The hematological parameters in children with scorpion sting: a study from upper Egypt

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Received 29 July 2023
Revised 18 September 2023
Accepted 25 September 2023
Published 23 December 2023

Journal of Current Medical Research and Practice
2023, 8:182–187

Background
Scorpion stings are common emergency events in Upper Egypt, with significant morbidity and mortality. We aimed to investigate the hematological parameter and their relation to the severity of envenomation in children presenting with scorpion stings.

Methods
The current study is an observational hospital-based case-control study that was carried out at the Emergency and Intensive Care Units, from January 2022 to December 2022. The hematological parameters were compared between these cases and those of controls.

Results
The study included 42 cases and 42 controls. The studied cases and those with moderate/severe envenomation had significantly higher total leucocyte count, absolute neutrophilic count (ANC), platelets count, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), d-dimer, and international normalized ratio (INR), compared with controls and those with mild envenomation, respectively. Multivariate logistic regression analysis showed that younger aged patients were more likely to suffer from severe scorpion envenomation compared with older aged ones (OR = 0.572, 95% confidence interval 0.356–0.919, $P = 0.021$), and patients with white blood cell (WBC) count greater than or equal to 11.6 were 7 times more likely to suffer from severe scorpion envenomation compared with those with WBC count less than 11.6 (OR = 75.607, 95% CI: 4.935–1158.258, $P = 0.002$).

Conclusions
Scorpion envenomation can cause many alterations in hematological parameters and platelet indices of affected victims. The use of these parameters to predict the severity of scorpion envenomation is simple, cheap, and easily applicable. Younger age and higher WBC count ($\geq$11.6) were significantly independent predictors of severe envenomation. Further studies are warranted.

Keywords:
children, hematological, neutrophil to lymphocyte ratio, platelets, platelet to lymphocyte ratio, predictive, scorpion sting, severity, upper Egypt

J Curr Med Res Pract 8:182–187

2357-0121

Introduction

Scorpion stings still represent common emergency events worldwide. Particularly, it is common in tropical and subtropical regions. In our locality, Upper Egypt, scorpions still represent a life-threatening hazard, especially to children [1]. The scorpion venom constitutes a mixture of cardiotoxins, hemolytic toxins, nephrotoxins, and neurotoxins [2]. The balance between those pro-inflammatory and anti-inflammatory cytokines released by the host -in varying proportions according to the different species of scorpions regulates the extent of inflammation, resulting in major clinical effects such as cardiac dysfunction, pulmonary edema, and shock [3]. Severe envenomation is usually associated with morbidity and mortality which in turn have an impact on hospitalization and increased costs [4].

Recently, there has been an interest in studying the changes in hematological parameters about scorpion envenomation. For example, parameters like the total leukocytic count (TLC), and the activated partial thromboplastin time (aPTT) are useful in predicting the severity of scorpion envenomation [5]. Moreover, some alterations in platelet counts and functions happen, due to an excessive systemic host inflammatory response to scorpion stings. [3].

Therefore, in this study, we aimed to investigate the relationship between the severity of envenomation and hematological parameters in pediatric patients presenting with scorpion stings.

Materials and methods

Study design, setting, and population

The current study is an observational hospital-based case-control study. It was carried out at the Emergency and Intensive Care Units, at Assiut University Children's Hospital during the period from January 2022 to December 2022. All children with scorpion envenomation who were admitted to the hospital during the study period were prospectively enrolled in the present study. As cases, they were compared with a group of matched healthy controls. Exclusion criteria included; patients with any other envenomation or intoxications, and patients or parents who refused to participate in the study.

Assessments

The study participants underwent the following:

(1) Full history: where the following data were inquired; age, sex, time and date of presentation, place of first referral, type of scorpion (if known), location, time and number of stings, region of residence (urban or rural), administration of antivenom, number of antivenoms, and the presenting symptoms.
(2) Full Clinical examination: vital signs, level of consciousness, general, systemic, and local examinations.
(3) Routine laboratory investigations:

The following laboratory workups were obtained; complete blood count (CBC) with differential count, with calculations of the neutrophil-to-lymphocyte ratio (NLR), d-dimer, platelet-to-lymphocyte ratio (PLR), and coagulation profile [prothrombin time (PT), prothrombin concentration, partial thromboplastin time (PTT), and international normalized ratio (INR)].

