International Journal of Research in Medical Sciences
Mukker P et al. Int J Res Med Sci. 2016 May;4(5):1423-1428
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20161203

Research Article

Comparative study of platelet indices in cirrhosis, cirrhosis with sepsis and normal population

Payal Mukker[1]*, Abhilash Haridas[2], Nishant Kallinkeel[1], Ajith P. G.[1]

[1]Department of Internal Medicine, Azeezia Medical College, KUH, Kollam, Kerala, India
[2]Consultant Gastroenterologist, KIMS Hospital, Sivagiri Sree Narayana Medical Mission Hospital,Varkala, Kerala State, India

Received: 16 February 2016
Accepted: 22 March 2016

***Correspondence:**
Dr. Payal Mukker,
E-mail: drpaayali@gmail.com

ABSTRACT

Background: Platelet indices are the first hematologic indices to be affected in cirrhosis. Cirrhosis patients are particularly susceptible to bacterial infections. The incidence of sepsis in cirrhosis is estimated to be at least 30-50% of hospital admissions. Sepsis also causes alterations in platelet indices. We studied and compared the platelet indices namely platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and platecrit in cirrhosis, cirrhosis with sepsis and normal control population.
Methods: This observational study included forty cirrhosis, forty three cirrhosis with sepsis and sixty one controls. Platelet indices were reviewed and compared between the groups and correlation of platelet indices with CTP score, MELD, platelet count and spleen size was also evaluated.
Results: Platelet indices were significantly altered in cirrhosis compared to normal population. MPV and PDW were significantly higher in cirrhosis compared to control population. Platelet count and platecrit were significantly lower in cirrhosis compared to control population. CTP score and MELD showed significant positive correlation with MPV and platelet count showed significant negative correlation with PD. Sepsis in cirrhosis was associated with significant decrease in platelet count and platecrit but caused significant increase in PDW compared to cirrhosis without sepsis. Cirrhosis with sepsis group had four patients with variceal bleeding with significantly higher mean PDW(19%) and significantly lower mean platecrit (0.04) compared to nonbleeding group (p value <0.05).
Conclusions: Platelet indices are useful parameters in cirrhosis. Other than platelet count, PDW and platecrit are useful indices to be monitored in cirrhosis with sepsis.

Keywords: Cirrhosis, Sepsis, Platelets, MPV, PDW, Platecrit

INTRODUCTION

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury that leads to portal hypertension and end stage liver disease. Abnormal hematological indices (HI) are common in cirrhosis with a prevalence ranging from 6% to 77% in various studies.[1] Platelets are non-nucleated cell fragments derived from megakaryocytes, most often present in the bone marrow. Studies show that platelets produced from megakaryocytes present in the microvasculature is governed by circulatory forces.[2] Thrombocytopenia was the most common and earliest HI abnormality to develop in cirrhosis.[1] MPV is the measure of average size of platelets in circulation, and PDW is an index reflecting the heterogeneity of platelets. Platelet activation leads to changes in platelet shape with increase in platelet size

and anisocytosis leading to an increase in MPV and PDW.[3] Platecrit is a measure of total platelet mass. Platecrit is an effective screening tool for detecting platelet quantitative abnormalities.

The etiopathogenesis of platelet abnormalities in cirrhosis include portal hypertension-induced splenic sequestration, alterations in thrombopoietin, bone marrow suppression mediated by toxins, consumptive coagulopathy due to low-grade disseminated intravascular coagulation, acquired intravascular coagulation, fibrinolysis and Increased blood loss.[1] Apart from their important role in hemostasis, it has become evident that platelets also are active players involved in inflammation and immunity. Direct interaction between platelets and bacteria leading to platelet activation has been reported in several studies *in vitro* and *in vivo*, recently reviewed by Fitzgerald et al.[4] Studies show that platelet indices are significantly altered in sepsis and septic shock due to increase in cytokines, endothelial damage, and bone marrow suppression. Platelet count was decreased in sepsis and decreased platelet counts parallel the severity of infection. Higher MPV and increased PDW have been found in sepsis.[5] The incidence of sepsis in cirrhosis is estimated to be at least 30-50% of hospital admissions.[6] There is scarcity of data on platelet indices in cirrhosis with sepsis.

