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ORIGINAL ARTICLE

Evaluate the incidence, topography, management, and outcomes in patients with polytrauma in the Suez Canal and Sinai areas



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ABSTRACT

Introduction: The global prevalence of trauma-related mortality ranges from 2% to 32%; however, In Egypt, it reaches 8%. Trauma chiefly affects people in the productive age group; seriously ill patients with multiple injuries present with various levels of polytrauma. Application of incorrect triage systems and improperly trained trauma teams increase mortality and morbidity rates in non-dedicated institutions; however, these rates can decrease with appropriate infrastructure. This study aimed to improve the quality of care for patients with polytrauma through improved knowledge of the different severity levels of polytrauma and defined databases, using a suitable triage trauma system, well-trained trauma team, and appropriate infrastructure.

Methods: This observational cross-sectional study was conducted at the emergency department (ED), over a study period of 7 months, from August 10, 2019, to March 09, 2020. This study included 458 patients with polytrauma who had met the inclusion and exclusion criteria and attended the ED of Suez Canal University Hospital.

Results: The incidence of trauma among all emergency cases in the ED was 5.3%. However, most multiple injuries are mild, accounting for 44.4%, while 27.3% of the cases had life-threatening injuries. Moreover, 41.9% of the patients were managed non-operatively, whereas 58.1% of the patients required surgical interventions. Concerning the outcome, 56% and 6.9% of patients with and without life-threatening injuries respectively, died. *Conclusion:* Facilities of the highest quality should be available for patients with polytrauma, especially those with life-threatening injuries. In addition, training emergency medical service staff for trauma triage is essential, and at least one tertiary hospital is required in every major city in the Suez Canal and Sinai areas to decrease trauma-related mortality.

African relevance

- Trauma is a leading cause of death in Africa.
- Trauma deaths range from 2% to 32% in prevalence but in Egypt accounted for 8%.
- Trained Emergency Medical Service (EMS) staff are essential.
- At least one Tertiary hospital is required in each big city in Canal and Sinai area to reduce mortality rates.
- Application of a formulated, updated, standardized trauma registry system solves a lot of problems in the resource-limited setting, for Emergency Care.

Introduction

The Berlin polytrauma definition (BPD) identifies multiple injury patients with a high risk of morbidity and mortality. The definition includes injuries with an Abbreviated Injury Scale score of ≥ 3 in ≥ 2 body regions (2AIS \geq 3) combined with the presence of \geq 1 physiological risk factors (PRFs) [1].

The PRFs based on Glasgow Coma Scale, age, acidosis, coagulopathy and hypotension at specific limit values.

Trauma is a major global health problem, the fifth-largest condition causing significant disability and remains a common cause of death in the first four decades of life. According to the World Health Organization, trauma accounts for approximately one in ten deaths worldwide. In Egypt, trauma-related death accounted for 8% of total fatalities and was the eighth leading cause of death in 2010. However, the high prevalence of traumatic injuries in Egypt is mostly due to under-reporting and misclassification [2].

In patients with severe polytrauma, mortality and morbidity may increase when using an incorrect triage system and improperly trained trauma teams outside of dedicated institutions; however, this can be prevented with appropriate infrastructure and system changes [3].

Patients with polytrauma may present with any of the following injury patterns: one major limb injury + two major system injuries; two

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major limb injuries + one major system injury; skeletal injury or one open grade fracture + one major system injury; or unstable pelvic fracture with visceral injuries [4].

The traditional protocol in Suez Canal University Hospital (SCUH) was unreliable, because it is based on the personal experiences of physicians and paramedical staff in the emergency room (ER), without a defined trauma triage system [13]. Thus, we attempted to apply an easy method for grouping patients with polytrauma into non-life-threatening polytrauma, which included three subgroups (mild, moderate, and major polytrauma), and life-threatening polytrauma.

Concerning the SCUH protocol, the ED is one of the busiest departments, providing care for all kinds of trauma. Thus, the increase in the number of patients presenting to the ED necessitates an efficient trauma system to avoid wasting resources and provide the best and most efficient care for patients. Furthermore, an efficient trauma system could help attain the trust of patients and boost their satisfaction.

No study has assessed the incidence, topography, management, and outcomes in patients with polytrauma. ED physicians did not know the different severity levels of polytrauma and other intervention tools to improve the outcomes of these cases, for example, an efficient triage system, well-trained trauma team, and appropriate infrastructure.

