF is quite common and linked to higher rates of morbidity and death **(21)**.

Study Limitations

There were some limitations to the current study. Firstly, this was a single-center study which limits the study's external validity (generalization). Secondly, the limited follow-up duration and the incomplete MACE parameter examinations.

CONCLUSION AND RECOMMENDATION

In conclusion,the addition of SGLT-2I to patients' existing guideline-directed medical therapy for non-valvular paroxysmal AF was found to be independently associated with reduction in the short-term adverse effects of the disease.

In recommendation, further studies are needed with multicenter cooperation and larger sample sizes to validate our findings. Interpretation and correlation ofSGLT2 cardiovascular benefits on cardiac mechanics by different conventional echo- cardio graphic parameters should be thoroughly studied. Longer follow-up periods are needed to support our study's findings.

Acknowledgement:

The authors wish to thankthe medical and administrative staff of the cardiology departments, Aswan University Hospital for the consistent help and support. It was not possible to complete this work without the help and support of the recruited patients.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (135-147) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Immunohistochemical Expression of Survivin and MUC5AC in Colorectal Cancer

Shimaa M.M.Bebars[1], Eman Muhammed Salah-Eldeen[2], Taghreed Mohammed Amin Mostafa[1], Rasha Mohamed Samir Sayed[1]

[1]Department of Human Pathology, faculty of medicine, Aswan university

[2]Department of Human Pathology, faculty of medicine, Sohag university

ABSTRACT

Keyword: Colorectal cancer, Survivin, MUC5AC, IHC

* **Corresponding author**: Taghreed Mohammed Amin Mostafa

Mobile: 01094384015

E-mail:

Taghreed.amin1234@gmail.com

Background: Colorectal cancer (CRC) is the third most frequently malignancy and the second leading cause of cancer-related deaths globally. Among emerging biomarkers, Survivin, an inhibitor of apoptosis, and MUC5AC, a mucin glycoprotein, have garnered attention due to their involvement in cell division, apoptosis regulation, and tumor progression. Their expression may hold potential diagnostic and prognostic value in CRC. **Objectives** to assess the expression of Survivin and MUC5AC in CRC tissues compared to normal colonic mucosa and explore their correlation with various clinico-pathological features, including tumor size, histological grade, lymph node metastasis (LNM), tumor budding, and lymphovascular invasion (LVI). and prognostic relevance in CRC patients. **Material and methods:** A total of 102 paraffin-embedded tissue samples (51 CRC, 51 normal mucosa) were evaluated using immunohistochemistry (IHC). An immunoreactivity score (IRS) was used, based on staining intensity and the percentage of positively stained cells. **Results:** revealed significantly elevated expression levels of Survivin and MUC5AC in CRC tissues ($p < 0.001$). Both markers were strongly associated with LNM and LVI, while Survivin alone correlated with tumor budding. Their co-expression was statistically significant, supporting their potential as diagnostic and prognostic biomarkers in CRC. **Conclusion:** Survivin and MUC5AC are promising biomarkers for CRC diagnosis and prognosis, showing strong associations with aggressive pathological features and potential clinical utility.

INTRODUCTION

By 2035, the incidence of colorectal cancer is predicted to increase by 60%, despite advancements in diagnostic techniques and preventative healthcare practices **[1].**

In 2020, there were 5231 (3.9%) new instances of colorectal cancer in Egypt, making it the sixth most common disease in both men and women. Similarly, CRC accounted for 2852 (0.2%) of all cancer-related fatalities, placing it eighth overall. Additionally, there have been some specific advancements in the screening of colorectal cancer **[2].**

Survivin belongs to the family of proteins that suppress apoptosis. In order to control chromosome separation and cell division, Survivin can function as a subunit of the chromosomal

passenger complex (CPC) and guide its other members, including Aurora-B, borealin, and the inner centromere protein **[3].** In most cancer types, poor outcomes are linked to high levels of Survivin expression **[4].** Note that Survivin has a variety of functions, including regulating apoptosis and cell proliferation. In addition to preventing cell death and reducing apoptosis, Survivin's presence in tumors is linked to chemotherapy resistance and the aggressive nature of malignancies **[5].**

Another potential biomarker in CRC is MUC5AC which is encoded on chromosome (11p15.5) **[6].** The stomach, lungs, ear, conjunctiva, nasopharynx, and gallbladder are the only organs that normally express the secretory mucin MUC5AC **[7].**

Tumor cell migration, invasion, adhesion, metastasis, and proliferation have all been linked to differential mucin expression **[8].** It is well known that the malignant behavior of cancer cells is caused by tissue-specific mucin genes and mucin carbohydrate antigens that alter in various forms of carcinoma **[9].** TNM (tumor, node, metastasis) categorization is used to stage the tumor in colorectal cancer (CRC), as is the case with all cancer types, in order to make basic therapeutic decisions. Additional immunohistochemistry (IHC) and genetic testing are used to determine the patients' eventual course of treatment, even if they share the same clinical diagnosis **[10].** The patients' treatment procedures have benefited immensely from the discovery of these extra prognostic indicators. Additionally, by examining the expression levels of different materials using IHC examination, the association with prognosis can be ascertained **[11].** Researchers have been looking for certain biomarkers that may be used to diagnose and track the effectiveness of treatment for people with colorectal cancer. But as of yet, no such indexes have been discovered **[12].**

AIMS OF THE WORK:

In the current study we aimed to a. analyze the expression of Survivin and MUC5AC in CRC patients in comparison with normal colonic mucosa, b. to study the association between Survivin and MUC5AC and clinico-pathological feature of CRC, c. to correlate the expression of Survivin and MUC5AC expression in CRC patients and their relation to prognostic parameters of the tumor.

MATERIAL AND METHODS:

This case-control study involved 102 formalin-fixed, paraffin-embedded tissue samples, comprising 51 colorectal cancer specimens and 51 matched normal colonic mucosae from the same patients. These instances were chosen from colorectal cancer patients who underwent surgical procedures at the Oncology Surgical Department. The specimens were submitted to the Pathology Lab of Aswan University Hospital and Aswan Oncology Center from January 2018 to September 2023.

The investigation encompassed specimens from radical right and left hemicolectomy, abdominoperineal resection, and low anterior resection. Cases involving colonoscopic and/or rectal biopsy, prior irradiation or chemotherapy, extensive necrosis and/or fibrosis, or positive/close margins were eliminated from this investigation. Clinical data were extracted from pathology reports, encompassing patient age, sex, tumor location, dimensions, and surgical type. Three serial sections from each tissue block were prepared at a thickness of 4 microns for the following purposes: One section was stained with

standard Hematoxylin and Eosin (H&E) for histological assessment, while the other two sections were immune -stained with Survivin and MUC5AC antibodies, respectively.

All H&E -stained sections were analyzed with a light microscope to determine histological type, grade, tumor invasion depth, lymphovascular invasion (LVI), tumor budding, lymph node metastasis (LNM), perineural invasion (PNI), and staging of colorectal cancer (CRC).

For IHC analysis, 4µm tissue sections were incubated with primary monoclonal antibodies: Survivin (Catalog; Cat#MA5-17035, Thermo Fisher Scientific) at a dilution of 1:500 and MUC5AC (Cat# MA1-21907, Thermo Fisher Scientific) at a dilution of 1:100. The negative control was established by omitting the main antibody, whilst stomach tissue functioned as a positive control. The streptavidin-biotin amplification technique was employed for immunostaining.

Tissue sections were affixed to positively charged slides, subjected to overnight deparaffinization in xylene, and subsequently rehydrated through a gradient of decreasing ethanol concentrations (95%, 85%, 70%). Subsequent to rinsing with tap water, they were rinsed with phosphate-buffered saline (PBS) at a pH of 7.2-7.6. A single drop of primary antibody was administered to tissue sections and incubated at ambient temperature for 60 minutes. Subsequently, a linking solution was applied for 15 minutes, after which rinse with PBS was conducted. The avidin-biotin complex (ABC) solution was administered for 15 minutes, succeeded by further washes with PBS. A chromogen was then introduced to interact with alkaline phosphatase, resulting in a colorimetric reaction. Tissue sections were rinsed with tap water, dehydrated using progressive concentrations of alcohol (70%, 85%, and 95%), and readied for assessment.

The immunoreactivity score (IRS) was evaluated based on the percentage of positive cells and the intensity of staining. The proportion of positive cells was assessed on a scale from (0) 0% to (4) 100% positive cells, while staining intensity was evaluated from none (0) to intense (3). The IRS was determined by multiplying the percentage score by the intensity score, resulting in the following categories: 0-1 (negative), 2-3 (mild), 4-8 (moderate), and 9-12 (strong) [12].

The results were analyzed utilizing IBM SPSS software (version 20.0, Armonk, NY: IBM Corp). Qualitative data were expressed as numerical values and percentages. The Kolmogorov-Smirnov test was employed to evaluate the normality of data distribution. Quantitative data were characterized by the range (minimum and maximum), mean ± standard deviation (SD), median, and interquartile range (IQR). The Wilcoxon signed-rank test was employed to compare irregularly distributed quantitative variables across two eras. The Chi-square test was utilized to compare categorical data across various groups. Monte Carlo adjustment was used to the Chi-square test if over 20% of the cells had an expected count of fewer than 5. The Student's t-test was employed to compare two groups of normally distributed quantitative data. The Mann-Whitney test was utilized for group analysis of abnormally distributed quantitative data. Statistical significance was defined as $p < 0.05$, extremely significant as $p < 0.01$, and non-significant as $p > 0.05$.

Approval was secured from the Ethics of Scientific Research Committee at the Faculty of Medicine, Aswan University, and the privacy and confidentiality of all acquired information were maintained., IRB NUM: Asw. Uni./488/10/20

RESULTS:

This study was conducted in tissue samples of 51 patients of CRC. The mean age of studied cases was 57 years. More than half of our participants (58%) were males, Specimens

were left sided in 60.8% of cases, rectal specimens were 27.5% of cases, and right side of the colon was the least common affected site (11.8%). It was found that 54.9% of cases had tumor size more than 5cm. The majority of the studied cases were diagnosed as conventional adenocarcinoma 48/51 (94.1%), and most of them 48/51 (82.4%) were Grade II carcinomas.

LNM was positive in 27/51 (52.9%), LVI was detected in 29/51 (56.9%), while PNI was found in 11/51 (21.6%) of cases and tumor stage II and III were the most frequent stages. The 51 normal colonic mucosae from the same patient were obtained for comparison.

Survivin expression was positive in 27/51 (52.9%) of CRC cases, while no evidence of expression in normal colonic mucosa 0/51 (100%) of cases. Significant statistical difference was detected when comparing Survivin expression in CRC and normal colonic mucosae ($p<0.001$) as shown in table (1), figure (1-3)

Table (1): Comparison between Survivin Expression in CRC and Normal Colonic Mucosae

Survivin expression	CRC (n=51)		Normal colonic (n=51)		χ^2	p
	No.	%	No.	%		
Negative	24	47.1	51	100.0	36.720*	<0.001*
Positive	27	52.9	0	0.0		

χ^2: **Chi square test**
p: p value for comparing between CRC and Normal colonic tissue
*: Statistically significant at $p \leq 0.05$

Comparing the IRS of Survivin with the clinco- pathological variables showed that there was a statistically significant association between Survivin expression and both LNM and LVI ($p<0.001$ for each). There was a Significant positive association between Survivin expression and tumor budding ($p = 0.028$). However, no significant correlation could be detected between Survivin expression and other variables including patient' age and sex, tumor size, grade or PNI (table 2).

Table (2): Relation between IRS of Survivin and clinico-pathological Studied Parameters

	IRS of Survivin								Test of sig.	p
	Negative (0 – 1) (n = 24)		Mild (2 – 3) (n = 6)		Moderate (4 – 8) (n = 12)		Strong (9 – 12) (n = 9)			
	No.	%	No.	%	No.	%	No.	%		
Sex										
Male	13	54.2	1	16.7	9	75.0	7	77.8	χ^2=	MCp=
Female	11	45.8	5	83.3	3	25.0	2	22.2	6.764	0.071
Age (years)										
Mean ± SD.	57.21 ± 10.84		63.33 ± 5.92		54.83 ± 8.49		57.67 ± 11.86			
Median (Min. – Max.)	60.0 (32.0 – 71.0)		63.50 (53.0 – 70.0)		55.0 (42.0 – 70.0)		62.0 (38.0 – 73.0)		F=0.953	0.423

Site										
Left colonic specimen	12	50.0	3	50.0	8	66.7	8	88.9	χ^2= 7.396	^{MC}p= 0.232
Right colonic specimen	4	16.7	1	16.7	0	0.0	1	11.1		
Rectal specimen	8	33.3	2	33.3	4	33.3	0	0.0		
Diagnosis										
Invasive adenocarcinoma	23	95.8	5	83.3	11	91.7	9	100.0	χ^2= 2.426	^{MC}p= 0.505
Mucinous carcinoma	1	4.2	1	16.7	1	8.3	0	0.0		
Grade										
I	2	8.3	0	0	2	16.7	0	0.0	χ^2= 4.905	^{MC}p= 0.491
II	21	87.5	5	83.3	9	75.0	7	77.8		
III	1	4.2	1	16.7	1	8.3	2	22.2		
Margin (Free)	24	100.0	6	100.0	12	100.0	9	100.0	–	–
Lymph node metastasis (LNM)										
Negative	18	75.0	4	66.7	2	16.7	0	0.0	χ^2= 21.655*	^{MC}p <0.001*
Positive	6	25.0	2	33.3	10	83.3	9	100.0		
T										
T1	1	4.2	1	16.7	0	0.0	0	0.0	χ^2= 6.322	^{MC}p= 0.717
T2	10	41.7	1	16.7	4	33.3	2	22.2		
T3	11	45.8	4	66.7	7	58.3	5	55.6		
T4	2	8.3	0	0.0	1	8.3	2	22.2		
N										
N0	18	75.0	4	66.7	2	16.7	0	0.0	χ^2= 29.376*	^{MC}p <0.001*
N1	4	16.7	0	0.0	2	16.7	1	11.1		
N2	2	8.3	1	16.7	7	58.3	7	77.8		
N3	0	0.0	1	16.7	1	8.3	1	11.1		
Tumor size										
≤5	13	54.2	3	50.0	5	41.7	2	22.2	χ^2=2.812	^{MC}p= 0.437
>5	11	45.8	3	50.0	7	58.3	7	77.8		
Mean ± SD.	4.72 ± 1.62		5.12 ± 1.60		5.43 ± 1.86		6.76 ± 1.72		H=7.379	0.061
Median (Min. – Max.)	4.75 (2.30 – 8.0)		5.50 (2.50 – 7.0)		5.80 (2.20 – 9.0)		7.50 (4.0 – 9.0)			
LVI										
No	18	75.0	0	0.0	3	25.0	1	11.1	χ^2= 19.543	^{MC}p <0.001*
Yes	6	25.0	6	100.0	9	75.0	8	88.9		
Perineural invasion (PNI)										
No	17	70.8	6	100.0	9	75.0	8	88.9	χ^2= 2.579	^{MC}p= 0.465
Yes	7	29.2	0	0.0	3	25.0	1	11.1		
Tumor budding										
No	23	95.8	4	66.7	8	66.7	6	66.7	χ^2= 7.808*	^{MC}p= 0.028*
Yes	1	4.2	2	33.3	4	33.3	3	33.3		

SD: **Standard deviation** χ^2: **Chi square test** MC: **Monte Carlo**
t: Student t-test **U: Mann Whitney test**
p: p value for comparing between different categories
*: Statistically significant at $p \leq 0.05$

High statistically significant difference was detected in the expression of MUC5AC between CRC and normal colonic mucosal tissue (p<0.001). All cases of normal colonic mucosa showed negative MUC5AC expression, while more than half of cases 31/51 (60.8%) of CRC showed highly positive MUC5AC expression as shown in table (3), figure (4, 5).

Table (3): Comparison between CRC and Normal colonic mucoase regarding to MUC5AC expression

MUC5AC expression	CRC (n = 51)		Normal colonic tissue (n = 51)		χ^2	P
	No.	%	No.	%		
Negative	20	39.2	51	100.0	44.535*	<0.001*
Positive	31	60.8	0	0.0		

χ^2: **Chi square test**
p: p value for comparing between CRC and Normal colonic tissue
*: Statistically significant at $p \leq 0.05$

As regard to the relation between MUC5AC IRS and clinic- pathological data, significant statistical association was found between the IRS of MUC5AC and LNM (p <0.001) and LVI (p <0.017), while no significant association was found between the IRS of MUC5AC and other variables (table 4).

Table (4): Relation between the IRS of MUC5AC and clinic-pathological variables

	Intensity of MUC5AC								Test of sig.	p
	Negative (0 – 1) (n = 20)		Mild (2 – 3) (n = 9)		Moderate (4 – 8) (n = 15)		Strong (9 – 12) (n =7)			
	No.	%	No.	%	No.	%	No.	%		
Sex										
Male	11	55.0	6	66.7	8	53.3	5	71	χ^2=	^{MC}p=
Female	9	45.0	3	33.3	7	46.7	2	28.6	1.015	0.860

Age (years)										
Mean ± SD.	57.70 ± 11.77		54.56 ± 10.38		58.0 ± 8.48		59.29 ± 8.96		F=0.329	0.804
Median (Min. – Max.)	61.50 (32.0 – 71.0)		53.0 (38.0 – 67.0)		59.0 (42.0 – 70.0)		61.0 (45.0 – 73.0)			
Site										
Left colonic specimen	11	55.0	7	77.8	9	60.0	4	57.1	χ^2= 9.287	^{MC}p= 0.114
Right colonic specimen	2	10.0	2	22.2	0	0.0	2	28.6		
Rectal specimen	7	35.0	0	0.0	6	40.0	1	14.3		
Diagnosis										
Invasive adenocarcinoma	18	90.0	9	100.0	14	93.3	7	100.0	χ^2= 1.230	^{MC}p= 1.000
Mucinous carcinoma	2	10.0	0	0.0	1	6.7	0	0.0		
Grade										
I	2	10.0	0	0.0	2	13.3	0	0.0	χ^2= 4.210	^{MC}p= 0.633
II	17	85.0	7	77.8	11	73.3	7	100.0		
III	1	5.0	2	22.2	2	13.3	0	0.0		
Margin (Free)	20	100.0	9	100.0	15	100.0	7	100.0	–	–
Lymph node metastasis (LNM)										
Negative	17	85.0	0	0.0	6	40.0	1	14.3	χ^2= 23.869*	^{MC}p <0.001*
Positive	3	15.0	9	100.0	9	60.0	6	85.7		
T										
T1	0	0.0	1	11.1	1	6.7	0	0.0	χ^2= 6.761	^{MC}p= 0.667
T2	7	35.0	1	11.1	7	46.7	2	28.6		
T3	11	55.0	6	66.7	6	40.0	4	57.1		
T4	2	10.0	1	11.1	1	6.7	1	14.3		
N										
N0	17	85.0	0	0.0	6	40.0	1	14.3	χ^2= 32.489*	^{MC}p <0.001*
N1	2	10.0	2	22.2	1	6.7	2	28.6		
N2	0	0.0	6	66.7	8	53.3	3	42.9		
N3	1	5.0	1	11.1	0	0.0	1	14.3		
Tumor size										
≤5	10	50.0	2	22.2	9	60.0	2	28.6	χ^2= 4.039	^{MC}p= 0.255
>5	10	50.0	7	77.8	6	40.0	5	71.4		
Mean ± SD.	4.84 ± 1.36		6.63 ± 2.05		4.77 ± 1.59		5.97 ± 2.26		H=8.025*	0.046*
Median (Min. – Max.)	5.15 (2.30 – 7.40)		7.50 (2.50 – 9.0)		5.0 (2.50 – 8.0)		6.10 (2.20 – 9.0)			
LVI										
No	14	70.0	2	22.2	5	33.3	1	14.3	χ^2= 9.946*	^{MC}p= 0.017*
Yes	6	30.0	7	77.8	10	66.7	6	85.7		
Perineural invasion (PNI)										
No	15	75.0	6	66.7	13	86.7	6	85.7	χ^2= 1.716	^{MC}p= 0.683
Yes	5	25.0	3	33.3	2	13.3	1	14.3		

Tumor budding										
No	18	90.0	6	66.7	11	73.3	6	85.7	χ^2=	^{MC}p=
Yes	2	10.0	3	33.3	4	26.7	1	14.3	2.970	0.447

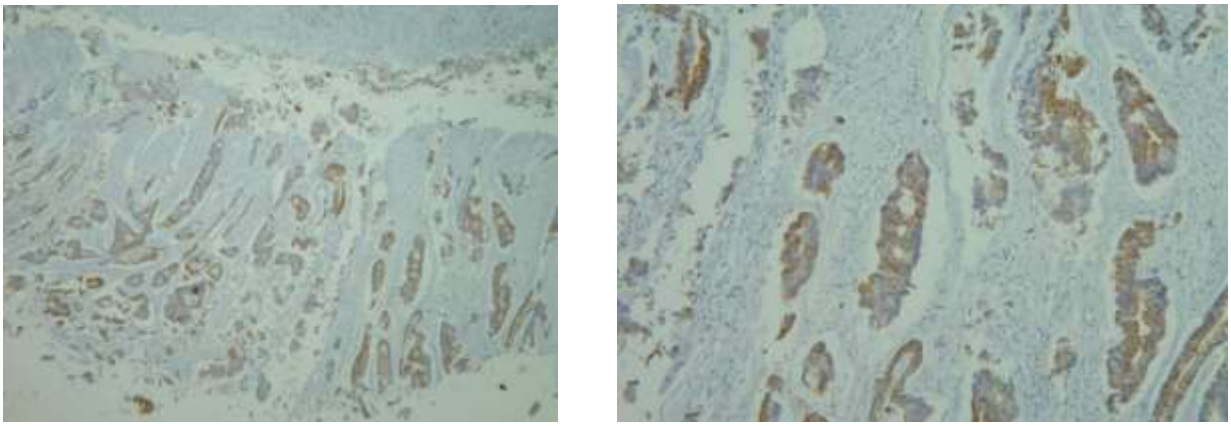
SD: **Standard deviation** χ^2: **Chi square test** MC: **Monte Carlo**
t: Student t-test **U: Mann Whitney test**
p: p value for comparing between different categories
*: Statistically significant at $p \leq 0.05$

Significant statistical association was detected between Survivin and MUC5AC expressions in CRC cases (p<0.001). Positive expression of Survivin and MUC5AC in CRC cases was found in 25/27 (92.6%) of cases as shown in table (5)

Table (5): Relation between Survivin and MUC5AC expressions in CRC cases

MUC5AC expression	**Survivin expression**				χ^2	**P**
	Negative (N = 24)		**Positive (N = 27)**			
	No.	**%**	**No.**	**%**		
Negative	18	75.0	2	7.4	24.353*	<0.001*
Positive	6	25.0	25	92.6		

χ^2**:** Chi Square Test



A: **B**:

Figure (1): Moderate positive Survivin expression (IRS 8) in tumor cells of CRC (A. x40, B, x100)

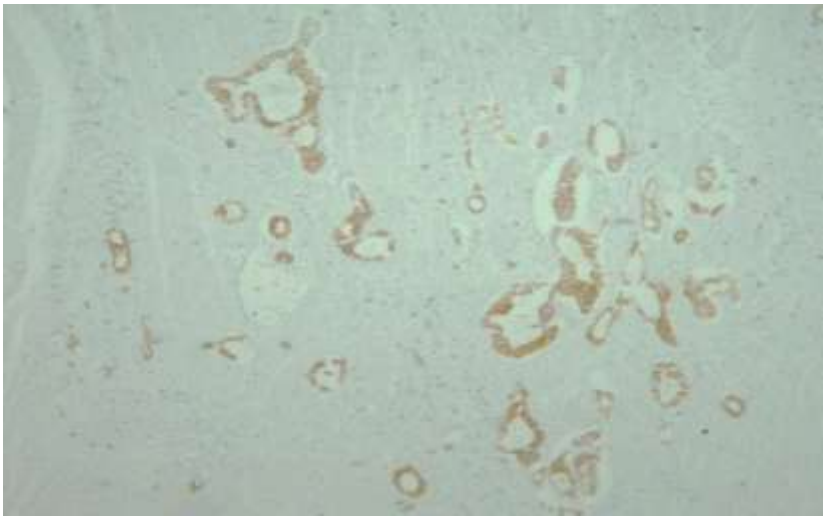
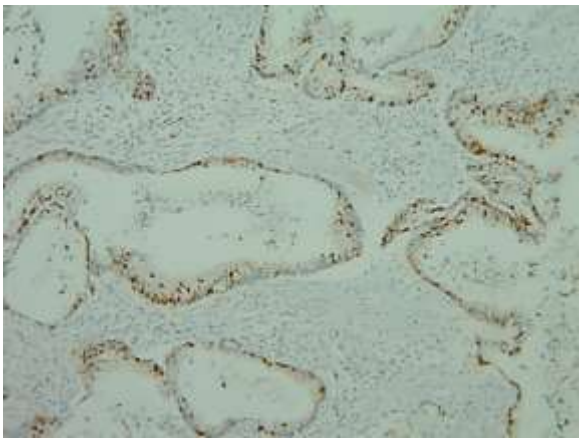


Figure (2): Strong positive Survivin expression (IRS 9) in tumor cells of CRC (x40)



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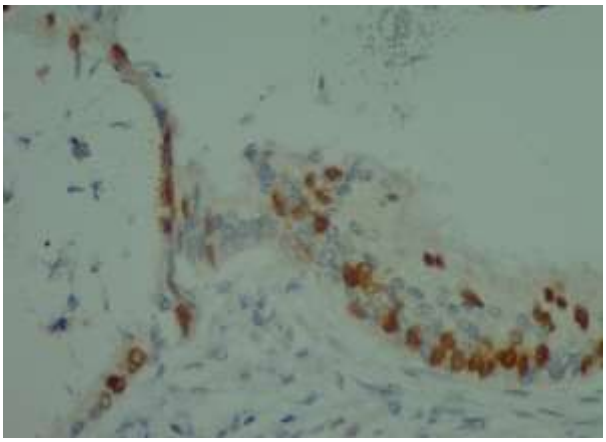
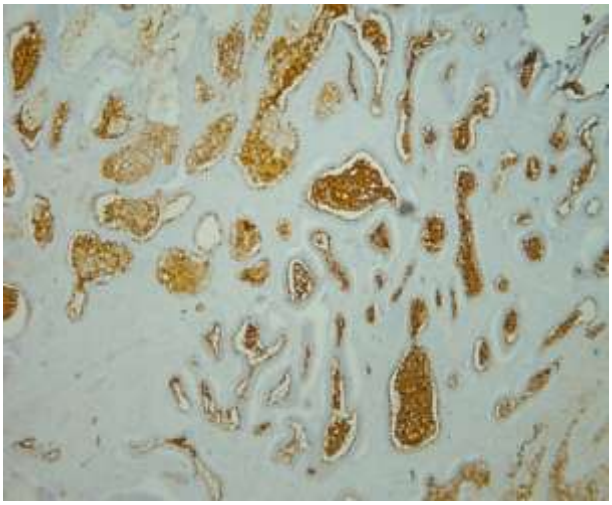
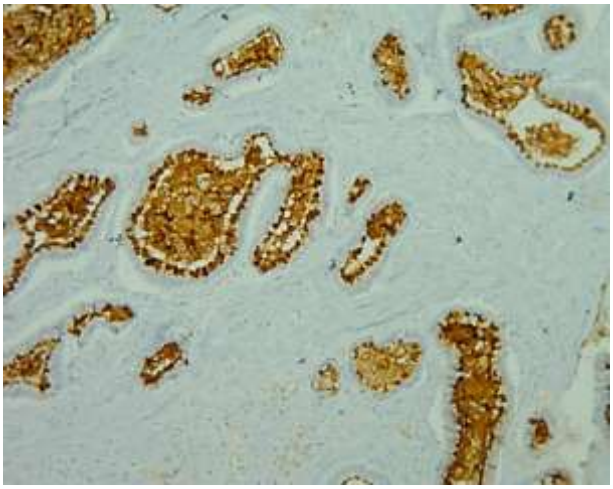


B:

Figure (3): CRC showing strong positive Survivin expression (IRS 12) in tumor cells (A. x40, B. x100)



A:



B:

Figure (4): CRC showing strong positive MUC5AC expression (IRS12) in tumor cells (A. x40, B. x100)

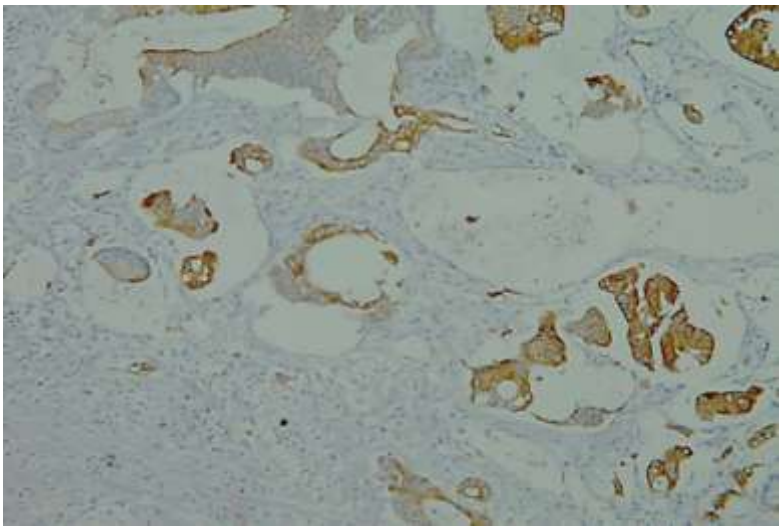


Figure (5): CRC showing strong positive MUC5AC expression (IRS 12) in tumor cells (x100).

