

The utility of the neutrophil-to-lymphocyte ratio in predicting urolithiasis in acute abdominal pain accompanied by flank pain

Feride Sinem Akgün¹, Orhun Sinanoğlu²

¹Department of Emergency Medicine, Maltepe University School of Medicine, İstanbul, Turkey

²Department of Urology, Maltepe University School of Medicine, İstanbul, Turkey

DOI: 10.18621/eurj.431227

ABSTRACT

Objectives: To evaluate whether the neutrophil-to-lymphocyte ratio (NLR), can differentiate between urinary stone disease and inflammatory conditions in patients admitted to emergency department having acute abdominal pain accompanied by flank pain.

Methods: Data of 191 patients with acute abdominal pain accompanied by flank pain admitted to emergency department in a single institution during 1 year period was retrospectively reviewed. Complete blood count and urine analysis were evaluated, the definitive diagnosis was established radiologically. The NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. The cut off value for the NLR in relation to stone status was calculated.

Results: Of the 191 patients 51.3% (n = 98) were males, 48.7% (n = 93) were females ($p > 0.05$). White blood counts of the patients according to the presence of stone does not show a statistically significant difference ($p > 0.05$). NLR measurement of patients according to the presence of stone shows a statistically significant difference ($p = 0.009$). NLR of patients with urinary stones were significantly lower than patients without urinary stones. NLR measurements did not differ significantly according to stone location. A cut-off point of ≤ 2.16 for the NLR was determined according to the stone status of the patients. NLR values were higher in patients with acute abdominal pain/flank pain due to inflammatory pathologies.

Conclusion: As the diagnosis and treatment of urolithiasis take long time and require elaborate methods, NLR may be used as a simple method in the differential diagnosis of pain due to urinary stone disease or inflammatory condition.

Keywords: Acute abdominal pain, emergency medicine, flank pain, neutrophil-to-lymphocyte ratio (NLR), urolithiasis

Received: June 6, 2018; Accepted: September 21, 2018; Published Online: November 16, 2018

Acute abdominal pain (AAP) is one of the leading symptoms among emergency department (ED) admissions and its diagnostic and management process takes long time [1]. AAP incidence is 7-10% among ED admissions [2, 3]. According to the Statis-

tical Institute in Turkey, 5% of hospitalized patients presenting to the emergency department are cases of AAP admitted to the emergency department, among them 30% cannot be diagnosed [4].

AAP may be due to multiple inflammatory and



Address for correspondence: Feride Sinem Akgün, MD., Maltepe University School of Medicine, Department of Emergency Medicine, İstanbul, Turkey
E-mail: bfsakgun@hotmail.com

Copyright © 2019 by The Association of Health Research & Strategy
Available at <http://dergipark.gov.tr/eurj>

noninflammatory conditions such as intestinal obstruction, acute appendicitis, pancreatitis and urinary stone diseases, aortic aneurysm rupture, mesenteric ischemia, ectopic pregnancy rupture [1].

AAP accompanied with flank pain suggest urinary stone disease and considered among the non-inflammatory pathologies [5, 6]. The abdominal pain is theoretically classified in textbooks as right/left/upper/lower quadrant pain, but the signs and symptoms are mostly presented as intermingled pictures [2].

Although pain localization, intensity and examination findings may be guiding for a probable diagnosis, a wide range of diagnostic tools from the simple urinalysis and complete blood count up to higher cost computerized tomography and magnetic resonance imaging may often be needed. A wide variety of pathologies are considered in the differential diagnosis of flank pain, AAP and many diseases which require elaborate work-up. Higher costs of these sophisticated diagnostic tools have led investigators to study cost-effective simple diagnostic methods including the neutrophil-to-lymphocyte ratio (NLR). Initially, The NLR was developed in 2001 by Záhorec [7] in order to provide a readily measurable parameter reflecting the severity of the stress and systemic inflammation in intensive care patients with shock, multiple trauma, major surgery or sepsis.

