Journal of Acute Disease

Original Article

doi: 10.4103/2221-6189.307391 jadweb.org

Association between community-acquired pneumonia and platelet indices: A case-control study

Hajar Motamed[1], Homayoon Bashiri[2], Farideh Yari[3], Arezoo Bozorgomid[2], Mosayeb Rostamian[2], Yousef Azarakhsh[4], Azam Hosseini[5], Roya Chegene Lorestani[2]✉

[1]*Department of Pathology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran*

[2]*Infectious Diseases Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran*

[3]*Clinical Research Development Center of Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran*

[4]*Department of Basic Sciences and Pathobiology, Faculty of Veterinary Medicine, Razi University, Iran*

[5]*Department of Microbiology, Faculty of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran*

ABSTRACT

Objective: To examine whether the platelet index would be applicable for the diagnosis of community-acquired pneumonia (CAP).

Methods: In this study, 64 CAP patients (the case group) and 68 healthy children (the control group) were included from 2017 to 2018. Baseline variables were recorded including total white blood cells, neutrophils, lymphocytes, red blood cells, platelet, mean platelet volume, platelet distribution width, erythrocyte sedimentation rate, and C-reactive protein, and compared between the case group and the control group. The cutoff value, sensitivity, and specificity of neutrophil-to-lymphocyte ratio, platelet, neutrophils, lymphocytes, and platelet larger cell ratio were calculated by receiver-operating characteristic curves.

Results: The median platelet count of the case group and the control group were (411.09±67.40) mm^3 and (334.48±78.15) mm^3, respectively (P=0.000). The median neutrophil count of the case group was higher than that of the control group (P=0.000), while the lymphocyte level of the case group was lower (P=0.000). Differences in other variables including the mean platelet volume, platelet distribution width, C-reactive protein, and erythrocyte sedimentation rate were not statistically significant between the two groups.

Conclusions: Due to the different levels of platelet, neutrophil and lymphocyte indices in the case and the control group, these indices can be used simultaneously for the diagnosis of CAP.

KEYWORDS: Community-acquired pneumonia; Platelet index; Hematological profile

1. Introduction

Community-acquired pneumonia (CAP) as a lower respiratory infection in children is one of the leading causes of hospitalization in the world[1,2]. Hospitalization of children with CAP is highly prevalent in developing countries, and CAP is one of the major causes of death of the infected children[3]. However, CAP is often misdiagnosed, leading to a delay in the treatment process[4,5]. Thus, timely diagnosis and treatment of CAP children play an important role in preventing and reducing the mortality[6].

Although the diagnosis of CAP in children is more clinical and usually confirmed by radiographic findings, laboratory findings can be also effective in CAP diagnosis[7]. The counting of blood cells [platelets (PLT), white blood cells (WBC), and red blood cells] is widely used to diagnose various diseases[8]. Thus, blood cell count has been used to diagnose or evaluate CAP patients in practice[9]. Besides, blood indices changes have been reported to be associated with lung diseases such as CAP, cystic fibrosis, and bronchiectasis as a reflection of the inflammatory response[10].

✉To whom correspondence may be addressed. E-mail: lorestani25@gmail.com

How to cite this article: Motamed H, Bashiri H, Yari F, Bozorgomid A, Rostamian M, Azarakhsh Y, et al. Association between community-acquired pneumonia and platelet indices: A case-control study. J Acute Dis 2021; 10(1): 23-27.

Article history: Received 2 September 2020; Revision 14 January 2021; Accepted 18 January 2021; Available online 25 January 2021

Leukocyte count in CAP patients is considered as a sign of systemic inflammatory response and the disease severity[11]. PLT is another important index involved in the immune response to infection with similar responses to leukocytes[12]. PLT is involved in the host antimicrobial defense mechanism by inducing inflammation through increasing inflammatory mediators, preventing inhibition of neutrophils and monocytes apoptosis, and increasing leukocyte infiltration[13]. An increased PLT count has been reported in the immune response to infections[14]. A change in the PLT number is an indicator of CAP severity[15]. PLT has long been known to act as acute-phase reactants in inflammatory diseases, but they are often neglected as a diagnosis indicator[16]. The role of the PLT index in different infectious diseases has been studied[17-20]. However, little is known about how this index changes during CAP infection. Therefore, our study aims to evaluate the role of this index in CAP diagnosing and its relation to children CAP.

