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Evaluation of the Potential Association of Platelet Levels, Mean Platelet Volume and Platelet Distribution Width with Acute Appendicitis

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Keywords: Platelet levels; Mean platelet volume (MPV); Platelet distribution width (PDW); Acute appendicitis

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Abstract

BACKGROUND: The occurrence and early management of acute appendicitis among children are especially important due to the difficult diagnosis and nonspecific symptoms of the disease. Diagnosis of appendicitis in children is very difficult due to similarity of its symptoms to other diseases, and also its self-limiting nature Platelet indexes such as mean platelet volume (MPV) and platelet distribution width (PDW) have been suggested as a biomarker of inflammation.

AIM: Therefore, we examined the association of MPV and PDW with acute appendicitis in children.

METHODS: This cross-sectional study was conducted on 464 patients with suspected acute appendicitis under the age of 18 years referred to the specialised hospitals of the ten studied provinces between October 2014 and October 2015. All data obtained regarding patient's lab tests, i.e. platelet count, MPV and PDW and also radiological studies and surgical reports were gathered in datasheets and analysed to evaluate the potential association of platelet levels, mean platelet volume (MPV) and platelet distribution width (PDW) with acute appendicitis

RESULTS: Our results showed that the MPV was significantly higher in acute appendicitis in comparison to perforated appendicitis as well as acute gangrenous appendicitis. PDW was significantly higher in acute appendicitis in comparison to perforated appendicitis and acute gangrenous appendicitis. The current project indicated that PDW < 10.05 had a sensitivity of 35% and specificity of 75%, platelet count < 229500 had a sensitivity of 24% and specificity of 75% and MPV < 8.95 had a sensitivity of 70% and specificity of 71%.

CONCLUSION: Our study suggested that platelet indexes such as MPV and PDW could significantly correlate with acute appendicitis in pediatric patients. Hence, we believe that both MPV and PDW could use as a simple and low-cost lab test for diagnosing acute appendicitis. Also, this study revealed that the MPV lower than 8.95 could be a novel index for diagnosing acute appendicitis with sensitivity of 70% and specificity of 71%.

Introduction

Acute appendicitis is one of the most common reasons for emergent surgery in all age subgroups around the world, only in the United States; the annual incidence of pediatric cases suffering acute appendicitis is estimated to be around 70.000 with notably higher incidence in the developed countries [1], [2], [3]. The incidence of disease in children aged birth to 4 years is about 1 to 2 cases per 10,000 children per year, reaching 25 cases per 10,000 children per year in older children [4]. The prevalence of disease in boys is twice that of girls with a brief distinction in different countries [5], [6]. The prevalence of acute appendicitis in developed countries is higher probably due to low fibre diet, genetic susceptibilities, as well as different patterns in gastrointestinal flora [7]. From the perspective of pathophysiology, acute appendicitis has been identified as a complex disease with quite a bit of variability in clinical manifestation and pathophysiology. The dominant pathophysiology of disease includes obstruction of the blind-ending appendix frequently due to lymphoid hyperplasia of the submucosal follicles in children following viral infections, dehydration, or fecalith. Other rare causes for appendicitis are parasitic infections, foreign bodies, or inflammatory reactions [8], [9], [10].

Overall, the occurrence and early

management of acute appendicitis among children are especially important due to the difficult diagnosis and nonspecific symptoms of the disease. Diagnosis of appendicitis in children is very difficult due to the similarity of its symptoms to other diseases and also its self-limiting nature [11]. It may not have the classic features seen in adults, and therefore hence, doctors may be challenged in terms of timely diagnosis and treatment. Its late diagnosis is common in children that one-third of preoperative children may suffer from perforation with increased the likelihood of mortality and morbidity [12]. Moreover, about 10 to 30% of appendectomies seem not to be necessary for children that can increase morbidity and healthcare costs [13].

Typically, decisions about appendectomy in acute abdominal pain refer to the other causes expressed by the patient (anorexia, nausea, vomiting and pain migration), examinations and clinical symptoms (fever, tenderness, and rebound tenderness, guarding, psoas sign and etc.) and serum tests (white blood cell count and polymorphonuclear neutrophils) [14]. However, various studies have been reported negative appendectomy in 15-30% of cases, especially in children. Negative appendectomy is associated with severe complications such as wound infections, obstruction and infertility due to damage to the uterine tubes. Imposing an unnecessary surgery may also lead to complications such as intestinal adhesions and loss of efficacy [15], [16].

