

Research Article

Importance of Neutrophil–Lymphocyte Ratio and Platelet–Lymphocyte Ratio for Determining the Prognosis and Hospitalization Period in Patients with Snakebites

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Abstract

Objectives: Snakebites can result in serious complications. Our country is a snakebite-endemic area. The parameters for the prognosis of snakebites are very valuable due to the inadequacy of acute inpatient services, as well as the excessively intense traffic at emergency rooms (ERs); therefore, we aimed to detect the importance of the neutrophil–lymphocyte ratio (NLR) and the platelet–lymphocyte ratio (PLR) as parameters in the prognosis for snakebites.

Methods: In this study, patients who presented at the ER within 24 hours after a snakebite were retrospectively analyzed. The sex, age, exposure duration, body part affected, hospitalization period, complications, mortality rate, and blood parameters of ER patients were assessed.

Results: Fifty healthy individuals who were suitable in terms of sex and age were included in the control group. It was detected that the average NLR ($p=0.000$) and PLR ($p=0.003$) values were statistically significantly higher in the patient group than in the control group. On comparing the patients discharged from the ER with those who remained hospitalized, no statistical difference was detected in the NLR value ($p=0.195$); however, the PLR value was significantly higher in the patients who remained hospitalized ($p=0.000$). The NLR ($p=0.000$) and the PLR ($p=0.000$) values in the patients who developed complications were significantly higher than those in patients who did not develop complications.

Conclusion: The hospitalization period, complication developments, and poor prognosis in snakebites may be predicted using the NLR and PLR values, which are easily available and inexpensive blood parameters.

Keywords: Neutrophil–lymphocyte ratio, platelet–lymphocyte ratio, snakebites

Although the total number of snake species present throughout the world is not precisely known, it is presumed to be between 2.500 and 3.000.^[1] Only 1/3rd of the snake species is venomous, which can be classified as dangerous to mankind. Only 8% of the snake species is dangerous to mankind.^[2] Snakebite is a significant mortality and morbidity cause, which occurs particularly in the summer months; in our country, it is encountered more frequently in South & Southeastern Anatolia Regions.^[3]

The snake venom comprises of a complicated structure,

comprising an aggregation of various toxic proteins and enzymes. The snake venom has cardiotoxic, neurotoxic, miotoxic, nephrotoxic, and hematotoxic characteristics, and local and systemic symptoms are observed in patients based on the intensity of the toxin.^[4, 5]

Many studies have reported that many complications such as necrosis^[6], amputation^[7], acute renal failure^[8], compartment syndrome^[7, 8], and mortality^[7] were encountered arising out of snakebites.

In the hospitals where snakebite cases are frequently en-

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countered and the inpatient bed availability is limited, follow-up is challenging and the patients return with further complications after being discharged from the hospital. Therefore, determining the prognosis is of vital importance, as the patient applies to the hospital.

In recent years, various studies have been conducted on the capability of prognosis and mortality predictions for many diseases with NLR and PLR, which are easily available and inexpensive blood parameters.^[9, 10, 11]

Reflecting the neutrophil level for the acute state in inflammation, and the lymphopenia developing after acute physiological stress, NLR was used with other inflammatory markers in the studies, thus recognized to be an efficient marker for inflammatory state.^[11]

Recently, it has been reported that PLR is a potential marker of inflammation and is an independent predictor of mortality in cardiac and various oncological diseases.^[12]

In this study, we aimed to analyze the role of NLR and PLR values measured during admission for determining poor prognosis in the early period for patients presenting to ER with snakebite.

Methods

In our study, 308 patients who presented to the ER of Batman Region State Hospital, which has a daily patient admission capacity of approximately 1500, within 24 h after snakebite between January 1, 2015 and January 1, 2017 were retrospectively analyzed. Ethical consent was taken from a local committee. The patient information was accessed through the hospital's records and automation system. The patients who were diagnosed with idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, and essential thrombocytosis; those who had a history of medication use leading to the disorders of platelets and neutrophils structure and function; and those with missing data were excluded.