Previously, the NLR was considered to be an indicator in inflammatory diseases, however, different conditions are currently known to cause NLR alteration as well [8-10]. The NLR has been reported to be a useful indicator in the diagnostic and treatment evaluation of many benign and malignant diseases [9, 11, 12]. A few limited studies have been recently published in which the diagnostic value of NLR in AAP was reported [13-15].

The aim of the present study is to evaluate the diagnostic distribution of patients with abdominal and flank pain admitted to ED with diagnosis of urinary stone disease and other inflammatory conditions as well as to compare them in terms of NLR and other parameters.

METHODS

After receiving approval from the ethics

committee, data of patients having right and/or left flank pain accompanied with AAP admitted to the emergency department of our institution between February 2015-February 2016 were retrospectively reviewed in the study. Demographic characteristics such as age, sex, medical history, comorbidities as well as blood count and urinalysis results immediately taken in the ED were noted. Additionally, definitive diagnoses of urinary stone disease, acute cholecystitis, appendicitis, ovarian cyst, urinary tract infection and cholecystitis, obtained with abdominal ultrasound (US), computed tomography (CT) and other laboratory work-up results in all patients were recorded. The NLR were calculated using data from the complete blood count (CBC). CBC and urinalysis were performed using a full assessment Sysmex XT-2000 and Erba Mannheim Uro-dipcheck 400e devices respectively.

Endocrinological, cardiological and other systemic comorbidities; regular medication; drug/alcohol abuse; nonsteroidal anti-inflammatory drug use within the last week; steroid use including ointment formulas within the last three months; upper respiratory infection within the last three weeks; pregnancy; insufficient history information on the evaluation form and any hematological, biochemical or serological abnormalities such as hyperlipidemia, hyperthyroidism, anemia, vitamin deficiency (D3 and B12), leukocytosis or leukopenia according to laboratory studies were exclusion criterion.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program for statistical analysis were used for statistical analyses. In order to evaluate study data, Mann-Whitney U test was used in descriptive statistical methods (mean, standard deviation, median, frequency, rate, minimum, maximum) as well as in the two-group comparisons of quantitative data with non normal distribution. For three or more groups with normal distribution Kruskal Wallis test was used. In the comparison of qualitative data, Pearson's chi-square test and Fisher-Freeman-Halton test were used. To determine cut-off values for parameters, diagnostic screening tests (sensitivity, specificity, PPV, NPV) and ROC curve analysis were used. Significance was considered when $p < 0.05$.

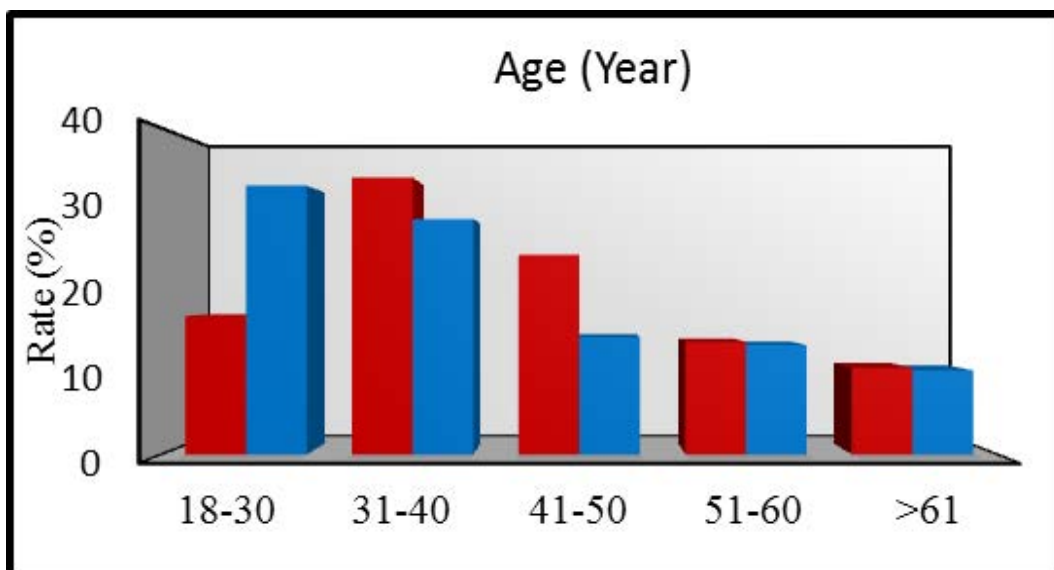


Figure 1. Age intervals according to stone status [Red: Stone (+), Blue: Stone (-)]

