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Role of platelet parameters as a biomarker in diagnosis of acute appendicitis: A retrospective case–controlled study

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ABSTRACT

Objective: To investigate the diagnostic value of platelet parameters in acute appendicitis.

Methods: This retrospective case-controlled study was performed among 200 healthy people and 200 patients with a primary diagnosis of acute appendicitis between October 2017 and June 2018. The patients were classified into three groups: the acute complicated appendicitis (suppurative and gangrenous) group, acute non-complicated appendicitis group and the control group. Red blood cell, white blood cell, lymphocyte, monocyte and platelets count, red blood cell distribution width, hemoglobin, hematocrit, mean platelet volume, platelet distribution width, and C-reactive protein were compared between the groups.

Results: Thirty-nine (19.5%) patients with acute appendicitis had no complication and 161 (80.5%) developed a complication. The white blood cell count, neutrophil count and C-reactive protein serum levels were significantly higher, whereas the mean age, lymphocyte count, monocyte count, red blood cell distribution width and platelet count were significantly lower in acute appendicitis patients with and without complications compared with the control group. Moreover, combined analysis of best diagnostic parameters (white blood cell, neutrophil and lymphocyte counts) showed that combined parallel sensitivity and specificity were 98.7% and 42.7%, respectively.

Conclusions: White blood cell, lymphocyte counts and neutrophil count could be used for diagnosis of acute appendicitis. More over the utility of mean platelet volume for differential diagnosis might be overestimated.

1. Introduction

Acute appendicitis (AA) is the most usual surgical reason for exigency laparotomy with approximate occurrence as 7%[1]. Even experienced surgeons sometimes find it hard to diagnose appendicitis, as demonstrated by the high rate of negative finding during appendectomy, which commonly reaches 20% to 30%[2]. This is mainly due to lack of pathognomonic signs or symptoms and neglect of the predictive values of related laboratory systems[3]. Rapid and accurate diagnosis is crucial because delayed diagnosis of appendicitis increase risk of perforation in acute appendicitis, thereby potentially resulting in sepsis and even death[4].

Imaging modalities such as ultrasound, computerized tomography, as well as diagnostic laparoscopy and modern laboratory tests have

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been more and more used to provide a fast and precise diagnosis[5]. Therefore, easily enforceable, widely available, time-saving and inexpensive new laboratory methods that can be exerted anywhere are necessary for the diagnosis of AA[6].

The complete blood count (CBC) with differential is a frequently requested test in clinical laboratories. Considerable amount of literature has been published on the accuracy of AA detection. These studies investigated many laboratory parameters, including red redistribution width (RDW)[4], platelet distribution width (PDW)[6], neutrophil-to lymphocyte ratio[7], platelets count (PLT)[8] and mean platelet volume (MPV)[4,6].

PLT, MPV and PDW are three CBC parameters related to platelets[9]. Full blood count analyzers show MPV as the main factor to determine platelet activity[10]. Inflammatory effect of MPV has been proven in several disease such myocardial infarction, acute pancreatitis, and pre-eclampsia[11-13]. PDW is an index of platelet heterogeneity, which would be an indication of active platelet release. Recent work by Dinc *et al.*[14] has suggested the PDW as a new index in the diagnosis of AA.

There are very few studies investigating the supporting role of platelet function parameters in cases of AA and the results of these experiments are very controversial. The purpose of this study was to investigate the diagnostic significance of platelet parameters including PLT, MPV and PDW in AA.

2. Patients and methods

2.1. Patients

Due to the retrospective nature of this study ethics committee approval was waived. The informed patient consent was waved by obtaining authorization from institutional review board committee. The retrospective analysis was performed during October 2017 to June 2018.

The control group was composed of 200 healthy persons who applied to check-up clinic. A total of 200 patients were diagnosed with AA according to abdominal examination findings, and/or based on the general clinical detection and symptoms of right lower quadrant or periumbilical pain, migration of pain to the right iliac fossa, nausea/vomiting, anorexia, and fever. The inclusion criteria were: patients had confirmed pathological diagnosis as AA. The exclusion criteria were described as follows: having infectious disease (acute or chronic), heart failure, comorbid conditions (*e.g.* cancer, respiratory, cardiac, endocrine, renal, and vascular disease, cancer, *etc.*), idiopathic thrombocytopenic purpura, peripheral vascular disease, using persistent medication (analgesics, oral contraceptives, antimetabolites, *etc.*), asthma, hematological disorders, chronic obstructive pulmonary disease, cancer, diabetes, rheumatologic disorder, atherosclerotic disease, renal and hepatic diseases.