Therefore, this study aimed to improve the quality of care for polytrauma patients by improving knowledge and establishing databases to determine the incidence, topography, and outcomes of the different severity levels of polytrauma at the ED of SCUH by developing a suitable and efficient triage system, deploying a well-trained trauma team, and adopting an appropriate infrastructure.

Methods

This was an observational cross-sectional study. This study was conducted at SCUH, a tertiary hospital and referral center for the Suez Canal and Sinai areas. The target population included all patients with polytrauma who met the inclusion and attended the ED of SCUH from August 10, 2019, to March 09, 2020.

The study included all polytrauma patients of any age, of both sexes and those who 1) died within 24hours; 2) had an Injury Severity Score (ISS) >15, or had an intensive care (ICU) stay exceeding 1 day, or who had 2 or more units of blood transfused.

Exclusion criteria were those self-discharged, transferred elsewhere or with injuries over 24 hours old on presentation.

The patients were classified into two groups according to the severity of the injuries:

- 1. Non-life-threatening polytrauma group, with three subgroups, namely, mild, moderate, and major polytrauma.
- 2. Life-threatening polytrauma group.

The mild polytrauma subgroup included patients with an Abbreviated Injury Scale (AIS) score of 1 plus AIS 2, for example, non-complex soft tissue injuries and fractures and rupture of the ligaments and tendons. The moderate polytrauma subgroup included patients with AIS 3 plus AIS 4, for example, skull injuries, arterial lesions, pelvic fractures or dislocations, intestinal lacerations, neurological, hepatic, or splenic injuries.

The major polytrauma subgroup included patients with AIS 5, for example spinal fractures or dislocations with cord injury.

The life-threatening polytrauma group included patients in prearrest conditions or even non-survival, for example, injuries to great vessels in the thorax, pneumothorax, and hemothorax [5].

First, all patients are assessed using the Advanced Trauma Life Support (ATLS) guidelines. As a routine workup for all injuries, plain X-rays (lateral cervical spine, posteroanterior chest, and anteroposterior pelvis) and focused assessment sonography for trauma are performed. However, for stable patients, selective plain X-rays of only the injured body part were obtained. Other specific investigations were performed according to the injured body parts, for example, brain computed tomography (CT) for patients with head trauma and a Glasgow Coma Scale (GCS) score of \leq 14. In addition, unstable patients were admitted to the resuscitation trauma area for urgent interventions.

All patients had complete history, including age, sex, occupation, mode and time of trauma, arrival, resuscitation, and secondary survey.

After the initial management and triage a tertiary survey was performed.

Progress notes with a definitive diagnosis of polytrauma and final decisions had to be made. Treatment may be surgical or conservative; moreover, according to the Egyptian law, all services for emergency cases within 48 h are free of charge. Thus, the short-term follow-up period was 48 h in the ED, with inpatient ward, or ICU follow up till 5 days.

Data enrolled and analyzed using Statistical Package for the Social Sciences, version 23.0 (IBM Corp., Armonk, NY, USA). Reported frequency distribution is presented as percentages, and descriptive statistics for polytrauma are presented as mean and standard deviation.

Ethical consideration: The Research Ethics Committee of the Faculty of Medicine approved the study, SCUH (reference number 3596) and individual patient consent for participation in this study was obtained, while for unconscious patients, informed consent was obtained from their relatives. The study did not affect the treatment decisions or treatment options.

Results

The total number of patients with different presentations who visited the ED from August 10, 2019, to March 09, 2020, was 28,301 (Figure (1)). Among them, 1,492 (5.3%) were patients with trauma. Of the 1,492 patients with trauma, 1,034 (69.3%) had minor injuries and did not meet the polytrauma criterion, and only 458 (30.7%) had polytrauma. Therefore, the total incidence of trauma among all cases in the ED was 5.3%; however, this rate increased to 9.3%, especially in the weekends.

Furthermore, the total number of cases admitted to SCUH during the study period was 7,509 (26.5%) of the 28,301 patients who visited the ED, among whom 762 (50.1%) were trauma cases; therefore, the total incidence of trauma admissions among the total admission cases that visited the ED was 10.2%.

