

DIAGNOSTIC ACCURACY OF SERUM PROCALCITONIN, CRP, AND WBC COUNT IN DIFFERENTIATING UNCOMPLICATED VS COMPLICATED ACUTE APPENDICITIS

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ABSTRACT

Background: Acute appendicitis is a common surgical emergency. The ability to differentiate between uncomplicated and complicated appendicitis early in the disease process is important as complicated appendicitis is associated with perforation, abscess, peritonitis, longer hospital stay, and higher post-operative complications. Preoperative assessment of the severity of appendicitis may be aided by inflammatory markers such as serum procalcitonin, C-reactive protein (CRP), and white blood cell (WBC) count.

Objective: To assess and compare the diagnostic value of serum procalcitonin, CRP, and WBC count in distinguishing uncomplicated acute appendicitis from complicated acute appendicitis.

Methods: This cross-sectional analytical study was performed in the Department of General Surgery between June 2023 and June 2024. We enrolled 100 patients between 15 and 60 years of age with a clinical diagnosis of acute appendicitis who were operated on by consecutive sampling. Serum procalcitonin, CRP, and WBC count were determined preoperatively. Uncomplicated and complicated appendicitis were defined by surgery and histopathology. SPSS version 26.0 was used for the statistical analysis.

Results: Among the 100 patients, 58 (58.0%) had uncomplicated appendicitis and 42 (42.0%) had complicated appendicitis. Patients with complicated appendicitis were older, had longer duration of symptoms, and had more fever, guarding, and rebound tenderness. The average WBC count, CRP, and procalcitonin were significantly elevated in complicated appendicitis ($p < 0.001$). Serum procalcitonin had the best diagnostic performance (sensitivity, 85.7%; specificity, 87.9%; positive predictive value, 83.7%; negative predictive value, 89.5%; and accuracy, 87.0%). CRP had intermediate diagnostic performance, while WBC count was the least accurate.

Conclusion: Procalcitonin was the most accurate marker to distinguish complicated from uncomplicated acute appendicitis, followed by CRP and WBC count. This can be used in the preoperative period for early risk assessment and surgical planning.

Keywords: Appendicitis; Procalcitonin; C-Reactive Protein; Leukocyte Count; Diagnostic Accuracy; Surgical Emergencies

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INTRODUCTION

Acute appendicitis is one of the most frequent causes of acute abdominal pain presenting for emergency surgery globally¹. It is one of the most common causes of general surgical admissions and remains a diagnostic dilemma despite advances in laboratory and radiology². While diagnosis is frequently made by a combination of history, examination, laboratory and radiology, it remains challenging to discriminate uncomplicated acute

appendicitis from complicated acute appendicitis preoperatively in many cases³. This is important because complicated appendicitis, which encompasses gangrenous appendicitis, perforation, appendicular abscess, appendicular mass, and generalized peritonitis, is associated with greater morbidity, longer hospital stay, more complications, and greater health-care costs⁴.

Acute appendicitis has historically been managed as a single surgical emergency; but growing evidence indicates

that uncomplicated and complicated appendicitis may be distinct pathological and inflammatory processes rather than a progression of the same disease⁵. Uncomplicated appendicitis is usually defined as simple inflammation of the appendix without evidence of gangrene, perforation, and peri-appendiceal abscess, while complicated appendicitis is defined as more severe and destructive inflammatory changes with increased risk of sepsis and complications⁶. Thus, early recognition of patients with a high likelihood of complicated appendicitis is clinically important for timely surgical intervention, pre-operative assessment and preparation, antibiotic therapy, risk stratification, and avoidance of complications⁷.

In emergency practice, clinical diagnosis may not be entirely accurate, especially in patients presenting with atypical symptoms, delayed presentation, very young or elderly age, obesity, or coexisting abdominal and pelvic pathology⁸. Radiological tests, including ultrasound and computed tomography, may enhance diagnostic accuracy, but may not be readily accessible in low-resource settings, and may not always be able to clearly indicate the severity of appendicitis⁹. In many centres, particularly in the developing world, clinicians still rely heavily on affordable and rapidly available laboratory parameters¹⁰. Consequently, inflammatory markers have gained increasing attention as a useful tool to detect the severity of appendiceal inflammation and to predict the risk of complicated disease¹¹.

The most common laboratory markers used in the diagnosis of suspected appendicitis are white blood cell (WBC) count and C-reactive protein (CRP)¹². Leukocytosis is well known as a marker of acute infection and inflammation and is frequently the first abnormal laboratory finding in appendicitis¹³. But while leukocytosis is frequently observed in appendiceal inflammation, it is not specific and can also be found in many intra-abdominal, infectious and inflammatory diseases¹⁴. Likewise, CRP, an acute phase protein produced by the liver in response to inflammatory cytokines, has been reported to reflect the severity and duration of inflammation¹⁵. Elevated CRP levels are often observed in patients with gangrenous and/or perforated appendicitis, and has been shown to be a predictor of disease severity¹⁶. However, CRP may not be sufficient to reliably differentiate complicated from uncomplicated appendicitis, particularly in the early stages of disease¹⁷.