Histologically, the appendices were divided into 3 groups. Group 1 consisted of 39 patients with acute non-complicated appendicitis, group 2 included 161 acute complicated appendicitis patients, while group 3 involved 200 healthy persons. Complicated appendicitis was described as gangrenous and/or suppurative appendicitis and non-complicated appendicitis was defined as simple AA.

2.2. Data collection and test

The patients were evaluated for age, gender, white blood cell (WBC) count, lymphocyte count, neutrophil count, monocyte count, PLT, PDW, MPV, RDW, and serum CRP level. All blood samples were obtained from the venous system and collected in potassium ethylenediaminetetraacetate tubes via the cephalic vein and assayed using an automated blood cell counter (Sysmex XT 1800 I, Japan).

2.3. Sensitivity and specificity value

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of these tests were also determined.

Through Pearson's correlation analysis, inter-correlations between parameters were calculated. The area under the receiver operating characteristic (ROC) curve was used to calculate the sensitivity, specificity, cut-off points, positive and negative predictive values and likelihood ratios. The confidence interval (*CI*) was set at 95% and P value < 0.05 was considered statistically significant. The cut-off point of MPV in our study was 7.6 FL. The reference values were (4-10)×1 000/mm^3 for WBC, (12-18) g/dL for hemoglobin (Hb), 40%-70% for neutrophil, (140-440)×1 000/mm^3 for PLT, 11%-16% for RDW, 8.5-12.5 FL for the MPV, 10-17 FL for the PDW, 17%-45% for platelet larger cell ratio and 36%-50% for the hematocrit. Besides, the sensitivity and specificity of combined tests which showed most area under curve was calculated with parallel method[15,16].

2.4. Statistical analysis

All analyses were performed using SPSS, version 20. Descriptive qualitative data were described as numbers and percentage values, while all quantitative parameters were expressed as mean scores, standard deviations, ranges, and medians with interquartile ranges (IQR). The Kolmogorov-Smirnov test was applied to evaluate normal distribution. Moreover, *Chi*-square test was conducted to compare qualitative data followed by independent t-test. The nonparametric data were compared by using the Mann-Whitney test. In addition, comparisons of quantitative variables with parametric distribution were done by the one-way analysis of variance and nonparametric multiple comparisons were carried out by the Kruskal-Wallis test.

3. Results

Of these AA patients, 117 (58.5%) were males and 83 (41.5%) were females, with a male to female ratio of 1.4:1. The age varied

Table 1. Main characteristic and complete blood count data.

