

MEAN PLATELET VOLUME AND PLATELET DISTRIBUTION WIDTH AS DIAGNOSIS MARKERS OF ACUTE PERFORATED APPENDICITIS IN PEDIATRIC PATIENTS

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Abstract: *Symptoms and findings in acute perforated appendicitis (APA) may not always typical in children, becomes difficult to establish the diagnosis preoperatively. Rapid and accurate diagnosis is important to reduce the risk of sepsis and even death. Another biomarkers for diagnosis are needed. This study investigated the diagnostic accuracy of indicators of platelet activation, namely mean platelet volume and platelet distribution width, in children with non perforated acute appendicitis (NPAA) and APA. This retrospective study compared 15 patients with APA (Group I), 15 patients with NPAA (Group II) between January 2016 to December 2018. Patient white blood cell (WBC) count, platelet (PLT) count, MPV, PDW, and hematocrit (HCT) were analyzed. Receiver operating characteristic (ROC) curves were used to evaluate the sensitivity and specificity of these indices in AP. Positive correlation was found between MPV and the degree of AP; as well as negative correlation between PDW and degree of AP. This is the first study to assess the MPV and PDW in pediatric patients with AP. This study showed the MPV is reduced and the PDW is normal in patients with AP. A decreased MPV value could serve as a marker to diagnose AP preoperatively. More studies are needed to establish relationship between PDW and MPV with AP.*

Keywords: *Appendicitis perforations; Mean Platelet Volume; Platelet distribution width*

INTRODUCTION

Appendicitis is the most common surgical condition that causes acute abdominal pain in children population, but its diagnosis can be difficult due to its vague signs and symptoms and particularly in preverbal children and its symptoms vary widely.^{1,2} Delay in its diagnosis is associated with increased morbidity and mortality. Thus, it is necessary to use more biomarkers are needed to clarify the diagnosis of patients with suspected appendicitis.^{3,4}

Recent studies have investigated the diagnostic accuracy of inflammatory markers.^{5,6} During inflammatory diseases such as appendicitis, there is a rapid recruitment of platelets to the site of inflammation where large active platelets decrease due to its consumption and sequestration.^{7,8}

Recent studies have investigated the diagnostic accuracy of inflammatory markers.^{9,10} Mean platelet volume (MPV) and platelet distribution width (PDW) are markers of the platelet activation that have relation with inflammation and can be helpful in diagnosis of acute appendicitis.¹¹

Relationship with MPV and acute appendicitis is only analyzed in one adult and one childhood study. The aim of this study is to research whether mean platelet volume and other platelet indices had diagnostic value to distinguish non perforated acute appendicitis (NPAA) and perforated appendicitis (PAA) on pediatric group.^{12,13}

RESEARCH METHOD

This retrospective, case-controlled study compared 30 patients who applied to general surgery and pediatric room in Brigjend H.Hasan Basry Hospital from January 2016 to January 2019 with acute appendicitis.

The data were classified into two groups according to perforated and non-perforated. Age, sex, hematocrit (HCT), white blood cell (WBC), thrombocyte, platelet distribution width, and mean

platelet volume were analyzed. Ultrasonographic examinations were performed by radiologists with 3.5 MHz convex and 7.5 MHz sector transducer. The criteria for the diagnosis of acute appendicitis counseled by USG were as follows: (1) the anteroposterior diameter of more than 6 mm, (2) periappendicular anechoic fluid, (3) periappendicular hypo-echoic inflammation, (4) significant thickness of the wall of the cecum and terminal ileum than the wall of the other intestinal segments, (5) appendicoliths, and (6) noncompressible and nonperistaltic appendix.^{12,13} Appendectomy was performed to all of the patients. All the specimens were analyzed by pathologists.

The exclusion criteria were the following: being more than 18 years of age, having acute or chronic infectious disease, comorbidities, history of severe anemia or hematological disease.

