European Review for Medical and Pharmacological Sciences 2016; 20: 2310-2314

Mean platelet volume in hepatitis A

H. ALMIŞ, I.H. BUCAK, V. ÇELIK, M. TEKIN, F. KARAKOÇ, Ç. KONCA, M. TURGUT

Department of Pediatrics, Adiyaman University School of Medicine, Adiyaman, Turkey

Abstract. – OBJECTIVE: Hepatitis A virus (HAV) still continues to be a serious public health problem worldwide. Mean platelet volume (MPV) is a marker of platelet function and activation. This study aimed to evaluate the relationship between MPV in acute hepatitis A patients as compared to the control group and to assess MPV as an acute phase reactant in acute hepatitis A.

PATIENTS AND METHODS: Seventy-six patients were enrolled in this study. The control group consisted of 41 healthy age- and sex-matched individuals. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, prothrombin time (PT), platelet count (PC), serum albumin (ALB), and mean platelet volume (MPV) levels were recorded. The diagnosis of HAV infection was based on anti-HAV Ig M positivity.

RESULTS: The mean levels of MPV in the study group were significantly statistically lower than in the control group ($p < 0.001$). The MPV levels revealed no correlation with the ALT, AST, ALP, and GGT levels ($p > 0.05$), but the MPV levels correlated with the platelet counts ($p < 0.05$). A 9.75 fL [area under the curve (AUC: 0.756)] optimal cutoff level of MPV with a sensitivity of 69.7% and specificity of 68.3% was determined in the children with acute hepatitis A.

CONCLUSIONS: MPV levels were significantly lower in the patients with acute hepatitis A as compared to the healthy control group. This study demonstrated that MPV may be a negative acute phase reactant for acute hepatitis A. Further studies will explain the role that MPV plays in inflammation and other viral infections.

Key Words:
Mean platelet volume, Hepatitis A, Child.

Introduction

Hepatitis A virus (HAV) is a non-enveloped RNA virus, with an icosahedral structure, that is in the genus of Hepatovirus in the family of Picornaviridae[1]. HAV is usually caused by self-limited acute hepatitis and is transmitted via the fecal oral route[2]. Although the course of HAV infection is usually asymptomatic it rarely develops into fulminant hepatitis[3,4]. Age is the main factor that determines the clinical course of HAV infection, and the infection is more severe with increasing age. Endemicity is closely linked to sanitation, hygiene, socioeconomic status, and vaccination. Outbreaks of HAV infection can occur, although that is less common in developed countries[5]. Hepatitis A is associated with various hematologic abnormalities, such as autoimmune hemolytic anemia, leukopenia, leukocytosis, thrombocytopenia, and thrombocytosis[6-8].

Platelets play a critical role in the inflammatory process. Many cytokines with different functions are secreted by platelets in inflammation[9,10]. Platelet volume is an indicator of platelet function and activation. Mean platelet volume (MPV) is readily measured by clinical hematology analyzers using sodium citrate as the anticoagulant[11]. Mean platelet volume and changes in the activity and function of platelets affect many diseases, such as acute pancreatitis, acute appendicitis, neonatal respiratory distress syndrome, retinal vein occlusion, inflammatory bowel disease, Crimean-Congo hemorrhagic fever, chronic hepatitis C and pulmonary tuberculosis[12-19].

This study aimed to evaluate the relationship between mean platelet volume in hepatitis A patients as compared to a healthy control group.

Patients and Methods

This study was conducted at the Outpatient Clinic of the Department of Pediatrics at Adiyaman University Hospital in Adiyaman City, Turkey. The study was approved by the Institutional Review Board. Seventy-six patients were enrolled in this study. The control group consisted of 41 healthy age- and sex-matched individuals. The data were obtained from patient records accessed from a computerized database system. The alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, prothrombin time (PT), platelet count (PC), serum albumin (ALB), and MPV laboratory findings of those patients were recorded.

Corresponding Author: Habip Almiş, MD; e-mail: drhabipalmis@yahoo.com

Exclusion criteria were the use of any drugs that might change platelet activity and function, and the presence of diabetes mellitus, asthma, peripheral and cerebrovascular disease, malignancies, and chronic diseases. In this study, cholestatic hepatitis was defined as serum bilirubin levels of 10 mg/dL or serum bilirubin levels that were high for more than 14 days.