Parameters	Acute noncomplicate appendicit (n=39)	Acute complicate appendicit (n=161)	Controls (n= 200)	P_1	P_2	P_3
Age (years)	25.76±14.24	26.75±15.48	43.64±18.05	NS	<0.001	<0.001
Gender						
Male [n (%)]	20 (51.3)	97 (60.2)	92 (46.0)	NS	NS	0.007
Female [n (%)]	19 (48.7)	64 (39.8)	108 (54.0)			
WBC count ($\times10^9$/L) [Median (IQR)]	11.3 (8.1–15.0)	13.4 (10.60–15.45)	8.3 (6.60–9.88)	0.014	<0.001	<0.001
RBC ($\times10^6$/μL)	4.85 ± 0.62	4.85 ± 0.56	4.8 ± 0.54	NS	NS	NS
Hct (%)[Median (IQR)]	39.4 (35.9–43.5)	39.3 (36.9–43.1)	40.2 (37.32–43.40)	NS	NS	NS
Hb [Median (IQR)]	13.6 (11.8–15.4)	13.6 (12.5–14.8)	13.6 (12.62–14.78)	NS	NS	NS
PLT [Median (IQR)]	221 (196.00–267.00)	224 (187.00–265.00)	241 (205.00–282.75)	NS	NS	0.005
MPV [Median (IQR)]	9.8 (9.20–10.30)	9.5 (8.8–10.2)	9.7 (9.02–1027.00)	0.092	NS	NS
PDW [Median (IQR)]	11.9 (11.20–13.60)	11.8 (10.70–12.95)	11.8 (10.70–13.47)	NS	NS	NS
PLRC [Median (IQR)]	24.7 (18.60–28.10)	21.9 (17.10–27.60)	23.55 (18.55–28.57)	NS	NS	0.05
RDW [Median (IQR)]	13.2 (12.7–14.1)	13.0 (12.6–13.5)	13.5 (12.9–14.5)	NS	NS	<0.001
Neutrophil [Median (IQR)]	70.8 (64.00–79.00)	80.0 (75.00–86.00)	61.9 (54.35–71.00)	<0.001	0.001	<0.001
Lymphocyte [Median (IQR)]	22.0 (15.90–28.00)	12.0 (9.50–18.00)	28.3 (19.60–34.37)	<0.001	0.004	<0.001
Mono [Median (IQR)]	7 (5.3–8.0)	6 (4.0–8.0)	7.3 (6.0–9.1)	0.095	0.074	<0.001
CRP						
Positive [n (%)]	21 (61.8)	103 (69.6)	36 (24.0)	NS	<0.001	<0.001
Negative [n (%)]	13 (38.2)	45 (30.4)	114 (76.0)			

WBC: white blood cell; RBC; red blood cell; Hct; hematocrit; Hb: hemoglobin; PLT: platelet; MPV: mean platelet volume; PDW: platelet distribution width; PLRC: Platelet large cell ratio; RDW: red blood cell distribution width; Mono: monocyte; CRP: C-reactive protein. P_1: Comparison between acute noncomplicate appendicit and acute complicate appendicit group; P_2: Comparison between acute noncomplicate appendicit and the controls; P_3: Comparison between acute complicate appendicit and the controls.

Table 2. Diagnostic value analysis for significant different data between appendicitis patients and control group.

Parameter	AUC	Cut-off	Sensitivity (%)	Specificity (%)	PPV	NPV	LR^+	LR^-
WBC	0.811	9.865	74.7	75.4	0.748	0.746	3.036	0.335
PLT	0.583	232.5	60.3	56.1	0.586	0.578	1.373	0.707
RDW	0.639	13.15	63.8	58.1	0.617	0.603	1.522	0.623
Neutrophil	0.812	71.9	77.8	76.9	0.768	0.776	3.367	0.288
Lymphocyte	0.804	19.2	76.4	73.7	0.755	0.745	2.904	0.320
Monocyte	0.650	7.05	52.3	64.6	0.575	0.597	1.477	0.738

WBC: white blood cell; RBC: red blood cell; Hct: hematocrit; Hb: hemoglobin; PLT: platelet; MPV: mean platelet volume; PDW: platelet distribution width; PLRC: Platelet large cell ratio; RDW: red blood cell distribution width; Mono: monocyte; CRP: C-reactive protein; PPV: positive predictive value; NPV: negative predictive value; LR: Likelihood ratios.

Table 3. Significant correlations between different parameters.

Parameter	Statistic parameter	Hb	RBC	WBC	PLT	MPV	PDW	PLRC	RDW	Neutr	Lymph	Mono
Age	r cofficient	NS	−0.149		−0.288	0.198	0.150	0.166	NS	NS	NS	NS
	P-value		0.035	NS	<0.001	0.005	0.034	0.019				
Hct	r cofficient	0.935	0.731	NS	−0.218	NS	NS	NS	−0.141	NS	NS	NS
	P-value	<0.001	<0.001		0.002							
Hb	r cofficient	–	0.704	0.218	−0.197	NS	NS	NS	−0.239	NS	−0.177	NS
	P-value		<0.001	0.002	0.005				0.001		0.013	
RBC	r cofficient	–	–	0.176	NS	NS	NS	NS	NS	NS	−0.156	0.159
	P-value			0.013							0.027	0.025
WBC	r cofficient	–	–	–	0.337	NS	NS	NS	NS	0.396	−0.418	−0.159
	P-value				<0.001					<0.001	<0.001	0.025
PLT	r cofficient	–	–	–	–	−0.458	−0.457	−0.474	NS	NS	NS	NS
	P-value					<0.001	<0.001	<0.001				
MPV	r cofficient	–	–	–	–	–	0.906	0.974	0.149	NS	NS	NS
	P-value						<0.001	<0.001	0.035			
PDW	r cofficient	–	–	–	–	–	–	0.919	NS	NS	NS	NS
	P-value							<0.001				
PLRC	r cofficient	–	–	–	–	–	–	–	NS	NS	NS	NS
	P-value											
RDW	r cofficient	–	–	–	–	–	–	–	–	NS	NS	NS
	P-value											
Neutrophil	r cofficient	–	–	–	–	–	–	–	–	–	−0.975	−0.522
	P-value										<0.001	<0.001
Lymphocyte	r cofficient	–	–	–	–	–	–	–	–	–	–	0.349
	P-value											<0.001