2. Materials and methods

2.1. Study design and patients

This case-control study was conducted in the Imam Reza Hospital, Kermanshah, Iran, from 2017 to 2018. The study included 64 children who were diagnosed with CAP as the case group and 68 non-pneumonia healthy individuals as the control group. CAP was diagnosed according to the clinical evidence (cough, fever, purulent sputum, and breathing difficulties) and supported by abnormal chest radiography.

2.2. Ethical approval

The study was approved by the Ethics Committee of the Kermanshah University of Medical Sciences (approval number: IR.KUMS.REC.1398.536).

2.3. Blood test

First, 5 mL of whole blood samples were drawn from a forearm vein, and then were stored into tubes containing EDTA and analyzed with Coulter HmX from Beckman Coulter at admission. The following demographic and laboratory variables were recorded: gender, age, hemoglobin, red blood cell count, WBC count, lymphocyte count, neutrophil count, PLT count, mean platelet volume (MPV), platelet distribution width (PDW), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), red blood cell distribution width, platelet large cell ratio. The reference values in the affiliated Imam Reza Hospital Laboratory were (3.5-9.5)×10^9/μL for WBC count, (1.8-6.3)×10^9/μL for the neutrophil count, 40%-70% for neutrophil percentage, (181-300)×10^9/μL for PLT, (9.4-12.5) fL for MPV, and 15.5%-18.1% for PDW. Thrombocytopenia and thrombocytosis were defined as PLT counts <150000/L and >400000/L, respectively.

2.4. Statistical analysis

Statistical analyses were carried out using SPSS software (version 20, SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was applied to evaluate the normal distribution of the data in each group. Continuous variables were presented as mean±standard deviation (SD) or median (IQR). Categorical variables were compared using the *Chi*-square test or Fisher's exact test and continuous variables were compared using *t*-test or the Mann-Whitney test (each when appropriate). The sensitivity, specificity, and area under curve (AUC) values were determined using receiver-operating characteristic (ROC) curves. Correlations between numerical variables were assessed using Pearson's or Spearman's correlation analysis. The significance level of this study was set at α=0.05.

3. Results

In total, 64 CAP infected patients (the case group) and 68 matched-healthy children (the control group) were included in this study. There were 34 male participants in the control group and 32 in the case group (P=1.000). The median age of the control and the case group was 3 (0-5) years and 1 (0-3) years, respectively (P=0.171).

The comparison of blood parameters between the case group and the control group are presented in Table 1. No significant difference was detected in the hemoglobin, WBC count, RBC count, CRP, ESR percentage, RDW, PDW, and MPV indices between the two groups (P>0.05).

The median NLR, neutrophil and mean PLT count were 1.00 (1.00-2.00), 57.50 (47.00-66.00), and 411.09±67.40 in the case group, which were significantly higher than those in the control group [0.64 (0.00-1.00), 36.00 (23.00-54.00), and 334.48±78.50, respectively (P<0.05)]. The lymphocyte count and platelet large cell ratio (PLCR) were

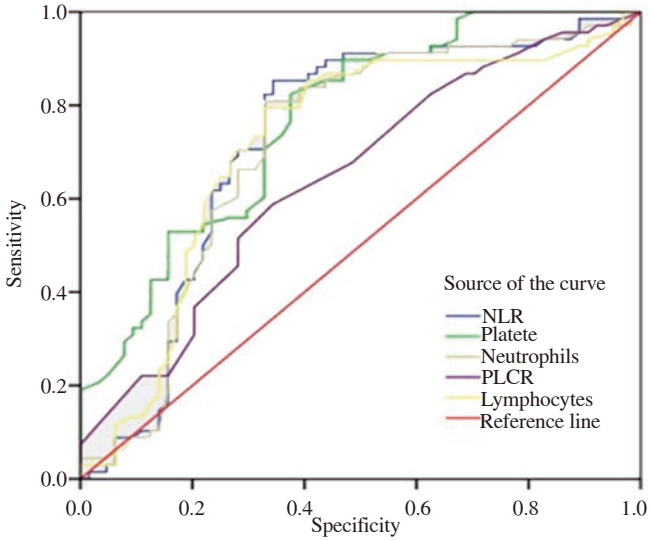

Figure 1. The ROC curve of PLT, neutrophil, lymphocyte, NLR, and PLCR for the diagnosis of community-acquired pneumonia. NLR: neutrophil-to-lymphocyte ratio; PLCR: platelet large cell ratio.

