Asian Journal of Pharmaceutical and Health Sciences
www.ajphs.com

Mean platelet volume and other platelet indices in adults patients with acute pyelonephritis

Mohammad Nassaji[1], Farahnaz Ghahremanfard[2]*, Majid Mirmohammadkhani[3], MohammadReza Tamadon[4], Soodabeh Manoochehri[5]

1 Associate professor of Infectious diseases, Research Center for Social Determinants of Health, Faculty of Medicine,
2 Assistant Professor of Hematology and Oncology, Department of Internal Medicine, Kowsar Hospital,
3 Assistant Professor of Epidemiology, Research Center for Social Determinants of Health, Department of Community Medicine, School of Medicine,
4 Associate professor of Nephrology, Department of internal medicine, Kowsar hospital,
5 MD of internal Medicine, Department of internal medicine, Kowsar hospital,
Semnan University of Medical Sciences, Semnan, Iran.

ARTICLE HISTORY

Received: 25.05.2014

Accepted: 27.06.2014

Available online: 30.08.2014

Keywords:

Acute pyelonephritis, Mean Platelet Volume, Platelet, Platelet Distribution Width

***Corresponding author:**

Email : f_ghahremanfard@yahoo.com
Tel.: +982333437821, +989121316725

ABSTRACT

Mean platelet volume (MPV) is a reflection of platelet size, which has been shown to correlate with platelet function and activation. Infections as inflammatory process are known to be associated with change in PLT indices. The purpose of this study was to evaluate platelet indices especially MPV in acute pyelonephritis and their changes after response to treatment. Adult patients who were admitted with diagnosis of acute pyelonephritis were considered for participation in the study. Control group were selected randomly from healthy adult normal population whom underwent medical check-ups at the same hospital. Platelet indices values in patients and control subjects were measured on admission and 3 days after response to treatment in patients. A total of 60 patients with acute pyelonephritis and 60 healthy people as a control group were included in the study. MPV and Platelet distribution width (PDW) were significantly different between patients and control group ($p=0.005$). Platelet count in patients was higher than control group but the difference was not significant. Platelet count and PDW values decreased significantly after response to treatment ($p<0.001$ and $p=0.007$ respectively). MPV and PDW may be useful markers in acute pylonephritis and as an auxiliary test in the diagnosis. PDW and platelet count also may be considered markers of response to treatment for acute pyleonephritis.

INTRODUCTION

Platelets (PLT) are the smallest cells in blood and are associated with hemostasis and blood coagulation. There is growing clinical evidence suggesting that platelets play an important role in the inflammatory responses [1]. PLT can be elevated as an acute phase reactionduring the inflammatory process. Multiple inflammatory mediators such as chemokines and cytokines are secreted by platelets that can exacerbate the immune response. Also their size increase when they are activated [2].

Infections as an inflammatory process are known to be associated with change in PLT indices [3]. Many bacteria are capable of interacting with platelets and inducing platelet activation and aggregation. These changes may be a direct or indirect interaction between a bacterial surface protein and a platelet receptor [4].

Platelet indices, including mean platelet volume (MPV), which is a measurement of the average size of platelets, platelet distribution width (PDW), which is a measure of variability in platelet sizes and plateletcrit (PCT), which indicates the volume of circulating platelets in a unit volume of blood, have been widely and routinely reported as part of complete blood counts[5]. In healthy populations MPV has showed an inverse relationship with platelet count and there is a direct relationship between MPV and PDW [6].

MPV and PDW have been attractive indices for research in

clinical settings during recent years. But their roles in the diagnosis and management of diseases have not been fully revealed yet [7]. They are reportedly associated with the platelet function and recording of both provide more reliable information [8]. Elevated MPV is associated with other markers of platelet activity, including increased platelet aggregation, increased thromboxane synthesis and β-thromboglobulin release, and increased expression of adhesion molecules [9].

Evidence has accumulated suggesting an important role of platelet indices especially MPV as a marker of inflammation and disease activity in several inflammatory disorders [5, 10]. Some other studies have been conducted on platelet parameters changes during infectious. However, clinical significance of these changes in infection is not obviously clear [11]. Most of these studies conducted on patients with sepsis. However, few previous studies evaluated such changes in local infections. The changes of platelet parameters and its clinical meaning have not been extensively identified in urinary tract infections.

