

Gross Hematuria in Patients with Wasp Sting: A Retrospective Study

wei wang (✉ wwei958@163.com)

Nephrology <https://orcid.org/0000-0001-5664-7725>

Maohe Wang

nephrology

Prince singh

nephrology

Yong Tang

nephrology

Xiang Zhong

nephrology

Shasha Chen

nephrology

Guisen Li

nephrology

Li Wang

nephrology

Research article

Keywords: Wasp sting, gross hematuria, risk factors, poisoning severity score

DOI: <https://doi.org/10.21203/rs.3.rs-35642/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Wasp sting is common in the world, and gross hematuria after wasp sting has been reported in Asia to occur before AKI. Gross hematuria is often used by clinicians as a sign indicated for intensive care and blood purification treatment. However, there is no study on the clinical characteristics and prognosis of wasp sting patients complicated with gross hematuria.

Methods: The demographic characteristics and clinical data of 363 patients with wasp sting admitted to Suining Central Hospital from January 2016 to December 2018 were retrospectively analyzed. At admission, the poisoning severity score was used as the criterion for severity classification. According to the presence of gross hematuria, the patients were divided into gross hematuria group and non-gross hematuria group. Multivariate logistic regression analysis was performed to explore the risk factors for gross hematuria.

Results: Of the 363 wasp sting patients, 219 were male and 144 were female, mean age was 55.9 ± 16.3 years. 51 (14%) had gross hematuria, 39(10.7%) had Acute Kidney Injury(AKI), 105 (28.9%) had rhabdomyolysis, 61(16.8%) had hemolysis, 56 (15.4%) had Multiple Organ Dysfunction Syndrome (MODS), 13 (3.6%) had Acute Respiratory Distress Syndrome (ARDS), 45(12.4%) went on to receive renal replacement therapy, and 14 (3.9%) died. Patients with gross hematuria group had significantly higher poisoning severity scores when admitted to the hospital than those without gross hematuria group (2.2 ± 0.5 vs. 1.1 ± 0.3 , $P < 0.001$).

Conclusion: Gross hematuria is one of the early clinical symptoms of severe wasp sting patients. AKI incidence and mortality of patients with gross hematuria are significantly increased. Prompt treatment should be taken for wasp sting patients complicated with gross hematuria. The poisoning severity score can be used for early assessment of the severity of wasp sting patients.

Introduction

Wasps belong to Hymenoptera order in the Animal kingdom[1]. Currently, there are more than 6000 species of wasps in the world and more than 200 species have been recorded in China[2, 3]. Wasp stings are common in the world. Epidemiological surveys in the United States show that wasp stings account for 27.4%-29.7% of all animal injuries and the annual mortality rate is 0.14–0.74/million population[4, 5]. In July-October 2013, 1,675 cases of wasp stings occurred in Shanxi Province of China, resulting in 42 deaths [6]. However, this global public health problem hasn't drawn adequate attention. There is a paucity of existing guidelines on the diagnosis and treatment of wasp stings. Chinese Society of Toxicology has prepared a consensus statement on the standardized diagnosis and treatment of wasp stings[7]. However a wide application of this consensus criteria is likely limited by the complex evaluation criteria. In Europe, the poisoning severity score is usually used to guide initial assessment and appropriate medical care assignment[8–11]. However, the poisoning severity score has not been reported specifically for evaluating the severity of wasp sting patients.

Local symptoms of wasp sting include redness, swelling, and pain. Xie[12], Liu[6], Sigdel[13], reported the occurrence rate of gross hematuria after wasp sting to be in the range of 10–55%. Gross hematuria occurring after wasp sting often alerts clinicians to the likelihood of a serious medical condition which may require intensive care admission, and in some cases even plasmapheresis[7, 14]. However, there has not been any study looking at the clinical characteristics and prognosis of wasp sting patients complicated with gross hematuria. Therefore, we undertook this study in which we looked at the 363 patients with wasp sting from January 2016 to December 2018 in Suining Central Hospital of Sichuan Province and we analyzed the clinical characteristics of patients with gross hematuria to identify risk factors to develop gross hematuria. In our study, we used the poisoning severity score to evaluate the severity of wasp sting patients upon admission, and ROC curve analysis was conducted to predict the occurrence of gross hematuria in wasp sting, so as to evaluate whether the poisoning severity score is meaningful to predict severe wasp sting patients in patients who show hematuria.

Materials And Methods

Research subjects

The research subjects were patients with wasp sting and hospitalized from January 1, 2016 to December 31, 2018 in the inpatient department of Suining Central Hospital in Sichuan province, China. The exclusion criteria were chronic kidney disease (CKD), age less than 14 years old, prolonged hospitalization or referral due to other previous medical history, and death upon admission. Acute kidney injury (AKI) was diagnosed based on the KDIGO criteria[15]. Among patients with wasp sting, we divided and compared them into gross hematuria and non–gross hematuria group. The study was approved by the Ethics Committee of Suining Central Hospital.

Data collection

EpiData3.1 software was used to input the following data: 363 patients' demographic indicators, including gender, age, number of stings, the time interval between sting and admission, and previous medical history; main symptoms and signs such as anaphylactic shock, rash, allergic reaction, gross hematuria, oliguria (or anuria); the poisoning severity score at admission, laboratory data of patients on admission, and on 2nd and 3rd day after admission and before discharge, severe complications such as Acute Kidney Injury (AKI) rhabdomyolysis, hemolysis, coagulation abnormalities, liver dysfunction, MODS, ARDS; interventions including dialysis, plasmapheresis, state at discharge (death or survival), length of hospital stay.