Complete blood counts were performed from the venous blood samples. All the samples were obtained with ethylenediamine tetra acetic acid (EDTA) anticoagulation. HCT, MPV, and PDW were analyzed via CBC. Reference values according to the openness of the impedance were accepted as 8.0–11.0 fl for MPV and 0.1–99.9 fl for PDW.

Statistical analyses were performed using SPSS for Windows 16.0 software. The parameters with normal distribution were expressed as mean and standard deviation. Comparisons of means were performed with Mann-Whitney U. Comparisons of non parametrics were analyzed by using chi-squared test. Logistic regression analysis was used to detect risk factors.

The parameters in the AA groups were described using a receiver operating characteristic (ROC) curve analysis. In addition, the sensitivity, specificity, positive and negative predictive values and likelihood ratios, and diagnostic accuracy were calculated by the area under the ROC curve. Results were evaluated within the

95%CI, and $P < 0.05$ was considered as statistically significant.

RESULTS AND DISCUSSION

The ages of patients with range 1-17 years. Groups were comprised of 53% boy and 47% girl in group I (NPAA), 47% girl and 53% boy in group II (PAA). There were no demographic differences among the groups.

In the comparisons of the laboratory values for all parameters, MPV was lower in Group II (PAA) ($p < 0.05$), whereas WBC in group II was higher than group I (NPAA)

($p > 0.05$). PDW and Platelet were normal in group I and II.

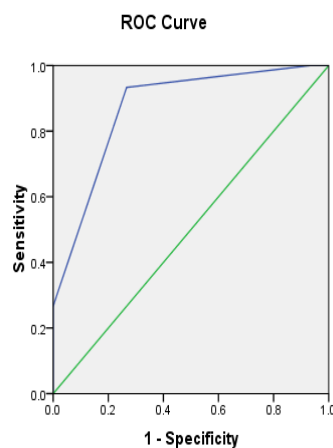
The diagnostic comparisons of the blood value evaluations are given in Table 2. MPV was the most important diagnostic parameter, followed by WBC and PDW. MPV showed 0,871 of AUC so can use to predict perforation status. As a result, the diagnostic accuracy for MPV is higher than WBC, PDW. In contrast, PDW has the lowest diagnostic accuracy. The ROC curves for these parameters are shown in Figure 1.

Table 1 Comparison of the laboratory values between the groups

Variable	Group I NPAA	Group II PAA	P values
WBC x 10 ⁹	8,6-34,2	11,3-31,7	0,126
MPV fL	7,3-9,3	6,3-8,1	<0,001
PDW %	9-12,3	8-10,9	0,744
HCT %	28-47,5	27,9-45,9	0,217
PLT x 10 ³	111-691	155-597	0,486

Table 2 Diagnostic comparison of blood parameters

Parameter	Cut Off	AUC (95%CI)	Sensitivity (%)	Specificity (%)
MPV	7,5	0,871	93,3	26,7
PDW	9,5	0,462	46,7	46,7
WBC	12650	0,667	80	53



Diagonal segments are produced by ties.

Figure 1 Receiver operating characteristic curves. MPV: Mean Platelet Volume;

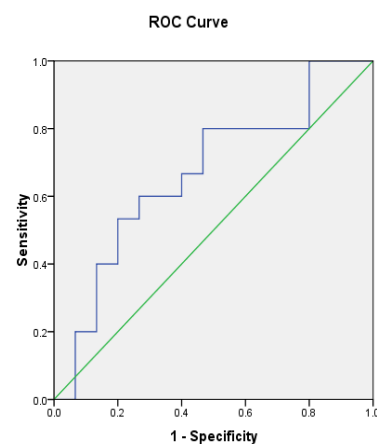


Figure 2 Receiver operating characteristic curves. WBC: White Blood Cell.