DISCUSSION:

Survivin plays a crucial role in cancer development and is involved in tumor cell resistance to radiation and chemotherapy. Mucins are high-molecular-weight glycoproteins. Over 20 mucin types have been identified and categorized into two classes according to their structure and function, playing a role in neoplasm growth **[13].** To our knowledge, no research have yet examined the link between Survivin and MUC5AC expressions in colorectal cancer among Egyptian patients.

This study aims to assess the immunohistochemical expressions of Survivin and MUC5AC and their relationship with colorectal cancer (CRC) in comparison to healthy colonic mucosa, as well as the correlation of their expression with clinico-pathological characteristics in CRC. This study revealed a substantial statistical difference in Survivin expression between colorectal cancer (CRC) and normal colonic mucosae ($p<0.001$). Survivin was expressed in 52.9% of CRC patients, but no expression was seen in normal colonic mucosae. This outcome aligned with the work of Al-Muttairi et al., which utilized Chromogenic In-Situ Hybridization (CISH) and demonstrated that the percentage of positive Survivin expression in colorectal cancer (CRC) was 63.3%, in contrast to 55% in benign equivalents. A significant proportion of cases in CRC exhibited the Survivin gene, with a moderate score observed in 26.7% of instances. They established that Survivin was absent in normal colorectal mucosa **[14].** Jourabchin et al. discovered that the expression rate of Survivin in colonic polyps was 81.6%, whereas in colorectal cancer (CRC) it was 94.6%. Survivin expression was elevated in colorectal cancer compared to colonic polyps [15]. Additionally, Al-Maghrabi et al. discovered that Survivin expression was present in 60.8% of the colorectal cancer samples examined **[16].** The present investigation found no significant correlations between Survivin expression and patients' age, sex, tumor location, size, or grade ($p > 0.05$ for all) in the analyzed cases. The findings concurred with those of Almuttairi et al., Wang et al., and Al-Maghrabi et al., who established that there were no significant relationships between age, sex, tumor site, tumor size,

or grade in the examined CRC cases and Survivin expression **[13],[14],[16].** Conversely, Shintani et al. discovered that females had significantly elevated levels of nuclear Survivin expression compared to males ($p < 0.05$). This variation may be attributed to the utilization of a different technology; the enzyme-linked immunosorbent assay method was employed to quantify the amount of Survivin **[17].**

This study identified a statistically significant association between Survivin expression and both lymph node metastasis (LNM) and lymphovascular invasion (LVI), with p-values less than 0.001 for each. This finding aligns with the work of Al-Maghrabi et al., who demonstrated a statistically significant association between positive Survivin immunostaining and both LNM and LVI **[16].**

Consistent with Zhang et al., a statistically significant correlation was seen between Survivin expression and tumor budding (p=0.028) **[18].**

This investigation, in agreement with Al-Muttairi et al., revealed no significant connection between Survivin expression and PNI **[14].**

This study identified a substantial statistical difference in MUC5AC expression between colorectal cancer (CRC) and normal colonic mucosae (p=<0.001). All instances of normal colonic mucosa exhibited negative MUC5AC expression, but over half of colorectal cancer cases (60.8%) demonstrated elevated MUC5AC expression.

Moreover, Jayanth et al. discovered that none of the normal individuals exhibited MUC5AC expression, but a significant majority of the CRC cases (88%) demonstrated moderate to high MUC5AC expression, particularly in mucinous carcinomas **[19].** Moreover, Wang et al. discovered that MUC5AC was highly expressed in 28.06% of colorectal cancer cases, whereas absent in normal colon tissues **[13].**

This study found no significant correlation between MUC5AC expression and factors such as patients' age, sex, tumor location, size, or grade in the examined CRC cases. This aligns with the findings of Wang et al. and Hazgui et al., who identified no significant statistical correlation between MUC5AC expression and the patients' age, sex, tumor location, size, or grade **[13],[20].**

Walsh et al. (2013) identified a significant statistical correlation between MUC5AC expression and female sex in a prospective cohort study involving 41,514 colorectal cancer (CRC) cases, demonstrating that MUC5AC-positive CRC was more frequently located proximally. This disparity may be attributed to the substantial sample size of 702 cases and differing geographic factors **[21].** The research by Kesari et al. shown a strong correlation between MUC5AC expression and higher grades of colorectal cancer (p= 0.006) **[22].**

The current investigation identified a statistically significant correlation between MUC5AC expression and lymph node metastasis (LNM). This discovery corresponds with the research conducted by Wang et al., which indicated elevated MUC5AC expression in colorectal cancer cases exhibiting lymph node metastasis. Nonetheless, Hazgui et al. discovered no significant link between MUC5AC expression and lymph node metastasis (LNM) in their investigation, which employed both immunohistochemistry (IHC) and reverse-transcription polymerase chain reaction (RT-PCR) to assess MUC5AC expression **[13],[20].**

Moreover, in alignment with Wang et al., the present investigation revealed a statistically significant correlation between MUC5AC expression and LVI. Conversely, Hazgui et al. could not identify a significant link between MUC5AC expression and PNI in their research **[13, 20].**

The current investigation identified a strong positive statistical connection between the expressions of Survivin and MUC5AC in colorectal cancer cases. Moreover, the positive association between Survivin and MUC5AC in colorectal cancer cases was 92.6%. This data

aligns with Wang et al., who identified a substantial positive connection between Survivin and MUC5AC expression in colorectal cancer cases **[13].**

CONCLUSION:

In conclusion, elevated expressions of Survivin and MUC5AC were observed in colorectal cancer cases, but no expression of either was detected in normal colonic mucosa. Furthermore, instances of CRC exhibiting elevated levels of Survivin and MUC5AC expression revealed markedly higher rates of LVI and LNM. Moreover, there were notable correlations between Survivin expression and tumor sprouting. The findings indicate that elevated levels of Survivin and/or MUC5AC may correlate with tumor growth and adverse prognostic indicators (LVI, tumor budding, and LNM) in colorectal cancer, and their expression could facilitate early detection of the disease.

RECOMMENDATION:

- Further studies with a larger number of patients, and in multi-centers are necessary to explore the role of Survivin and MUC5AC in CRC patients.
- Studying the correlation between studied markers and other prognostic parameters such as overall survival and disease-free survival rate.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (148-159) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Surgical Site Infections Following Non-Instrumental Lumbar Spine Surgery: A 4-Year Retrospective Analysis in Neurosurgery department in Aswan University Hospitals (2021–2024)

Ahmed Aly[1], Ahmed Abdallah Ismaeil 2, Khaled Ismail[1]

[1] Neurosurgery Department, Faculty of Medicine, Aswan University, Egypt

2Neurosurgery Department, Faculty of Medicine, Assiut University, Egypt

ABSTRACT

Keyword: Spinal infection, lumbar spine surgery, post-operative infection.

*** Corresponding author:**
Khaled Ismail
Mobile: 01065544104
E-mail:
Khaled.ismail6060@gmail.com

Background: While extensive research has investigated surgical site infections (SSIs) following instrumental spine surgery, few studies have addressed infection rates after non-instrumental lumbar procedures. This study aims to estimate the rate of SSI following non-instrumental lumbar spine surgery and identify contributing risk factors. **Material and Methods:** A retrospective review of 117 patients who underwent non-instrumental lumbosacral spine surgery at Aswan University Hospitals between January 2021 and December 2024 was conducted. Patients were grouped as: - Needing surgical washout due to SSI: 6 patients (5.13%) - Not requiring washout: 111 patients (94.87%) **Results:** No statistically significant differences were found between the two groups in terms of age, gender, BMI, or revision vs de novo surgery. However, several key risk factors were associated with the washout group: higher prevalence of osteoporosis, more frequent discectomy procedures, operations at L2–L3 level, and significant intraoperative blood loss. Staphylococcus aureus was the most frequently isolated organism. Two-thirds of affected patients required antibiotics for ≥6 weeks.**Conclusion:** SSI is a notable risk even in non-instrumental lumbar spine surgery. Independent risk factors include osteoporosis, significant intraoperative blood loss, discectomy, and procedures at the L2–L3 level

INTRODUCTION

Instrumentation in spine surgery has been reported to increase the incidence of postoperative surgical site infections (SSIs) by up to 28%[2]. This increase is attributed to factors such as extended exposure of the wound, extensive tissue dissection, and prolonged operative duration [3]. While extensive literature exists on SSIs in instrumental spinal surgeries, data concerning infection rates and contributing factors in non-instrumental procedures are limited.

Pourtaheri group [4] compared the outcomes of 23 instrumented and 11 non-instrumented consecutive patients who had undergone a lumbar laminectomy, bilateral partial facetectomy, and posterolateral fusion and found that 43% of the instrumented group and 64% of the non-

instrumented group required reoperation with no differences in the reoperation rate. Suresh et al [5] in their systematic review found that decreased preoperative Hb/Hct were significant predictors of increased postoperative morbidity, including return to the operating room. Preoperative anemia has been associated with an increased need for blood transfusions and postoperative complications in various surgical procedures, including cardiac and spinal procedures ([6],[7, 8]).

Other predictors for washout were pulmonary complications, intraoperative blood transfusion, return to operating theatre and duration of hospital stay (> 5 days)[5]. Hypothyroidism constitutes an important factor in delaying wound healing[9, 10]. Surgical site infection (SSI) is a clinically important complication of SS[11].

Many studies have investigated risk factors associated with SSI following instrumental SS however there is a lack of clinical data concerning SSI risk factors for non-instrumental lumbosacral spinal surgeries.

The present study was designed to investigate the incidence and risk factors associated with SSI in non-instrumental lumbar spine surgeries. We hypothesized that despite being considered less invasive, non-instrumental surgeries also present a measurable risk of SSI, possibly linked to different predictive factors compared to their instrumental counterparts.

SUBJECT AND METHODS

This retrospective study was conducted at Aswan University Hospitals, Egypt. It reviewed medical records of 117 patients who underwent non-instrumental lumbosacral spine surgery between January 2021 and December 2024. Patients with spinal infection, tumor, tuberculosis, fracture, scoliosis, or spondylolisthesis were excluded.

Collected data included demographic variables, comorbidities, type of surgery, surgical level, estimated blood loss, operative time, and postoperative infection details. Cases were grouped based on the presence of SSI requiring surgical washout (n=6) and those without SSI (n=111).

Statistical analysis

Data analysis was performed using SPSS 19.0 software (IBM, Chicago, IL). Our patients were classified into two groups: SSI needing washout and non-SSI. Descriptive statistics, crosstabs and frequency tables were used to describe some of the basic variables. Mann-Whitney and Chi-square tests compared groups. Logistic regression assessed independent predictors.

RESULTS

A total of 117 patients underwent non-instrumental lumbar spine surgery at Aswan University Hospitals between January 2021 and December 2024. Of these, 6 patients (5.13%) developed surgical site infections (SSIs) requiring operative washout, while 111 patients (94.87%) had no such complications.

Demographic and Clinical Characteristics (Table 1)

Patients who developed SSIs and required washout had a higher mean age (66.25 years, 95% CI: 51.08–81.42) than those who did not require washout (54.41 years, 95% CI: 51.79–57.02). This difference was statistically significant, with a Cohen's d of 0.835, indicating a large effect size and suggesting age is a meaningful risk factor for infection.

In terms of Body Mass Index (BMI), the washout group had a mean BMI of 28.82 (95% CI: 24.10–33.54), compared to 28.22 (95% CI: 27.19–29.24) in the non-washout group. However, the Cohen's d was only 0.120, denoting a small, likely insignificant effect.

Comorbidities and Risk Factors

All 6 patients in the washout group had at least one comorbidity. Osteoporosis was significantly more prevalent among these patients (16.7%) than in the non-washout group (0.8%, p = 0.011). Although other comorbidities (e.g., diabetes, smoking, anemia) were present, only osteoporosis showed a strong association with postoperative infection in this cohort.

Table 1: Demographic factor and associated comorbidities among studied groups

	Group needed wash out (N=6)	**Group without wash out (N=111)**	**Total participants (N=117)**	**X^2 or z value**	**P value**
Age (mean ± SD)	59.5 ± 24.2372.5 (14–85)	54.6 ± 16.753 (21–87)	54.82 ± 17.1254 (14–87)	-1.206	0.228
Gender					
Male	4 (66.7%)	57 (51.4%)	61 (52.1%)	2.556	0.143
Female	2 (33.3%)	54 (48.6%)	56 (47.9%)		
Body Mass Index (BMI)	27.71 ± 5.4925.8 (19–38)	29.50 ± 5.7729.49 (16.5–46.4)	29.42 ± 5.7629.4 (16.5–46.4)	-0.926	0.354
Other Disease Comorbidities					
Without comorbidity	0 (0%)	50 (45.0%)	50 (42.7%)	9.308	0.002*
With comorbidity	6 (100%)	61 (55.0%)	67 (57.3%)		
Hypothyroidism	0 (0%)	6 (5.4%)	6 (5.1%)	0.659	0.534

	Group needed wash out (N=6)	**Group without wash out (N=111)**	**Total participants (N=117)**	**X^2 or z value**	**P value**
Anemia	1 (16.7%)	3 (2.7%)	4 (3.4%)	1.175	0.317
Diabetes mellitus (DM)	0 (0%)	12 (10.8%)	12 (10.3%)	1.450	0.620
Hypertension	2 (33.3%)	31 (27.9%)	33 (28.2%)	1.540	0.745
Cardiac diseases	1 (16.7%)	12 (10.8%)	13 (11.1%)	0.098	0.606
Chest disease	1 (16.7%)	16 (14.4%)	17 (14.5%)	0.064	0.528
CNS diseases	1 (16.7%)	10 (9.0%)	11 (9.4%)	0.841	0.304
Malignancy	0 (0%)	4 (3.6%)	4 (3.4%)	0.398	0.683
Osteoporosis	1 (16.7%)	1 (0.9%)	2 (1.7%)	19.090	0.011
Previous spine operation	1 (16.7%)	4 (3.6%)	5 (4.3%)	4.830	0.085
Smokers	2 (33.3%)	19 (17.1%)	21 (17.9%)	0.531	0.440

DM: diabetes mellitus, High BMI: high body mass index, COPD: Chronic obstructive pulmonary.

Surgical Characteristics (Table 2)

- Despite the fact that SSI was more likely with discectomy (66.7% vs. 27.9%), no statistical significance was found between microdiscectomy and laminectomy
- Laminectomy, was more common in the non-washout group.
- The most frequently affected spinal level in the washout group was L2–L3 (66.7%), whereas the non-washout group primarily involved L4–L5 and L5–S1 levels. This anatomical distinction reached statistical significance ($p = 0.001$).
- Blood loss exceeding 300 ml was documented in 83.3% of patients with SSI, compared to 5.6% in those without ($p = 0.001$), reinforcing its role as a procedural risk factor.

Table 2: Factor related to spinal surgery among studied groups.

	Group needed wash out (N=6)	Group without wash out (N=111)	Total participants (N=117)	X^2 or t value	P value
Discectomy	4 (66.7%)	31 (27.9%)	35 (29.9%)	2.436	0.119
Laminectomy	2 (33.3%)	80 (72.1%)	82 (70.1%)		
De-novo or revision					
De-novo	6 (100%)	101 (91.0%)	107 (91.5%)	0.000	0.985
Revision	0 (0%)	10 (9.0%)	10 (8.5%)		
Level of surgery				57.709	0.001*
L2–3	4 (66.7%)	6 (5.4%)	10 (8.5%)		
L3–4	0 (0%)	5 (4.5%)	5 (4.3%)		
L4–5	2 (33.3%)	39 (35.1%)	41 (35.0%)		
L5–S1	0 (0%)	29 (26.1%)	29 (24.8%)		
Multiple levels	0 (0%)	32 (28.8%)	32 (27.4%)		
Duration of operation (min)	150.55 ± 56.28165 (96–270)	148.84 ± 52.41139 (45–316)	148.92 ± 51.19143 (45–316)	-1.198	0.231
Blood loss				47.680	<0.001*
< 100 ml	1 (16.7%)	92 (82.9%)	93 (79.5%)		
100–200 ml	0 (0%)	8 (7.2%)	8 (6.8%)		
200–300 ml	1 (16.7%)	5 (4.5%)	6 (5.1%)		
300–400 ml	1 (16.7%)	4 (3.6%)	5 (4.3%)		
400–500 ml	0 (0%)	1 (0.9%)	1 (0.9%)		
> 500 ml	3 (50.0%)	1 (0.9%)	4 (3.4%)		

Microbiological Findings (Table 3)

Among the 6 patients requiring washout:

- Staphylococcus aureus was the most commonly isolated organism (2 cases, 33.3%)
- Proprionobacterium acnes was identified in 1 case (16.7%)
- 2 cases (33.3%) showed no microbial growth
- 1 case (16.7%) had other less common organisms

Table 3: Infection data of Group needed wash out (Microbiology and Treatment Duration) (n=6)

Microorganism / Treatment Duration	Frequency
Staphylococcus aureus	2 (33.3%)
Proprionobacterium	1 (16.7%)
No growth detected	2 (33.3%)
Other organisms	1 (16.7%)
Antibiotic ≥ 6 weeks	4 patients (66.7%)

Antibiotic Treatment

Two-thirds (4 out of 6 patients) required long-term antibiotic therapy of six weeks or more, either due to persistent symptoms or positive intraoperative cultures. The prolonged need for antibiotic intervention highlights the clinical and economic burden of postoperative SSIs.

Table 4: Multivariate Logistic Regression Analysis to Detect the Risk Factors of Wash-out

Variable	B	Std. Error	z	P value	Lower 95% CI	Upper 95% CI
const	-4.303	2.904	-1.481	0.138	-9.996	1.390
Age	0.065	0.038	1.719	0.086	-0.009	0.140
Gender	-22.261	25701.359	-0.001	0.999	-50396.000	50351.478

Osteoporosis	1.673	2.146	0.780	0.436	-2.533	5.879
Discectomy	1.471	1.050	1.401	0.161	-0.586	3.528
Blood Loss >300ml	-26.383	490069.929	-0.000	1.000	-960545.793	960493.027
Multiple Level Surgery	-13.555	729.047	-0.019	0.985	-1442.460	1415.350
BMI	-0.082	0.088	-0.927	0.354	-0.255	0.091

DISCUSSION

This study confirms that even in non-instrumental lumbar spine surgeries, SSI remains a significant complication, with a 5.13% incidence rate. The key risk factors identified through multivariate regression include osteoporosis, significant blood loss, discectomy, and procedures involving the L2–3 level.

The findings align with prior literature focusing on instrumental procedures, underscoring that surgical complexity alone does not dictate infection risk. Comorbidities and operative variables such as blood loss play an important role.

Surgical site infection (SSI) is one of the most serious complications following spinal surgery. Its prevalence has been reported to be between 0.7% to 12.0% [12, 13]. Most previous studies focused on instrumental spine surgery. Patel group [11], investigated SSI rates after spine operations, found that instrumentation increases the rate of post-operative infections [1] by up to 28% [2]; this may be is attributed to increased exposure of the wound to air, soft tissue dissection, and muscle/skin retraction [Kasliwal et al 2013][3]. A recent systematic review and meta-analysis was published by Hirase et al 2022[14]. They found that seven studies (274 non-instrumented, 398 instrumented) were analyzed but there was no difference between them in functional improvement and no difference in reoperation or complication rates.

In the present study we selected non-instrumental lumbar spine surgery to estimate the frequency of spine surgery infection (SSI) and analyse the possible risk factors. The main finding was the high frequency of SSI after non-instrumental lumbar spine surgery (5.13%). Koutsoumbelis et al 2011[15] found that the rate of postoperative SSI after lumbar spinal surgery was 2.6% out of 3218 patients based on a single institution analysis. Klemencsics et al[16] found that the prevalence of SSI was 3.6% out of 1030 patients after routine degenerative lumbar surgeries. The difference in the results may be related to the small sample size of our group, and the methodology for selection of cases.

Demographic factors and associated comorbidities related to SSI.

Age, obesity, smoking, osteoporosis, previous SSI, long surgical time, increased blood loss, revision surgery, multilevel surgical segments and other have all been considered as risk factors for SSI [17-21].

In the present study we failed to find any association between SSI and age, sex or BMI. However all patients who developed SSI were more likely to have co-morbidities, particularly osteoporosis, compared with the non-SSI group (0.002*), while no other risk significant factors can be detected in the present study which could be related to the small sample size. In contrast Khurana 2021[22] in his review concerning the adverse effects of smoking on spine surgery found that smoking impaired spinal vascular supply and induced local hypoxia, inflammation and proteolysis that could delay wound healing. Zhang et al 2018[23] in their meta-analyses found that smokers have a significantly increased rate of SSI complications including more skin incision necrosis, delayed wound healing and increased possibility of infection [24-27]. The higher risk of infection is typically attributed to smoking impairing the normal phagocytic activity of neutrophils and macrophages against pathogens [27].

Preoperative anaemia has been associated with an increased need for blood transfusions and postoperative complications in various surgical procedures, including cardiac and spinal procedures. Leichtle et al 2011[7], Beattie et al 2009[8], Musallam et al 2009[28]). Phan K, et al 2017 [6]found that preoperative anaemia was a significant predictor of pulmonary intraoperative blood transfusion, return to operating theatre and length of hospital stay.

In hypothyroidism, a decrease type-IV collagen and hydroxyproline was described during the proliferative phase of wound healing. This indicates that hypothyroidism is an important factor in delaying wound healing [9, 10].However in the current study we failed to find significant association of hypothyroidism and SSI.

Factors related to the operative procedure

Previous studies have reported that many different risk factors for SSI are related to the operative procedure[15, 29, 30]). Long surgical time, high levels of estimated blood loss, revision surgery, and intervention over multiple surgical segments are all risk factors for SSI.

A-Blood loss

Consistent to prior research, increased estimated blood loss has been significantly associated with a higher risk of postoperative surgical site infections (SSI). During spinal surgery, greater blood loss often necessitates allogenic blood transfusions, which can lead to relative immunosuppression and impaired wound healing, thereby elevating the risk of postoperative SSI. Furthermore, significant intraoperative blood loss commonly results in lower postoperative hemoglobin levels, which themselves constitute an independent risk factor for SSI. Koutsoumbelis et al. [15] reported that postoperative hemoglobin levels were significantly lower in patients who developed SSI compared to those who did not following lumbar spinal instrumented surgery. Similarly, Tominaga et al. [31] identified low hemoglobin levels as a contributing factor to SSI and suggested that correcting anemia may reduce the likelihood of infection. Additionally, anemia often requires more extensive use of allogenic blood transfusion, further compounding the risk of postoperative SSI.

B- The type and level of spine surgery

SSI rates are affected by the type of surgical procedures [2]. Instrumentation has been used in most of spine operations for the treatment of spinal abnormalities[3]. Meredith et al 2012 [1]and Smith et al 2011[2]found that instrumentation increases the rate of post-operative infections. This was attributed to increased exposure of the wound to air, soft tissue dissection, and muscle/skin retraction[3]. In the present study discectomy was significantly higher among the group needing washout than the other group. Regarding the level of surgery, most patients needing washout were operated at L2-3 while most patients in the other group were operated at L4-5, followed by L5-S1 with significant difference between groups (0.001). However, there was no significant difference between groups regarding whether the operation was de-novo or revision.

C-Duration of surgery

Most reports comparing SSI and controls reported longer hospital stays for patients with SSIs. The average SSI-associated re-admission rate within 30 d from discharge was reported in 4 studies. A number of studies have shown that both prolonged time surgery, and prolonged hospital stays were considered as risk factors of SSIs [32, 33]. In contrast to the result of the current study that found no significant differences in duration of operation and time of hospital stay between groups which may be related to small sample size.

Involvement of Staphylococcus aureus

A recent review reported that 33.3% of MRSA was caused by of *S. aureus* SSIs. Instrumented spinal surgery had the highest average SSI rate (3.8%), followed by spinal decompression (1.8%) and spinal fusion (1.6%), while none recorded SSI in non-instrumental SS [11].In the present study we focussed only on non-instrumental lumbosacral spine surgery and found that 5.13 % had SSI.

The leading causal agent of SSI after spine operations is *Staphylococcus aureus* [34], with several studies reporting that the pathogen was responsible for 41% to 90% of spinal SSIs [35-40]. These results were consistent with our own in which Staphylococcus aureus was found in 33.3 % cases that needing washout, followed by Proprionobacterium acnes (1 case 16.7%) and another 2 cases (33.3%) had no detected growth. However, half of those infected needed antibiotic for 6 months or more. Propionibacterium acnes (P. acnes), an anaerobe, is reported to cause SSI orthopedic surgeries. In contrast, recent studies have shown that the prevalence is probably underestimated according to several points: slow and low growing bacteria, anaerobic conditions not always well-performed[41].This microorganism has been recognized as the cause of various types of implant-associated infections, including neurosurgical shunts[42], internal fracture fixation devices, spinal hardware[43], and prosthetic joints [44]. The present study is the first study that detected P. acnes in non-instrumental spinal surgical procedure.

Limitations of the study: It was a retrospective study in which some information from the patients were incomplete and resulted in some patients being excluded from the sample. A second problem is the small sample size as they recruited from single centre.

While the study provides new insights into infection dynamics in non-instrumental surgeries, its retrospective design and single-center data limit generalizability. Future multicenter prospective studies are warranted.