A recent study in Iran showed that the number of white blood cells, the percentage of neutrophils and CRP are some diagnostic factors of acute appendicitis [17]. Recently, it has been shown that platelet count and its morphological assay in the lab test can have valuable predictive values in different gastrointestinal disorders and their surgical outcomes [18]. Also, it has been shown that higher platelet counts are associated with negative outcomes in critically ill patients. Thus, considering the need for determining better diagnostic methods for appendicitis specifically in children, in this study we have evaluated the potential association of platelet levels, mean platelet volume (MPV) and platelet distribution width (PDW) with the incidence of acute appendicitis.

Material and Methods

This study was a descriptive cross-sectional conducted on 464 patients with suspected appendicitis under the age of 18 years referred to the specialised hospitals of the studied provinces between October 2014 and October 2015. Ten provinces (Tehran, Arak, Kashan, Tabriz, Bandar-e-Abbas, Karaj, Hamadan, Kermanshah, Zanjan, Mashhad and Shiraz) out of the 31 provinces were randomly selected from Iran. The criteria for suspected acute appendicitis were included fever (temperature > 38ºC), vomiting, history of anorexia and vague periumbilical pain following migration of pain to the right lower quadrant, tenderness, rebound tenderness in physical examination and increased white blood cell (elevation of the neutrophil or band count can be seen without elevation of the total WBC count). In abdominal radiography, the main criteria for acute appendicitis were convex lumbar scoliosis, obliteration of the right psoas margin, right lower quadrant air-fluid levels, air in the appendix, and localised ileus. In abdominal ultrasonography, main finding was a non-compressible tubular structure 6 mm or wider in the right lower quadrant with local tenderness. The diagnosis of appendicitis was finally approved according to the surgical findings and post-operative pathological assessments. The patient's data collected and entered into the checklist by reviewing the hospital records including gender, age, chief complaints and clinical manifestations, laboratory tests, histopathology reports, findings on physical examination and imaging assessments, preoperative prophylaxis, surgery report, in-hospital complications, and length of hospitalisation.

Descriptive analysis was used to describe the data, including mean ± standard deviation (SD) for quantitative variables and frequency (percentage) for categorical variables. Comparison of numerical data means was based on ANOVA, Tukey's post hoc test and student’s t-test. Also, Spearman correlation was used for indicated the correlation of study variables, i.e. platelet count, MPV and PDW with appendicitis incidence. Correlated variables were then analysed with the ROC curve to indicate their sensitivity and specificity for predicting appendicitis incidence and the decent cut-off values.

Results

In this study, 464 patients admitted to the university hospital with appendicitis symptoms were studied among whom 179 (38.6%) were female, and 285 (61.4%) were male. These patients had a mean age of 110 months which had a standard deviation of 40.8 months (range 1-216).

Through their admission, clinical and preclinical assessments confirmed the final diagnosis of appendicitis in 90.3% of these cases. Among these cases, 411 patients (88.6%) underwent open surgery while 52 were operated with laparoscopy (11.2%) and only one patient did not undergo surgical treatment (0.2%) due to denying consent for the operation.

Post-operative assessments on the obtained tissue were performed to determine the underlying pathology. As it is demonstrated in Table.1 acute appendicitis, perforated appendicitis, acute

gangrenous appendicitis and reactive follicular hyperplasia were the most frequent findings whereas 22 operated patients were revealed to have normal appendix tissue.

The obtained blood tests at the time of admission in these patients revealed a mean platelet count of 279271 ± 113806 platelets per microliter of blood, mean platelet volume (MPV) of 9.18 ± 4 fL and platelet distribution width (PDW) of 11.41 ± 2.2 Fl.