Statistical methods

The data were analyzed by SPSS software version 19.0. Results are expressed as median (IQR) for continuous variables and as percentages for categorical variables. The enumeration data are represented by rate, and the chi-square test was used for comparison between the two groups. The measurement data conforming to the normal distribution are represented by mean \pm standard deviation ($\bar{x} \pm s$), and the non-

conforming normal distribution by median M (P25, P75). Variables of the two groups were compared by Mann-Whitney U test. Multivariate logistic regression model was used to screen the risk factors of gross hematuria, and then ROC curve analysis was performed on the selected risk factors. A p-value of less than 0.05 for 95% confidence was set and used as a cut-off point to examine the statistical association between the variables.

Results

Demographic characteristics

From January 2016 to December 2018, 390 patients with wasp sting were admitted to Suining Central Hospital, 363 of whom were included in the study. Of the 27 patients excluded, 14 refused to be hospitalized after admission, and 13 prolonged hospitalization due to their previous medical history such as chronic kidney disease, chronic obstructive pulmonary disease, gastrointestinal ulcer, diabetes. 60% patients were male with a mean age of 55.9 ± 16.3 years (Table 1). The time interval between sting and admission was 3(0.5–144) hours, and the poisoning severity score was 1.2 ± 0.5 points on admission. Fourteen patients died, with a fatality rate of 3.9%. Eight patients died on the first day of admission, three each on second and third day. Most common cause of death was ARDS (9/14) followed by MODS (4/14) (Table 1). Monthly distribution of patients with gross hematuria, AKI, ICU and death after wasp sting (Fig. 1.)

Table 1
Clinical data of wasp sting patients (n = 363)

Variable	Value
Age (years)	55.9 ± 16.3
Gender (M: F)	219:144
Number of stings	9(4,15)
Interval (hours)	3(2,5)
Poisoning severity score	1.2 ± 0.5
Hospitalization Days (day)	4(3,6)
Rash <i>n</i> (%)	50(13.8)
Shock <i>n</i> (%)	20(5.5)
AKI <i>n</i> (%)	39(10.7)
Rhabdomyolysis <i>n</i> (%)	105(28.9)
Hemolysis <i>n</i> (%)	61(16.8)
Oliguria or anuria <i>n</i> (%)	27(7.4)
Coagulation abnormalities <i>n</i> (%)	139(38.3)
Liver damage <i>n</i> (%)	82(22.6)
Dialysis <i>n</i> (%)	45(12.4)
MODS <i>n</i> (%)	56(15.4)
ARDS <i>n</i> (%)	13(3.6)
ICU <i>n</i> (%)	7(1.9)
Death <i>n</i> (%)	14(3.9)
Note: the interval (hours) is the time interval between sting and admission	

Clinical manifestations

Almost all patients (100%) had local symptoms such as redness, swelling, and pain at the sting site. 51 patients (14%) had gross hematuria, 39 patients (10.7%) had AKI, 61 patients (16.8%) developed hemolysis, with 105 patients (28.9%) developing rhabdomyolysis. Forty-five patients (12.4%) underwent blood purification treatment, and 7 patients (1.9%) were admitted to ICU (Table 1).

Comparison of clinical data between the two groups

There was no statistical difference in gender composition between patients with gross hematuria and patients with non-gross hematuria ($P = 0.089$) (Table 2). The average age of patients with gross hematuria was higher than that of patients with non-gross hematuria (65 years vs 54 years, $p < 0.001$). The number of stings, the time interval between stings and admission, and the poisoning severity score on admission in patients with gross hematuria group were higher than those in patients with non-gross hematuria group, and the hospitalization days were significantly prolonged ($p < 0.001$). 13 patients (25.5%) died in the group with gross hematuria, and 1 patient (0.3%) died in the group without gross hematuria ($p < 0.001$). The patient in the non-gross hematuria group died of respiratory failure in the setting of chronic obstructive pulmonary disease (Table 2).

Table 2

Comparison of clinical data between non-gross hematuria group and gross hematuria group

Variable	non-gross hematuria group (<i>n</i> = 312)	gross hematuria group (<i>n</i> = 51)	<i>P</i>
Age (years)	54.4 ± 16.7	65.2 ± 9.5	< 0.001
Gender (M: F)	194:118	25:26	0.089
Number of stings	7(3,10)	30(19,33)	< 0.001
Interval (hours)	3(2,4)	6(4,12)	< 0.001
Poisoning severity score	1.1 ± 0.3	2.2 ± 0.5	< 0.001
Hospitalization Days (day)	4(3,6)	11(3,21)	< 0.001
Rash <i>n</i> (%)	50(16)	0(0)	0.001
Shock <i>n</i> (%)	19(6.1)	1(2)	0.332
AKI <i>n</i> (%)	3(1)	36(70.6)	< 0.001
Rhabdomyolysis <i>n</i> (%)	55(17.6)	50(98)	< 0.001
Hemolysis <i>n</i> (%)	15(4.8)	46(90.2)	< 0.001
Oliguria or anuria <i>n</i> (%)	1(0.3)	26(51)	< 0.001
Coagulation abnormalities <i>n</i> (%)	90(28.8)	49(96.1)	< 0.001
Liver damage <i>n</i> (%)	35(11.2)	47(92.2)	< 0.001
Dialysis <i>n</i> (%)	5(1.6)	40(78.4)	< 0.001
Dialysis time (day)	3.8 ± 2.4	11.9 ± 11.8	0.268
MODS <i>n</i> (%)	8(2.6)	48(94.1)	< 0.001
ARDS <i>n</i> (%)	0(0)	13(25.5)	< 0.001

Variable	non-gross hematuria group (n = 312)	gross hematuria group (n = 51)	P
ICU n (%)	0(0)	7(13.7)	< 0.001
Death n (%)	1(0.3)	13(25.5)	< 0.001

Note: the interval (hours) is the time interval between sting and admission

Comparison of complications between the two groups

No rash was seen in hematuria group (p = 0.001) (Table 2). One patient developed shock in hematuria group compared to 19 in non-gross hematuria group (p = 0.332). The incidence of oliguria (or anuria), rhabdomyolysis, hemolysis, coagulation abnormalities, liver damage, MODS, ARDS in the gross hematuria group was higher than that in the non-gross hematuria group. 7 patients (13.7%) in the gross hematuria group were admitted to ICU, while no patients in the non-gross hematuria group were admitted to ICU (p < 0.001). 36 (70.6%) patients with gross hematuria developed AKI, compared to 3 (1%) patients with non-gross hematuria. (p < 0.001). Forty patients (78.4%) in the gross hematuria group received dialysis compared to 5 (1.6%) in the non-gross hematuria group (p < 0.001) (Table 2).

