

# Diagnostic value of platelet indices in acute appendicitis and comparison with histopathology



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## Diagnostic value of platelet indices in acute appendicitis and comparison with histopathology

**BACKGROUND:** Acute appendicitis is one of the most common surgical emergencies. An early and accurate diagnosis of acute appendicitis is vital. Evidence for a link between platelets indices and inflammation disease comes from recent studies. We aimed to evaluate preoperative diagnostic values of platelet indices (Mean platelet volume-MPV, Platelet Distribution Width-PDW, Plateletcrit-PCT) and leukocyte count (WBC) in comparison with post-operative histopathology results in patients who underwent appendectomy.

**METHODS:** The 165 patients who underwent appendectomy, were evaluated retrospectively. Patients' demographic characteristics, imaging findings, preoperative laboratory markers and postoperative histopathology results were recorded. The patients were divided into three groups based on the histopathologic findings; perforated appendicitis, acute appendicitis without perforation and negative appendectomy group. The specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) of the laboratory markers were measured. Additionally potential correlation among laboratory markers analysed.

**RESULTS:** The negative appendectomy rate was 15.1% in 165 patients. The leukocyte count was statistically higher in acute appendicitis ( $14.9 \times 10^3/\mu\text{L}$ ) group than negative appendectomy ( $6.9 \times 10^3/\mu\text{L}$ ) group. There was also statistically significant difference between groups according to the PCT levels. The leukocyte count achieved sensitivity, specificity, PPV, and NPV of 95.9, 24, 99.1, and 92.7% respectively. A significant positive correlation between WBC and PCT were obtained. Inflammatory markers were not directly related to the severity of the disease.

**CONCLUSIONS:** Elevated leukocyte count and PCT levels support diagnosis of acute appendicitis in correlation with pathological findings. Thereby combination of the inflammatory markers, positive clinical and radiological findings would improve diagnostic accuracy in acute appendicitis.

**KEY WORDS:** Acute appendicitis, Inflammatory markers, Platelet indices

## Introduction

Acute appendicitis is one of the most common intra abdominal surgical emergencies <sup>1</sup>. The progression from acute inflammation to perforation generally occurs within few days <sup>2</sup>. Therefore delay in the diagnosis and surgical intervention for AA may lead to perforation of appendix, peritonitis and systemic septic complications

with the increase of morbidity and mortality rates.<sup>3</sup> Besides it has been documented that the negative appendectomy rate varies between 5 to 15% in recent series.<sup>4</sup> However early and accurate diagnosis of disease is depend on combination of careful history, physical examination, scoring systems, laboratory and imaging evaluation, acute appendicitis is mostly diagnosed with clinical findings such as fever, right lower quadrant pain and tenderness in routine clinical practice <sup>5,6</sup>. On the other hand, the accuracy of the clinical diagnosis of acute appendicitis is reported between 76 percent and 92 percent <sup>7</sup>. Since the introduction of ultrasonography and computed tomography, the negative appendectomy rates have considerably decreased but the higher perforation rate is still remain <sup>8,9</sup>. Therefore, due to these difficulties in diagnosis, an early and accurate diagnosis for acute appen-

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ditis may contribute to reduce the perforation rates, risk of peritonitis or sepsis and the number of unnecessary operations. It can be achieved preoperatively before an invasive surgical procedure with additional tests<sup>10</sup>. The severity of acute appendicitis associated with inflammation.<sup>11</sup> Additionally platelet indices (PCT, PDW, MPV) and WBC play prominent roles in inflammatory processes<sup>12</sup>. Recently MPV, PCT, PDW and WBC has been evaluated as an inflammatory marker in several inflammatory diseases such as cardiovascular, cerebrovascular disorders, endometriosis, pulmonary disease and also in acute appendicitis, additionally it was highlighted that platelet indices can be used as a marker of inflammatory disease<sup>13-18</sup>. Therefore widely available, simple, minimally invasive and cost-effective blood tests suggest potential clinical benefits for diagnosis of acute appendicitis.

