Original Article *Iran J Ped Hematol Oncol. 2019, Vol 9.No 3, 159-165*

Platelet Indices as Useful Indicators of Urinary Tract Infection

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Received: 27 January 2019 **Accepted:** 20 May 2019

Abstract

Background: The changes of platelet parameters can be a useful index for rapid diagnosis of urinary tract infection (UTI), since platelet changes are routinely determined through complete blood count (CBC) test. The correlation between platelet indices, included number (PLTs), mean platelet volume (MPV) and platelet distribution width (PDW), which are the indicators of production and function of platelets, with UTI was evaluated in this study.

Materials and Methods: In this descriptive-analytical study, 97 patients with UTI (patient group) and 117 healthy people (control group). The average age for the patient and the control group was 10.84±6.68 and 11.34±7.1 years old, respectively. This study was done during 2016-2018 in Imam Reza Hospital, Kermanshah, west of Iran. The PLT, MPV, PDW, and other inflammatory indices, including white blood cell, neutrophils, lymphocytes, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were evaluated. The diagnosis of bacteria was done using routine microbiological and biochemical methods. The platelet indices were statistically compared between the patients and the control groups (T test and Chi square test).

Results: The most common isolated gram negative and gram positive bacteria were *E. coli*, *Citrobacter*, and *Staphylococcus aureus*, respectively. In the patient group, PLT number was significantly higher than that in the control group (p=0.0007), while difference of other indices such as MPV, PDW, neutrophils, lymphocytes, CRP, and ESR were not statistically significant between the two groups. In case of UTI with gram positive bacteria, PLT number (p=0.05) was lower but MPV (p=0.02) and PDW (p=0.045) was higher compared to the UTI with gram negative bacteria.

Conclusion: The results of this study showed that the platelet number could be a useful diagnostic index for urinary tract infection. However, more studies need to be done with higher number of patients to evaluate the more details of platelet changes during UTIs.

Keywords: Platelet count, indicators, Urinary Tract Infection

Introduction

Urinary tract infection (UTI) is one of the most common microbial infections which causes severe complications. To prevent bacteremia and kidney damages, as well as, to eliminate infection, rapid diagnosis and antibiotic therapy should be started. Otherwise, there may be the risk of UTI complications and antibiotics resistance (1). Although urine culture is the gold standard for diagnosis of urinary tract infection, it is time consuming and needs 48 h for the result confirmation (2). Therefore, alternative methods of UTI diagnosis which can be faster and more effective are needed. Chang in platelet parameters has been reported as an index for rapidly presumptive diagnosis of urinary tract infection without waiting for urine culture results (3). It has been reported that platelet parameters, especially mean platelet volume (MPV),

can be used as an inflammatory index of immune response during infections (4-7).

Platelets are the smallest blood cells derived from bone marrow megakaryocyte cells and are involved in the hemostasis and coagulation processes (8). When activated, they participate in host defense system through the phagocytosis and the production of free cytotoxic radicals and oxidative molecules (9). Platelets can also enhance the inflammatory process by increasing the leukocyte recruitment and apoptosis prevention of monocytes and neutrophils, as well as, increasing inflammatory mediators such as chemokine and cytokines (3, 10). It has been reported that thrombocytosis occur during the urinary tract infection, which is actually the bone marrow response to the platelet usage during the infection, as they are involved in the host defense system (1). Further, cytokines produced by epithelial cells and leukocytes associate with urinary tract cause thrombocytosis during UTIs (3).

Hematologic markers for infections are included white blood cell count, platelet count (PLTs), Mean platelet volume (MPV), platelet distribution width (PDW), red cell distribution width (RDW), neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), and C-reactive protein (CRP) (9). PLT, as an acute phase reaction, usually increases during the inflammatory process. MPV is the mean size of the platelets, indicating the production rate and stimulation of the platelets (11). In severe inflammation, the MPV increases, which actually shows the increase of platelet activity (12). Another factor indicative of the platelet activation is PDW (13). Both MPV and PDW have been attractive indices for researchers in recent years. However, their roles in diagnosis and management of diseases have not been completely understood (8). The role of platelet parameters in various diseases has been studied, and the information on these parameters is also available for urinary tract infections (4-7). There is no additional cost to the patient for testing platelet parameters, because they are routinely determined with the complete blood count (CBC) test (14). However, there is conflicting information about the effect of urinary tract infection on these platelet parameters. The aim of this study was to evaluate the changes in PLT, MPV, PDW, erythrocyte sedimentation rate (ESR), and CRP in patients with urinary tract infection.