Blood from the study group and the healthy group was obtained by venipuncture. The patients were evaluated for anti-HAV Ig M and anti-HAV Ig G antibodies. The diagnosis of HAV infection was based on anti-HAV Ig M positivity. Each sample of whole blood was collected in tubes containing ethylenediaminetetraacetic acid. The Sysmex XT 2000i (Roche Diagnostics GmbH, Mannheim, Germany) automated analyzer was used for the blood counts. The reference range for MPV was between 7.0 fL and 11 fL.

Statistical Analysis

SPSS (Statistical Package for Social Sciences Statistical Software) 16.0 Version (SPSS, Inc., Chicago, IL, USA) was used to assess the patient data. The Mann-Whitney U test was performed to compare gender distribution in both groups. The independent two sample t-test was used to compare the age distribution and MPV levels in both groups. The Pearson's test was used to evaluate the correlations among the MPV levels and the other laboratory parameters. The data were expressed as mean ± standard deviation (x±SD). Significance of statistical analysis was defined at a value of $p < 0.05$. To define the optimal cutoff level of MPV measured in the acute hepatitis A, the reason why characteristic (ROC) curve analysis was used.

Results

Seventy-six children (42 males; 34 females) with acute hepatitis A and 41 healthy control subjects (22 males; 19 females) were included in this study. The mean age for the study group was 7.2 ± 3.1 and the mean age for the control group was 5.56 ± 2.56 years. There was no statistically significant difference with regard to age and gender between the groups ($p > 0.05$). The laboratory findings and demographic data for the study group and the control group are shown in Table I. The mean levels of MPV in the study group were statistically significantly lower than in the control group ($p < 0.05$). The MPV levels showed no correlation with the ALT, AST, ALP, and GGT levels ($p > 0.05$), but we detected a correlation between the MPV levels and the platelet counts ($p < 0.05$). We measured the CRP, leukocyte count, and ESR levels in the acute hepatitis A patients and we found no statistically significant correlation between these levels and the MPV levels ($p > 0.05$).

A 9.75 fL [area under the curve (AUC: 0.756)] optimal cutoff level of MPV with a sensitivity of 69.7% and specificity of 68.3% was determined in the children with acute hepatitis A (Figure 1). None of our patients developed fulminant hepatitis. Death did not occur in any of the studied cases.

Discussion

The most important finding of our study showed that MPV levels significantly decreased in patients with acute hepatitis A compared to the healthy control group. This study showed that MPV may be a negative acute phase reactant in acute hepatitis A.

Platelets have three types of granules: α-granules, dense bodies, and lysosomes. The α-granules and the dense bodies play a role in the activation of hemostasis and in the production of inflammation and cytokine; they are also modulators of inflammation[20]. Platelets are not only required for primary hemostasis, they also play an important pro-inflammatory role[21]. Platelets are activated by different cytokines. IL-6 and TNF-a contribute to

Table I. Demographic and platelet parameters and laboratory findings of the control and acute hepatitis A groups.

	Acute hepatitis A	Control	*p* value
Age (years)	7.44 ± 2.93	5.56 ± 2.56	> 0.05
Gender (male/female)	42 (55.3%)/34 (34.7%)	22 (53.7%)/19 (46.3%)	> 0.05
ALT	1342.32 ± 763.24	19.24 ± 5.73	< 0.05
AST	1186.03 ± 860.6	28.53 ± 6.29	< 0.05
Platelet count (10^3 µL)	263.12 ± 80.12	249.61 ± 71.22	< 0.05
MPV (fL)	8.75 ± 1.24	10.02 ± 1.40	< 0.05