NS: no significant.

from 3 to 75 years with a mean of (26.55±15.22) years (Table 1).

The WBC count, neutrophil count, and CRP serum level were significantly higher, while the mean age, lymphocyte count, monocyte count, RDW and PLT count were significantly lower in AA patients with and without complications compared with the control group. Higher mean neutrophil count of the patients (P<0.001) and lower mean lymphocyte (P<0.001) were found in patients with complication compared with those with non-complication.

The sensitivity, specificity, PPV, NPV for WBC were 74.7%, 75.4%, 74.6%, and 74.8%. Moreover, sensitivity, specific ity, PPV and NPV of NP were 77.8%, 76.9%, 76.8% and 77.6, respectively. The sensitivity, specificity, PPV, NPV for lymphocyte count were 76.4%, 73.7%, 75.5% and 74.5%. While the sensitivity, specificity, PPV, NPV for RDW were 63.8%, 58.1%, 61.7% and 60.3%.

For primitive diagnosis of appendicitis, OR state of combined tests has a most sensitivity (98.7%). Meanwhile, to exclude normal individuals AND state of combining tests has a most specificity (98.5%) (Table 2).

A positive relationship between Hb and HCT, MPV and PDW, MPV and PLCR and PDW and PLCR were observed. PLT and MPV, PLT and PDW, PLT and PLCR also had a negative correlation (Table 3).

Predictive power of variables in AA and ROC analysis are given in Table 3 and Figure 1. WBC, neutrophil, and lymphocyte count were the most specific and sensitive parameters (Table 2, Figure 1).

4. Discussion

AA is common case for exigency surgery[17]. Despite the advances in the diagnostic field, the diagnosis remains quite hard for surgeons. It is imperative to provide a fast and precise diagnosis before the complications[18]. This study assayed the diagnostic value of platelet parameters in AA[19].

Appendicitis is more common in the age group 10 to 30 years old[20]. With a male to female ratio of 1.4:1, apparently incidence of AA is high in males[21]. In the present study, the mean age was (26.55±15.22) years (range: 3 to 75 years), and the male to female ratio was 1.4:1, that are compatible with the current literature.

In the present investigation, mean age was lower in AA patients with and without complication compared with the control group. This finding is contrary to previous studies which have proposed that there are no significant differences between patients with AA and the control group regarding age[6,9]. Also, this outcome is contrary to that of Boshnak *et al.* who found AA patients have a older mean age[22].

In recent years, the function of platelets in inflammation has been extensively studied[23,24]. The metabolic activity and functions of platelets are associated with its size, larger platelets are presumably to be younger and more reactive[25]. There are studies suggested that size of platelets is determined at the progenitor cell stage (i.e. the megakaryocyte) and by some innumerable cytokines, such as interleukin-3 or interleukin-6 which affect megakaryocyte ploidy and produce larger and more active platelets[6,19]. Accordingly, platelet volume is an indicator of platelet reactivity[26]. MPV, a marker of platelet activation, can be calculated by apportioning the plateletcrit by the number of platelets[22]. Increased production of young platelets enhances the MPV value, and according to this, MPV is a reliable marker of platelet activity[27].

PDW is a platelet heterogeneity indicator associated with platelet activation, which causes change from discoid form to spherical, and the formation of pseudophobia to acquire a large surface. An increase in PDW and MPV indicates that young platelets are entering peripheral circulation[14].