RESULTS

Of the 191 patients 51.3% (n = 98) were males, 48.7% (n = 93) were females (*p* > 0.05). The age ranged from 18 to 86, with average of 40.30 ± 13.96 years. Stone status according to gender was statistically significant (*p* < 0.01). Urinary stone disease incidence was frequent between ages 31-40 (Figure 1).

The diagnoses of the patients with flank pain admitted to emergency department were urolithiasis

(48.7%), urinary tract infection (26.4%), unidentified abdominal pain (13.7%), acute appendicitis (3.6%), ovarian cyst (1%) and acute cholecystitis (0.5%).

The white blood cell count (WBC), NLR and platelet (PLT) counts of the patients included in the study were evaluated. WBC and PLT values of patients did not show a statistically significant difference related to stone status (*p* = 0.456; and *p* = 0.876; respectively) (Table 1). NLR of stone patients showed a statistically significant difference without gender discrimination (*p* = 0.009; *p* < 0.01) and NLR values of the patients

Table 1. CBC evaluation of the patients

		Total (n = 191)	Stone (+) (n = 94)	Stone (-) (n = 97)	<i>p</i> value
WBC	Min-Max (Median)	2.8-29.1 (9.3)	4.6-16.5 (9.1)	2.8-29.1 (9.5)	0.456
	Mean ± SD	9.89 ± 3.45	9.64 ± 2.88	10.14 ± 3.92	
NLR	Min-Max (Median)	0.7-20.8 (2.4)	0.7-10 (2)	1-20.8 (2.9)	0.009**
	Mean ± SD	3.37 ± 3.00	2.68 ± 1.86	4.04 ± 3.67	
PLT	Min-Max (Median)	80-571 (238)	106-400 (243)	80-571 (235)	0.876
	Mean ± SD	248.52 ± 62.54	245.71 ± 56.28	251.25 ± 68.25	

CBC = complete blood count, NLR = neutrophil-to-lymphocyte ratio, PLT = platelet, SD = standard deviation, WBC = white blood cell, *MannWhitney U Test: ***p* < 0.05

Table 2. Diagnostic screening tests and ROC curve results

	Diagnostic Scan				ROC Curve	
	Cutoff	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Area 95% Confidential Interval
NLR	≤ 2.16	59.57	61.86	60.20	61.20	0.610 0.530-0.689

NLR = neutrophil-to-lymphocyte ratio

with stone were significantly lower than those without stone. After radiological examinations performed in 94 patients with stone, it was seen that 29.8% of the stones were in the kidney, 23.4% in the proximal ureter and 46.8% in the distal ureter (NLR respectively; 2.45 ± 1.41 ; 3.28 ± 2.60 ; 2.52 ± 1.65). The anatomic location of urinary stone and the NLR values did not show a statistically significant relationship ($p = 0.667$).

Considering the significance of NLR, a cut-off point was calculated using ROC analysis and diagnostic screening tests; NLR cut off points for stone (+) patients was assessed as ≤ 2.16 . Standard error of 61.1% under ROC curve was 4.1% (Table 2 and Figure 2).

There is a statistically significant relationship between NLR cut-off value 2.16 and stone status ($p = 0.003$). When NLR value is 2.16 or less, the risk of stone positivity is 2.34 fold increased. Odds ratio for NLR was 2.390 (95% CI: 1.337-4.272).

DISCUSSION

In this study the relationship between NLR, WBC and PLT measurement and urinary tract stones (renal and ureteral stones) was evaluated in patients admitted to ED with abdominal pain accompanied by flank pain. Lower NLR was found to be more significant than WBC and PLT assessment in patients with stones compared to those without stones.