Acute pyelonephritis is an infection of the upper urinary tract, specifically the renal parenchyma and renal pelvis. It can lead to significant morbidity and sometimes mortality in patients. Better diagnosis and appropriate therapy can significantly reduce the morbidity and mortality associated with this illness [12].

The aims of this study were to investigate the platelet indices values especially MPV in patients with acute pyelonephritis and their changes after response to treatment.

MATERIALS AND METHOD

This cross-sectional study was conducted from June 2012 to March 2013 in a university affiliated hospital of Semnan University of Medical Science, Iran. Adult patients (≥ 18 years old) who were admitted with diagnosis of acute pyelonephritis were considered for participation in the study. Control group were selected from healthy adult normal population whom underwent medical check-ups at the same hospital.

Informed written consent was obtained from all subjects before enrollment. The study protocol was approved by Research Council and Ethical Committee of the Semnan University of Medical Science.

The diagnosis of acute pyelonephritis was based on the clinical findings of fever (>38°C), flank pain and/or tenderness, with pyuria and positive urine culture [13]. In all participant blood samples were collected by venipuncture in tubes containing EDTA anticoagulant. Complete blood count, including PLT counts, PDW, MPV and PCT, was determined using an automatic blood cell counter (Sysmex Xs 800I Japan). The reference range in our laboratory was as follow; platelet count 150-400×10^9/L, MPV 7.0-12 fL, PDW 15-18% and PCT 0.108-0.292.

For all patients antibiotic therapy was started immediately after diagnosis and three days after response to treatment complete blood count was repeated.

Patients were classified into two subgroups according to their fever temperature on admission as mild (T≤38.5) and sever pyelonephritis (T>38.5) [14].

Data about gender, age and complete blood count were registered for individuals who met inclusion criteria. Individuals with history of infection in recent month, platelet disorders, atherosclerosis events, treatment with anticoagulant and immunosuppressive agents were excluded.

Statistical analysis was performed by Mann-Whitney, Wilcoxon Signed Ranks tests and multivariate analysis using SPSS 16.0. P-values of less than 0·05 were considered statistically significant.

RESULTS

Of all patients admitted with acute pyelonephritis that were screened 60 met inclusion criteria and were enrolled. Same numbers of controls were selected.

Among patients 25 (41.7%) and among controls 31(51.7%) were men. The gender distribution of both groups was not statistically difference (p=0.272). Mean (±SD) age of patients was 69.8±13.8 years and for controls was 57.83±17.06 years (p<0.001).

The mean ± standard deviation platelet counts and indices of both groups are presented in table 1. Patients with acute pyelonephritis had a significantly higher mean MPV value compared to healthy controls (p=0.005). PDW was significantly lower in patients than controls (p=0.005).

Adjusting for age by multivariate analysis also showed

Table 1. The mean and standard deviation of platelet parameters in patients with acute pyelonephritis and controls

Index	Mean± SD		P*
	Cases (n=60)	Controls (n=60)	
PLT	274,100±92,974	250,200±65,826	0.307
MPV	9.74±1.39	9.05±1.23	0.005
PCT	0.240±.09	0.230±.06	0.661
PDW	16.37±.81	16.81±.92	0.005

* Mann-Whitney Test ,

Table 2. The mean and standard deviation of platelet counts and indices of sub-groups according to severity of disease in cases

Index	Mean± SD		P*
	Severe (n=17)	mild (n=43)	
PLT	267,500±93,486	276,700±93,749	0.652
MPV	9.43±.99	9.86±1.52	0.441
PCT	0.230±.07	0.240±.09	0.948
PDW	16.22±.59	16.42±.87	0.470

* Mann-Whitney Test

Table 3. The mean and standard deviation of platelet parameters in patients before and after treatment

Index	Mean± SD		P*
	before treatment	After treatment	
PLT	274,100±92,974	231,450±73,487	<.001
MPV	9.74±1.39	11.22±11.78	0.830
PCT	0.240±.09	0.220±.09	0.330
PDW	16.37±.81	15.95±1.04	0.007

* Wilcoxon Signed Ranks Test

significant difference for MPV (p=0.007) and PDW (p=0.011) between two groups. When two subgroups of patients (mild and sever) compared, all platelet parameters were lower in sever group but with no significant differences (Table 2).