The following characteristics and parameters were analyzed for the included patients: patients' sex, age, profession, vital findings, duration of exposure, bitten body part, hospitalization period, complications developed, mortality rate, including the blood parameters as applying to the hospital. Fifty healthy individuals who were suitable in terms of sex and age were included in the control group.

The cases were split into the following paired groups: patients and controls; those who developed complications and those who did not; those who remained hospitalized and those who were discharged from the hospital; and lower extremity and upper extremity snakebites. The NLR and PLR values of these groups were compared.

In univariate statistical analyses, chi-square test was applied for categorical variables, whereas Student-t test was applied for continuous variables. Numeric variables were stated as mean±SD. $P < 0.05$ was considered as statistically significant. Pearson correlation analysis was performed for the measurement of linear relationship level between two continuous variables. Regarding the Pearson correlation coefficient (r), a value of 0.00–0.25 was considered as very poor correlation, 0.26–0.49 as poor correlation, 0.50–0.69 as medium correlation, 0.70–0.89 as high correlation, and 0.90–1.00 as very high correlation.

Results

In total, 351 patients presented with snakebite to the ER of Batman Region State Hospital between January 1, 2015 and January 1, 2017. We excluded 43 patients whose automation records and file information could not be accessed. In the study, 69.8% (215) of the patients were male and 30.1% (93) were female. We calculated the age average of the patients as $43\% \pm 19.70\%$ (35) of the control group was male, while 30% (15) of the group was female; the age average was 42 ± 13 years. There was no statistically significant difference regarding age ($p = 0.712$) and sex ($p = 0.813$) between the control and patient groups.

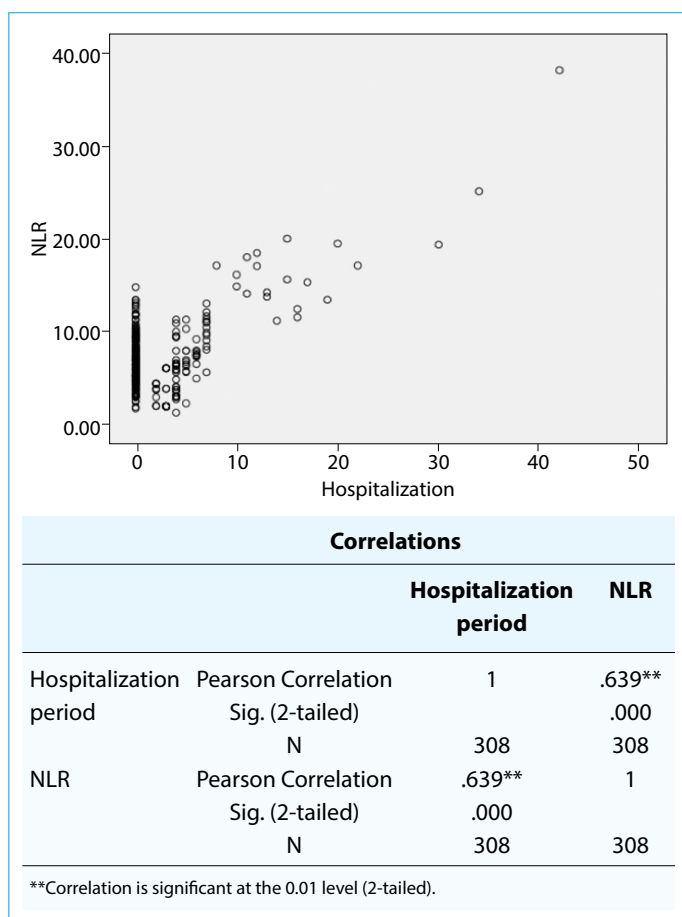
Analyzing the patients as distributed by months, the highest rate of patient application was during the months of June, July, August, and September. Of all patients, 63% were farmers, and 92% were from the countryside and 8% were from the town center. Furthermore, 53% of the patients ($n = 163$) were bitten in the lower extremity and 47% ($n = 145$) were bitten in the upper extremity. Also, 59.4% ($n = 183$) of the patients were discharged after treatment and monitored in ER, while 40.5% ($n = 125$) of them remained hospitalized. The average hospitalization period of the patients who remained hospitalized was 6.35 ± 6.12 . In addition, 6.8% ($n = 21$) of the 308 patients developed complications while being monitored and nine of them developed compartment syndrome, while seven of these complications were finger amputations, three were coagulopathy and two were acute renal failure. There was no case of exitus.