Table 1. Comparison of clinical and laboratory data of the study children.

Variables	Control group (n=68)	Case group (n=64)	t/U	P-value
Hemoglobin (g/dL) [median (IQR)]	10.90 (9.00-13.00)	11.20 (10.00-11.00)	736.00	1.000
RBC (mm^3) [median (IQR)]	3.85 (3.00-4.00)	4.10 (3.00-4.00)	574.50	0.110
WBC (mm^3) [median (IQR)]	10.00 (8.00-16.00)	10.60 (8.00-13.00)	734.00	0.980
PLT (mm^3) [mean±SD]	334.48±78.50	411.09 ±67.40	-6.03	0.000
MPV (fL) [mean±SD]	9.02±1.05	8.78±0.82	-1.12	0.260
PDW (%) [median (IQR)]	10.60 (9.00-12.00)	10.00 (9.00-11.00)	627.50	0.290
Neutrophile (mm^3) [median (IQR)]	36.00 (23.00-54.00)	57.50 (47.00-66.00)	1243.00	0.000
Lymphocyte (mm^3) [median (IQR)]	54.50 (35.00-65.00)	31.00 (23.00-41.00)	1231.00	0.000
NLR [median (IQR)]	0.64 (0.00-1.00)	1.00 (1.00-2.00)	1.19	0.000
ESR (%) [median (IQR)]	20.50 (8.00-32.00)	28.50 (14.00-44.00)	884.50	0.150
CRP [n(%)]				
Negative (no agglutination)	29.00 (42.60)	35.00 (54.70)		
1+ (small agglutinated particles)	14.00 (20.60)	14.00 (21.90)	3.00	0.391
2+ (medium agglutinated particles)	9.00 (13.20)	6.00 (9.40)		
3+ (coarse agglutinated particles)	16.00 (23.50)	9.00 (14.10)		
RDW (%) [Median (IQR)]	14.30 (13.00-15.00)	14.15 (13.00-14.00)	656.00	0.440
PLRC (%) [Median (IQR)]	18.00 (14.00-23.00)	15.00 (12.00-18.00)	1.54	0.000

RBC: red blood cell; WBC: white blood cell; PLT: platelet; MPV: mean platelet volume; PDW: platelet distribution width; NLR: neutrophil-to-lymphocyte ratio; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RDW: red blood cell distribution width; PLRC: platelet large cell ratio.

Table 2. Sensitivity, specificity, PPV, NPV of variables for diagnosis of community-acquired pneumonia in children.

Variables	Cutoff point	AUC ROC	Sensitivity	Specificity	PPV	NVP
NLR	0.91	0.726	0.85	0.66	0.72	0.81
Platete	347.50	0.767	0.82	0.62	0.70	0.77
Neutrophils	45.45	0.714	0.81	0.67	0.72	0.77
PLRC	16.50	0.646	0.59	0.66	0.65	0.60
Lymphocytes	45.40	0.717	0.79	0.67	0.72	0.75

NLR: neutrophil-to-lymphocyte ratio; PLRC: platelet large cell ratio; PPV: positive predictive value; NPV: negative predictive value.

54.50 (35.00-65.00) and 18.00 (14.00-23.00) in the control group, which were significantly lower than that in the case group [31.00 (23.00-41.00) and 15.00 (12.00-18.00)] (P<0.05). Based on the ROC analysis, in the case group, the cut-off values of the PLT, neutrophil count, lymphocyte count, PLCR, and NLR were 347.50, 45.45, 45.40, 16.50, and 0.91, respectively (Table 2). The area under the curve (AUC) of the PLT, neutrophil count, lymphocyte count, PLCR, and NLR is presented in Figure 1.