Urinary tract stones usually develop between the ages of 20-49 and make peak in 3rd and 4th decades. It is usually more common in men than in women [16]. In our study, the mean age was 31-40 years and most of the patients with urinary stones most were male as well ($n = 65/94$, 69.1%).

NLR, platelet/lymphocytes ratio (PLR) and systemic immune inflammatory index have been subject of many studies [17-20]. Previously the link between NLR ratio and cardiovascular diseases as well as malignancies were evaluated in numerous

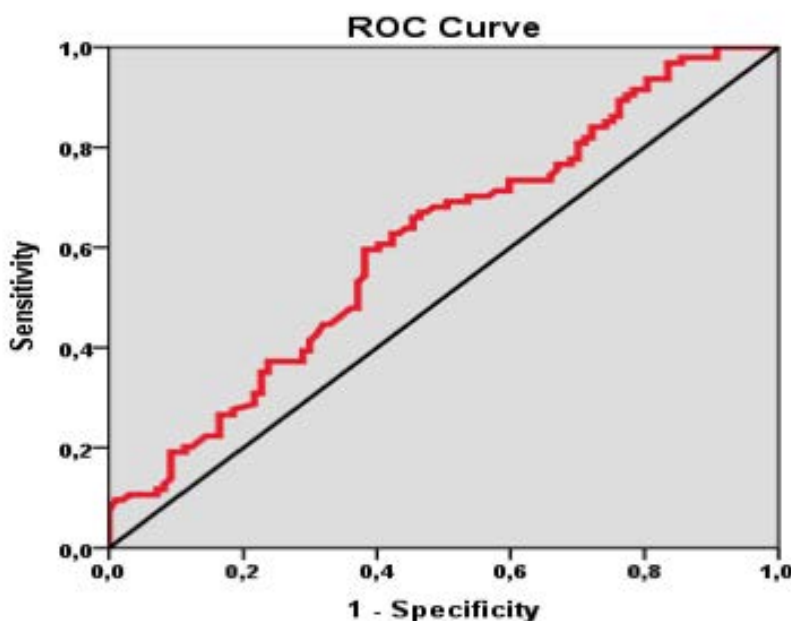


Figure 2. ROC curve according to stone status

reports [21-23]. Later, the importance of NLR among diagnostic and prognostic parameters of miscellaneous illnesses were reported [10, 24-26]. In our study, we investigated the role of NLR in differential diagnosis of patients presenting with flank pain to ED. There are relatively few publications evaluating NLR in patients admitted to ED due to abdominal pain, flank pain and similar symptoms [13, 14, 27-29].

In a study of Acar *et al.* [6] in which acute appendicitis and renal colic were compared, NLRs for acute appendicitis and renal colic were calculated as 8.48 ± 0.39 and 4.96 ± 0.16 respectively with a cut-off value of 3.30. Likewise, inflammation markers such as WBC, red cell distribution width (RDW), mean platelet volume (MPV), PLR and NLR were cited to be useful in the differential diagnosis of renal colic with acute appendicitis in this study.

In 2014 Uyeturk *et al.* [27] grouped patients in urinary stone positive and stone free arms, they have found a higher NLR [app. 2.5 (0.7-8.4)] in stone arm versus stone free arm. In parallel to these data, NLR value in our study was lower in flank pain due to urinary stone disease compared to no stone group (2.68 ± 1.86) which was statistically significant. However, our cut-off value was 2.16 and lower than those of Acer *et al.* [6] and Uyeturk *et al.* [27]. Additionally, WBC and PLT results were not statistically significant in the present study.

There were mostly inflammation related cases in the group which we compared to stone cases. In renal colic, intraluminal pressure increases due to ureteral obstruction during the acute phase and then, nerve endings in the mucosa and muscular layer are stimulated, leading to pain. Evidence of inflammation is not usually observed [30].