Comparison of laboratory examination results between the two groups

At the time of admission and the 2nd-3rd day after admission, the serum creatinine (CREA), creatine kinase (CK), aspartate aminotransferase (AST), indirect bilirubin (IBIL), alanine transaminase (ALT), prothrombin time (PT), activated partial thromboplastin time (APTT), lactate dehydrogenase (LDH), leukocyte(WBC) values in the gross hematuria group were higher than those in the non-gross hematuria group (p < 0.001). Serum CREA and LDH tested before discharge were still significantly higher in the gross hematuria group than that in the non-gross hematuria group (p < 0.001) (Table 3).

Table 3

Comparison of laboratory examination between non-gross hematuria group and gross hematuria group

Variable		non-gross hematuria group (n= 312)	gross hematuria group (n= 51)	P
Creatinine (59-104umol/l)	On admission	68.8 ± 50.1	153.9 ± 181.0	< 0.001
	The 2nd-3rd day	74.5 ± 56.4	222.1 ± 189.7	< 0.001
	Pre-discharge	66.9 ± 25.6	236.0 ± 237.4	< 0.001
Creatine kinase (40-200U/l)	On admission	235.7 ± 562.6	5222.0 ± 8867.4	< 0.001
	The 2nd-3rd day	1620.7 ± 3479.1	10781.6 ± 11103.8	< 0.001
	Pre-discharge	263.6 ± 392.0	1438.1 ± 6562.4	0.603
Aspartate aminotransferase (13-35U/l)	On admission	51.4 ± 90.9	922.3 ± 1574.1	< 0.001
	The 2nd-3rd day	87.1 ± 133.1	1134.7 ± 2138.3	< 0.001
	Pre-discharge	36.9 ± 23.8	246.3 ± 1296.2	0.332
Indirect bilirubin (0-18.0umol/l)	On admission	11.0 ± 10.3	45.8 ± 26.4	< 0.001
	The 2nd-3rd day	7.6 ± 11.2	33.2 ± 29.7	< 0.001
	Pre-discharge	7.0 ± 7.7	10.9 ± 24.9	0.947
Alanine transaminase (7-40U/l)	On admission	32.4 ± 52.0	310.1 ± 459.5	< 0.001
	The 2nd-3rd day	48.8 ± 52.4	275.5 ± 405.6	< 0.001
	Pre-discharge	46.7 ± 39.5	87.1 ± 201.6	0.576
Prothrombin time (11-14.5s)	On admission	13.9 ± 1.4	14.9 ± 1.7	< 0.001
	The 2nd-3rd day	13.2 ± 1.0	14.8 ± 2.4	< 0.001

Variable		non-gross hematuria group (n= 312)	gross hematuria group (n= 51)	P
	Pre-discharge	12.8 ± 0.9	12.7 ± 0.9	0.091
APTT	On admission	64.2 ± 38.4	121.2 ± 47.7	< 0.001
(26-40s)	The 2nd-3rd day	37.6 ± 17.9	90.8 ± 62.4	< 0.001
	Pre-discharge	33.0 ± 4.3	40.2 ± 16.0	0.003
Lactate dehydrogenase	On admission	233.54 ± 110.0	1580.2 ± 1447.6	< 0.001
(120-250U/l)	The 2nd-3rd day	306.0 ± 266.0	2012.9 ± 1929.6	< 0.001
	Pre-discharge	241.2 ± 146.8	720.5 ± 1359.0	< 0.001
Leukocyte	On admission	11.7 ± 4.9	22.3 ± 7.4	< 0.001
(3.5–9.5*10 ⁹ /l)	The 2nd-3rd day	12.8 ± 12.2	19.3 ± 7.4	< 0.001
	Pre-discharge	9.0 ± 2.7	10.8 ± 6.0	0.306
Note: APTT is a shorthand for activated partial thromboplastin time				

Multivariate logistic regression analysis

We used the patient's age, the number of stings, the time interval between stings and admission, the poisoning severity score and the season as independent variables to establish a logistics regression model for screening the risk factors related to gross hematuria at admission. The results showed that the poisoning severity score, the number of stings and season are independent risk factors for gross hematuria in patients with wasp sting (Table 4).

Table 4
Multivariate logistic regression analysis of gross hematuria in wasp sting patients

Variable	β	Wald χ^2	P	OR	95%CI
Poisoning severity score	4.601	43.241	< 0.001	99.551	25.26-392.27
The season	1.472	7.066	0.008	4.357	1.47–12.90
Number of stings	0.025	3.574	0.059	1.025	1.00-1.05

ROC curve analysis

Further ROC curve analysis of independent risk factors for gross hematuria in wasp sting patients showed that the AUC corresponding to poisoning severity score and number of stings are 0.928 and 0.892 respectively (Fig. 2).

The AUC of serum LDH on admission to predict AKI of wasp sting patients was 0.980 (Fig. 3).

Discussion

Gross hematuria after wasp sting is not rare in Asian countries [6, 12, 13]. Current study did a retrospective analysis of 363 cases of wasp sting patients admitted to Suining Central Hospital in Sichuan Province of China. Our research found that 14% of the patients with wasp sting had gross hematuria, and this was only seen in the summer and fall months from July through December. More than half of patients with hematuria (51%) developed oliguria (or anuria). More than 70% of patients with hematuria had AKI, and the fatality (mortality) rate was 25.5%. The poisoning severity score in patients with gross hematuria was significantly higher than that in patients with non-gross hematuria. The poisoning severity score, the season and number of stings turned out to be independent risk factors for gross hematuria in wasp sting patients.