For coagulation parameters, blood samples were collected from patients and controls in two citrated tubes containing buffered sodium citrate (0.109 M, 3.2%) in the blood: anticoagulant 9:1 ratio. The plasma was run on a fully automated coagulometer (Sysmex CA 1500; Sysmex Corporation, Kobe, Japan), and values of PT, PC, INR, and PTT were recorded. The rest of the plasma was used for the calculation of D-dimer levels by a semiquantitative rapid latex agglutination slide test (D-Di test, Diagnostica Stago S.A.S., France).

Assessment of severity

As per Shamoon *et al.* [6], the patients were classified into four groups:

(1) Grade 1: local pain and paresthesia at the sting site. scorpion sting.
(2) Grade 2: local pain and paresthesia at the sting site as well as proximal to it.
(3) Grade 3: grade 2 with added cranial nerve (blurry vision, increased oral secretions, rapid tongue movement, nystagmus), or skeletal neuromuscular dysfunction (flailing of the extremities, tetanus-like arching of the back) which can also be accompanied by autonomic dysfunction.
(4) Grade 4: unlike that of grade 3 where the patient will experience either cranial nerve or skeletal muscle dysfunction, grade 4 includes both. This can cause hyperthermia (up to 40°C), rhabdomyolysis, pulmonary edema, and multiple organ failures.

Ethical consideration

Informed written consent was obtained from the guardians of the study participants. The protocol of the study had been approved by the Local Medical Ethical Review Board of the Faculty of Medicine, Assiut University (IRB no: 17101317).

Statistical analysis

The software SPSS (statistical package for the social science; SPSS Inc., Chicago, IL, USA) version 22 was used. Data were described in terms of mean ± standard deviation, or median and range when not normally distributed. The Student *t*-test was used for the comparison of quantitative variables for normally distributed data whereas Mann–Whitney *U* test was used for non-normally distributed data. For comparing categorical data, a Chi-square (χ^2) test was performed. An exact test was used instead when the expected frequency was less than 5. The receiver operating characteristic curve (ROC) analysis was used to find out the best cut-off values to validate the prediction of scorpion envenomation severity using different markers. Odds ratio (OR) with a 95% confidence interval (CI) and Logistic Regression was calculated for the prediction of severe scorpion envenomation. A *P* value was set as significant at less than 0.05 level.

Results

Demographic and clinical characteristics

The study included two groups: 42 cases and 42 controls. It was found that there were no significant differences between the two groups about age, sex, and body weight. 71.4% of the cases came from rural areas. The most common sites for the sting were the hand (42.9%) and leg (40.5%). (Table 1).

Myocarditis, arrhythmia, depressed ST segment, and heart failure were seen in 38.1, 31, 31, and 31% of

cases, respectively. 38.1% of cases developed pulmonary edema. In comparison to the control group, the studied cases had significantly higher heart rate (HR) and respiratory rate (RR), but lower body temperature and blood pressure (BP). Table 2 shows these data.

Laboratory findings

With regards to the blood counts, the studied cases had significantly higher total leucocyte count, ANC, ALC, platelets count, PDW, NLR, and PLR, compared with controls, respectively. On the other hand, cases had significantly lower lymphocyte count, hematocrit, and MPV, than controls, respectively.

With regards to the coagulation profile, the studied cases had significantly lower prothrombin concentration, but higher INR and d-dimer values than controls, respectively. There were no significant differences about PT and PTT. These data are detailed in Table 3.