This study included 458 patients with polytrauma who presented to the ED within 12 h from the time of trauma. All patients underwent routine and advanced investigations for the initial diagnosis and management decisions. In addition, this study revealed that most patients (64.6%) belonged to the age group of 18–60 years; moreover, most patients (87.5%) were male, thereby indicating male predominance.

The total number of patients with polytrauma without lifethreatening injuries was 333, and the total number of patients of polytrauma with life-threatening injuries was 125 (Table (1)).

According to the trauma mechanism, the trauma mechanism for half of the patients under study (n=229, 50%) was a motor vehicle crash. The next commonest categories were assault (n=124, 27.1%) and falling from height (FFH) (n=95, 20.8%). (Table (2)).

In addition, 29.4% of patients with polytrauma without lifethreatening injuries and 100% of patients with polytrauma without lifethreatening injuries had a respiratory rate of more than twenty-nine per minute, however in 64.7% of patients with polytrauma with lifethreatening injuries, the respiratory rate was not recorded (Table (3)). Tachycardia (more than 100 beats per minute) was present in 11.8% of patients with polytrauma with life-threatening conditions and 9.7% of patients with polytrauma without life-threatening conditions, while for 58.8% of patients with polytrauma with life-threatening conditions, the heart rate was not recorded. Furthermore, 3.2% of patients with polytrauma without life-threatening conditions had a systolic blood pressure of <90 mmHg, and in 41.2% of patients with polytrauma with lifethreatening conditions, systolic blood pressure not recorded. Significant differences in respiratory rate, heart rate, and systolic blood pressure



Fig. 1. Summary algorithm for selection of the study patients

were observed between the polytrauma with life-threatening injuries and polytrauma without life-threatening injuries groups, but no significant difference was observed in the GCS score between both groups.

According to the site of polytrauma, most patients (n = 59; 47%) had head and facial injuries, and 41.2% of the patients in the polytrauma with life-threatening injuries group had injuries to their extremities (Table (2)). Meanwhile, in the polytrauma without life-threatening injuries group, the most common site of polytrauma was the head and neck (n = 171; 51.6%), whereas the most common site of polytrauma without life-threatening injuries (n = 129; 38.8%) in the polytrauma without life-threatening injuries group.

Most patients (n = 76; 60.8%) in the polytrauma with lifethreatening injuries group and 188 (56.5%) patients in the polytrauma without life-threatening injuries group arrived at the hospital at night (Table (4)).

The distributions of Types of Polytrauma of the studied cases were Mild 203(44.4%), Moderate 94(20.5%), Major 36(7.8%) and Life threatening 125(27.3%) Moreover, most injuries in both sex groups were mild (n = 203; 44.4%), but 125 (27.3%) patients had life-threatening injuries.

Statistically significant differences were observed in contributing factors for determining the causes and definitive diagnosis between the polytrauma with and without life-threatening injuries groups (Table (4)); six (40%) and nine (30%) cases were due to insufficient physical examination, zero and three (10%) cases were caused by incomplete assessment due to patient instability, six (40%) and nine (30%) cases were caused by incorrect interpretation of imaging, respectively.

Table 1 Demographic characteristics					
Age (years)	Total	Polytrauma with life-threatening conditions	Polytrauma without life-threatening conditions	P-value	
<18	143(31.2%)	41(33.6%)	102(30.6%)	0.9	
18-60	296(64.6%)	79(61.6%)	217(65.1%)		
<60	19(4.2%)	5(4.8%)	14(4.2%)		
Sex					
Male	401(87.5%)	108(86.4%)	293(87.5%)	0.08	
Female	57(12.5%)	17(13.6%)	40(12.5%)		

Table 2

Mode and Site of polytrauma

	Traumatic patient		
Mode of trauma	No.	%	
Motor vehicle crash (MCA)	229	50%	
Assault	124		
		27.1%	
Falling From Height (FFH)	95		
		20.8%	
Falling Downstairs (FDS)	0	0	
Falling To Ground (FTG)	0	0	
Direct Head Trauma (DHT)	10	2.1%	

Variable		Polytrauma with life-threatening conditions	Polytrauma without life-threatening conditions	<i>P</i> -value
Site of polytrauma	Head Thorax Abdomen and pelvis Face Extremities Spine	0 7(5.9%) 7(5.9%) 59(47%) 52(41.2%) 0	53(16%) 11(3.2%) 11(3.2%) 118(35.6%) 129(38.8%) 11(3.2%)	<0.05*

