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RESEARCH ARTICLE

EVALUATION OF HEMATOLOGICAL PARAMETERS IN DIFFERENTIAL DIAGNOSIS OF ACUTE PYELONEPHRITIS AND CYSTITIS IN ADULTS

***Alper Bitkin, Mustafa Aydın, Lokman Irkilata, Ebubekir Akgüneş and Mustafa Kemal Atilla**

Samsun Training and Research Hospital Urology Clinic, University of Health Sciences, Samsun, Turkey

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ABSTRACT

Objectives: This study aimed to evaluate the usefulness of several hematological parameters in the diagnosis of acute pyelonephritis and cystitis, as well as in differentiating between these two diseases. **Materials and Methods:** The patients were divided into two groups: those treated for acute pyelonephritis (APN) and those treated for cystitis. Complete blood counts were obtained from all the patients, including the mean platelet volume (MPV), platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), and platelet count. These parameters were recorded and compared between the 2 groups. **Results:** The mean MPV and platelet count values were not significantly different between the two groups ($p=0.473$ and $p=0.977$, respectively). However, the median NLR and PLR values were significantly higher in the pyelonephritis group than in the cystitis group ($p<0.001$ and $p=0.001$, respectively). **Conclusions:** The NLR and PLR appear to be useful in differentiating between acute pyelonephritis and cystitis. However, there is a need for additional prospective studies with larger patient numbers.

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INTRODUCTION

Cystitis is characterized by symptoms of dysuria, frequent urination, urgency, and suprapubic pain, and it is identified as a lower urinary tract infection (UTI) (Rhyn *et al*., 1998). Acute pyelonephritis (APN) is an upper UTI involving the kidney parenchyma and renal pelvis. Clinically, frequent urination, dysuria, side pain, and fever (>38.5°C) can be seen in pyelonephritis cases. With regard to the laboratory findings, pyuria, bacteriuria, and positive urinary cultures can be seen in both of these diseases. Additionally, during the acute phase reaction in pyelonephritis, the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and white blood cells may increase (Donnenberg *et al*., 1996). The identification of APN is most commonly done clinically. However, the existence of lower urinary tract symptoms does not exclude APN, even if there are no upper urinary tract symptoms (Norris *et al*., 2008). APN is correlated with morbidity and mortality, and it may result in renal failure and sepsis if there is an early diagnosis but no treatment (Bergeron, 1995). Therefore, clinicians require better methods to differentiate between these diseases more quickly and practically. Recently, there have been a lot of studies involving the hematological parameters, such as the lymphocytes, neutrophils, and platelets, as inflammatory signs (Zahorec, 2001; Bitkin *et al*., 2018).

Corresponding author: Alper Bitkin,
Samsun Training and Research Hospital Urology Clinic, University of Health Sciences, Samsun, Turkey.

One of these hematological parameters, the mean platelet volume (MPV) is an indicator of platelet activation. It has been shown previously that the MPV is useful for the characterization of inflammatory disorders (Gunluoglu *et al*., 2017). Additionally, it has also been shown that the MPV is a marker that can be used for the differentiation between APN and cystitis in pediatric patients (Tekin *et al*., 2015). In this study, we evaluated the hematological parameters of APN and cystitis in adults in order to determine whether these parameters could be useful in the discrimination between APN and cystitis.

MATERIALS AND METHODS

From January 2016 through February 2018, we retrospectively examined the patients in our clinic who were treated for cystitis and APN. A diagnosis of cystitis was made in those patients with symptoms of frequent urination, a sense of pressure, and suprapubic pain, in addition to pyuria based on the results of a urine test (10 or more leukocytes per mm^3). A diagnosis of APN was made in those patients with flank pain, fever (>38°C), nausea, and vomiting, in addition to cystitis symptoms and pyuria (based on a urine test), a positive urine culture (>10^4colony-forming units (CFU)/ml in a midstream urine), leukocytosis, and high CRP and ESR values. The patient exclusionary criteria were as follows: history of smoking, recent antibiotic treatment, inflammatory, autoimmune, or chronic infectious diseases, anemia,