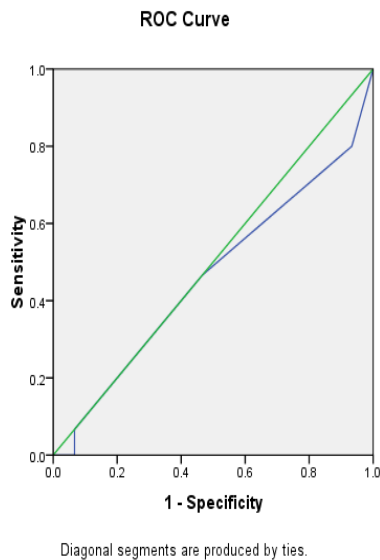


Figure 3 Receiver operating characteristic curves. PDW: Platelet Distribution Width

Acute appendicitis is acute inflammation of the appendix vermiformis, which is the most frequent condition leading to emergent abdominal surgery in children.¹⁴ The diagnosis of appendicitis can be difficult in children because its symptoms vary widely, and a delay in its diagnosis is associated with increased morbidity and mortality.¹⁵ It is important to use more laboratory tests in patients with suspected acute appendicitis with perforation or non-perforation.¹⁶

As acute appendicitis is an inflammatory process, many authors consider using biomarkers for diagnosis. Among these, WBC is the one most commonly used. Many studies support that WBC is the first indicator to be elevated in appendix inflammation.¹⁷ In our study the sensitivity and specificity of WBC is 80% and 53%, with cutoff values 12650 and AUC 0,67. As of these results, increasing WBC value on children with AA is not reliable to differentiate NPAA and PAA.

Platelet activation is related to pathophysiology of disorders with a tendency for inflammation and thrombosis. MPV, a marker of platelet activation, is being investigated for its correlation with

both inflammation and thrombosis. Low MPV values may occur in high-grade inflammatory diseases. a decrease in MPV occurs in acute cases, whereas an increase occurs with chronic events.¹⁸ The proinflammatory activities of platelets are maintained by bioactive molecules stored within their alpha and dense granules.^{19,20} After activation, these molecules are rapidly secreted. However, the exact organelle activity that controls the thrombocyte volume has not yet been clearly identified.¹⁹ Danese et al.²⁰ speculated that the reduced MPV could be due to the consumption or sequestration of the large activated platelets in the intestinal vasculature.²¹

MPV is a measurement that describes the average size of platelets and is a marker of platelet function and activation. It has been suggested that the changes of MPV in many inflammatory diseases.²² Bilici et al.,²³ Albayrak et al.,²⁴ Tanrikulu et al.,²⁵ and Erdem et al.²⁶ have suggested that the MPV was significantly lower in the acute appendicitis group compared to the control group at childhood and adult patients, respectively.

Our results agree with those studies. In the current trial, we detected a lower MPV in pediatric patients with PAA. The cause of this remains unclear. We found positive correlation between low MPV value with PAA ($p < 0,05$), from 14 from 15 samples (93,3%) with PAA show the low value of MPV. We found the results of sensitivity and specificity of MPV 93% and 27%, with good AUC 0,871. These results show that low MPV could serve as a marker to diagnose AP preoperatively.

This study is one of rare study in the literature to present the correlation between PAA and NPAA with MPV in pediatric population, as a case controlled. Detection of low MPV values in the AA groups with the high values of sensitivity and diagnostic accuracy detected for PAA are promising for future studies in diagnosis and early prediction of potential complications. Even though the specificity still low so low MPV

should always be combined with clinical. This may provide an opportunity for making a diagnosis of PAA without requiring additional analysis, increased cost, or loss of time, and is practically applicable in the emergency department. MPV could be an important laboratory evaluation, but should always be associated with additional signs (right lower quadrant tenderness, elevated temperature, rebound tenderness), symptoms (migration of pain, vomiting) and other laboratory tests (leukocytosis, C-reactive protein). More studies are needed to establish relationship between MPV and PAA with a larger sample size.

