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ORIGINAL RESEARCH

Prognostic Value of Red Blood Cell Width Distribution-to-Platelet Ratio in Patients with Snakebite-Associated Multiple Organ Dysfunction Syndrome: A Retrospective Observational Study

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Background: Snakebite-induced organ dysfunction emerging as the primary determinant of morbidity and mortality. This study aims to explore the prognostic value of red blood cell distribution width (RDW) to platelet ratio (RPR) on multi-organ dysfunction (MODS) in patients with snake bites.

Methods: A retrospective study included 637 patients with snakebite between 2015 and 2020 from two hospitals in Anhui province, China. Data were collected at two time points: on the 1st-day and the 5th-day after treatment. All patients were divided into two groups according to the presence or absence of MODS. *T*-tests, chi-square tests, and univariate and multivariate logistical analyses were used to identify the prognostic factors for the development of MODS.

Results: 56 (8.8%) patients developed MODS following snakebite. Logistics analyses indicated that from being bitten at the hospital, the 1st-day of red blood cell distribution width-to-platelet ratio (RPR) and creatinine (CR) levels, and the 5th-day of aspartate aminotransferase (AST) were significantly associated with the development of MODS. The sensitivity and the specificity of the 1st-day RPR were calculated by the received operating characteristic curve (AUC=0.720, 95% CI, 0.642–0.798). The 1st day RPR=0.110 and the 5th day RPR=0.085.

Conclusion: The study found that the RPR is an independent risk factor for predicting multi-organ dysfunction in patients with snake bites. The 1st-day RPR >0.110 is prone to be a new independent predictive factor for the development of MODS after snakebite.

Keywords: RPR, red blood cell width distribution-to-platelet ratio, MODS, snakebite, inflammation

Introduction

Snakebite is a profoundly deleterious affliction that poses a significant threat to human life, primarily through venom injection and the subsequent development of organ damage syndromes caused by toxins. Recent statistics reported by the World Health Organization (WHO) indicate that snakebites have resulted in a range of 81000 to 138000 fatalities, and at least 400000 patients suffering from permanent disability. The snakebite predominantly threatens roughly 5.8 billion people, affecting those residing in impoverished and rural communities.[1,2] According to WHO guidelines for grading snakebite severity,[3] patients are classified into three categories: mild, moderate, and severe. This grading system is based on local symptoms (such as the extent of swelling and necrosis), systemic symptoms (such as neurotoxicity and coagulopathy), and laboratory findings (such as platelet count and coagulation function).

The mountainous population is particularly prone to snake encounters, due to their predominant engagement in agricultural activities, livestock rearing, poultry farming, and fish cultivation.[4] The prevalent snake species in this region

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comprise aquatic snakes (*Enhydris chinensis*) and pit vipers (*Gloydius brevicaudus*). Pit viper bites are common in clinical practice, Pit viper venom is a mixture of neurotoxin and hemotoxin. Compared with other vipers, envenomation caused by these vipers has generally resulted in relatively low fatality rates. However, the symptoms are tremendously biased toward systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS), attributed to the widespread utilization of the target antivenom treatments.

Systemic Inflammatory Response Syndrome (SIRS) is a widespread inflammatory state triggered by infection or non-infectious insults, characterized by dysregulation of the body's immune response.[5] It is diagnosed by the presence of at least two of the following criteria: abnormal body temperature (>38°C or <36°C), tachycardia (>90 beats/min), tachypnea (>20 breaths/min or $PaCO_2$ <32 mmHg), and abnormal white blood cell count (>12,000/μL, <4,000/μL, or >10% immature forms). SIRS is often an early stage of severe conditions such as sepsis, and it plays a critical role in the progression of multiple organ dysfunction syndrome (MODS) and increased mortality in critically ill patients. Early recognition and management of SIRS are essential to prevent further complications.

Multiple organ dysfunction syndrome (MODS), is the simultaneous failure of two or more organs during infection and other systematic inflammation. This condition has been considered a primary contributor to both mortality and mobility among critically ill patients.[6] Several studies have reported the significance of organ damage such as acute kidney injury (AKI), and coagulation disorders played an important role in snakebite envenoming development.[7,8] Red blood cell distribution width (RDW) and platelet count as part of the standard complete blood count (CBC) were widely used in disease diagnosis. With the inflammation and oxidative stress induced by disease, there is a persistent process of destruction and regeneration of red blood cells and platelets. However, the magnitude of these changes was extremely inconsistent. Red blood cell distribution to platelet ratio (RPR) is calculated by the ratio of the red blood cell distribution/platelet count, which has become an important marker used for the prognostic of mortality and mobility in severe burns, hepatitis, cancer, breast cancer, colorectal cancer and glioblastoma.[9–13] We have previously demonstrated that RPR plays an important role in the prognostic of mortality in severe burns.[10]

In this study, we investigated the potential indicators to predict multiple organ dysfunction failure in snakebite patients, and to determine the prognostic value of associating factors, particularly the RPR after snakebite.

