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Original Article

Could platelet indices be prognostic biomarkers for mild or severe acute pancreatitis?

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Abstract: The aim of this study was to show the relation of platelet indices with the severity of acute pancreatitis (AP) and if they have any correlation with the severity of AP. Forty-seven patients with AP hospitalized in Department of Gastroenterology, Inonu University Faculty of Medicine were divided into two groups, namely, the severe AP group (n=15) and the mild AP group (n=32). The scores of these patients at days 0, 3 and at the beginning of remission according to the prognostic scoring systems (Ranson, APACHE II, and BISAP criteria), CRP, sedimentation and platelet indices (platelet count, MPV, PDW and PCT) were noted. Mann-Whitney U test was used to compare the groups. Spearman's Rho test was used to evaluate the correlations between the platelet indices and other prognostic factors. Significant differences were found between the groups as regards platelets (P<0.02), PDW (P<0.001), AST (P<0.001), ALT (P<0.001), Total bilirubin (P<0.007), LDH (P<0.001), CRP (P<0.001), sedimentation (P<0.001), APACHE-II (P<0.001), Ranson (P<0.002) parameters. When considered for the correlation between the platelet indices and other prognostic factors, it was seen that all the platelet indices showed strong positive or negative correlation in mild AP with other prognostic scoring systems, CRP and sedimentation. In contrast, it was seen that platelet indices in severe AP cases did not show strong correlation with other prognostic scoring systems, CRP and sedimentation. We showed that platelet derivatives can be used as a good prognostic biomarker for the course of mild AP. In severe AP cases, however, usability of platelet indices must be supported with further studies.

Keywords: Acute pancreatitis, prognostic markers, platelet indices

Introduction

Acute pancreatitis (AP) is a systemic inflammatory disease that can have various clinical courses. While majority of the AP cases heal without sequels, 10-20% of these can have a severe course, and can be fatal in 30% [1, 2]. Mortality can be prevented with treatment given by diagnosing the high-risk patients in the early period [3]. AP diagnosis requires the presence of two features out the three below. The first of these is the abdominal pain consistent with AP (severe and permanent pain in the epigastric area with acute onset and radiating to the back), the second is the amylase and lipase levels that had increased more than 3 folds of the normal limit, and the third is the imaging of the characteristic findings of AP in computerized tomography (CT) with contrast, magnetic resonance imaging (MRI) or trans abdominal ultrasonography (US) [1]. As regards the course of AP, it is clinically important to determine the severity of AP, since outcomes of mild AP is better than that of severe AP [4].

According to revised Atlanta Criteria, AP is divided into three groups as mild, moderate and severe. There are no local/systemic complications or organ failure in mild AP, pancreatitis episode becomes milder or limits itself within a period less than 7 days. In AP with medium severity, transient organ failure lasting less than 48 hours or local complications (peripancreatic fluid collection, pancreatitic necrosis) or

systemic complications (exacerbation of a previously existing disease) are observed. In severe AP however, organ failure lasts for more than 48 hours [5]. Modified Marshall Classification is used for the diagnosis of organ failure. According to this classification, impairment two systems out of respiratory, cardiac and renal organ systems is defined as organ failure [6].

Several prognostic scoring systems and inflammatory markers have been studied with the purpose of determining the severity of AP and establishing the mortality risk accordingly. In this context, the most frequently used scoring systems include the Ranson criteria, Imrie criteria, Computed tomography severity index (CTSI), Acute Physiology and Chronic Health Evaluation II (APACHE-II) and Bedside index for severity in acute pancreatitis (BISAP) scoring systems. Together with this, all the scoring systems have their own pros and cons. Ranson criteria is the method that is used most frequently in practice to assess the severity of AP. Together with this, its failure in providing the possibility of a clear assessment before the completion of the first 48 hours following admission and failure in determining the mortality risk are its most important disadvantages [7]. The most important advantage of the APACHE-II scoring system is that it can be used to determine the severity of pancreatitis even on the day of application to the hospital. However, multitude and complexity of parameters in APACHE II system are the most important disadvantages [8]. CTSI scoring system allows evaluation of pancreatic and peripancreatic local complications through the use of contrast tomography. However, it is rather insufficient as regards the systemic inflammatory response developing secondary to AP. In 2008, Wu *et al* [9] developed the BISAP score (BUN >258 mg/dL, Impaired mental Status, development of systemic inflammatory response syndrome, age >60 age, and presence of pleural effusion) with the purpose of both reducing the number of parameters of the scoring systems and showing the severity of systemic complications.

