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Mean platelet volume is increased in patients with chronic hepatitis B

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ABSTRACT

Objectives. Hepatitis secondary to infection with the hepatitis B virus (HBV) is one of the most common causes of viral hepatitis worldwide. Multiple extrahepatic manifestations of HBV infection have been recognized. However, the effect of HBV infection on the mean platelet volume (MPV) is unknown. The aim of this study was to assess the MPV, an indicator of platelet activation, in patients with chronic hepatitis B. ***Methods.*** The study group consisted of 50 patients with chronic hepatitis B. An age, gender, and body mass index-matched control group consisted of 50 healthy volunteers. All patients and control participants underwent echocardiographic examination. We measured the serum MPV values in patients and control participants. ***Results.*** Mean platelet volume was significantly higher among patients with HBV when compared with the control group (9.2±2.2 vs 7.1±1.6 fl, respectively; $p<0.001$). ***Conclusions.*** We have shown that MPV was significantly elevated in patients with chronic hepatitis B compared to control participants. According to our knowledge, there has been no previous study of MPV in chronic HBV patients. Therefore, we have investigated the possible association between HBV infection and MPV.

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Keywords: Platelets; arrhythmia; hepatitis B virus; mean platelet volume; thromboembolism

Introduction

The hepatitis B virus (HBV) infection is a major public health problem worldwide. It is known that chronic HBV infection triggers autoimmune disorders. A strong relationship has been found with essential mixed cryoglobulinemia, glomerulonephritis, and porphyria tarda. Additionally, HBV infection has been associated with extrahepatic involvements such as Sjogren's syndrome, lichen planus, and Hashimato's thyroiditis [1, 2].

Recent studies revealed that the virus has extensive reservoirs of extrahepatic replication. Hepatitis C virus (HCV) and HBV proteins and nucleic acids have been found in a number of non-hepatic tissues including lymph nodes, spleen, bone marrow, kidney, colon, stomach, periadrenal ganglia, skin, thyroid, pancreas, testis, ovaries, brain, heart and lung tissue [3-6]. It is also considered that there is a relation between HBV and HCV and coronary artery

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disease. Conflicting findings on the possible association between HBsAg positivity, indicating inactive HBsAg carrier status, and atherosclerosis have been reported [7, 8]. However, there is no consensus on this issue.

Recent studies suggest that mean platelet volume (MPV) is a potentially useful prognostic biomarker in patients with cardiovascular disease such as acute coronary syndrome, valvular heart disease, pulmonary thromboembolism and hypertension [9-12].

Our present study was conducted to research the effect on MPV among the persons with HBV infection.

Methods

Selection of the patients

50 patients with mean age of 43±13 years, who has been followed in the outpatient clinic of infection diseases department because of the chronic hepatitis B, with normal liver enzymes and who has not received antiviral treatment, are included in the study. The control group was consisted of 50 successive persons, with mean age of 39±13 years who appealed to the cardiology and Infectious disease outpatient clinics because of various reasons and did not have any structural cardiac pathologies identified.

The physical examination, the medical history of patients, complete blood count and the blood biochemistry were evaluated in all groups. The subjects were defined as hypertensive if their blood pressure was ≥140/90 mmHg or if they were receiving any antihypertensive medication. Diabetes mellitus was defined as the presence of a history of antidiabetic medication usage or fasting glucose level above 126 mg/dl. Smoking status was classified as smokers or those who never smoked.

Patients with coronary artery disease, heart failure, valve disease, cardiomyopathy, hypertension, diabetes mellitus, chronic lung disease, thyroid dysfunction, anemia, malignancy, renal and hepatic insufficiency, chronic inflammatory disease, pregnancy, septicemia, cerebrovascular accident, and thrombocytopenia were excluded from the study. All of the patients were in sinus rhythm and none of them were taking cardioactive medications like antiarrhythmics, antiplatelet, antipsycotics, and antihistaminics. Each patient signed an informed consent form and the local ethics committee approved the study.

For the analysis of MPV, blood samples with K3 EDTA were analyzed after one hour of venipuncture by the Sysmex XT-2000i analyzer (Sysmex, Kobe, Japan).

Echocardiographic Measurements

Two-dimensional, M-mode, pulsed and color flow doppler echocardioagraphic examinations of all subjects were performed by the same examiner with a commercially available machine (Vivid 7 pro, GE , Horten, Norway, 2-5 mHz phased array transducer). During echocardiography, a single-lead electrocardiogram was recorded continuously. M-mode measurements were performed according to the criteria of the American Society of Echocardiography [13,14]. The right atrium , left atrium (LA) diameter, LV end-systolic and end-diastolic diameters were measured. LV ejection fraction (EF) was estimated by Simpson's rule.

Statistical Analyses

The SPSS 16.0 statistical program (SPSS, Chicago, IL, USA) was used for the statistical study. Data were expressed as mean±standard deviation (SD). Student t-test, one-way ANOVA- and chi-square test were used to compare the variables. P value of less than 0.05 was considered significant.

Results

There was no statistically significant difference between patient group and the control with regard to age, gender, diameters of the left atrium, right atrium and the left ventricle, pulmonary artery systolic pressure, body mass index and smoking status (Table 1). Additionally, there were no significant differences between the two groups with regard to lipid profile, fasting glucose levels, creatinine, white and red blood cell and platelet counts. However, MPV was found to be significantly higher in patients with HBV infection (9.2±2.2 fl vs 7.1±1.6 fl, $p<0.001$, Table 2).