Table 1: Underlying pathologies in the study population

Pathology	Frequency	Per cent	Valid Percent
Normal	22	4.7	4.8
Acute appendicitis (Acute suppurative, early acute & acute appendicitis)	253	54.5	54.6
Eosinophilic appendicitis	2	0.4	0.4
Perforated appendicitis	39	8.4	8.4
Mucosal lymphoid follicular hyperplasia	1	0.2	0.2
Lymphoid follicular hyperplasia	12	2.6	2.6
Vermiform appendicitis	1	0.2	0.2
Obliteration appendix	1	0.2	0.2
Vermiform appendix	1	0.2	0.2
Acute gangrenous appendicitis	69	14.9	14.9
Serosal edema and congestion	1	0.2	0.2
Suppurative Appendicitis	7	1.5	1.5
Necrotic	1	0.2	0.2
Appendicitis	4	0.9	0.9
Congestion	6	1.3	1.3
Reactive follicular hyperplasia	41	8.8	8.9
Embedded	2	0.4	0.4
Total	463	99.8	100.0
Missing	1	0.2	
Total	464	100.0	

Comparison of platelet count, MPV and PDW between different acute appendicitis, perforated appendicitis and acute gangrenous appendicitis pathologies

Results of one-way ANOVA revealed a significant difference between the three types of acute appendicitis, perforated appendicitis and acute gangrenous appendicitis regarding PDW (F (2.355) = 27.57, p-value < 0.001) and MPV (F (2,354) = 26.22, p-value < 0.001). However, no significant difference was observed in platelet counts between these groups.

Furthermore, results of the Tukey's post-hoc test revealed that mean MPV was significantly higher in acute appendicitis compared to perforated appendicitis (p-value = 0.001) and acute gangrenous appendicitis (p-value < 0.001) while there was no significant difference between acute gangrenous appendicitis and perforated appendicitis in this regard (p-value = 0.248). Also, it was shown that mean PDW was significantly higher in acute appendicitis compared to perforated appendicitis (p-value < 0.001) and acute gangrenous appendicitis (p-value < 0.001) while there was no significant difference between acute gangrenous appendicitis and perforated appendicitis in this regard (p-value = 0.333). Table 2 represents the mean of platelet count, MPV and PDW in each group.

Table 2: Mean of platelet count, MPV and PDW in each appendicitis pathology group

Appendicitis pathology	Platelet		MPV		PDW	
	Mean	SD*	Mean	SD	Mean	SD
Acute appendicitis	271538	114966	9.1	1.0	10.9	1.5
Perforated appendicitis	311030	88228	8.1	1.1	12.3	3.5
Acute gangrenous appendicitis	289021	120619	8.4	1.0	13.0	3.0

*SD: Standard deviation.

Evaluation of correlation between platelet count, MPV and PDW and incidence of acute appendicitis, perforated appendicitis and acute gangrenous appendicitis pathologies

Results of spearman's correlation test for platelet count, MPV and PDW and incidence of acute appendicitis, perforated appendicitis and acute gangrenous appendicitis pathologies revealed a significant negative correlation between acute appendicitis and PDW (correlation coefficient -0.150, p-value = 0.001) and also the platelet count (correlation coefficient -0.1, p-value = 0.048). However, there was a significant positive correlation between acute appendicitis and MPV (correlation coefficient 0.188, p-value < 0.001). Moreover, it was shown that perforated appendicitis had a significant negative correlation with MPV (correlation coefficient -0.260, p-value < 0.001). Finally, analysis results revealed a significant positive correlation between acute gangrenous appendicitis and PDW (correlation coefficient 0.221, p-value < 0.001) and a significant negative correlation between this type of appendicitis and MPV (correlation coefficient -0.245, p-value < 0.001).

Predictive value of platelet count and PDW for appendicitis

To evaluate the Predictive value of platelet count, MPV and PDW for appendicitis ROC curve analysis was performed according to correlation analysis results. In this regard, as most of the correlations were negative, test was set as smaller test indicated more positive test, and for those with positive correlation, the 1/variable was considered for analysis.

Acute appendicitis

ROC curve analysis for variable correlated with acute appendicitis revealed that PDW, platelet count and 1 / MPV are sensitive and specific for determining the incidence of this type of appendicitis (Figure 1).