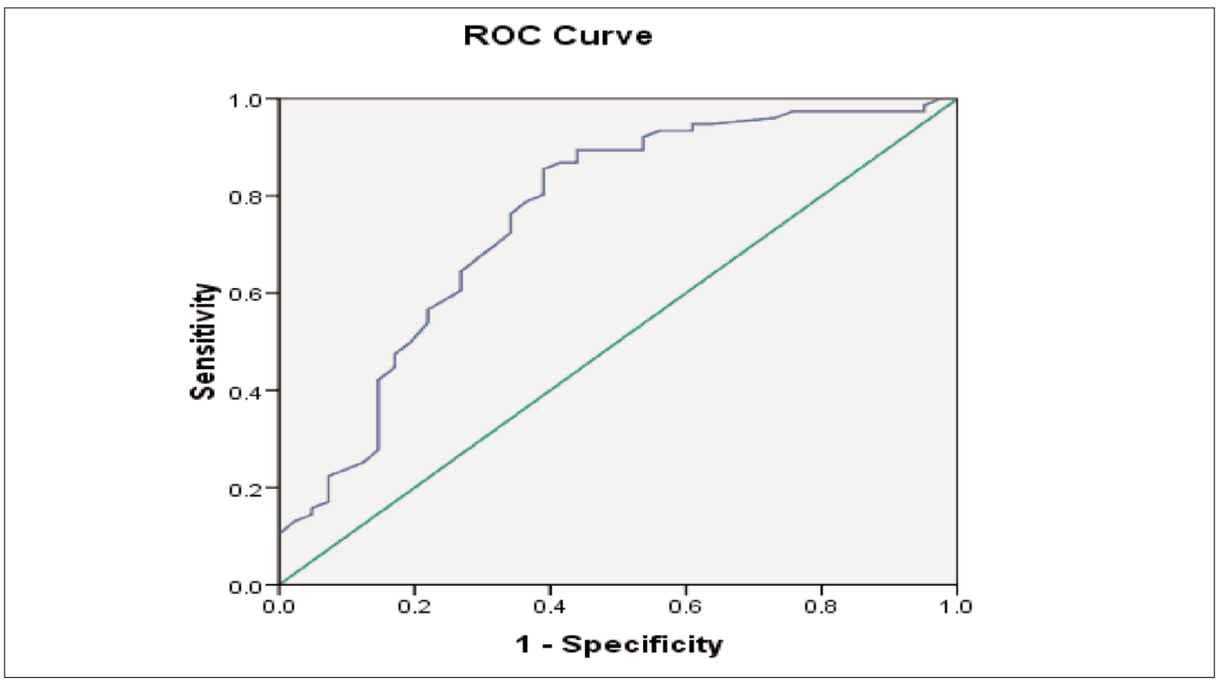

Figure 1. Mean platelet volume and differentiation between acute hepatitis A and the control group, ROC (receiver operating characteristic) curve; the optimal cutoff level of the mean platelet volume (MPV) was 9.75 fL (sensitivity, 69.7%; specificity, 68.3%; AUC, 0.756).

the inflammatory process by which the platelets are activated[22]. After degranulation, the size of the platelets is reduced. Anti-TNF-a agents increase MPV and the size of the platelets[23].

Platelet size varies depending on the platelet function and activity. MPV can be easily measured by whole blood analysis[24]. Nowadays, MPV is a marker widely used to detect platelet function and activity and acute phase reactant[24,25].

Many studies have shown that the MPV levels decreases during the acute and active inflammatory period of some diseases. Liu et al[26] showed that MPV levels decreased in Kawasaki disease. Beyazit et al[12] demonstrated that a statistically significant decrease in MPV levels occurred in acute pancreatitis. Kisacik et al[27] demonstrated that MPV levels significantly decreased in ankylosing spondylitis and rheumatoid arthritis patients with active disease. Yuksel et al[28] reported that MPV levels decreased in ulcerative colitis. Danese et al[29] detected that MPV levels decreased in active inflammatory bowel disease. Mete et al[25] showed that MPV levels decreased in children with acute rotavirus gastroenteritis and that study suggested that MPV could be used as an acute phase reactant in children with rotavirus gastroenteritis.

Ekiz et al[30] showed that increased MPV was statistically significant in patients with chronic hepatitis B. Karaman et al[18] demonstrated that high MPV levels (especially those over 8.4 fL) may help predict advanced fibrosis in patients with chronic hepatitis C. Turhan et al[31] demonstrated that MPV levels significantly increased in inactive HBs Ag carrier patients.

There are a few limited studies on the MPV levels in hepatitis B. More recently, Hu et al[32] showed that MPV levels were significantly increased in chronic hepatitis B patients compared with acute hepatitis B patients and healthy control group. This study suggests that high MPV levels are an indicator of disease severity in hepatitis B.