Wasp venom contains a variety of bioactive components, such as enzymes (including phospholipase, hyaluronic acid), amines (including histamine, serotonin, catecholamine), peptides (including wasp venom peptide, wasp kinin)[16]. Phospholipase damages the cell membrane by attacking the phospholipid structure, which has a toxic effect on skeletal muscle and erythrocyte membrane, leading to rhabdomyolysis and intravascular hemolysis[17–19]. Wasp venom peptide can also cause muscle necrosis and cell apoptosis[16, 20]. Venom induced rhabdomyolysis leads to a release of muscle enzymes such as creatine kinase and muscle protein such as myoglobin, free hemoglobin (from red blood cells) in the intravascular circulation[21]. Once in the circulation, these muscle (heme) proteins gets freely filtered through the glomeruli and eventually exceed the tubular reabsorption capacity of renal tubules resulting in gross hematuria[22]. Kidney biopsy study in wasp sting-induced kidney injury has demonstrated deposition of myoglobin and hemoglobin in renal tubules[23–25].

Prior study has shown that gross hematuria associated with wasp sting generally occurs 4–12 hours after sting, and tends to occur earlier than AKI [26]. In our cohort, 14% of wasp sting patients presented with gross hematuria. These patients also had a higher poisoning severity score at the time of admission. The incidence of serious complications such as AKI, MODS, ARDS, and mortality were significantly higher than those reported by Xie [12]. Therefore, gross hematuria can be used as one of the early indicators of severe wasp sting patients and requires active intervention. Multivariate logistic regression analysis showed that the poisoning severity score was an independent risk factor for patients suffering from wasp stings to develop gross hematuria. One point increase in the poisoning severity score correlated with 99.6 times increased risk of developing gross hematuria. The poisoning severity score is widely used in Europe

to assess the severity of poisoned patients (including environmental toxins), with simple and accurate characteristics [9, 27]. However, it has not been reported specially for the evaluation of wasp sting patients. ROC curve analysis of poisoning severity score for predicting gross hematuria in wasp sting patients shows that when the poisoning severity score is greater than 1.5, the risk of gross hematuria is significantly increased with high accuracy (AUC = 0.928). In brief, gross hematuria reflects a high poisoning severity score and thus can be used as a surrogate marker of worse clinical outcome following a wasp sting. Meanwhile, the poisoning severity score can be used for early assessment of the severity of wasp sting patients and is worthy of promotion in clinical practice.

In developed countries, wasp stings are mainly manifested in varying degrees of allergic-reactions, therefore their treatment mainly focuses on desensitization and antiallergic treatment[5, 28, 29]. On the other hand, In China, wasp sting patients are mainly characterized by toxic reactions and the main causes of death of wasp sting patients are MODS, ARDS and non-allergic shock[12, 30], which is consistent with our conclusion. Epidemiology in the United States and Sweden shows that wasp stings mostly occur in summer and autumn when the climate is warm, which is related to the increase in the number of wasps and the increase in people's outdoor activities[31, 32]. Multivariate logistic regression analysis also confirmed that gross hematuria is related to the season. In summer and autumn, swarms of wasps are more likely to hurt people. This regional and seasonal difference may be related to the different wasp species in different regions and seasons, and the different components and virulence of wasp venom[17, 33, 34].

The serum creatine kinase, aspartate aminotransferase, lactate dehydrogenase, and indirect bilirubin of patients with gross hematuria were significantly higher than those of patients with non-gross hematuria on admission and the 2nd-3rd day after admission. Creatine kinase and aspartate aminotransferase are laboratory indicators of rhabdomyolysis [35], while lactate dehydrogenase and indirect bilirubin are laboratory indicators of hemolysis [36], which indicated that patients with gross hematuria experienced more severe and prolonged rhabdomyolysis and intravascular hemolysis. So that patients who develop gross hematuria are likely those who are most severely affected by the venom. While rhabdomyolysis and intravascular hemolysis can cause AKI, the renal injury can be exacerbated in the states of shock [35, 37–39]. However it is rather difficult to explain why patients in the gross hematuria group had developed less shock than in non-gross hematuria group. We further analyzed 51 patients with gross hematuria (Table 5). Serum leucocyte, indirect bilirubin, and creatine kinase had no statistical difference on admission for patients with gross hematuria complicated with AKI (n = 36) and patients without AKI (n = 15). However, serum LDH of patients with gross hematuria complicated with AKI was significantly higher than that of patients without AKI on admission (P = 0.003). This has previously been shown by Li and Zhang that elevated serum LDH is associated with AKI in wasp sting patient population[26, 30]. ROC curve analysis of LDH for predicting AKI in wasp sting patients shows that when LDH was greater than 463.5 U/L, the risk of AKI in wasp sting patients was significantly increased. In the gross hematuria group, AKI group had higher mortality than in the non-AKI group but it was not statistically significant. The serum creatinine of 25 patients with gross hematuria complicated with AKI

did not return to normal at discharge (119-925umol/l). According to Zhang's report, 10.7% of patients with wasp sting complicated with AKI will progress to CKD [30]. We have evidence from population based studies that a subset of patients with AKI progress to CKD[40]. It would be therefore be advisable for such patients to be followed in nephrology clinic after their discharge. However, this result may also be related to the short hospitalization time of our patients (average 11 days), because, according to Ambarsari's report, the cure of acute kidney injury after wasp sting takes 3–6 weeks[41].

