

➔ Original Article



Do Platelet Indices Serve as Biomarkers for Differentiating Complicated Appendicitis From Simple Appendicitis in Adults?

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Abstract

Background: Acute appendicitis (AA) is known as a prevalent surgical emergency on a global scale. The objective of this study was to analyze laboratory parameters in individuals diagnosed with both simple and complicated forms of appendicitis.

Methods: In this cross-sectional study, the medical records of patients diagnosed with AA were retrospectively reviewed through histopathological examination from March 2021 to February 2022. The patients were categorized into simple and complicated groups. Furthermore, the association between appendicitis subcategories and various laboratory parameters, such as mean platelet volume (MPV), platelet distribution width (PDW), white blood cell count (WBC), and platelet count, was analyzed within these groups.

Results: Overall, 317 AA patients with a mean age of 30.6 ± 12.4 years were enrolled in this study. Simple appendicitis was more frequent among the patients, accounting for 62.77% of cases. Moreover, complicated appendicitis was higher in males than in females (44.37% vs. 42.03%, respectively, $P = 0.012$). The mean MPV/platelet index was elevated in the simple appendicitis group when compared to the complicated appendicitis group (10.01 ± 7.34 vs. 9.52 ± 1.06). On the other hand, the mean WBC/platelet index was higher in the complicated appendicitis group than in the simple appendicitis group (13.16 ± 4.8 vs. 11.72 ± 4.3). A notable discrepancy was found in the differentiation between complicated AA and simple appendicitis based on the WBC/platelet index ($P = 0.016$).

Conclusion: Differences in age and gender were significant between patients with simple and complicated appendicitis. The WBC value demonstrated a significant elevation in the complicated appendicitis group compared to patients with simple appendicitis, indicating its potential significance in distinguishing between complicated and simple AA.

Keywords: Acute appendicitis, Complicated appendicitis, Laboratory, Platelet indices

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Background

Acute appendicitis (AA) stands as a prevalent surgical emergency on a global scale (1). The yearly occurrence of AA is 9.4 cases per 10000 individuals, with a steady rise noted in emerging industrialized nations (2). Appendicitis manifests in simple or uncomplicated (involving the inflammation of the appendix with or without phlegmonous changes in neighboring tissues) and complicated (involving the inflammation of the appendix leading to gangrene or perforation with or without abscess development) forms (3). Perforation can be observed in 13–20% of patients presenting with AA (4). Although conventional thinking suggests the progression from simple to complicated appendicitis, recent findings cast uncertainty on the existence of distinct biological forms of appendicitis (5). Despite a decline in overall appendicitis rates, there has been no decrease in the proportion of patients presenting with

perforated appendicitis or delayed symptom onset (6).

The management of AA is firmly established, yet diagnosing the condition in an emergency context continues to pose challenges (7). Even seasoned surgeons often find the clinical diagnosis challenging, as evidenced by the significant rate of negative explorations, commonly reaching 20–30% (8). A delay in diagnosing AA is linked to an elevated risk of perforation and additional complications (9). Various efforts have been undertaken to reduce the rate of unnecessary surgeries following clinical suspicion of AA (10). Despite comprehensive clinical history, physical examinations, and standard laboratory tests, there is a lack of definitive decision-making tools for early detection of AA (11).

Traditionally, a combination of clinical evaluation along with elevated levels of leukocytes and C-reactive protein has been utilized to diagnose AA; however, their sensitivity and specificity are deemed inadequate

(12, 13). Radiological methods, including magnetic resonance imaging, are frequently utilized, with some medical facilities employing magnetic resonance imaging for a conclusive diagnosis (14). Various scoring systems have been devised to enhance diagnostic precision (15). Platelet (PLT) indices play a crucial role in responding to systemic inflammation and sepsis (16). Elevated inflammatory activity leads to increased activation, sequestration, and destruction of PLT, consequently releasing smaller PLT into the bloodstream (17). These PLT indices encompass mean platelet volume (MPV) and platelet distribution width (PDW), which are determined through a routine complete blood count test (16). Hence, the reduction of MPV and PDW parameters could serve as indicators reflecting the acute inflammation burden and the severity of diseases such as rheumatoid arthritis, acute pancreatitis, and inflammatory bowel disease (18).