Table 1. Comparison of parameters according to group

	Acute Pyelonephritis(n:32)	Cyctitis(n:32)	p
Age± ss (years)	40±13.6	4.7±14.6	0.111
BMI± ss (kg/m²)	25.5±3.5	25.5±2.86	0.975
Platelet (x10^3 µL)*	260.53 ± 78.72	261.06 ± 72.10	0.977
MPV(fL)*	8.45 ± 0.77	8.60 ± 0.91	0.473
Leukocytes(x10^3 µL)*	14.16 ± 5.00	8.16 ± 2.30	<0.001
Lymphocytes (x10^3 µL)*	1.43 ± 0.69	2.03 ± 0.90	0.004
ESR**	60 (18 - 133)	8 (1 - 39)	<0.001
CRP**	14.1 (2.16 - 30)	0.3 (0.1 – 5.1)	<0.001
Neutrophil (x10^3 µL)**	10.8 (3.68 – 21.1)	4.8 (2.5 – 11.6)	<0.001
NLR**	9.19 (1.55 - 24)	2.69 (0.7 - 36)	<0.001
PLR**	207.5 (48.67 – 434.29)	132.42 (57.58 - 2920)	0.001

*arithmetic mean ± standard deviation, **median (min-max)

Table 2. ROC analysis for the acute pyelonephritis group

	Cutoff	Sensitivity	Specificity	PPV	NPV	AUC(area under curve)(95% confidence interval)
NLR	5.71	85.3	78.1	80.6	83.3	0.869
PLR	150	70.6	78.1	77.4	71.4	0.736

hypercholesterolemia, high blood pressure, chronic kidney failure, a liver function disorder, and hematological disease.

Ultrasonography (USG) and computed tomography (CT) imaging were conducted in all of the patients. Each patient's demographic data, complete blood count, biochemistry, urine test, and urine culture parameters were recorded. All the patients were phlebotomized from a peripheral vein, and each blood sample was placed in a blood tube containing ethylene diamine tetra acetic acid for a complete blood count and flow cytometry evaluation (LH 780 hematology analyzer; Beckman Coulter Inc., Miami, FL, USA). The CRP levels were measured via thespectrophotometric method using the Cobas c501 module of the Cobas 6000 series auto analyzer (Roche Diagnostics GmbH, Mannheim, Germany). The ESR levels were measured with an Alifax SIR20 analyzer (Sire Analytical Systems, Udine, Italy). The normal range values for the blood samples were as follows: thrombocytes 130–400 x 10^3 µl, leukocytes 4–10 x 10^3 µ, neutrophils 2–7 x 10^3 µl, lymphocytes 0.8–4 x 10^3 µl, and MPV 7.57–11.58 fl. In addition to these parameters, the platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR) values were determined in all the groups. The specificity, sensitivity, positive predictive values (PPV), and negative predictive values (NPV) of the hematological parameters were compared between the groups.

Statistical Analysis

The data was analyzed using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to determine whether the data was normally distributed. The normally distributed data was compared using the independent samples t-test, while the non-normally distributed data was compared using the Mann-Whitney U test. The cut-off points for the NLR and PLR were determined using a receiver operating characteristic (ROC) analysis. The level of significance was $p<0.05$.

RESULTS

Sixty-four patients with complete medical records were included in this study. The first group consisted of 32 APN inpatients (26 females and 6 males), while the second group consisted of 32 cystitis outpatients (22 females and 10 males). The clinical and demographic data of both groups is shown in Table 1.

The mean platelet counts differed between the groups ($p=0.977$). Similarly, the mean MPV values also differed between the groups ($p=0.473$). The median ESR and CRP levels in the APN group were found to be significantly higher than those in the cystitis group ($p<0.001$). Likewise, the median NLR and PLR levels in the APN group were found to be significantly higher than those in the cystitis group ($p<0.001$ and $p=0.001$, respectively). ROC analyses were conducted due to the significant NLR and PLR levels. The cut-off value for the NLR was found to be 5.71, and those patients with values above this were identified as having APN, while those with values below this were identified as having cystitis. For the NLR, the sensitivity was 85.3% and the specificity was 78.1%. For the PLR, sensitivity was 70,6% and specificity was 78,1%. The data for ROC analysis are shown in Table 2.