METHODS

A retrospective cohort study was conducted between November 2014 and August 2015 in two tertiary level hospitals in Kerala, India and study group includes patient data from medical records were examined retrospectively.

Study group; Patients diagnosed with cirrhosis based on a combination of clinical, radiologic and biochemical criteria. In all cirrhosis patients child–pugh score and MELD score were recorded. Sepsis in cirrhosis was diagnosed by the conventional criteria of the presence of bacteremia and two or more of the criteria required to diagnose the presence of systemic inflammatory response syndrome (SIRS); (1) a core temperature ≥38°C or ≤36°C; (2) a heart rate ≥90 beats/min; (3) tachypnea ≥20 breaths/min or the need of mechanical ventilation and (4) a white blood cell count ≥12×109/L or ≤4×109/L or >10% of immature neutrophils.

The study included cirrhosis group with 40 patients with mean age of 59 years. 62.5% were males. Etiology of cirrhosis was alcohol in 58%.The mean CTP score was 9 and mean MELD score was 14. The mean spleen size was 13cm.

In the cirrhosis with sepsis group there were 43 patients. Mean age was 52 years. 84% were male patients. The most common etiology for cirrhosis in this group was also alcohol in 51%. The mean CTP score was 9.7 and mean MELD score was 21. The cause for sepsis was SBP in 48%, urinary tract infection in 26%, cellulitis in 14% and respiratory tract infection in 12%. In the sepsis group four patients had developed variceal bleeding during hospitalization.

Control group; Age and sex matched patients were selected as controls. A total of 61 controls were selected for comparative study.

- Selection criteria for the control group were: (1) no evidence for cirrhosis; (2) no active infection.
- Normal ESR and C-reactive protein (CRP) level in laboratory examination.
- Normal leukocyte count in laboratory examination.
- No systemic inflammatory response syndrome (SIRS) criteria.
- Not on antiplatelet drugs or NSAIDS
- No DM, metabolic syndrome, CAD, CKD or stroke

The first complete blood counts (CBCs) performed after admission was reviewed and platelet indices including platelet count, mean platelet volume, platelet distribution width, and platecrit were obtained. The CBCs were performed using a Sysmex XN 1000 analyzer (Japan). The normal range of PLT, MPV, PDW and PCT were 100–300×10^9/L, 7–13 fl, 9–17% and 0.11–0.28% respectively.

Statistical analysis

The cohort was divided into 3 groups as cirrhosis group, cirrhosis with sepsis and control population group. Continuous variables were expressed as means with standard deviations and categorical variables as numbers with percentages. In order to compare groups, either one-way ANOVA or students T test were used for continuous variables, accordingly to the homogeneity of variance *test.* The pearson correlation coefficient was used to measure the strength of the linear relationship between two variables. All p-values of less than 0.05 were considered statistically significant. Statistical analysis was conducted with SPSS 18.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline characteristics of the three groups are shown in Table 1. The age and sex variables are comparable in the three groups. In both cirrhosis and cirrhosis with sepsis groups alcohol was the predominant etiology. CTP score and MELD score was significantly higher in the cirrhosis with sepsis group (p value<0.05). The spleen size was significantly higher in both the cirrhosis groups compared to control group (13 versus 8.9 cm, p value<0.05).

Table 1: Patient characteristic of the three groups.