Table 1. Comparison of patient and control groups for their NLR and PLR values

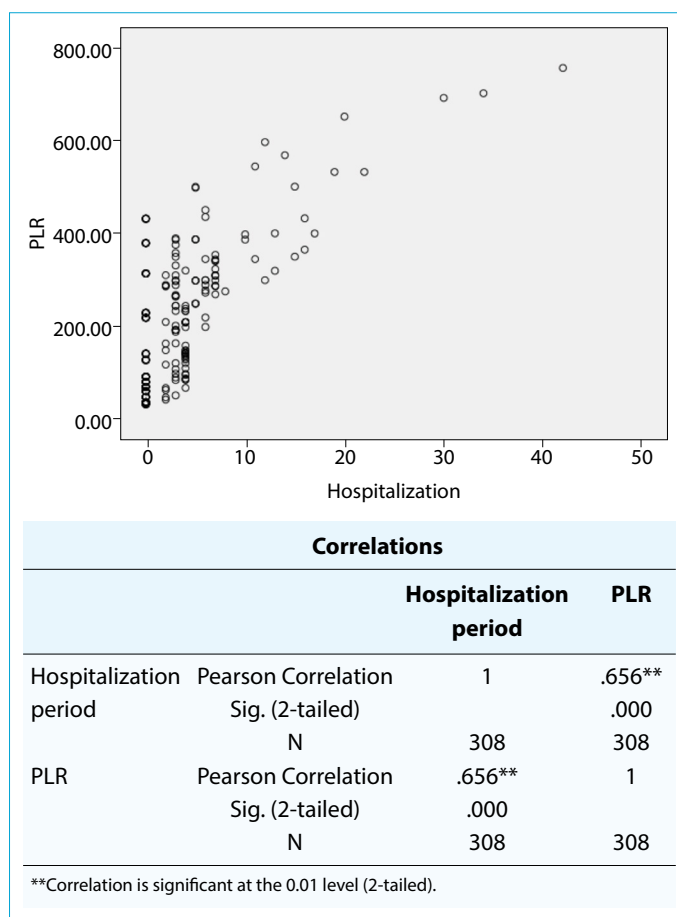
	Patient (n=308)	Control (n=50)	P value
NLR (mean+SD)	7.12±4.15	2.34±1.08	0.000
PLR (mean+SD)	194.40±145.88	130.42±70.44	0.003

Table 2. Relationship between the NLR and PLR values and treatment process (discharge, hospitalization), development of complication, and bitten body part

		(n)	NLR (mean±SD)	P value	PLR (mean±SD)	P value
Treatment process	Discharge	183	6.87±2.58	0.195	138.05±118.59	0.000
	Hospitalization	125	7.49±5.71		276.91±143.16	
Complication	Developing	21	17.24±5.75	0.000	478.49±142.22	0.000
	Not developing	287	6.38±2.85		173.61±122.75	
Bitten body part	Lower extremity	163	4.94±2.58	0.425	187.12±116.56	0.382
	Upper extremity	145	7.32±5.40		201.69±170.31	