CONCLUSION

SSIs in non-instrumental lumbar spine surgeries, while less studied, occur with a frequency warranting clinical attention. Surgeons should be particularly vigilant in cases involving osteoporosis, high intraoperative blood loss, discectomy, and high lumbar levels like L2–3. Prophylactic strategies and early interventions may mitigate risks.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (160-171) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Combating Antimicrobial Resistance in ICU-Related CAUTIs: Insights and Strategies" (A Cross Sectional Study)

Ola A. Mohamed[1]. Ahmed Sadek[2], Mohamed A. Hassany[3], Amal H. Ali[1]

[1]Department of Medical Microbiology and Immunology, Faculty of Medicine, Aswan University
[2]Department of Medical Microbiology and Immunology, Faculty of Medicine, Assuit University
[3]Department of Internal Medicine, Faculty of Medicine, Aswan University

ABSTRACT

Keyword: Catheter-associated urinary tract infections, Antimicrobial resistance, Multidrug-resistant pathogens, ICU infections, Carbapenems, Amikacin, Therapeutic strategies

*** Corresponding author:** Ola A. Mohamed
Mobile: 01144480087
E-mail: Drolaa.mohamed@gmail.com

Background and Objective: Catheter-associated urinary tract infections (CAUTIs) are a major source of morbidity in ICU patients, with antimicrobial resistance (AMR) complicating treatment. This study assesses resistance patterns and therapeutic options for CAUTIs in ICU patients at Aswan University Hospital. M**ethodology:** A total of 200 ICU patients with indwelling Foley catheters were included between June 2023 and June 2024. Urine samples were collected 48 hours post-catheterization under sterile conditions. Samples (10–20 cc) were processed for Gram staining and culture, with incubation at 37 °C for 18–24 hours. Antimicrobial susceptibility was tested using the Kirby-Bauer disc diffusion method per CLSI guidelines. **Results:** Gram-negative isolates showed high resistance to ampicillin, amoxicillin-clavulanic acid, and cephalosporins. Carbapenems and amikacin were the most effective antibiotics. Predominant pathogens included multidrug-resistant (MDR) Klebsiella spp. and E. coli. Most Gram-negative isolates were classified as MDR. Additionally, *E. coli* and *Klebsiella spp*. were more frequently isolated in patients with hypertension and diabetes, indicating a potential association with these comorbidities. **Conclusion:** The high prevalence of MDR organisms in CAUTIs highlights the urgent need for antimicrobial stewardship, routine resistance monitoring, and new therapeutic approaches to improve infection control in ICU settings.

INTRODUCTION

Catheter-associated urinary tract infections (CAUTIs) are a leading healthcare-associated infection globally, particularly in intensive care units (ICUs). These infections account for a significant proportion of hospital-acquired complications, often resulting in prolonged hospital stays and increased morbidity and mortality. The widespread emergence of antimicrobial resistance (AMR) among CAUTI pathogens exacerbates the challenge, limiting treatment options and increasing healthcare costs.(1)

In medical literature, the terms "multidrug-resistant" (MDR), "extensively drug-resistant" (XDR), and "pan drug-resistant" (PDR) are commonly used to describe the various resistance patterns seen in AMR bacteria. XDR was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e., bacterial isolates remain susceptible to only one or two categories), PDR as non-susceptibility to all agents in all antimicrobial categories, and MDR as acquired non-susceptibility to at least one agent in three or more antimicrobial categories.(2) The risk factors for UTIs caused by multidrug resistant organisms (MDROs) can be divided into two categories: individual variables, such as a history of UTIs, a diagnosis of dementia or malfunction, diabetes mellitus (DM), and prostate illness, and demographic factors, such as age and female sex. Urinary catheter use is one risk factor, as is previous hospitalization, residing in a nursing home, and prior antibiotic treatment.

Few research are available to assess the endemic antimicrobial resistance profile in low- and middle-income countries, despite the fact that numerous reports have shown the incidence and resistance patterns of numerous diseases(3).As a result, empirical antimicrobial therapy and the treatment of particular diseases are thought to require evidence-based understanding of the local pattern of antibiotic resistance.(4)

ICU patients are particularly vulnerable to CAUTIs due to factors such as extended catheterization periods, immunosuppression, and exposure to broad-spectrum antibiotics (5). Understanding pathogen resistance patterns and tailoring therapeutic approaches is critical to improving outcomes. This study aims to investigate the antimicrobial resistance profiles of CAUTI pathogens and update he antibiogram in Aswan University Hospital.

PATIENTS AND METHODS

Study Design

This prospective observational study was conducted at Aswan University Hospital between June 2023 and June 2024. Data collected from patients' records included: demographic data, diagnosis on admission, history of chronic diseases, duration of hospital stay, insertion of a urinary catheter and duration of the catheter in days.

Patients >18 years of age, having at least two calendar days of urinary catheterization after being admitted to the intensive care unit, and giving informed written consent was included in the study.

The exclusion criteria for this study include patients who are not catheterized, those younger than 18 or older than 70, pregnant women, and patients undergoing chemotherapy. Additionally, patients with a history of sexually transmitted diseases or those who have been on antimicrobial therapy at least 48 hours prior to catheter insertion are excluded. If more than two types of organisms are grown from a clinical sample, the sample will be considered contaminated, and such cases will also be excluded from the study.

Methods:

Sample Collection

Samples were taken based on clinical suspicion in ICU patients who had been catheterized for more than 48 hours.

Following hospital guidelines and standard operating procedures, skilled medical professionals placed sterile indwelling urethral catheters in patients using aseptic techniques to minimize the risk of introducing bacteria into the bladder. To further reduce contamination during urine sample collection, strict aseptic protocols were adhered to, including performing hand hygiene, wearing gloves, and disinfecting the catheter sampling port with 70% isopropyl alcohol prior to aspiration. Urine was collected using a sterile syringe and transferred into a sterile container. If no urine was present in the catheter tubing, it was clamped to allow accumulation before collection.

After obtaining the sample, the tubing was unclamped, and all materials were properly disposed of. Samples were promptly transported to the laboratory or refrigerated if there was a delay. These procedures, in line with CDC and NICE guidelines[6], ensure sample sterility, reduce contamination risk, and enhance diagnostic accuracy.

In patients with short-term catheterization (<7 days), urine specimens were obtained via the catheter port using aseptic technique or, if no port was present, by puncturing the catheter tubing with a needle and syringe after clamping. For patients with long-term catheterization (>7 days), fresh catheter replacement was performed before urine collection.

Laboratory Analysis

• Gram Staining and Culture: Samples were subjected to Gram staining and inoculated onto culture media (Cysteine Lactose Electrolyte Deficient (CLED) agar, blood agar and MacConkey agar). Culture plates were incubated at 37 °C for 18–24 hours.

Routine methods for identifying pathogens in this study included Gram staining and biochemical reactions. In cases where biochemical results were inconclusive, the Vitek-2 compact system (Biomerieux) was utilized to ensure precise pathogen identification. However, the study primarily relied on the Kirby-Bauer disc diffusion method for antimicrobial susceptibility testing, adhering to CLSI guidelines.

The selective use of Vitek-2 in specific cases allowed the study to balance methodological rigor with practical constraints. Uniform application of automated systems could have further enhanced the reliability and accuracy of the resistance data.

• Antimicrobial Susceptibility Testing: The Kirby-Bauer disc diffusion method was used to evaluate susceptibility patterns, following Clinical Laboratory Standards Institute (CLSI) guidelines.

Each isolate's bacterial suspension was made in 0.5 milliliters of nutrient broth medium, and the turbidity was corrected to meet 0.5 McFarland standards. After dipping a sterile brush into the suspension, it was placed in the middle of the Muller Hinton agar plate and spread equally across the medium. After each isolate was seeded onto Muller Hinton agar, antibiotic discs were put on top and incubated for 24 hours at 35–37˚C. Inhibition zone (IZ) diameter was measured using a caliper and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guideline. as susceptible (S), intermediate (I), or resistant (R). *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), and *Pseudomonas aeruginosa* (ATCC 27853) were used as quality control strains (LSI2019).

Classes of antibiotics used. Antibiotic disc used in the present study were: Aminoglycosides (Gentamicin 10µg, Amikacin 10µg, Tobramycin 10µg), Cephalosporins (Cefotaxime 30µg, Ceftazidime 30µg Ceftriaxone 30µg) Nitrofurantoin (Nitrofurantoin 300µg),tetracyclines (tetracycline 30µg),Folate Pathway Inhibitors (trimethoprim- sulfamethoxazole 25µg), Penicillins (oxacillin 30µg, penicillin10µg, Ampicillin 10µg), Glycopeptides (vancomycin 30µg), Carbapenems (Imipenem 10µg, Meropenem 10µ), Fluoroquinolones(ciprofloxacin 5µg). All the antibiotics used in the study were the products of Oxoid, Basingstoke, and Hampshire, England

According to the recently updated CLSI standards[7], interpretative criteria for antibiotic susceptibility testing are revised annually to reflect current best practices.

Data management and Analysis:

Pathogen prevalence and antibiotic resistance patterns were analyzed, focusing on commonly used antibiotics and emerging multidrug-resistant organisms. Data was analyzed using SPSS statistical package (version 28).

RESULTS

Table 1: Distribution of Gram Negative and Gram Positive Organisms Isolated

Classification	Number	Percentage (%)
Gram-negative	194	96.98
Gram-positive	6	3.02

The table shows that Gram negative organisms were predominant, representing approximately 97% of the total isolates, while Gram positive organisms constituted only 3%.

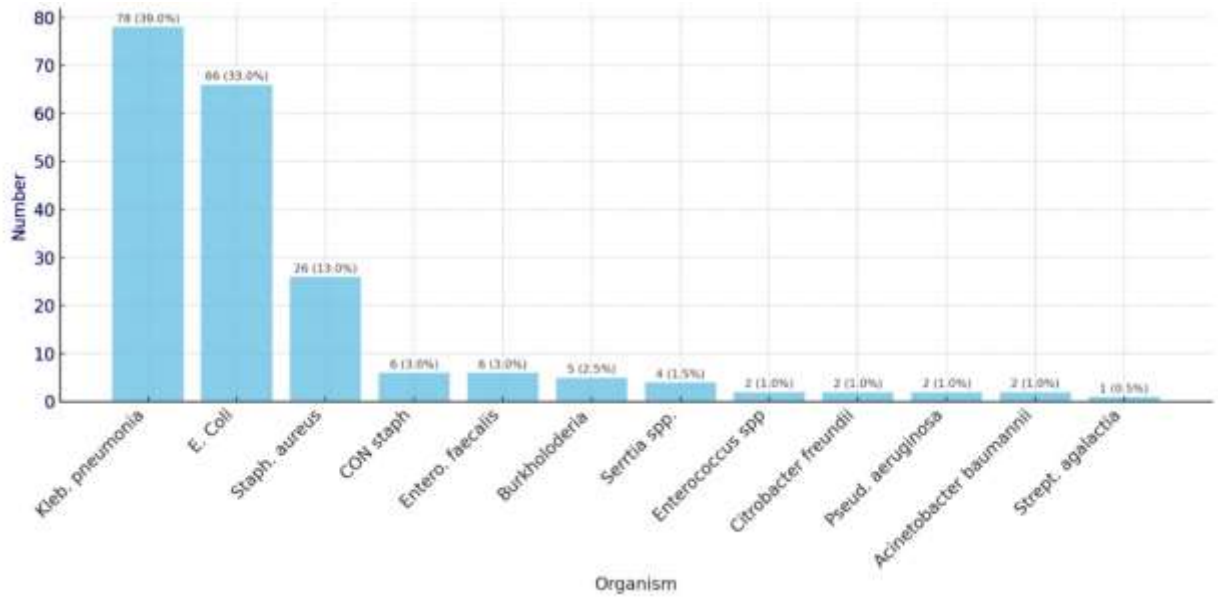

Figure 1: Bar chart showing Distribution of Clinical Bacterial Isolates

Note: *Klebsiella pneumoniae* was the most commonly isolated organism, representing 78 cases (39.0%) of the total isolates. In contrast, *Streptococcus agalactiae* was the least frequent, identified in only 1 case (0.5%).

Table 2: Antimicrobial Susceptibility and Resistance Distribution Across Major Bacterial Isolates and Antibiotics

All values reflect categorical interpretations (Sensitive (S)/Resistent (R)) based on standard clinical breakpoints (e.g., CLSI guidelines).

Antimicrobial Agents	**S/ R**	**Total No.(%)**	***E.coli No.(%)***	***Kleb.pneumoniae No.(%)***	***Staph.aureus No.(%)***	***Enterococcus spp. No.(%)***	***Serratia spp. No.(%)***	***Citrobacter freundii No.(%)***	***Pseud. aeruginosa No.(%)***
Amikacin	S	110 (69%)	50 (90%)	35 (60%)	7 (58%)	5 (63%)	4 (67%)	3 (75%)	2 (22%)
	R	50 (31%)	6 (10%)	23 (40%)	5 (42%)	3 (37%)	2 (33%)	1 (25%)	7 (78%)
Gentamicin	S	125 (72%)	55 (93%)	40 (65%)	8 (62%)	6 (66%)	5 (71%)	4 (80%)	2 (20%)
	R	48	4	22	5	3	2	1	8

		(28%)	(7%)	(35%)	(38%)	(34%)	(29%)	(20%)	(80%)
Meropenem	S	100 (64%)	45 (85%)	30 (55%)	0 (0%)	4 (50%)	3 (75%)	3 (60%)	4 (44%)
	R	56 (36%)	8 (15%)	25 (45%)	0 (0%)	4 (50%)	1 (25%)	2 (40%)	5 (56%)
Nitrofuranto-in	S	90 (60%)	38 (79%)	30 (55%)	8 (50%)	6 (70%)	4 (57%)	2 (50%)	0 (0%)
	R	60 (40%)	10 (21%)	25 (45%)	8 (50%)	3 (30%)	3 (43%)	2 (50%)	3 (100%)
Ciprofloxacin	S	80 (50%)	30 (55%)	25 (45%)	6 (40%)	4 (44%)	3 (43%)	2 (40%)	2 (22%)
	R	80 (50%)	25 (45%)	30 (55%)	9 (60%)	5 (56%)	4 (57%)	3 (60%)	7 (78%)
TMP-SMX	S	70 (56%)	28 (60%)	22 (50%)	6 (46%)	5 (58%)	3 (60%)	3 (67%)	1 (25%)
	R	55 (44%)	19 (40%)	22 (50%)	7 (54%)	4 (42%)	2 (40%)	1 (33%)	3 (75%)
Piperacillin-Tazobactam	S	60 (53%)	25 (62%)	20 (50%)	5 (42%)	3 (50%)	2 (67%)	2 (50%)	1 (17%)
	R	53 (47%)	15 (38%)	20 (50%)	7 (58%)	3 (50%)	1 (33%)	2 (50%)	5 (83%)
Vancomycin	S	65 (67%)	-	-	35 (78%)	20 (63%)	-	-	-
	R	32 (33%)	-	-	10 (22%)	12 (37%)	-	-	-
Ceftriaxone	S	50 (41%)	20 (48%)	15 (40%)	4 (44%)	3 (50%)	2 (50%)	2 (50%)	1 (17%)
	R	72 (59%)	22 (52%)	23 (60%)	5 (56%)	3 (50%)	2 (50%)	2 (50%)	5 (83%)

The table shows high resistance rates among Gram-negative bacteria, particularly *Klebsiella pneumoniae, Citrobacter freundii, and Pseudomonas aeruginosa*, to commonly used antibiotics such as ciprofloxacin, TMP-SMX, and ceftriaxone. P. aeruginosa exhibited the highest resistance, reaching 100% for ciprofloxacin and 83% for ceftriaxone. In contrast, amikacin and meropenem showed better efficacy across most isolates, especially *E. coli and Enterococcus spp.*.

Table 3: Association of Top Comorbidities with Pathogen Distribution and Statistical Significance calculated using the Chi-square test (Fischer's exact test was applied when counts where below 5).

Note: * refer to p value with significant importance (p value < 0.05).

Organism	HTN(n/%) P-value	DM(n/%) P-value	CKD P-value
Kleb.pneumonia	30(38%) 0.03*	28(36%) 0.04*	10(13%) 0.08
E. coli	35(53%) 0.02*	20(30%) 0.05*	11(17%) 0.06
Staph.aureus	12(46%) 0.07	6(23%) 0.09	3(12%) 0.12
Enterococcus spp.	1(50%) 0.15	1(50%) 0.18	0(0%) 0.20
Pseud.aeruginosa	1(50%) 0.22	-	-

This table reveals that hypertension and diabetes are significantly associated with **Klebsiella pneumoniae** and **Escherichia coli* infections, suggesting these comorbidities may influence pathogen susceptibility patterns. Chronic kidney disease did not show significant organism-specific associations.

DISCUSSION

When it comes to health sector governance, antimicrobial stewardship is more stringent in underdeveloped nations. Antimicrobial resistance levels differ among hospital settings and geographical regions, making it difficult to assess the severity of the issue. MDR pathogen infections cause therapy to be delayed, which has a detrimental effect on the patient's health, particularly in immunocompromised patients. [8] Furthermore, one of the main causes of the development of resistance is the lack of awareness on the appropriate use of antibiotics in each community. The goal of the current study was to identify the most common diseases in our community and the patterns of antibiotic resistance they exhibit.

The data presented in Table 1 highlights a statistically significant disparity in the distribution of Gram-negative versus Gram-positive organisms isolated in the clinical setting. Gram-negative bacteria accounted for 96.98% of isolates. Compared to Gram-positive organisms, which consti-

tuted only 3.02%. This finding is similar to **Poddar et al.'s** study, reported a clear predominance of Gram-negative isolates.

The distribution pattern seen in the bar chart further emphasizes the clinical dominance of Gram-negative pathogens, particularly *Klebsiella pneumoniae* and *Escherichia coli*, which together represent over 60% of all bacterial isolates. *Klebsiella pneumoniae*, being the most prevalent organism (n = 78, 39.0%), is known for its capacity to acquire multidrug resistance and cause a broad range of infections. *E. coli* follows closely with 66 cases (33.0%), a finding consistent with its role as a common etiological agent in both community- and hospital-acquired infections. The presence of other Gram-negative organisms such as *Pseudomonas aeruginosa, Citrobacter freundii, and Acinetobacter baumannii*, although in smaller numbers, is clinically significant due to their intrinsic resistance mechanisms and association with high morbidity in hospitalized patients.

In contrast, Gram-positive organisms such as *Staphylococcus aureus* (13.0%), *coagulase-negative staphylococci* (3.0%), and *Enterococcus spp*. (3.0%) were considerably less frequent. Of note, *Streptococcus agalactiae* was detected in only one instance (0.5%), reinforcing its relatively minor role in the infection. This disparity in prevalence could be influenced by several factors, including differences in host susceptibility, hospital infection control practices, and local antibiotic prescribing patterns. The higher standard deviation observed among Gram-positive isolates also suggests greater variability and less predictability in their distribution. These findings underline the urgent need for Gram-negative-targeted infection control measures and guide empirical therapy toward coverage of the most prevalent and resistant organisms.

Additionally, **The Bereanu et al.'s** study [10] published in Antibiotics in 2024 reported that *Klebsiella pneumoniae* was the most commonly isolated microorganism in ICU patients, accounting for 38.7% of infections, followed by *Acinetobacter baumannii* (20.6%) and *Pseudomonas aeruginosa* (8.7%). Similarly, research in the Journal of Infection and Public Health identified *Acinetobacter baumannii* (30.6%), *Klebsiella pneumoniae* (27%), and *Pseudomonas aeruginosa* as the most prevalent Gram-negative bacterial species in healthcare-related infections.

According to **Ma et al.** [11] the prominence of these pathogens is particularly concerning due to their association with multidrug resistance (MDR). The ESKAPE group of pathogens—*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter species*—are known for their ability to "escape" the effects of antibacterial drugs, leading to challenging treatment scenarios.

The comprehensive antimicrobial susceptibility profile table 2 demonstrated notable variability in resistance patterns among common clinical bacterial isolates. *Escherichia coli* exhibited high susceptibility to aminoglycosides such as amikacin (90%) and gentamicin (93%), as well as to carbapenems like meropenem (85%). However, resistance was more pronounced against commonly used oral agents, with ciprofloxacin and TMP-SMX showing lower susceptibility rates of 55% and 60%, respectively. *Klebsiella pneumoniae* displayed a more resistant phenotype overall, with moderate susceptibility to amikacin (60%) and meropenem (55%), but considerably lower sensitivity to fluoroquinolones and β-lactam/β-lactamase inhibitor combinations. *Staphylococcus*

aureus isolates showed expected high susceptibility to vancomycin (78%) and moderate resistance to other tested agents including gentamicin (62%) and ceftriaxone (44%). These findings emphasize the continued efficacy of certain broad-spectrum agents, especially aminoglycosides and carbapenems, against Gram-negative pathogens.

Among other organisms, *Enterococcus spp*. showed moderate susceptibility to vancomycin (63%) and gentamicin (66%), underscoring the need for vigilant monitoring of resistance among Gram-positive cocci. Non-fermenting Gram-negative bacilli such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii* demonstrated high resistance levels across most tested agents, particularly piperacillin-tazobactam and ciprofloxacin, with susceptibility rates as low as 17–22%. Rare isolates like *Serratia spp*. and *Citrobacter freundii* displayed relatively preserved sensitivity to gentamicin, amikacin, and TMP-SMX, albeit from limited sample sizes.

These results align with **Saleem et al.'s** [(12)] findings, which noted *Klebsiella pneumoniae* isolates exhibited high resistance rates to ceftriaxone, tigecycline, and nitrofurantoin, with 80% resistance to the former two antibiotics. Similarly, *Escherichia coli* isolates demonstrated some sensitivity to nitrofurantoin and amikacin (both 19.2%), followed by gentamicin (18.8%) and meropenem (13.9%).

For *Staphylococcus aureus*, susceptibility was highest for nitrofurantoin (13.2%) and gentamicin (10.5%), with lower responses to rifampin, levofloxacin, and vancomycin. *CoNS* exhibited modest sensitivity to vancomycin, gentamicin, and nitrofurantoin (20% each), which remains consistent with current treatment recommendations, although resistance is emerging as in **Kawasuji et al.'s** study. [(13)]

Additionally, the study by **Sader et al.** [(14)] reported that *Klebsiella spp*. exhibited high resistance rates to multiple antibiotics, including ampicillin and cephalosporins, while *E. coli* strains showed significant resistance to cephalosporins but retained susceptibility to carbapenems.

The table 3 illustrates the statistical association between major bacterial pathogens and common comorbidities—Hypertension (HTN), Diabetes Mellitus (DM), and Chronic Kidney Disease (CKD)—. The analysis employed the Chi-square test, with Fisher's exact test applied for low-frequency values (counts < 5). Among the pathogens analyzed, *Klebsiella pneumoniae* and *E. coli* demonstrated statistically significant associations with both HTN and DM, with p-values of 0.03 and 0.04 for *Klebsiella* and 0.02 and 0.05 for *E. coli*, respectively. These findings suggest that patients harboring these organisms were more likely to have these metabolic comorbidities, supporting the hypothesis that such conditions may influence microbial colonization or infection susceptibility.

In contrast, *Staphylococcus aureus, Enterococcus spp.*, and *Pseudomonas aeruginosa* did not show statistically significant associations with any of the studied comorbidities, as indicated by p-values above the 0.05 threshold. For CKD, none of the organisms reached statistical significance, although *E. coli* and *Klebsiella* displayed higher frequencies among CKD patients (17% and 13%, respectively), suggesting a possible trend that may warrant further investigation with a larger sample size. Overall, the data highlight a noteworthy association between gram-

negative pathogens and metabolic diseases such as HTN and DM, potentially guiding targeted prevention and therapeutic strategies in susceptible patient populations.

Preventive antibiotic treatment may theoretically reduce the risk of CAUTIs. However, such prophylaxis is generally not recommended due to concerns about cost, potential adverse effects, and the promotion of antibiotic resistance. The Health Service Executive (HSE) advises against long-term antibiotic prophylaxis in catheterized patients, citing risks such as adverse events and the development of antimicrobial resistance.

Effective CAUTI prevention strategies include appropriate use of urinary catheterization and prompt catheter removal. The National Institute for Health and Care Excellence (NICE) emphasizes the importance of removing or changing catheters as soon as possible when no longer needed to reduce infection risk. Additional preventive measures involve maintaining unobstructed urine flow, using a sterile closed drainage system, and ensuring that trained personnel insert and maintain catheters aseptically. Also, non-antibiotic strategies, such as catheter coatings, probiotics, and bacteriophage therapy, represent promising avenues for future research. CDC recommend these practices as part of a comprehensive approach to prevent CAUTIs.[15]

CONCLUSION

This study confirms the high prevalence of multidrug-resistant pathogens in ICU-related CAUTIs, particularly among *Klebsiella spp.* and *E. coli*. While carbapenems and amikacin remain effective therapeutic options, the reliance on these drugs must be balanced with antimicrobial stewardship initiatives. Hypertention and diabetes are significantly associated with *Klebsiella spp* and *E. coli*. Ongoing surveillance, innovative therapies, and infection prevention measures are critical to mitigating the impact of AMR in ICU settings.

ETHICS AND LIMITATIONS

The study was conducted in accordance with ethical guidelines and approved by the institutional ethics committee at Aswan University Hospital. Informed written consent was obtained from all participants.
Despite its strengths, the study has limitations. The single-center design restricts the generalizability of findings. The exclusion of patients with prior antibiotic use or advanced age (>70 years) may have led to an underestimation of resistance prevalence. Future multicenter studies incorporating broader patient demographics are needed to validate and extend these results.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (172-186) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Potential Impact of Blood Pressure Variability on Right Ventricular Remodeling in Pregnant Women with Pre-Eclampsia or Gestational Hypertension

Aml Mohammed Soliman*, Mahmoud Elsayed Abdellatif, Hossam El-Dein Mohammed, Amr Hanafy Mahmoud

Department of Cardiology, Faculty of Medicine, Aswan University, Aswan, Egypt.

Abstract

Background: Hypertensive disorders of pregnancy complicate as much as ten percent of pregnancies and represent a significant cause of maternal and perinatal morbidity and death. **Objective** of this research was to assess right ventricular (RV) and blood pressure (BP) variability remodeling in females had gestational HTN (GH) and PE, in addition to their correlation. **Methodology**: This observational comparative investigation involved 40 female patients with pregnancy-related hypertensive disorders (Group A) and 20 healthy pregnant women as a control group (Group B) at Aswan University hospital. **Results**: At three-month follow-up, systolic/diastolic BP, RV dimensions, and RV strain remained significantly higher in the cases group, whereas SD of systolic BP and S' were lower (P<0.05). RV structure and function were similar between preeclampsia and gestational hypertension groups, except for higher RAVI, global RV, and free wall RV strain in preeclampsia (P<0.05). Maternal and fetal complications showed no significant difference between groups. **Conclusions**: BP variability significantly impacts RV remodeling in pregnant women with GH and PE. Despite similar maternal and fetal complication rates between groups, the persistence of elevated BP and RV abnormalities postpartum underscores the need for ongoing cardiovascular monitoring and management.

Keyword: Blood Pressure, Right Ventricular Remodeling, Pregnancy, Pre-Eclampsia, Gestational Hypertension.

*** Corresponding author**
Mahmoud Elsayed Abdellatif
Mobile: 01021728001
E-mail:
mahmoud.abdellatief124@gmail.com

INTRODUCTION:

Hypertensive disorders of pregnancy, involving preexisting and gestational hypertension (GH), pre-eclampsia (PE), and eclampsia, complicate approximately ten percent of gestations and represent a significant etiology of maternal and perinatal death and morbidity [1].

Any hypertensive disorder during pregnancy might lead to PE. It presents in as much as thirty-five percent of females with GH and as much as twenty-five percent of those with chronic hypertension (HTN) [2].