	Cirrhosis (n=40)	Cirrhosis with sepsis (n=43)	Control (n=61)
Age (years)	59±6	52±10	55±7
Sex	Male 25(62.5%) Female 15 (37.5%)	Male 36 (84%) Female 7 (17.5%)	Male 44 (72%) Female 17(28%)
Cirrhosis etiology	Alcohol 23 (58%)	Alcohol 22 (51%)	
	Cryptogenic 11 (16%)	Cryptogenic 14 (33%)	
	HBV 4 (10%) HCV 2 (6%)	HBV 3 (7%) HCV 4 (9%)	
CTP	9±1.7	9.7±0.86	
MELD	14.0±4.352	21.28±4.18	
Spleen size(cm)	13.10±1.48	13.07±2.33	8.9±2.10
Infectious Foci		SBP 21(48%)	
		UTI 11(26%)	
		Respiratory 5(12%)	
		Cellulitis 6(14%)	

In Table 2, platelet indices of the three groups are shown. The mean platelet count is significantly lower in cirrhosis groups compared to control population (p value <0.05). Mean platelet count is significantly lower in cirrhosis with sepsis group compared to cirrhosis only group (p value <0.05). MPV was significantly higher in cirrhosis groups compared to control group (~9fl versus. 7.7fl, p value <0.05) but between cirrhosis and cirrhosis with sepsis group it was not significantly different (8.9 Vs. 9.1fl, p value >0.05). Mean platecrit was significantly different between the three groups (p value <0.05), lowest in cirrhosis with sepsis group of 0.05%, highest in control population with 0.22% and cirrhosis group had a mean value of 0.09%. Four patients in cirrhosis with sepsis developed variceal bleed and mean PDW and mean platecrit were 19% and 0.04 respectively, which was significantly lower than cirrhosis without sepsis group.

In Table 3, correlation of platelet indices with important parameters of cirrhosis namely CTP score, MELD, spleen size and platelet count is shown. A significant positive correlation was seen between CTP score and MPV (r= 0.4, p<0.05). A significant positive correlation was seen between MELD and MPV (r=0.4, p<0.02). So as liver cirrhosis progresses MPV also increases. A significant negative correlation was seen between platelet count and PDW (r= -0.3, p value <0.01).

Table 2: Platelet Indices of the three groups.

	Cirrhosis (n=40)	Cirrhosis with sepsis (n=43)	Control (n=61)
Platelet count (x1000)	101.900± 41.900	75.470± 30.850	292.01± 78.783
MPV (fl)	8.98± 0.891	9.12± 0.956	7.70± 0.803
PDW	17.83±0.48	18.23±0.764	16.56±0.501
Platecrit	0.092±0.048	0.055±0.022	0.224±0.130

Table 3: Correlation of CTP score, MELD score and spleen size with platelet indices.

	Platelet count	MPV	PDW	Platecrit
CTP score	Negative, r=-0.2 (p value >0.05)	Positive, r=0.4 (p<0.05)	Positive=0.3 (p value >0.05)	Negative, r=-0.3 (p value >0.05)
MELD score	Negative=0.2 (p value>0.05)	Positive, r=0.4 (p value <0.02)	Positive, r=0.2 (p value >0.05)	Negative, r=-0.2 (p value >0.05)
Spleen size	Negative, r=0.4, (p >0.05)	Positive, r=0.3 (p value >0.05)	Positive, r=0.2 (p value >0.05)	Negative, r=-0.4 (p value >0.05)
Platelet count		Negative, r=-0.3 (p value >0.05)	Negative, r=-0.3, (p<0.01)	Positive=0.2 (p>0.05)

DISCUSSION

Thrombocytopenia is the most common and first hematologic index abnormality to develop in cirrhosis.[1] Changes in platelet parameters accompany the progression of various forms of liver disease. This explains the use of platelet count as an indirect marker in some of the noninvasive assessments of hepatic fibrosis.[7]

With availability of newer high performance design automated blood cell analyzers, platelet indices are also being estimated with better standardization and thus have greater clinical utility. Most important parameters among them are platecrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW). We studied platelet indices in cirrhosis, cirrhosis with sepsis and normal control population also.