The biochemical markers most frequently studied in the literature to predict the severity and prognosis of AP include the trypsinogen activation peptide, CRP, procalcitonin, erythrocyte sedimentation rate, PMN-elastase, Phospholipase A2, TNF-α, IL-6 and IL-8. Almost all of these markers are related to inflammation, which plays an important in the physiopathology of pancreatitis. The number of studies in the literature related to the relation between the severity and prognosis of AP and the mean platelet volume (MPV) [10-14]. Together with this, no studies have been performed on the effects of platelet indices including plateletcrit (PCT) and platelet distribution width (PDW) on the prognosis of AP to the best of our knowledge. In this study, we aimed at determining if there is any correlation between the Ranson, BISAP, APACHE-II, CRP, and erythrocyte sedimentation rate parameters, of which the relation to the prognosis of AP is known, with the Platelet count, MPV, PCT and PDW.

Material and methods

Data of forty-seven patients followed up with the diagnosis of AP in Department of Gastroenterology, Inonu University Faculty of Medicine between September 2014 and October 2015 were evaluated retrospectively. It was considered that two features out of the three below was considered required for AP diagnosis: 1- Characteristic abdominal pain consistent with AP; 2- Amylase and lipase levels increased to 3 folds of the normal limit; and 3- imaging of characteristic findings of AP with contrast CT, MR or US [1]. Patients with hematologic diseases, with body mass indices greater than 30, patients with biliary pancreatitis, with inflammatory known previously, those using drugs causing thrombocytopenia, and patients with advanced cardiac failure were excluded from the study. Blood test results and scores of patients on day of application and day 3 and on the beginning day of remission were noted. Based on the Revised Atlanta Criteria [5], patients were divided into two groups as the mild (n=32) and severe (n=15) pancreatitis. Informed consent forms were obtained from all the patients. Data were summarized using the median value and the min. and max. values. Consistence of data with the normal distribution was examined with the Shapiro Wilk test.

The primary objective of this study was to determine which variables differed statistically between mild and severe cases of AP. Therefore, the two groups were compared as regards age, sex, hemoglobin (Hb), platelet count, PDW, PCT,

Table 1. Comparison of pancreatitis patients according to severity of disease

Parameters	Mild Pancreatitis (n=32)	Severe Pancreatitis (n=15)	P
Age	57 (23-85)	77 (65-87)	0.001
Gender (female/male)	25/7	6/9	0.025
Hb	13.9 (10.7-16.3)	13.4 (10.8-15.4)	0.07
Plateletes	334 (195-524)	440 (312-535)	0.02
PDW	14.9 (12.1-18.5)	17.8 (15.2-19.8)	0.001
PCT	0.23 (0.15-0.37)	0.22 (0.13-0.40)	0.76
MPV	8.1 (6.1-11)	7.8 (5.4-10.4)	0.36
AST	108 (57-341)	302 (168-452)	0.001
ALT	125 (68-367)	421 (280-760)	0.001
T Bil	0.96 (0.35-2.93)	2.47 (0.82-3.73)	0.007
I Bil	0.42 (0.12-1.48)	1.1 (0.39-1.69)	0.003
LDH	269 (138-589)	569 (365-854)	0.001
Amylase	1503 (276-6186)	1322 (532-5382)	0.71
Lipase	1297 (568-4258)	1023 (741-4256)	0.89
CRP	2 (0.3-8.4)	9.6 (4.2-20.4)	0.001
Sedimentation	32 (10-69)	51 (36-84)	0.001
APACHE II	3 (0-8)	9 (5-12)	0.001
Ranson	2 (0-4)	3 (1-4)	0.002
BISAP	2 (0-4)	2 (1-4)	0.058
Hospitalization days	5 (4-14)	10 (6-48)	0.0001

PDW: Platelet Distribution Width; PCT: Plateletcrit; MPV: Mean Platelet Volume; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; T Bil: *Total Bilirubin;* I Bil: *Indirect Bilirubin;* LDH: *Lactate Dehydrogenase;* CRP: *C-Reactive Protein;* APACHE II: Acute Physiology and Chronic Health Evaluation II; BISAP: Bedside ındex for Severity in Acute Pancreatitis.