Materials and Methods

This study was approved by Kermanshah University Ethics Committee (approval number: IR.KUMS.REC.1398.137).

This research was performed during 2016-2018 in Imam Reza hospital of Kermanshah city, west of Iran. A total of 97 patients with clinical and laboratory signs of UTI were selected. The clinical findings were included dysuria, frequent urination, flank pain, and cloudy urine. The laboratory findings were included the increase in the number of neutrophils and leukocytes as well as raise of CRP and ESR in blood (15, 16). All 97 patients (test group) showed positive clinical signs and symptoms with the presence of ≥105 bacteria per milliliter of midstream urine (17). As a control group, 117 individuals with the similar age distribution but without any infectious disease were used.

Exclusion criteria were as follows: those with chronic diseases (chronic infectious disease, chronic kidney disease, liver disease, hypothyroidism, rheumatoid arthritis and diabetes, etc.), patients with hematological disorders (iron deficiency anemia or hemolytic anemia, Leukopenia and thrombocytopenia), and those who received antibiotics.

All midstream urine samples from the suspected patients with UTI were immediately sent to the laboratory for urine testing and culturing. The urine samples were cultured on blood agar, Eosin methylene blue agar, and MacConkey agar followed by incubation

for 24 hours at 37 ° C. Then, microbiological and biochemical tests were used to identify grown colonies (17).

To perform CBC, each blood sample was collected into tubes contained EDTA (ethylene diamine tetra acetic acid) and analyzed with automatic hematological analysis system (sysmex, XT-2000i). The white blood cells (WBCs), hemoglobin (Hb), Red blood cells (RBCs), platelet count, MPV, and PDW values were obtained from CBC test. The normal ranges for PLTs, MPV, and PDW were 150,000-400,000/ml, 8.5-12.5 fl, and 10-17%, respectively. Further, for each participant, blood samples for the CRP and ESR testing were collected and tested.

Version 21 of SPSS was applied for the statistical analysis. The data were analyzed using Chi-square and t-test. The $p<0.05$ was considered statistically significant.

Results

The average age for the patient and the control group was 10.84±6.68 and 11.34±7.1 years old, respectively. Out of 214 participants, 94 (43.9%) were males and 120 (56.1%) were females. The microbial etiology of UTIs have been shown in Table I. The frequency of microorganisms used UTIs for gram-negative, gram-positive bacteria, and Candida were 70.1%, 18.5% and 11.3%, respectively. The most frequently isolated bacteria were Escherichia coli species.

Laboratory results showed that PLT was significantly higher in patient group in compared to the control group (p=0.0007). However, there was no significant difference between patient and control groups in terms of WBC, RBC, Hb, Lymphocyte, Neutrophil, MPV, and PDW (Table II).

Table III shows the values of Hb, RBCs, WBCs, PLTs, MPV, PDW, Neutrophil, ESR, and CRP among gram-negative and gram-positive bacteria caused UTIs. MPV value in patients infected with gram-positive bacteria was higher than gram-negative cases (p=0.028). Further, patients with gram-negative bacterial UTI showed higher MPV value than Candida infected patients (p=0.044). However, there was no significant difference between MPV value of gram-positive and Candida infected patients (p=0.0846). PDW value in gram-negative infected patients was lower than gram-positive infected patients (p=0.046).

In term of CRP value, there was no significant difference between the patient and control groups based on the Fisher and Pearson's chi-squared tests (p=0.075, p=0.452).

Based on Pearson's chi-squared test, there was no significant difference between the organism condition of the patients and healthy controls. However, the prevalence of gram-positive bacteria was higher in adults, while in pediatric, Candida species were more common (p=0.005).