DISCUSSION

APN exhibits a large spectrum of symptoms ranging from mere ailments to sepsis (Bass *et al*., 2003). Each year in the USA, approximately 250,000 APN cases are diagnosed, and more than 100,000 patients require inpatient treatment (Hooton *et al*., 1997). The mortality rate connected with pyelonephritis ranges between 1.2% and 33% (Lee at al., 2012; Yoshimura *et al*., 2005). For the diagnosis of APN, evidence of a UTI (found in the urinary system or in culture) and upper UTI signs (fever, trembling, side pain, nausea, vomiting, costovertebral angle sensitivity) are useful. At the same time, cystitis symptoms (frequent urination, a sense of pressure, suprapubic pain) may also be found in these patients (Ramakrishnan *et al*., 2005). While a fever is a significant finding in discriminating between cystitis and pyelonephritis, one in three elderly patients shows no sign of fever. The dominant symptoms in 20% of these patients are gastrointestinal or pulmonary complaints (Bass *et al*., 2003).The laboratory findings of pyelonephritis include pyuria, bacteriuria, and a positive urinary culture, in addition to acute phase reactants, such as increases in the ESR, CRP, and white blood cells (Donnenberg *et al*., 1996). In our study, both the clinical and laboratory findings of the patients were used. Among the clinical findings of pyelonephritis, in addition to the lower urinary tract findings, fevers and costovertebral angle sensitivity were observed. Moreover, in the laboratory findings, the leukocyte count, CRP, and ESR were higher in the APN group ($p<0.001$). However, the diagnostic criteria in the literature are not homogenous (Piccoli *et al*., 2006).

Radiological imaging is not usually performed in non-complicated renal infection patients. The role of imaging lies primarily in the examination of patients who have undergone conventional treatments, but the infection has recurred, or in cases with unusual or permanent symptoms (Stunell *et al*., 2007).In the evaluation of patients with acute bacterial pyelonephritis, CT is the preferred imaging method. It is superior in determining focal parenchymal abnormalities, the extent of the disease, perinephric fluid collection, and abscesses when compared with USG and intravenous pyelography (IVP) (Goldman *et al*., 1991).The sensitivity and specificity of CT in the diagnosis of APN are 86.8% and 87.5%, respectively, while they are 74.3% and 56.7%, respectively for USG (Majd *et al*., 2001). We do not perform imaging in every patient with a UTI in our clinic. However, we do perform USG and/or CT examinations in those patients with side pain and fever, as well as those with continuous symptoms despite treatment. Only those patients with USG and/or CT results were included in our study. Overall, imaging methods are used primarily to determine whether there is a complication, rather than to make a diagnosis. A delay in an APN diagnosis can cause chronic pyelonephritis that may result in sepsis, kidney abscesses, secondary high blood pressure, and renal failure (Tekin *et al*., 2015) Distinguishing between APN and cystitis can sometimes be difficult with standard clinical and laboratory findings, which may cause a latency in the diagnosis. However, imaging procedures are both time consuming and expensive. A complete blood count is an uncomplicated, cheap, and easily accessible method that can be used in almost all laboratories. One of the complete blood count parameters, the leukocyte count, is a commonly used marker for neutrophils and other related parameters, as well as in inflammatory processes (Barbu *et al*., 2011; Thomsen *et al*., 2013). In APN, the leukocyte count is significantly increased (Piccoli *et al*., 2006). In our study, the average leukocyte count in the APN group was 16.1x 10^3 µl, and it was 8.1x 10^3 µl in the cystitis group, which was a statistically significant difference ($p<0.001$). In addition, platelets play a huge role in a variety of inflammatory and infective disease pathogeneses (Hamzeh-Cognasse *et al*., 2015; Nording *et al*., 2015). The MPV is one of the platelet parameters that can be obtained with a complete blood count, but it remains largely ignored by clinicians. The MPV is an indirect sign of thrombocyte function. For example, large thrombocytes are metabolically and enzymatically more active than other thrombocytes because they contain intense granules with more thromboxane A2 (Alper *et al*., 2009). It is believed that the MPV increases in cases of serious inflammation because the platelets are roaming peripherally; in contrast, it is reduced in mild inflammation cases because the large platelets are gathered in the inflammatory area (Gasparyan *et al*., 2010). The platelet count and MPV can be examined as inflammatory signs of disease activity in upper UTIs (Giles, 1981). In addition, it has been shown previously that the MPV is an inflammatory marker of various infective diseases, including acute appendicitis and sepsis (Albayrak *et al*., 2011; Aydemir *et al*., 2015). The MPV is increased in pediatric patients with UTIs, and it has been determined that it can be used to differentiate between APN and cystitis (Bass *et al*., 2003; Lee *et al*., 2015). In our study, there was no difference in the average MPVs between the APN and cystitis groups ($p=0.473$). Contrary to pediatric patients, we found that the MPV cannot be used to differentiate between these diseases in adults. It has been shown that the hematological parameters are simple and practical inflammatory signs that can play predictive roles (especially the NLR and PLR) in systemic inflammatory processes (Azab *et al*., 2013; Dirican *et al*., 2013).They are also some of the most sensitive and specific biological markers in the classification of patients with inflammation during the perioperative period in cancer surgery, and as suggested by cardiologists (Dirican *et al*., 2013; Proctor *et al*., 2011). In our study, the median NLR value in the APN group was 9.19, and in the cystitis group it was 2.69; this difference was found to be statistically significant ($p<0.001$). Similarly, the median PLR value in the APN group was found to be higher than in the cystitis group ($p=0.001$, 207.5 – 132.42, respectively). After conducting the ROC analyses of the NLR and PLR values, the cut-off value for the NLR was 5.71; the sensitivity for the APN group was 85.3% and the specificity was 78.1% (PPV=80.6%, NPV=83.3%). The PLR cut-off value was 150, with a sensitivity of70.6% and a specificity of 78.1% (PPV=77.4%, NPV=71.7%).