MPV, AST, ALT, total bilirubin, indirect bilirubin, LDH, amylase, lipase, CRP, erythrocyte sedimentation rate, APACHE-II, Ranson and BISAP criteria. Platelet indices were measured with the hemogram device Sismex XN-1000, Japan. Mann-Whitney U test and Yates' corrected chi-square tests were used to evaluate the differences between the groups.

The secondary objective of this study is to evaluate the correlations between platelet indices, CRP, erythrocyte sedimentation rate and other prognostic scoring systems within the two groups. The correlations between the APACHE-II, BISAP, Ranson, CRP and erythrocyte sedimentation rate and platelet indices including Platelet count, PDW, MPW and PCT were evaluated with Spearman's Rho test. Separate analyses were carried out for the three different results of prognostic indices and platelet derivatives at days 0 and 3 and the remission date. Spearman's Rho coefficient (r) was used to determine the direction, power and significance of correlation. P<0.05 value was accepted as the statistical significance threshold. IBM SPSS Statistics ROC curve analysis was used to determine optimal prognostic values for PDV, MPV, PCT and PLT. Also, multiple logistic regression analysis was carried out to identify the association between PDV, MPV, PCT, PLT and prognosis. P<0.05 value was accepted as the statistical significance threshold. IBM SPSS Statistics 23.0 and Minitab package programs were used for analyses.

Results

Forty-seven patients were included in this study with ages ranging between 23 and 87 years. Thirty-one of the patients were females and 16 were males. While thirty-two of the patients were mild AP cases, 15 were severe AP cases. Differences were found between patient groups were mild and severe AP in parameters including age (P<0.001), sex (P<0.025), platelet (P<0.02), PDW (P<0.001), AST (P<0.001), ALT (P<0.001), total bilirubin (P<0.007), indirect bilirubin (P<0.003), LDH (P<0.001), CRP (P<0.001), erythrocyte sedimentation rate (P<0.001), APACHE-II (P<0.001), Ranson (P<0.002), and days of hospital stay numbers (P<0.0001). In contrast, no statistical differences were found between the groups in Hb, amylase, lipase, PCT and MPV values. Although BISAP value did not differ statistically (P<0.058), *p* value was rather close to the significance level of 0.05. Results are shown in **Table 1**.

While a significant positive relation was found between platelet, PDW and Apache II, BISAP, Ranson, CRP and erythrocyte sedimentation rate in the study carried out using Spearmen rho test in the patient group with mild AP; significant negative relation was found between MPV and APACHE-II, BISAP, Ranson, CRP and erythrocyte sedimentation rate. No significant

Table 2. The statistical correlation bewtween plateletes indices and prognostic scoring system (APACHE, BISAP, Ranson, CRP and Sedimentation) in patients with mild pancreatitis

	APACHE	BISAP	Ranson	CRP	Sedim
Plateletes-0	+0.794***	+0.659***	+0.371*	+0.813**	+0.668**
Plateletes-3	+0.60***	+0.499**	+0.540**	+0.721***	+0.592***
Plateletes-R	+0.552***	+0.598***	+0.567**	+0.503**	+0.613***
PDW-0	+0.718***	+0.608***	+0.445**	+0.792**	+0.617***
PDW-3	+0.622***	+0.556***	+0.490**	+0.680***	+0.377*
PDW-R	+0.478**	+0.489**	+0.710***	+0.526**	+0.442**
MPV-0	-0.662***	-0.582***	-0.552***	-0.477**	-0.584***
MPV-3	-0.668***	-0.583***	-0.717***	-0.631***	-0.667***
MPV-R	-0.541***	-0.376*	-0.596***	-0.488**	-0.502**
PCT-0	-0.68	+0.48	-0.006	-0.10	+0.004
PCT-3	+0.67	+0.45	+0.003	-0.190	-0.219
PCT-R	-0.118	-0.159	-0.276	-0.242	-0.162

*P<0.05, **P<0.01, ***P<0.001: Statistical comparetion of the parameters in the same line and column. (+) r: Positive correlation, (-): Negative correlation.