Multiple studies have shown contradictory results on the relationship between MPV and AA. These discrepant results may be ascribed to differences in ethnicity and geographic distribution. Some studies indicate MPV reduction in AA[6,14], while others reported that MPV is higher in AA compared to the control group[4,28]. Meanwhile, Fan *et al.*[29] and Boshnak *et al.*[22] proposed that there was no significant increase or decrease in the

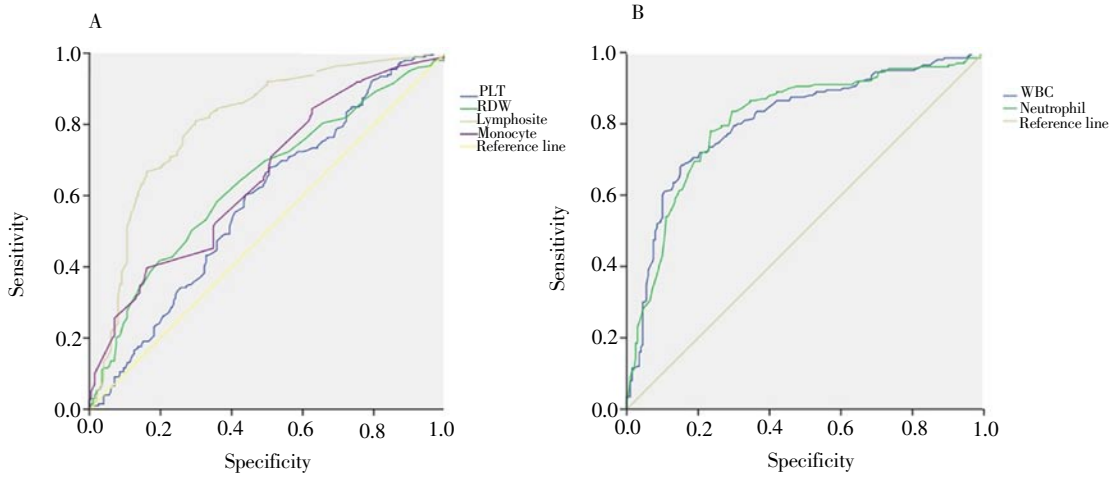

Figure 1. Receiver operating characteristic curve for predictors of cases with acute appendicitis. A: PLT, RDW, lymphocyte, monocyte; B: WBC, neutrophil. PLT: Platelet count; RDW: Red blood cell distribution width, WBC: white blood cell.

MPV between patients with appendicitis and the control group. The results of our study are consistent with these studies, showing that there is a significant relationship between the groups regarding MPV. Influencing the MPV by other inflammatory processes may provide a feasible elucidation for this result[30].

Dink *et al.*[14] reported that PDW is higher in AA compare to the control group. The result of this experiment is in agreement with those obtained by Ceylan *et al.*[31] reported that there is no difference in the PDW between people with AA and the control group and people with acute complicated appendicitis and acute non-complicated appendicitis. This finding may support the hypothesis of up-regulation or down-regulation of platelets volumes in one direction in AA patients, which leads to no significant difference between the groups[31].

It is interesting to note that in this study AA patients had lower PLT count when compared to the control group. This finding was also showed by Lee *et al.*[32] who found that PLT count is lower in AA patients in comparison with the control group. This result is in contrary to some studies which have reported no significant discrepancy between the groups regarding PLT[22,29]. Boshnak *et al.*[22] reported that positive appendectomy group have lower PLT count (P=0.020) compared to negative appendectomy patients, but it is not significant.

Several reports indicate that the first laboratory parameters for inflammation of the appendix is WBC count, and many patients with appendicitis show leucocytosis[33,34]. The present study confirms that WBC count is significantly higher in AA.

RDW represents the heterogeneity of red blood cell dimensions, and is applied in the differential diagnosis of anemia. It is reported as a percentage of the standard deviation of red blood cell volume to mean corpuscular volume. RDW may be used as an indicator of inflammatory disease, like inflammatory bowel diseaseand rheumatoid arthritis[35,36]. In addition, RDW indicates an drastic correlation with parameters like erythrocyte sedimentation rate and CRP in inflammatory conditions[37,38]. Similar to this article, Narci *et al.*[4] reported that patients with complicated appendicitis had a significantly lower RDW value in comparison with the control group. On the other hand,,Boshnak *et al.*[22], Aktimur *et al.* and Tanrikulu *et al.*[9] reported that there is no statistically significant difference regarding RDW .