Cut off point, sensitivity, and specificity based on the positive predictive value (PPV) and negative predictive value (NPV) of PLT (for diagnosis of UTI), MPV, and PDW factors (for UTI patients based on the causative of gram positive and gram negative bacteria) are shown in Table IV and Table V. The ROC curves of the mentioned factors are shown in Figure 1 and Figure 2.

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Table I: Types and frequency of microbes isolated from urinary cultures

Rows	Bacteria	Number (%)
1	*Escherichia coli*	39(40.2)
2	*Citrobacter*	13(13.4)
3	*Candida*	11(11.3)
4	*Staphylococcus aureus*	9(9.2)
5	*Entrocooci*	9(9.2)
6	*Proteus*	9(9.2)
7	*Entrobacter*	3(3.1)
8	*Pseudomonas*	3(3.1)
9	*Acintobacter*	1(1)
	Total	97(100)

Table II: The results for blood tests of patient and control groups

Parameters	Patient group	Control group	p value
WBC (/µ L)	10.30	10.36	0.727
RBC	4.13	4.55	0.575
Hb (g/dL)	11.54	11.47	0.406
Lymphocyte	33.7	38.3	0.083
ESR (mm/hr)	38.6	31.6	0.217
Neutrophil (%)	54.1	52.4	0.613
PLTs (X103/µ L)	329.2	277.48	0.007
MPV (fL)	9.28	9.21	0.611
PDW (%)	11.3	11.1	0.456

Table III: The results of blood tests for UTI patients based on the causative of gram positive and gram negative bacteria

Parameters	Gram stain		p value
	Negative (Mean ± SE)	Positive (Mean ± SE)	
Hb(g/dL)	11.6	11.22	0.960
RBCs	4.25	3.76	0.084
WBCs(/µ L)	10.1	10.5	0.637
PLTs (X103/µ L)	294.6	236.9	p=0.053
MPV (fL)	9.11	9.61	p=0.022
PDW (%)	11.06	11.96	p=0.045
Neutrophils (%)	52.82	55.65	0.525
Lymphocytes (%)	34.82	33.40	0.501
ESR (mm/hr)	38.28	32.77	0.286

Table IV: Sensitivity, specificity, PPV, and NPV of variables for diagnosis of UTI

Parameters	Cut off point	AUC Roc	Sensitivity	Specificity	PPV	NVP
PLT (X103/µ L)	200.50	0.609	0.81	0.37	0.61	0.61

Table V: Sensitivity, specificity, PPV and NPV for UTI patients based on the causative of gram positive and gram negative bacteria

Parameters	Cutoff point	AUC Roc	Sensitivity	Specificity	PPV	NVP
MPV (fL)	9.15	0.668	0.72	0.60	0.60	0.61
PDW (%)	11.45	0.650	0.65	0.67	0.36	0.89