Table 3. The statistical correlation bewtween plateletes indices and prognostic scoring system (APACHE, BISAP, Ranson, CRP and Sedimentation) in patients with severe pancreatitis

	APACHE	BISAP	Ranson	CRP	Sedim
Plateletes-0	+0.362	+0.443*	+0.134	+0.755***	+.0429
Plateletes-3	+0.645**	+0.615*	+0.667**	+0.781***	+0.088
Plateletes-R	+0.539**	+0.662**	+0.726	+0.643*	+0.674**
PDW-0	+0.270	+0.253	+0.395	+0.277	+0.106
PDW-3	+0.568*	+0.585*	+0.622*	+0.526*	+0.273
PDW-R	+0.553*	+0.608*	+0.746**	+0.819***	+0.704**
MPV-0	-0.257	-0.164	+0.156	-0.274	-0.820***
MPV-3	-0.560*	-0.431	-0.193	-0.076	-0.803***
MPV-R	-0.556*	-0.480	-0.571*	-0.416	-0.645**
PCT-0	+0.320	+0.402	-0.641*	-0.140	-0.146
PCT-3	+0.430	+0.244	-0.236	-0.050	-0.242
PCT-R	+0.009	-0.007	-0.027	-0.090	-0.477

*P<0.05, **P<0.01, ***P<0.001, (+) r: Positive correlation, (-): Negative correlation.

relation was found between the PCT value and APACHE-II, BISAP, Ranson, CRP and erythrocyte sedimentation rate. Results are shown in **Table 2**.

In the study carried out on the patient group with severe AP using Spearmen's rho test, while positive correlation at day 0 was found between Apache II and platelet, PDW and MPV, this correlation was not statistically significant. While significant positive relation was found at day 3 and at remission between APACHE-II and platelet and PDW, significant negative relation was found between APACHE-II and MPV. While significant positive relation was found at day 3 and at remission between BISAP and platelet, a significant positive relation was found at day 3 and at remission between BISAP and PDW. While a significant positive relation was found between Ranson and platelet (day 3) and PDW (day 3 and the day of remission), significant negative relation was found between Ranson and MPV (day 0) and PCT (day 0). While significant positive relation was found with CRP and platelet on all days, significant positive relation was found with CRP and PDW on day 3 and on the day of remission. Significant negative relation was found between erythrocyte sedimentation rate and MPV on all days. Results are shown in **Table 3**.

ROC Curve analysis shows that the optimal cut-off point for prognostic values, sensitivity, specificity, area under curve for PDW, MPV, PCT and PLT levels were [14.6, 81.25%, 41.94%, 0.55± 0.089 (SE)], [7.3, 50.0%, 67.7%, 0.56±0.090 (SE)], [0.31, 93.75%, 19.15%, 0.53±0.089 (SE)] and [343, 75%, 48.39%, 0.55±0.086 (SE)] respectively. ROC Curve results shows in **Figures 1**-**4**.

Multiple logistic Regression analysis shows that MPV (P=0.74), PCT (P=0.84), PDW (P=0.57) and PLT (P=0.91) levels were not statistically significant effect on prognosis. Area under the ROC Curve for this Multiple logistic Regression was 0.585±0.086 (SE).