CONCLUSION

Low MPV with the high values of sensitivity and diagnostic accuracy. Even though the spesifity is not high, it can help to making diagnosis with should always be combined with additional sign . This may provide an opportunity for making a diagnosis of PAA without requiring additional analysis, increased cost, or loss of time, and is practically applicable in the emergency department. This is promising for future studies in diagnosis and early prediction of potential complications in AA. So, more studies are needed to establish relationship between MPV and PAA with a larger sample size

REFERENCES

1. Brogden TG, Streets CG. The management of acute appendicitis. *J R Nav Med Serv.* 2013;99:106-10.
2. Kim JS. Acute abdominal pain in children. *Pediatr Gastroenterol Hepatol Nutr.* 2013;16:219-24.
3. Bundy DG, Byerley JS, Liles EA, Perrin EM, Katznelson J, Rice HE. Does this child have appendicitis? *JAMA.* 2007;298:438-51
4. van Heurn LW, Pakarinen MP, Wester T. Contemporary management of abdominal surgical emergencies in infants and children. *Br J Surg.* 2014;101:e24-33.
5. Bilici S, Sekmenli T, Göksu M, Melek M, Avci V. Mean platelet volume in diagnosis of acute appendicitis in children. *Afr Health Sci* 2011; 11: 427-432 [PMID: 22275934]
6. Andersson M, Rubér M, Ekerfelt C, Hallgren HB, Olaison G, Andersson RE. Can new inflammatory markers improve the diagnosis of acute appendicitis? *World J Surg* 2014; 38: 2777-2783 [PMID: 25099684]
7. 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.
8. Pawelski H, Lang D, Reuter S. Interactions of monocytes and platelets: implication for life. *Front Biosci (Schol Ed).* 2014;6:75-91.
9. Groselj-Grenc M, Repse S, Vidmar D, Derganc M. Clinical and laboratory methods in diagnosis of acute appendicitis in children. *Croat Med J.* 200;48:353-61.
10. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis.* 1996;7:157-61.
11. Martin JF, Trowbridge EA, Salmon G (1983) The biological significance of platelet volume: its relationship to bleeding time, thromboxane B2 production and megakaryocyte nuclear DNA concentration. *Thromb Res* 32:443–460 [http://dx.doi.org/10.1016/0049-3848(83)90255-4] [PMID: 6658722]
12. Rioux M (1992) Sonographic detection of the normal and abnormal appendix. *AJR Am J Roentgenol* 158:773–778
13. Siegel MJ (1992) Acute appendicitis in childhood: the role of US. *Radiology* 185:341–342
14. Kim JS. Acute abdominal pain in children. *Pediatr Gastroenterol Hepatol Nutr.* 2013;16:219-24.
15. van Heurn LW, Pakarinen MP, Wester T. Contemporary management of abdominal surgical emergencies in

- infants and children. *Br J Surg*. 2014;101:e24-33.
16. Groselj-Grenc M, Repse S, Vidmar D, Derganc M. Clinical and laboratory methods in diagnosis of acute appendicitis in children. *Croat Med J*. 200;48:353-61.
17. 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: 27-32 [PMID: 16460636]
18. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitis GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des* 2011; 17: 47-58 [PMID: 21247392]
19. Kayahan H, Akarsu M, Ozcan MA, Demir S, Ates H, Unsal B, Akpınar H. Reticulated platelet levels in patients with ulcerative colitis. *Int J Colorectal Dis* 2007; 22: 1429-1435 [PMID: 17549498]
20. 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 [PMID: 15128364]
21. Andersson M, Rubér M, Ekerfelt C, Hallgren HB, Olaison G, Andersson RE. Can new inflammatory markers improve the diagnosis of acute appendicitis? *World J Surg* 2014; 38: 2777-2783 [PMID: 25099684]
22. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis*. 1996;7:157-61.
23. Bilici S, Sekmenli T, Göksu M, Melek M, Avci V. Mean platelet volume in diagnosis of acute appendicitis in children. *Afr Health Sci*. 2011;11:427-32
24. Albayrak A, Albayrak F, Aylu B, Uyanik A, et al. Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis. *Clin Appl Thromb Hemost*. 2011;17:3626.
25. 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:e10211.
26. Erdem H, Aktimur R, Cetinkunar S, Reyhan E, Gokler C, Irkorucu O, et al. Evaluation of mean platelet volume as a diagnostic biomarker in acute appendicitis. *Int J Clin Exp Med*. 2015;8:1291-5.