Materials and Methods

A total of 1239 patients with snake attacks and clinical wounds were treated at the First Affiliated Hospital of Anhui Medical University and the First Affiliated Hospital of Anhui University of Chinese Medicine between 2015 and 2020 and were enrolled in the retrospective study. Snakebite patients should visit one of the two hospitals within 48 hours after injury; The exclusion criteria were as follows: 1) patients who visited the hospital for more than 48 hours after injury or discharged against medical advice. 2) patients with known cancer, immune diseases, and organ functional lesions such as cardiac disease, kidney disease, hepatopathy, hematological, biochemical, or serological abnormality were also excluded. 3) patients infected before being sent to the hospital or had surgery within 1 month. 4) patients had incomplete or missing information records. Finally, 637 snakebite patients were included in the study. All patients were notified in writing that their demographic data and clinical results of hospitalization might be used for scientific research.

The treatment of snakebite patients in this study was based on the World Health Organization (WHO) guidelines for the management of snakebites and the Chinese guideline for management of snakebites.[3,14] Key principles included the timely administration of antivenom for systemic envenoming, supportive care, and wound management to prevent infection. Regular laboratory monitoring of coagulation profiles, platelet counts, and renal function was conducted to guide treatment and ensure optimal patient outcomes.

All patients in this study were victims of viper bites and received intravenous antivenom serum (Shanghai Serum Biotechnology Co., Ltd.) upon hospital admission. A 6000U dose was administered in 200 mL of saline solution. This antivenom has been confirmed to be free of hemorrhagic, neurotoxic, and cytotoxic effects, demonstrating excellent biosafety and serving as a reliable treatment for venom neutralization.

Steroids, such as dexamethasone (10mg in 250mL of saline solution), were administered for three days to reduce edema and mitigate inflammatory responses. Prophylactic measures were also taken to protect vital organs, such as intravenous administration of 1.8g of glutathione, along with the infusion of 1000–2000mL of fluids. The bite site was

treated with wound debridement and dressing changes. For areas of significant swelling, needle puncture and cupping therapy were performed daily to promote the reduction of swelling. Additionally, a topical mixture of ground Jidesheng snake medicine tablets, honey, and white vinegar was applied around the bite site and the swollen areas once per day until the swelling subsided (Figure 1).

Data Collection

The clinical data collected from the electronic medical record included demographics (gender, age), medical history, specialized medical, results of laboratory tests (The blood routine, biochemical test, coagulation function), and

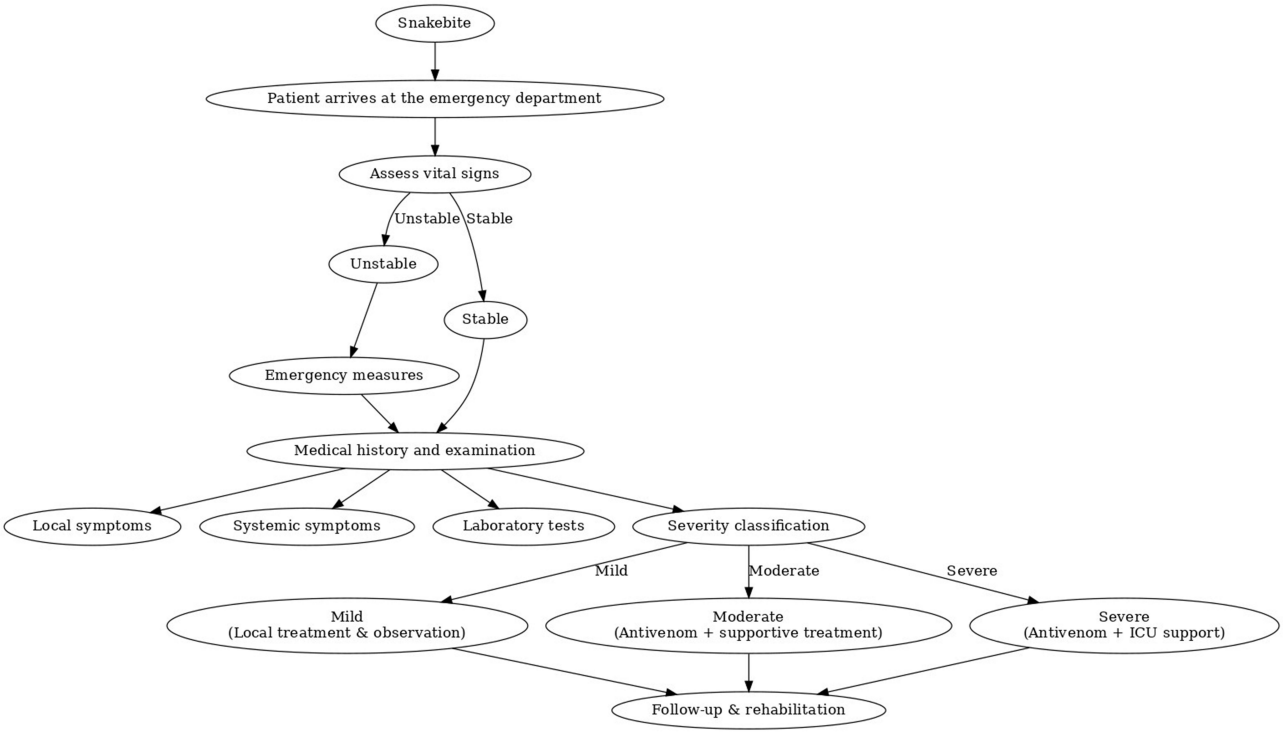

Figure 1 Patient care flow chart.