Discussion

The present study showed that MPV was significantly higher in patients with chronic HBV infection compared to controls.

Recently, it has been emphasized the importance

Table 1. Comparison of clinical and echocardiographic features of HBV patients and controls group

	Patients (n=50)	Controls (n=50)	*p*
Age (years)	43.0±13.0	39.0±13.0	0.26
Male/female	19/31	22/28	0.20
LA diameter (mm)	33.5±3.5	34.2±3.6	0.69
LV EDD (mm)	45.2±4.2	44.2±4.5	0.24
LV ESD (mm)	23.4±2.1	24.4±2.7	0.61
RA diameter (mm)	37.6±3.8	32.8±3.0	0.48
LVEF (%)	64.0±5.2	64.8±5.9	0.33
BSA (m2)	1.8±0.4	1.8±0.3	0.25
Heart rate (bpm)	78.1±8.2	69.3±8.3	0.12
SPAP (mmHg)	28.8±3.9	25.4±3.4	0.19
SBP (mmHg)	127±25	122.5±24	0.66
DBP (mmHg)	72.5±9	79.3±12	0.88
BMI (kg/m2)	28±4.9	24±3.1	0.52
Smoking	11	12	0.70

BMI=body mass index, BSA=body surface area, DBP=diastolic blood pressure, HBV=hepatitis B virus, LA=left atrium, LVEDD=left ventricular end-diastolic dimension, LVEF=left ventricular ejection fraction, LVESD=left ventricular end-systolic dimension, RA= right atrium, SBP=systolic blood pressure, SPAP= systolic pulmonary artery pressure,

Table 2. Comparison of biochemical and hematological parameters of HBV patients and controls group

	Patients (n=42)	Controls (n=50)	*p*
Glucose (mg/dl)	98.2±13.0	93.5±11.0	0.53
Creatinin (mg/dl)	0.8±0.2	0.75±0.3	0.28
Total cholesterol (mg/dl)	201.0±55.0	195.0±52.0	0.17
Trigliserid (mg/dl)	132.0±25.0	125±23	0.86
HDL- holesterol (mg/dl)	42.0±7.0	44.2±7.5	0.22
White-blood cell count ($x10^3/mm^3$)	7.9±2.8	8.6±2.6	0.23
Hemoglobin (g/dl)	14.1±2.6	13.3±2.2	0.41
Platelet count ($x10^3$)	265.4±63.4	282.3±89.3	0.65
Mean platelet volume (fl)	9.2±2.2	7.1±1.6	<0.001

dl=deciliter, fl=femtolitre, HBV=hepatitis B virus, HDL=high density lipoprotein

of HCV infection in myocarditis and cardiomyopathy. HBV and HCV has been associated with atherosclerosis and HBV sero-positivity in the patients with coronary artery disease was found to be related to cardiac failure and increased mortality [15, 16].

Matsumori *et al.* [6] found anti-HCV positivity in 10.6% of the patients with hypertrophic cardiomyopathy and in 6.3% of the patients with dilated cardiomyopathy. Additionally, they found arrhythmia in 21.5% of anti-HCV positive patients; hence, the authors suggested that HCV might play a role in several cardiac disorders with formerly unidentifiable etiology.

In our previous study, an association was also found between HBV infection and the left and right ventricular dysfunction [17]. There are some conflicting studies in the literature about the relation between HBV/HCV and atherosclerosis and coronary

artery disease [7, 8,18].

Wang *et al.* [19] found higher NT-proBNP levels, increasing with the heart failures in the HBV/HCV patients not having liver failure, in comparison with the control group. Similarly, Kucukazman *et al.* [20] found higher BNP levels in asymptomatic hepatitis B virus positive patients. According to this situation, it is considered that both HBV and HCV infections may increase heart failure. Despite a large number of studies done about the relation between cardiomyopathy, myocarditis and heart failure, the data about cardiac effects of HBV is limited.

Recent studies suggest that MPV is a potentially useful prognostic biomarker in patients with cardiovascular disease such as acute coronary syndrome, valvular heart disease pulmonary and systemic thromboembolism and hypertension [21]. However, relationship between MPV and chronic HBV infection is not defined.

The present study showed that MPV was significantly higher in patients with chronic HBV infection compared to controls. It is known that platelets having dense granules are more active biochemically, functionally, and metabolically and are a risk factor for developing coronary and pulmonary thrombosis, leading to myocardial infarction. In previous studies, increased MPV was demonstrated in acute myocardial infarction [22, 23], mitral and aortic stenosis [9, 10], deep vein thrombosis [11], and hypertension [12].

The Limitation of the Study

The most significant limitation of our study was the insufficient number of patients. The other limitation of our study was the method, so it was not prospective.

Conclusions

In conclusion, our findings show that MPV is increased in patients with chronic HBV infection, compared to controls. The increased MPV may predict the possible increase of the prevalence of cardiovascular events in patients with HBV. Further prospective studies are required to establish the clinical significance of increased MPV and to investigate the role of anti-platelet agents in chronic HBV patients.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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