Comparisons of the PLT parameters of the study population before and after treatment are shown in table 3. Platelet count and PDW values decreased significantly after response to treatment (p<0.001 and p=0.007 respectively).

DISCUSSION

Platelets are believed to be active participants in the host defense. The platelet volume has been found to be associated with PLT function and activation and is a reflection of both proinflammatory and prothrombotic conditions [10].

Different studies showed conflicting results about PLT counts in patients with infectious diseases. In our study, mean PLT count was higher in patients than control but without significant difference. In consistent with this finding, Karadag-Oncel et al in a study on children with community acquired pneumonia reported a higher PLT count with no significant difference between patients and control groups[15]. Similarly, in another study PLT count was not significantly different between patients with severe sepsis and normal control group [16].

In contrast, Catal et al in their study reported that mean PLT count was significantly higher in children with upper urinary tract infection than controls [17]. In another study mean platelet count was significantly higher in the patients with active pulmonary tuberculosis compared to the non- tuberculosis group [18].

A study compared PLT count and MPV in HIV-infected and uninfected women and identified that mean PLT count was lower in HIV-infected than uninfected women [19]. In another study that conducted on patients with sepsis and positive blood culture authors reported that the average PLT count decreased during sepsis [20]. Gofrit et al in their study concluded that thrombocytosis in patient with upper UTI is not a random phenomenon. It is a marker of complications like kidney obstruction or perinephric abscess [21].

Platelet responses to different infections have not been extensively characterized in humans. Acute infection is usually not associated with thrombocytosis because megakaryopoiesis is inhibited during acute infection by mediators such as bacterial lipopolysaccharide, tumor necrosis factor and transforming growth factor b. In contrast, chronic inflammation and infections is often associated with reactive thrombocytosis [22].

MPV has recently been recognized as an inflammatory marker in various conditions including myocardial infarction, cerebrovascular diseases, acute pancreatitis, respiratory distress syndrome, ulcerative colitis, sepsis and periodontitis [9, 23-25].

The results for infectious diseases seem to be conflicting. While some investigators reported a negative correlation between MPV and infections, other studies have demonstrated direct association between increased MPV and infectious diseases.

Our study revealed that MPV was significantly higher in patients with acute pyelonephritis compared with healthy controls. It implicates activation of PLT in these patients as previously reported in some studies. Catal et al studied children with upper UTI and determined a statistically significant higher MPV value in the patients than control children [17]. In three study findings showed that the average MPV level increased significantly in patients with sepsis [16, 20, 26]. Others authors reported higher MPV in patients with active tuberculosis [18], malaria [17] and infective endocarditis [28, 29].

The reason for this change has not been elucidated fully. One possible mechanism may be suggested that involves a characteristic pathogen-induced platelet activation process during infections. Infections caused an increased production of younger platelets as a response to destruction of platelet. Younger platelets that have been released from the bone marrow have larger size and therefore lead to the rise in MPV. Biochemical factor that involves a direct or indirect interaction between bacteria and platelets contributes to these changes [30]. Elevated inflammatory cytokines such as IL-3 and IL-6 during infections can also lead to the production of more reactive and larger platelets as reported previously [31].

In contrast few studies reported reduced MPV in infections. A study conducted in children with pneumonia showed lower MPV in patients compared to healthy controls. But patients with more severe pneumonia that required hospitalization were found to have significantly higher MPV values compared to patients who were followed-up on an outpatient basis [15]. Wiwanitkit et al reported that statistically significant decrease of MPV values was detected in the patients with hookworm infection [32]. In Qadri et al study, HIV infected women had lowers MPV values than uninfected women [19].

The difference in these findings might at least partly be explained by differences in the study design, types of infections, number of samples and confounding variables.

There are few studies that evaluated PDW changes in infectious diseases. We found significantly lower PDW in patients with acute pyelonephritis when compared with the control group. In Catal et al study, although PDW was higher in children patients with upper UTI than controls, this difference was not statistically significant [17].