Preeclampsia is correlated with two percent to eight percent globally pregnancy-related complications. It leads to nine percent to twenty-six percent of maternal mortalities in low-income countries and sixteen percent in high-income countries. The variables for the initial diagnosis of preeclampsia are specifically described as a systolic blood pressure of 140 millimeters of mercury or greater or a diastolic blood pressure of 90 millimeters of mercury or greater on 2 occasions a minimum of four hours apart; or shorter interval timing a systolic blood pressure of 160 millimeters of mercury or above or a diastolic blood pressure of 110 millimeters of mercury or above may be recorded within a shorter interval, all of that must occur following twenty weeks of pregnancy [3].

The initial presentation of PE usually occurs in near-term pregnancies. Additional significant results that might or might not be present in the clinical presentation involve proteinuria, signs of end-organ damage like thrombocytopenia, compromised hepatic function, severe persistent pain in the

right upper quadrant or epigastric, excluding all alternative diagnoses, new-onset headache unresponsive to all treatment forms, kidney insufficiency, or pulmonary edema with abnormal lab values **[4].**

GH, formerly referred to as pregnancy-induced hypertension, is an onset of hypertension following twenty weeks of gestation. The diagnosis needs that the patient demonstrates [5] high blood pressure (systolic not less than 140 or diastolic not less than 90 millimeters of mercury, with the latter assessed via the 5th Korotkoff sound), previous history of normal blood pressures, absence of protein in the urine, and absence of manifestations of PE or eclampsia. Additionally referred to as HTN, GH is identified retrospectively when the case doesn't develop to preeclampsia and if blood pressure returns to normal by the twelve-week postpartum visit. 50% of females identified with GH among twenty-four and thirty-five weeks develop PE. The diagnosis of GH mandates raised monitoring. Women who progress to severe GH due to elevated blood pressure demonstrate worse perinatal results compared to those with mild preeclampsia and need treatment like to that of severe preeclampsia **[6].**

Dramatic cardio-vascular (CV) changes occur during pregnancy to meet the maternal and growing fetal metabolic requirements. Blood volume increases, and PVR decreases along with progressive placental growth. Increase also in heart rate and cardiac output during pregnancy **[7]**. Cardiac remodeling, involving progressive mild dilation of all cardiac chambers and rise in LV mass, occurs as a compensatory response for such changes. PVR throughout normal gestation keeps low despite raised renin and angiotensin II blood concentrations. This lack of vascular response to activated renin-angiotensin system may be related to the humoral factors such as prostaglandin and progesterone. Abnormal pressure overloading in pregnancy complicated by HTN would result in variant cardiac remodeling compared with that of normal gestation **[8].**

Whereas BP measurements are widely accepted as essential for diagnosing and managing heart failure and HTN, the possible importance of blood pressure variability (BPV), alone or in tandem with heart rate variability (HRV), remains unexamined because of the lack of wearable, convenient, continuous blood pressure monitors **[9].**

Blood pressure variability is characterized as an alteration in arterial blood pressure over a described duration. The complex physiology of blood pressure variability is dependent on the interactions among hemodynamic, humoral, neuronal, in addition to behavioral factors (lifestyle, anxiety, as well as postural alters), environmental factors (atmospheric pressure and climate). and the interaction of aortic compliance and systemic capacitance and is complicated by concurrent antihypertensive and heart failure medical treatments **[10].**

The potential clinical significance of blood pressure variability is not yet fully established; nevertheless, three aspects must be deemed. Blood pressure variability introduces uncertainty in evaluating a subject's blood pressure state, particularly when utilizing spot clinic assessments. The evaluation of BPV may enhance cardiovascular risk stratification, though the size of its independent contribution in this regard still to be superior recorded. Elevated blood pressure variability may serve as a therapy target, with the objective of enhancing results, probably without generating further costs. The option of long-acting medications, in particular dihydropyridine calcium antagonists and combinations of long-lasting compounds, may be indicated for people with raised blood pressure variability; though, the potential clinical advantages of this method remain inadequately demonstrated **[11].** So, in this study we aimed to evaluate RV and BPV remodeling in females with PE and GH, in addition to their correlation.

PATIENTS AND METHODS

In this observational comparative study, we enrolled sixty pregnant women > 18 years old after 20 weeks of gestation collected from those admitted to labour and delivery unit or during a routine

prenatal visit at Aswan university Hospital obstetrics and Gynaecology clinic and we divided them into two groups:

Group A (n=40): with GH or PE and **group B** (n=20): with normal pregnancy serve as control group.

We ruled out patients with gestation period below twenty weeks, congenital heart diseases, moderate to severe valvular heart diseases, cardiomyopathy whatever its reason, underlying RV dysfunction and poor image quality.

Procedure: All cases have been subjected to complete history taking, clinical examination, laboratory investigations [complete blood count (CBC), coagulation profile, platelet count (PLT), international normalization ratio (INR), activated partial thromboplastin time (aPTT), prothrombin time (PT), blood sugar, alanine transaminase (ALT), aspartate aminotransferase (AST), serum creatinine, blood urea, urine albumin (dipstick) and albumin/creatinine ratio in urine] and ECG or any additional research that is needed based on the patients' clinical situation.

- **Office BP measurements:**

  In each visit diastolic blood pressure (DBP) and systolic blood pressure (SBP) have been assessed 2 to 3 times, taking the average of the last 2 readings, the visit-to-visit variability has been identified by coefficient of variation (CV) or standard deviation of either diastolic or systolic blood pressure from baseline, then 3 months post-partum to evaluate BP variability.

- **Non-invasive Imaging:**

Two-dimensional transthoracic echocardiography [12]:

It was performed during pregnancy after 20 weeks of gestation and at 3 months post-partum follows up to evaluate the following parameters:

- RV Basal, mid, and longitudinal diameters.
- RV function by TAPSE and S Velocity methods.
- **Speckle tracking (STE) analysis of RV:**

The examination began by positioning the case in the left lateral decubitus position and the probe was moved across his chest to determine the RV strain [13]. Image acquisition has been conducted from an RV-focused view at the apical four-chamber view to fully visualize the right ventricular free wall, right ventricular apex, and tricuspid valve/annulus within the imaging sector throughout systole and diastole. At a suitable intermediate depth (intermediate depth), any excessive anterior tilt (left ventricular outflow tract not observed) or posterior tilt (coronary sinus not observed) has been avoided. All strain measurements have been automatically given via the software with color coding. The image has been evaluated for tracking quality. Manual corrections have been done when needed. Each segment region of interest (ROI) was carefully discovered for proper placement along the RV-free wall and ventricular septum. region of interest thickness has been set at five millimeters in a non-hypertrophied right ventricular free wall and has been raised in a hypertrophied RV. Pericardial tracking was completely prevented or, at best, minimized to the lowest extent possible for the outer contour. The inner contour was along the endocardial border, excluding trabeculations and papillary muscle. The tracking stopped at the tricuspid annulus and wasn't into the right ventricular or the right ventricular, and away from the tricuspid annulus. right ventricular global longitudinal strain (RV GLS): Involved the RV-free wall and the ventricular septum. Normal range: 20%–25%. right ventricular -free wall strain (RV FWS): excluded the ventricular septum. Normal range: 23%–33%.

Statistical analysis

Statistical analysis has been carried out by SPSS v26 (IBM Inc., Chicago, IL, United States of America). Quantitative parameters have been presented as mean and standard deviation (SD) and compared among the 2 groups applying unpaired Student's t-test. Qualitative parameters have been presented as percentage (%) and frequency and examined utilizing the Chi-square or Fisher's exact

test when suitable. Association among numerous parameters has been conducted utilizing Pearson moment correlation equation. A two-tailed P value under 0.05 has been deemed statistically significant.

Ethical Consideration:

The Medical Ethic Committee of Aswan University's Faculty of Medicine granted IRB permission (IRB?????). Clinical trial.gov was used to prospectively register the study Clinical trial.gov ID:NCT06100484) . The research has been performed following the principles outlined in the Helsinki Declaration [14] and in accordance with CONSORT checklist for research ethics [15]. Prior to the beginning of the research, the title and goal of the study were completely clarified and informed consent from each patient was acquired. All information gathered was kept private and utilized exclusively for scientific study. Each research participant was free to leave the research at any moment without affecting the quality of the medical care they received.

RESULTS

This observational study was performed on 60 pregnant women after 20 weeks of pregnancy and divided into two groups.

Age, parity, gestational age and diabetes, creatinine, Hb, SD of systolic, diastolic Bl P and EF were insignificantly different between both groups. Base line BMI, 24-hrs urine protein level, mean systolic, diastolic Bl P, LVEDD, LVESD, RV basal, mid and longitudinal diameter, RV thickness, RAVI, global RV and free wall RV strain were significantly greater in cases group in comparison with control group (P below 0.05). TAPSE and S' were significantly decrease in cases group compared to control group (P below 0.05). Cases group includes 17 patients (42.5%) with PE and 23 patients (57.5%) with gestational diabetes. **Table 1, Figures (1-4).**

Table 1: Comparison of all examined groups according to demographic, baseline laboratory data, mean systolic, diastolic Bl P, LV, RV parameters and RV strain and description of diagnosis in cases group

	Cases group (n= 40)	Control group (n= 20)	Test	P
Age (years)	30.7±5.2	32.8±4.1	T= -1.550	0.126
BMI (kg/m^2)	31±3.6	28.9±3.7	T= 2.294	**0.025***
Parity	2.4±1.2	2.1±1	T= 1.026	0.309
Gestational age	32±3.9	32.5±4.6	T= -0.372	0.711
Gestational diabetes	4(10.0%)	2(10.0%)	X^2= 0	1
Antihypertensive therapy	20(50.0%)	0(0.0%)	X^2= 15	**<0.001***
Laboratory data				
Creatinine (mg/dL)	86.1±15	79.8±11.4	T=1.646	0.105
Hb (g/dl)	11.2±1.4	11.6±1.3	T=-1.094	0.279
24-hrs urine protein level (mg/day)	894±939	91.4±19.9	T=3.809	**<0.001***
Mean systolic Bl P	152±3.6	120±1.8	T=36.341	**<0.001***
SD of systolic Bl P	3.6±1.8	3±1.8	T=1.137	0.260
Mean diastolic Bl P	92±2	75±3.4	T=24.756	**<0.001***
SD of diastolic Bl P	3±1.7	2.6±1.4	T=0.845	0.402
LV parameters				
EF (%)	60.7±3.5	62.1±2.5	T=-1.582	0.119
LVEDD (mm)	47.9±2.7	45.8±3.8	T=2.462	**0.017***
LVESD (mm)	30.8±3.8	26±3.7	T=4.649	**<0.001***
RV parameters				

RV basal diameter (mm)	33.4±6.5	23.6±2	T=6.578	**<0.001***
RV mid diameter (mm)	32.1±3.4	26.2±2	T=7.227	**<0.001***
RV longitudinal diameter (mm)	75.5±5.1	62±4.9	T=9.797	**<0.001***
RV thickness (mm)	3.3±0.4	3±0.4	T=2.296	**0.025***
TAPSE (mm)	21.6±3.3	23.9±1.9	T=-2.947	**0.005***
S' (cm/s)	11.8±2.4	14±3.3	T=-2.913	**0.005***
RAVI (ml/m^2)	24.1±4.4	17.4±3.1	T=6.068	**<0.001***
RV strain				
Global RV	-19.6±2.2	-23.2±2	T=6.025	**<0.001***
Free wall RV strain (%)	-21.7±2.3	-27.2±2.7	T=8.063	**<0.001***
	Cases group (n= 40)			
Diagnosis				
PE	17(42.5%)		--	--
Gestational HTN	23(57.5%)			

Data are presented as mean ± SD or frequency (%). * Significant P value below 0.05. T: independent sample t test, X^2: chi-square test, BMI: body mass index, Hb: hemoglobin, Bl P: blood pressure, SD: standard deviation, EF: ejection fraction, LVEDD: left ventricular end-diastolic diameter, RV: right ventricular, TAPSE: tricuspid annular plane systolic excursion, RAVI: right atrial volume index, LVESD: left ventricular end-systolic diameter, PE: preeclampsia.

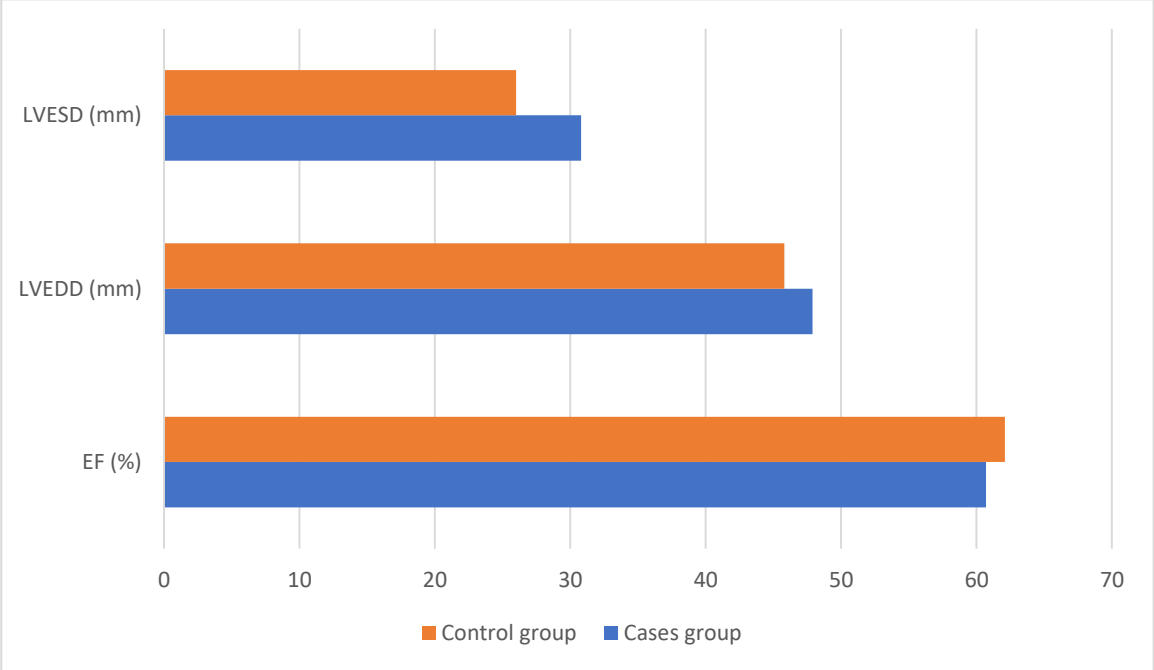

Figure (1): Comparison among the cases and controls according to the baseline mean values of LV parameters.

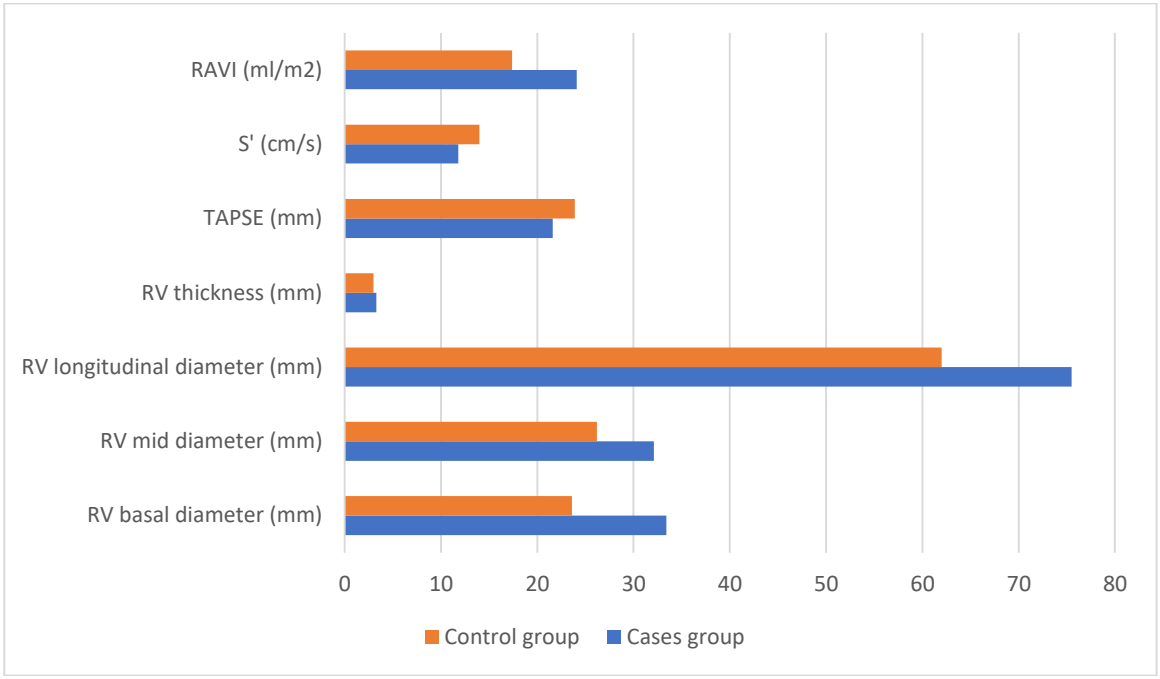

Figure (2): Comparison among the cases and controls as regards the baseline mean values of RV parameters.

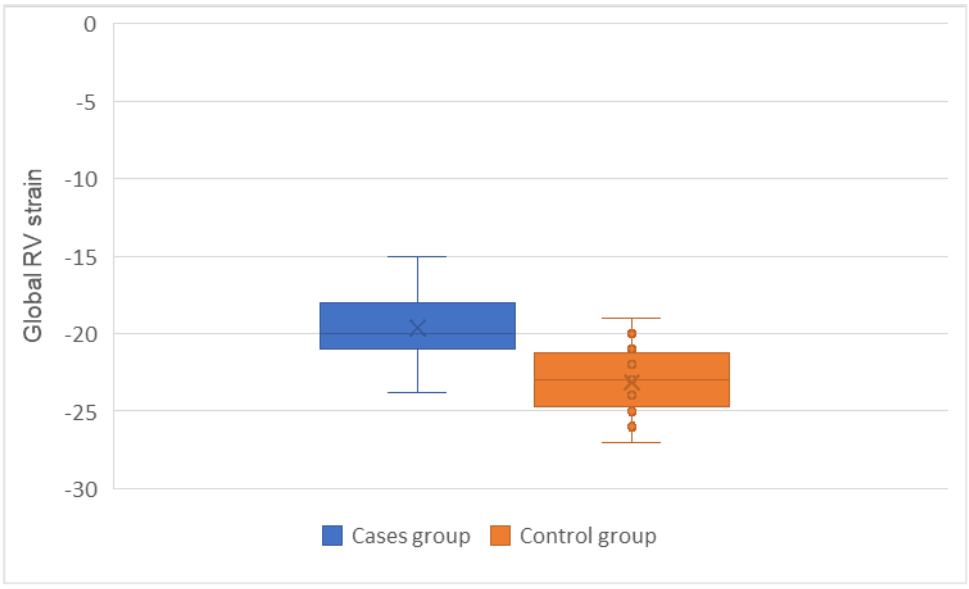

Figure (3): Comparison among the cases and controls as regards the baseline global RV strain.

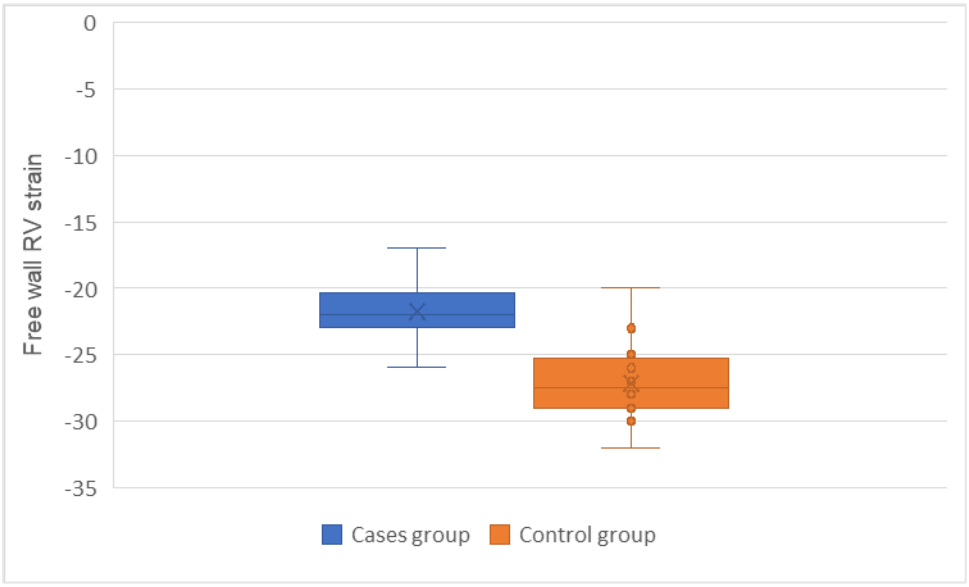

Figure (4): Comparison between the cases and controls regarding the baseline free wall RV strain.

Three months follow up mean systolic and diastolic Bl P, RV basal, mid and longitudinal diameter, global RV and free wall RV strain were significantly greater in cases group compared to control group (P below 0.05). SD of systolic Bl P and S' were significantly reduce in cases group in comparison with control group (P below 0.05). SD of diastolic Bl P, TAPSE, Δ global RV and Δ free wall RV strain were insignificantly variant among both groups. **Table 2, Figure (5-7).**

Table 2: Comparison of all examined groups regarding mean systolic and diastolic Bl P, RV parameters, RV strain and its delta after 3 months

		Cases (n= 40)	Controls (n= 20)	T test	P
After 3 months					
Mean systolic Bl P		125±12.3	117±2.3	3.082	**0.003 ***
SD of systolic Bl P		3.1±1.4	4.2±1.7	-2.700	**0.009 ***
Mean diastolic Bl P		78±7.2	71±2.1	4.229	**<0.001***
SD of diastolic Bl P		3.9±1.9	3.1±1.3	1.709	0.093
RV parameters	**RV basal diameter (mm)**	31±5.1	25±1.9	5.136	**<0.001***
	RV mid diameter (mm)	31.2±3.6	27.2±2	4.628	**<0.001***
	RV longitudinal diameter (mm)	73.6±4.8	63.8±4.1	7.853	**<0.001***
	TAPSE (mm)	23.3±2.7	24.2±1.6	-1.324	0.191
	S'(cm/s)	12.2±2.3	14±3.2	-2.479	**0.016***
RV strain	**Global RV**	-22.3±2.3	-25.3±1.6	5.291	**<0.001***
	Free wall RV strain (%)	-24.3±2.4	-28.6±2.3	6.602	**<0.001***
Δ RV strain	**Δ Global RV**	-13.98±13	-10±9.3	-1.21	0.18
	Δ Free wall RV strain	-12.7±12.1	-6.8±16.4	-1.58	0.12

Δ: delta.

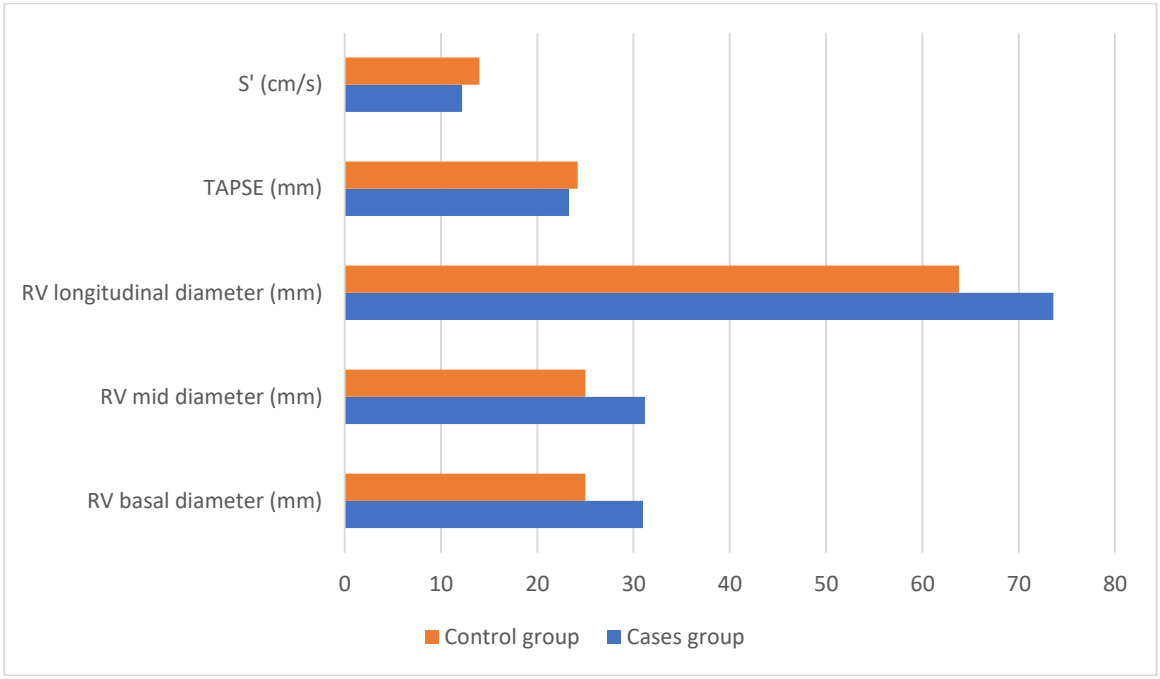

Figure (5): Comparison among the cases and controls according to the mean values of RV parameters after 3 months.