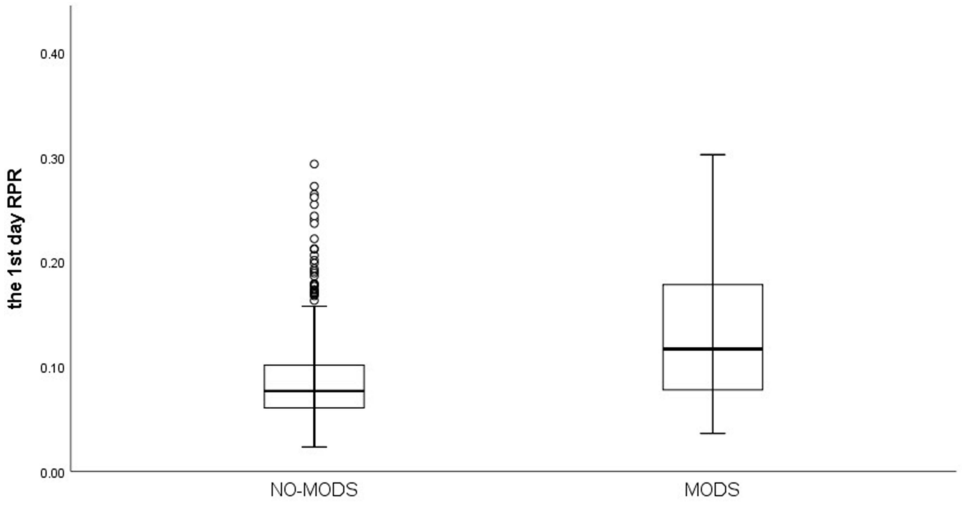

Figure 2 The 1st-day RPR values for snakebite patients with MODS and NO-MODS. Data represented as mean, standard deviation (SD), and individual patient value markers.

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complication record. Blood draws were performed on the first 24 hours of enrollment and the fifth 24 hours after enrollment for dynamically measuring the internal environment of the snakebite patients. All patients had a 60-day follow-up to determine the endpoint and ensure complete wound healing. The diagnosis of MODS was based on organ failure criteria and the Sequential Organ Failure Assessment (SOFA) score, for evaluating and monitoring organ dysfunction in critically ill patients, particularly in intensive care units. The SOFA score assesses six organ systems: respiratory, coagulation, liver, cardiovascular, renal, and neurological (Table 1). Higher scores indicate more severe dysfunction and are generally linked to poorer outcomes.

Organ Failure Diagnostic Criteria

The diagnostic criteria of organ failure were as described:[15–17]

1. Circulation dysfunction was defined as shock status with systolic blood pressure <90 mmHg or mean arterial pressure <70 mmHg.
2. Respiratory dysfunction was defined as PaO2/FiO2 ratio <300 or required mechanical ventilation more than 24 hours.
3. Renal dysfunction was defined as serum creatinine level >1.2 mg/dL or a urine output <0.5 mL/kg/h for more than 6–12 h.
4. Hepatic dysfunction was defined as serum bilirubin level >20.5 umol/L or alanine aminotransferase and aspartate aminotransferase more than two times the upper limit of normal.
5. Hematologic dysfunction was defined as a blood platelet count <100,000/μL.
6. Coagulopathy was defined as an international normalized ratio >1.5.
7. Nervous system dysfunction was defined as Glasgow Coma Scale < 14.

Patients with MODS after snakebite must satisfy the two following conditions: two or more organ function disorders occurred simultaneously or sequentially during hospitalization and the SOFA scores were higher than 2.

Table 1 Sequential Organ Failure Assessment (SOFA)

SOFA Component	Score 0	Score 1	Score 2	Score 3	Score 4
Respiratory Dysfunction (PaO_2/FiO_2 ratio)	>400	300–400	200–300	100–200	<100 or mechanical ventilation >24h
Coagulation Dysfunction (Platelet count $\times 10^3/\mu L$)	>150	100-	15,050–100	20–50	<20
Liver Dysfunction (Total bilirubin mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12
Cardiovascular Dysfunction	Normal BP / no vasopressors	SBP <90 mmHg or vasopressor use	SBP <70 mmHg or higher dose vasopressors	Requires high-dose vasopressors or cardiac support	Uncontrolled BP despite maximum vasopressors
Neurological Dysfunction (Glasgow Coma Scale)	15	13–14	10–12	6–9	<6
Renal Dysfunction (Serum creatinine / Urine output)	Normal	Cr 1.2–1.9 or UO <0.5 mL/kg/h for 6–12h	Cr 2.0–3.4 or UO <0.5 mL/kg/h for >12h	Cr 3.5–4.9 or requires dialysis	Cr >5.0 or requires dialysis

Notes: Interpretation of Scores: The higher the total SOFA score, the more severe the organ dysfunction and the higher the mortality risk. A SOFA score ≥2 is an indication of organ dysfunction, and a continuously increasing score suggests worsening clinical status.