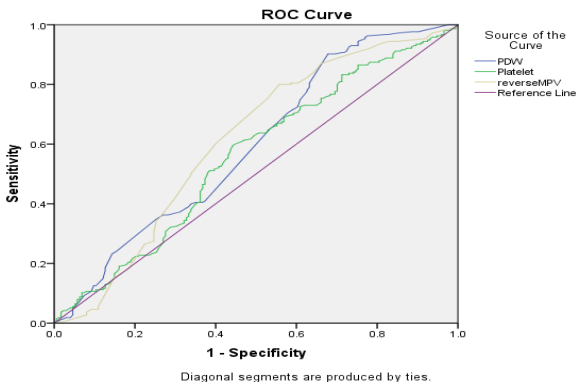

Figure 1: ROC curve analysis for variable correlated with acute appendicitis

In this regard the area under curve and p-value were as (AUC:0.594, p-value = 0.001) for PDW, (AUC:0.560, p-value = 0.041) for platelet count and (AUC:0.594, p-value < 0.001) for 1 / MPV.

Furthermore, the coordinate of the curves indicated that PDW < 10.050 had a sensitivity of 35% and specificity of 75%, platelet count < 229500 had a sensitivity of 24% and specificity of 75% and 1/MPV < 0.1058 had a sensitivity of 35% and specificity of 75%.

Perforated appendicitis

ROC curve analysis for variable correlated with acute appendicitis revealed that MPV is sensitive and specific for determining the incidence of this type of appendicitis (Figure 2)

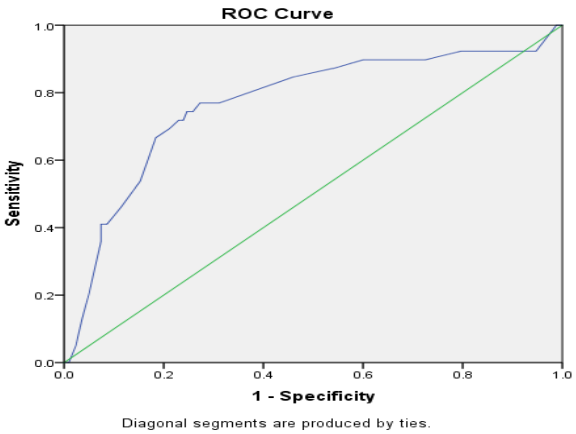

Figure 2: ROC curve analysis for variable correlated with perforated appendicitis

In this regard, the area under curve and p-value was as (AUC:0.768, p-value < 0.001) for MPV and coordinate of the curves indicated that MPV < 8.25 had a sensitivity of 70% and specificity of 80%.

Acute gangrenous appendicitis

ROC curve analysis for variable correlated with acute appendicitis revealed that MPV and 1/PDW are sensitive and specific for determining the incidence of this type of appendicitis (Figure 3).

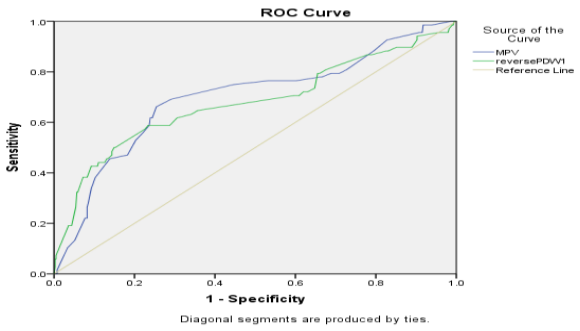

Figure 3: ROC curve analysis for variable correlated with acute gangrenous appendicitis

In this regard the area under curve and p-value were as (AUC:0.698, p-value = 0 < 001) for MPV and (AUC:0.679, p-value = 0 < 001) for 1 / PDW.

Furthermore, the coordinate of the curves indicated that MPV < 8.95 had a sensitivity of 70% and specificity of 71% and 1/PDW < 229500 had a sensitivity of 59% and specificity of 76%.

Discussion

According to our reports, on all children who were suspected of acute appendicitis according to initial manifestations, 10% suffered definitively from disease according to surgical findings as the gold diagnostic standard. Although clinical assessment along with different imaging modalities especially ultrasonography can be very helpful to discriminate abnormal from healthy conditions, but could not play a key role in this goal. The obtained prevalence of childhood appendicitis among suspected children is much closer to the rates previously reported. As shown by Wiersma et al. in 2009, the prevalence of appendicitis, proven by surgery and/or pathology, in this study was 34% [15].