Mild versus moderate/severe envenomation

For the severity of envenomation; 12, 14, 8, and 8 cases had grades 1, 2, 3, and 4, respectively. These grades were grouped into two groups: group I (mild envenomation); 26 (61.9%) cases, and group II (moderate and severe envenomation); 16 (38.1%) cases.

Group II had significantly higher total leucocyte count, ANC, platelets count, PDW, MPV, and PLR, compared with group I, respectively. Group II had significantly prolonged PT, and longer PTT, higher INR and d-dimer levels, compared with group I patients, respectively with mild envenomation.

Predictors of severity of envenomation

The WBC, PLR, and d-dimer had areas under the curve (AUC) of 0.921, 0.805, and 0.841, with *P* values of less than 0.001, 0.001, and less than 0.001, respectively. (Table 4).

Univariate logistic regression analysis had shown that younger age, lower GCS score, higher WBC count, higher platelets count, higher PDW, MPV, and PLR were significant predictors for severe scorpion envenomation. Multivariate logistic regression analysis showed that younger age and higher WBC count (≥11.6) were significantly independent predictors of severe envenomation. Younger aged patients were more likely to suffer from severe scorpion envenomation compared with older aged ones (OR = 0.572, 95% CI: 0.356–0.919, *P* = 0.021), and patients with WBC count greater than or equal to 11.6 were 7 times more likely to suffer from severe scorpion envenomation compared with those with WBC count less than 11.6 (OR = 75.607, 95% CI: 4.935–1158.258, *P* = 0.002). (Table 5).

Table 1 Demographic Features and site of the sting

Item	Cases (*n*=42, %)	Controls (*n*=42, %)	*P*
Age (y)			
Mean±SD	5.18±4.12	5.19±3.85	0.982
Sex			
Male	31 (73.8)	28 (66.7)	0.474
Female	11 (26.2)	14 (33.3)	
Weight			
Mean±SD	19.95±8.57	25.17±13.21	0.091
Residency			
Urban	12 (28.6)	24 (57.1)	0.008
Rural	30 (71.4)	18 (42.9)	

Table 2 Clinical presentations and signs of scorpion sting among the study participants

Item	Cases (*n*=42, %)	Controls (*n*=42, %)	*P*
Signs			
Heart rate			<0.001
Normal	14 (33.3)	42 (100.0)	
Tachycardia	26 (61.9)	0	
Bradycardia	2 (4.8)	0	
Mean±SD	121.43±24.27	106.19±14.95	
Respiratory rate			<0.001
Normal	14 (33.3)	42 (100.0)	
Tachypnea	26 (61.9)	0	
Bradypnea	2 (4.8)	0	
Mean±SD	29.50±9.86	23.24±5.45	
Temperature (°C)			0.008
Normal	12 (28.6)	24 (57.1)	
Hyperthermia	26 (61.9)	18 (42.9)	
Hypothermia	4 (9.5)	0	
Mean±SD	37.76±1.00	37.61±0.62	
Blood Pressure			0.001
Normal	28 (66.6)	42 (100.0)	
Hypertension	0	0	
Hypotension	4 (9.5)	0	
Shocked	10 (23.8)	0	
GSC			0.001
Mean±SD	12.64±4.09	14.81±0.59	
Presenting symptoms among cases; *n*=42 (%)			
Gastrointestinal	No (%)		
Excessive salivations	26 (61.9)		
Vomiting	25 (59.5)		
Diarrhea	16 (38.1)		
Abdominal pain	27 (64.3)		
Neurological			
Agitation	19 (45.2)		
Paresthesia	42 (100.0)		
Disturbed conscious level	10 (23.8)		
Cardiovascular			
Myocarditis	16 (38.1)		
Arrhythmia	13 (31.0)		
Depressed ST segment	13 (31.0)		
Heart failure	13 (31.0)		
Pulmonary			
Pulmonary edema	16 (38.1)		

Discussion

CBC is an inexpensive and easy-to-perform diagnostic test. Recently, numerous studies focused on the proportion of different types of leukocytes in various medical conditions [7,8].