Previous studies have supported the findings that MPV levels are elevated in some chronic viral diseases, such as chronic hepatitis B and C, whereas MPV levels decrease in some acute viral diseases, such as rotavirus gastroenteritis, HIV, and RSV[25,31-35]. MPV is inversely correlated with platelet count[10]. Therefore, MPV is usually increased in patients with thrombocytopenia caused by a viral infection.

There is no specific study on MPV in acute hepatitis A. Jørgensen et al[36] demonstrated that

MPV levels were significantly lower in patients with liver disease. According to our knowledge, this current study is the first to assess the relationship between MPV and acute hepatitis A.

The present study has some limitations. First was the absence of a group of patients with fulminant hepatitis, which in our determination prevented the ability to evaluate whether a relationship exists between MPV and disease severity. Another limitation is that this work is retrospective.

Conclusions

MPV may be a negative acute phase reactant for acute hepatitis A. Further studies are needed to explain the role that MPV plays in inflammation and other viral infections.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

1) Nainan OV, Xia G, Vaughan G, Margolis HS. Diagnosis of hepatitis A virus infection: a molecular approach. Clin Microbiol Rev 2006; 19: 63-79.
2) Mulyanto Wibawa ID, Suparyatmo JB, Amirudin R, Ohnishi H, Takahashi M, Nishizawa T, Okamoto H. The complete genomes of subgenotype IA hepatitis A virus strains from different islands in Indonesia form a phylogenetic cluster. Arch Virol 2014; 159: 935-945.
3) Koff RS. Hepatitis A. Lancet 1998; 351: 1643-1649.
4) Stapleton TJ, Lemon SM. Infectious diseases. In: Hoeprich PD, Jordan MC, Ronald AR. Hepatitis A and hepatitis E. 5. Philadelphia, 1994; pp. 790-800.
5) Franco E, Meleleo C, Serino L, Sorbara D, Zaratti L. Hepatitis A: epidemiology and prevention in developing countries. World J Hepatol 2012; 4: 68-73.
6) Çetinkaya B, Tezer H, Özkaya Parlakay A, Revide Sayli T. Evaluation of pediatric patients with hepatitis A. J Infect Dev Ctries 2014; 8: 326-330.
7) Maiga MY, Oberti F, Rifflet H, Ifrah N, Calès P. Hematologic manifestations related to hepatitis A virus. 3 cases. Gastroenterol Clin Biol 1997; 21: 327-330.
8) Kumar KJ, Kumar HC, Manjunath VG, Anitha C, Matha S. Hepatitis A in children- clinical course, complications and laboratory profile. Indian J Pediatr 2014; 81: 15-19.
9) Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 2011; 17: 47-58.
10) Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996; 7: 157-161.
11) Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. Platelets 2002; 13: 301-306.
12) Beyazit Y, Sayilir A, Torun S, Suvak B, Yesil Y, Purnak T, Oztas E, Kurt M, Kekilli M, Ibis M. Mean platelet volume as an indicator of disease severity in patients with acute pancreatitis. Clin Res Hepatol Gastroenterol 2012; 36: 162-168.
13) Albayrak Y, Albayrak A, Albayrak F, Yildirim R, Aylu B, Uyanik A, Kabalar E, Güzel IC. Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis. Clin Appl Thromb Hemost 2011; 17: 362-366.
14) Canpolat FE, Yurdakök M, Armagangil D, Yigit S. Mean platelet volume in neonatal respiratory distress syndrome. Pediatr Int 2009; 51: 314-316.
15) Örnek N, Ogurel T, Örnek K Onaran Z. Mean platelet volume in retinal vein occlusion. Eur Rev Med Pharmacol Sci 2014; 18: 2778-2782.
16) Öztürk ZA, Dag MS, Kuyumcu ME, Cam H, Yesil Y, Yilmaz N, Aydinli M, Kadayifci A, Kepekci Y. Could platelet indices be new biomarkers for inflammatory bowel diseases? Eur Rev Med Pharmacol Sci 2013; 17: 334-341.
17) Ekiz F, Gürbüz Y, Basar Ö, Aytekin G, Ekiz Ö, Sentürk ÇS, Aktas B, Yilmaz B, Altinbas A, Çoban S, Sencan I. Mean platelet volume in the diagnosis and prognosis of Crimean-Congo hemorrhagic fever. Clin Appl Thromb Hemost 2013; 19: 441-444.
18) Karaman H, Karakükcü Ç, Karaman A, Kayman T, Yalçin S, Ta demir AE, Zararsiz G, Poyrazoglu OK. Mean platelet volume as a fibrosis marker in patients with chronic hepatitis C. Turk J Med Sci 2013; 1: 39-45.
19) 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: 1009-1013.
20) Jenne CN, Urrutia R, Kubes P. Platelets: bridging hemostasis, inflammation, and immunity. Int J Lab Hematol 2013; 35: 254-261.
21) Zarbock A, Polanowska-Grabowska RK, Ley K. Platelet-neutrophil-interactions: linking hemostasis and inflammation. Blood Rev 2007; 21: 99-111.
22) Kaser A, Brandacher G, Steurer W, Kaser S, Offner FA, Zoller H, Theurl I, Widder W, Molnar C, Ludwiczek O, Atkins MB, Mier JW, Tilg H. Interleukin-6 stimulates thrombopoiesis through thrombopoietin: role in inflammatory thrombocytosis. Blood 2001; 98: 2720-2725.