In contrast, PDW values in patients with pulmonary tuberculosis were significantly higher than controls [18]. Also, comparing of PDW between patients with sepsis and the control group showed significantly higher level in patients [16].

In our patients PLT count and PDW values decreased significantly after response to treatment. MPV increased after treatment but this increase was not statistically significant. This finding confirmed the results of some previous studies. In patients with tuberculosis, the levels of all parameters including PLT count and PDW decreased significantly after anti-tuberculous therapy [18]. In Zareifar et al study, platelet count reduction and MPV increase proposed as markers of recovery in children with infectious and inflammatory diseases [33].

In contrast, the total platelet counts of patients with bacterial endocarditis increased significantly but, MPV values decreased significantly after treatment [29]. A study on patients with pulmonary hydatid cyst demonstrated that MPV decreased after operation with statistically significant difference but, there were no statistical difference change in PLT counts before and after operation [34]. In Kitazawa et al study the MPV levels in patients with sepsis remained higher in the non-survivors than in the survivors but the average platelet count was similar between the two groups [20].

Our study has some limitations. First, the eligible patient number was relatively small in this study, owing to the restrictive inclusion criteria. Second, we evaluated patients for a short time after response to treatment; this reduced our ability to compare the changes in PLT indices over longer time.

CONCLUSION

In conclusion, our findings suggest that MPV and PDW, which is performed for almost all patients admitted to hospital, may be useful markers in upper urinary tract infections and may be used as an auxiliary test in the diagnosis. PDW and platelet count also may be considered markers of response to treatment for acute pyleonephritis. Further prospective studies with larger samples are needed to better identification of platelet parameters responses to different types of infections as an indicator of disease activity or for the evaluation of response to treatment.

ACKNOWLEDGMENT

The research was supported by Research Committee of Semnan University of Medical science.

REFERENCES

1. Ghoshal K, Bhattacharyya M. Overview of Platelet Physiology: Its Hemostatic and Nonhemostatic Role in Disease Pathogenesis. Scientific World Journal 2014; 2014:781857.
2. Ware J, Corken A, Khetpal R. Platelet function beyond hemostasis and thrombosis. Curr Opin Hematol 2013; 20:451-6.
3. Griesshammer M, Bangerter M, Sauer T, Wennauer R, Bergmann L, Heimpel H. Aetiology and clinical significance of thrombocytosis: analysis of 732 patients with an elevated platelet count. J Intern Med 1999; 245: 295 - 300.
4. Kerrigan SW, Cox D. Platelet-bacterial interactions. Cell Mol Life Sci 2010; 67:513-23.
5. Leader A, Pereg D, Lishner M. Are platelet volume indices of clinical use? A multidisciplinary review. Ann Med 2012; 44(8): 805-16.