4. Discussion

It has been reported that ESR, WBC count, and CRP, which are assumed as general indicators of infectious disease, are also valuable in the diagnosis of CAP[21,22]. Leukocyte count, ESR, and CRP are the most common acute phase reactants[16]. Changes in these indices can be used to diagnose infectious and inflammatory diseases[23]. Thomas *et al.* reported that the average CRP level was higher in patients with bacterial pneumonia than in patients with viral pneumonia. In another study performed by Zhao *et al.*, abnormally increased CRP and IL-6 in pneumonias patients were observed. Although CRP plays a key role in the inflammatory process of sepsis and CAP, in our study the CRP index did not show a predictive value for CAP detection[24,25]. That may be due to the small sample size.

Neutrophils and lymphocytes have been reported to play an important role in the inflammatory processes. Physiological immune responses are characterized by a decrease of lymphocytes and an increase of neutrophils[26]. In CAP patients, some indices such as WBC and neutrophils counts are important in the disease screening and improvement of the diagnosis[7]. In our study, there was an increase in the number of neutrophils but a decrease in the number of lymphocytes in the case group compared to the control group. There was a negative correlation between the neutrophil count with the lymphocyte count of CAP patients. These findings are similar to the results of Curbelo *et al.*, who confirmed that abnormally low lymphocytes with elevated neutrophil count, have good predictive power in pneumonia[27]. Besides, NLR can be a useful index for predicting CAP infections, although it works better in combination with other indices[28]. Jager *et al.* reported that the predictive power of NLR in CAP is better than CRP and WBC[29].

PLT, which are important inflammatory cells and release a large number of inflammatory molecules under the process of chemotaxis, can also act as acute phase reactants[16]. PLT, in addition to their role in host defense through phagocytosis, are considered inflammatory indicators because they play an important role in inflammatory reactions by increasing vascular permeability and inflammatory mediators such as cytokines and chemokines. Therefore, it has been reported that changes in PLT can be used to diagnose various inflammatory diseases[30]. A study also reported in the prognosis of patients with CAP, PLT abnormalities are a more useful indicator than leukocyte abnormalities[16]. PLT would increase against respiratory tract infections due to elevated levels of inflammatory

cytokines so that the commonest cause of reactive thrombocytosis has been reported in respiratory infections[31,32]. In another study, an increase in PLT count was observed in children with pneumonia[33]. In a study by Şahin *et al.*, the number of PLT in the patient group was significantly higher than the control group. The results of these studies are consistent with our results[16].

MPV and PDW are two important PLT indicators that are related to PLT activity and function[34,35]. Different changes in MPV levels have been observed in different clinical conditions[16]. In our study, the amount of MPV value was lower in CAP patients in comparison to the controls, although this difference was not statistically significant. Similarly, in other studies, the amount of MPV in patients with pneumonia was lower than that in the control group[16,36,37]. Their findings showed that the amount of MPV varies depending on the severity of the infection suggesting it as a good indicator for CAP diagnosis[38].

It is noteworthy that our study has some limitations as follows: (1) our sample size is not large; (2) the study is done only in one health center. Considering that, we suggest that a more comprehensive and multicenter study with a larger sample size should be conducted to confirm the relationship between PLT and CAP.

The result of this study showed the different levels of platelet, neutrophil, lymphocyte, neutrophil to lymphocyte ratio, and platelet large cell ratio in the case and the control group, it could be concluded that these indices can be used simultaneously for the diagnosis of CAP. However, a single index is not accurate enough to predict CAP, and a combination of clinical history, clinical signs and symptoms, and the use of more than one index are recommended to diagnose CAP patients.

Conflict of interest statement

The authors report no conflict of interest.

Acknowledgments

We would like to thank the Clinical Development Research Unit of Imam Reza Hospital the Kermanshah University of Medical Sciences.

Authors' contributions

H.M.: Study concept and design; R.C., F.Y. and S.M. and A.H.: Acquisition of data; B.A.: Analysis and interpretation of data; A.B. and R.C.: Drafting of the manuscript, critical revision of the manuscript for important intellectual content; M.R., H.B. and B.A., Y.A.: Statistical analysis; R.C. and A.B.: Administrative, technical, and material support; H.M.: Study supervision.