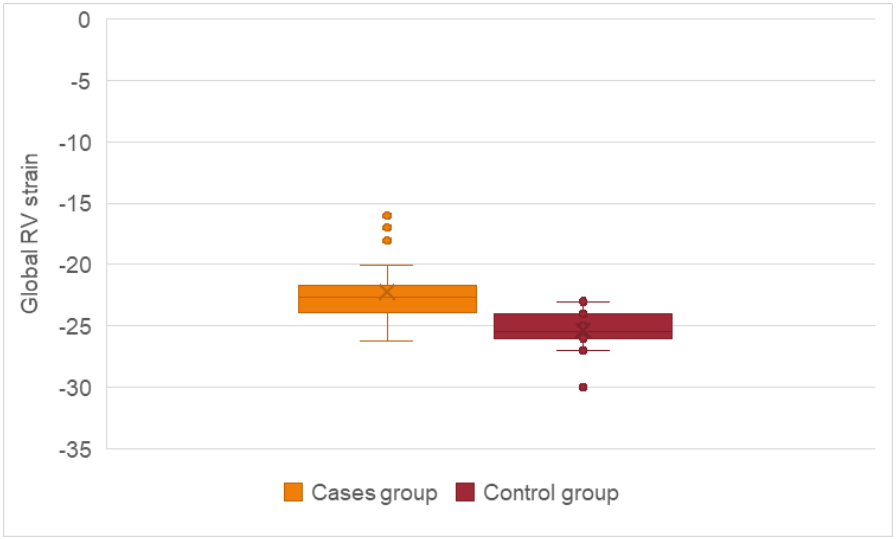

Figure (6): Comparison among the cases and controls as regards the global RV strain after 3 months

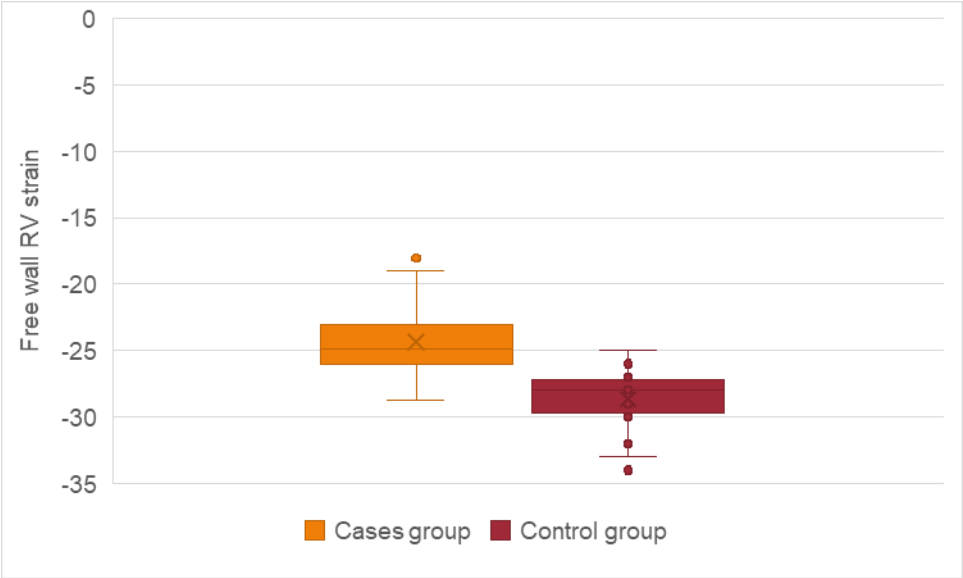

Figure (7): Comparison among the cases and controls as regards the free wall RV strain following three months

There was a significant negative association among mean systolic blood pressure and age and TAPSE in cases group (P below 0.05). There was a significant positive association among mean systolic blood pressure and creatinine, RV mid and longitudinal diameter, RAVI, global RV and free wall RV in cases group (P below 0.05). There was a significant positive association among mean diastolic BP and BMI, creatinine, RV basal and longitudinal diameter, global RV and free wall RV in cases group. There was a significant negative association among mean diastolic BP and TAPSE and S'. There were no significant association among mean systolic and diastolic BP and other parameters in cases and control group. There was a significant negative association among mean diastolic BP and BMI and parity in control group (P below 0.05). **Table 3**

Table 3: Relation among mean systolic and diastolic BP and other studied parameters in cases and control group

	Mean systolic Bl P		**Mean diastolic Bl P**		**Mean systolic Bl P**		**Mean diastolic Bl P**	
	R	**P**	**r**	**P**	**r**	**P**	**r**	**P**
Cases group					**Control group**			
Age	-0.330	**0.037***	-0.178	0.273	0.078	0.744	0.202	0.394
BMI	0.123	0.449	0.340	**0.032***	-0.002	0.993	-0.547	**0.012***
Parity	0.002	0.988	-0.039	0.812	0.004	0.987	-0.482	**0.031***
Gestational age	0.033	0.841	-0.077	0.639	0.320	0.169	0.039	0.870
Creatinine	0.325	**0.041***	0.316	**0.047***	-0.228	0.334	-0.069	0.773
Hb	-0.179	0.268	-0.296	0.064	-0.018	0.938	-0.304	0.193
24h urine protein	0.235	0.145	0.118	0.469	0.317	0.173	-0.053	0.823
EF	-0.002	0.990	-0.096	0.556	-0.070	0.769	0.245	0.298
LVEDD	0.094	0.564	0.067	0.679	0.266	0.257	-0.166	0.485
LVESD	0.124	0.447	0.139	0.393	-0.122	0.607	-0.194	0.412
RV basal diameter	0.280	0.081	0.336	**0.034***	0.036	0.880	-0.045	0.850
RV mid diameter	0.353	**0.026***	0.272	0.089	0.069	0.773	0.087	0.716
RV longitudinal diameter	0.459	**0.003***	0.332	**0.036***	0.233	0.322	-0.035	0.884
RV thickness	0.200	0.217	0.283	0.076	-0.109	0.648	-0.333	0.152

TAPSE	-0.349	**0.027**	-0.316	**0.047***	0.428	0.060	-0.361	0.118
S'	-0.283	0.077	-0.379	**0.016***	0.339	0.144	-0.053	0.826
RAVI	0.320	**0.044***	0.194	0.231	0.174	0.463	-0.252	0.283
Global RV	0.429	**0.006***	0.396	**0.011***	0.037	0.876	-0.197	0.406
Free wall RV strain	0.440	**0.005***	0.391	**0.013***	-0.074	0.758	0.139	0.560

r: correlation coefficient.

There was a significant positive relation among mean systolic and diastolic BP and right ventricular basal, mid and longitudinal diameter, global RV and free wall RV strain in cases group after three months (P below 0.05). There was a significant negative association among mean systolic and diastolic BP and TAPSE, S' (P below 0.05). There was insignificant relation among mean diastolic and systolic BP and other parameters in control group after 3 months. There was a significant negative association among mean diastolic BP and S' in control group after 3 months (P below 0.05). **Table 4**

Table 4: Relation among mean systolic and diastolic BP and other studied parameters following three months of monitoring in cases and control group

	Mean systolic Bl P		**Mean diastolic Bl P**	
	R	**P**	**r**	**P**
After 3 months follow up in cases group				
RV basal diameter	0.735	**<0.001***	0.724	**<0.001***
RV mid diameter	0.542	**<0.001***	0.617	**<0.001***
RV longitudinal diameter	0.686	**<0.001***	0.779	**<0.001***
TAPSE	-0.363	**0.021***	-0.369	**0.019***
S'	-0.422	**0.007***	-0.410	**0.009***
Global RV	0.803	**<0.001***	0.775	**<0.001***
Free wall RV strain	0.717	**<0.001***	0.637	**<0.001***
After 3 months follow up in control group				
RV basal diameter	0.048	0.841	-0.025	0.918
RV mid diameter	0.038	0.873	0.098	0.681
RV longitudinal diameter	-0.174	0.463	-0.188	0.427
TAPSE	0.207	0.381	-0.136	0.567
S'	-0.147	0.537	-0.454	**0.044***
Global RV	0.142	0.549	0.149	0.530
Free wall RV strain	0.078	0.745	0.129	0.586

RV basal, mid and longitudinal diameter, right ventricular thickness, TAPSE and S' were insignificantly different among both groups. RAVI, global right ventricular and free wall RV strain were significantly greater in pre-eclampsia group in comparison with gestational HTN group (P below 0.05). RV parameters and RV strain were insignificantly variant among both groups after 3 months. **Table 5**

Table 5: Comparison of PE and gestational HTN patients regarding RV parameters and RV strain and after 3 months in cases group

		PE (n= 17)	**Gestational HTN (n= 23)**	**T test**	**P**
RV parameters	**RV basal diameter (mm)**	34.8±7.3	32.4±5.8	1.1	0.25
	RV mid diameter (mm)	33±3.7	31.4±3.1	1.5	0.15
	RV longitudinal diameter (mm)	76.5±6.1	74.8±4.3	1.1	0.3
	RV thickness (mm)	3.4±0.4	3.3±0.5	0.7	0.49
	TAPSE (mm)	20.8±3.4	22.1±3.2	-1.3	0.2

	S'(cm/s)	11.9±2.2	11.8±2.5	0.13	0.9
	RAVI (ml/m^2)	25.8±3.8	22.8±4.5	2.22	**0.032***
RV strain	**Global RV**	-18.4±2	-20.6±1.8	2.5	**0.001***
	Free wall RV strain (%)	-20.8±2.1	-22.4±2.3	2.3	**0.028***
After 3 months					
RV parameters	**RV basal diameter (mm)**	32.1±6	30.2±4.3	1.2	0.25
	RV mid diameter (mm)	30.8±3.7	31.4±3.6	-0.58	0.57
	RV longitudinal diameter (mm)	73.9±5.6	73.4±4.2	0.36	0.72
	TAPSE (mm)	22.6±3.1	23.9±2.4	-1.5	0.15
	S'(cm/s)	12.2±2.8	12.2±2	-0.04	0.97
RV strain	**Global RV**	-21.7±2.5	-22.6±2.2	1.2	0.24
	Free wall RV strain (%)	-24.2±2.6	-24.4±2.3	0.28	0.78

Maternal and foetal complications were insignificantly variant between both groups. **Table 6, Figures (8-9).**

Table 6: Comparison of all studied groups regarding maternal and fetal complications

		Cases group (n= 40)	**Control group (n= 20)**	**X^2**	**P**
Maternal complications	**Eclampsia**	3(7.5%)	0(0.0%)	1.58	0.21
	Haemorrhage	10(25.0%)	4(20.0%)	0.186	0.67
	Pre-term labor	13(32.5%)	3(15.0%)	2.1	0.15
Fetal complications	**IUFD**	4(10.0%)	2(10.0%)	0	1
	IUGR	12(30.0%)	3(15.0%)	1.6	0.21
Complications after 3 months					
Persistent HTN		6(15.0%)	0(0.0%)	3.33	0.068
Post-partum haemorrhage		7(17.5%)	1(5.0%)	1.8	0.179
Post partum fits		3(7.5%)	0(0.0%)	1.58	0.21
Fetal deaths		3(7.5%)	1(5.0%)	0.134	0.714

IUGR: intrauterine growth restriction, IUFD: intrauterine fetal demise, HTN: hypertension.

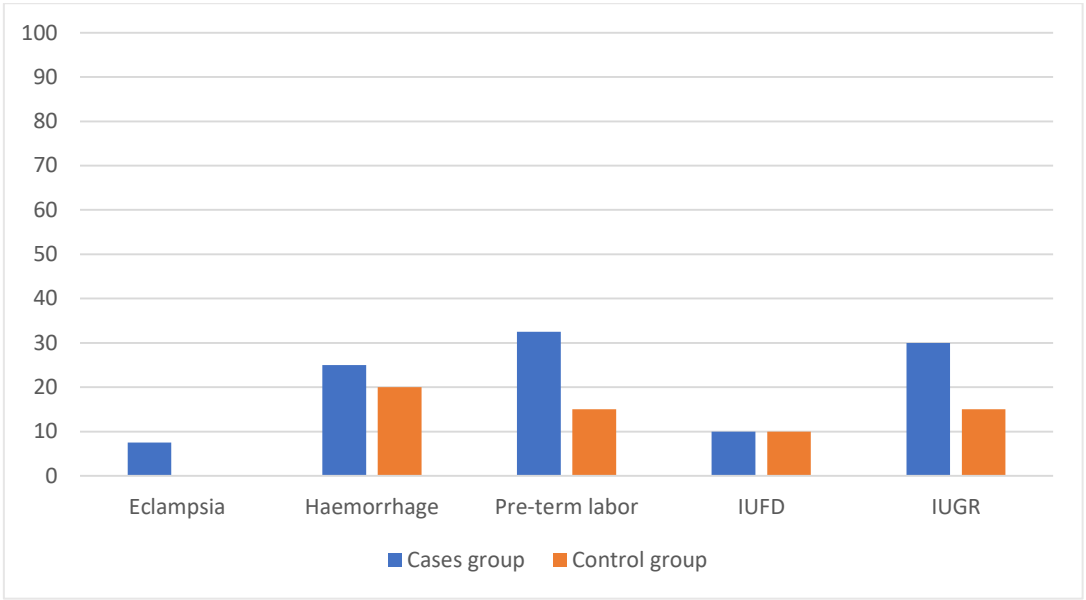

Figure (8): Comparison between cases and controls regarding complications.

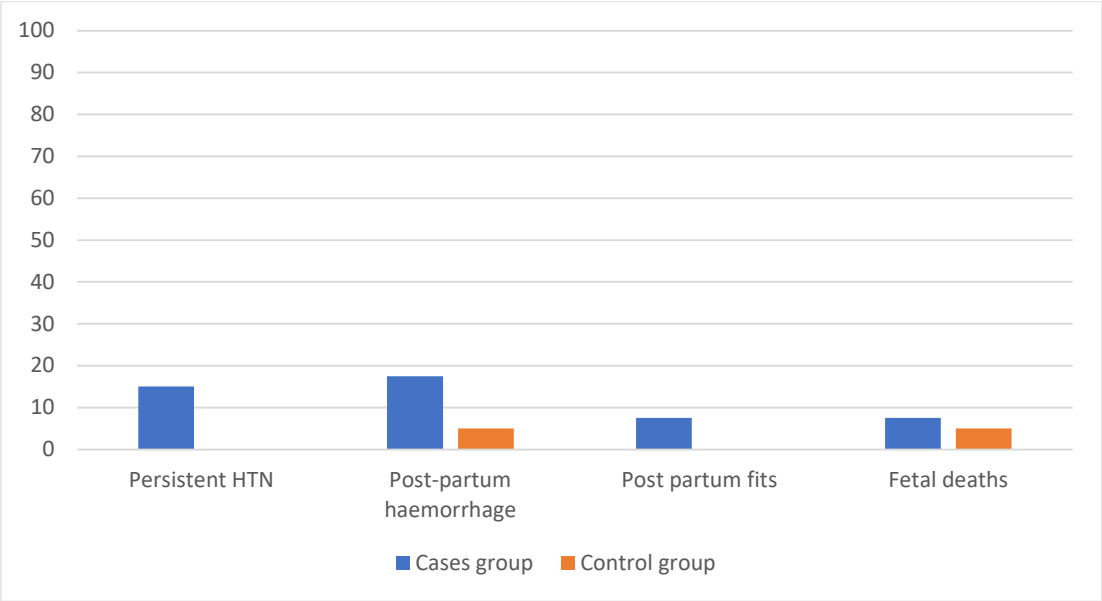

Figure (9): Comparison between cases and controls regarding complications after 3 months.

DISCUSSION

Hypertensive disorders in pregnancy (HDP) represent one of the most frequent complications throughout pregnancy. This entity involves numerous hypertensive disorders and all of them are related to raised death and morbidity throughout gestation and especially in its late stage [13].

Regarding comparison of all studied groups as regard maternal and fetal complications. There were non-significant variances among the groups for eclampsia, maternal hemorrhage, preterm labor, IUFD, IUGR, persistent HTN, post-partum hemorrhage, post-partum fits and fetal deaths. Our study disagrees with Masoura et al. [16] stated that there was statistically significant greater IUGR in the PE group in comparison with controls. Additionally, Davies et al. [7] stated that a significant positive correlation was found among PE and preterm birth.

In our study cases had significantly greater mean diastolic and systolic BPs compared to controls. No significant difference has been observed in the SD of systolic and diastolic BP. After 3 months, cases had significantly higher mean systolic BP compared to controls and significantly lower SD of systolic BP compared to controls. Mean diastolic BP was significantly higher in cases vs. controls. No significant difference in SD of diastolic BP. Large study by Jieyu et al. [17] stated comparable outcomes with significantly greater blood pressure variability among females has GH and PE in comparison with in normotensive controls. Additionally, Mesquita et al. [18] reported hypertensive pregnancy disorders exhibited higher systolic and diastolic BP than females whose diagnosis of HTN didn't occur throughout gestation.

In agreement with our result about LV, RV parameters and RV strain, Paudel et al. [19] illustrated that preeclamptic cases had a significantly greater left atrium, a thicker interventricular septum, greater systolic pulmonary artery pressure, and an increased mitral E/e′ ratio in comparison with controls throughout gestation, whereas left ventricular ejection fraction remained comparable. Preeclamptic cases demonstrated significantly decreased left ventricular and RV GLS throughout gestation in comparison with controls. Çağlar et al. [20] stated a significant enlargement of right ventricular and RA, and deterioration of right ventricular diastolic and systolic function in females had PE in comparison with controls.

In cases, mean systolic BP correlated significantly with age, creatinine, RV mid diameter, RV longitudinal diameter, TAPSE, RAVI, global RV and free wall RV strain. No significant correlations were found with other parameters. Mean diastolic BP significantly correlated with

BMI, creatinine, RV basal diameter, RV longitudinal diameter, TAPSE, S, global RV and free wall RV strain. No significant correlations were found with other parameters. In controls, mean systolic BP shows no significant correlations with other parameters. Mean diastolic BP significantly negatively correlates with BMI and parity. No other significant correlations are found. A study by Melchiorre et al. [21] reported that global diastolic dysfunction has been discovered more frequently in PE against control pregnancies. Raised cardiac work and left ventricular mass indices recommend that left ventricular remodeling was an adaptive response to sustain myocardial contractility with PE at term. Furthermore Ganesh et al. [22] reported significant risk factors recognized in univariate analysis involved pre-pregnancy body maa index above twenty-five, history of chronic hypertension, history of kidney illness, history of diabetes, family history of hypertension, history of pre-eclampsia in previous gestation and numerous gestation.

After 3 months in cases, mean systolic BP significantly positively correlated with RV mid diameter, right ventricular basal diameter, RV longitudinal diameter, global right ventricular and free wall RV strain. It negatively correlated with TAPSE, and S. Mean diastolic BP significantly positively correlated with right ventricular basal diameter, RV longitudinal diameter, right ventricular mid diameter, global RV and free wall RV strain. It negatively correlated with TAPSE and S. In controls after 3 months, mean systolic BP showed no significant correlations with other parameters. Mean diastolic BP had a significant negative correlation with S. No other significant correlations were found. A study by Countouris et al. [23] revealed that Compared with females with normotensive pregnancies, those with Hypertensive disorders in pregnancy history were more likely to have present HTN. Following adjusting for race, age, MVM lesions, current HTN, BMI, and hemoglobin A1c, females have hypertensive disorders in pregnancy history had greater interventricular septal thickness and relative wall thickness.

In agreement with our result about PE and gestational HTN patients regarding RV parameters and RV strain and after 3 months in cases group, Tadic et al. [13] reported that twenty-four hours, daytime, and nighttime diastolic and systolic blood pressures, in addition to visit-to-visit diastolic and systolic blood pressures, were significantly raised in females with pre-eclampsia and gestational hypertension compared to the control group. The parameters of short- and long-term blood pressure variability gradually raised from the control group, through those with pre-eclampsia, to those with GH. The right ventricular diameter, E/e′ ratio, and PAP were significantly greater in females with GH and PE compared to the control group.

Limitations of the study:

- The research was in an only one center.
- the sample size was comparatively small.
- The monitoring of cases has been restricted for relatively short duration.
- the observational nature of the study means that causality cannot be definitively established between BP variability and RV remodeling. Variations in individual treatment regimens and adherence to antihypertensive therapy may have influenced the outcomes, potentially introducing variability in the results.

CONCLUSIONS

BP variability significantly impacts RV remodeling in pregnant women with PE and GH. Elevated BP during pregnancy is associated with pronounced RV structural changes and impaired function, as evidenced by increased RV dimensions, decreased TAPSE, and altered RV strain measurements. Despite similar maternal and fetal complication rates between groups, the persistence of elevated BP and RV abnormalities postpartum underscores the need for ongoing CV monitoring and management. These results emphasize the critical importance of early intervention and comprehensive postpartum care to address the long-term CV risks associated with HDP.

Disclosure Statement: There were no conflicts of interest for the authors.

Financial support and sponsorship: None.

Author Contribution:

Mahmoud Elsayed Abdellatif (MEA); design, concept, clinical studies, literature search, statistical analysis, manuscript preparation. **Hossam Eldein Mohammed Mohammed (HMM);** design, literature search, manuscript preparation and review**. Amr Hanafy Mahmoud (AHM);** design, literature search, clinical investigations, final draft review. **Aml M. Soliman (AMS):** literature search, clinical investigation, manuscript editing and final draft preparation and review**.**

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (187-196) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Gastric Ultrasound as a Predictor of Postoperative Vomiting in Pediatric Emergency Surgery: A Randomized Controlled Study.

Ayman Mohamady Eldemrdash, Zaher Zaki Zaher, Tarek S. Hemaida, Soudy S. Hammad, Doaa Hamdy Hassaneen*, Mohammed Ahmed Alazhary.

Anesthesiology, Intensive Care and Pain Management Department, Faculty of Medicine, Aswan University

ABSTRACT

Keyword: : NT, NICU, PMI Guideline, PC Guideline.

* **Corresponding author**: Doaa Hamdy Hassaneen

Mobile: 01113542707

E-mail: hdoaa520@gmail.com

Introduction: Postoperative nausea and vomiting (PONV) are common in pediatric surgery. This study compared peri-operative risk factors and gastric volume using ultrasound in pediatric traumatic and non-traumatic emergency surgeries. **Methods:** A double-blinded RCT at Aswan University Hospital included 50 patients (2-13 years) undergoing urgent surgery. Gastric ultrasound measured anteroposterior diameter (APD), craniocaudal diameter (CCD), and cross-sectional area (CSA) in supine and right lateral decubitus (RLD) positions. Risk scores for PONV were calculated, and data were analyzed using R software**. Results**: Traumatic cases (82%) showed lower risk scores than non-traumatic cases ($p<0.001$). In the RLD position, non-traumatic cases had higher APD ($p=0.03$). Pre-operative vomiting cases were older (10 vs. 5 years, $p=0.001$) and had higher risk scores ($p<0.001$). CCD was smaller in non-vomiting cases in the supine position ($p=0.011$). No significant differences were found in predicted gastric volume. **Conclusion:** Gastric ultrasound aids in assessing peri-operative risk in pediatric emergency surgery. Individualized risk assessment is crucial, particularly in traumatic cases and younger patients. Gastric ultrasound can help refine risk assessment and perioperative management strategies for pediatric emergency surgeries.

INTRODUCTION

Postoperative nausea and vomiting (PONV) are common complications after pediatric surgery and are often associated with pain. In view of the markedly increase in prevalence between pediatric patients, it is vital to discover the key PONV risk factors in order to enhance treatment approaches (1.)

In addition to its impact on patient well-being, PONV has been reported to affect both child and family satisfaction and sometimes cause statistically noteworthy resource usage, including prolonged hospital recovery time and unexpected hospitalization (2) Furthermore, serious medical complications may

occur, as aspiration, dehydration associated with electrolyte imbalance , post-operative bleeding, airway obstruction, increase in intracranial pressure and surgical sutures dehiscence. (3)

The technique of anesthetic induction also the airway management practices could vary between elective and urgent surgical procedures. Risk factors as trauma, opioid administration, and intra-abdominal procedures may challenge the usefulness of recommended NPO protocols and guidelines in having an empty stomach, aiming outcome free from preoperative vomiting and aspiration risks throughout typical induction procedures.(4)

Gastric ultrasound is a valuable non-invasive tool for assessing gastric content and volume in real time, helping predict postoperative vomiting and aspiration risk. Lots of previous studies have proved the efficacy of gastric ultrasound in assessing post-operative vomiting and aspiration risk then guiding the anesthetic practice decisions in pediatric patients experiencing both elective and emergency procedures (4) . Moreover, routine point-of-care ultrasound (POCUS) assessments have been revealed to modify anesthesia management strategies in trauma patients by exactly predicting the gastric volume and limit the risk of post-operative vomiting (5)

This study aims to evaluate and compare peri-operative risk factors in pediatric traumatic and non-traumatic surgical cases, with a specific focus on gastric volume assessments via gastric ultrasound measurements. Through identifying significant differences and correlations, this study aims to inform evidence-based perioperative management strategies. for pediatric patients undergoing emergency surgery.

PATIENTS AND METHODS

This study is derived from a double blinded randomized controlled (RCT) that was conducted in Aswan University hospital as a secondary analysis of a previous RCT.

The study enrolled pediatric patients aged 2-13 years who were scheduled for urgent surgery, defined as surgery that could not be postponed for more than 48 hours after clinical onset. Patients were divided into two groups: traumatic and non-traumatic surgical cases. Exclusion criteria included severely shocked patients, those with diffusely distended abdomens that could obstruct gastric ultrasound (US), patients with a history of hypersensitivity to famotidine, and those with hepatic or renal impairments.

All patients underwent gastric ultrasound assessments to evaluate gastric content and volume. The ultrasound measurements were taken in both the supine and right lateral decubitus (RLD) positions. The anteroposterior diameter (APD), craniocaudal diameter (CCD), and cross-sectional area (CSA) of the gastric antrum were measured. Predicted gastric volume (GV) was calculated based on these measurements.

Additionally, Data on patient demographics, surgical duration, pre-operative vomiting, and risk scores for post-operative nausea and vomiting (PONV) were collected. The risk scores were calculated based on factors such as age, duration of surgery, and type of surgery. The degree of risk was categorized as low, moderate, or high.

Analysis:

Analyses were conducted using the R Statistical language (version 4.1.2; R Core Team, 2021) on Windows 10 x64 (build 19045). The Kruskal. Test. function is used for non-normally distributed continuous data and is equivalent to Wilcox. Test when comparing two groups. For categorical data, we use the Chi-square test to compare categories when there are only two groups, while the Kruskal-Wallis Rank Sum Test is used for more than two groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Risk Factor for Vomiting and Scoring of Risk for Patients Undergoing Emergency Pediatric Surgery:

This table shows significant differences in the risk scores and degree of risk between traumatic and non-traumatic surgeries, with non-traumatic cases presenting a higher risk of vomiting. No significant differences were found for age, surgery duration, or pre-operative vomiting. The findings suggest that surgery type is a key factor in assessing vomiting risk.

Table 1 : Risk factor for vomiting and Scoring of risk for patients undergo emergency pediatric surgery

	Overall (n = 50)	**Traumatic** (n = 41)	**Non Traumatic** (n = 9)	p-value
Age (Years)	8.50 [5.00, 11.00]	8.00 [5.00, 11.00]	11.00 [7.00, 11.00]	0.647
Duration of Surgery (Min)	90.00 [60.00, 97.50]	90.00 [60.00, 90.00]	90.00 [60.00, 120.00]	0.359
Scoring of Risk	21.00 [13.00, 21.00]	21.00 [13.00, 21.00]	36.00 [21.00, 36.00]	**0.002**
Degree of Risk				**<0.001**
High risk	6 (12.0)	0 (0.0)	6 (66.7)	
Moderate risk	37 (74.0)	34 (82.9)	3 (33.3)	
Low risk	7 (14.0)	7 (17.1)	0 (0.0)	
Gender = male	41 (82.0)	33 (80.5)	8 (88.9)	0.908
Pre-operative Vomiting	33 (66.0)	26 (63.4)	7 (77.8)	0.663

Data presented, Median - [IQR] , n(%)

There was no significant difference between the Traumatic and non- Traumatic groups regarding the age or duration of surgery (p = 0.647 and p 0.359, respectively). Most patients had a moderate risk score (74%), while 12% had a high-risk score. Although two other risk factors were included, none of the 50 patients had a history of previous PONV or were predisposed to multiple opioid doses (**Table 1**).

Table 2: Type of Emergency Pediatric Surgery

Comment: Traumatic surgeries comprised 82% of the cases, with orthopedic fractures being the most common (46%). The table highlights the diversity in surgical types, with non-traumatic surgeries representing a smaller proportion (18%). Significant differences were observed in risk scores and degree of risk between traumatic and non-traumatic groups.

Table 2 : Type of emergency pediatric surgery		
Type of surgery	**surgery Category**	**N (%)**
Orthopedic fracture trauma	Traumatic	23 (46%)
Soft Tissue trauma	Traumatic	12 (24%)
Abdominal Surgery	Non Traumatic	9 (18%)
Neuro-eye Trauma	Traumatic	4 (8%)
Compartmental Syndrome	Traumatic	2 (4%)

Our study included 50 patients with a median age of 8.5 years, of which 41 (82%) were male. Traumatic surgeries made up 82% of the cases, with orthopedic fracture repair being the most common (46%), followed by soft tissue trauma (24%) (**Table 2**). Non-traumatic surgeries accounted for 9 cases (18%). There is significant difference in the risk score and degree of risk traumatic and non-traumatic surgery ($p = 0.02$ and $p < 0.001$, respectively).