Statistical Analysis

SPSS 22.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. Continuous variables were described as mean ± standard deviation (SD), and other data were represented by frequency (%). All patients were divided into the MODS group and NO-MODS group and took the 1st day and 5th day as time points respectively. Student's *t*-test and Pearson's χ^2-test were employed to evaluate the differences between the MODS and NO-MODS groups. Before conducting the *t*-test, normality tests and assessed homogeneity of variance were performed to confirm that the data were normally distributed and that the assumption of sample independence was satisfied. The receiving operating characteristic (ROC) curves were constructed for RPR at two different time points the area under the ROC curves (AUC) was used for assessing the prognostic performance, and the Youden index (Youden index = sensitivity + specificity – 1) was used for calculating the best cutoff points. The T-tests, chi-square tests, and univariate logistic regression were performed to analyze the potential variables, and then the candidate variables were subjected to multivariate logistic regression to determine the independent prognostic factors for MODS after snakebite.

Results

602 patients were excluded due to hospitalization exceeding 48 hours (n=146). Incomplete cure patients discharged from the hospital (n=104). Patients with known cancer (n=6), immune diseases (n=22), and organ functional lesions such as cardiac disease, kidney disease, and hepatopathy. Hematological, biochemical, or serological abnormalities were also excluded (n=62), incomplete or missing information records (n=262).

A total of 637 patients were included in the study. According to the (Table 2), the mean age was 52.81±17.78 (range: 1–88). The gender balance remains roughly equal in the snakebite patients (male to female; 57.5% to 42.5%). As far as the patients are concerned, the majority of snakebite wounds were located in the lower limb (61.4%), 245 patients (38.5%) in the upper limb, and only one patient in the shoulder for the snake coiled around the branch before attacking. The snake attack happened commonly in summer (74.9%), the incidence rate in the autumn (21.2%) was not far behind, it was very low in the spring (3.8%) and winter (0.2%).

During the hospitalization, 56 (8.8%) patients developing MODS were recorded, 61 (9.6%) patients developed shock and received fluid resuscitation, 5 (0.8%) patients received mechanical ventilation for respiratory dysfunction, 13 (2.0%) patients developed renal dysfunction, 118 (18.5%) patients occurred liver dysfunction, 97 (15.2%) patients developed hematologic dysfunction, 20 (3.1%) patients developed coagulation dysfunction, and 3 (0.5%) patients developed nervous system dysfunction (Table 2).

Table 2 Baseline Clinical Characters for the Snakebite Patients

	Snakebite Patients(N=637)
Age, years	52.81±17.78
Female, n (%)	271(42.5)
The site of bite, n (%)	
Upper limb	245(38.5)
Lower limb	391(61.4)
Other sites	1(0.2)
Bite to hospital time, hours (IQR)	8(4–15)
Season of injury, n (%)	
Spring	24(3.8)
Summer	477(74.9)
Autumn	135(21.2)
Winter	1(0.2)
LOS, days	8.20±4.24
Organ dysfunction, n (%)	
Circulation dysfunction	61(9.6)
Respiratory dysfunction	5(0.8)

(*Continued*)

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Table 2 (Continued).

	Snakebite Patients(N=637)
Renal dysfunction	13(2.0)
Hepatic dysfunction	118(18.5)
Hematologic dysfunction	97(15.2)
Coagulopathy	20(3.1)
Nervous system dysfunction	3(0.5)
MODS	56(8.8)

Notes: Data are presented as mean ± SD, or number (%).
Abbreviations: LOS, length of stay; IQR, interquartile range; MODS: multiple organ dysfunction syndrome.

Table 3 shows the comparison of baseline clinical characteristics. The endpoint of this study was the occurrence of MODS, all snakebite patients were divided into the MODS group (56 cases) and the NO-MODS group (581 cases). Gender and the site of the bite were considered without difference between the two groups. In the MODS group, age and bite-to-hospital time were higher than in the NO-MODS group.

Table 4 compared the clinical subjects between the MODS group and the NO-MODS group at two different time points. Compared to the NO-MODS patients, the MODS patients had significantly higher WBC, Neutrophils, PLT, RPR, ALT, AST, TBIL, DBIL, and CR in the 1st-day laboratory result. However, on the 5th-day post-snakebite, significant hematological and biochemical differences were observed between patients with MODS and those NO-MODS. The

Table 3 Comparisons of Baseline Clinical Characters Between MODS and NO-MODS Patients

	NO-MODS (n=581)	MODS (n=56)	p
Age, years	52.18±17.94	59.25±14.73	0.001
Sex			0.816
Male, n (%)	333(57.3%)	33(58.9%)	
Female, n (%)	248(42.7%)	23(41.1%)	
The site of bite, n (%)			0.401
Upper limb	228(39.2%)	17(30.4%)	
Lower limb	352(60.6%)	39(69.9%)	
Other sites	1(0.2%)	0(0%)	
Bite to hospital time, hours	11.08±10.62	21.48±15.37	0.001
Season of injury, n (%)			0.002
Spring	21(3.6%)	3(5.4%)	
Summer	442(76.1%)	35(62.5%)	
Autumn	118(20.3%)	17(30.4%)	
Winter	0(0%)	1(1.8%)	
LOS, days	7.87±3.25	11.66±9.14	<0.001
Organ dysfunction, n (%)			
Circulation dysfunction	30(5.2%)	31(55.4%)	<0.001
Respiratory dysfunction	0(0%)	5(8.9%)	<0.001
Renal dysfunction	4(0.7%)	9(16.1%)	<0.001
Hepatic dysfunction	78(13.4%)	40(71.4%)	<0.001
Hematologic dysfunction	64(11.0%)	33(58.9%)	<0.001
Coagulopathy	8(1.4%)	12(21.4%)	<0.001
Nervous system dysfunction	0(0%)	3(5.4%)	<0.001

Abbreviation: LOS, length of stay.