Mean platelet count in cirrhosis and control group (100×10^9/L versus 290×10^9/L, p value <0.05) in our study was lower than the Chinese study by Xianghoung et al (43×10^9/L versus 95×10^9/L, p value <0.05).[8] MPV in cirrhosis and control group (8.98fl versus 7.7fl, p value <0.05) was also lesser than in the Chinese study by Xianghong et al (13.26 fl versus 9.73fl, p value <0.05).[8] Platecrit in cirrhosis and control group (0.09% versus 0.22%, p value <0.05) was also lower than Chinese study (1.06% versus 1.98 %, p value <0.05).[8] A recent study on the Indian population revealed that blood donors from North Eastern India had mean platelet count of 132 (range 71-267)$\times10^9$/L, MPV of 13.1fl (12-21.9), platecrit of 0.17% (0.10 - 0.38) and PDW of 17.4 fl (14.9-19.6). The corresponding values in South Indian blood donors were 252×109/L (160-478) for platelet count, 7.35fl (6-9.2) for MPV, 0.19% (1.13-1.28) for platecrit and 16.38 fl (15.2-18.5) for PDW.[9] The data from South Indian blood donors are comparable to our data for normal control population. Platelet count was lower and MPV was higher in the north-eastern population and the reason is attributed to existence of Harris platelet syndrome, a well-known entity in northeast and it is the most common cause for inherited giant platelet disorder also.[10]

In another interesting study differences in platelet indices between healthy Han population and Tibetans in China found a significant difference in platelet indices in spite of same genetic background but difference in environment of high altitude with hypoxia in Tibetans. Tibetans had higher platelet count (P<0.01) but lower mean platelet volume (MPV), platelet distribution width (PDW) and platelet-large cell ratio (P-LCR) (P<0.01) compared to Han people. Thus genetic and environmental factors can influence platelet indices of different populations.[11]

In our study MPV in cirrhosis was significantly higher than control population (8.98 versus 7.70f l, P<0.05) and PDW in cirrhosis was significantly higher than control population (17.83 versus 16.56 fl, p value<0.05). The platelets originate by fragmentation of larger precursor cells called megakaryocytes and thereafter interact with monocyte-macrophage system in spleen. In cirrhosis endotoxemia due to gut bacterial translocation, oxidative stress, hyperkinetic circulation, antiplatelet antibody formation, splenic sequestration all influence platelet activity. Thompson et al postulated that large-volume platelets contain more body density, higher activity, more rapid metabolism, more powerful adhesive capacity, and also more bleeding.[12] Xianghoung et al found that MPV and CD62P-a granular protein on platelet surface and marker of activation were higher in liver cirrhosis patients than in the control group.[8] Increase in CD62P and MPV could cause hypersplenism and can destroy platelets. Several other markers of platelet activation like serum beta-thromboglobulin, platelet factor 4 alpha-granule contents, P-selectin expression on resting platelets was considerably higher in cirrhosis patients.[13] Splenic sequestration of platelets not only occurs in cirrhosis with portal hypertension but also in conditions like congestive splenomegaly due to homozygous sickle cell disease in children, hemoglobin C (HbC) disease, HbSC disease, thalassemia major, chronic infections, Gaucher's disease, myeloproliferative disorders, lymphomas.[14]

Studies have found that MPV is increased in coronary artery disease and cerebrovascular accident. It is widely used surrogate marker of platelet function and shown as marker of inflammation in ulcerative colitis, Crohn's disease, rheumatoid arthritis, chronic kidney and liver disease, hepatitis B, pre-eclampsia, metabolic syndromes like diabetes mellitus and nonalcoholic fatty liverdisease.[15]

PDW was significantly higher in the cirrhosis group compared to control group (17.83 versus 16.56fl, p value <0.05). PDW is a more specific marker of platelet activation, since it does not increase during simple platelet swelling. Van Cott and coworkers also observed a decreased effect of storage time on PDW.[16] According to Luzzatto et al increased proportion of giant platelets and platelet distribution width are better indicators of altered platelet homeostasis than mean platelet volume in liver cirrhosis.[17]