References

[1] Cevey-Macherel M, Galetto-Lacour A, Gervaix A, Siegrist CA, Bille J, Bescher-Ninet B. Etiology of community-acquired pneumonia in hospitalized children based on WHO clinical guidelines. *Eur J Pediatr* 2009; **168**(12): 1429-1436.

[2] Nascimento-Carvalho CM. Community-acquired pneumonia among children: the latest evidence for an updated management. *J Pediatr* 2020; **96**(S1): 29-38.

[3] Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, et al. Global, regional, and nationalcauses of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* 2012; **379**(9832): 2151-2161.

[4] Gupta D, Agarwal R, Aggarwal AN, Singh N, Mishra N, Khilnani GC, et al. Guidelines for diagnosis and management of community-and hospital-acquired pneumonia in adults: Joint ICS/NCCP(I) recommendations. *Lung India* 2012; **29**(Suppl 2): S27-S62.

[5] Morens DM, Folkers, KG, Fauci SA. The challenge of emerging and re-emerging infectious diseases. *NPG Asia Mater* 2004; **430**(8): 242-249.

[6] Karimi A, Armin Sh, Fahimzad Sa. Acute Childern Pneumonia. *J Med Council I.R.I* 2009; **26**(4): 541-554.

[7] Ning J, Sha X, Ma Y, Lv D. Valuable hematological indicator for the diagnosis and severity assessment of Chinese children with community-accquired pneumonia prealbumin. *Medicine* 2016; **95**(47): e5452.

[8] Shah AR, Chaudhari SN, Shah MH. Role of platelet parameters in diagnosing various clinical conditions. *Natl J Integr Res Med* 2013; **3**(2):162-165.

[9] Shaaban LH, Ahmed Y. Hemogram values in community acquired pneumonia. *Egypt J Chest Dis Tuberc* 2015; **64**(3): 617-623.

[10]Tekin R, Aktar F, Ayaz C. Comparison of inflammatory markers between adult and pediatric brucellosis patients. *Open Forum Infect Dis* 2017; **4**(1): S350-S351.

[11]Elmaraghy AA, Abdelfattah EB, Ahmad MS. Platelet count: Is it a possible marker for severity and out come of community acquired pneumonia? *Egypt J Chest Dis Tuberc* 2016; **65**(2): 499-504.

[12]Mirsaeidi M, Peyrani P, Aliberti S, Filardo G, Bordon J, Blasi F, et al. Thrombocytopenia and thrombocytosis at time of hospitalization predict mortality in patients with community-acquired pneumonia. *Chest* 2010; **137**(2): 416-420.

[13]Yeaman MR. The role of platelets in antimicrobial host defense. *Clin Infect Dis* 1997; **25**(5): 951-968.

[14]Prina E, Ferrer M, Ranzani OT, Polverino E, Cilloniz C, Moreno E, et al. Thrombocytosis is a marker of poor outcome in community-acquired pneumonia. *Chest* 2013; **143**(3): 767-775.

[15]KazeraniM, Moghadamnia F. Survey of relationship between platelet count and complications community acquired pneumonia in teaching hospitals of Mashhad Islamic Azad University (2014). *Med J Mashhad Uni Med Sci* 2016; **59**(5): 300-308.

[16]Sahin M, Duru NS, Elevli M, Civilibal M. Assessment of platelet parameters in children with pneumonia. *J Pediatr Infect* 2017; **11**(3): e106-e112.

[17]Aydemir H, Piskin N, Akduman D, Kokturk F, Aktas E. Platelet and mean platelet volume kinetics in adult patients with sepsis. *Platelets*

2015; **26**(4): 331-335.

[18]Albayrak Y, Albayrak A, Albayrak F, Yildirim R, Aylu B, Uyanik A, et al. Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis. *Clin Appl Thromb Hemost* 2011; **17**(4): 362-366.

[19]Turhan O, Coban E, Inan D, Yalcin AN. Increased mean platelet volume in chronic hepatitis B patients with inactive disease. *Med Sci Monit* 2010; **16**(4): Cr202-205.

