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Original Article

Mean platelet volume in patients with biliary and non-biliary acute pancreatitis

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Abstract: Introduction: Acute pancreatitis (AP) is a systemic inflammatory disease. We aimed to detect whether there was a change of mean platelet volume (MPV) level on onset and remission patients with biliary and non-biliary acute pancreatitis. Materials and methods: In our emergency service patients diagnosed with biliary and nonbiliary AP were analyzed retrospectively. Laboratory results measured in onset and remission were recorded and compared. Results: Total number of patients enrolled in our study was 331 (177 female). 194 cases were classified as biliary and 137 were as non-biliary AP. Average age and numbers of female patients of biliary cases were higher than that of nonbiliary cases. Initial MPV values were lower than remission values in all patients with AP. In biliary group initial MPV was 8.42 ± 1.04 and remission value was 8.71 ± 1.12. In nonbiliary group initial MPV was 8.07 ± 1.02 and remission value was 8.4 ± 1.06. In both groups on onset had lower mean MPV levels than those in remission (P = 0.0001 both of them). Conclusions: MPV values were higher than initial values in remission period in patients both of groups. MPV was lower in non-biliary AP group than biliary AP group that can be an indicator of early-onset infection.

Keywords: Biliary acute pancreatitis, nonbiliary acute pancreatitis, mean platelet volume

Introduction

Acute pancreatitis (AP) is an inflammatory disease with a highly variable clinical course. The incidence is estimated as 30-113/100,000. Most patients develop mild AP, whereas 10-20% suffers the severe form, and the mortality rate for all cases is 10-15% [1]. The most common causes of acute pancreatitis are gallstones and alcoholism. The clinical course of biliary pancreatitis is mild in most cases, and cholecystectomy minimizes the risk of recurrent biliary pancreatitis or other complications [2]. An accurate diagnosis of the underlying etiology is essential for follow-up procedures and the treatment. Serum aspartate aminotransferase (AST), total bilirubin and alkaline phosphatase (ALP) levels and imaging methods are useful in the discrimination of biliary vs. non-biliary acute pancreatitis [3]. Since the diagnostic sensitivity by abdominal ultrasonography, the first imaging modality to be performed in emergency conditions is about 67-87%, biliary AP, which requires urgent operation, is sometimes misdiagnosed as non-biliary AP [4]. However, fast, inexpensive and non-invasive serum biomarker tests are needed to differentiate between patients with biliary and non-biliary AP. Mean platelet volume (MPV) is a parameter of complete blood count (CBC) analysis and measures the average size of the platelets. In many studies MPV is used as an indicator of platelet function in thrombotic and inflammatory diseases [5]. High grade inflammatory conditions like inflammatory bowel disease, rheumatoid arthritis and familial Mediterranean fever are characterized by small sized platelets, and the disease remission is characterized by large platelets [6]. However, there are studies in the literature reporting decrease or increase in

Table 1. Liver and pancreas enzymes show in bilier and nonbilier acute pancreatitis group

Variables	Bilier group, at admission n: 195	Non-Bilier group at admission n: 137	*P*
Age (years)	47.69 ± 17.64	58.29 ± 17.43	0.0001
Gender	Male 88 64.2%	64 33%	0.0001
	Female 49 35.8%	130 67%	
Glucose (mg/dl)	148.53 ± 82.42	167.04 ± 115.48	0.095
BUN (mg/dl)	36.68 ± 24.7	39.44 ± 34.34	0.398
Creatinine (mg/dl)	0.87 ± 0.57	0.99 ± 0.89	0.159
AST (U/l)	203.08 ± 213.18	77.83 ± 139.32	0.0001
ALT U/l)	216.99 ± 208.76	71.4 ± 126.99	0.0001
ALP (U/l)	175.56 ± 150.23	111.58 ± 67.48	0.0001
GGT (U/l)	325.42 ± 319.37	136.35 ± 280.92	0.0001
LDH (U/l)	374.14 ± 220.21	291.75 ± 232.4	0.001
Amylase (U/l)	790.5 (354.5-1470.25)	528 (204-1141)	0.005
Lipase (U/l)	1365 (585-3967.5)	982 (316-2420)	0.016
TotalBilirubin (mg/dl)	2.17 ± 2.21	1.39 ± 2.05	0.001
Direct.Bilirubin (mg/dl)	1.31 ± 1.65	0.73 ± 1.53	0.001
Calcium (mg/dl)	8.9 ± 0.8	9 ± 0.91	0.312
Na (mmol/L)	137.48 ± 10.12	135.62 ± 4.63	0.047

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatases; BUN, blood urea nitrogen; CRP, C reactive protein; GGT, gama-glutamyl-transferase; LDH, lactate dehydrogenase; Na, sodium.