Platecrit was also significantly lower in cirrhosis than control population (0.09 versus 0.22%, p value<0.05). Multiple factors contribute to this and include splenic platelet sequestration, immune mediated destruction, bone marrow suppression by toxins and chronic viral infection. Also a low platecrit develops due to reduced levels or activity of the hematopoietic growth factor thrombopoietin (TPO). TPO synthesis is mainly dependent on hepatic function. TPO stimulates the production and differentiation of megakaryocytes into mature platelets. Serum TPO levels correlate inversely with the severity of liver disease as reflected by the degree of fibrosis and child-pugh class. TPO levels and platelet counts increase after orthotopic liver transplantation, strongly supporting impaired TPO

production as a primary cause of decreased platelet mass in at least some patients.[17]

In cirrhosis with sepsis group, mean platelet count was $75x10^9$/L and mean platecrit was 0.055% respectively, which was significantly lower than mean platelet count of 100 x 10^9/L, mean platecrit of 0.09% in cirrhosis without sepsis group. Fitzgerald and colleagues have proposed a mechanism by which platelet activation can be stimulated by bacterial pathogens.[4] In sepsis bacterial ligands like gram negative bacteria-derived LPS, gram positive-derived lipoteichoic acids, bacterial cell wall peptidoglycans bind to toll-like receptor (TLR) family of membrane proteins. TLR-1, TLR-2, TLR-4, TLR-6, TLR-8 and TLR-9 are known to be expressed by platelets. Also bacterial cell wall or membrane proteins interact with platelet membrane proteins and stimulate signaling pathways culminating in thromboxane A2 release and platelet activation. Activated platelets engulf the bacteria in a heterogeneous aggregate and degranulate alpha granules containing thrombocidins, members of a family of anti-bacterial proteins with bactericidal activity against *E. coli*, *staphylococcus aureus* etc.[18] Also bacterial endotoxin induces expression of adhesion molecules on endothelial cells. Endotoxemia induces Increased rolling and adherence of platelets within liver sinusoids.[19] Moreover, decreased survival of circulating platelets and increased removal of platelets from circulation due to phagocytosis by the macrophages in reticuloendothelial system also plays important role. Thus the described changes induced by cirrhosis and sepsis contribute to significant decrease in platecrit and also increases the risk of bleeding.

In our study in the sepsis with cirrhosis group four patients had variceal bleed during admission and data of this subgroup showed mean PDW 19% was significantly higher and mean platecrit 0.04 which was significantly lower than nonbleeding group (p value <0.05). In a Korean study, major bleeding occurred in 12.2% of critically ill cirrhotic patients admitted to the MICU. Sepsis and thrombocytopenia were associated with an increased risk of major bleeding during the MICU stay.[20] So a lower platelet mass with high turnover rate and predominantly immature platelets would predispose to variceal bleeding in sepsis. PDW and platecrit can be useful markers for assessing risk of bleeding in cirrhosis with sepsis and can guide platelet transfusions. Replacement of platelet count with platecrit as a standard for transfusions in a human neonatal intensive care unit resulted in fewer transfusions with no increased incidence of bleeding, indicating the potential value of platecrit to guide clinical decision making, assuming the risk of bleeding would be decreased as functional platelet mass increases.[21]

PDW in cirrhosis with sepsis was significantly higher than in cirrhosis without sepsis (18.03 versus 17.83, p<0.05) The PDW increases during platelet depletion when turnover is accelerated, as occurs in sepsis. A higher value of PDW suggests a large range of platelet size due to swelling, destruction, and immaturity as a result of cirrhosis and superadded sepsis.