CRP is an acute inflammatory phase protein, can act as a good diagnostic marker in inflammatory diseases. Boshnak *et al.*[22] reported that there was a significant increase in CRP in the positive appendectomy group compare with the negative appendectomy group, which is analogous to our result.

In the present study, the number of lymphocytes and neutrophil in the patients with AA was significantly lower and higher than the control group, respectively. This finding is consistent with the study of Pehlivanlı *et al.*[39].

In one study about the diagnosis of AA, the sensitivity of WBC was 85.8%, specificity was 31.9%. The sensitivity of neutrophil count was 87.2%, and specificity was 33.1%[40]. And the sensitivity, specificity, PPV, NPV for WBC were 74.7%, 75.4%, 74.6%, and 74.8%, respectively in our study, consis tent with the literature. Moreover, sensitivity, specific ity, PPV and NPV of NP were 77.8%, 76.9%, 76.8% and 77.6, respectively. The sensitivity, specificity, PPV, NPV for lymphocyte count were 76.4%, 73.7%, 75.5% and 74.5% which are in agreement with Boshnak *et al.* [22] who found the sensitivity, specificity, PPV, NPV for lymphocyte count were 82.76%, 63.64%, 85.7 % and 58.3%. In this study, the sensitivity, specificity, PPV, NPV for RDW were 63.8%, 58.1%, 61.7% and 60.3%. Tanrikulu *et al.*[9] reported that sensitivity, specificity, PPV, NPV for RDW were 18.5%, 92.4%, 80% and 46.4%. The type of the designed study and the diversity of individuals is probably the reason for the difference in these rates.

In this study, combined tests of best diagnostic parameters (WBC or neutrophil or lymphocyte counts) by an “or” rule enhanced the sensitivity to 98.7%. Morover, AND state of combining tests has a most specificity to exclude normal individuals. Gulnaz *et al.*[41] reported that OR state of combining tests (Total leucocyte count or neutrophil or CRP) has a sensitivity and specificity of 77.82% and 82.80%.

There is a positive correlation between parameters such as MPV and PDW, MPV and PLCR and PDW and PLCR and negative correlation between PLT and MPV, PLT and PDW and PLT and PLCR. Aydogan *et al.*[8] found that there was a linear correlation between MPV and numbers of platelets and MPV and PDW. In contrast, Narci *et al.*[4] did not find any significant correlation between, CRP, MPV and leukocyte levels.

In conclusion, WBC, lymphocyte and neutrophil counts could be used to evaluate the diagnosis of AA. Moreover, for best diagnostic protocol according to CBC results, both OR and AND state should be considered. PLT was significantly lower in patients with appendicitis, but the discriminatory power of this value and AUC is low. Therefore, this index is not useful in diagnosing patients with appendicitis.

Our results require validation in multicentre prospective studies with greater sample size. On the other hand, we found no statistically significant difference between appendicitis patients and the control group regarding the MPV and PDW levels. The most important limitation of this study is that it is inconceivable to prove the existence of other inflammatory conditions from blood sampling. Another limitation is that this is retrospective. The study was conducted on patients with clinical diagnosis of AA; also, patients with complicated and non-complicated appendicitis were separately compared. However, some studies compared only AA patients with the control groups and has limitation to evaluate the diagnostic function of platelet indices in AA[28]. Notably platelet parameters are extremely specific to the exclusive technologies, and are affected by factors such as the anticoagulant lag time from sampling to analysis, leading to unreliable results[42].

Conflict of interest statement

The authors report no conflict of interest.

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References

[1] Omari AH, Khammash MR, Qasaimeh GR, Shammari AK, Yaseen MKB, Hammori SK. Acute appendicitis in the elderly: risk factors for perforation. *World J Emerg Surg* 2014; **9**(1): 6.