In a similar study, WBC and neutrophil ratio varied depending on stone size and location, additionally these values were higher in secondary renal colic cases [28]. In the present study NLR was lower in urinary stone cases and yet, neither the location (kidney or ureter) nor the size had a significant effect on these values. This data remains to be evaluated in further prospective studies.

Limitations

Our study has some limitations; first, the comparative group displayed a wide variety of diagnoses in contrast to urolithiasis patients, hence

different statistical evaluation would be more suitable for each of these conditions but the number of patients in our subgroups were low. However, all these subgroups had inflammatory pathologies which lead us to assign inflammatory conditions as the comparison group. The retrospective nature of the study is another limitation. Since smoking and obesity have been previously reported to have a link with increased NLR, the fact that we did not take body mass index and smoking status into consideration in our patients is another limitation [18, 19]. Lastly, not all patients with AAP and flank pain, but only the patients undergone advanced imaging methods were included in the study due to retrospective nature of the study.

CONCLUSION

In conclusion, as the diagnosis and treatment of urolithiasis cases are time consuming and require elaborate methods, NLR may be a simple method in the differential diagnosis of pain due to urinary stone disease or inflammatory condition. Our results should be further evaluated with comprehensive prospective studies.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

- [1] O'Brien MC. Acute abdominal pain. Tintinalli's emergency medicine: a comprehensive study guide New York: McGraw-Hill. 2011;p. 2120.
- [2] van Randen A, Laméris W, van Es HW, van Heesewijk HPM, van Ramshorst B, Ten Hove W, et al. A comparison of the accuracy of ultrasound and computed tomography in common diagnoses causing acute abdominal pain. *Eur Radiol* 2011;21:1535-45.
- [3] Pitts SR, Niska RW, Xu J, Burt CW. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Natl Health Stat Report* 2008;6:1-38.
- [4] Emet M, Eroğlu M, Aslan Ş, Öztürk G. [Approach to patient

with abdominal pain]. *Eurasian J Med* 2007;39:136-41. [Article in Turkish]

[5] Marincek B. Nontraumatic abdominal emergencies: acute abdominal pain: diagnostic strategies. *Eur Radiol* 2002;12:2136-50.

[6] Acar E, Ozcan O, Deliktaş H, Beydilli H, Kırılı İ, Alataş ÖD, et al. Laboratory markers has many valuable Parameters in the discrimination between acute appendicitis and renal colic. *Ulus Travma Acil Cerrahi Derg* 2016;22:17-22.

[7] Zahorec R. Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratisl Lek Listy* 2001;102:5-14.

[8] Koh CH, Bhoo-Pathy N, Ng KL, Jabir RS, Tan GH, See MH, et al. Utility of pre-treatment neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as prognostic factors in breast cancer. *Br J Cancer* 2015;113:150-8.

[9] Durmus E, Kivrak T, Gerin F, Sunbul M, Sari I, Erdogan O. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are predictors of heart failure. *Arq Bras Cardiol* 2015;105:606-13.

[10] Bahadır A, Baltacı D, Türker Y, Türker Y, Iliev D, Öztürk S, et al. Is the neutrophil-to-lymphocyte ratio indicative of inflammatory state in patients with obesity and metabolic syndrome? *Anatol J Cardiol* 2015;15:816-22.

[11] Kurtul S, Sarlı B, Baktir AO, Demirbas M, Saglam H, Doğan Y, et al. Neutrophil to lymphocyte ratio predicts SYNTAX score in patients with non-ST segment elevation myocardial infarction. *Int Heart J* 2015;56:18-21.

[12] Hyun S, Kwon S, Cho S, Park S, Jung W. Can the neutrophil-to-lymphocyte ratio appropriately predict carotid artery stenosis in patients with ischemic stroke?-A retrospective study. *J Stroke Cerebrovasc Dis* 2015;24:2646-51.

[13] Küçük E. The change of neutrophil lymphocyte ratio in acute appendicitis. *Med-Science* 2015;4:2379-87.