Table 3: Gastric Ultrasound Measurement in Pediatric Patients by Surgery Category

In the supine position, no significant differences were found between traumatic and non-traumatic cases for APD, CCD, or CSA. However, in the RLD position, non-traumatic cases had a significantly higher APD ($p = 0.03$). Other measurements, such as gastric volume, did not show significant differences between the two groups.

Table3 : Gastric Ultrasound Measurement in Pediatric Patients by Surgery Category					
Position	Variables	Overall (n = 50)	Traumatic (n = 41)	Non Traumatic (n = 9)	p-value
Supine Position	APD	1.10 [0.90, 1.40]	1.10 [0.85, 1.40]	1.20 [1.10, 1.40]	0.34
	CCD	2.85 (0.54)	2.85 (0.56)	2.82 (0.47)	0.89
	CSA	2.64 (0.97)	2.62 (1.01)	2.73 (0.83)	0.78
RLD	APD	1.18 (0.25)	1.15 (0.25)	1.34 (0.24)	**0.03**
	CCD	2.95 [2.40, 3.30]	2.90 [2.50, 3.30]	3.00 [2.30, 3.20]	0.81
	CSA	2.62 (0.76)	2.55 (0.73)	2.94 (0.86)	0.16
	Predicted GV	104.85 (36.43)	101.03 (36.32)	122.29 (33.44)	0.11

Data presented Mean ± SD, Median - [IQR] , n(%)

In our study comparing traumatic and non-traumatic cases, we found that in the supine position, there were no significant differences between the two groups for anteroposterior diameter (APD), craniocaudal diameter (CCD), and cross-sectional area (CSA). However, in the right lateral decubitus (RLD) position, a significant difference was observed in APD ($p = 0.03$), with non-traumatic cases showing higher values. No significant differences were found in CCD, CSA, or predicted gastric volume (GV) in the RLD position. (**Table 3**).

Table 4: Risk Factor and Gastric Ultrasound Measurement in Patients Undergoing Emergency Pediatric Surgery by Pre-operative Vomiting

Non-vomiting patients were younger and had lower risk scores compared to vomiting patients, with significant differences observed. In the supine position, CCD was significantly smaller in non-vomiting cases. No significant differences were found in pre-operative gastric volume or RLD position measurements between the two groups.

Table4 : Risk factor and Gastric Ultrasound Measurement in the patients undergo emergency pediatric surgery by Pre-operative Vomiting

	Overall (n = 50)	**Vomiting** (n = 33)	**Non Vomiting** (n = 17)	p-value
Age (Years)	8.50 [5.00, 11.00]	10.00 [7.00, 12.00]	5.00 [3.00, 8.00]	**0.001**
Duration of Surgery (Min)	90.00 [60.00, 97.50]	90.00 [60.00, 90.00]	90.00 [60.00, 120.00]	0.438
Scoring of Risk	21.00 [13.00, 21.00]	21.00 [21.00, 21.00]	13.00 [13.00, 13.00]	**<0.001**
Degree of Risk				0.091
High risk	6 (12.0)	6 (18.2)	0 (0.0)	
Moderate risk	7 (14.0)	3 (9.1)	4 (23.5)	
Low risk	37 (74.0)	24 (72.7)	13 (76.5)	
Gender = male	41 (82.0)	28 (84.8)	13 (76.5)	0.732
Supine APD	1.10 [0.90, 1.40]	1.10 [0.91, 1.40]	1.10 [0.88, 1.30]	0.622
Supine CCD	2.85 (0.54)	2.98 (0.54)	2.58 (0.44)	**0.011**
Supine CSA	2.64 (0.97)	2.79 (0.99)	2.35 (0.89)	0.132
RLD APD	1.18 (0.25)	1.18 (0.29)	1.19 (0.18)	0.931
RLD CCD	2.95 [2.40, 3.30]	3.10 [2.50, 3.30]	2.70 [2.10, 3.00]	0.085
RLD CSA	2.62 (0.76)	2.71 (0.82)	2.45 (0.61)	0.243
Pre-Operative GV	104.85 (36.43)	100.32 (34.52)	113.65 (39.45)	0.224

Data presented Mean ± SD , Median - [IQR] , n(%)

In our study comparing Pre-Operative vomiting and non-vomiting cases, we found significant differences in several variables. non-vomiting cases were younger (median age 5 years) compared to vomiting cases (median age 10 years) with a p-value of **0.001**. The scoring of risk was also significantly different, with non-vomiting cases having a lower median score (13) compared to vomiting cases (21), and a p-value of less than **0.001**. No significant differences were observed in the duration of surgery, gender distribution, or pre-operative gastric volume. In the supine position, the craniocaudal diameter (CCD) was significantly smaller in non-vomiting cases (**p = 0.011**), while other measurements such as anteroposterior diameter (APD) and cross-sectional area (CSA) showed no significant differences. In the right lateral decubitus (RLD) position, no significant differences were found in APD, CCD, or CSA between the two groups. (**Table 4**).

DISCUSSION

Our present study aimed to compare gastric volume, risk scores, and pre-operative risk factors between traumatic and non-traumatic pediatrics emergency surgical cases and their relation to post-operative

vomiting as a common complication. Our study included 50 patients with a median age of 8.5 years, of which 41 (82%) were male. Traumatic surgeries made up 82% of the cases, with orthopedic fracture repair being the most common (46%), followed by soft tissue trauma (24%). Non-traumatic surgeries accounted for 9 cases (18%). There is significant difference in the risk score and degree of risk between traumatic and non-traumatic surgery ($p = 0.02$ and $p < 0.001$, respectively).

There was no significant difference between the Traumatic and non- Traumatic groups regarding the age or duration of surgery ($p = 0.647$ and p 0.359, respectively). Most patients had a moderate risk score (74%), while 12% had a high-risk score. In alignment to these findings,(6) found a PONV prevalence of 27% and 28% in children aged 1–12 and 13–24 months, respectively. Studies of children under 14 years of age found a sharp increase in PONV at 3 years of age (7) , with an increase of 0.2%–0.8% per year up to puberty (8) . (9) estimated an average PONV prevalence rate of 40% in children aged 3 years and older.

Although two other risk factors were included, none of the 50 patients had a history of previous PONV or were predisposed to multiple opioid doses. This is important factors to be considered as (10) and (7) reported that opioid administration during anesthesia induction is not by itself a risk factor for PONV, but the application of it is an important stimulus on the matter when opioids were re-applied at time of surgery or in the post-operative period. Consequently "multiple opioid dose" converts to be a single-important risk factor of PONV in the "VPOP-score" which was created by (10) , along with age (>3 and ≤13), time of anesthesia duration (>45 min), surgery procedures at risk like (tympanoplasty, tonsillectomy, and strabismus surgery), and the pre-disposition to any (previous personal history , previous motion sickness attaches ,positive familial history of any pre-disposing factor).

Besides, Operations that lasts (30 min) duration and anesthesia time over (45 min) have been recognized as possible risk factors in scoring PONV risks in children as (8) (10) proved. Also, the PONV prevalence rate could rise from (34% to 48%) (11) The cause could be the longer exposure to emetogenic substance (12)

In our study comparing traumatic and non-traumatic cases, we found that in the supine position, there were no significant differences between the two groups for anteroposterior diameter (APD), craniocaudal diameter (CCD), and cross-sectional area (CSA). However, in the right lateral decubitus (RLD) position, a significant difference was observed in APD ($p = 0.03$), with non-traumatic cases showing higher values. No significant differences were found in CCD, CSA, or predicted gastric volume (GV) in the RLD position.

These findings are in line with previous study representing that gastric content distribution varies with patient positioning and how it can affect ultrasound measurements of the antrum (13) . (5) also confirmed that the antral CSA is more surely evaluated in the RLD position in comparison to the supine position, signifying that gravitational effects boost the sensitivity of gastric volume estimation.

Moreover, a study done by (4) reported that the RLD position delivers a more accurate assessment of gastric content, mostly in emergency situations where fasting status is undefined. Their conclusions

support the concept that variances in antral measurements between traumatic and non-traumatic cases could be related to variations in stress-related gastric motility or to delayed emptying due to opioid use. In the same way, (14) described that in case of emergency surgery, patients had a more prevalence of high gastric volume, that accentuate the need for detailed peri-operative ultrasound assessments to evaluate possible vomiting risks.

Despite differences in APD in the RLD position, CCD, CSA, and GV showed no significant differences. This aligns with conclusions by (15), who highlighted that despite the fact that gastric volume assessment models are useful, they should be taken in conjunction with qualitative ultrasound results for better risk stratification. Moreover, (16) emphasized that while the RLD position is perfect for volume assessment, variances in antral measurements may not constantly associate with an increased risk of aspiration, predominantly in pediatric patients.

In our study comparing Pre-Operative vomiting and non-vomiting cases, we found significant differences in several variables. non-vomiting cases were younger (median age 5 years) compared to vomiting cases (median age 10 years) with a p-value of **0.001**. These findings align with previous study showing that younger pediatric patients often show faster gastric emptying and lower gastric volumes preoperatively, dropping their possibility of perioperative nausea and vomiting (PNV) (14)

The scoring of risk was also significantly different, with non-vomiting cases having a lower median score (13) compared to vomiting cases (21), and a p-value of less than **0.001**. No significant differences were observed in the duration of surgery, gender distribution, or pre-operative gastric volume. In the supine position, the craniocaudal diameter (CCD) was significantly smaller in non-vomiting cases (**p = 0.011**), while other measurements such as anteroposterior diameter (APD) and cross-sectional area (CSA) showed no significant differences. In the right lateral decubitus (RLD) position, no significant differences were found in APD, CCD, or CSA between the two groups.

This supports findings by (15), who verified that differences in CCD might reflect changes in gastric accommodation and motility. A comparable study by (17) start that while overall gastric volume did not vary significantly between patients with delayed gastric emptying predisposing factors (DGEF) and those without, antral CSA and CCD measurements varied, suggesting altered gastric motility and compliance in higher-risk patients.

Furthermore, the absence of significant differences in APD, CSA, or predicted gastric volume (GV) between vomiting and non-vomiting cases in the right lateral decubitus (RLD) position is constant with findings from (4) .Their study noted that while variations in antral diameter can be position-dependent, overall gastric emptying dynamics remain constant across patient clusters with different vomiting tendencies. (14) further has added proof to an account this by representing that RLD positioning increases imagining of gastric content but not essentially interpret to differences in gastric volume between high- and low-risk groups.

The clinical implications of these findings support the importance of individualized risk assessment policies in perioperative stage management. Granting that preoperative vomiting is a multifactorial situation —including surgery type, patient age, the opioid administration, and stressful conditions

specially at time of emergency—ultrasound-based measurement tools present valuable insights into gastric motility forms and risk stratification patterns. Certain the significant differences detected in age and risk scores between specific patient groups, upcoming studies should see the sights whether specific medical prophylactic interventions, as antiemetic prophylaxis or adapted fasting protocols, can improve perioperative clinical outcomes specially in high-risk pediatric patients.

We hypothesize that gastric ultrasound can identify differences in gastric volume and risk factors between traumatic and non-traumatic pediatric emergency surgeries, thereby improving risk stratification for postoperative vomiting.

Study limitations:

- Small sample size (n=50) may limit generalizability.

- Lack of control for opioid doses and preoperative fasting durations.

CONCLUSION

This study suggests that gastric ultrasound could be integrated into perioperative assessment protocols to refine risk stratification in pediatric emergency surgery. Larger studies are needed to validate gastric ultrasound's predictive value for PONV.").

Sponsors and funding sources: There are none to be declared.

Acknowledgment: There is none to be declared.

Conflict of interests: None to be declared.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (197-203) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Traumatic and non-traumatic Ped surgeries degree of risk and gastric ultrasound as an instrument for assessment of post-Operative nausea and vomiting

Ayman Mohamady Eldemrdash, Zaher Zaki Zaher, Tarek S. Hemaida, Soudy S. Hammad, Doaa Hamdy Hassaneen*, Mohammed Ahmed Alazhary.

Anesthesiology, Intensive Care and Pain Management Department, Faculty of Medicine, Aswan University

ABSTRACT

Keyword: Famotidine; Placebo; Pediatric Surgery; Nausea.

* **Corresponding author**: Doaa Hamdy Hassaneen
Mobile: 01113542707
E-mail: hdoaa520@gmail.com

Background: The classification of pediatric surgeries as traumatic or non-traumatic depends on factors such as surgery type, age, medical conditions, and procedure complexity. **Methods:** This prospective observational study was performed in the Department of Anesthesiology, Intensive Care, and Pain Management at Aswan University Hospital. The study included 50 pediatric patients who underwent emergency surgeries, categorized into traumatic and non-traumatic procedures. The research was permitted via the institutional review board, and informed consent was attained from the parents or legal guardians of all participants. **Results**: Orthopedic fracture trauma accounted for 46% of emergency pediatric surgeries, followed by soft tissue trauma (24%), abdominal surgery (18%), neuro-ophthalmic (eye-related) trauma (8%), and compartment syndrome (4%). Additionally, we compared preoperative and postoperative gastric ultrasound measurements in 100 patients. In the supine position, there were no significant variances between the pre- and post-surgery values for the anteroposterior diameter (APD), the craniocaudal diameter(CCD), and the cross-sectional area (CSA), with p-values of 0.371, 0.759, and 0.905, correspondingly. Similarly, for the right lateral decubitus (RLD) position, there were no significant variances in anteroposterior diameter, craniocaudal diameter, cross-sectional area, and gastric volume(GV) among the both groups, with p-values of 0.449, 0.527, 0.637, and 0.874, correspondingly. **Conclusion:** The study found no significant differences in postoperative nausea and vomiting risk in trauma surgeries, indicating ultrasound as a valuable bedside tool for anesthesia planning.

INTRODUCTION:

Pediatric surgeries can be broadly categorized into traumatic and non-traumatic procedures, each with distinct risks and postoperative considerations. The degree of risk associated with pediatric surgeries depends on several factors, including the type of surgery, the child's age, underlying medical conditions, and the nature of the surgical procedure itself **(1)**.

Traumatic surgeries, which are usually caused by accidents or injuries, may have a higher risk of complications because of the trauma. Non-traumatic surgeries, on the other hand, tend to be elective procedures, like those for birth defects or long-term illnesse**s (1).**

Ultrasonography can evaluate the elevated volume of gastric content, which could lead to pulmonary aspiration and regurgitation. As suggested by the European Society of Anesthesiology and Intensive Care, bedside point of care ultrasound (POCUS) is a safe and non-invasive way to assess the stomach **(2).**

This method improves our understanding of gastric emptying in various cases and clinical circumstances, assisting in the identification of potential risk factors related to gastric content. Nil per os (NPO) protocols are currently the standard preventive measures against aspiration **(3)**.

Postoperative nausea and vomiting can lead to longer discharge times, which could cause slower turnover in the ambulatory outpatient setting. PONV can also lead to aspiration, unwarranted hospital admissions, and patient dissatisfaction. Patients would rather spend extra money to avoid nausea **(4)**.

As a treatment for PONV prevention, famotidine is often compared to placebo in clinical studies to evaluate its effectiveness in reducing these symptoms after pediatric surgeries. The potential benefits of famotidine in this setting have been studied, but its exact role in preventing PONV in pediatric emergency surgery remains a subject of ongoing research **(5)**.

Although anesthetists are aware of postoperative nausea and vomiting (PONV/POV) as a prevalent complication in pediatric anesthesia, its incidence in daily routine is still too great. Anesthesia risk factors are volatile agents, nitrous oxide, opioids, and the length of the anesthetic **(6)**.

Point-of-care ultrasonography (POCUS) has emerged as a valuable instrument to assess critically ill cases, and it has been confirmed to be effective in evaluating gastric contents and volume in various clinical settings. Point-of-care ultrasonography can assist in identifying cases that are at risk for aspiration, consequently guiding the decision to employ an RSI and assisting in determining the most appropriate airway treatment method throughout anesthesia **(**7**)**.

This research aimed to assess the variance of the gastric volume via quantitative measurements of the gastric antrum before and after surgery.

PATIENTS AND METHODS:

This prospective observational study has been performed on the Department of Anesthesiology, Intensive Care, and Pain Management at Aswan University Hospital. The study included 50 pediatric patients who underwent emergency surgeries, categorized into traumatic and non-traumatic procedures. The study has been permitted via the institutional review board, and informed consent has been attained from the parents or legal guardians of all participants.

Inclusion Criteria: Patients aged 1 to 18 years, scheduled for emergency pediatric surgeries (both traumatic and non-traumatic), and able to undergo a gastric ultrasound assessment.

Exclusion Criteria: History of gastrointestinal disorders, recent food intake within the last 6 hours, receipt of antiemetic medications within 24 hours before surgery, and inability to undergo gastric ultrasound assessment due to technical or clinical reasons.

Patient Selection

Cases that met the inclusion criteria and didn’t meet any of the exclusion criteria have been enrolled in the research. Depending on the type of surgery, we separated the cases into two groups: traumatic (number=41) and non-traumatic (number=9).

Data Collection

Demographic information, involving sex, age, and weight, has been documented for each patient. The type of surgery, duration of surgery, and preoperative risk factors for postoperative nausea and vomiting (PONV) were also documented. Risk factors for PONV included age, duration of surgery, history of motion sickness, and the presence of preoperative vomiting.

Gastric Ultrasound Assessment

Gastric ultrasound assessments were performed preoperatively and postoperatively using a portable ultrasound machine with a high-frequency linear probe. The following measurements were taken in both the supine and right lateral decubitus (RLD) positions:

· Anterior-posterior diameter (APD) of the gastric antrum
· Cross-sectional diameter (CCD) of the gastric antrum
· Cross-sectional area (CSA) of the gastric antrum
· Gastric volume (GV) has been estimated utilizing the formula: $GV = \pi \times (APD/2)^2 \times CCD$

The ultrasound measurements have been conducted through a single experienced operator to diminish interobserver variability.

Postoperative Management

All patients received standard postoperative care, including routine monitoring of vital signs and administration of analgesics as needed. The incidence of postoperative nausea and vomiting was recorded within the first 24 hours postoperatively. Patients who experienced PONV were treated with standard antiemetic protocols.

Statistical Analysis:

Information has been analyzed utilizing statistical software (SPSS version 26). Continuous variables have been represented as mean ± standard deviation (SD) or median [interquartile range (IQR)], and categorical variables have been represented as percentages and frequencies. Comparisons between groups have been made utilizing the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. A p-value of below 0.05 has been considered statistically significant.

RESULTS:

Table 1: Risk factor for vomiting and scoring of risk for patients undergo emergency pediatric surgery

	Overall (n = 50)	**Traumatic** (n = 41)	**Non Traumatic** (n = 9)	p-value
Age (Years)	8.50 [5.00, 11.00]	8.00 [5.00, 11.00]	11.00 [7.00, 11.00]	0.647
Duration of Surgery (Min)	90.00 [60.00, 97.50]	90.00 [60.00, 90.00]	90.00 [60.00, 120.00]	0.359
Scoring of Risk	21.00 [13.00, 21.00]	21.00 [13.00, 21.00]	36.00 [21.00, 36.00]	**0.002**
Degree of Risk				**<0.00**

				1
High risk	6 (12.0)	0 (0.0)	6 (66.7)	
Moderate risk	37 (74.0)	34 (82.9)	3 (33.3)	
Low risk	7 (14.0)	7 (17.1)	0 (0.0)	
Gender = male	41 (82.0)	33 (80.5)	8 (88.9)	0.908
Pre-operative Vomiting	33 (66.0)	26 (63.4)	7 (77.8)	0.663
Data presented, Median [IQR] , n(%)				

Our study included 50 patients with a median age of 8.5 years, of whom 41 (82%) were male. Traumatic surgeries made up 82% of the cases, with orthopedic fracture repair being the most common (46%), followed by soft tissue trauma (24%). Non-traumatic surgeries accounted for 9 cases (18%). There is a significant difference in the risk score and degree of risk between traumatic and non-traumatic surgery ($p = 0.02$ and $p < 0.001$, respectively). There was no significant difference between the traumatic and non-traumatic groups regarding the age or duration of surgery ($p = 0.647$ and $p = 0.359$, respectively). Most patients had a moderate risk score (74%), while 12% had a high-risk score. Although two other risk factors were included, none of the 50 patients had a history of previous PONV or were predisposed to multiple opioid doses (**Table 1**).

Table 2: Type of emergency pediatric surgery		
Type of surgery	**surgery Category**	**N (%)**
Orthopedic fracture trauma	Traumatic	23 (46%)
Soft Tissue trauma	Traumatic	12 (24%)
Abdominal Surgery	Non Traumatic	9 (18%)
Neuro-eye Trauma	Traumatic	4 (8%)
Compartmental Syndrome	Traumatic	2 (4%)

According to the type of emergency pediatric surgery, the current study revealed that orthopedic fracture trauma was represented 46%, soft tissue trauma was represented 24%, abdominal surgery was represented 18%, neuro-eye trauma was represented 8%, and compartmental syndrome was represented 4%. (**Table 2**).

Table3: Gastric Ultrasound Measurement in Pediatric Patients by before and after surgery					
		Overall	Pre-operative	Post-operative	p-value
Supine	APD	1.10 [0.85, 1.40]	1.10 [0.90, 1.40]	1.00 [0.81, 1.40]	0.371
	CCD	2.83 (0.62)	2.85 (0.54)	2.81 (0.69)	0.759

	CSA	2.66 (1.24)	2.64 (0.97)	2.67 (1.47)	0.905
RLD	APD	1.16 (0.30)	1.18 (0.25)	1.14 (0.35)	0.449
	CCD	2.80 [2.30, 3.30]	2.95 [2.40, 3.30]	2.70 [2.20, 3.30]	0.527
	CSA	2.57 (1.01)	2.62 (0.76)	2.53 (1.21)	0.637
	GV	104.10 (47.26)	104.85 (36.43)	103.34 (56.43)	0.874
Data presented Mean ± SD, Median] IQR] , n(%)					

The study compared before and after surgery measurements in 100 patients. For supine measurements, an insignificant variance has been observed among values before and after surgery for APD, CCD, and CSA (p-values: 0.371, 0.759, and 0.905, respectively). Similarly, for RLD measurements, APD, CCD, CSA, and GV showed insignificant variances among the 2 groups (p-values: 0.449, 0.527, 0.637, and 0.874, respectively) **(Table 3).**

DISCUSSION:

Regarding risk factors for vomiting and scoring of risk for patients undergoing emergency pediatric surgery, the current study showed that cases had a median age of 8.5 years, of which 41 (82%) were male. Traumatic surgeries made up 82% of the cases, with orthopedic fracture repair being the most common (46%), followed by soft tissue trauma (24%). Non-traumatic surgeries accounted for 9 cases (18%); there was a significant difference in the risk score and degree of risk between traumatic and non-traumatic surgery (p-value equal to 0.02 and p-value below 0.001, correspondingly). An insignificant variance has been observed among the traumatic and non-traumatic groups regarding the age or duration of surgery (p-value equal to 0.647 and p-value equal to 0.359, respectively). Most patients had a moderate risk score (74%), while 12% had a high-risk score. Although two other risk factors were included, none of the 50 patients had a history of previous PONV or were predisposed to multiple opioid doses.

Traumatic surgeries, especially those involving orthopedic fractures and soft tissue trauma, often lead to more severe and complex cases requiring a higher level of intervention and postoperative care. These cases are typically associated with greater pain, inflammation, and potential for complications, which may increase the risk of postoperative nausea and vomiting (PONV). Additionally, traumatic injuries might involve more extensive surgical procedures, which could further increase the risk of PONV due to factors like longer anesthesia times, higher levels of pain management required (often with opioids), and the physical stress associated with trauma **(8)**.

Corresponding to our result, **(9)** assessed postoperative nausea and vomiting and incidence in kids. They reported that the incidence of postoperative nausea and vomiting in kids was still too great in outpatients and inpatients, and there were simple strategies to decrease baseline risk.

Famotidine is an antihistamine that has an impact on improving duodenal and gastric ulcers. Numerous researches have demonstrated that famotidine has the potential to be effective in the management of gastric inflammation, gastroesophageal reflux, stress ulcers, upper gastrointestinal bleeding, and prevention of acid aspiration into the lungs. Despite this, there is restricted research available concerning the effects of famotidine on pain control after surgery **(10)**.

According to the type of emergency pediatric surgery, the current study revealed that orthopedic fracture trauma was represented 46%, soft tissue trauma was represented 24%, abdominal

surgery was represented 18%, neuro-eye trauma was represented 8%, and compartmental syndrome was represented 4%.

Orthopedic fracture trauma represented 46% of the cases in this study, likely because fractures are among the most common injuries in pediatric emergency surgery. Children are more prone to accidents, falls, and sports-related injuries, which often result in fractures, particularly in the context of trauma **(11)**.

This study compared before and after surgery measurements in 100 patients. For supine measurements, an insignificant variance among values before and after surgery for APD, CCD, and CSA (p-values: 0.371, 0.759, and 0.905, respectively). Similarly, for RLD measurements, APD, CCD, CSA, and GV showed insignificant variances among the 2 groups (p-values: 0.449, 0.527, 0.637, and 0.874, respectively**, (12)** used US to diagnose gastric distension. They reported that fluid-filled stomachs observed on ultrasound may also be useful to expect cases who may suffer emesis; ultrasonography (US) is frequently utilized in medicine as a means of diagnosis. This method is noninvasive, accessible, inexpensive, and doesn't need to be subjected to radiation or contrast. Ultrasonography is a rapid and practical tool for bedside assessment. Ultrasonography is user dependent, but it is routinely utilized by surgeons for venous access and focused assessment with sonography for trauma exams.

Inconsistent with **, (13)** used ultrasonographic assessment of gastric content and volume in pediatric cases having elective operations. They found that ultrasound results of solid content in the antrum and/or a calculated volume of the stomach above 1.25 milliliters per kilogram. Before surgery, they conducted both supine and right lateral decubitus ultrasound examinations on the antrum. We assessed the gastric fluid content using a qualitative grading scale ranging from zero to two. The cross-sectional area of the antrum has been determined in the right lateral decubitus position, assisting the calculation of the gastric fluid volume regarding an established formula by Perlas. Ultrasound measurements of kids have been assessed. The median fasting period was four hours for liquids and nine hours for thick liquids and solids. Solid content was absent in all the kids. Five kids (5.2%) exhibited a grade two antrum, implying that fluid content was visible in both the supine and right lateral decubitus positions. The proportion of kids with a gastric fluid volume above 1.25 milliliters per kilogram, ranging from 0.1 to 4.7 percent, was lower than those above 0.8 and 1 milliliters per kilogram. These results reinforce the idea that surpassing 1.25 milliliters per kilogram of gastric fluid volume is rare in kids who have fasted before elective operation and may serve as a significant threshold to distinguish normal from elevated gastric fluid volume, consistent with earlier research **, (14)**. Even in the absence of apparent risk factors, her gastric volume has been categorized as "high-risk." The literature points to incremental growth in overall gastric volume with a constant right lateral decubitus and cross-sectional area as age develops. For example, a four-year-old child weighing seventeen kilograms with a right lateral decubitus and a cross-sectional area of four cm^2 would have an estimated total gastric volume of twelve milliliters (0.7 mL/kg^{-1}), while a ten-year-old child weighing twenty-nine kilograms would have an estimated twenty-one milliliters **(14)**.