In present study we aimed to evaluate preoperative diagnostic values of platelet indices (MPV, PDW, PCT) and WBC in comparison with post-operative histopathology results in patients who underwent appendectomy, to examine whether preoperative platelet indices and WBC count would contribute as non-invasive biomarkers for preoperative diagnosis of acute appendicitis.

## Materials and Methods

This study was performed in Bayrampasa State Hospital and Esencan Hospital, Department of Surgery between January 2015-January 2016. Total number of 165 patients who underwent appendectomy, were evaluated retrospectively in this study. Patients' demographic characteristics, imaging findings, preoperative laboratory markers (MPV, PDW, PCT, WBC) and postoperative histopathology results were recorded.

Patients presented with appetite loss, nausea and vomiting, supporting signs in history as well on admission. Clinical and physical findings of acute appendicitis examined by the surgeon and at least one clinical finding was suggestive of acute appendicitis. The clinical findings included right lower abdominal pain, percussion and rebound tenderness, localized and diffuse rigidity of the abdominal wall were evaluated. The final diagnosis was based on the histopathologic assessment. The patients were divided into three groups based on the histopathologic findings; perforated appendicitis, acute appendicitis without perforation and negative appendectomy group.

Cell blood count analysis was performed on patients' venous blood samples. Haematological parameters were analysed using a haematology analyser (Cell-Dyne 3700, Abbott, Abbott Park, IL, USA). Normal values were defined as follows: WBC 4.0 to 10.0  $\times 10^3/\mu\text{L}$ , MPV 6 to 11 fL, PDW 8 to 18 fL and PCT 0.2 to 0.5%.

The specificity, sensitivity, positive predictive value and negative predictive value of the laboratory markers were

measured. Additionally the correlation between laboratory markers and histopathology outcomes were examined.

## STATISTICAL ANALYSIS

All the data were analysed with SPSS (Statistical Package for the Social Sciences) software for Windows (v21.0; IBM, Armonk, NY, USA). Individual and aggregate data were summarized using descriptive statistics including mean, standard deviations, medians (min-max), frequency distributions and percentages. Normality of data distribution was verified by Kolmogorov-Smirnov test. Comparison of the variables with normal distribution was made with Student t test. Evaluation of categorical variables performed by Chi-Square test. We used Spearman correlation to examine the relationship between laboratory markers and histopathology results. P-Values of  $<0.05$  were considered statistically significant.

## Results

The 165 patients included in this study were 93 (56.4%) male and 72 (43.6%) female and the mean age of 165 patients was  $29.15 \pm 12.174$  (Ranged: 5-70 ages) years. The patients diagnosed with acute appendicitis ( $n=140$ ) in this study were 79 (56.4%) male and 61 (43.6%) female and the mean age of acute appendicitis patients was  $28.71 \pm 11.915$  years. The negative appendectomy rate was 15.1% ( $n=25$ ). The mean age of negative appendectomy group was  $31.6 \pm 13.54$  years (Table I). There were no statistically significant differences between the acute appendicitis and negative appendectomy groups according to the age and gender ( $p>0.05$ ). In addition of the 140 patients diagnosed with acute appendicitis, 6 (4.3%) were histopathologically reported as perforated appendicitis. There were no statistically significant differences found between the acute appendicitis and perforated appendicitis groups according to the age and gender (respectively;  $p=0.619$ ,  $p=0.697$ ).

The mean WBC was  $14.9 \times 10^3/\mu\text{L}$  (SD:  $\pm 4.3$ ; Ranged: 5.45 to  $27.7 \times 10^3/\mu\text{L}$ ) in the acute appendicitis group, whereas in negative appendectomy group was  $6.9 \times 10^3/\mu\text{L}$  (SD:  $\pm 2.3$ ; Ranged: 2.1 to  $11.9 \times 10^3/\mu\text{L}$ ). The leukocyte count was found statistically higher in acute appendicitis group than negative appendectomy group ( $p=0.000$ ). The mean PCT levels were  $0.25 \pm 0.06\%$  and  $0.20 \pm 0.04\%$  in the acute appendicitis and negative appendectomy groups, respectively, there was also statistically significant difference between acute appendicitis and negative appendectomy groups according to the PCT levels ( $p=0.001$ ). The median MPV level was  $9.65 \pm 1.08$  fL in the acute appendicitis group and  $9.90 \pm 1.11$  fL in negative appendectomy group. There was no statistically significant difference found accord-

ing to MPV values between groups ( $p > 0.05$ ). The median PDW level was  $12.4 \pm 2.1$  fL in the acute appendicitis group and  $13.4 \pm 2.73$  fL in negative appendectomy group. There was no statistically significant difference found according to PDW levels between groups ( $p > 0.05$ ) (Table II).