Despite numerous studies addressing the prediction of complicated appendicitis, a definitive method to distinguish preoperatively between complicated appendicitis and simple appendicitis is lacking (19, 20). Thus, this study aims to explore the preoperative laboratory features of simple and complicated appendicitis in patients histopathologically diagnosed with AA.

Methods

This cross-sectional study was retrospectively performed on the medical records of the patients who were diagnosed with acute abdomen and underwent appendectomy (open and laparoscopic) between March 2021 and February 2022 in Urmia Imam Khomeini Hospital, Urmia, Iran. The study was started after the approval of the Ethics Committee of Urmia University of Medical Sciences (IR.UMSU.REC.1399.012).

The study encompassed all patients who underwent appendectomy for AA. The exclusion criteria comprised patients under 15 years of age, individuals with liver and rheumatological disorders, those with inflammatory bowel disease, liver transplantation, thrombocytopenia, and patients receiving treatment with aspirin or other medications that impact PLT function.

The study documented the demographic features of all patients and recorded laboratory parameters, namely, MPV, PDW, white blood cell (WBC) count, and PLT count values. Additionally, the surgical records and histopathology reports were reviewed, and the maximum dimensions of the resected appendix specimen were documented. The presence of polymorphonuclear cell infiltration in the muscularis propria was indicative of histological AA.

The patients were categorized into simple and complicated appendicitis groups. The complicated appendicitis group comprised patients with a perforated or gangrenous appendix or those with a periappendiceal abscess. Patients initially assigned to the simple

appendicitis group based on intraoperative assessment but later found to have histopathological evidence of perforation or gangrene were reclassified into the complicated appendicitis group. Conversely, patients lacking intraoperative and histopathological signs of perforation or gangrene, as well as those without a periappendiceal abscess, were designated as the simple appendicitis group.

Statistical Analysis

The obtained data were statistically analyzed using SPSS, version 15.0 (SPSS Inc., Chicago, IL, USA). The normality of continuous variables was evaluated by the Kolmogorov-Smirnov test. Continuous and categorical variables were expressed as means $\pm$ standard deviations (SD), as well as numbers and percentages, respectively. The Chi-square test was used for comparisons between categorical variables. An independent sample T-test and Mann-Whitney U test were utilized to compare normally and non-normally distributed parameters, respectively. Statistical significance was accepted as $P < 0.05$.

Sample Size Calculation

Overall, 325 patients were included in this study considering the following formula, the amount of MPV in patients with uncomplicated appendicitis compared to patients with complicated appendicitis, and previous data (21), taking into account a confidence interval of 90% and a test power of 90%.

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 [P_1(1-P_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

Results

The study retrieved the medical records of 325 patients who underwent appendectomy within a one-year timeframe. Seven patients were excluded from the analysis due to concurrent medical conditions. Therefore, the research was conducted on a cohort of 317 patients who underwent appendectomy specifically for AA.

The mean age of the patients was 30.6 ± 12.4 years, ranging from 15 years to 75 years. In the complicated appendicitis group, the average age was 50.5 ± 8.5 years, with a range of 41–79 years. Notably, the mean age of the patients in the complicated appendicitis group (36.5 ± 10.9 years) was higher than that of patients in the simple appendicitis group (29.5 ± 7.7 years) ($P = 0.002$).

Of the participants, 160 (50.5%) were male. The incidence of complicated appendicitis was found to be higher in male patients compared to female patients (44.37% vs. 42.03%, respectively, $P = 0.012$). Conversely, a larger proportion of patients (62.77%) presented with simple appendicitis. Among the study cohort, 79 patients (50.6%) were male. Table 1 provides detailed information regarding laboratory values for cases with simple and complicated appendicitis.