6. Farias MG, Schunck EG, Dal Bo S, de Castro SM. Definition of reference ranges for the platelet distribution width (PDW): a local need. Clin Chem Lab Med 2010; 48: 255-7
7. Buttarello M, Plebani M. Automated blood cell counts: state of the art. Am J Clin Pathol 2008; 130:104-16.
8. Jackson SR, Carter JM. Platelet volume: laboratory measurement and clinical application. Blood Rev 1993; 7(2):104-13.
9. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996; **7:**15761.
10. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 2011;17(1):47-58.
11. Becchi C, Al Malyan M, Fabbri LP, Marsili M, Boddi V, Boncinelli S. Mean platelet volume trend in sepsis: is it a useful parameter? Minerva Anestesiol 2006; 72(9):74956.
12. Ramakrishnan K, Scheid DC. Diagnosis and management of acute pyelonephritis in adults. Am Fam Physician 2005; 71: 933-42.
13. Lane DR, Takhar SS. Diagnosis and management of urinary tract infection and pyelonephritis. Emerg Med Clin North Am 2011; 29: 539-52.
14. Gupta K,Traunter BW. Urinary Tract Infection, Pyelonephritis and prostatitis. In: Longo DL, Kasper DL, Jameson Jel (ed). Harrison's Principles of Internal Medicine. 18 th ed. New York: MC Graw Hill, 2012; 2387-95.
15. Karadag-Oncel E, Ozsurekci Y, Kara A, Karahan S, Cengiz AB, Ceyhan M. The value of mean platelet volume in the determination of community acquired pneumonia in children. Ital J Pediatr 2013; 8; 39:16.
16. Guclu E**,** Durmaz Y, Karabay O. Effect of severe sepsis on platelet count and their indices. Afr Health Sci 2013; 13: 333-8.
17. Catal F, Bavbek N, Bayrak O et al. Platelet parameters in children with upper urinary tract infection: is there a specific response? Ren Fail 2008; 30: 377-81.
18. Tozkoparan E, Deniz O, Ucar E, Bilgic H, Ekiz K. Changes in platelet count and indices in pulmonary tuberculosis. Clin Chem Lab Med 2007; 45: 1009-13.
19. Qadri S, Holman S, Dehovitz J, Crystal H, Minkoff H, Lazar JM. Mean platelet volume is decreased in HIV-infected women. HIV Med 2013;14: 549-55.
20. Kitazawa T, Yoshino Y, Tatsuno K, Ota Y, Yotsuyanagi H. Changes in the mean platelet volume levels after bloodstream infection have prognostic value. Intern Med 2013; 52:1487-93.
21. Gofrit ON, Shapiro A, Rund D et al. Thrombocytosis accompanying urinary tract infection suggests obstruction or abscess. Am J Emerg Med 2006; 24: 118-21.
22. Klinger MH, Jelkmann W. Role of blood platelets in infection and inflammation. J. Interferon. Cytokine Res 2002; 22: 913- 22.
23. Chu SG, Becker RC, Berger PB et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. J Thromb Haemost. 2010; 8:148-56.
24. Bilici S, Sekmenli T, Göksu M, Melek M, Avci V. Mean platelet volume in diagnosis of acute appendicitis in children. Afr Health Sci 2011;11: 427-32.
25. Wang X, Meng H, Xu L, Chen Z, Shi D, Lv D. Mean platelet volume as an inflammatory marker in patients with severe periodontitis. Platelets 2014.
26. Aydemir H, Piskin N, Akduman D, Kokturk F, Aktas E. Platelet and mean platelet volume kinetics in adult patients with sepsis. Platelets 2012 June 25. Early Online:16
27. Ladhani S, Lowe B, Cole AO, Kowuondo K, Newton CR. Changes in white blood cells and platelets in children with falciparum malaria: relationship to disease outcome. Br J Haematol 2002;119**:** 839-47.
28. Cho SY, Jeon YL, Kim W et al. Mean platelet volume and mean platelet volume/platelet count ratio in infective endocarditis. Platelets 2013 Nov 8**.** Early Online: 13
29. Icli A, Tayyar S, Varol E et al. Mean platelet volume is increased in infective endocarditis and decreases after treatment. Med Princ Pract 2013; 22: 270-3.
30. Cox D, Kerrigan SW, Watson SP. Platelets and the innate immune system: Mechanisms of bacterial-induced platelet activation. J Thromb Haemost 2011; 9:10971107.
31. Debili N, Masse JM, Katz A, Guichard J, Breton-Gorius J, Vainchenker W. Effects of the recombinant hematopoietic growth factors interleukin-3, interleukin-6, stem cell factor, and leukemia inhibitory factor on the megakaryocytic differentiation of CD34+ cells. Blood 1993; 82: 8495.
32. Wiwanitkit V, Soogarun S, Saksirisampant W , Suwansaksri J. Platelet parameters in subjects infected with hookworm. Platelets 2003; 14: 391-3.
33. Zareifar S, Farahmand Far MR, Golfeshan F, Cohan N. Changes in Platelet Count and Mean Platelet Volume During Infectious and Inflammatory Disease and Their Correlation With ESR and CRP. J Clin Lab Anal 2014; 28: 245248 (2014)
34. Küçükbayrak A, Oz G, Fındık G, Karaoğlanoğlu N et al. Evaluation of platelet parameters in patients with pulmonary hydatid cyst. Mediter J Hematol Infect Dis 2010; 2(1): e2010006.