Discussion

AP is an inflammatory disease with various clinical presentations and classified under two headlines primarily as the biliary and non-biliary disease. The process following the onset of inflammation is the same in almost all the

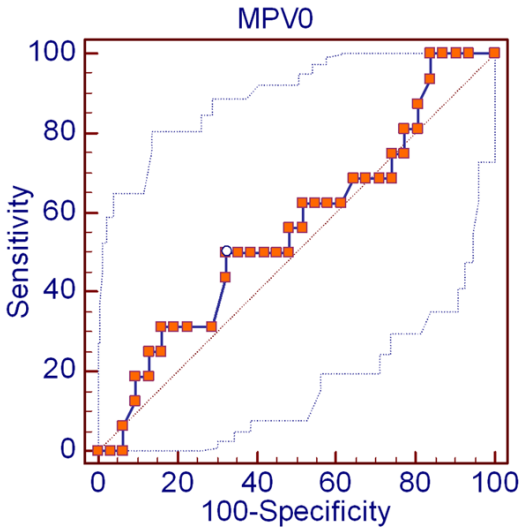

Figure 1. ROC curve for MPV.

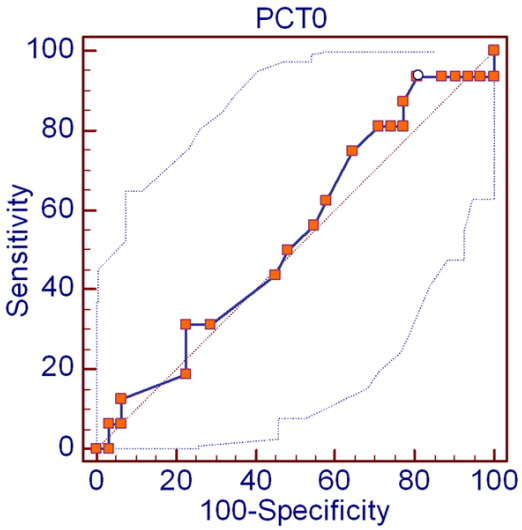

Figure 2. ROC curve for PCT.

patients, whatever the underlying cause is. Clinical diagnosis of AP is made based on the revised. Prediction of the course and prognosis of the disease is rather difficult. With this reason, several prognostic scoring systems and biochemical markers have been studied to predict the prognosis of the disease and risks of mortality and morbidity. The most commonly used biochemical markers include the trypsinogen activation peptide, CRP, Procalcitonin, erythrocyte sedimentation rate, PMN-elastase, Phospholipase A2, TNF-α, IL-6 and IL-8. It has rarely been reported in the literature that platelet count and platelet derivatives are used as biochemical markers.

Platelets were known as non-immune blood cells originating from megakaryocytes. It was believed that platelets were involved only in primary hemostasis until the recent years. However, it has been shown in the studies of the recent years that platelets play a role as the proinflammatory cells in many inflammatory processes as well as their hemostatic functions [15, 16]. In the literature, many studies have been reported related to the roles of platelet count, distribution and platelet indices including MPV, PCT and PDW in inflammatory diseases. It has been shown that differences in the ratios or distributions of platelet derivatives occur in many autoimmune and inflammatory diseases with inflammatory bowel disease in the first place [17-19]. It has been reported in many studies that MPV value in the active phase of inflammation are lower as compared to the control groups or the patient population in remission. Ozturk *et al* [18] showed that MPV and PDW levels are reduced in the active phase of the inflammatory bowel disease, and the PCT level increased as compared to the control group. In the conclusion section of this study of their, the authors have reported that these changes seen in the platelet indices in inflammatory bowel disease are notable, and therefore they can be used as inflammatory markers in the follow-up of the disease. Danese *et al* [15] found a lower MPV level in inflammatory bowel diseases. The suggested that such low levels were related to the sequestration and destruction of the large activated platelets. Makay *et al* [20] reported that MPV value markedly reduced during the FMF attacks as compared to the attack-free periods. In the same study, it was shown that thrombocyte count increased markedly during the attack. Albayrak *et al* [21] found that MPV values were lower in the acute appendicitis cases as compared to the control group. In contrast, it has been reported in some studies that MPV value increased during the course of inflammatory diseases [22]. Therefore, further prospective studies are needed in order to be able to express a definite opinion.