Table 5
Comparison of gross hematuria without AKI group and gross hematuria with AKI group

Variable	Non-AKI group(<i>n</i> = 15)	AKI group(<i>n</i> = 36)	<i>P</i>
Age (years)	64.5 ± 11.4	65.4 ± 8.7	0.828
Gender (M: F)	5:10	20:16	0.220
Number of stings	28(20,45)	30(17,31)	0.820
Interval (hours)	6(3,24)	6(4,11.5)	0.747
Poisoning severity score	1.9 ± 0.6	2.25 ± 0.5	0.070
Hospitalization Days (day)	9(7,12)	12.5(2,29)	0.080
serum WBC at admission	20.5 ± 5.6	23.0 ± 8.0	0.321
serum IBIL at admission	34.5 ± 19.7	50.8 ± 27.7	0.062
serum CK at admission	4113.4 ± 6270.1	5678.4 ± 9786.1	0.602
serum LDH at admission	864.1 ± 366.3	1854.0 ± 1610.2	0.003
serum CREA at admission	66.6 ± 14.4	186.4 ± 203.1	< 0.001
serum CREA at discharge	61.4 ± 15.3	316.5 ± 248.8	< 0.001
Shock <i>n</i> (%)	0(0)	1(2.8)	1.000
Rhabdomyolysis <i>n</i> (%)	14(93.3)	36(100)	0.294
Hemolysis <i>n</i> (%)	12(80)	34(94.4)	0.144
Oliguria or anuria <i>n</i> (%)	0(0)	26(72.2)	< 0.001
Dialysis <i>n</i> (%)	8(53.3)	32(88.9)	0.009
MODS <i>n</i> (%)	12(80)	36(100)	0.022
ARDS <i>n</i> (%)	0(0)	13(36.1)	0.006
ICU <i>n</i> (%)	1(6.7)	6(16.7)	0.658
Death <i>n</i> (%)	2(13.3)	11(30.6)	0.297
Note: WBC is a shorthand for Leukocyte, IBIL is a shorthand for Indirect bilirubin, CK is a shorthand for Creatine kinase, LDH is a shorthand for Lactate dehydrogenase, CREA is a shorthand for Creatinine			

Our research also has limitations. Ours is a retrospective study and hence there may be selection bias in addition to possible confounding. Study comes from a single center and we did not have complete information such as wasp species, sting site, prognosis and follow-up of patients with AKI.

To our knowledge, this is the largest study in terms of numbers to study this phenomenon. We also had an extensive biochemical and clinical data available for our cohort. Added to this is the use of

multivariate logistic regression analysis and ROC curves to study the association.

In conclusion, the poisoning severity score can be used for early assessment of the severity of wasp sting patients. Gross hematuria is one of the early but serious markers of adverse outcomes in patients with wasp sting and hence should alert clinicians about more aggressive and closer monitoring of such patients.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Suining Central Hospital (Suining, China). and all the patients signed informed consents to participate in this study.

Consent for publication

Not applicable.

Availability of data and material.

All data and material were obtained from Suining Central Hospital.

Competing interests

The authors report no conflicts of interest.

Funding

This work was supported by This work was supported by under Grant from the University of Electronic Science and Technology of China Central University Research Fund[ZYGX2019J104], under Grant from the National Natural Science Foundation of China (No. 81970641) and under Grant from Renal Department and Institute of Nephrology, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Sichuan Clinical Research Center for Kidney Diseases. These grants played a role in data collection of these patient, as well as the interpretation of data and the manuscript writing.

Authors' contributions

Data collection (MHW ,YT, XH, CSS), study design (WW, GSL, LW), statistical analyses (MHW, WW), writing (MHW SP, WW) language modification (SP). All authors have read and approved the manuscript.

Acknowledgments

We are grateful to all the subjects who participated in this work.

References

1. Pesek RD, Lockey RF. Management of insect sting hypersensitivity: an update. *Allergy Asthma Immunol Res.* 2013;5(3):129–37.
2. Walker AA, Robinson SD, Yeates DK, Jin J, Baumann K, Dobson J, Fry BG, King GF. Entomo-venomics: The evolution, biology and biochemistry of insect venoms. *Toxicon.* 2018;154:15–27.
3. Yang X, Chai L, Liu C, Liu M, Han L, Li C, Guo H, Sun Y, Rao X, Xiao M, et al. Serum Metabolomics Analysis in Wasp Sting Patients. *Biomed Res Int.* 2018;2018:5631372.
4. Forrester JA, Weiser TG, Forrester JD. An Update on Fatalities Due to Venomous and Nonvenomous Animals in the United States (2008–2015). *Wilderness Environ Med.* 2018;29(1):36–44.
5. Forrester JA, Holstege CP, Forrester JD. Fatalities from venomous and nonvenomous animals in the United States (1999–2007). *Wilderness Environ Med.* 2012;23(2):146–52.
6. Liu Z, Li XD, Guo BH, Li Y, Zhao M, Shen HY, Zhai Y, Wang XL, Liu T. Acute interstitial nephritis, toxic hepatitis and toxic myocarditis following multiple Asian giant hornet stings in Shaanxi Province, China. *Environ Health Prev Med.* 2016;21(4):231–6.
7. Chinese Society Of. Toxicology P, Treatment Of Specialized C, Hubei Emergency Medicine Committee Of Chinese Medical Hubei Provincial A, Occupational Disease P, Yang U, Xiao X. M: Expert consensus statement on standardized diagnosis and treatment of wasp sting in China. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2018, 30(9):819–23.
8. Casey PB, Dexter EM, Michell J, Vale JA. The prospective value of the IPCS/EC/EAPCCT poisoning severity score in cases of poisoning. *J Toxicol Clin Toxicol.* 1998;36(3):215–7.
9. Cairns R, Buckley NA. The Poisoning Severity Score: If It Did Not Exist, We Would Have To Invent It. *J Med Toxicol.* 2017;13(2):131–4.
10. Mong R, Arciaga GJ, Tan HH. Use of a 23-hour emergency department observation unit for the management of patients with toxic exposures. *Emerg Med J.* 2017;34(11):755–60.
11. Persson HE, Sjoberg GK, Haines JA, Pronczuk de Garbino J. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol.* 1998;36(3):205–13.
12. Xie C, Xu S, Ding F, Xie M, Lv J, Yao J, Pan D, Sun Q, Liu C, Chen T, et al. Clinical features of severe wasp sting patients with dominantly toxic reaction: analysis of 1091 cases. *PLoS One.* 2013;8(12):e83164.
13. Sigdel MR, Raut KB. Wasp bite in a referral hospital in Nepal. *J Nepal Health Res Council.* 2013;11(25):244–50.
14. Yao Rong. Expert Consensus on Standardized Diagnosis and Treatment of Bee Sting in Sichuan Province. *West China Medicine.* 2013;28(09):1325–8.
15. Section 2: **AKI Definition.** *Kidney Int Suppl (2011)* 2012, 2(1):19–36.
16. Gong J, Yuan H, Gao Z, Hu F. Wasp venom and acute kidney injury: The mechanisms and therapeutic role of renal replacement therapy. *Toxicon.* 2019;163:1–7.