Conclusions

After reviewing all the values, we did not detect significant statistical differences in the MPV and platelet counts between the APN and cystitis groups. These parameters seemed to have no diagnostic value in the differentiation between APN and cystitis. When considering the fact that APN group exhibited significantly higher NLR and PLR values than the cystitis group, these two parameters can be used in the discrimination between these diseases. The circumstances that limited our study include the fact that it was retrospective, and that we did not have a sufficient number of patients. Because it is cheap, fast, and easily accessible, a complete blood count can be used for the immediate diagnosis of APN in order to begin treatment more quickly, so that it does not lead to life-threatening situations (such as sepsis). However, more data is required, as well as additional prospective studies with more patients, in order to determine the reliability of these values.

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REFERENCES

Albayrak, Y., Albayrak, A., Albayrak, F., Yildirim, R., Aylu, B. *et al*. 2011. Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis. *Clin Appl Thromb Hemost.* 17, 362–366.

Alper, A.T., Sevimli, S., Hasdemir, H., Nurkalem, Z., Guvenc, T.S. *et al*. 2009. Effects of high altitude and sea level on mean platelet volume and platelet count in patients with acute coronary syndrome. *J Thromb Thrombolysis*. 27: 130–134.

Aydemir, H.,Piskin, N., Akduman, D., Kokturk, F., Aktas, E. 2015.Platelet and mean platelet volume kinetics in adult patients with sepsis. *Platelets.* 26, 331–335.

Azab, B., Chainani, V., Shah, N., McGinn, J.T. 2013. Neutrophil-lymphocyte ratio as a predictor of major adverse cardiac events among diabetic population: a 4-year follow-up study. Angiology. 64:456-65.

Barbu, C., Iordache, M., Man, M.G. 2011. Inflammation in COPD: pathogenesis, local and systemic effects. *Rom J Morphol Embryol.* 52:21-7.

Bass, P.F. 3d, Jarvis, J.A., Mitchell, C.K. 2003. Urinary tract infections. Prim Care. 30:41-61.

Bergeron, M.G. 1995. Treatment of pyelonephritis in adults. *Med Clin North Am.,* 79:619-49.

Bitkin, A., Aydın, M., Özgür, B.C., Irkilata, L., Akgunes, E. *et al*. 2018. Can haematologic parameters be used for differential diagnosis of testicular torsion and epididymitis? Andrologia. Feb;50(1).

Dirican, A., Ekinci, N., Avci, A., Akyol, M., Alacacioglu, A. *et al*. 2013. The effects of hematological parameters and tumor-infiltrating lymphocytes on prognosis in patients with gastric cancer. *Cancer Biomark.* 13:11-20.

Donnenberg, M., Welch, R. 1996. Virulence determinants in uropathogenic E. coli. In: Mobley H, Warren J (eds) Urinary tract infection: molecular pathogenesis and clinical management. American Society for Microbiology Washington, DC. 135–174.