MPV during the inflammatory process of acute pancreatitis. Most studies have described biomarkers that can differentiate biliary AP from non-biliary AP. In our study, we aimed to determine the variability of MPV in differentiating biliary from non-biliary AP.

Materials and methods

We evaluated the medical records retrospectively of 362 patients admitted to the emergency department with biliary or non-biliary AP from December 2011 to December 2012 study after the approval of the Research Ethics Committee was obtained. Thirty-one patients who had pregnancy, malignancy or end-stage renal disease, or had admitted to the Intensive Care Unit or had died before were excluded from the study. The patients presenting with abdominal pain, those with > 3 times increase in pancreatic enzymes (amylase and lipase), diagnosed with AP, and those in whom the clinical diagnosis was supported by imaging techniques were included in the study [7]. The first day of hospitalization was set as the onset, and the day that a patient was discharged from the hospital since she/he could have started oral intake and was relieved of pain was set as remission. MPV values from the first CBC and before discharge were documented. Haemoglobin concentration, leukocyte counts, thrombocyte counts, and MPV values of the two groups at the beginning of illness and in clinical remission were recorded and compared. Serum concentrations of C-reactive protein (CRP), glucose, blood urea nitrogen (BUN), creatinine, AST, alanine aminotransferase (ALT), ALP, gama-glutamyl-transferase (GGT), lactate dehydrogenase (LDH), amylase, lipase, total bilirubin, direct bilirubin, calcium, and sodium levels were also compared.

The data of this study were analysed by using the statistical software of Number Cruncher Statistical System (NCSS) version 2007 (Utah, USA). Data were expressed by descriptive statistics (mean, standard deviation, median and interquartile range). For a comparison of variables of normal distribution, the t-test for independent samples was used and Mann-Whitney U test was used for the comparison of variables with non-normal distribution. The Chi-square test and the Fisher's exact test were used to analyse qualitative variables and Pearson correlation analyses were used to determine relationships between variables. The results were considered significant at $P < 0.05$.

Results

Of the 362 patients diagnosed with AP, 331 patients were included in the study. The mean

Table 2. Full blood counts shown in bilier and nonbilier acute pancreatitis group

variables		Bilier	Non-Bilier	*P* (bilier and nonbilier)
		n ± st. dv	n ± st. dv	
n = 331		n = 195	n = 137	
Haemoglobin (g/dl)	Onset	13.03 ± 1.89	13.24 ± 2.49	0.387
	Remission	11.77 ± 1.77	12.33 ± 1.95	0.007
	P (onset and remission)	0.0001	0.0001	
Leukocyte (µl)	Onset	11610 ± 5040	12050 ± 5470	0.457
	Remission	8190 ± 4830	8320 ± 3900	0.799
	P onset and remission)	0.0001	0.0001	
Thrombocyte (µl)	Onset	246170 ± 79560	266770 ± 102780	0.041
	Remission	238510 ± 85460	270980 ± 93250	0.001
	P (onset and remission)	0.118	0.585	
MPV	Onset	8.42 ± 1.04	8.07 ± 1.02	0.003
	Remission	8.71 ± 1.12	8.4 ± 1.06	0.011
	P (onset and remission)	0.0001	0.0001	

MPV, mean platelet volume.