17. Habermann E. Bee and wasp venoms. *Science*. 1972;177(4046):314–22.
18. Fernandez ML, Quartino PY, Arce-Bejarano R, Fernandez J, Camacho LF, Gutierrez JM, Kuemmel D, Fidelio G, Lomonte B. Intravascular hemolysis induced by phospholipases A2 from the venom of the Eastern coral snake, *Micrurus fulvius*: Functional profiles of hemolytic and non-hemolytic isoforms. *Toxicol Lett*. 2018;286:39–47.
19. Perez-Riverol A, Lasa AM, Dos Santos-Pinto JRA, Palma MS. Insect venom phospholipases A1 and A2: Roles in the envenoming process and allergy. *Insect Biochem Mol Biol*. 2019;105:10–24.
20. Konno K, Kazuma K, Nihei K-i: **Peptide Toxins in Solitary Wasp Venoms**. *Toxins* 2016, 8(4).
21. Silva GBDJ, Vasconcelos AGJ, Rocha AMT, Vasconcelos VR, Barros JN, Fujishima JS, Ferreira NB, Barros EJJ, Daher EF. Acute kidney injury complicating bee stings - a review. *Rev Inst Med Trop Sao Paulo*. 2017;59:e25.
22. Bagley WH, Yang H, Shah KH. Rhabdomyolysis. *Intern Emerg Med*. 2007;2(3):210–8.
23. Chao YW, Yang AH, Ng YY, Yang WC. Acute interstitial nephritis and pigmented tubulopathy in a patient after wasp stings. *Am J Kidney Dis*. 2004;43(2):e15–9.
24. Dhanapriya J, Dineshkumar T, Sakthirajan R, Shankar P, Gopalakrishnan N, Balasubramaniyan T. Wasp sting-induced acute kidney injury. *Clin Kidney J*. 2016;9(2):201–4.
25. Kularatne K, Kannangare T, Jayasena A, Jayasekera A, Waduge R, Weerakoon K, Kularatne SA. Fatal acute pulmonary oedema and acute renal failure following multiple wasp/hornet (*Vespa affinis*) stings in Sri Lanka: two case reports. *J Med Case Rep*. 2014;8:188.
26. Li F, Liu L, Guo X, Luo Z, Zhang Y, Lu F, Wang G, Chen T, Chen D. Elevated cytokine levels associated with acute kidney injury due to wasp sting. *Eur Cytokine Netw*. 2019;30(1):34–8.
27. Wang IJ, Yeom SR, Park SW, Lee SH, Han SK, Park SC, Ryu JH, Hwang SY. Poison severity score and sequential organ failure assessment score: Carbon monoxide poisoning prognosis. *PLoS One*. 2019;14(3):e0212025.
28. Welton RE, Williams DJ, Liew D. Injury trends from envenoming in Australia, 2000–2013. *Intern Med J*. 2017;47(2):170–6.
29. Warrell DA. Venomous Bites, Stings, and Poisoning: An Update. *Infect Dis Clin North Am*. 2019;33(1):17–38.
30. Zhang L, Yang Y, Tang Y, Zhao Y, Cao Y, Su B, Fu P. Recovery from AKI following multiple wasp stings: a case series. *Clin J Am Soc Nephrol*. 2013;8(11):1850–6.
31. Mowry JB, Spyker DA, Brooks DE, McMillan N, Schauben JL. 2014 **Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 32nd Annual Report**. *Clin Toxicol (Phila)* 2015, **53**(10):962–1147.
32. Johansson B, Eriksson A, Ornehult L. Human fatalities caused by wasp and bee stings in Sweden. *Int J Legal Med*. 1991;104(2):99–103.
33. Vikrant S, Jaryal A, Gupta D, Parashar A. Epidemiology and outcome of acute kidney injury due to venomous animals from a subtropical region of India. *Clin Toxicol (Phila)*. 2019;57(4):240–5.

34. Burdmann EA, Jha V. The Authors Reply. *Kidney Int.* 2017;92(5):1288–9.
35. Vanholder R, Sever MS, Ereğ E, Lameire N. Rhabdomyolysis. *J Am Soc Nephrol.* 2000;11(8):1553–61.
36. Siddon AJ, Tormey CA. The chemical and laboratory investigation of hemolysis. *Adv Clin Chem.* 2019;89:215–58.
37. Basnayake K, Cockwell P, Hutchison CA. Rhabdomyolysis and acute kidney injury. *N Engl J Med.* 2009;361(14):1411–2. author reply 1412–1413.
38. Bee DE, James GP, Paul KL. Hemoglobinuria and hematuria: accuracy and precision of laboratory diagnosis. *Clin Chem.* 1979;25(10):1696–9.
39. Dvanajscak Z, Walker PD, Cossey LN, Messias NC, Boils CL, Kuperman MB, Larsen CP. Hemolysis-associated hemoglobin cast nephropathy results from a range of clinicopathologic disorders. *Kidney Int.* 2019;96(6):1400–7.
40. Devarajan P, Jefferies JL. Progression of Chronic Kidney Disease after Acute Kidney Injury. *Prog Pediatr Cardiol.* 2016;41:33–40.
41. Ambarsari CG, Sindih RM, Saraswati M, Trihono PP. Delayed Admission and Management of Pediatric Acute Kidney Injury and Multiple Organ Dysfunction Syndrome in Children with Multiple Wasp Stings: A Case Series. *Case Rep Nephrol Dial.* 2019;9(3):137–48.