Table 3

Clinical predictors of the study groups

		Polytrauma with life-threatening	Polytrauma without life-threatening	
		conditions	conditions	P-value
Respiratory rate	<29	37(29.4%)	333(100%)	< 0.05*
	>29	7(5.9%)	0(0%)	
	Not assessed	81(64.7%)	0(0%)	
Pulse rate	<100 bpm	37(29.4%)	301(90.3%)	< 0.05*
	>100 bpm	15(11.8%)	32(9.7%)	
	Not assessed	73(58.8%)	0(0%)	
Systolic blood pressure	<90 mmHg	0(0%)	11(3.2%)	< 0.05*
	>90 mmHg	74(58.8%)	322(96.8%)	
	Not assessed	51(41.2%)	0(0%)	
Glasgow Coma Scale	<8	0(0%)	0(0%)	0.4
	8-12	0(0%)	11(3.2%)	
	13–15	125(100%)	322(96.8%)	

Table 4

Time and methods of diagnostic injuries

Diagnostic methods	Polytrauma with life-threatening conditions	Polytrauma without life-threatening conditions
Full examination	36(40%)	100(30%)
Radiological assessment by:		
СТ	13(13.4%)	122(36.6%)
X-ray	45(100%)	33(10%)
MRI	0(0%)	48(14.4%)
US	45(100%)	30(9%)
The time of injuries		
Night	76 (60.8%)	145 (43.5%)
Day	49 (39.2%)	188 (56.5%)

A significant correlation was observed between severity levels of polytrauma and management modalities (p = 0.034) (Table (5)). Surgical interventions were performed for 103 of the 125 patients (82.1%) in the polytrauma with life-threatening injuries group but only 199 of the 333 patients (59.7%) in the polytrauma without life-threatening injuries group. However, non-operative treatment with follow-up was offered to twenty-two of the 125 patients (17.9%) in the polytrauma with life-threatening injuries group and 134 of the 333 patients (40.3%) in the polytrauma without life-threatening injuries group.

A significant difference in the number of patients with ward admission observed between the polytrauma with and without life-threatening injuries groups. Among the patients in the polytrauma with lifethreatening injuries group, 36% were admitted to a ward compared to 29.1% of the patients in the polytrauma without life-threatening injuries group; however, no significant difference in the length of ward stay was observed between the groups.

In addition, a significant difference in the number of patients admitted to the ICU was noted between the polytrauma with and without lifethreatening injuries groups (p = 0.01). Sixty-four percent of the patients in the polytrauma with life-threatening injuries group were admitted to the ICU compared with 59.7% of the patients in the polytrauma without life-threatening injuries group. In addition, a significant difference

Table 5

Ward, ICU admission, outcome, and management for the study groups

	Polytrauma without life-threatening conditions (n = 333)		Polytrauma with life-threatening conditions (n = 125)			
	n	%	n	%	χ[2]	P-value
Ward admission	97	29.1	45	36	5.8	0.01*
Ward stay (days) Mean <u>±</u> SD Range	4.96 <u>+</u> 0-	- 4.799 -25	5.64 1-	± 5.6 30	0.866*	0.387
ICU admission	199	59.7	80	64	6.11	0.01*
ICU stay (days) Mean ±SD Range	2.74 ± 5.59 0-27		0.36 ± 0.91 0-4		2.5*	0.0*
No admission	37	11.1	0	0		
Outcome: Died Discharged after complete recovery Not admitted	23 273 37	6.9 81.9 11.1	70 55 0	56 44 0	5.8	0.055
Treatment offered Conservative Surgical	134 199	40.3 59.7	22 103	17.9 82.1	4.51	0.034

in the length of ICU stay observed between both groups (p = 0.01) since patients in the polytrauma without life-threatening injuries group were admitted to the ICU for 2.74 ± 5.59 days compared with 0.36 ± 0.91 days for patients in the polytrauma with life-threatening injuries group (Table (5)).

Regarding outcomes, 70 patients (56%) in the polytrauma with lifethreatening injuries group died, whereas of the 333 patients in the polytrauma without life-threatening injuries group, 273 (81.9%) were discharged after treatment, only 23 (6.9%) died, and 37 (11.1%) were not admitted to a ward as no lesions were found during the initial investigation and follow-up at the ED (Table (5)).