**Figure 1.** Relation between hospitalization period and NLR value.

We analyzed the NLR and PLR values of the patient and control groups as applying to the hospital, involved in our study. We detected that the average NLR ($p=0.000$) and PLR ($p=0.003$) values were statistically significantly higher in the patient group than in the control group (Table 1). Comparing the patients who were discharged from ER and those who remained hospitalized, no statistical difference was detected for NLR value ($p=0.195$); however, the PLR value was significantly higher in the patients who remained hospitalized ($p=0.000$) (Table 2). The NLR ($p=0.000$) and PLR ($p=0.000$)

**Figure 2.** Relation between hospitalization period and PLR value.

values in the patients who developed complications were significantly higher than those in the patients who did not develop complications. Being bitten on the lower or upper extremity by the snake did not constitute any significant change on the NLR ($p=0.425$) and PLR ($p=0.382$) values.

We analyzed the relation between the hospitalization period and blood parameters of the patients and detected a positive and medium correlation between the NLR ($p=0.000$, $r=0.639$) and PLR ($p=0.000$, $r=0.656$) values and hospitalization period (Fig. 1, Fig. 2).

Discussion

Snakebite is one of the most common causes of admission to ER within our region, particularly in the summer months. The Viperidae family of snakes is frequently seen in this region due its geographical position, and snakebites are considered as a serious public health problem, since the temperature is above seasonal normal and the people mainly work in rural areas in the summer months.

Local and systemic symptoms are observed in patients depending on the density of the snake venom. The local findings are edema, hematoma, and gangrenous lesions, while the systemic findings are pyrexia, nausea, vomiting, circulatory failure, mild hepatitis, delirium, convulsion, and coma. Mortality may occur due to secondary infections, disseminated intravascular coagulopathy, neurotoxicity, acute renal failure, intracranial hemorrhage. Besides, progressing anemia, leukocytosis, thrombocytopenia, hyperfibrinogenemia, failure in coagulation tests, proteinuria, and azotemia have also been reported.^[3,13]

Snake venom contains phospholipase, acetylcholinesterase, hyaluronidase, collagenase, RNA and DNA, leukotrienes, antibactericidin, neurotoxins, procoagulant, anticoagulant, cardiotoxin, hemotoxin, and certain electrolytes. It also causes secretion of quinine, histamine, and serotonin via cytolytic enzymes in the bitten area. Apart from the aforementioned, the snake venom also contains proteolytic and hemolytic factors, amino-acid oxidants, as well as other enzymes.^[14, 15] These enzymes, contained within the venom, may generate anti-inflammatory response, apart from tissue and cell damage.

We analyzed the relationship between the NLR and PLR values, as anti-inflammatory parameters, and poor prognosis, development of complication, and hospitalization period in patients who presented to the hospital with snakebites. We confirmed that the NLR and PLR values may be significant in poor prognosis. Elbey et al. confirmed a significant relation between NLR value and poor prognosis in his studies on snakebites.^[16] Apart from obtaining a similar result in our study, we also confirmed that PLR value comprises a predictive value concerning poor prognosis, development of complication, and hospitalization period for these patients, and to the best of our knowledge, no other study concerning the PLR value in snakebites has been conducted. We think that there is a need for extensive prospective studies.

Recently, the NLR and PLR values have been used for prognosis in many diseases.^[17, 18, 19, 20] We believe that the prediction of poor prognosis and the development of complication in snakebites are of vital importance, particularly in crowded hospitals with limited inpatient bed availability,

including snakebite endemic regions, for patient monitoring and discharging.

Conclusion

We believe that it is possible to make predictions on hospitalization periods and development of complications using the NLR and PLR values, which are measured in patients while applying to ER for snakebites.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship contributions: Concept – N.G.K., M.O., M.U.; Design – N.G.K., M.O., M.U.; Supervision – N.G.K., M.O., M.U.; Materials – N.G.K., M.O., M.U.; Data collection &/or processing – N.G.K., M.O., M.U.; Analysis and/or interpretation – N.G.K., M.O., M.U.; Literature search – N.G.K., M.O., M.U.; Writing – N.G.K., M.O., M.U.; Critical review – N.G.K., M.O., M.U.

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