Figures

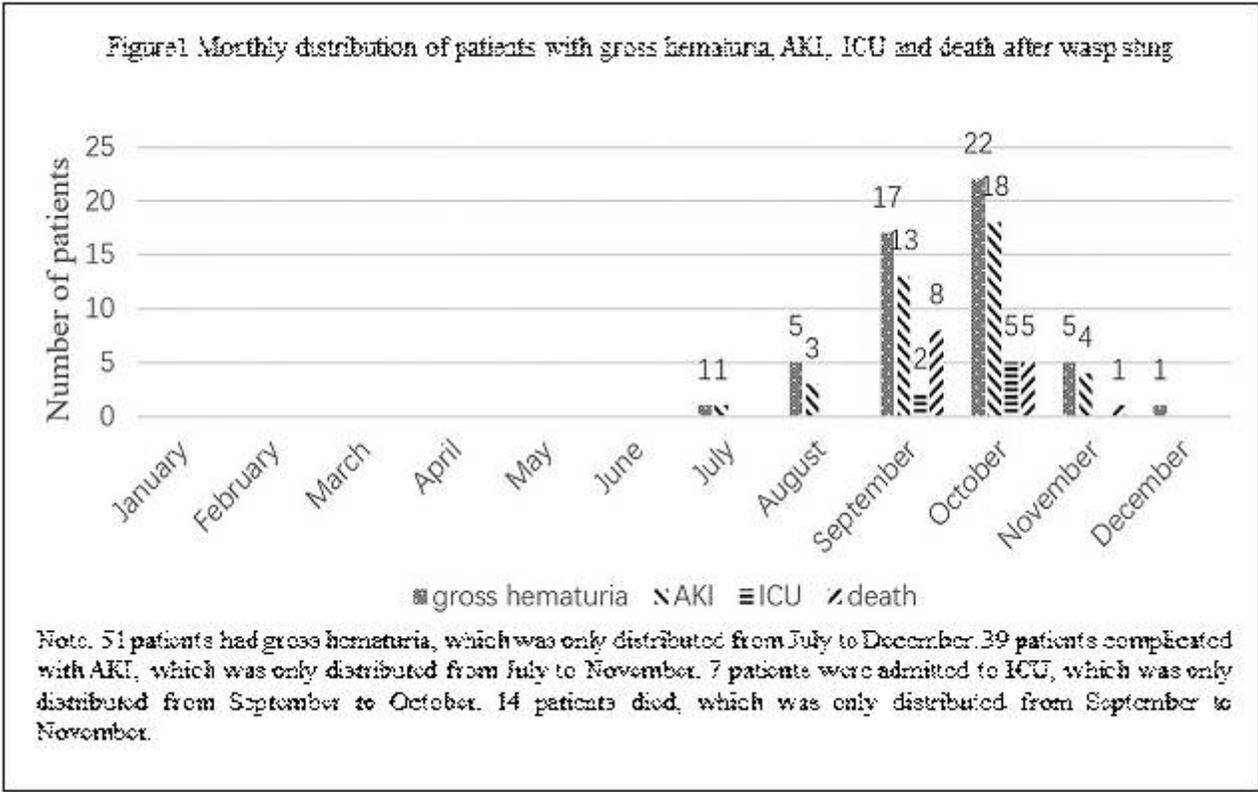


Figure 1

Monthly distribution of patients with gross hematuria, AKI, ICU and death after wasp sting

