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ORIGINAL ARTICLE

The Role of the NLR and PLR in Urinary Tract Infection

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SUMMARY

Background: **Urinary tract infections are common diseases especially seen in bedridden patients. Urine culture, which is the gold standard in the diagnosis of this disease, is an expensive examination, results take a long time, and not available in every center. The objective of this study is to explain the role of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) in urinary tract infections.**

Methods: **For the research, urine culture, NLR, and PLR values of 406 patients, who had urinary tract infections and were registered in Antalya Training and Research Hospital home health services unit, were examined from the health records. In the study, NLR and PLR were studied in blood. In addition, NLR and PLR values of 414 participants were examined as the control group.**

Results: **The mean NLR and PLR values of the participants with urinary tract infection were 4.624 ± 5.818 and 176.645 ± 110.051. The mean NLR and PLR values of the participants without urinary tract infection were 2.117 ± 1.266 and 121.945 ± 53.735. NLR and PLR values of the participants with and without urinary tract infection were compared, and the result was statistically significant (p = 0.000 and p = 0.000, respectively). Urine culture, NLR and PLR values were compared in the patients with urinary system infection. NLR and PLR were lower in the patients with positive urine culture than the patients with negative urine culture; however, the result was statistically insignificant (p = 0.610 and p = 0.702, respectively).**

Conclusions: **According to our results, NLR and PLR were higher in the patients with urinary tract infection than the in healthy volunteer control group. Therefore, it is thought that the clinical judgement of symptoms and complaints comes first and then the NLR and PLR can be used as inflammatory markers in patients with urinary tract infection.**

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KEY WORDS

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INTRODUCTION

Patients, who receive home healthcare service are bedridden or semi-bedridden individuals with many chronic diseases, and most of them are elderly and frail. In these patients, the use of invasive catheters such as urinary catheters, nasogastric tubes and percutaneous endoscopic gastroscopy is common. Therefore, the frequency of infectious diseases is higher in patients who receive home healthcare service compared to the community. Urinary tract infections cover infections in the kidneys, ureters, bladder or urethra. While different symptoms

can be observed in each urinary tract organ infection, these symptoms may also coexist in complex urinary tract infections. While back and flank pain, high fever, shivering, nausea and vomiting are frequently encountered in kidney and ureter infections, dysuria is prominent in cystitis and urethritis. All urinary tract infections are common diseases seen in bedridden patients [1].

Some complications that may be caused by untreated urinary tract infections are perinephric cellulitis and abscesses, septic shock, renal dysfunction, hematological dysfunctions such as anemia or thrombocytopenia and preeclampsia in pregnant women. The first way to prevent complications caused by urinary tract infections is to diagnose the disease early and start the treatment in the early phase [1,2].

Complete urinalysis, which is frequently used to diagnose urinary tract infections, may give inaccurate results due to contamination in bedridden patients receiving home healthcare service. Urine culture, which is the gold standard in the diagnosis of this disease, is an expensive examination that gives results after 1 to 3 days and cannot be performed in every center. On the other hand, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are increasingly used as inflammation markers, and are easily accessible markers providing quick results. In recent years, they have been the subject of research in different medical fields [3-5]. The reason for conducting the study is to look for an answer to the following question: "Can an alternative examination that can help the diagnosis in bedridden patients with urinary tract infection be provided?" The objective of this study is to determine the role of NLR and PLR in urinary tract infections.

MATERIALS AND METHODS

For the study, the records of people who received home healthcare services from Antalya Training and Research Hospital between November 1, 2017, and April 30, 2020, were retrospectively scanned. The patients with urinary tract infection and receiving home healthcare services constituted the case group, and the healthy individuals who applied to polyclinics for other reasons constituted the control group. The sample size was not calculated in the study, and all patients who met the inclusion criteria for the case group were included in the study. Four hundred and six people in total were suitable for the research criteria and included in the study. For the control group, the records of the people who applied to the report polyclinic between November 1, 2017, and December 31, 2018, were retrospectively scanned, and 414 people were included in the study. The total number of the participants included in the study was 820. All results of the participants were obtained from their health records.

Research Inclusion Criteria:

For the case group:

1. Being registered in the home healthcare services unit between November 1, 2017, and April 30, 2020
2. Presenting with the complaints of dysuria
3. Having hemogram and urine culture tests performed on the same day
4. The diagnosis of urinary tract infection established as a result of the physician assessment

For the control group:

1. Absence of an active complaint
2. Being 18 years old and above
3. Applying to the family medicine polyclinic for administrative reasons between November 1, 2017, and December 31, 2018. These participants were the people who applied to the family medicine polyclinic to obtain an ability to work report.