Our demographic data showed that males were more affected by scorpion stings than females. This finding is in agreement with several studies [9] and could be explained by the fact that boys go outdoors more often than girls. Upper and lower limbs were the most frequent sites for scorpion envenomation. This finding is by the study of Baseer and Naser [10]. This could be attributed to that the upper and lower extremities were the exposed area, so easy to be liable for envenomation.

Table 3 Hematological parameters and coagulation profile among the study participants

Item	Cases (*n*=42, %)	Controls (*n*=42, %)	*P*
CBC parameters			
WBC (10^3/ul)			<0.001
Mean±SD	10.16±3.08	5.99±1.78	
Leukocytosis	30 (71.4)	15 (35.7)	
Leucopenia	2 (4.7)	6 (14.2)	
Normal	10 (23.8)	33 (78.5)	
Neutrophils (10^3/ul)			0.053
Mean±SD	49.45±19.35	40.67±21.65	
ANC (cells/microL)			<0.001
Mean±SD	5321.45±2596.95	2456.95±1574.33	
Lymphocyte (10^3/ul)			0.027
Mean±SD	39.74±19.82	49.93±21.73	
ALC (cells/microL)			0.003
Mean±SD	4385.12±2609.62	2960.79±1557.75	
Hemoglobin (g/dl)			0.613
Mean±SD	11.69±0.98	11.78±0.77	
Platelets (10^3/ul)			<0.001
Mean±SD	333.29±150.16	207.17±52.38	
NLR			0.019
Mean±SD	1.94±1.59	1.69±1.39	
PLR			0.045
Mean±SD	11.49±9.39	7.98±6.57	
Coagulation profile			
PT (sec)			0.098
Mean±SD	13.66±1.81	12.68±0.94	
PC (%)			<0.001
Mean±SD	74.88±21.05	93.93±11.16	
PTT (sec)			0.108
Mean±SD	34.79±9.08	30.68±5.59	
INR			0.034
Mean±SD	1.29±0.48	1.06±0.33	
D-dimer (mg/l)			<0.001
Mean±SD	0.82±1.04	0.25±0.21	

The studied cases and those with moderate to severe envenomation have significantly higher HR, RR, lower mean BP, and lower GCS scores compared with their counterparts of controls and those of mild envenomation. These findings could be explained by the anaphylactic reaction as a result of releasing the allergenic proteins which leads to hypotension with vasodilation and decreased intravascular volume with reduced myocardial perfusion [3,6,9]. Moreover, the scorpion venom inhibits the angiotensin-converting enzyme (ACE), leading to the accumulation of bradykinin, which is implicated in the development of pulmonary edema [3,11].

Agitation and disturbed level of consciousness was seen in 45.2 and 23.8%, of cases, respectively. Myocarditis, arrhythmia, depressed ST segment, and heart failure were seen in 38.1, 31, 31, and 31% of cases, respectively. 38.1% of cases developed pulmonary edema.

In contrast, Baseer and Naser [10] reported that the most frequent clinical manifestations were vomiting and tachycardia, while local manifestations such as pain, and induration were documented in 37.0 and 11.3%, respectively. The most frequent general manifestations were fever and sweating which were documented in 30.5 and 50.0%, respectively [10].

Valdivia *et al.* [12] reported a series of 32 children with scorpion bites, 50% exhibited myocarditis, 12.5% had subclinical disease, and 63% had observed ECG changes [12]. These differences could be attributed to differences in the inclusion criteria and the severity of envenomation.