In this study, all patients received treatment for different polytrauma levels. In the mild polytrauma subgroup, 41.9% and 58.1% of the patients received conservative and surgical treatments, respectively. In the moderate polytrauma subgroup, 39.4% and 60.6% of the patients received conservative and surgical treatments, respectively. In the major polytrauma subgroup, 33.3% and 66.7% of the patients received conservative and surgical treatments, respectively. In the major polytrauma subgroup, 33.3% and 66.7% of the patients received conservative and surgical treatments, respectively. In addition, in the polytrauma with life-threatening injuries group, 17.9% and 82.1% of the patients received conservative and surgical treatments, respectively.

Discussion

Data on injuries over a number of years in this large trauma care center would provide a reliable prediction of what is happening in terms of injuries among the Suez Canal and Sinai populations [6].

This study recognized trauma as a significant problem in the Suez Canal and Sinai areas, with a special concern regarding the incidence, topography, and outcomes of the different severity levels of polytrauma. This has the implication that all ED staff should trained in trauma management.

Thus, factors in the Suez Canal and Sinai areas may have decreased the incidence of trauma compared with the incidence of trauma in other areas, such as appropriate infrastructure (new and high-quality roads and less-crowded motor flows). In this study, most patients arrived at the ED at night. This finding conforms to those of Elbaih et al. who noted higher rates of life-threatening injuries in patients arriving at night (59.2%) than in patients arriving during the day (40.8%) [4].

The high rates of life-threatening injuries among patients who arrived at night may be explained by the fact that during the day, speed limits imposed according to the designated function of particular roads are observed. In addition, the attitude of drivers may influence by knowledge about preventive measures: helmet use; and fear of the police, deployed during the day. Road safety equipment is mostly unavailable at night,worsened by lack of streetlights. In addition, well-trained physicians are vital in the rapid transportation of injured patients. In our resource-limited setting, where staff shortage is a problem, the redistribution of available staff should occur to address this problem. Since trauma is common at night and weekends - this has implications for the staffing of emergency departments. More than 2%–3% of patients with trauma have minor injuries, which may be due to several measures, including stressing the importance of infrastructure and road safety maintenance.

According to the study by Elbaih et al., the most common diagnostic cause of instability and life-threatening injuries was hypovolemic shock (64%), whereas the least common cause was cardiogenic shock (10%) [4].

Providing care to trauma cases is one of the main responsibilities of ED staff, which include prehospital and hospital phase management. Emergency physicians, Emergency Medical Services (EMS) teams, and the availability of resources play an essential role in stabilizing injuries. After resuscitation, cases of polytrauma with various levels of severity must be transported to a tertiary hospital for more investigations. Thus, the availability of these recourses is essential, especially in low-income countries. Studies on the incidence of polytrauma with different severity levels is limited, so this study is comparatively innovative.

This study revealed that most patients belonged to the age group of 18–60 years; moreover, with a male predominance. It is a disease of young men, associated with road traffic crashes - with the implication that there is the potential for trauma prevention with improved infrastructure and road safety messages targeted to this section of the population.

This study revealed that most injuries in both sex groups were mild at 44.4%, with moderate and severe only constituting 28.5%, and only 27.3% were unstable life-threatening polytrauma cases. This is similar to the findings of Fouda et al., which reported cases with minor, moderate, and major injuries after MVC (n = 746) and 200 (21.1%) of the 946 patients with trauma had life-threatening injuries, also half of these patients had mild polytrauma [7].

In addition, the respiratory rate and heart rate was not recorded in many of the patients. This implies the need for additional training of nurses and doctors. Facilities of the highest quality, for example tertiary hospitals, should be suitably located and available for patients with life-threatening injuries. Thus, at least one mandatory tertiary hospital will be required in every major city in Suez Canal and Sinai areas to decrease fatalities. Well-trained physicians and senior health providers are vital in the rapid transportation of injured patients. Also, EMS and the availability of resources play an essential role in stabilizing patients with trauma. The availability of the ambulance service in the "Golden Hour" for patients with life-threatening injuries is essential for the patient to reach a hospital early.

Khorsandi et al. have revealed an insignificant difference in hospital stay between patients with blunt trauma and those with penetrating life-threatening injuries [8]. Lema et al., in an 11-year review of outcomes of life-threating polytrauma in hospitals in England, have reported an insignificant difference in ICU stay between patients with polytrauma without life-threatening injuries and those who sustained life-threatening polytrauma [9].