Hemogram, urine culture and, if evaluated, sedimentation and CRP values of 406 participants included in the case group were analyzed. Only the hemogram values of 414 participants included in the control group were examined. Primary outcomes in the study were NLR, PLR, and urine culture. In the study, NLR and PLR were studied in blood.

The ethics committee approval was obtained from SBU Antalya Training and Research Hospital Clinical Researches Ethics Committee with the decision number 12/30 and date May 2nd, 2019.

RESULTS

Eight hundred twenty participants were included in the study. Among the participants, those with urinary system infection were included in the first group (n = 406); those who did not have a health problem but came to the polyclinic to have a health check-up for administrative purposes were included in the second group (n = 414). The mean age of the participants was 53.5 ± 25.3. In the study, the number of females was higher in the group with urinary tract infection. The mean age of the group was 73.9 ± 18. The control group consisted of the individuals who did not have any complaints and applied to have a routine health check-up. In this group, males constituted the majority. In addition, the mean age of the control group participants was quite low, with an average of 33.3 ± 11.4. Of the participants, 85.221% (n = 346) with urinary tract infection had urinary catheters; there were no participants with urinary catheters in the control group.

When the distribution of chronic diseases of the participants was examined, 97.5% of the participants in the group with urinary tract infection had at least one chronic disease. According to their frequencies, the diseases were as follows: hypertension (40.9%), diabetes mellitus (24.1%), dementia (24.1%), malnutrition (21.9%), cerebrovascular disease (CVD) (18.5%), hemiplegia (17.2%), coronary artery disease (15%), chronic obstructive pulmonary disease (COPD) (10.3%), hyper-

Table 1. Distribution of inflammatory markers in urine culture.

Groups	Urine culture negative (n = 189)		Urine culture positive (n = 217)		p-value
	Mean	Standard deviation	Mean	Standard deviation	
NLR	4.8	6.7	4.5	4.9	0.610
PLR	178.9	117.7	174.7	103.2	0.702

Table 2. Distribution of laboratory markers in the presence of urinary tract infection.

Groups	Case (n = 406)		Control (n = 414)		T	p
	Mean	SD	Mean	SD		
Hemoglobin	11.7	1.9	14.5	6.5	-8.0	0.000
Hematocrit	36.0	5.8	41.7	4.9	-15.2	0.000
Neutrophil	6.3	4.2	4.7	1.7	7.3	0.000
Platelet	271.6	109.2	273.5	70.6	-0.3	0.763
Lymphocyte	1.9	1.2	2.4	0.7	-7.8	0.000
MCV	86.0	8.3	84.0	6.4	3.8	0.000
WBC	9.1	4.7	8.2	4.1	3.2	0.001
RBC	4.3	1.0	5.0	0.6	-13.2	0.000
NLR	4.6	5.8	2.1	1.3	8.6	0.000
PLR	176.6	110.1	121.9	53.8	9.1	0.000
Mentzer Index	21.2	5.5	17.1	3.0	13.2	0.000

Table 3. Distribution of laboratory markers in the presence of a chronic disease.

Groups	Chronic disease no (n = 373)		Chronic disease yes (n = 447)		t	p
	Mean	Sd	Mean	Sd		
Hemoglobin	14.5	6.9	12.0	2.0	7.4	0.000
Hematocrit	41.7	5.1	36.5	5.9	13.3	0.000
Neutrophil	4.8	1.8	6.1	4.0	-5.7	0.000
Platelet	277.9	73.0	268.2	104.7	1.5	0.121
Lymphocyte	2.4	0.7	1.9	1.2	6.9	0.000
MCV	83.8	6.6	86.0	8.0	-4.1	0.000
WBC	8.3	4.3	9.0	4.5	-2.3	0.024
RBC	5.0	0.6	4.3	0.9	12.1	0.000
NLR	2.2	1.4	4.6	5.6	-7.3	0.000
PLR	124.3	56.2	169.7	107.1	-7.4	0.000
Mentzer Index	17.1	3.2	20.9	5.4	-12.0	0.000

lipidemia (9.4%) and Parkinson's (8.6%). Of the participants in the control group, 12.3% had at least one chronic disease. Their distribution was as follows: hypertension (2.7%), diabetes mellitus (2.7%), hypothyroidism (1.2%), depression (1%), asthma (1%), COPD (0.7%), hyperlipidemia (0.7%) and others (2.3%).