[20]Tanju C, Ekrem G, Emel AB, Nur A. Mean platelet volume as a negative marker of inflammation in children with rotavirus gastroenteritis. *Iran J Pediatr* 2014; **24**(5): 617-622.

[21]Melbye H, Straume B, Brox J. Laboratory tests for pneumonia in general practice: the diagnostic values depend on the duration of illness. *Scand J Prim Health Care* 1992; **10**(3): 234-240.

[22]Blot M, Croisier D, Pechinot A, Vagner A, Putot A, Fillion A, et al. A leukocyte score to improve clinical outcome predictions in bacteremic pneumococcal pneumonia in adults. *Open Forum Infect Dis* 2014; **1**(4): ofu075.

[23]Lee IR, Shin JI, Park SJ, Oh JY, Kim JH. Mean platelet volume in young children with urinary tract infection. *Sci Rep* 2015; **5**(9): 18072.

[24]Thomas J, Pociute A, Kevalas R, Malinauskas M, Jankauskaite L. Blood biomarkers differentiating viral versus bacterial pneumonia aetiology: a literature review. *Ital J Ped* 2020; **46**(1): 4.

[25]Zhao D, Yao F, Wang L, Zheng L, Gao Y, Ye J. A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias. *Clin Infect Dis* 2020; **71**(15): 756-761.

[26]Bozdemir SE, Altıntop YA, Uytun S, Aslaner H, Torun YA. Diagnostic role of mean platelet volume and neutrophil to lymphocyte ratio in childhood brucellosis. *Korean J Intern Med* 2017; **32**(6): 1075-1081.

[27]Curbelo J, Bueno SL, Galván-Román JM, Ortega-Gomez M, Rajas O, Fernandez-Jimenez G. Inflammation biomarkers in blood as mortality predictors in community-acquired pneumonia admitted patients: Importance of comparison with neutrophil count percentage or neutrophil-lymphocyte ratio. *PLoS One* 2017; **12**(3): e0173947.

[28]Yang T, Wan C, Wang H, Qin J, Chen L, Shen Y, et al. The prognostic and risk-stratified value of neutrophil-lymphocyte count ratio in Chinese patients with community-acquired pneumonia. *Eur J Inflamm* 2017; **15**(1): 22-27.

[29]de Jager CPC, Wever PC, Gemen EFA, Kusters R, van Gageldonk-Lafeber AB, van der Poll T, et al. The neutrophil-lymphocyte count ratio in patients with community-acquired pneumonia. *PLoS One* 2012; **7**(10): e46561.

[30]Cros A, Ollivier V, Ho-Tin-Noe B. Platelets in inflammation: regulation of leukocyte activities and vascular repair. *Front Immunol* 2015; **5**: 678.

[31]Ozcan C, Sayli TR, Kosan-Culha V. Reactive thrombocytosis in children. *Turk J Pediatr* 2013; **55**(4): 411-416.

[32]Subramaniam N, Mundkur S, Kini P, Bhaskaranand N, Aroor S. Clinicohematological study of thrombocytosis in children. *ISRN Hematol* 2014: 389257.

[33]Choudhury J, Rath D. Thrombocytosis in under-five children with lower respiratory tract infection. *Arch Pediatr Infect Dis* 2018; **6**(1): e61605.

[34]Togan T, Narci H, Turan H, Ciftci O, Kursun E, Arslan H. The impact of acute brucellosis on mean platelet volume and red blood cell distribution. *Jundishapur J Microbiol* 2015; **8**(2): e20039.

[35]Zayed KMS, Abdelhakeem AM, Gafar HS, Eldahshan TAEK. Diagnostic of platelet parameters versus interleukin-6 in children with urinary tract infection. *Egypt Paediatr Assoc* 2016; **64**(3): 142-148.

[36]Karadagoncel E, Ozsurekci Y, 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; **39**: 16.

[37]Afyon M, Artuk C. Could mean platelet volume be a useful marker for infectious diseases? a review of literature. *Med Sci* 2016; **5**(4): 1059-1062.

[38]Robbins G, Barnard DL. Mean platelet volume change in infection. *J Clin Pathol* 1983; **36**(11): 1320.