Table 4 Comparison of Laboratory Subjects Between MODS and NO-MODS Patients at Two Different Time Points

	Day 1		P	Day 5		P
	NO-MODS	MODS		NO-MODS	MODS	
Laboratory variables						
WBC (×10^9;/L)	9.59 ± 3.48	11.35± 5.01	0.001	7.51 ± 2.64	7.50 ± 3.07	0.947
Neutrophils (×10^9/L)	7.91 ± 3.28	9.87 ± 4.80	0.000	4.69 ± 2.37	5.11 ± 2.96	0.216
Lymphocytes (×10^9/L)	1.20 ± 0.73	1.01 ± 0.86	0.064	2.09± 0.90	1.68 ± 0.82	0.001
RBC (×10^{12}/L)	4.55 ± 0.57	4.60 ± 0.64	0.551	4.26 ± 0.71	3.98 ± 0.55	0.004
Hemoglobin (g/L)	137.03 ± 19.60	140.68 ± 25.49	0.197	127.86 ± 16.60	121.00 ± 18.06	0.004
RDW (%)	13.41 ± 1.08	13.78 ± 1.71	0.117	13.40 ± 1.14	13.69 ± 1.92	0.267
PLT (×10^9/L)	180.06 ± 66.11	130.02 ± 65.45	0.000	184.97 ± 66.28	148.50 ± 75.70	0.000
RPR	0.087 ± 0.039	0.140 ± 0.091	0.000	0.085 ± 0.050	0.119 ± 0.081	0.003
ALT (U/L)	30.38±38.87	155.50±329.82	0.006	43.43±37.38	179.84±307.54	0.002
AST (U/L)	54.58±112.21	512.09±1232.46	0.007	33.52±29.43	241.25±604.46	0.013
TBIL (mg/dL)	13.72±6.27	16.48±8.68	0.024	10.32±4.28	12.99±6.34	0.003
DBIL (mg/dL)	5.24±2.90	6.85±4.20	0.007	3.65±1.75	4.73±2.39	0.002
IBIL (mg/dL)	8.43±4.33	9.42±5.80	0.221	6.67±3.02	8.26±4.41	0.011
BUN (mg/dL)	6.57±1.86	6.78±2.36	0.512	5.83±3.73	8.67±7.88	0.014
CR (mg/dL)	46.66±13.02	54.68±26.66	0.030	57.86±16.13	100.55±112.20	0.009

Abbreviations: WBC, white blood cell count; RBC, red blood cell count; RDW, red cell distribution width; PLT, platelet count; RPR, red blood cell distribution to platelet ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; IBIL, Indirect bilirubin; BUN, blood urea nitrogen; CR, creatinine;

MODS group exhibited lower lymphocyte, RBC, hemoglobin, and PLT, suggesting immune dysregulation and inflammation associated with organ dysfunction. cBiochemical markers in the MODS group revealed elevated ALT, AST, TBIL, DBIL, and IBIL, reflecting impaired liver function or rhabdomyolysis. The myotoxicity of snake venom can induce rhabdomyolysis, leading to muscle breakdown and the release of intracellular components, including CK, LDH, myoglobin, and AST.[18] This process may contribute to the development of acute renal dysfunction. Additionally, significantly higher BUN and CR levels in MODS patients indicated renal dysfunction.

Figure 2 shows the 1st-day RPR values for snakebite patients with MODS and NO-MODS. The significantly elevated RPR on MODS group suggests increased inflammation and coagulopathy. Figure 3 presents the ROC curves of the RPR on the 1st day and 5th day and the occurrence of the MODS in the snakebite patients. The sensitivity and specificity of the 1st-day RPR (AUC=0.720 95% CI,0.642–0.798). The Youden Index was used to calculate the optimal cut-off value of the RPR (the 1st day RPR=0.110, the 5th day RPR=0.085).

The results of the Student's *t*-test and Pearson's $\chi 2$ test were included in the univariate logistic regression analysis to identify the potential factors influencing outcomes. The statistically significant variables were performed using the multivariate logistic regression analysis for estimating the independent prognostic value between the MODS status and the potential predictors (Table 5).

Discussion

The occurrence of MODS emerges as a serious complication in infectious or non-infectious stimuli due to its rapid progression and deterioration.[19] In this progress, the detection of the organ dysfunction and the early identification of the MODS are crucial factors for assessing the prognosis of snakebite.