23) Gasparyan AY, Sandoo A, A Stavropoulos-Kalinoglou A, Kitas GD. Mean platelet volume in patients with rheumatoid arthritis: the effect of anti-TNF-therapy. Rheumatol Int 2010; 30: 1125-1129.

24) Martin JF, Trowbridge EA, Salmon G, Plumb J. The biological significance of platelet volume: its relationship to bleeding time, platelet thromboxane B2 production and megakaryocyte nuclear DNA concentration. Thromb Res 1983; 32: 443-460.

25) Mete E, Akelma AZ, Cizmeci MN, Bozkaya D, Kanburoglu MK. Decreased mean platelet volume in children with acute rotavirus gastroenteritis. Platelets 2014; 25: 51-54.

26) Liu R, Gao F, Huo J, Yi Q. Study on the relationship between mean platelet volume and platelet distribution width with coronary artery lesion in children with Kawasaki disease. Platelets 2012; 23: 11-16.

27) Kisacik B, Tufan A, Kalyoncu U, Karadag O, Akdogan A, Ozturk MA, Kiraz S, Ertenli I, Calguneri M. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine 2008; 75: 291-294.

28) Yüksel O, Helvaci K, Basar O, Köklü S, Caner S, Helvaci N, Abayli E, Altiparmak E. An overlooked indicator of disease activity in ulcerative colitis: mean platelet volume. Platelets 2009; 20: 277-281.

29) Danese S, Motte CD Cde L, Fiocchi C. Platelets in inflammatory bowel disease: clinical, pathogenic, and therapeutic implications. Am J Gastroenterol 2004; 99: 938-945.

30) Ekiz F, Yüksel O, Koçak E, Yilmaz B, Altindas A, Çoban S, Yüksel I, Üsküdar O, Köklü S. Mean platelet volume as a fibrosis marker in patients with chronic hepatitis B. J Clin Lab Anal 2011; 25: 162-165.

31) 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: 202-205.

32) Hu Y, Lou Y, Chen Y, Mao W. Evaluation of mean platelet volume in patients with hepatitis B virus infection. Int J Clin Exp Med 2014; 7: 4207-4213.

33) Purnak T, Olmez S, Torun S, Efe C, Sayilir A, Ozaslan E, Tenlik I, Kalkan IH, Beyazit Y, Yuksel O. Mean platelet volume increased in chronic hepatitis C patients with advanced fibrosis. Clin Res Hepatol Gastroenterol 2013; 37: 41-46.

34) 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: 549-555.

35) Renshaw AA, Drago B, Toraya N, Gould EW. Respiratory syncytial virus infection is strongly correlated with decreased mean platelet volume. Int J Infect Dis 2013; 17: e678-e680.

36) Jørgensen B, Fischer E, Ingeberg S, Hollaender N, Ring-Larsen H, Henriksen JH. Decreased blood platelet volume and count in patients with liver disease. Scand J Gastroenterol 1984; 19: 492-496.