Table 1. Demographic Features of Studied Patients

	Total N = 317	Simple Appendicitis n= 199 (62.77%)	Complicated Appendicitis n = 118 (37.22%)	P value
*Mean age (years)	30.6 ± 12.4	29.5 ± 7.7	36.5 ± 10.9	0.002
**Gender				
Male	160 (50.5%)	89 (55.62%)	71 (44.37%)	0.012
Female	157 (49.5%)	91 (57.96%)	66 (42.03%)	

Note. *Independent sample T-test, **Chi-square test.

Based on the results (Table 2), the mean MPV/platelet index was greater in the simple appendicitis group compared to patients with complicated appendicitis (10.01 ± 7.34 vs. 9.52 ± 1.06). However, no statistically significant difference was observed in distinguishing between complicated AA and simple appendicitis based on the MPV/platelet index ($P = 0.473$).

The mean PDW and PLT indices exhibited similar values across both groups, with no significant variations noted in differentiating complicated AA from simple appendicitis based on PDW and PLT/platelet indices ($P = 0.078$, $P = 0.720$, respectively).

Furthermore, the mean WBC/platelet index was higher in the complicated appendicitis group in comparison to patients with simple appendicitis (13.16 ± 4.8 vs. 11.72 ± 4.3). A significant difference was found in discriminating between complicated AA and simple appendicitis based on the WBC/platelet index ($P = 0.016$).

Discussion

The diagnosis of AA poses challenges, and ongoing research is exploring alternative methods for diagnostic confirmation. Appendectomy is the primary treatment for severe appendicitis, while the management of mild cases remains uncertain, as some instances may resolve without intervention (22). Complicated AA represents a significant issue, leading to extended recovery periods, prolonged hospital stays, and increased costs, all of which can have negative impacts on clinical outcomes and treatment effectiveness (23). Distinguishing between simple and complicated cases is crucial when determining the appropriate treatment approach for appendicitis (24). The present study investigated preoperative laboratory values in adult patients with AA, demonstrating the significance of these values in differentiating between complicated and simple forms of the disease.

Our findings confirmed notable distinctions among the groups concerning demographic factors, including age and gender. Patients in the complicated appendicitis group exhibited a higher mean age compared to those in the simple appendicitis group. Confirming findings from the existing literature (23, 25), this observation can be attributed to the higher occurrence of AA with atypical symptoms in elderly individuals, making diagnosis more challenging than in younger counterparts (26). Furthermore, consistent with previous research, our study revealed a greater prevalence of complicated

Table 2. Comparison of Simple and Complicated Groups According to Laboratory Values of Studies Patients

Laboratory Values	Complicated Appendicitis	Simple Appendicitis	P value
	Mean ± SD	Mean ± SD	
MPV (fL)	9.52 ± 1.06	10.01 ± 7.34	0.473
PDW (%)	13.51 ± 1.35	13.01 ± 2.46	0.078
WBC (mcL)	13.16 ± 4.8	11.72 ± 4.3	0.016
PLT (mcL)	23.45 ± 7.2	23.18 ± 5.7	0.720

Note. MPV: Mean platelet volume; PDW: Platelet distribution width; WBC: White blood cell; PLT: Platelet; SD: Standard deviation; Independent sample T-test.

appendicitis in male patients.

AA is a prevalent condition affecting individuals of all age groups and both genders (27). Within this investigation, the mean age of patients in the complicated appendicitis cohort surpassed that of individuals in the simple appendicitis group. Typically, AA manifests in relatively youthful individuals (28). It is widely recognized that diagnosing appendicitis in older patients poses greater challenges than in their younger counterparts (29). Numerous prior studies have shown how older patients may occasionally lack not only the conventional symptoms of appendicitis but also exhibit atypical laboratory data abnormalities (30, 7). Consequently, a higher proportion of elderly patients may present with gangrenous appendicitis. Consistent with the existing literature (31), our study also identified a higher prevalence of complicated appendicitis among male patients.