The leukocyte count achieved a sensitivity, specificity, positive predictive value, and negative predictive value of 95.9, 24, 99.1, and 92.7% respectively in our study. The sensitivity, specificity, positive predictive value and negative predictive value for PCT were found 72.5, 48, 82.5, and 62.5% respectively. The sensitivity, specificity, positive predictive value, and negative predictive value were found 39.6, 48, 56.9, and 31.9% for PDW; 44.4, 60, 52.4, and 26.9% for MPV respectively (Table III).

The correlation analysis was performed to identify any significant correlation between the laboratory markers in this study. Analysis showed a significant positive-low correlation between WBC and PCT ( $r: 0.391$ ,  $p: 0.000$ ). There was also a significant negative-low correlation between PCT and the PDW ( $r: -0.177$ ,  $p: 0.023$ ).

Moreover, there was a significant positive-low correlation between MPV and the PCT ( $r: 0.306$ ,  $p: 0.000$ ). Besides no significant correlations were observed between WBC and MPV ( $r: 0.134$ ,  $p: 0.087$ ) or between WBC and PDW ( $r: -0.134$ ,  $p: 0.086$ ) (Table IV).

The mean values of leukocyte count, plateletcrit, mean platelet volume, and platelet distribution width were  $15.3 \pm 3.4 \times 10^3/\mu\text{L}$  and  $14.9 \pm 4.4 \times 10^3/\mu\text{L}$ ;  $0.31 \pm 0.11\%$  and  $0.25 \pm 0.06\%$ ;  $9.7 \pm 0.7$  fL and  $9.6 \pm 1.09$  fL;  $12.1 \pm 1.70\%$  and  $12.5 \pm 2.18\%$  in perforated appendicitis and acute appendicitis group, respectively (Table V). There was no statistically significant difference among the groups with respect to the platelet indices ( $p > 0.05$ ). Also, no significant difference found among groups according to the leukocyte count ( $p > 0.05$ ).

## Discussion

Acute appendicitis is generally classified into three types; focal, suppurative, or gangrenous-perforated. Besides in

TABLE I - Distribution of acute appendicitis and negative appendectomy patients according to the age and gender.

	Acute appendicitis	Negative appendectomy	Total	P Value
Female	n=61 (43.6%)	n= 11 (44%)	n= 72 (43.6%)	0.968
Male	n= 79 (56.4%)	n= 14 (56%)	n= 93 (56.4%)	
Total	n= 140 (84.8%)	n= 25 (15.2%)	n= 165 (100%)	
Mean Age	$28.1 \pm 11.915$ (min: 5; max: 60)	$31.6 \pm 13.4$ (min: 5; max: 70)	$29.15 \pm 12.174$ (min: 5; max: 70)	0.276

TABLE II - Comparison of platelet indices (MPV, PDW, PCT) and WBC levels between acute appendicitis and negative appendectomy groups.

	Acute appendicitis (n=140)	Negative appendectomy (n=25)	p value
WBC	$14.921929 \pm 4.395020$	$6.958400 \pm 2.310885$	0.000*
PCT	$0.254164 \pm 0.066292$	$0.206600 \pm 0.042037$	0.001*
MPV	$9.52143 \pm 1.083258$	$9.900000 \pm 1.114675$	0.296
PDW	$12.495714 \pm 2.159799$	$13.432000 \pm 2.734002$	0.057

$p^* < 0.05$

TABLE III - Diagnostic evaluation of platelet indices (MPV, PDW, PCT) and leukocyte count.