Herein, we conducted an investigation into potential hematological indicators at early time points to predict the occurrence of MODS in snakebite patients to raise awareness of the systematic inflammation and potential adverse outcomes. This is the first study to explore the clinical implications of MODS in snakebite patients, with a specific focus on evaluating the prognostic value of the RPR. In our study, 56 (8.79%) patients developed MODS after snakebite. The most common organ failure was hepatic dysfunction (n=118,18.5%) followed by hematologic dysfunction (n=

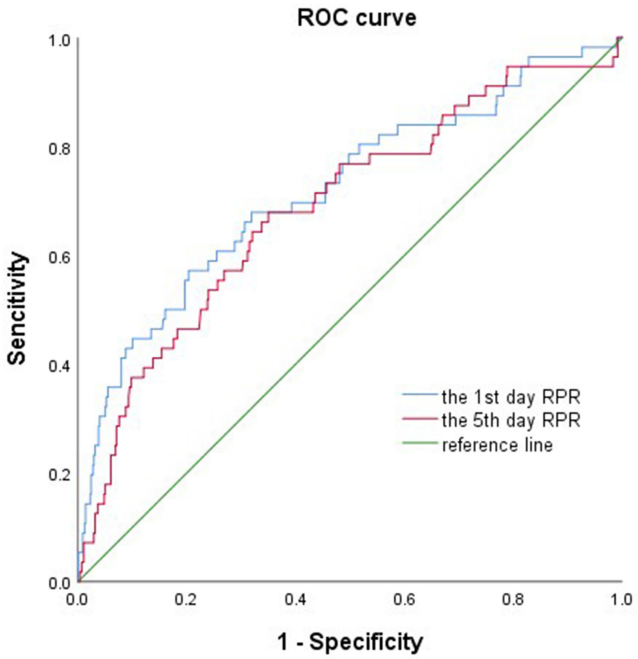

Figure 3 Received operating characteristic curve of the 1st-day RPR (AUC=0.720 95% CI,0.642–0.798) and the 5th-day RPR (AUC=0.689 95% CI,0.612–0.767) for prediction of MODS in snakebite injury.

97.15.2%). In the multiple logistics analysis, bite to hospital, the 1st day RPR, CR and the 5th day AST were identified as independent prognostic factors associated with the occurrence of MODS after snakebite.

Organ dysfunction frequently occurs in snakebite cases. Rapid venom release into the bloodstream and its interaction with major organs play a critical role in snakebite pathology, leading to infection, inflammation, neurotoxicity, and multi-organ damage.[20] Previous studies have extensively reported the poor outcomes after snakebite, including circulation dysfunction with hemodynamic instability, respiratory dysfunction, renal dysfunction, hepatic dysfunction,

Table 5 Univariate and Multivariate Logistic Regression Analysis for MODS and NO-MODS Patients at Two Different Time Points

Variable	Day 1				Day 5			
	Univariate		Multivariate		Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age	1.028 (1.008–1.048)	0.005	1.016(0.987–1.047)	0.278	1.028 (1.008–1.048)	0.005	1.016(0.987–1.047)	0.278
Bite to hospital time, hours	1.057(1.038–1.076)	0.000	1.056(1.027–1.085)	0.000	1.057(1.038–1.076)	0.000	1.056(1.027–1.085)	0.000
Season of injury		0.256		NS		0.256		NS
WBC ($\times 10^9$/L)	1.141 (1.062–1.226)	0.000		NS		NS		NS
Neutrophils ($\times 10^9$/L)	1.145(1.064–1.232)	0.000		NS		NS		NS
Lymphocytes ($\times 10^9$/L)		NS		NS	0.478 (0.310–0.737)	0.001		NS
RBC ($\times 10^{12}$/L)		NS		NS	0.430 (0.261–0.707)	0.001		NS
Hemoglobin		NS		NS	0.976 (0.960–0.992)	0.004		NS
PLT ($\times 10^9$/L)	0.985 (0.980–0.991)	0.000		NS	0.990 (0.985–0.995)	0.000		NS
RPR(>cutoff value)	5.232 (2.969–9.219)	0.000	3.679 (1.071–12.637)	0.039	3.536 (1.993–6.271)	0.000		NS
ALT (U/L)	1.009 (1.005–1.013)	0.000		NS	1.013 (1.008–1.017)	0.000		NS
AST (U/L)	1.003 (1.002–1.005)	0.000		NS	1.013 (1.008–1.019)	0.000	1.014 (1.005–1.023)	0.002
TBIL (mg/dL)	1.050 (1.016–1.086)	0.004		NS	1.105(1.052–1.161)	0.000		NS
DBIL (mg/dL)	1.120 (1.045–1.200)	0.001		NS	1.255(1.112–1.416)	0.000		NS
IBIL (mg/dL)		NS		NS	1.136(1.057–1.222)	0.001		NS
BUN (mg/dL)		NS		NS	1.094(1.028–1.165)	0.005		NS
CR (mg/dL)	1.026(1.012–1.041)	0.000	1.030 (1.008–1.053)	0.006	1.021(1.009–1.033)	0.001		NS

thrombocytopenia, and nervous system dysfunction.[7,21–27] Exploring the mechanism and manifestation of MODS following snakebite is essential. However, clinical identification is challenging since humans are not the primary targets of snake venom, and its metabolism in the human body remains complex.

Snakebite can be divided into three kinds according to the poisoning situation: the absence of venom being injected (dry bites), isolated local symptoms, and snakebite with systemic envenoming.[18] It is difficult to diagnose snakebite and take appropriate treatment for human symptoms at the early stage, such as hyperventilation, syncope, vomiting, and other clinical features.[20] Therefore, we can regard the occurrence of MODS as an exacerbation condition, and early intervention offers a large opportunity for controlling MODS in snakebites.