age of the 194 patients (130 women and 64 men) in the biliary AP group was 58.29 ± 17.43 years, and of the 137 patients (49 women and 88 men) in the non-biliary AP group was a 47.69 ± 17.64 years. The risk of biliary pancreatitis was 3.64 times greater in the female patients than in males. **Table 1** shows the levels of liver enzymes, pancreatic enzymes and the biochemical data in both groups. Mean serum CRP, blood glucose, BUN, creatinine and calcium levels were not significantly different between biliary and non-biliary AP groups ($P \geq 0.05$), while mean AST ($P = 0.0001$), ALT ($P = 0.0001$), ALP ($P = 0.0001$), GGT ($P = 0.0001$) and LDH ($P = 0.001$) levels was significantly higher in biliary AP group than the non-biliary AP patients. Also, the mean levels of serum amylase ($P = 0.005$), lipase ($P = 0.016$), total bilirubin ($P = 0.001$) and sodium ($P = 0.047$) were higher in the biliary AP group patients. The length of hospital stay in biliary AP patients (4.91 ± 4.41 days) was significantly lower than those in the non-biliary AP group (10.02 ± 7.15 days) ($P = 0.0001$).

Table 2 shows the variations of haemoglobin, leukocyte and thrombocyte count and MPV on admission and in remission in both groups. In both groups the patients on admission had lower mean MPV levels than those in remission ($P = 0.0001$). The mean MPV on admission was higher in the group of patients with biliary AP than in those with non-biliary AP ($P = 0.003$). Also, mean MPV was higher in biliary AP group patients in remission period ($P = 0.011$).

In biliary AP patients, there was no relationship between MPV values and the variations of age, length of hospital stay, haemoglobin, leukocyte count, blood glucose and serum creatinine levels, AST, ALT, ALP, GGT, amylase and lipase activities, total bilirubin and direct bilirubin, calcium and sodium levels ($P > 0.05$). A positive correlation was found between MPV and LDH ($r = -0.143$, $P = 0.048$).

There was also no relationship between MPV values and the variations of age, length of hospital stay, haemoglobin, leukocyte count, CRP, blood glucose and serum creatinine levels, ALT, ALP, GGT, LDH and lipase activities, total bilirubin, direct bilirubin, calcium and sodium levels in non-biliary AP patient group ($P > 0.05$). Also, there was a positive correlation between MPV and AST ($r = -0.223$, $P = 0.009$) and amylase ($r = 0.203$, $P = 0.018$) in non-biliary AP patient group.

In biliary AP ($r = -0.32$ $P = 0.0001$) and non-biliary AP ($r = -0.44$, $P = 0.0001$) groups, a negative correlation was observed between MPV values and platelet values.

Discussion

MPV reflects the platelet size and is an indicator of platelet function or reactivity. The throm-

bocytes play an important role in the pathogenesis of several disorders, including inflammatory processes. The role of MPV was investigated in several disorders. It was shown to increase in the presence of cardiovascular risk factors, and to decrease in diseases with prominent inflammation, and also to increase following treatment with non-steroidal anti-inflammatory drugs [8-11]. These findings were associated with the changes in thrombocytes related to the severity of systemic inflammation.

AP is an inflammatory process associated with tissue damage caused by free radicals, oxidative stress and cytokine release [12]. Increased levels of serum amylase and serum lipase caused by tissue damage, are the most popular laboratory markers for the diagnosis and follow-up of AP [13]. Platelet activating factor (PAF) serves as a primary mediator of inflammation in the pathogenesis of AP. PAF contributes to local tissue damage and bleeding. MPV, an indicator of thrombocytic activity, has been investigated in various proinflammatory and prothrombotic clinical states [5]. However, the relationship between MPV and AP has remained unclear. In addition, the studies conducted in this area are limited and the results are conflicting. Furthermore, AP patients were not grouped according to disease etiology and etiological investigation of MPV variations was not performed in these publications. In our study, patients were grouped as having biliary and non-biliary AP to investigate whether there were any differences between these groups. There was a significant difference between onset and remission of acute pancreatitis in both groups. In addition, both the onset and the remission MPV levels were significantly different between two groups. The alteration from onset to remission in MPV was found to be negatively correlated to the severity of inflammation.