	WBC	PCT	PDW	MPV
Sensitivity	95.9%	72.5%	39.6%	44.4%
Specificity	24%	48%	48%	60%
PPV	99.1%	82.5%	56.9%	52.4%
NPV	92.7%	62.5%	31.9%	26.9%

TABLE IV - Correlation of platelet indices (MPV, PDW, PCT) and leukocyte count.

			WBC	PCT	MPV	PDW
Spearman Test	WBC	Correlation coefficient (r)	1,000	,391**	,134	-,134
		p -Value	.	,000	,087	,086
		N	165	165	165	165
	PCT	Correlation coefficient (r)	,391**	1.000	,173*	-,177*
		p -Value	,000	.	,026	,023
		N	165	165	165	165
	MPV	Correlation coefficient (r)	,134	,173*	1,000	,306**
		p -Value	,087	,026	.	,000
		N	165	165	165	165
	PDW	Correlation coefficient (r)	-,134	-,177*	,306**	1.000
		p -Value	,086	,023	,000	.
		N	165	165	165	165

TABLE V - Comparison of platelet indices (MPV, PDW, PCT) and WBC levels between perforated appendicitis and acute appendicitis groups.

	Perforated appendicitis (n=6)	Acute appendicitis (n=134)	p value
WBC	15.3483 ± 3.4617	14.9028 ± 4.429977	0.809
PCT	0.31817 ± 0.113790	0.25130 ± 0.062555	0.211
MPV	9.750 ± 0.7556	9.648 ± 10.975	0.822
PDW	12.150 ± 1.7050	12.511 ± 2.1818	0.690

eastern countries acute appendicitis mostly classified as catarrhal, phlegmonous, or gangrenous types based on the inflammatory characteristic of disease<sup>11</sup>. Although recent series recommends a negative appendectomy rate as high as 15 percent and also new approaches in antibiotic therapy currently being developed, surgery is still the first choice for acute appendicitis particularly in gangrenous appendicitis<sup>10,19</sup>. In accordance with published data the negative appendectomy rate was 15.1% in present study. Therefore inflammatory markers such as leukocyte count and platelet indices suggest potential clinical benefits for diagnosis of acute appendicitis.

Xharra et al. reported a mean age of 19.7±10,5 years (Ranged: 5-59), of the 148 patients with acute appendicitis; 90 (52.02%) were male and 83 (47.97%) were females, additionally researchers reported that 83.5% of patients were under aged 30 years<sup>20</sup>. In another study Aren et al. determined male gender and age between 15-30 years as potential risk factors for acute appendicitis in their study which conducted with 302 cases of appendectomy<sup>21</sup>. Consistent with this results, of the 140 patients with acute appendicitis; 79 (56.4%) were male, 61 (43.6%) were female and the mean age was 28,71±11,915 years in our study. There were no statistically significant differences found between groups according to the age and gender. Guler K. et al. evaluated the 101 patients (65.3% male, 34.7% female) into

two groups based on the histopathologic findings as perforated appendicitis (n=17) and acute appendicitis (n=84). Researchers reported mean age of 31.58 and 28,5 years in perforated appendicitis and acute appendicitis groups respectively, additionally no statistically significant differences found between the groups according to the age and gender<sup>22</sup>. We also divided patients as perforated appendicitis and acute appendicitis, similarly there were no statistically significant differences found between the acute appendicitis and perforated appendicitis groups according to the age and gender.

The relationship between the rise of leukocyte count and appendicitis diagnosis have been examined and demonstrated in numerous published data. Aren A. et al designed 3 groups to assess leukocyte count in patients with acute appendicitis; < 10 x103/μL, 10 to 15 x103/μL and >15x103/μL. Researchers observed 2,5 times higher risk (p=0.042) for developing acute appendicitis in >15x103/μL leukocyte group<sup>21</sup>. Narci H. et al. also noted the increase of leukocyte count in acute appendicitis group.<sup>23</sup> Yang HR. et al. showed a relationship between higher leukocyte count and histological inflammation in acute appendicitis<sup>24</sup>. Andersson RE et al. and Guraya SY et al. suggested that leukocyte count is a reliable indicator of acute appendicitis<sup>25,26</sup>. Xharra et al. reported elevated WBC in 126 (85.1%) cases with positive histopathology (mean 12.6 and 15.6 x109/l in acute