The platelet factors such as MPV and PDW are markers that could be easily studied with complete blood count and which is an indicator of platelet function and activation. These markers volume were found to be associated with platelet function and activation [19], [20]. In general, platelet production increases as the platelet count decreases, and young platelets become larger and more reactive, and therefore, the MPV values are higher [21], [22]. In recent years, in some studies in which MPV was tested as a simple inflammatory marker, MPV was reported to have been affected by inflammation, and that it increases significantly in myocardial infarction, sepsis, cerebrovascular diseases, respiratory distress syndrome and chronic pulmonary diseases [23], [24].

In the literature, MPV has been reported to decrease in some inflammatory bowel diseases such as ulcerative colitis, especially in the active period, and that it could be used for determination of the disease activity [25], [26]. This condition is thought to have been related to the release of bioactive molecules of pro-inflammatory active platelets in the presence of inflammation. Also, numerous studies have been evaluated the role of platelet indexes such as MPV and PDW in acute appendicitis. In this regard, Boshnak et al., showed that Increased PDW combined with elevated white blood cells and neutrophil counts might be used as diagnostic tests in the cases of acute appendicitis, while MPV and RDW levels were not useful diagnostic markers, while studies are not in consist with each other [27].

Our results showed that the mean MPV was

significantly higher in acute appendicitis in comparison to perforated appendicitis as well as acute gangrenous appendicitis. Besides, current study demonstrated that the mean PDW was significantly higher in acute appendicitis in comparison to perforated appendicitis and acute gangrenous appendicitis. In contrast, Arian Nia et al. found no association between MPV and final diagnosis of acute appendicitis in children between the ages of 1 and 15 years; and also, they suggested that the MPV is not an effective index in the diagnosis of acute appendicitis and cannot be involved as a reliable index in making decision. However, Bilici et al. found that the mean MPV was found to be lower than normal in 48 cases in the acute appendicitis group (MPV = 7.55) [28]. However, the study by Uyanik et al. supports the findings which are in contrast with our study. They found that the mean MPV was 7.9 in the appendicitis group and 7.7 in the control group and that there was no statistically significant difference between the two groups [29]. Interestingly, MPV in Erdem et al., study was 7.4 in the appendicitis group and 9.1 in the control group [30]. Similarly, Fan et al. reported that the MPV value in gangrenous appendicitis group was significantly lower than in the controls group [31].

Although numerous studies have been reported the effectiveness of PDW and MPV in diagnosis of various types of appendicitis, few reports have been conducted to evaluate the sensitivity and specificity of platelet indexes for diagnosis of acute appendicitis. In this regard, MPV was evaluated by Bilici et al., [28]. In the recent mentioned study, the specificity was determined as 54%, and sensitivity was found as 87% for the decrease in MPV (< 7.4 fL). The current project indicated that PDW < 10.05 had a sensitivity of 35% and specificity of 75%, platelet count < 229500 had a sensitivity of 24% and specificity of 75% and 1/MPV < 0.1058 had a sensitivity of 35% and specificity of 75%. Furthermore, our results indicated that MPV < 8.95 had a sensitivity of 70% and specificity of 71% and 1 / PDW < 229500 had a sensitivity of 59% and specificity of 76%.

Finally, the results obtained from this study showed a significant negative correlation between acute appendicitis and PDW and also the platelet count. However, our results revealed that there was a significant positive correlation between acute appendicitis and MPV. Moreover, it was shown that perforated appendicitis had a significant negative correlation with MPV. Finally, analysis results revealed a significant positive correlation between acute gangrenous appendicitis and PDW and a significant negative correlation between this type of appendicitis and MPV.

In conclusion, our study suggested that platelet indexes such as MPV and PDW could significantly correlate with acute appendicitis in pediatric patients. Hence, we believe that both MPV and PDW could use as a simple and low-cost lab test for diagnosing acute appendicitis. Also, this study revealed that the MPV lower than 8.95 could be a novel index for diagnosing acute appendicitis with sensitivity of 70% and specificity of 71%.

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