RPR has been recognized as a valuable prognostic indicator of inflammation diseases.[28] The aggressive inflammation-promoting destruction of red blood cells decreased the production of red blood cells and elevated the red blood cell distribution (RDW) value.[29] Moreover, dysfunction in the hemostatic system, particularly thrombocytopenia was associated with acute systemic inflammation for rapid trapping and consumption of platelets.[30] Several studies propose that thrombocytopenia is associated with heightened disease severity and worsened outcomes.[31,32] Therefore, the combination and conversion of the RDW and platelet are biologically feasible for predicting the development of MODS. Chen, B. et al [9] first proposed RPR as a novel, simple noninvasive index for predicting hepatic fibrosis and cirrhosis. Further, Cetinkaya, E. et al[33] analyzed 102 acute pancreatitis patients' data and the result showed that RPR was associated with mortality and the severity of the inflammation. Equally significant, our previous study has demonstrated that RPR was independently associated with mortality in patients with burns.[10]

Snakebite is a prevalent clinical issue that significantly impacts patients' quality of life and gives rise to economic or social consequences. This paper retrospective analyzed 637 patients with snakebites coming from two major teaching hospitals. However, this study has several limitations. Firstly, the qualitative data is mainly from the two major hospitals in the Anhui Province in China, and may not fully represent the current status in other regions. Secondly, the retrospective study introduces inevitable bias. Thirdly, there were differences in the species, living habits, and characteristics of the snake among regions and countries. Lastly, differences in medical treatment levels and resources have resulted in the omission of data on medical equipment and pharmaceuticals in the study.

Conclusion

MODS represents a serious morbidity syndrome with snakebite. This study demonstrates that the red blood cell distribution to platelet ratio exhibits an independent prognostic value for the occurrence of MODS in snakebite patients. Specifically, the 1st day-higher RPR ($\geq$0.110) could serve as a predictive tool for identifying organ dysfunction.

Abbreviations

WBC, White Blood Cell Count; PLT, Platelet; RPR, red blood cell distribution width-to-platelet ratio; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; IBIL, indirect bilirubin; RBC, Red Blood Cell Count; RDW, red cell distribution width; BUN, Blood Urea Nitrogen; CR, Creatinine.

Data Sharing Statement

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Ethical Approval and Consent to Participate

This study was performed by the Declaration of Helsinki and approved by the committee on medical ethics of the First Affiliated Hospital of Anhui Medical University, Hefei, Anhui (reference number: PJ 2022-10-33). All patients gave written informed consent for treatment and were aware that all information could be used anonymously for scientific purposes only.

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This paper has been uploaded to ResearchGate as a preprint: https://www.researchgate.net/publication/376778581_Prognostic_value_of_red_blood_cell_width_distribution-to-platelet_ratio_in_patients_with_snakebite-associated_multiple_organ_dysfunction_syndromeA_retrospective_observational_study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Abdullahi SA, Habib AG, Hussaini N, Abd-Alla AMM. Control of snakebite envenoming: a mathematical modeling study. *PLoS Negl Trop Dis*. 2021;15(8):e0009711. doi:10.1371/journal.pntd.0009711
2. Kasturiratne A, Wickremasinghe AR, de Silva N, et al. The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med*. 2008;5(11):e218. doi:10.1371/journal.pmed.0050218
3. Web Regional Office for South-East Asia. World Health Organization. Guidelines for the management of snakebites, 2nd ed 2016. Available from: https://iris.who.int/handle/10665/249547. Accessed April 14 2025.
4. Lin B, Zhang JR, Lu HJ, et al. Immunoreactivity and neutralization study of Chinese Bungarus multicinctus antivenin and lab-prepared anti-bungarotoxin antisera towards purified bungarotoxins and snake venoms. *PLoS Negl Trop Dis*. 2020;14(11):e0008873. doi:10.1371/journal.pntd.0008873
5. Luo P, Ji Y, Liu X, et al. Affected inflammation-related signaling pathways in snake envenomation: a recent insight. *Toxicon*. 2023;234:107288. doi:10.1016/j.toxicon.2023.107288
6. American College of Chest Physicians (ACCP) headquarters in Northbrook. American college of chest physicians/society of critical care medicine consensus conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Critical Care Medicine*. 1992;20(6):864–874. doi:10.1097/00003246-199206000-00025
7. Noutsos T, Currie BJ, Lek RA, Isbister GK. Snakebite associated thrombotic microangiopathy: a systematic review of clinical features, outcomes, and evidence for interventions including plasmapheresis. *PLoS Negl Trop Dis*. 2020;14(12):e0008936. doi:10.1371/journal.pntd.0008936
8. Isbister GK. Snakebite doesn't cause disseminated intravascular coagulation: coagulopathy and thrombotic microangiopathy in snake envenoming. *Semin Thromb Hemost*. 2010;36(4):444–451. doi:10.1055/s-0030-1254053
9. Chen B, Ye B, Zhang J, Ying L, Chen Y. RDW to platelet ratio: a novel noninvasive index for predicting hepatic fibrosis and cirrhosis in chronic hepatitis B. *PLoS One*. 2013;8(7):e68780. doi:10.1371/journal.pone.0068780
10. Qiu L, Chen C, Li SJ, et al. Prognostic values of red blood cell distribution width, platelet count, and red cell distribution width-to-platelet ratio for severe burn injury. *Sci Rep*. 2017;7(1):13720. doi:10.1038/s41598-017-13151-3
11. Bilgin B, Sendur MAN, Hizal M, et al. Prognostic effect of red cell distribution width-to-platelet ratio in colorectal cancer according to tumor stage and localization. *J Cancer Res Ther*. 2019;15(1):54–60. doi:10.4103/jcrt.JCRT_624_17
12. Takeuchi H, Abe M, Takumi Y, et al. Elevated red cell distribution width to platelet count ratio predicts poor prognosis in patients with breast cancer. *Sci Rep*. 2019;9(1):3033. doi:10.1038/s41598-019-40024-8
13. Schneider M, Schäfer N, Apallas S, et al. Red blood cell distribution width to platelet ratio substantiates preoperative survival prediction in patients with newly-diagnosed glioblastoma. *J Neuro-Oncol*. 2021;154(2):229–235. doi:10.1007/s11060-021-03817-4
14. Lyu C, Zhang G, Zhu H, et al. The Chinese guideline for management of snakebites. *J World Emerge Med*. 2024;15(5):333–355. doi:10.5847/wjem.j.1920-8642.2024.076
15. Vincent JL, Moreno R, Takala J, et al. The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. on behalf of the working group on sepsis-related problems of the European society of intensive care medicine. *Inten Care Med*. 1996;22(7):707–710. doi:10.1007/bf01709751
16. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intens Care Med*. 2021;47(11):1181–1247. doi:10.1007/s00134-021-06506-y
17. Feng JY, Chien JY, Kao KC, et al. Predictors of early onset multiple organ dysfunction in major burn patients with ventilator support: experience from a mass casualty explosion. *Sci Rep*. 2018;8(1):10939. doi:10.1038/s41598-018-29158-3
18. Pucca MB, Knudsen C, So I, et al. Current knowledge on snake dry bites. *Toxins*. 2020;12(11):668. doi:10.3390/toxins12110668