In the study, 53.4% (n = 217) of the participants with urinary tract infection had bacterial growth in their urine culture. The rates of reproduction in urine culture were as follows: 58.5% *E. coli*, 13.4% *klebsiella*, 10.1% *pseudomonas*, 4.1% *enterococcus*, 3.7% *candida* and 10.1% other.

In the study, urine culture, NLR, and PLR values of patients with urinary tract infection were compared in order to evaluate the relationship between urinary culture, NLR, and PLR. Accordingly, the NLR and PLR values of the participants with negative urine culture were higher than those with positive urine culture. However, the result was not statistically significant. The distribution is shown in Table 1.

When the correlation analyses between the ages of the participants and their hemoglobin, hematocrit, neutrophil, platelet, lymphocyte, MCV, NLR and PLR values were examined, it was found that the relationship of age with hemoglobin was r = -0.247 negative (p = 0.000), with hematocrit r = -0.422 negative (p = 0.000), with lymphocyte r = -0.19 negative (p = 0.000), with neutrophil r = 0.195 positive (p = 0.000), with MVC r = 0.171 positive (p = 0.000), with NLR r = 0.216 positive (p = 0.000), and with PLR r = 0.21 positive (p = 0.000).

When the correlation analysis between NLR and PLR was examined by including all participants, a positive relationship was found (r = 0.131), a positive relationship was found only in the group with urinary tract infection (r = 0.568), and a positive relationship was found in the control group a result of NLR and PLR correlation (r = 0.616).

Receiver operating characteristic (ROC) curve analysis was used to determine prediction points of NLR and PLR levels for urinary tract infection. The optimal cutoff value of NLR was 6.593, sensitivity 18.0%, specificity 86.2%, and under the ROC curve (AUROC) 0.509. The optimal cutoff value of PLR was 328.062, sensitivity 10.8%, specificity 91.5%, and under the ROC curve (AUROC) 0.495.

In the study, females had more chronic diseases than males, and chronic drug use was more common in females compared to males (p = 0.000 and p = 0.000). When urine cultures were evaluated by gender, the ratio of females with positive urine culture was higher compared to males, but the difference was not statistically significant (p = 0.470).

When the participants are divided into groups as those with urinary tract infection and the control group, the distribution of their laboratory values is as in Table 2. NLR and PLR values of the participants with urinary tract infection were statistically significantly higher than the control group.

In the study, while determining the group with urinary tract infection, those who had urine culture and hemogram tests performed on the same day were selected. If CRP and sedimentation were also measured on the same day apart from hemogram and urine culture, those results were also recorded. Accordingly, CRP of 298 participants and sedimentation values of 113 participants from this group were recorded. When the correlation analyses between NLR and sedimentation and CRP were examined, it was found that the relationship of NLR with CRP was r = 0.409 positive and with sedimentation it was r = 0.287 positive. When the correlation analyses between PLR and sedimentation and CRP were examined, it was found that the relationship of PLR with CRP was r = 0.334 positive and with sedimentation it was r = 0.318 positive.

When the participants were evaluated without being divided into groups, hemoglobin, hematocrit, and RBC values of males were statistically significantly higher than females (p = 0.000, p = 0.000, p = 0.000). NLR and PLR values of the participants by gender are as follows: NLR is 3.3 ± 3.9 in females and 3.4 ± 4.7 in males (p = 0.873), and PLR is 150.6 ± 82.3 in females and 147.6 ± 97.6 in males (p = 0.631).

Four hundred forty-seven (54.5%) of the participants had at least one chronic disease, while 373 (45.5%) of the participants had no known chronic diseases. The distribution of laboratory values according to the presence of a chronic disease is shown in Table 3.

DISCUSSION

The gold standard test in the diagnosis of urinary tract infections is urine culture. However, urine culture is an examination where results take a long time, cannot be performed in every center, and is difficult and expensive compared to NLR and PLR measurements. Therefore, we compared urinary culture results and NLR and PLR values of the participants with urinary tract infection. Urine culture results of 406 participants were evaluated. Accordingly, 189 (46.6%) participants had negative urine culture, while 217 (53.5%) participants had positive urine culture. As a result of our research, we expected NLR and PLR values to increase in the participants with positive urine culture (Table 1). It means NLR and PLR are correlated to symptoms better than to bacteriology. However, the comparison results were different contrary to our expectation. The mean NLR and PLR values of the participants with negative urine culture were higher than the participants with positive urine culture, but the result was statistically insignificant. In other words, NLR and PLR are correlated to symptoms better than to bacteriology. Different results were obtained in the studies comparing the NLR and PLR values of participants with positive culture results in different diseases. High NLR (≥ 5) and high PLR (≥ 200) have been shown to be associated with pulmonary cavitation in 137 patients with pulmonary cavitation and positive sputum culture in Japan [6]. In a study where the laboratory markers of malaria patients in Thailand were evaluated, the mean NLR values were 2.8 in P. falciparum, 2.7 in P. vivax, and 2.2 in healthy volunteers, and the difference was statistically significant (p < 0.0001) [7]. In another study, NLR and PLR values of the patients diagnosed with COVID19 were evaluated