Though MPV in cirrhosis was significantly greater than control group there was no significant difference in MPV between the cirrhosis with and without sepsis group (9.12 versus 8.98, p>0.05). Studies are inconclusive in regards to MPV in sepsis and have shown any number of MPV change during sepsis (increase, decrease or biphasic). Van der Lelie et al showed that MPV was elevated in 13 of the 25 septicemia patients, and returned to normal values as soon as the disease was under control.[22] On the other hand, Bessman et al found that MPV decreased during sepsis.[23] An increase in MPV, a sign of larger platelet size, usually is indicative of compensated bone marrow platelet production following stress-induced platelet destruction, as sepsis develops; in fact, the MPV is inversely proportional to the degree of platelet maturity. A decrease in MPV is seen in conditions which reduce platelet production in the bone marrow. A decreased MPV may be related to the presence of endotoxins and suppression of bone marrow , as well as to endotoxins and increased immunoglobulin, both having the ability to induce sustained platelet activation, thereby leading to the release of active compounds that cause granular exhaustion, platelet shrinkage, and decreased preservation and resulting low MPV.[8] Low values of MPV are obtained in hypersplenism, myeloproliferative disorders, sepsis and postchemotherapy.[24].

Despite design advances, there are technical limitations to generation of platelet indices by automated hematology analyzers and these include imprecision in the identification of very small and very large platelets based on internal thresholds in the instrument software, variation in results among different analyzers even within the reference range and so comparison between different studies may be affected. The other limitations of our study are that since it is a retrospective study artifactual alteration like due to prolonged EDTA storage cannot be prevented. MPV can be affected by cardiovascular diseases and many cardiovascular risk factors like, obesity, hypertension, smoking, hyperlipidemia, diabetes mellitus, prediabetes, atrial fibrillation, metabolic syndrome, fatty liver disease. In addition rheumatic and inflammatory chronic diseases also affect MPV value.[25,26] Because this is a retrospective study it is impossible to exclude all these factors in all patients.

CONCLUSION

Platelet indices are useful parameters in cirrhosis. Other than platelet count, PDW and platecrit are useful indices to be monitored in cirrhosis with sepsis.