Gasparyan, A.Y., Sandoo, A., Stavropoulos-Kalinoglou, A., Kitas, G.D. 2010. Mean platelet volume in patients with rheumatoid arthritis: the effect of anti-TNF-alpha therapy. *Rheumatol Int.* 30, 1125–1129.

Giles, C. 1981. The platelet count and mean platelet volume.*Br J Haematol.*48,31–37.

Goldman, S.M., Fishman, E.K. 1991. Upper urinary tract infection: the current role of CT, ultrasound and MRI. Semin Ultrasound CT MR. 12:335–360.

Gunluoglu, G., Yazar, E.E., Veske, S.N., Seyhan, E.C., Altin, S.2017. Mean platelet volume as an inflammation marker in active pulmonary tuberculosis. Multidiscip Respir Med. 9:11.

Hamzeh-Cognasse, H.,Damien, P., Chabert, A., Pozzetto, B., Cognasse, F., Garraud, O. 2015. Platelets and infections - complex interactions with bacteria. *Front Immunol.* 6, 82.

Hooton, T.M., Stamm, W.E. 1997. Diagnosis and treatment of uncomplicated urinary tract infection. Infect Dis Clin North Am. 11:551-81.

Lee, I.R., Shin, J.I., Park, S.J., Oh, J.Y., Kim, J.H. 2015. Mean platelet volume in young children with urinary tract infection. Sci Rep. Dec 15;5:18072.

Majd, M., Nussbaum Blask, A.R., Markle, B.M., Shalaby-Rana, E., Pohl, H.G. *et al*. 2001. Acute pyelonephritis: comparison of diagnosis with 99 m-Tc DMSA, SPECT, spiral CT, MR imaging and power Doppler US in and experimental pig model. Radiology. 218 (1):101–108.

Lee, J.H., Lee, Y.M., Cho, J.H. 2012. Risk factors of septic shock in bacteremic acute pyelonephritis patients admitted to an ER. J Infect Chemother. 18:130-3.

Nording, H.M., Seizer, P., Langer, H.F. 2015. Platelets in inflammation and atherogenesis. *Front Immunol.* 6, 98.

Norris, D.L., Young, J.D. 2008. Urinary tract infections: diagnosis and management in the emergency department. *Emerg Med Clin N Am.* 26: 413.

Piccoli, G.B., Consiglio, V., Colla, L., Mesiano, P., Magnano, A. *et al*. 2006. Antibiotic treatment for acute 'uncomplicated' or 'primary' pyelonephritis: a systematic, 'semantic revision'. *Int J Antimicrob Agents*. Aug; 28.

Proctor, M.J., Morrison, D.S., Talwar, D., Balmer, S.M., Fletcher, C.D. *et al*. 2011. A comparison of inflammation-based prognostic scores in patients with cancer. A Glasgow Inflammation Outcome Study. *Eur J Cancer.* 47:2633–41.

Ramakrishnan, K., Scheid, D.C. 2005. Diagnosis and management of acute pyelonephritis in adults. *Am Fam Physician.* Mar 1;71(5):933-42.

Rhyn, R.L., Roche, R.J.1998. Infection in the elderly. In Brilman JC, Quenze RW eds. Infectious Disese in Emergency Medicine. 2nd ed Phıladelphia: Lippincott Raven. 291-316.

Stunell, H., Buckley, O., Feeney, J., Geoghegan, T., Browne, R.F. *et al*. 2007. Imaging of acute pyelonephritis in the adult. *Eur Radiol.* Jul;17(7):1820-8.

Tekin, M., Konca, C., Gulyuz, A., Uckardes, F., Turgut, M. 2015. Is the mean platelet volume a predictive marker for the diagnosis of acute pyelonephritis in children? *Clin Exp Nephrol.* Aug; 19(4):688-93.

Thomsen, M., Ingebrigtsen, T.S., Marott, J.L., Dahl, M., Lange, P. *et al*. 2013. Inflammatory biomarkers and exacerbations in chronic obstructive pulmonary disease. JAMA. 309:2353- 61.

Yoshimura, K., Utsunomiya, N., Ichioka, K., Ueda, N., Matsui, Y. *Et al*. 2005. Emergency drainage from urosepsis associated with upper urinary tract calculi. *J Urol.* 173:458-62.

Zahorec, R. 2001. Ratio of neutrophil to lymphocyte counts—rapid and simple parameter of systemic inflammation and stress in critically ill. Bratislavské Lekárske Listy.102, 5–14.

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