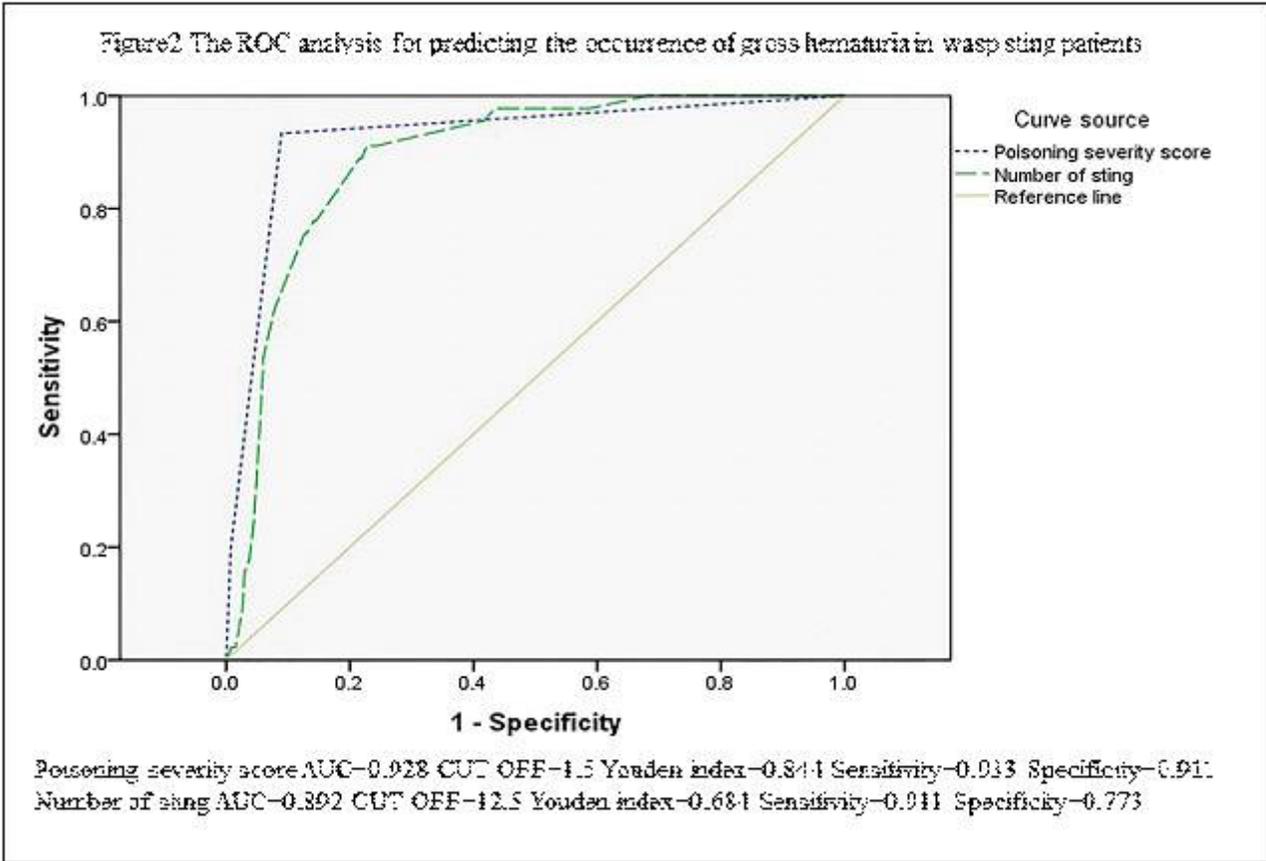


Figure 2

The ROC analysis for predicting the occurrence of gross hematuria in wasp sting patients

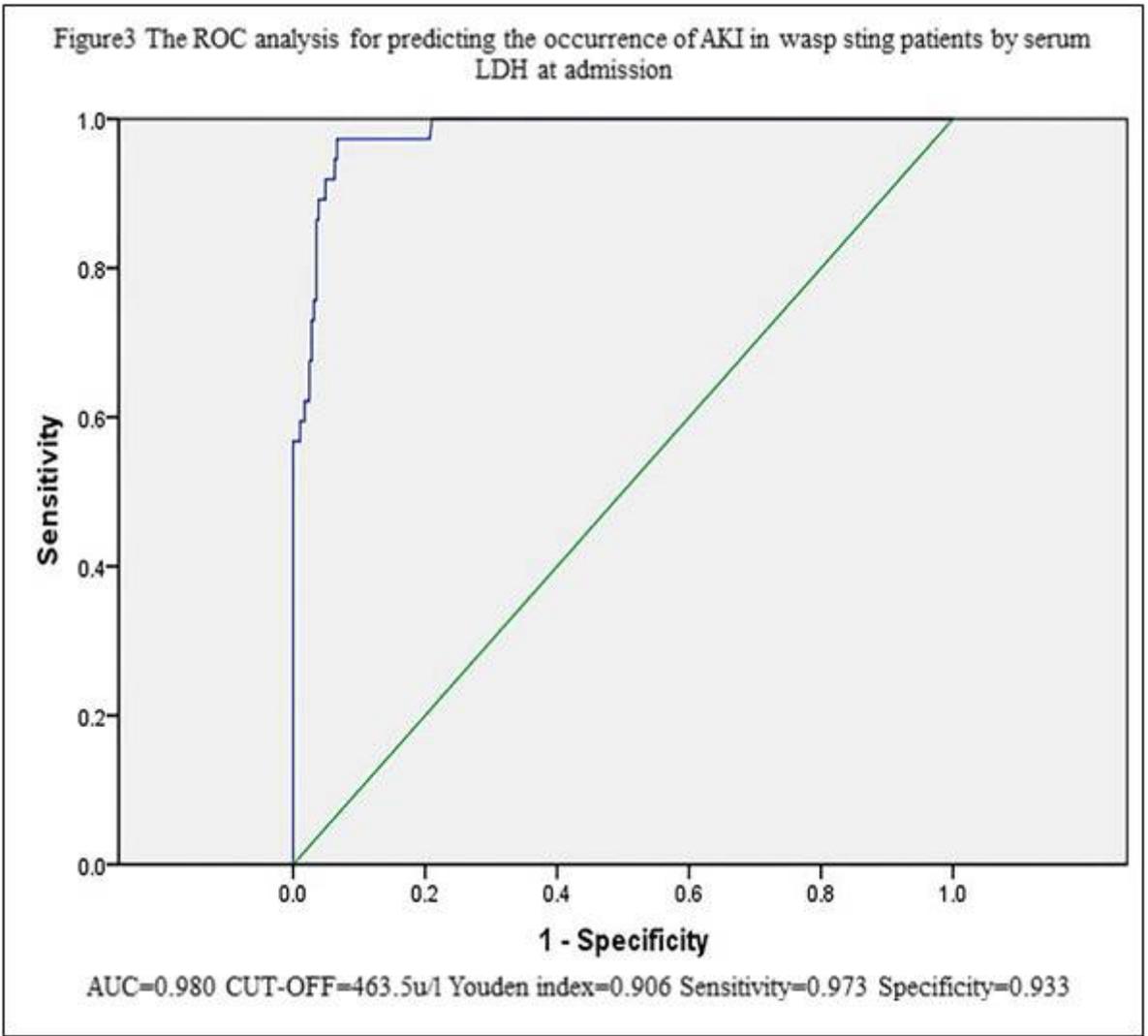


Figure 3

The ROC analysis for predicting the occurrence of AKI in wasp sting patients by serum LDH at admission