Some studies (32, 33) have addressed the correlation between complete blood count parameters and underlying inflammatory or infectious conditions. It is unsurprising that the levels of known acute inflammatory cells significantly differ in distinguishing between complicated and non-complicated appendicitis, aligning with the results of previous research (34). MPV, utilized as an indicator of PLT activation, is derived from dividing the plateletcrit by the PLT (35). Elevated levels of immature PLT contribute to an increased MPV measurement, establishing MPV as a dependable marker of PLT functionality (36).

The literature presents conflicting views on the fluctuations of MPV in cases of AA. While some studies indicate a decrease in MPV during AA (37), others suggest an increase (38). Boshnak et al (35), investigating

the alterations in mean MPV, PDW, and RDW in AA diagnoses, found that elevated PDW levels, in conjunction with a high WBC and neutrophil count, could potentially serve as a diagnostic indicator for AA. However, MPV and RDW levels were not deemed effective diagnostic markers in their research. Recent studies have underscored the role of PLT in inflammation, establishing a link between PLT activation and the pathophysiology of inflammatory conditions, which contradicts the outcomes of their study.

Furthermore, some literature reports indicated no significant association between MPV and AA (12). In our study, no notable disparity was observed in MPV values between the simple and complicated AA groups. It can be speculated that this lack of differentiation could be attributed to the influence of other inflammatory factors on MPV, factors that were not accounted for in our analysis.

Aydogan et al (39) reported a noteworthy elevation in PDW levels in cases of perforated AA. Contrastingly, Fan et al (40) found an increase in PDW levels among patients with acute gangrenous appendicitis when compared to a healthy control group. However, some studies demonstrated no significant disparity in PDW values in cases of complicated AA (16). Dinç et al (27) and Ceylan et al (21) noted no discernible distinction in PDW levels between individuals with and without AA. Similarly, in our investigation, no significant variance was observed in PDW values between the groups with simple and complicated AA.

The initial and most common diagnostic indicator for AA is an elevation in the WBC count and ratio of neutrophils to lymphocytes, as noted by researchers (41). In our study, a significant difference was detected in distinguishing between complicated and uncomplicated AA based on this WBC value. Specifically, the results revealed higher WBC levels in cases of complicated AA compared to uncomplicated ones. Studies have shown the positive predictive value of WBC results in differentiating between uninflamed, uncomplicated, and complicated appendicitis (42). Withers et al reported a direct relationship between escalating WBC levels and the likelihood of complicated appendicitis (43). The likelihood of a patient having appendicitis while exhibiting normal values of both WBC and C-reactive protein is exceedingly low (43). A WBC count of 10000 cells/mm³ is highly indicative of AA, with levels likely to be higher in cases of complicated appendicitis (42). Moreover, a WBC count equal to or above 17000 cells/mm³ is associated with complications of AA, such as perforation and gangrene (7).

Limitations of the Study

Several limitations were identified in our study. Firstly, it is important to acknowledge that our study was conducted

at a single center, which restricts the generalizability of the findings to the broader population. Furthermore, assessments were based solely on data from a single laboratory, consequently precluding any definitive statements regarding alterations observed post-follow-up or in response to treatment.

Conclusion

In this study, notable distinctions were observed in the age and gender profiles of patients with simple versus complicated appendicitis. Additionally, the WBC count demonstrated a significant elevation in the complicated appendicitis cohort compared to those with simple appendicitis, indicating a potentially key indicator in distinguishing between complex and straightforward cases of AA.

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Authors' Contribution

Conceptualization, Investigation, Formal Analysis, Original Draft Writing, Reviewing, and Editing: N. K.

Conceptualization, Supervision, and Project Administration: M. R.
Investigation and Original Draft Writing: K. M.

Conflict of Interests

There is no conflict of interests among the authors.

Ethical Approval

The study was approved by the Ethics Committee of Urmia University of Medical Sciences (ethical code IR.UMSU.REC.1399.012).

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