The article published on the relation between AP and platelet counts and platelet indices are limited in number, and almost all such articles

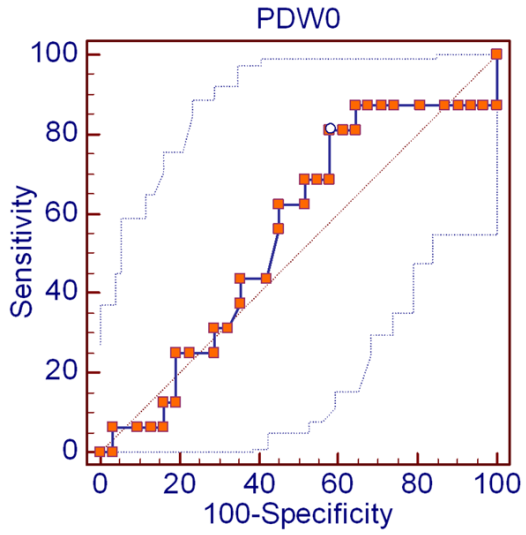

Figure 3. ROC curve for PDW.

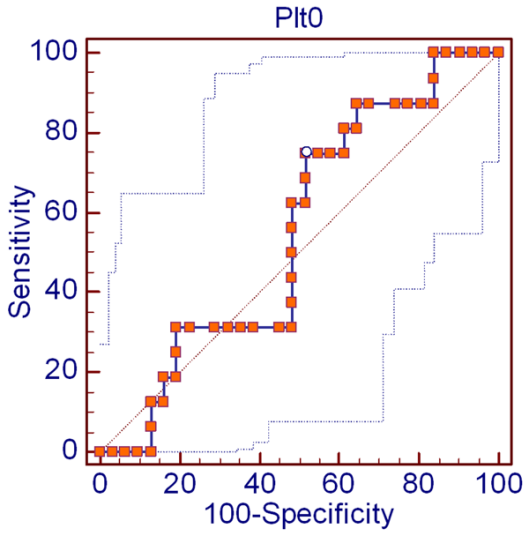

Figure 4. ROC curve for PLT.

are on MPV and platelet count [10-14]. Akbal *et al* [10] reported in their study on biliary pancreatitis that the MPV ratio was higher than that of the control group, and stated in conclusion that high MPV values could reflect hyper coagulation related to pancreatitis. Okuturlar *et al* [11] showed in their study on biliary and non-biliary pancreatitis cases that the MPV values at admission were markedly lower as compared to those during remission, and stated in conclusion that MPV value can be used as an indicator to show the inflammation in the early period. Beyazit *et al* [12] showed that MPV value could be significantly lower as compared to the control group, and stated that assessment of the MPV value together with other inflammatory markers is useful in the prediction of the severity of AP. Mimidis *et al* [13] reported that MPV, PDW and platelet-large cell ratio increased markedly in the remission phase of pancreatitis and stated that thrombocytes directly participated in the inflammatory process that develops during pancreatitis. Yilmaz *et al* [14] showed that MPV value markedly increased in AP cases, while the platelet count decreased markedly as compared to the control group. The authors stated that the increased MPV value could be used as a marker for diagnosis.

In these studies, the relation between MPV, platelet count and AP was studied; however, no clear consensus could be obtained in the studies. The MPV value was found lower than that of the control group, while the MPV value was found higher than that of the control group. The relation of PDW and PCT with AP has been almost not touched at all. In this study, one of the most important factors that limit us is the lack of a control group, and the other one is the small number of cases. Lack of the control group prevents us to interpret if the platelet indices increase in AP cases or not. However, the results we obtain from this study allow us to interpret if the platelet indices are related with the severity of AP or not. We showed that there are no differences between mild and severe AP cases as regards MPV and PCT values. In contrast, we found that platelet counts and PDW rates were higher in severe AP cases. These results have shown us that there is no relation between the severity of inflammation and MPV.