with healthy volunteers with nasopharyngeal culture. In that study, the mean NLR and PLR values of COVID19 patients were found as 3.3 ± 2.8 and 169.5 ± 97.5, respectively, and these results were again high compared to healthy volunteers ($p < 0.001$) [8]. In all these studies, a single factor was identified with the culture result and compared with healthy volunteers. However, in our study, the results were grouped as culture positive and culture negative and the compared. The differences in the results are thought to result from this difference. However, there is a need for comprehensive research comparing culture results and inflammatory markers. The use of NLR and PLR markers in diseases with inflammation is increasing day by day. In our study, when the NLR and PLR values of the patients with complaints and symptoms of urinary tract infection and were compared with the control group. NLR and PLR values were found to be statistically significantly higher than the control group. While the mean NLR was 4.6 in the group with infection, the mean NLR was 2.1 in the control group. Similarly, the mean PLR in the group with infection was 176.6, while the mean PLR was 121.9 in the control group. A meta-analysis was published in the Journal of Infection in 2019 [9]. This analysis evaluated the relationships between blood leukocyte ratios and infectious diseases. As a result of this study, it was reported that blood leukocyte ratios increased in bacterial infections such as urinary tract infections, community-acquired pneumonia, diabetic foot infection, and respiratory system diseases, and its use was beneficial [9]. This result was also consistent with our research. Similarly, in a study evaluating inflammatory markers in children with febrile urinary tract infection, WBC, CRP, ESR, and NLR values of the children with acute pyelonephritis were found to be higher than those with lower urinary tract infection ($p < 0.001$) [10]. Furthermore, while NLR was found to be statistically significantly beneficial in a study regarding neonatal sepsis, PLR was not found to be beneficial in the same way [11]. In another study comparing chronic otitis media patients with effusion and healthy individuals, NLR and PLR values were found as 2 and 112.7, respectively, in patients with chronic otitis media with effusion; these values were found as 1.9 and 114.6 in healthy volunteers, respectively. The difference is statistically insignificant [12]. For this reason, it is thought that it would be more accurate to evaluate each infectious disease separately and to determine the appropriate evidence.

Among the participants included in the study, 54.5% had at least one chronic disease, while 45.5% had no known chronic diseases. In the group with urinary tract infection, 97.5% of the participants had at least one chronic disease. NLR and PLR values of those with chronic diseases (mean values, 4.3 and 169.7, respectively) were statistically significantly higher than those without any chronic disease (mean values, 2.2 and 124.3, respectively). The five most common chronic diseases observed in the participants of our study were hypertension, diabetes mellitus, dementia, malnutrition and CVD, respectively. There are studies investigating NLR and PLR values in these chronic diseases, and generally, a relationship has been found between these chronic diseases and inflammatory markers. Studies have revealed that NLR and PLR values increase in coronary artery diseases [13,14]. In a study comparing NLR and PLR values with healthy individuals in terms of diabetes mellitus, it was found that both NLR and PLR values were higher in diabetic patients compared to healthy individuals, with p-values of 0.004 and 0.021 [15]. In fetal malnutrition seen in newborn infants, NLR and PLR values were found to be statistically and significantly higher compared to healthy newborn infants, and p-values were as follows: $p = 0.011$ and $p < 0.001$, respectively [16]. In another study conducted in the elderly population, NLR was found to be higher in patients with malnutrition compared to patients with normal nutritional status ($p = 0.004$) [17]. In a study, where the individuals with ischemic cerebrovascular disease were compared with a healthy control group, WBC, CRP, homocysteine and NLR were found to be higher than healthy individuals ($p < 0.001$) [18]. Therefore, it would not be accurate to explain the high NLR and PLR values in our study only with urinary tract infections. NLR and PLR values increase in many disease types as well as urinary tract infections. The clinical judgement of symptoms and complaints comes first and after that the NLR and PLR can be used as inflammatory markers in patients with urinary tract infection.

Declaration of Interest:
There is no conflict of interest for the author.

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