ACKNOWLEDGEMENTS

We would like to thank Mrs. Jeffy Binu (lecturer and statistician, Azeezia medical college, Kollam, Kerala, India) for assisting us with statistics of this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Qamar AA, Grace ND. Abnormal hematological indices in cirrhosis. Can J Gastroenterology. 2009;23(6):441-5.
2. Luff SA, Papoutsakis ET. Megakaryocytic Maturation in Response to Shear Flow is mediated by the Activator Protein 1 (AP-1) Transcription Factor via Mitogen-Activated Protein Kinase (MAPK) Mechanotransduction. J Biol Chem. 2016;291(15):7831-43.
3. Shah AR, Chaudhari SN, Shah MH. Role of platelet parameters in diagnosing various clinical conditions. Nat'l J Med Res. 2013;3(2):162-5.
4. Fitzgerald JR, Foster TJ, Cox D. The interaction of bacterial pathogens with platelets. Nat. 2006;4(6):445-57.
5. Gao Y, Li Y, Yu X, Guo S, Ji X, Sun T, et al. The impact of various platelet indices as prognostic markers of septic shock. PLoS One. 2014;9(8).
6. Wong F, Bernardi M, Balk R, Christman B, Moreau R, Garcia-Tsao G, et al. Sepsis in cirrhosis: report on the 7th meeting of the International Ascites Club. Gut. 2005;54(5):718-25.
7. Chuks S, Nwokediuko, Ibegbulam O. Quantitative platelet abnormalities in patients with hepatitis b virus-related liver disease. Gastroenterology Research. 2009;2(6):344-9.
8. Xianghong G, Guanping C, Fenghua Y, Jiayin W. Changes in platelet functional parameters and CD62 P expression in liver cirrhosis. Afr Health Sci. 2013; 13(4):1079-83.
9. Naina HV, Harris S. Platelet and red blood cell indices in Harris platelet syndrome. Platelets. 2010;21(4):303-6.
10. Roy AD, Choudhury N, Ray D. Giant Platelets in Platelet Donors - A Blessing in Disguise? J Clin Diagn Res. 2015;9(6):EC01-3.
11. Niu Q, Zhang R, Zhao M, Zeng S, Huang X, Jiang H, et al. Differences in Platelet Indices between Healthy Han Population and Tibetans in China. PLoS One. 2013;8(6):1-5.
12. Thompson CB, Eaton KA, Princiotta SM, Rushin CA, Valeri CR. Size dependent platelet subpopulations: relationship of platelet volume to ultrastructure, enzymatic activity, and function. Br J Haematol. 1982;50(3):509-19.
13. Panasiuk A, Prokopowicz D, Zak J, Matowicka-Karna J, Osada J, Wysocka J. Activation of blood platelets in chronic hepatitis and liver cirrhosis P-selectin expression on blood platelets and secretory activity of β-thromboglobulin and platelet factor-4. Hepato-Gastroenterology. 2001;48(39):818-22.
14. George JN, Rizvi MA. Examination of the blood. Thrombocytopenia. Williams Textbook of Haematology. Chapter 2, Chapter 117. New York: McGraw-Hill Co.; 2001.
15. Ekiz F, Yüksel O, Koçak E, Yilmaz B, Altinbas A, Çoban S, et al. Mean platelet volume as a fibrosis marker in patients with chronic hepatitis B. J Clin Lab Anal. 2011;25(3):162-5.
16. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I.Hippokratia. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. 2010;14(1):28-32.
17. Luzzato G, de Franchis G, Fabris F, Gerunda GE, Girolami A. Increased proportion of giant platelets and platelet distribution width are better indicator of altered platelet homeostasis than mean platelet volume in liver cirrhosis. Folia Hematol Int Mag Klin Morphol Blutforsch. 1988;115(5):719-26.
18. Gangireddy VGR, Kanneganti PC, Sridhar S, Talla S, Coleman T. Management of Thrombocytopenia in Advanced Liver Disease. Canadian Journal of Gastroenterology and Hepatology. 2014;28(10);558-64.
19. Croner RS, Hoerer E, Kulu Y, Hackert T, Gebhard MM, Herfarth C, et al. Hepatic platelet and leukocyte adherence during endotoxemia. Crit. Care. 2006;10: R15:1-6.
20. Cho J, Choi SM, Yu SJ, Park YS, Lee CH, Lee SM, et al. Bleeding complications in critically ill patients with liver cirrhosis. Korean J Intern Med. 2016;31(2):288-95.
21. Gerday E, Baer VL, Lambert DK, Paul DA, Sola-Visner MC, Pysher TJ, Christensen RD. Transfusion, Testing platelet mass versus platelet count to guide platelet transfusions in the neonatal intensive care unit. 2009;49(10):2034-9.
22. Van der Lelie J, Von dem Borne AK. (1983) Increased mean platelet volume in septicemia. J Clin Pathol. 1983;36:693-6.
23. Bessman JD, Gardner FH. Platelet size in thrombocytopenia due to sepsis. Surg Gynecol Obstet. 1983;156:177-80.
24. Greer JP, Arber DA, Glader. Disorders of haemostasis and coagulation. The diagnostic approach to the bleeding disorders. Thrombocytopenia caused by immunological destruction. Wintrobe's Clinical Haematology. 10th Edition, Part V, Chapter 60, Chapter 62. Philadelphia: Williams and Wilkins; 1998.
25. Vizioli L, Muscari S, Muscari A. The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. Int J Clin Pract. 2009;63(10):1509-15.
26. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des. 2011;17:47-58.

Cite this article as: Mukker P, Haridas A, Kallinkeel N, Ajith PG. Comparative study of platelet indices in cirrhosis, cirrhosis with sepsis and normal population. Int J Res Med Sci 2016;4:1423-8.