One of the most important results of this study is that it has been shown it there are relations between the platelet indices and the classical prognostic markers. In mild AP cases, increases in platelet count and PDW values positively parallel the increases in APACHE-II, BISAP, Ranson, CRP and erythrocyte sedimentation rate. Together with this, we showed that there is a significant negative relation between the MPV value and the classical prognostic markers. That is, decrease in MPV values were observed in parallel with the increases in APACHE-II, BISAP, Ranson, CRP and erythrocyte sedimentation rate. No significant relation was found between the PCT and the classical prognostic

markers. Similar correlations were found in severe AP cases also. However, no statistical significance was found in the majority of cases.

In conclusion, it has been shown that there is a statistically significant correlation in classical prognostic scores and platelets and platelet indices including PDW and MPV in cases with mild AP. In contrast, we were unable to find a powerful correlation in severe AP between platelet indices and classical prognostic liken in mild AP. Platelet indices, which are both inexpensive and accessible, can be used as a prognostic marker in the follow-up of AP. New prospective studies are required in this issue.

Disclosure of conflict of interest

None.

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References

[1] Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006; 101: 2379-2400.

[2] Fagenholz PJ, Castillo CF, Harris NS, Pelletier AJ, Camargo CA Jr. Increasing United States hospital admissions for acute pancreatitis, 1988-2003. Ann Epidemiol 2007; 17: 491-497.

[3] Forsmark CE, Baillie J; AGA Institute Clinical Practice and Economics Committee; AGA Institute Governing Board. AGA Institute technical review on acute pancreatitis. Gastroenterology 2007; 132: 2022-2044.

[4] Papachristou GI, Clermont G, Sharma A, Yadav D, Whitcomb DC. Risk and markers of severe acute pancreatitis. Gastroenterol Clin North Am 2007; 36: 277-96.

[5] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS; Acute Pancreatitis Classification Working Group. Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013; 62: 102-11.

[6] Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Crit Care Med 1995; 23: 1638-52.

[7] Ranson JH, Pasternack BS. Statistical methods for quantifying the severity of clinical acute pancreatitis. J Surg Res 1977; 22: 79-91.

[8] Yeung YP, Lam BY, Yip AW. APACHE system is better than Ranson system in the prediction of severity of acute pancreatitis. Hepatobiliary Pancreat Dis Int 2006; 5: 294-9.

[9] Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population-based study. Gut 2008; 57: 1698-1703.

[10] Akbal E, Demirci S, Koçak E, Köklü S, Başar O, Tuna Y. Alterations of platelet function and coagulation parameters during acute pancreatitis. Blood Coagul Fibrinolysis 2013; 24: 243-6.

[11] Okuturlar Y, Soylu A, Dogan H, Cakmak S, Kirac Utku I, Oztosun B, Akarsu C, Ocak Serin S, Avci A, Kones O, Ozucelik DN, Guzey D, Harmankaya O, Kumbasar A. Mean platelet volume in patients with biliary and non-biliary acute pancreatitis. Int J Clin Exp Pathol 2015; 8: 2051-6.

[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: 162-8.

[13] Mimidis K, Papadopoulos V, Kotsianidis J, Filippou D, Spanoudakis E, Bourikas G, Dervenis C, Kartalis G. Alterations of platelet function, number and indexes during acute pancreatitis. Pancreatology 2004; 4: 22-7.

[14] Yilmaz N, Ozkan OV, Buyukbas S, Can Y, Ozturk OH, Aydogan A, yonden Z. Mean platelet volume in patients with acute pancreatitis. J Clin Exp Invest 2011; 2: 362-365.

[15] Danese S, Motte Cd Cde L, Fiocchi C. Platelets in inflammatory bowel disease: clinical, pathogenic, and therapeutic implications. Am J Gastroenterol 2004; 99: 938-45.

[16] 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.

[17] Threatte GA. Usefulness of the mean platelet volume. Clin Lab Med 1993; 13: 937-950.

[18] Ozturk 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: 334-41.

[19] Yüksel O, Helvaci K, Başar 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: 277-81.

[20] Makay B, Turkyilmaz Z, Unsal E. Mean platelet volume in children with familial Mediterranean fever. Clin Rheumatol 2009; 28: 975-8.
[21] 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: 362-6.
[22] Coban E, Adanir H. Platelet activation in patients with Familial Mediterranean Fever. Platelets 2008; 19: 405-8