Notably, many studies have been conducted with the help of hematological parameters, especially, the total and differential leukocytic count and platelet indices as potential biomarkers to predict the worse clinical course of scorpion envenomation [4]. In the current study, cases had significantly higher total leucocyte count, ANC, ALC, platelets count, PDW, NLR, and PLR, compared with controls, respectively. On the other hand, cases had significantly lower lymphocyte count, hematocrit, and MPV, than controls, respectively. These findings were similar to

Table 4 The sensitivity and specificity of hematological parameters in predicting severe envenomation

Parameter	Cut off	95% CI	Sensitivity	Specificity	AUC	*P*
WBCs (10^3/ul)	≥11.6	0.833–1.0	87.5%	88.5%	0.921	<0.001
MPV (fL)	≥0.85	0.491–0.840	62.5%	100.0%	0.666	0.074
PLR	≥8.2	0.661–0.950	75.0%	61.5%	0.805	0.001
D-dimer (mg/dl)	≥0.85	0.702–0.981	62.5%	100.0%	0.841	<0.001

Table 5 Predictors of severe envenomation among the study cases

Variables	*n*	Univariate analysis			Multivariate analysis		
		OR	95% CI	*P*	OR	95% CI	*P*
Age	42	0.732	0.570–0.939	0.014	0.572	0.356–0.919	0.021
GCS	42	0.463	0.270–0.794	0.005			
WBCs							
<11.6		ref					
≥11.6		53.67	7.958–361.897	<0.001	7.607	4.935–115.258	0.002
Platelets	42	1.015	1.006–1.024	0.001			
PDW	42	1.961	1.167–3.297	0.011			
MPV	42	2.785	1.044–7.430	0.041			
D-dimer	42						
<0.85	32	ref					
≥0.85	10	0.977	0.011–0.657	0.999			
PLR							
<8.2	20	ref					
≥8.2	22	4.800	1.207–19.082	0.026	5.963	0.443–80.342	0.178

previous studies [4,5,13] and could be explained by the induction of a venom-mediated systemic inflammatory response-like syndrome.

Thrombocytosis has been seen among our cases, particularly those with severe envenomation. This may reflect the stimulatory effect of released catecholamines, especially adrenaline, on platelet synthesis [14]. NLR and PLR are novel inflammatory markers that can be applied in many diseases for predicting inflammation. In the current study, it was found that the mean NLR and PLR ratios were statistically significantly higher in studied cases compared with healthy controls. Moreover, the WBC, PLR, and d-dimer had areas under the curve (AUC) of 0.921, 0.805, and 0.841, with *P* values of less than 0.001, 0.001, and less than 0.001, respectively. Horoz *et al.* [4] found that the mean NLR and PLR were significantly higher among scorpion sting patients compared with matched controls. Moreover, the NLR can predict mortality and major adverse cardiac events in acute coronary syndrome [15].

With regards to the coagulation profile, the studied cases had significantly lower prothrombin concentration, but higher INR and d-dimer values than controls, respectively. These findings are in concordance with the previous literature that the coagulation disorders, including bleeding diathesis and disseminated intravascular coagulation (DIC), were reported as a complication in severe forms of envenomation [16].

This could be explained by the fact that the toxin released by the sting stimulates the autonomic nervous system, which activates the coagulation cascade [17] The elevated d-dimer level could be explained by activation of the coagulation system and subsequent fibrinolysis and has a high predictive value for venous thromboembolism (VTE), which may occur either locally or diffusely [18].

As predictors of severity of envenomation, our data showed that younger age and higher WBC count (≥11.6) were significantly independent predictors of severe envenomation.

In daily clinical practice, these parameters can be used as surrogate markers for scorpion envenomation severity and have the advantages of being simple, cheap, easily measured, and reproducible. Further prospective studies using simple applicable and cheap biomarkers namely (MPV, NLR, PLR, and PDW) are needed to determine the best combination of these hematological biomarkers to detect those with high risk to receive earlier appropriate management to achieve better outcomes.

Conclusion

Our data showed that scorpion envenomation can lead to many alterations in hematological parameters and platelet indices. The use of these parameters to predict the severity of scorpion envenomation is simple, cheap, and easily applicable. Younger age and higher WBC count (≥11.6) were significantly independent predictors of severe envenomation. Further studies are warranted.

Acknowledgments

The authors thank Omar Abdelwahab (omaromar44666@gmail.com), Al Faisal University, Riyadh, KSA, for his great help in this research.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Chippaux JP. Emerging options for the management of scorpion stings. Drug Des Devel Ther 2012; 6:165–173.