appendicitis and perforated appendix groups respectively) moreover researchers demonstrated a positive correlation between WBC and severity of inflammation<sup>20</sup>. Bates MF et al. concluded absence of an increased WBC count is a risk factor for negative appendectomy<sup>27</sup>. Supportively in present study the mean WBC was  $14.9 \times 10^3/\mu\text{L}$  in acute appendicitis group and the leukocyte count was statistically higher in acute appendicitis group than negative appendectomy group.

In recent studies, the sensitivity of WBC was reported to range from 60 to 87% and specificity from 53 to 100%.<sup>20,21,28</sup> Xharra et al. reported a sensitivity, specificity, positive predictive value, and diagnostic accuracy of 85.1, 68, 94, 82.6%, respectively with WBC<sup>20</sup>. In accordance with published data the leukocyte count achieved a sensitivity, specificity, positive predictive value, and negative predictive value of 95.9, 24, 99.1, and 92.7% respectively in our study.

Inflammation paves the way for increased platelet production and platelet production may cause differentiation of platelet volume. Finally this process results with increased MPV and PDW levels<sup>29</sup>. In addition reduction of platelet and PCT levels occurs during excessive consumption of platelets. Increased platelet volume has been widely examined, on the contrary MPV might decrease in high-grade inflammation due to excessive consumption as well<sup>30</sup>. Numerous published data demonstrated diagnostic value for platelets indices in certain inflammatory diseases<sup>14</sup>. Narci et al. reported higher MPV values in patients with acute appendicitis, with 66% sensitivity and 51% specificity<sup>23</sup>. Meanwhile, Kılıç et al. showed no significant difference between acute appendicitis and patient groups<sup>31</sup>. Ceylan et al. stated that the MPV was lower in 363 acute appendicitis patients than in control groups and no significant difference between groups according to PDW levels<sup>32</sup>. Yılmaz Y. et al. analysed 224 pediatric patients who underwent appendectomy and researchers reported a platelet count, MPV, PCT and PDW value of  $305 \pm 94 \times 10^3/\mu\text{L}$ ;  $7.37 \pm 0.90$  fL;  $0.220 \pm 0.057$  % and  $16.3 \pm 0.5$ %, respectively in acute appendicitis group. Researchers found no statistically significant difference between between acute appendicitis and normal appendix group with regard to platelet indices<sup>33</sup>. Uyanık B. et al. stated that MPV has no diagnostic value in pediatric acute appendicitis<sup>34</sup>. In accordance with published data there were no statistically significant differences found according to MPV and PDW values between groups in our study ( $p > 0.05$ ). Besides the published data particularly available on MPV is seem to be conflicting and confusing, thus the relationship between platelet indices and inflammation grade would benefit from additional studies.

Tanrikulu CS. et al. reported a sensitivity, specificity, PPV, NPV and diagnostic accuracy of 45, 89.2, 87.3, 49.6 and 61.7% respectively for MPV. Researchers also found no significant difference between the groups

according to the PDW and platelet values<sup>35</sup>. In our study the sensitivity, specificity, positive predictive value, and negative predictive value were found 39.6, 48, 56.9, and 31.9% for PDW; 44.4, 60, 52.4, and 26.9% for MPV respectively. This two markers found to be a poor sensitivity to utilize as diagnostic tool in present study.

On the contrary in our study there was statistically significant difference between acute appendicitis and negative appendectomy groups according to the PCT levels ( $p=0.001$ ). Moreover the PCT achieved a sensitivity, specificity, positive predictive value, and negative predictive value of 72.5, 48, 82.5, and 62.5% respectively. Supportively Oylumlu M. demonstrated that PCT may be a predictive marker for the cardiac syndrome X which is well-known as a inflammatory disease<sup>36</sup>. In the present study, we also found a positive correlation between WBC and PCT levels. Moreover, there was a significant positive-low correlation between MPV and the PCT levels. These findings support a requirement of combination assessment of inflammatory markers in acute appendicitis.