Conclusion

This research found no significant differences in gastric volume or antrum measurements preoperatively and postoperatively in pediatric emergency surgeries, regardless of surgery type or medication. While traumatic surgeries had a higher PONV risk, no correlation was observed with gastric volume changes, suggesting famotidine and surgical factors had minimal impact. Ultrasound is a simple, non-invasive bedside tool that should be integrated into best practice guidelines to aid anesthesia planning and decision-making.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (204-211) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Age-related differences in functional and post-operative outcomes in spinal anesthesia for open appendectomy with Dexmedetomidine

Soudy S. Hammad, Ahmed Mohsen hagag*, Ayman Mohammady Eldemrdash , Tarek S. Hemaida

Anesthesiology, Surgical Intensive Care and Pain Managment Department, Faculty of Medicine, Aswan University

ABSTRACT

Keyword
Dexmeditomidine, ASA classification, Bromage score.
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***Corresponding author:**
Ahmed Mohsen hagag
Email: ahmed2019mohsen@gmail.com
Phone : 01141097536

Background: Dexmedetomidine , a selective α2 adrenergic agonist, preserves neurological function and mitigates neuronal damage. **Objectives:** This study examined age-related variations in the efficacy and postoperative outcomes of DEX in patients undergoing open appendectomy under spinal anesthesia. **Patients and Methods:** A prospective observational study was conducted on 74 patients receiving DEX perioperatively. Participants were stratified into four age groups: <20 years (n=12), 20-30 years (n=43), 30-40 years (n=8), and >40 years (n=11). **Results**: Intraoperative adverse events (e.g., bradycardia, hypotension) and postoperative outcomes (analgesia duration, VAS scores, Bromage score) showed no significant age-related differences. However, older patients exhibited higher ASA scores (P<0.001), indicating greater comorbidities. VAS scores at 1-hour post-surgery differed significantly (P=0.017), with younger patients reporting lower pain. **Conclusion:** While most outcomes were consistent across age groups, the disparity in ASA classification underscores the impact of aging-related comorbidities on perioperative management. The stability of intraoperative and postoperative parameters, including pain and sensory recovery, suggests Dexmeditomidine reliability as a therapeutic agent across diverse ages.

INTRODUCTION

Dexmedetomidine is a highly selective α2 adrenergic receptor agonist that maintains neurological function and reduces neuronal damage. It provides a protective effect against cognitive impairments by suppressing the hippocampus inflammatory response and neuronal apoptosis triggered by surgical trauma (1).

Dexmedetomidine sedation in the intensive care unit has demonstrated advantageous effects on sleep quality and minimal impacts on breathing. Scheduled intravenous injection of Dexmedetomidine postoperatively was shown to diminish in-hospital delirium (2).

Dexmedetomidine utilized for case-controlled analgesia (PCA) diminished discomfort and undesirable effects while enhancing case satisfaction post-surgery (3).

In elderly cases (aged sixty years or older) undergoing spinal surgery, intravenous and endotratracheal dexmedetomidine decreased the occurrence of early postoperative delirium in comparison to intranasal administration (4).
In pediatric patients undergoing surgery for congenital heart disease, dexmedetomidine was related to a shortened length of mechanical ventilation, diminished postoperative opioid use, attenuated stress response, & a decreased incidence of delirium in comparison to placebo or other anesthetics (5). Nonetheless, it may elevate the possibility of bradycardia and hypotension. In infants and toddlers with congenital heart disease, dexmedetomidine was effectively utilized as the principal sedative for invasive operations while preserving spontaneous respiration (6).
This study aimed to investigate how age influences the effectiveness and postoperative outcomes of using dexmedetomidine in patients undergoing open appendectomy surgery under spinal anethesia.

PATIENTS AND METHODS

This prospective, observational research has been conducted on 74 cases who received dexmedetomidine as part of their perioperative management. Patients were classified into four age groups: <20 years included 12 patients, 20-30 years included 43 patients, 30-40 years included 8 patients, and >40 years included 11 patients.

Inclusion Criteria: Cases aged eighteen years and older who had elective surgery and received dexmedetomidine for sedation and analgesia were included. All participants were scheduled for general anesthesia and had no history of allergies or adverse reactions to dexmedetomidine. Informed consent has been collected from all participants.

Exclusion Criteria: Cases with a known history of severe cardiovascular conditions (e.g., bradycardia, hypotension), renal or hepatic impairment, a history of chronic drug or alcohol abuse, or those who were pregnant or breastfeeding. Cases with a history of neurological disorders or cognitive impairment were also excluded from the study.

Ethical Considerations: The research has been performed in accordance with the Declaration of Helsinki, and ethical clearance has been secured from the institutional review board (IRB). All cases provided informed consent prior to their involvement in the research.

Methods

Intervention: All patients received dexmedetomidine as part of their perioperative care regimen. The drug was administered according to standard clinical practice guidelines, with doses adjusted depending on the individual case's clinical condition and response to therapy. Dexmedetomidine was administered intravenously either as a continuous infusion or bolus, as per the anesthesiologist's discretion.

Patient Stratification: Patients were stratified into four age groups for analysis:
Group 1: below twenty years
Group 2: twenty to thirty years
Group 3: thirty to forty years
Group 4: above forty years
Each group was assessed for intraoperative adverse events, postoperative analgesia, sensory recovery, and functional outcomes. Age-related differences in outcomes were the primary focus of the analysis.

Data Collection:

Demographic data: Age, sex, smoking history, and American Society of Anesthesiologists (ASA) physical status classification were recorded.

Intra-operative data: Operation time, incidence of adverse events (e.g., bradycardia, hypotension, nausea, vomiting, respiratory depression), and any interventions required have been documented.

Postoperative data: Duration of postoperative analgesia, time to sensation, and the Visual Analog Scale (VAS) scores for pain were recorded at specified intervals (1, 2, 4, 6, and 8 hours postoperatively). The Bromage score, which assesses motor block, was also recorded at 5 minutes, one hour, two hours, four hours, and six hours after surgery.

Outcome Measures:

Primary outcome: Age-related differences in functional and postoperative outcomes, including postoperative pain (VAS scores), motor block (Bromage score), and sensory recovery time.

Secondary outcomes: The prevalence of intraoperative adverse events, including bradycardia, hypotension, nausea, vomiting, and respiratory depression.

Statistical Analysis: The data have been examined utilizing suitable statistical techniques. Descriptive statistics (mean, standard deviation) have been utilized for continuous variables, while categorical data have been assessed utilizing chi-square or Fisher's exact tests. Comparisons among age groups have been conducted utilizing analysis of variance (ANOVA) or the Kruskal-Wallis test, where applicable. A p-value below 0.05 has been deemed statistically significant.

RESULTS

Table (1): Distribution of case's characteristics between age groups in Dexmedetomidine group.

	<20 years N = 12	**20-30 years N = 43**	**30-40 years N = 8**	**>40 years N = 11**	**P-value**
Sex					
Male	7 (58.3%)	21 (48.8%)	7 (87.5%)	7 (63.6%)	0.221
Female	5 (41.7%)	22 (51.2%)	1 (12.5%)	4 (36.4%)	
Smoking	0 (0%)	3 (7%)	2 (25%)	3 (27.3%)	0.07
ASA					
I	11 (91.7%)	40 (93%)	5 (62.5%)	3 (27.3%)	**<0.001**
II	1 (8.3%)	3 (7%)	3 (37.5%)	8 (72.7%)	
Operation time (min) Mean ±SD	51.67 ±2.77	52.72 ±2.85	53.13 ±1.46	53.64 ±4.18	0.443

P value >0.05: Not significant, P value <0.05 is statistically significant, p<0.001 is highly significant, SD: standard deviation, ASA: American Society of Anesthesiologists.

Table 1 demonstrates that there was statistically insignificant difference among age groups in the dexmedetomidine group regarding sex, smoking, and operation time, while there was a highly statistically significant difference among age groups in the dexmedetomidine group regarding ASA.

Table (2): Distribution of Intra-Operative Adverse events between age groups in Dexmedetomidine group.

	<20 years N = 12	**20-30 years N =43**	**30-40 years N =8**	**>40 years N =11**	**P-value**
Abdominal	2 (16.7%)	4 (9.3%)	0 (0%)	1 (9.09%)	0.667

discomfort					
Visceral pain	1 (8.3%)	5 (11.6%)	0 (0%)	2 (18.2%)	0.638
Nausea	1 (8.3%)	4 (9.3%)	0 (0%)	2 (18.2%)	0.608
Vomiting	1 (8.3%)	3 (7%)	0 (0%)	1 (9.09%)	0.867
Bradycardia	3 (25%)	9 (20.9%)	3 (3.75%)	4 (36.4%)	0.625
Hypotension	7 (58.3%)	12 (27.9%)	2 (25%)	5 (45.5%)	0.196
Respiratory depression	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1
Shivering	1 (8.3%)	10 (23.25%)	2 (25%)	3 (27.3%)	0.664
Pruritus	0 (0%)	2 (4.65%)	0 (0%)	0 (0%)	0.686

Table 2 demonstrates that there was statistically insignificant difference among age groups in the dexmedetomidine group regarding intraoperative adverse events (abdominal discomfort, visceral pain, nausea, vomiting, bradycardia, hypotension, respiratory depression, shivering, and pruritus).

Table (3): Distribution of Post-operative data between age groups in Dexmedetomidine group.

Mean ±SD	**<20 years N = 12**	**20-30 years N =43**	**30-40 years N =8**	**>40 years N =11**	**P-value**
Duration-postoperative analgesia (min)	342.50±81.37	408.84±116.38	435 ±127.28	381.82±81.71	0.201
Time to sensation (min)	287 ±27.08	300.35 ±36.72	307.13 ±31.17	300.64±41.34	0.603

Table 3 demonstrates that there was statistically insignificant difference among age groups in the dexmedetomidine group regarding duration of postoperative analgesia and time to sensation.

Table (4): Distribution of VAS at interval times between age groups in Dexmedetomidine group.

VAS Mean ±SD	**<20 years N = 12**	**20-30 years N =43**	**30-40 years N =8**	**>40 years N =11**	**P-value**
After 1 hour	0.50 ±0.80	0.05 ±0.31	0.25 ±0.71	0.00 ±0.00	**0.017**
After 2 hours	3.25 ±1.49	2.49 ±1.56	1.50 ±1.85	2.36 ±1.21	0.107
After 4 hours	1.00 ±1.21	0.53 ±0.86	0.25 ±0.46	0.45 ±0.69	0.242
After 6 hours	4.33 ±1.23	3.58 ±1.10	3.25 ±1.49	3.64 ±0.92	0.155
After 8 hours	5.67 ±1.44	4.86 ±1.13	4.63 ±1.19	5.27 ±1.27	0.147

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Table 4 shows that there was statistically insignificant difference among age groups in the dexmedetomidine group regarding VAS after 2, 4, 6, and 8 hours, while there was statistically significant difference among age groups in the dexmedetomidine group regarding VAS after 1 hour.

Table (5): Distribution of Bromage at interval times between age groups in Dexmedetomidine group.

Bromage	**<20 years**	**20-30 years**	**30-40 years**	**>40 years**	**P-value**

Mean ±SD	**N = 12**	**N =43**	**N =8**	**N =11**	
After 5 mins	0.83 ±1.19	0.30 ±0.64	0.13 ±0.35	0.36 ±0.51	0.108
After 1 hour	0.50 ±0.52	0.23 ±0.48	0.13 ±0.35	0.36 ±0.67	0.309
After 2 hours	1.17 ±1.03	0.58 ±0.93	0.25 ±0.71	0.64 ±1.21	0.185
After 4 hours	2.75 ±1.60	2.30 ±1.15	1.88 ±0.64	2.27 ±1.19	0.449
After 6 hours	3.92 ±1.44	3.56 ±1.05	3.00 ±0.76	3.55 ±1.04	0.348

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Table 5 demonstrates that, there was statistically insignificant different among age groups in Dexmedetomidine group regarding Bromage after 5 min, after 1, 2, 4, and 6 hours.

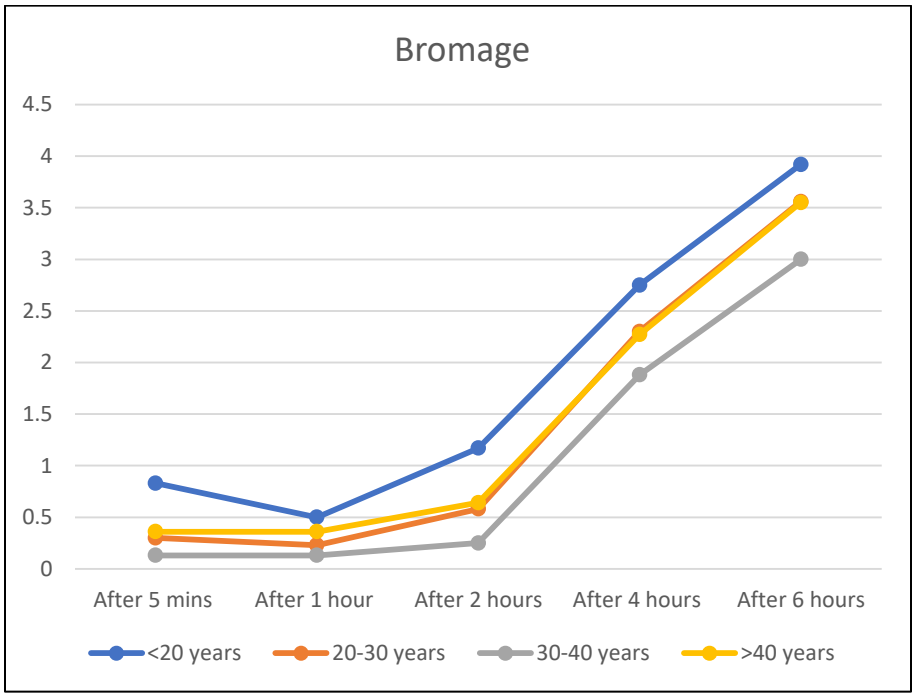

Figure (3): Bromage distribution between age groups in Dexmedetomidine group.

DISCUSSION

Our findings demonstrated that there was statistically insignificant difference among age groups in the Dexmedetomidine group regarding sex, smoking, and operation time, while there was a highly statistically significant difference among age groups in the Dexmedetomidine group regarding ASA.

Older patients often have higher ASA scores due to increased comorbidities and reduced physiological reserve. Our findings align with **Li et al. (7), who** reported that older age is independently related to higher ASA physical status assignments, with an adjusted odds ratio of 1.39 per ten years of age (ninety-five percent CI 1.37 to 1.41).

On the other hand, **Zaib et al. (8),** focusing on patients aged 60 years and above, reported that the ASA score did not demonstrate a significant correlation in this older population.

Our findings demonstrated that there was statistically insignificant difference among age groups in the dexmedetomidine group regarding intraoperative adverse events (abdominal discomfort,

visceral pain, nausea, vomiting, bradycardia, hypotension, respiratory depression, shivering, and pruritus).

In line with Weerink **et al. (9),** who conducted a review to examine various current therapeutic applications of dexmedetomidine, indicating that post-operative pediatric ICU cases over one month exhibited an identical safety profile to that of the adult population.

Gao et al. (10) found that dexmedetomidine use in patient-controlled epidural analgesia reduced the prevalence of itching, nausea, and vomiting compared to opioids, without elevating other adverse events.

A systematic review by **Sin et al. (11)** reported that dexmedetomidine was related to decreased incidence of emergence agitation, pain, cough, post-surgery nausea and vomiting, and shivering in the post-anesthesia care unit. It did increase the prevalence of hypotension, but not residual sedation or bradycardia.

On the other hand, dexmedetomidine's effects appear to vary with age, particularly in younger patients. **Tervonen et al. (12)** reported that neonates and infants (0-3 months) experienced bradycardia more frequently than older infants (3-6 months) when given dexmedetomidine (86% vs 50%, p=0.001). Severe bradycardia was also more common in the youngest patients (17% in neonate's vs 0% in three- to six-month-olds, p-value equal to 0.005).

Our findings demonstrated that there was statistically insignificant difference among age groups in the dexmedetomidine group regarding time to postoperative analgesia and time to sensation.

In line with **Potts et al. (13),** aimed to enhance an understanding of dexmedetomidine pharmacokinetics in pediatric populations, it has been observed that children's drug responses maintain a common receptor, cellular, and physiological foundation with adults, irrespective of age or developmental stage.

Our results showed that there was statistically insignificant difference among age groups in the dexmedetomidine group according to VAS after 2, 4, 6, and 8 hours, while there was statistically significant difference among age groups in the dexmedetomidine group regarding VAS after 1 hour.

Sane et al. (14) reported lower postoperative pain in the dexmedetomidine group for 24 hours in patients aged twenty to sixty years undergoing upper extremity orthopedic operations.

Gao et al. (10) also noted lower VAS scores at multiple time points postoperatively in patients receiving dexmedetomidine compared to opioids.

Interestingly, **Wu et al. (15)** focused on older patients (over 65 years) and found that intranasal dexmedetomidine improved postoperative sleep quality, which may indirectly affect pain perception.

Our findings demonstrated that there was statistically insignificant difference among age groups in the dexmedetomidine group regarding Bromage after 5 min and after 1, 2, 4, and 6 hours.

Sane et al. (14) and Singh et al. (16) examined the impacts of dexmedetomidine as an adjuvant in brachial plexus blocks for adult patients. These studies generally found that adding dexmedetomidine prolonged the motor block period longer than local anesthetic alone.

Interestingly, **Agrawal et al. (17)** used the Bromage score to assess motor block in adult patients (18-60 years) receiving intravenous dexmedetomidine with spinal anesthesia. It reported a longer time to regression of motor block to Bromage 0/1 in the dexmedetomidine group compared to control (274 ± 21.25 min vs 130.12 ± 20.70 min).

CONCLUSION

In conclusion, we found that, despite the absence of age-related differences in most of the outcomes, the significant difference in the ASA classification suggests that comorbidities associated with aging may play an essential role in the general perioperative management of patients receiving dexmedetomidine. The lack of significant variation in other parameters such as intraoperative adverse events, postoperative pain, and sensory recovery highlights the potential of dexmedetomidine to provide consistent therapeutic benefits across different age groups.
Further studies with larger and more diverse patient populations may be necessary to confirm these findings and explore potential mechanisms underlying the observed differences.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (212-218) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Video Laryngoscope for Nasal Intubation in Maxillofacial Trauma: A Comparative Study of Mandibular and Zygomatic Fractures

Soudy S. Hammad, Ayman Mohammady Eldemrdash, Mohamed A. Alazhary , Mohammed Essam Yahia

Department of anesthesiology, surgical Intensive care & pain management, Faculty of medicine, Aswan University

ABSTRACT

Keyword: Maxillofacial Trauma, Video Laryngoscope, Mandibular Fracture, Zygomatic Fracture, Airway Management.

Corresponding author: Mohammed Essam Yahia

Email: muhammadessam962@gmail.com

Phone: 01125257916

Background: Maxillofacial trauma complicates airway management due to anatomical distortion and bleeding. Video laryngoscopy (VL) enhances visualization and improves intubation success rates. This study evaluates VL's effectiveness in nasotracheal intubation for mandibular and zygomatic fractures, focusing on success rates, intubation time, and complications. **Methods:** This prospective, randomized clinical trial was conducted at Aswan University Hospital .A total of 27 patients requiring nasal intubation due to maxillofacial trauma were included in this study. Patients were divided into two groups: Group A (14 patients) with mandibular fractures and Group B (13 patients) with zygomatic fractures. **Results:** Mandibular fracture patients had a significantly longer intubation duration. First-attempt success, Magill forceps use, cervical spine extension, and bleeding incidence showed no significant differences between groups. Complication rates were similar. **Conclusion:** patients with mandibular fractures may pose additional challenges due to airway misalignment and soft tissue obstruction, video laryngoscopy remains an effective tool to mitigate these difficulties. The comparable first-attempt success rates and low complication rates across both fracture groups reinforce its utility in trauma care.

INTRODUCTION

Maxillofacial trauma poses a significant challenge in airway management due to the distortion of normal anatomy, bleeding, and swelling. Effective airway control is crucial to prevent hypoxia and ensure patient stability, particularly in emergency settings. While direct laryngoscopy remains a common technique for intubation, it can be difficult in cases of facial fractures due to restricted mouth opening, airway obstruction, and poor visualization of the glottis. Recent advancements in airway management have led to the widespread adoption of video laryngoscopy, which has been shown to improve intubation success rates and reduce complications in patients with difficult airways **(1).**

Managing the airway during nasotracheal intubation (NTI) presents specific challenges in oral and maxillofacial surgery. The upper airway's complex structure, often impacted by facial abnormalities or trauma, requires careful and flexible intubation techniques. The nasal anatomy plays a vital role in both breathing and the sense of smell by filtering, humidifying, and detecting odors. Externally, the nasal vestibule, septum, bone, and cartilage are key to NTI, while internally, structures such as the turbinates (conchae), posterior nasal aperture, adenoids, Eustachian tube openings in the nasopharynx, and nasal

mucosa are significant. Video laryngoscopy (VL) provides a clear view of the nasopharynx and oropharynx—through which the nasotracheal tube passes—along with the laryngopharynx, including the epiglottis, arytenoids, and vocal cords **(8).**

The choice of intubation technique in patients with maxillofacial fractures is particularly important as these injuries can compromise airway patency and make conventional intubation methods challenging. Mandibular fractures can result in airway misalignment and soft tissue obstruction, whereas zygomatic fractures may contribute to swelling and bleeding that obscure the visual field during laryngoscopy. Studies have suggested that video laryngoscopy provides better glottic visualization, reduces cervical spine movement, and enhances first-attempt intubation success in trauma patients compared to direct laryngoscopy **(3).**. However, there remains a need for further comparative studies to determine its effectiveness in specific fracture patterns.

In addition to improving visualization, video laryngoscopy has been associated with a reduced need for external airway manipulation and adjunctive intubation techniques, such as the use of Magill forceps. Research has indicated that it minimizes the risk of esophageal intubation and facilitates a more controlled intubation process, which is particularly beneficial in maxillofacial trauma cases where securing the airway is time-sensitive **(2).**. Given these advantages, this study aims to assess and compare the effectiveness of video laryngoscope-assisted intubation in patients with mandibular and zygomatic fractures by evaluating parameters such as intubation time, first-attempt success rate, incidence of bleeding, and the necessity for additional airway management techniques.

SUBJECTS AND METHODS

This prospective, randomized clinical trial was conducted at Aswan University Hospital .A total of 27 patients requiring nasal intubation due to maxillofacial trauma were included in this study. Patients were divided into two groups: **Group A** (14 patients) with mandibular fractures and **Group B** (13 patients) with zygomatic fractures.

Preoperative assessments: included informed consent, detailed medical history, nasal examination, and airway assessment. Patients fasted for at least 8 hours before surgery without premedication. **Intraoperative Procedure**: standard monitoring was applied, and anesthesia was induced with fentanyl, propofol, and rocuronium, followed by face mask ventilation with oxygen and sevoflurane. Atropine was administered to reduce secretions, and oxymetazoline nasal spray was used for nasal preparation. A lubricated bougie was inserted through the nostril and guided past the nasopharynx, followed by placement of a reinforced, cuffed endotracheal tube (7.0 mm ID for men, 6.5 mm ID for women) using C-MAC® video laryngoscope, with Magill forceps IF needed. Certified anesthetists performed all intubations. and the following parameters were assessed: intubation time, first attempt success rate, bleeding, use of Magill forceps, and cervical spine extension.

Ethical Consideration:

The study was approved by the Ethical Committee of Aswan University Hospital (IEC Ref No: Asw. Uni./911/3/24) and registered on ClinicalTrials.gov (ID: NCT06386757). Written informed consent was obtained from all participants

Statistical examination

Data were entered into the computer and analyzed using version 20.0 of the IBM SPSS software program. (Armonk, New York: IBM Corporation) Quantitative and percentage descriptions were provided for qualitative data. The Kolmogorov-Smirnov evaluation was used to determine the distribution's normality. The range (minimum &maximum), mean, standard deviation, median and interquartile range (IQR) were used to describe quantitative data. At the 5% significance level, the derived results were deemed significant.

The used Evaluations were:

1 - **Chi-square test** for categorical variables, to compare among different groups

2 - **Student t-test** for normally distributed quantitative variables, to compare between two studied groups

RESULTS

In this study we included 27 patients, 14 patients with mandibular fractures, and 13 with zygomatic. The mean age in mandibular fracture and Zygomatic fracture group are 31.7 (12.3) and 32 (12.5) years respectively, while the BMI were 25.2 (3.6) and 23.6 (3.1) minutes, moreover, ASA I were 12 (85.7%) and 4 (30.8%), respectively.We found that the difference between mandibular fracture and Zygomatic fracture in inter-incisor Distance (cm) was not statistically significant p-value 0.17. While the thyromental Distance (cm) was significantly longer in mandibular group compared to zygomatic p-value = 0.04. Regarding Mallampati score, class I was 55% and 61% while class II was 50% and 38.5 % in mandibular fracture and Zygomatic fracture, respectively.Apart from thyromental distance there were no significant differences regarding demographic data **Table 1**.

Regarding the intubation duration, participants in mandibular fractures needed statistically significant longer intubation time compared to zygomatic group **Table 2 and Figure 1** . First trial success rate was not statistically significant between both groups. While the need for Magil forceps higher in the mandibular group but was not statistically significant compared to Zygomatic fracture p-value < 0.07 **Table 2 and Figure 2**, Moreover, the difference in the need for cervical spine extension between the two groups was statistically insignificant. Regarding the Occurrence of nasal and oropharyngeal bleeding, incidence of bleeding were statistically insignificant in both groups, moreover there were two cases found to be mild bleeding in the mandibular group. No moderated, severe or massive bleeding were reported in either group **Table 2**. The rate of complications were similar in both groups

Table 1: Comparison between the studied groups as regard patients data and preoperative parameters

		Mandibular n= 14	Zygomatic n= 13	p-value
Age (years)		31.7 (12.3)	32 (12.5)	0.9
BMI		25.2 (3.6)	23.6 (3.1)	0.2
Gender (male)		12 (85.7%)	10 (76.9%)	0.9

Smoking		11 (78.6%)	8 (61.5%)	0.58
ASA I		12 (85.7%)	4 (30.8%)	0.57
Inter-incisor Distance (cm)		4.6 (0.7)	5 (0.6)	0.17
Thyromental Distance (cm)		6.5 (0.6)	7 (0.6)	0.04 *
Mallampati score	1	7 (50.0%)	8 (61.5%)	0.82
	2	7 (50.0%)	5 (38.5%)	
Nasal Anatomy Abnormalities		2 (14.3%)	1 (7.7%)	1
Nasal Trauma History		13 (92.9%)	10 (76.9%)	0.53

Table 2: Comparison between the studied groups as regard Primary Outcome, Secondary Outcomes.