Mimidis et al., in a study of 54 AP patients, have found that MPV values were different between onset (9.1 fL) and remission (9.8 fL) of the disease that was increased in remission [14]. The results of our study are consistent with that. Furthermore, we have detected differences in MPV levels at onset and remission of both biliary and non-biliary AP. We have also determined MPV decreased during the acute phase of pancreatitis (MPV was 8.42 ± 1.04 in the biliary, and 8.07 ± 1.02 in the non-biliary AP patients), whereas it increased after the treatment (biliary AP group's MPV: 8.71 ± 1.12, non-biliary AP group's MPV: 8.4 ± 1.06) (P = 0.0001 for both). MPV changes can be explained by reduction of inflammation and recovery of the disease. In addition, when biliary pancreatitis was compared to non-biliary pancreatitis, MPV values were found to be different at onset (P = 0.003) and remission (P = 0.011) phases (**Table 2**). The MPV values showed an increase in remission phase in both groups. The mean MPV level was the lowest (8.0 fL) at onset in non-biliary AP group, while the mean level in remission (8.4 fL) of biliary AP patients was the same with that at onset (8.4 fL) in the biliary AP group. The highest MPV level was detected in remission in the biliary AP group (8.7 fL). This finding can be attributed to the more acute onset of biliary AP compared to non-biliary AP and short duration of inflammatory processes.

Multi-factorial scoring systems such as modified Glasgow Prognostic Scores (mGPS), Ranson, Acute Physiology Chronic Health Evaluation (APACHE II), and imaging techniques such as computed tomography severity index (CTSI) are used to predict the severity of acute pancreatitis [15]. In a study of 144 patients, where mGPS and CTSI scoring systems were used to predict the severity of AP, a significant correlation was found between MPV and mGPS. In addition, ROC analysis suggested 7.85 fL as the cut-off value for MPV in severe AP as predicted by mGPS [16]. Our patients could not be assessed with clinical severity scores due to retrospective nature of our study. As is known, the activity of AP affects length of hospital stay. In our study, longer length of hospital stay among patients with low MPV in non-biliary AP group (10.02 ± 7.15) compared to biliary AP group (4.91 ± 4.41) can be interpreted as a positive correlation between severity of disease and low MPV.

Akbal et al. investigated international normalized ratio (INR), D-dimer, fibrinogen and MPV levels at onset and remission in their study of 24 patients with AP. No difference was found between onset (8.6 fL) and remission (8.5 fL) MPV values, but these values were higher compared to healthy controls [17]. However, these results are inconsistent with those of our study and some other studies [14, 16]. In that paper, they found a positive correlation between MPV

and liver and pancreatic enzymes [17]. We have found a positive correlation between MPV and AST and amylase in non-biliary AP group and also between MPV and LDH in biliary AP group. However, consistent with other studies [14, 16] we detected a significant difference in MPV levels between onset and remission periods. The findings reported by Akbal et al. can be explained by small number of patients included in the study, and long storage time of blood samples before the measurements, as noted in the critiques of this study [18, 19]. In our study, blood samples have been tested immediately on admission and the day of discharge.

There was no significant difference in platelet count between onset and remission periods in biliary and non-biliary AP groups. However, significantly elevated platelet counts were found both at onset (P = 0.041) and remission (P = 0.001) periods in non-biliary AP group. In addition, there was a negative correlation between MPV and platelet count both in biliary and non-biliary AP groups. Platelets are acute-phase reactants therefore they increase in response to inflammation [19]. The negative correlation between MPV and platelet count at onset, where inflammatory activity is prominent, supports a relationship between MPV and thrombocytes and inflammation [10]. The fact that MPV was lower and platelet count was higher in non-biliary AP group compared to biliary AP group can be an indicator of early-onset infection in non-biliary AP group.

Our results would be stronger if we had conducted a comparison between MPV and CRP at admission, follow-up and discharge.

In conclusion, the difference in MPV levels between different times during the disease in patients with acute pancreatitis and also between biliary and non-biliary AP groups has been considered to be associated with the course of inflammation. This difference also affects length of hospital stay. The negative correlation between decrease in MPV and thrombocyte count reflects the relationship of MPV, as other acute phase reactants, with inflammation. The changes of MPV at admission and discharge and increase in MPV during recovery in both groups can be used as a parameter in evaluating the course of disease. The lower level of MPV in non-biliary AP patients compared to biliary AP patients can be used to establish the etiology. Further studies including correlation with CRP are necessary to establish whether MPV is a parameter to indicate the course of disease.

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Disclosure of conflict of interest

None.

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