Therefore, training medical teams and building more trauma centers for life-threatening injuries and emergency resuscitation are essential, and supplementing these centers with different equipment and trained ED physicians and surgeons and increasing ICU beds for patients with trauma is important.

The study by Ekpe et al. revealed a mortality rate of 5.4% in patients with polytrauma, which is comparable to 6.9% in patients with polytrauma without life-threatening injuries. However, 56% of the patients in the polytrauma with life-threatening injuries group died in our study, which were associated with life-threatening and extra-organ injuries, delayed presentation of injury of longer than 24 h, and life-threating injuries as characterized by chest involvement [10].

Outcome of admitted patients with life-threatening polytrauma in this study may be explained by the presence of ED physicians who rapidly treated critical cases according to the ATLS protocol. Moreover, by applying a new emergency approach rather than the traditional methods, a dramatic decrease in the length of stay was observed, which may be due to the suitable new patient-sorting system, and the use of the resuscitation room in the ICU trauma triage for selected critical cases, with acceptable over-triage and provision of rapid and proper management without delay, resulting in improved ICU outcomes.

Elbaih et al. conducted a prospective study involving two hundred patients with life-threatening polytrauma and observed that surgical interventions were performed on 162 patients, indicating that surgery is the most commonly used treatment, which conforms to our study [11]. Therefore, all ED physicians should train in emergency surgical interventions for patients with polytrauma, such as tube or needle thoracotomy, pericardiocentesis, ED thoracotomy, and other urgent surgical interventions [12].

This study has reported a specific association between male sex and increased incidence of trauma, which might be due to the more active behavior of males than females. MVC, assault, and FFH were the most common injury mechanisms in Egyptian patients. The care of injured patients includes prehospital and hospital phase management. EMS and the availability of tools play an essential role in providing care for patients with trauma.

Trauma is a significant problem in the Suez Canal and Sinai areas, with a special concern regarding the incidence, topography, and outcomes of the different severity levels of polytrauma. Most trauma patients had minor injuries and did not meet the polytrauma criterion. The total incidence of trauma among all cases in the ED increased in the weekends and most the patients with life-threatening injuries arrived at the hospital at night.

According to the site of polytrauma, most patients had head and facial injuries, in the polytrauma with life-threatening injuries group while in those without life-threatening injuries group, the most common site of polytrauma was the extremities. Statistically significant differences were observed in contributing factors for determining the causes and definitive diagnosis between the polytrauma with and without life-threatening injuries groups, being due to insufficient physical examination, incomplete assessment due to patient instability, and incorrect interpretation of imaging, respectively.

A significant correlation observed between severity levels of polytrauma and management modalities. Surgical interventions were performed more often for polytrauma with life-threatening injuries.

Conclusions

Trauma remains a significant problem in the Suez Canal and Sinai areas, concerning regarding the incidence, topography, and outcomes for the different severity levels of polytrauma. To improve the quality of interventions for patients with polytrauma, a suitable infrastructure should be developed in Egypt (for example, high-quality roads with regular road maintenance, less-crowded traffic flows, and the proper behavior of motorcycle riders). Training of EMS staff is essential and mandatory. In addition, at least one tertiary hospital is required in every major city in Suez Canal and Sinai areas to decrease the mortality rate. All ED staff should train and be qualified for urgent surgical procedures for patients with polytrauma, such as tube thoracotomy, pericardiocentesis, ED thoracotomy, and other emergency surgical interventions. The application of a trauma registry system solves problems in this resourcelimited setting. The old ED patient registry for Emergency Care can be reformulated, updated, and standardized for trauma cases. The facility must deploy an efficient charting system and trauma registry to eliminate bias due to differences in personal data collection methods and to reduce significant information gaps in patient's charts.

Dissemination of results

Results of this study were presented locally at the Emergency Department scientific day with staff members at Suez Canal University.

Authors' contributions

Authors contributed as follows to the conception or design of the work, the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: AHE contributed 50%; MTI contributed 30%, and BSA contributed 20%. All authors approved the version submitted and agreed to be accountable for all aspects of the work.

Declaration of Competing Interest

The authors declared no conflicts of interest.

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