		Mandibular n= 14	**Zygomatic n= 13**	**p-value**
Intubation time (seconds)		55.8 (8.5)	47.9 (5.7)	0.009
Rate of first trial success		13 (92.9%)	13 (100.0%)	1
Number of 2nd trial success		1 (7.1%)	0 (0 %)	
Need for use of Magil forceps		9 (64.3%)	3 (23.1%)	0.07
Need for cervical spine extension		6 (42.9%)	3 (23.1%)	0.49
Need for fibro optic		0 (0 %)	0 (0 %)	1
Bleeding	No bleeding	5 (35.7%)	6 (46.2%)	0.35
	Minimal bleeding	7 (50.0%)	7 (53.8%)	
	Mild	2 (14.3%)	0 (0.0%)	
	Moderate	0 (0.0%)	0 (0.0%)	
	Severe	0 (0.0%)	0 (0.0%)	
	Massive	0 (0.0%)	0 (0.0%)	
Complications (lip or dental injury)		2 (14.3%)	3 (23.1%)	0.9
Desaturation		0 (0 %)	0 (0 %)	1

Figure 1: Comparison between the studied groups regarding mean intubation duration

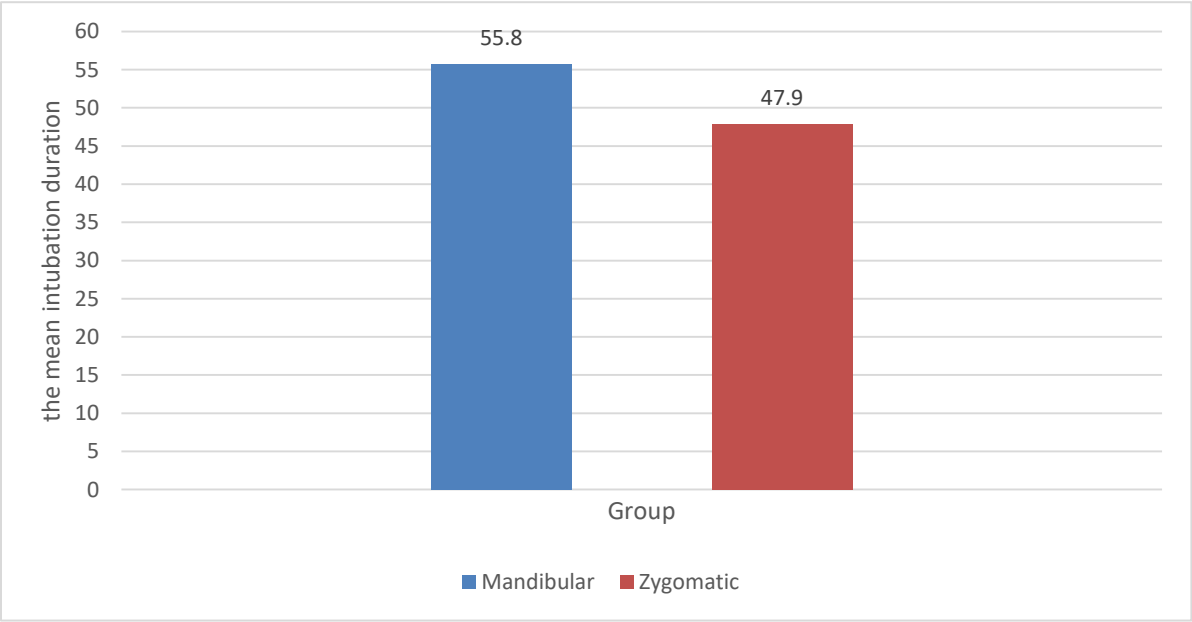
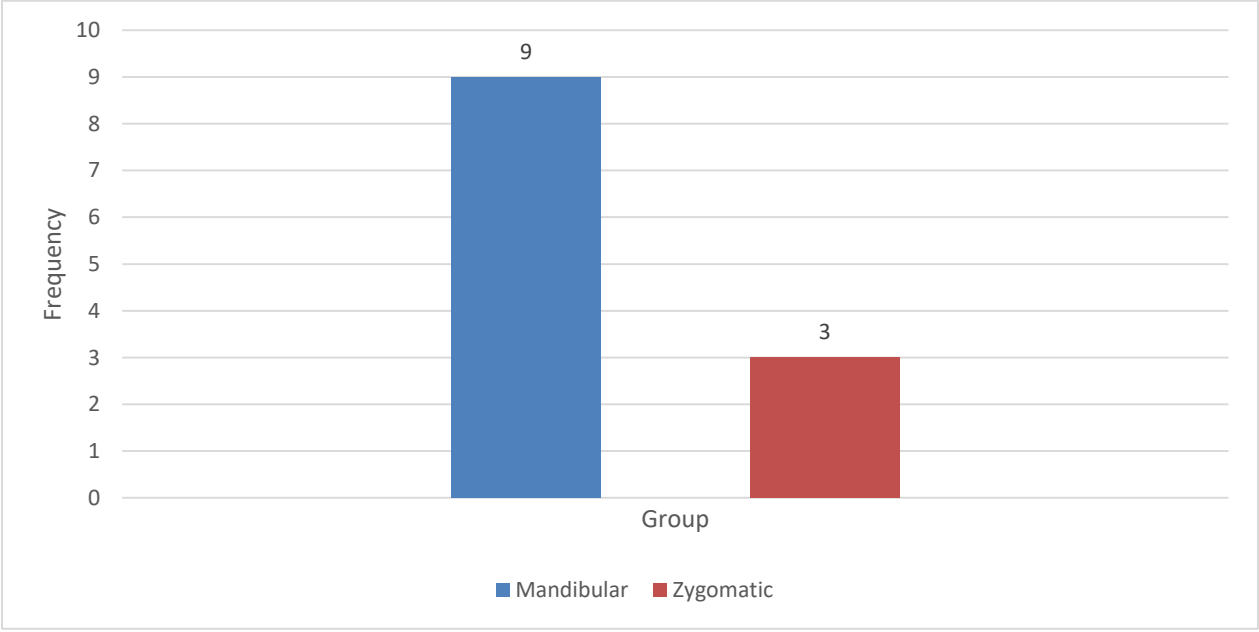


Figure 2: Comparison between the studied groups regarding frequency of Magill forceps usage



DISCUSSION

The findings of this study reinforce the advantages of video laryngoscopy in patients with maxillofacial trauma. Consistent with previous research, patients with mandibular fractures exhibited longer intubation times and required additional airway management maneuvers compared to those with zygomatic fractures **(10)**. This is likely due to the anatomical distortion caused by mandibular instability, which complicates direct passage of the endotracheal tube. However, video laryngoscopy facilitated better visualization and minimized cervical spine extension, making it a safer alternative to direct laryngoscopy**.**

First-attempt success rate is a critical measure of intubation efficiency, particularly in trauma patients where securing the airway rapidly is essential. In this study, first-attempt success rates were not statistically different between the two groups, indicating that video laryngoscopy provides a comparable level of effectiveness regardless of fracture type. However, the slightly lower success rate in mandibular fracture patients may be attributed to greater airway misalignment and soft tissue obstruction. Prior research suggests that patients with mandibular fractures often require multiple intubation attempts due to these factors, reinforcing the need for careful pre-intubation assessment and adjunctive airway management strategies **(7,9).**

Additionally, the incidence of nasal and oropharyngeal bleeding was similar in both groups, with no cases of moderate or severe bleeding reported. This finding suggests that video laryngoscopy may help mitigate bleeding-related complications by providing a clear airway view and reducing the need for excessive manipulation. However some studies report increased incidence of bleeding in mandibular fractures **(6,9).**

The requirement for Magill forceps was observed to be higher in cases of mandibular fractures compared to zygomatic fractures, although this difference did not reach statistical significance (p-value < 0.07). The increased reliance on Magill forceps in these cases suggests that airway management in mandibular fractures often presents greater challenges, necessitating the use of additional instruments to facilitate successful intubation. This finding aligns with previous research, which has reported similar trends and underscores the importance of utilizing adjunctive airway techniques when dealing with complex trauma cases. The need for specialized tools in such scenarios highlights the difficulties associated with airway access and emphasizes the critical role of appropriate airway management strategies in optimizing patient outcomes **(4).**

Another significant finding was the comparable need for cervical spine extension in both groups. Given that trauma patients may have concomitant cervical spine injuries, minimizing cervical movement during intubation is a priority. The ability of video laryngoscopy to facilitate successful intubation with minimal cervical spine extension has been well-documented **(5)**. This supports its role as the preferred technique in maxillofacial trauma cases

The overall rate of complications like dental fracture or lip injury was similar in both groups, further supporting the safety and effectiveness of video laryngoscopy in maxillofacial trauma patients. Future studies should explore larger patient cohorts and randomized controlled trials to confirm these findings and refine airway management protocols for trauma patients.

CONCLUSIONS

Video laryngoscopy represents a valuable advancement in airway management for patients with maxillofacial trauma. Its ability to improve glottic visualization, minimize cervical spine movement, and facilitate successful intubation makes it a preferred technique in emergency settings. While patients with mandibular fractures may pose additional challenges due to airway misalignment and soft tissue obstruction, video laryngoscopy remains an effective tool to mitigate these difficulties. The comparable first-attempt success rates and low complication rates across both fracture groups reinforce its utility in trauma care. Future research should focus on optimizing protocols for intubation in maxillofacial injuries to enhance patient safety and outcomes.

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Aswan University Medical Journal, volume 5 / No.3/ September 2025 (219-227) Online ISSN: **2735-3117**

ORIGINAL ARTICLE

Pathogens Distribution and Risk Factors of Catheter-Associated Urinary Tract Infections in ICU Patients (A Cross-Sectional Study)

Ola A. Mohamed[1]. Ahmed Sadek[2], Mohamed A. Hassany[3], Amal H. Ali[1]

[1]Department of Medical Microbiology and Immunology, Faculty of Medicine, Aswan University
[2]Department of Medical Microbiology and Immunology, Faculty of Medicine, Assuit University
[3]Department of Internal Medicine, Faculty of Medicine, Aswan University

ABSTRACT

Keyword: Catheter-associated urinary tract infections, ICU, Klebsiella, Nosocomial infections, Uropathogens

*** Corresponding author:** Ola A. Mohamed
Mobile: 01144480087
E-mail: Drolaa.mohamed@gmail.com

Background and Objectives: Catheter-associated urinary tract infections (CAUTIs) represent the most frequent nosocomial infections, accounting for 80% of all UTIs in healthcare settings. Common causative pathogens include *Klebsiella spp., Escherichia coli, Staphylococcus aureus, Enterococcus spp., and Pseudomonas aeruginosa*. This study aims to identify uropathogens associated with CAUTIs in ICU patients at Aswan University Hospital to guide empirical therapy and enhance infection prevention strategies. **Methodology:** A total of 200 patients with indwelling Foley catheters in the ICU at Aswan University Hospital were enrolled between June 2023 and June 2024. Urine samples were collected 48 hours post-catheterization, processed under sterile conditions, and cultured using standard microbiological techniques. **Results:** *Klebsiella pneumoniae* was the most frequently isolated pathogen (39%), followed by *E. coli* (33%), *Staphylococcus aureus* (13%), *Coagulase-negative staphylococci* (3%), *Enterococcus spp.* (4%), *Serratia spp.* (2%), and *Pseudomonas aeruginosa* (1%). CAUTIs were more prevalent among females and patients aged 30-39 and 60-69 years. **Conclusion:** CAUTIs remain a significant source of morbidity and healthcare costs. *Klebsiella pneumoniae and E. coli* are the leading pathogens. Effective CAUTI prevention requires catheter management strategies, reducing catheter duration, and enhancing infection control practices.

INTRODUCTION

The Centers for Disease Control and Prevention (CDC) defines CAUTI as a urinary tract infection that occurs in a patient with an indwelling urinary catheter in place for more than two calendar days on the date of the event, with day of catheter placement being Day 1, and was either present on the day of or the day before removal of the catheter. CAUTI is typically confirmed through urine culture results showing significant microbial growth, often defined as ≥10^5 CFU/ml of urine with no more than two species of microorganisms. Symptoms such as fever, suprapubic tenderness, or costovertebral angle pain may be present but are not always required for diagnosis in asymptomatic bacteriuria cases. (1)

CAUTIs are among the most common healthcare-associated infections, particularly in intensive

care unit (ICU) settings where the use of indwelling urinary catheters is often necessary for critically ill patients. [2] CAUTIs contribute significantly to patient morbidity and mortality, increased hospital stays, and heightened healthcare costs. [3] The presence of a catheter disrupts the natural defense mechanisms of the urinary tract, creating a direct route for pathogens to enter the bladder and establish infection. [4]

Pathogens responsible for CAUTIs in ICU patients often differ in prevalence, resistance profiles, and virulence from those found in other hospital wards, largely due to the unique pressures and conditions within ICUs. [5] Critically ill patients frequently undergo multiple invasive procedures and are exposed to broad-spectrum antibiotics, factors that contribute to the selection of multidrug-resistant organisms (MDROs). [6] These pathogens include, but are not limited to, Gram-negative bacteria such as *Escherichia coli*, *klebsiella spp*. and *Pseudomonas aeruginosa*, as well as Gram-positive organisms like *Enterococcus spp.* and *Staphylococcus aureus*. [7]

The understanding of microbial profiles and resistance patterns of pathogens responsible for CAUTIs in ICU settings is essential for effective prevention, timely diagnosis, and targeted antimicrobial therapy. This paper reviews the prevalent pathogens associated with CAUTIs in ICU patients and the risk factors contributing to infection in this vulnerable population. [8]

Despite the global burden of CAUTI, limited data exist on pathogen profiles in critically ill ICU patients in Egypt. This study seeks to address this gap by identifying predominant uropathogens and risk factors of CAUTI at Aswan University Hospital.

PATIENTS AND METHODS

Study design

A descriptive cross-sectional study conducted in ICUs at Aswan University Hospital, including both medical and surgical ICUs. The study spanned one year From June 2023 to June 2024 and involved 200 patients selected based on calculations from the EpiInfo software.

ICU-admitted patients included from both medical and surgical units who are catheterized, irrespective of gender. Eligible patients must be between the ages of 18 and 70 and meet the criteria for CAUTI.

The excluded patients in this study who are not catheterized, those younger than 18 or older than 70, pregnant women, and patients undergoing chemotherapy.

Additionally, patients with a history of sexually transmitted diseases. If more than two types of organisms are grown from a clinical sample, the sample will be considered contaminated, and such cases will also be excluded from the study.

Methods:

Demographic information such as name, age, sex, underlying clinical condition, date of admission to the ICU, and any history of previous antibiotic intake were recorded.

Sterile urethral indwelling catheters were aseptically placed to patients by qualified physicians in accordance with hospital rules or standard operating procedures, thereby reducing the danger of introducing bacteria to the bladder.

Samples for urine were taken depending on the clinical suspicion of the patients admitted to ICU for more than 48 hours. A freshly voided clean catch midstream urine sample (10–20 mL) was collected with a wide-mouth sterile container with a screw cap before catheter insertion. In patients with short-term (<7 days) catheterization, urine specimens were obtained by sampling through the catheter port using aseptic technique (disinfecting with 70% alcohol) or, if a port was not present, by puncturing the catheter tubing with a needle and syringe after clamping (catheter urine was taken in this case because the risk of contamination is low). In patients with long-term (> 7 days) indwelling catheters, urine samples were collected after the catheter was replaced with a freshly placed catheter.

The urine sample was promptly brought to the microbiology section for culture and wet-mount testing. Urine was cultivated on Cysteine Lactose Electrolyte Deficient (CLED) agar, blood agar and MacConkey agar using a 0.001 ml calibrated wire loop and incubated at 37 °C for 24 hours. An uncentrifuged urine sample was examined using wet mount and Gram staining techniques.

In this study, the identification of uropathogens was carried out using a combination of biochemical tests to differentiate bacterial species based on their metabolic characteristics. Following initial culture, suspected colonies were subjected to a series of standard biochemical reactions for confirmation.

Gram-Negative Bacteria: *E. coli, Klebsiella spp., Proteus spp., and Pseudomonas aeruginosa* were identified using Indole, Methyl red, Voges Proskauer, Citrate, Triple Sugar Iron, Urease, Oxidase, and Motility tests based on their metabolic characteristics. Gram-Positive Bacteria: *Staphylococcus spp., Streptococcus spp., and Enterococcus spp.* were differentiated using Catalase, Coagulase, Bile Esculin, and Mannitol fermentation tests.

The identification of all isolated pathogenic organisms was performed using routine microbiological methods, including Gram staining, culture, and biochemical reactions. When further confirmation was required, an automated identification system, such as VITEK-2(BioMérieux), was employed. Additionally, API-20E (BioMérieux), a manual biochemical identification system, was used for the identification of specific bacterial isolates.

Data Management and Analysis:

Data were analyzed using SPSS v28. Descriptive statistics (percentage) and inferential tests (p-values) determined significance ($p<0.05$).

RESULTS

Our study on 200 catheterized patients identified female gender, hypertension, and diabetes mellitus as key risk factors for catheter-associated urinary tract infections (CAUTI). The culture positivity rate was slightly higher in females (55%) and more frequent in patients over 60 years old. Among bacterial isolates, Gram-negative bacteria dominated, with *Klebsiella spp. and E. coli* most prevalent, while *Staphylococcus aureus* led among Gram-positive bacteria. These findings emphasize the importance of risk factor awareness in CAUTI management.

Table 1: Characteristics of patients.

Difference between groups were analyzed using the Chi-square test although no p-values are reported in this table

Characteristics	**Categories**	**Number**	**%**
Length of stay in the ICU	<7 days	105	52.5
	>7 days	95	47.5
Prior antibiotic treatment	Yes	133	66.5
	No	67	33.5
Age groups (years)	20-29	21	10.05
	30-39	50	25.13
	40-49	31	15.58
	50-59	34	17.09
	60-69	64	32.16
Sex	Male	90	44.72
	Female	110	55.28
Site of admission	Surgical ICU	130	65
	Medical ICU	70	35
Comorbidities	Hypertension (HTN)	53	26.5
	Diabetes Mellitus (DM)	34	17
	Chronic Kidney disease (CKD)	20	10
	Benign Prostatic Hyperplasia (BPH)	10	5

Table 2: The prevalence of CAUTI bacteriuria and the causative organisms.

Note: * refer to p value with significant importance (p value < 0.05).

P-values were calculated using the Chi-square test (Fisher's exact test was applied when counts were below 5).

Organism	**Number**	**%**	**P-value**
Klebsiella pneumonia	78	39	0.65
Escherichia coli	66	33	0.02*
Staphylococcus aureus	26	13	0.47
Enterococcus spp.	8	4	0.72
Coagulase-negative Staphylococcus (CoNS)	6	3	0.51
Burkholderia	5	2.5	0.88
Serratia spp.	4	1.5	0.79
Citrobacter freundii	2	1	0.91
Pseudomonas aeruginosa	2	1	0.68
Acinetobacter baumanni	2	1	0.56
Streptococcus agalactiae	1	0.5	0.73

Table 3: Organisms distribution by patients' characteristics.

Note: * refer to p value with significant importance (p value < 0.05).

P-values were calculated using the Chi square test (Fisher's exact test was applied when counts were below 5).

HTN: Hypertension, DM: Diabetes mellitus, CKD: Chronic kidney disease

Organism	**Age Group (n/%) (p-value)**	**Sex (n/%) (p-value)**	**Top Comorbidities (n/%) (p-value)**	**Total Cases (n)**
Klebsiella pneumonia	**20-39:**12 (15%) (p=0.04) *	**Male:**32 (41%) (p=0.17)	**HTN:**30 (38%) (p= 0.03) *	**78**
	40-59:40 (51%) (p=0.03) *	**Female:**46 (59%) (p=0.21)	**DM:**28 (36%) (p= 0.04) *	
	60-69:26 (34%) (p=0.06)		**CKD:** 10 (13%) (p= 0.08)	
E. Coli	**20-39:**9 (14%) (p=0.02) *	**Male:**25 (38%) (p=0.12)	**HTN:**35 (53%) (p= 0.02) *	**66**
	40-59:33 (50%) (p=0.02) *	**Female:** 41 (62%) (p=0.02) *	**DM:**20 (30%) (p= 0.05) *	
	60-69:24 (36%) (p=0.05) *		**CKD:**11 (17%) (p= 0.06)	
Staphylococcus aureus	**20-39:**7 (27%) (p=0.15)	**Male:**10 (38%) (p=0.10)	**HTN:**12 (46%) (p= 0.07)	**26**
	40-59:12 (46%) (p=0.10)	**Female:**16 (62%) (p=0.30)	**DM:**6 (23%) (p= 0.09)	
	60-69:7 (27%) (p=0.12)		**CKD:**3 (12%) (p= 0.12)	
Enterococcus spp.	**20-39:**1 (50%) (p=0.45)	**Male:**1 (50%) (p=1.00)	**HTN:**1 (50%) (p= 0.15)	**2**
	40-59:1 (50%) (p=0.50)	**Female:**1 (50%) (p=1.00)	**DM:**1 (50%) (p= 0.18)	
	60-69:0 (0%) (p=0.20)		**CKD:**0 (0%) (p= 0.20)	
Pseudomonas aeruginosa	**20-39:**1 (50%) (p=0.50)	**Male:** 2 (100%) (p=0.05) *	**HTN:**1 (50%) (p= 0.22)	**2**
	40-59:1 (50%) (p=0.55)	**Female:**0 (0%) (p=0.20)		
	60-69:0 (0%) (p=0.30)			

DISCUSSION

Urinary tract infections (UTIs) are the most common nosocomial infections, accounting for approximately 35% of all hospital-acquired infections (HAIs). These infections are predominantly linked to the use of equipment for urinary drainage, with urethral catheterization responsible for about 80% of nosocomial UTIs in hospital settings. In cases where catheterization is essential, the

risk of UTI increases with the duration of catheter placement, rising between 3% and 7% daily. A study of 200 patients, confirming that prolonged catheter use significantly elevates infection rates, underscoring the need for limiting catheter use and removing catheters as soon as possible. [(9)]

The statistical analysis of patient characteristics revealed key associations related to ICU admissions. Among the 200 patients, 52.5% (105 patients) had an ICU stay of less than 7 days, while 47.5% (95 patients) stayed 7 days or more. The nearly even distribution suggests that prolonged ICU admission is common, potentially due to severe infections, complications, or

underlying health conditions. Patients with extended ICU stays may have increased exposure to nosocomial pathogens, prolonged antibiotic use, and higher risks of multidrug-resistant infections.

According to **Lee et al.** [10] age group distribution showed the largest proportion of patients belonged to the 60–69 age group (32.16%), followed by 30–39 years (25.13%) and 40–49 years (15.58%). The presence of a substantial number of middle-aged and older adults suggests that age-related immune decline, comorbidities, and hospitalization risks may contribute to ICU admissions. Conversely, younger patients (20–29 years: 10.05%) were the least represented, potentially reflecting their better baseline health status and lower susceptibility to severe infections.

Also **Mohamed et al.** [11] discovered the role of prior antibiotic treatment. A significant majority, 66.5% (133 patients), had received prior antibiotic treatment, whereas 33.5% (67 patients) had not. This highlights the widespread use of antibiotics, possibly for empirical therapy or prior infections. The high proportion of antibiotic-exposed patients raises concerns about antimicrobial resistance, which can complicate treatment outcomes and increase ICU length of stay.

Our findings were also consistent with **Modra et al.*'s*** study [12], Sex-based analysis indicated there was a female predominance (55.28%) compared to males (44.72%), suggesting that women were slightly more likely to be admitted to the ICU in this cohort. This could be attributed to higher rates of urinary tract infections (UTIs), sepsis, and chronic conditions such as diabetes and hypertension in females, which may predispose them to critical illness requiring intensive care.

In terms of ICU type, the majority of patients (65% or 130 patients) were admitted to the Surgical ICU, while 35% (70 patients) were in the Medical ICU. The high proportion of surgical ICU admissions may be due to postoperative infections, complications, and the need for intensive monitoring following major surgical procedures. Medical ICU admissions likely include patients with severe infections, respiratory failure, and chronic disease exacerbations requiring intensive medical management. In contrast, **khanna et al.** [13] A retrospective analysis of unplanned ICU admissions highlighted that medical patients were the majority.

Among comorbidities, the most common comorbidity among ICU patients was hypertension (HTN) (26.5%), followed by diabetes mellitus (DM) (17%), chronic kidney disease (CKD) (10%), and benign prostatic hyperplasia (BPH) (5%). The predominance of hypertension and diabetes underscores their role as major risk factors for severe infections, organ dysfunction, and ICU admission. Chronic kidney disease further contributes to immune suppression and increased susceptibility to sepsis, while BPH, though less prevalent, may be linked to urinary retention and recurrent infections in elderly male patients. [14]

The distribution of bacterial isolates revealed that *Klebsiella pneumoniae* (39.0%) and *E. coli* (33.0%) were the most prevalent pathogens, indicating a high burden of urinary tract and nosocomial infections, whereas the **Venkataraman et al.*'s*** study [15] reported a higher prevalence of *E. coli* (35.7%) and a lower incidence of *Klebsiella species* (28.6%). *Staphylococcus aureus* (13.0%) and *Enterococcus spp.* (4.0%) represent common Gram-positive isolates, while less frequent pathogens, including *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (1.0% each), highlight the presence of opportunistic and multidrug-resistant infections.

E. coli showed a statistically significant difference between groups (p = 0.02), suggesting a meaningful variation in its distribution. In contrast, other organisms had non-significant p-values, indicating no notable differences. Further investigation is needed to understand the factors influencing E. coli prevalence. The findings emphasize the need for effective infection control and antimicrobial stewardship to prevent the spread of resistant bacteria in healthcare settings.

According to the most prevalent organisms in table 2, The statistical analysis of bacterial infections across different patient demographics revealed several significant associations ($p < 0.05$) with age, sex, and comorbidities. *Klebsiella pneumoniae* was significantly more prevalent among the 20–39 (p = 0.04) and 40–59 (p = 0.03) age groups, suggesting that younger and middle-aged individuals were more susceptible to this pathogen. Additionally, a strong correlation was observed between *Klebsiella pneumoniae* and hypertension (p = 0.03) as well as diabetes mellitus (p = 0.04), indicating that underlying metabolic and cardiovascular conditions may increase the risk of infection.

Similarly, *E. coli* exhibited a broad age distribution, with significant associations in 20–39 (p = 0.02), 40–59 (p = 0.02), and 60–69 (p = 0.05) age groups. Notably, *E. coli* showed a female predominance (p = 0.02), aligning with its established role as the leading cause of urinary tract infections (UTIs). Furthermore, *E. coli* was significantly linked to hypertension (p = 0.02) and diabetes (p = 0.05), reinforcing the hypothesis that vascular and metabolic disorders contribute to its pathogenesis.

While *Staphylococcus aureus* and *Enterococcus spp*. did not exhibit statistically significant sex- or age-based differences, *Pseudomonas aeruginosa* was found exclusively in males (p = 0.05), suggesting a potential sex-related predisposition. These findings emphasize that age, sex, and preexisting conditions play a critical role in bacterial infection susceptibility, with metabolic and cardiovascular diseases emerging as key risk factors.

The significant associations identified in this study highlight the importance of targeted prevention strategies, early detection, and personalized treatment approaches for high-risk patient populations, particularly those with hypertension, diabetes, and recurrent infections.

CONCLUSION

This study highlights the high prevalence of nosocomial infections, with *Klebsiella pneumoniae* (39.0%) and *E. coli* (33.0%) as the dominant pathogens, particularly affecting older adults and patients with hypertension and diabetes. *E. coli* showed a female predominance (p = 0.02), while *Pseudomonas aeruginosa* was found exclusively in males (p = 0.05). Prolonged ICU stays (47.5% ≥7 days) and prior antibiotic use (66.5%) further increased infection risks, emphasizing the need for strong infection control and antimicrobial stewardship. These findings underscore the importance of early detection, targeted prevention strategies, and personalized treatment to reduce ICU-related infections and improve patient outcomes.

LIMITATIONS

One potential limitation is selection bias, as patients were only selected from one hospital's ICU, which may not represent other ICUs with different protocols. Additionally, ICU patients often have complex comorbidities, which could influence infection rates and microbial susceptibility. Future

studies should consider multicenter data to enhance representativeness and control for varying healthcare practices.

CONFLICT OF INTEREST

The authors report no conflicts of interest. The study was conducted independently, following ethical guidelines to ensure transparency and impartiality. No external funding or personal relationships influenced the research or its outcomes.

Abbreviation list

1. CAUTI – Catheter-associated urinary tract infection
2. CDC – Centers for Disease Control and Prevention
3. CHD – Chronic heart disease
4. CKD – Chronic kidney disease
5. CONS – Coagulase-negative staphylococci
6. HAIs – Hospital-acquired infections
7. ICU – Intensive care unit
8. MDRO – Multi-drug resistant organisms
9. UTI – Urinary tract infection

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