Recently elevated leukocyte count was found to be related to perforated appendicitis in published data<sup>37</sup>. On the other hand Lin CJ. et al. concluded that leukocyte count only increases during the early stages or prior to perforation and they found no statistically significant differences in patients with perforated appendicitis.<sup>38</sup> Supportively a study conducted by Guler K. et al. found no significant differences between perforated appendicitis (mean WBC:  $14.6 \times 10^3/\mu\text{L}$ ) and acute appendicitis group (mean WBC:  $13.2 \times 10^3/\mu\text{L}$ ) in terms of leukocyte count<sup>22</sup>. Similarly Wu CT. et al. found no significant differences between perforated appendicitis and acute appendicitis group in terms of leukocyte count in a study consisted of 120 patients<sup>39</sup>. Moreover Aydoğan et al. divided acute appendicitis patients into two groups; perforated appendicitis and acute appendicitis. Researchers found lower MPV and higher PDW levels in the perforated appendicitis group<sup>40</sup>. In accordance with published data there was no statistically significant difference among the groups with respect to the platelet indices and leukocyte count in our study.

In conclusion, the findings of the present study suggest that elevated leukocyte count and PCT levels support diagnosis at the early stage of acute appendicitis in significantly correlation with pathological findings. Furthermore preoperative leukocyte count achieved a highest sensitivity, positive predictive value, and negative predictive value in present study. Thus combination of the inflammatory markers and positive clinical findings would improve diagnostic accuracy in acute appendicitis. Besides inflammatory markers were not directly related to the severity of the disease. Consequently further researches should be perform with larger study groups to achieve more assuring results.

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## Riassunto

L'appendicite acuta è una delle più comuni emergenze chirurgiche, ed una sua diagnosi tempestiva e precisa è della massima importanza. Da studi recenti è emerso un evidente collegamento tra gli indici piastrinici e le malattie infiammatorie. Con questo studio ci siamo proposti di valutare il valore diagnostico preoperatorio degli indici piastrinici (volume piastrinico medio – MPV, distribuzione dello spessore piastrinico – PDW, piastrinocrito – PCT) e conta leucocitaria (WBC) in raffronto con i dati istopatologici postoperatori in pazienti sottoposti ad appendicectomia.

Lo studio è stato condotto su 165 pazienti appendicetomizzati, e valutati retrospettivamente, rilevando le loro caratteristiche demografiche, la diagnostica per immagini ed i dati di laboratorio preoperatori ed i risultati istopatologici postoperatori. I pazienti sono stati suddivisi in tre gruppi in relazione ai rilievi istopatologici: appendicite perforata, appendicite acuta senza perforazione e appendice indenne. Sono stati presi in considerazione specificità, sensibilità e valore predittivo positivo (PPV) e negativo (NPV) dei dati di laboratorio, analizzando ulteriori correlazioni potenziali tra questi dati.

L'incidenza delle appendicectomie con appendice indenne è risultata del 15,1% sui 165 pazienti. La conta leucocitaria è risultata statisticamente più elevata nel gruppo delle appendicitis acute ( $14,9 \times 10^3/\mu\text{L}$ ) rispetto al gruppo delle appendici indenni ( $6,9 \times 10^3/\mu\text{L}$ ). Sono risultate differenze statisticamente significative tra i gruppi in relazione ai livelli del piastrinocrito. La conta leucocitaria ha dimostrato sensibilità, specificità, PPV e NPV rispettivamente del 95,9%, 24%, 99,1% e 92,7% ed una correlazione positiva tra WBC e PCT senza una diretta correlazione tra i markers della flogosi e la sua gravità.

In conclusione una conta leucocitaria elevata ed alti livelli del PCT sono diagnostici nell'appendicite acuta in correlazione con i dati istopatologici. Pertanto la combinazione dei markers infiammatori con i reperti clinici e radiologici sono in grado di migliorare l'accuratezza diagnostica nell'appendicite acuta.

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