[2] Andersson R, Hugander A, Thulin A. Diagnostic accuracy and perforation rate in appendicitis: association with age and sex of the patient and with appendicectomy rate. *Eur J Surg* 1992; **158**(1): 37-41.

[3] Pinto F, Pinto A, Russo A, Coppolino F, Bracale R, Fonio P, et al. Accuracy of ultrasonography in the diagnosis of acute appendicitis in adult patients: review of the literature. *Crit Ultrasound J* 2013; **5**(1): S2.

[4] Narci H, Turk E, Karagulle E, Togan T, Karabulut K. The role of red cell distribution width in the diagnosis of acute appendicitis: a retrospective case-controlled study. *World J Emerg Surg* 2013; **8**(1): 46.

[5] Andersson M, Andersson RE. The appendicitis inflammatory response score: a tool for the diagnosis of acute appendicitis that outperforms the Alvarado score. *World J Emerg Surg* 2008; **32**(8): 1843-1849.

[6] Albayrak Y, Albayrak A, Albayrak F, Yildirim R, Aylu B, Uyanik A, et al. Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis. *Clin Appl Thromb Hemost* 2011; **17**(4): 362-366.

[7] Ishizuka M, Shimizu T, Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *Int Surg* 2013; **97**(4): 299-304.

[8] Aydogan A, Akkucuk S, Arica S, Karakus A, Ozkan OV, Yetim I, et al. The analysis of mean platelet volume and platelet distribution width levels in appendicitis. *Indian J Surg* 2015; **77**(2): 495-500.

[9] Tanrikulu CS, Tanrikulu Y, Sabuncuoglu MZ, Karamercan MA, Akkapulu N, Coskun F. Mean platelet volume and red cell distribution width as a diagnostic marker in acute appendicitis. *Iran Red Crescent Med J* 2014; **16**(5): e10211.

[10]Sandhaus LM, Meyer P. How useful are CBC and reticulocyte reports to clinicians? *Am J Clin Pathol* 2002; **118**(5): 787-793.

[11]Avramakis G, Papadimitraki E, Papakonstandinou D, Liakou K, Zidianakis M, Dermitzakis A, et al. Platelets and white blood cell subpopulations among patients with myocardial infarction and unstable angina. *Platelets* 2007; **18**(1): 16-23.

[12]Beyazit Y, Sayilir A, Torun S, Suvak B, Yesil Y, Purnak T, et al. Mean platelet volume as an indicator of disease severity in patients with acute pancreatitis. *Clin Res Hepatol Gastroenterol* 2012; **36**(2): 162-168.

[13]Dadhich S, Agrawal S, Soni M, Choudhary R, Jain R, Sharma S, et al. Predictive value of platelet indices in development of preeclampsia. *J SAFOG* 2012; **4**(1): 17-21.

[14]Dinc B, Oskay A, Dinc SE, Bas B, Tekin S. New parameter in diagnosis of acute appendicitis: platelet distribution width. *World J Gastroenterol* 2015; **21**(6): 1821.

[15]Sergeant E, Perkins N. *Epidemiology for field veterinarians: An Introduction*. CABI; 2015.

[16]Weinstein S, Obuchowski NA, Lieber ML. Clinical evaluation of diagnostic tests. *Am J Roentgenol* 2005; **184**(1): 14-19.

[17]Ishikawa H. Diagnosis and treatment of acute appendicitis. *Japen Med Assoc J* 2003; **46**(5): 217-221.

[18]Yüksel Y, Dinç B, Yüksel D, Dinç SE, Mesci A. How reliable is the Alvarado score in acute appendicitis. *Ulus Travma Acil Cerrahi Derg* 2014; **20**(1): 12-18.

[19]Uyanik B, Kavalci C, Arslan ED, Yilmaz F, Aslan O, Dede S, et al. Role of mean platelet volume in diagnosis of childhood acute appendicitis. Emerg Med Int 2012; **2012**: 823095.

[20]Spirt MJ. Complicated intra-abdominal infections: a focus on appendicitis and diverticulitis. *Postgrad Medi* 2010; **122**(1): 39-51.

[21]Emil S, Gaied F, Lo A, Laberge JM, Puligandla P, Shaw K, et al. Gangrenous appendicitis in children: a prospective evaluation of definition, bacteriology, histopathology, and outcomes. *J Surg Res* 2012; **177**(1): 123-126.