2 Abd El-Aziz FEA, El Shehaby DM, Elghazally SA, Hetta HF. Toxicological and epidemiological studies of scorpion sting cases and morphological characterization of scorpions (Leiurusquin questriatus and Androctonus crassicauda) in Luxor, Egypt. Toxicol Rep 2019; 6:329–335.

3 Petricevich VL. Scorpion venom and the inflammatory response. Mediators Inflamm 2010; 2010: 903295.

4 Horoz ÖÖ, Yıldızdaş D, Aslan N, Gökay SS, Ekinci F, Erdem S, *et al.* Is there any relationship between initial hematological parameters and the severity of scorpion envenomation?. Turk J Pediatr 2020; 62:394–404.

5 Nour Eldin A, Sakr M, Khater A. Study of Hematological Parameters in Patients with Scorpion Envenomation Presented to the Poison Control Center of Ain Shams University Hospitals. Ain Shams J Forensic Med Clin Toxicol 2022; 38:92–102.

6 Shamoon Z, Peterfy RJ, Hammoud S, Khazaeni B. Scorpion Toxicity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available from: https://www.ncbi.nlm.nih. gov/books/ NBK430928/. [Last updated on 2022 Aug 08].

7 Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Res Notes 2017; 10:12.

8 Stefaniuk P, Szymczyk A, Podhorecka M. The Neutrophil to Lymphocyte and Lymphocyte to Monocyte Ratios as New Prognostic Factors in Hematological Malignancies - A Narrative Review. Cancer Manag Res 2020; 12:2961–2977.

9 Mohamad IL, Elsayh KI, Mohammad HA, Saad K, Zahran AM, Abdallah AM, Tawfeek MS, *et al.* Clinical characteristics and outcome of children stung by scorpion. Eur J Pediatr 2014; 173:815–818.

10 Baseer KA, Naser MAA. Predictors for Mortality in Children with Scorpion Envenomation Admitted to Pediatric Intensive Care Unit, Qena Governorate, Egypt. Am J Trop Med Hyg 2019; 101:941–945.

11 Agrawal A, Kumar A, Consul S, Yadav A. Scorpion bite, a sting to the heart! Indian J Crit Care Med 2015; 19:233–236.

12 Valdivia HH, Kirby MS, Lederer WJ, Coronado R. Scorpion toxins targeted against the sarcoplasmic reticulum Ca(2+)-release channel of skeletal and cardiac muscle. Proc Natl Acad Sci U S A 1992; 89:12185–12189.

13 Konca C, Tekin M, Colak P, Uckardes F, Turgut M. An overview of platelet indices for evaluating platelet function in children with scorpion envenomation. EXCLI J 2014; 13:801–808.

14 Sulai NH, Tefferi A. Why does my patient have thrombocytosis? Hematol Oncol Clin North Am 2012; 26:285–301. viii

15 Dong CH, Wang ZM, Chen SY. Neutrophil to lymphocyte ratio predicts mortality and major adverse cardiac events in acute coronary syndrome: A systematic review and meta-analysis. Clin Biochem 2018; 52:131–136.

16 Khataminia A, Razi Jalali M, Jalali SM, Jafari H. The Effect of Various Fractions of Hemiscorpius lepturus Scorpion (Scorpionida: Hemiscorpiidae) Venom on Hemostatic System in Peripheral Blood of Rats in Comparison to Whole Venom. Jundishapur J Health Sci 2020; 12:e102586.

17 Godoy DA, Badenes R, Seifi S, Salehi S, Seifi A. Neurological and Systemic Manifestations of Severe Scorpion Envenomation. Cureus 2021; 13:e14715.

18 Köse A, Biricik S, Bozkurt S, Cavuşoğlu C, Ayrık C. Toxic Hepatitis and Coagulopathy due to Scorpion Sting. Ann Clin Case Rep 2016; 1:1212.