19. Beal AL, Cerra FB. Multiple organ failure syndrome in the 1990s. systemic inflammatory response and organ dysfunction. *JAMA*. 1994;271(3):226–233. doi:10.1001/jama.1994.03510270072043
20. Gutierrez JM, Calvete JJ, Habib AG, Harrison RA, Williams DJ, Warrell DA. Snakebite envenoming. *Nat Rev Dis Primers*. 2017;3(1):17063. doi:10.1038/nrdp.2017.63
21. Kim OH, Lee JW, Kim HI, et al. Adverse cardiovascular events after a venomous snakebite in Korea. *Yonsei Med J*. 2016;57(2):512–517. doi:10.3349/ymj.2016.57.2.512
22. Valenta J, Stach Z, Michalek P. Exotic snake bites in the Czech Republic--epidemiological and clinical aspects during 15-year period (1999-2013). *Clin Toxicol*. 2014;52(4):258–264. doi:10.3109/15563650.2014.902066
23. Cruz LS, Vargas R, Lopes AA. Snakebite envenomation and death in the developing world. *Ethnic Dis*. 2009;19(Suppl 1):S1–42–6.
24. Albuquerque P, Mota SM. Snakebite-associated kidney injury. *Contribu Nephrol*. 2021;199:244–251. doi:10.1159/000517725
25. Waiddyanatha S, Silva A, Siribaddana S, Isbister GK. Long-term effects of snake envenoming. *Toxins*. 2019;11(4):193. doi:10.3390/toxins11040193
26. Bhikane AU, Jadhav RK, Masare PS, Chavhan SG. Clinical, hematobiochemical, and pathological findings and therapeutic management of viperine snake envenomation in zebu cattle. *Trop Anim Health Prod*. 2020;52(6):3425–3437. doi:10.1007/s11250-020-02376-6
27. Sachetto ATA, Jensen JR, Santoro ML, Lacerda MV. Liver gene regulation of hemostasis-related factors is altered by experimental snake envenomation in mice. *PLoS Negl Trop Dis*. 2020;14(6):e0008379. doi:10.1371/journal.pntd.0008379
28. Dervisevic A, Muhic A, Zaciragic A, et al. Red blood cell distribution width-to-platelet ratio inversely correlates with indicators of disease activity status in rheumatoid arthritis patients. *Rom J Intern Med*. 2021;59(2):180–186. doi:10.2478/rjim-2020-0044
29. Lehmann F, Schenk LM, Bernstock JD, et al. Elevated red cell distribution width to platelet ratio is associated with poor prognosis in patients with spontaneous, deep-seated intracerebral hemorrhage. *Front Neurol*. 2021;12:751510. doi:10.3389/fneur.2021.751510
30. Stohlawetz P, Folman CC, von Dem Borne AE, et al. Effects of endotoxemia on thrombopoiesis in men. *Thromb Haemost*. 1999;81(4):613–617. doi:10.1055/s-0037-1614534
31. Habets KL, Huizinga TW, Toes RE. Platelets and autoimmunity. *Europ J Clin Invest*. 2013;43(7):746–757. doi:10.1111/eci.12101
32. Hepburn AL, Narat S, Mason JC. The management of peripheral blood cytopenias in systemic lupus erythematosus. *Rheumatology*. 2010;49(12):2243–2254. doi:10.1093/rheumatology/keq269
33. Cetinkaya E, Senol K, Saylam B. Red cell distribution width to platelet ratio: new and promising prognostic marker in acute pancreatitis. *World J Gastroenterol*. 2014;20(39):14450–14454. doi:10.3748/wjg.v20.i39.14450