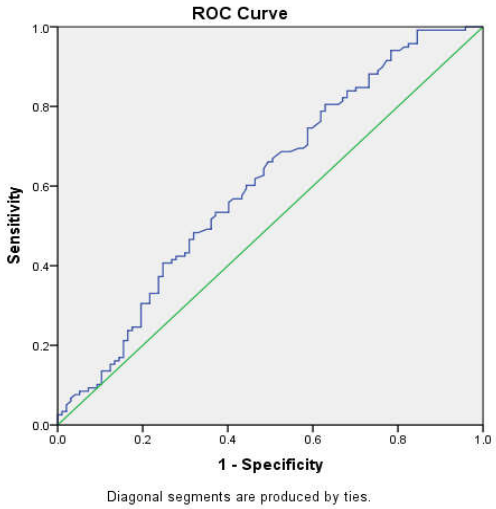

Figure 1: Receiver operating characteristic curve (ROC) of PLT

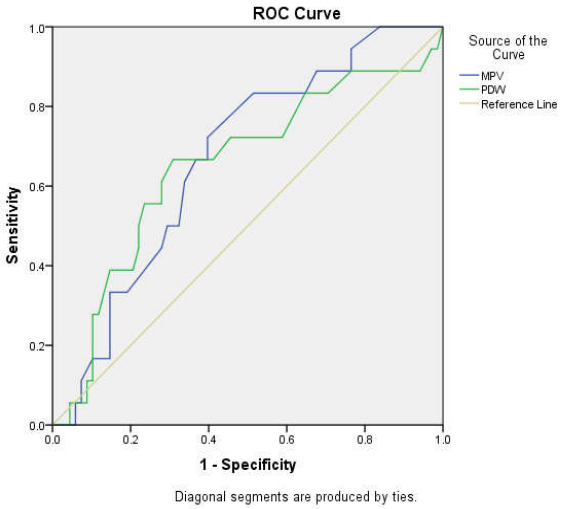

Figure 2: Receiver operating characteristic curve (ROC) of MPV and PDW

Discussion

Infection is among common human diseases, which is sometimes difficult to be diagnosed (18). Although the diagnostic techniques of infectious diseases have been improved, they still need more effective and simple practical diagnosis methods (11, 19). Blood cells counting (platelets, white blood cells and red blood cells) of patients is widely used to evaluate various diseases (20). In patients with urinary tract infection, blood cell indices are also routinely examined and their changes are easily determined using automatic blood cell analyzers (14). Further, platelet parameters are also easily tested using automatic blood cell analyzers (18, 20). Increase in the number of leukocytes as well as the rising of ESR or CRP are mostly happen in infections, including UTIs (15). ESR and CRP are routine tests prescribed for the evaluation of patients in case of infection diseases. These tests indicate the systemic inflammations in human bodies; however, it is suggested that these two testes be analyzed together for more sensitivity and specificity (21). During the inflammatory process, platelet count increases as part of the acute phase reaction (1). Changes in these indices are used to diagnose infectious and inflammatory diseases (15). Some studies have reported that platelets play an important role in the pathogenesis of various inflammatory diseases, including inflammatory bowel disease, colitis, ankylosing spondylitis, and rheumatoid arthritis (22-27). Platelets were also referred to as an indicator of urinary tract infection (3). The results of present study indicated that the number of platelets was significantly higher in UTIs, but with no significant difference between the patient and the control groups was observed in terms of MPV, which is similar to the results by Togan (28). It has been observed that there is a difference in platelet indices, including PLT, MPV, and PDW regarding the different clinical conditions (1, 3, 14, 21). However, in contrast to our results, previous reports have shown that MPV is a useful index in the diagnosis of infectious and inflammatory diseases such as endocarditis, Crohn's disease, and ulcerative colitis (29-31). Moreover, in several studies, changes in the amount of MPV in patients with acute rheumatoid arthritis, tuberculosis, acute pyelonephritis, and urinary tract infections have been observed (14, 32-36). In the present study, a small increase was noted in MPV among UTIs, although it was not statistically significant, which may explain the fact that

the number of patients and the accuracy of measuring MPV play a role for difference between our results and above studies. It has been reported that in gram-negative bacteria, lipid A in lipopolysaccharide leads to an increase in the platelet number which can make a deference with UTIs with gram positive bacteria (14). The results of the present study indicated a decrease in platelet number and an increase in MPV and PDW in gram-positive bacterial UTIs compare to gram-negative bacterial UTIs. One possible explanation for these differences can be the small number of UTIs with gram positive bacteria in our study. On the other hand, in some reports, the MPV and PDW levels have been reported higher in urinary tract infection caused by gram-positive bacteria, which make this issue more controversial (1, 3). Similar to our study, inverse relationship between platelet count and MPV and a direct relation between MPV and PDW have been reported in several other studies (20, 32). Conversely, in some other studies, a direct relationship between platelets number and MPV level has been observed (1, 3, 14).

Conclusion

Altogether, our results showed that platelet indices can be used as diagnostic markers to evaluate the urinary tract infection. However, more studies need be done with greater number of patients and bacterial causative agents to better show platelet indices changes in UTIs.

Conflict of interest

The authors declared that there was no conflict of interest to publish this article.

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