[22]Boshnak N, Boshnaq M, Elgohary H. Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis. *J Invest Surg* 2018; **31**(2): 121-129.

[23]Morrell CN, Aggrey AA, Chapman LM, Modjeski KL. Emerging roles for platelets as immune and inflammatory cells. *Blood* 2014; **123**(18): 2759-2767.

[24]Thachil J. Platelets in inflammatory disorders: a pathophysiological and clinical perspective. *Semin Thromb Hemost* 2015; **41**(6): 572-581.

[25]Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. *Hippokratia* 2010; **14**(1): 28.

[26]Shannon O. Platelets interact with bacterial pathogens. *Thromb Haemost* 2009; **102**(4): 613-614.

[27]Ozdemir O, Soylu M, Alyan O, Geyik B, Demir AD, Aras D, et al. Association between mean platelet volume and autonomic nervous system functions: Increased mean platelet volume reflects sympathetic overactivity. *Exp Clin Cardiol* 2004; **9**(4): 243.

[28]Aktimur R, Cetinkunar S, Yildirim K, Ozdas S, Aktimur SH, Gokakin AK. Mean platelet volume is a significant biomarker in the differential diagnosis of acute appendicitis. *Inflamm Cell Signaling* 2015; **2**(2): e930.

[29]Fan Z, Pan J, Zhang Y, Wang Z, Zhu M, Yang B, et al. Mean platelet volume and platelet distribution width as markers in the diagnosis of acute gangrenous appendicitis. *Dis Markers* 2015; **2015**: 542013.

[30]Kilic T. Diagnostic value of mean platelet volume in acute appendicitis. *J Clin Analyti Med* 2014; **7**(113): 368-370.

[31]Ceylan B, Aslan T, Çınar A, Kurt AR, Akkoyunlu Y. Can platelet indices be used as predictors of complication in subjects with appendicitis? *Wien Klin Wochenschr* 2016; **128**(8): 620-625.

[32]Lee WS, Kim TY. Is mean platelet volume a new predictor in confirming a diagnosis of acute appendicitis? *Clin Appl Thromb Hemost* 2011; **17**(6):

E125-E6.

[33]Andersson R. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. *Br J Surg* 2004; **91**(1): 28-37.

[34]Birchley D. Patients with clinical acute appendicitis should have pre-operative full blood count and C-reactive protein assays. *Ann R Coll Surg Engl* 2006; **88**(1): 27-32.

[35]Clarke K, Sagunarthy R, Kansal S. RDW as an additional marker in inflammatory bowel disease/undifferentiated colitis. *Dig Dis Sci* 2008; **53**(9): 2521-2523.

[36]He Y, Liu C, Zeng Z, Ye W, Lin J, Ou Q. Red blood cell distribution width: a potential laboratory parameter for monitoring inflammation in rheumatoid arthritis. *Clin Rheumatol* 2018; **37**(1):161-167.

[37]Tonelli M, Sacks F, Arnold M, Moye L, Davis B, Pfeffer M. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. *Circulation* 2008; **117**(2): 163-168.

[38]Weiss G, Goodnough LT. Anemia of chronic disease. *New Engl J Med* 2005; **352**(10): 1011-1023.

[39]Pehlivanlı F, Aydin O. Role of platelet to lymphocyte ratio as a biomedical marker for the pre-operative diagnosis of acute appendicitis. *Surg Infect (Larchmt)* 2019; doi: 10.1089/sur.2019.042.

[40]Yang HR, Wang YC, Chung PK, Chen WK, Jeng LB, Chen RJ. Laboratory tests in patients with acute appendicitis. *ANZ J Surg* 2006; **76**(1-2): 71-74.

[41]Gulnaz N, Tasleem S, Abdullah F, Afzal A. Clinical accuracy of inflammatory markers combined with ultrasound in acute appendicitis. *Ann PIMS–Shaheed Zulfiqar Ali Bhutto Med Univ* 2018; **14**(2):161-168.

[42]Banfi G, Germagnoli L. Preanalytical phase in haematology. *J Med Biochem* 2008; **27**(3): 348-353.