[14] Shimizu T, Ishizuka M, Kubota K. A lower neutrophil to lymphocyte ratio is closely associated with catarrhal appendicitis versus severe appendicitis. *Surg Today* 2016;46:84-9.

[15] Yardımcı S, Ugurlu MU, Coskun M. Neutrophil-lymphocyte ratio and mean platelet volume can be a predictor for the severity of acute appendicitis. *Ulus Travma Acil Cerrahi Derg* 2016;22:163-8.

[16] Serinken M, Karcioğlu O, Turkcuer I, Ozkan HI, Keysan MK, Bukiran A. Analysis of clinical and demographic characteristics of patients presenting with renal colic in the emergency department. *BMC Res Notes* 2008;1:79.

[17] Akdag S, Akyol A, Asker M, Duz R, Gumrukcuoglu HA. Platelet-to-lymphocyte ratio may predict the severity of calcific aortic stenosis. *Med Sci Monit* 2015;21:3395-400.

[18] Furuncuoğlu Y, Tulgar S, Dogan AN, Cakar S, Tulgar YK, Cakiroglu B. How obesity affects the neutrophil/lymphocyte and

platelet/lymphocyte ratio, systemic immune-inflammatory index and platelet indices: a retrospective study. *Eur Rev Med Pharmacol Sci* 2016;20:1300-6.

[19] Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res* 2014;20:6212-22.

[20] Tulgar YK, Cakar S, Tulgar S, Dalkilic O, Cakiroglu B, Uyanik BS. The effect of smoking on neutrophil/lymphocyte and platelet/lymphocyte ratio and platelet indices: a retrospective study. *Eur Rev Med Pharmacol Sci* 2016;20:3112-8.

[21] Chua W, Charles KA, Baracos VE, Clarke SJ. Neutrophil/lymphocyte ratio predicts chemotherapy outcomes in patients with advanced colorectal cancer. *Br J Cancer* 2011;104:1288-95.

[22] Akpek M, Kaya MG, Lam YY, Sahin O, Elcik D, Celik T, et al. Relation of neutrophil/lymphocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. *Am J Cardiol* 2012;110:621-7.

[23] Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol* 2008;102:653-7.

[24] Günay E, Sarınc Ulaşlı S, Akar O, Ahsen A, Günay S, Koyuncu T, et al. Neutrophil-to-lymphocyte ratio in chronic obstructive pulmonary disease: a retrospective study. *Inflammation* 2014;37:374-80.

[25] Kalelioglu T, Akkus M, Karamustafalioglu N, Genc A, Genc ES, Cansiz A, et al. Neutrophil-lymphocyte and platelet-lymphocyte ratios as inflammation markers for bipolar disorder. *Psychiatry Res* 2015;228:925-7.

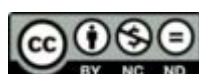
[26] Wu G, Yao Y, Bai C, Zeng J, Shi D, Gu X, et al. Combination of platelet to lymphocyte ratio and neutrophil to lymphocyte ratio is a useful prognostic factor in advanced nonsmall cell lung cancer patients. *Thorac Cancer* 2015;6:275-87.

[27] Uyeturk U, Dagistan E, Aktas G, Ozyalvacı ME, Tekce H, Yilmaz B. Association between urinary stone disease and perirenal tissue thickness. *Nat J Med Res* 2014;4:193-6.

[28] Sfoungaristos S, Kavouras A, Katafigiotis I, Perimenis P. Role of white blood cell and neutrophil counts in predicting spontaneous stone passage in patients with renal colic. *BJU Int* 2012;110(8 Pt B):E339-45.

[29] Küçük A, Erol MF, Senel S, Eroler E, Yumun HA, Uslu AU, et al. The role of neutrophil lymphocyte ratio to leverage the differential diagnosis of familial Mediterranean fever attack and acute appendicitis. *Korean J Intern Med* 2016;31:386-91.

[30] Müslümanoğlu AY, Tepeler A. Renal colic, diagnosis and treatment. *Marmara Med J* 2008;21:187-92



This is an open access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.