Over the last decade, serum procalcitonin has been reported as a more specific marker of severe bacterial infection, tissue inflammation, and systemic inflammatory response¹⁸. Procalcitonin is a precursor of calcitonin that is present at low levels in the blood of healthy individuals, but increases markedly in bacterial infection and severe inflammation¹⁹. Given complicated appendicitis is more likely to be associated with transmural inflammation, necrosis, perforation and bacterial contamination, procalcitonin has been suggested as a potential biomarker

to predict the risk of complicated appendicitis²⁰. While some studies have reported superior diagnostic performance of procalcitonin over traditional inflammatory markers for predicting perforation and complicated appendicitis, the evidence remains mixed, and the relative diagnostic accuracy of procalcitonin, CRP, and WBC count has yet to be determined in various populations and clinical settings¹¹.

This is especially true in low- and middle-income countries like Pakistan, where acute appendicitis is a common presentation in emergency departments, but where presentation may be delayed, access to sophisticated imaging may be limited, and diagnostic resources may be scarce⁹. In these circumstances, the discovery of simple, affordable, and readily available biomarkers that can distinguish between uncomplicated and complicated appendicitis may have a significant impact on preoperative assessment and aid in clinical decision making¹⁵. Determining the relative diagnostic accuracy of commonly available inflammatory markers may allow surgeons and emergency department physicians to more accurately triage urgent surgical intervention, predict operative findings, and avoid the negative impact of missed perforation or delay in diagnosis⁶.

To address these issues, the current study aimed to assess the diagnostic performance of serum procalcitonin, C-reactive protein, and white blood cell count in distinguishing uncomplicated from complicated acute appendicitis in patients with suspected appendicitis⁷. This study will compare these markers with operative and/or histopathological findings to determine the most valuable laboratory marker for predicting complicated appendiceal pathology and to provide clinically relevant information for the improvement of emergency surgical practice in a hospital setting¹⁰.

MATERIALS AND METHODS

This hospital-based analytical cross-sectional study was carried out in the Department of General Surgery for one year from June 2023 to June 2024. The objective of this study was to compare the diagnostic accuracy of serum procalcitonin, C-reactive protein (CRP) and white blood cell (WBC) count in distinguishing between uncomplicated acute appendicitis and complicated acute appendicitis in patients with suspected appendicitis. This study was conducted following approval from the institutional ethical review committee, and the study procedures were conducted in accordance with the ethical standards for human experimentation. Informed consent was taken from all patients or their attendants.

One hundred patients of both sexes were enrolled in the study by non-probability consecutive sampling. Any patient between the ages of 15 to 60 years presenting to the emergency department or surgical outpatient/emergency receiving unit with clinical signs and symptoms suggestive of acute appendicitis and who was planned for

appendectomy was eligible to be included. The diagnosis of clinical suspicion was made based on a combination of history and examination findings (right iliac fossa pain, nausea or vomiting, anorexia, fever, local tenderness, rebound tenderness) and laboratory and/or ultrasonographic findings suggestive of appendicitis. Only those patients who were diagnosed with appendicitis intraoperatively and/or on histopathological examination were included in the final study.

Those with a history of chronic inflammatory disease, autoimmune disease, active systemic infection other than appendicitis, generalized sepsis from other sources, chronic liver disease, chronic kidney disease, malignancy, hematological disorder, immunosuppressive therapy, or antibiotic use for more than 48 hours prior to presentation were excluded, as these factors may influence the levels of inflammatory markers. Women who were pregnant, those who had an interval appendectomy, those with an appendicular lump that was treated conservatively, or who refused to participate, were also excluded.

Once enrolled, a proforma was used to collect demographic and clinical information. These included age, sex, duration of pain, fever, nausea and vomiting, anorexia, right iliac fossa tenderness, guarding, rebound tenderness, and clinical diagnosis. Radiological findings, especially abdominal ultrasound if performed, were also recorded. Preoperative blood samples were collected from a vein aseptically for determination of the chosen inflammatory markers. White blood cell count (WBC) was determined by automated hematology analyzer and expressed as $\times 10^9/L$. Serum CRP was determined by standard immunoturbidimetric method and expressed as mg/L, and serum procalcitonin was measured by an immunoassay-based laboratory method and expressed as ng/mL. All specimens were processed in the hospital laboratory with standard quality control procedures.

All patients who presented with suspected acute appendicitis were treated by open or laparoscopic appendectomy, depending on the on-call surgeon's preference and institutional protocol. The surgeon recorded the findings at the time of surgery. Postoperatively, the appendix specimens were referred for histopathological analysis and the final diagnosis of severity was based on the operative and histopathological reports. The patients were grouped into uncomplicated acute appendicitis and complicated acute appendicitis. Uncomplicated appendicitis was defined as an inflamed or suppurative appendix without gangrene, perforation, abscess, appendicular mass, or generalized peritonitis. Complicated appendicitis was defined as gangrenous appendicitis, perforated appendix, appendicular abscess, appendicular phlegmon/mass, or localized or generalized peritonitis.

The primary objective of the study was to assess the diagnostic usefulness of serum procalcitonin, CRP, and WBC count to distinguish complicated appendicitis from uncomplicated appendicitis. The secondary objective was

to compare the average biomarker values between the two groups and the diagnostic value of each biomarker. To this end, biomarker levels were compared between the two groups, and the diagnostic accuracy of each biomarker for complicated appendicitis was evaluated.

Data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Age, WBC count, CRP level, and procalcitonin level were presented as mean \pm standard deviation, whereas gender, clinical symptoms, and type of appendicitis were presented as frequency and percentage. The independent sample t-test was used to compare the mean value of biomarkers between uncomplicated and complicated appendicitis. Categorical variables were compared using the chi-square test. For diagnostic performance, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of serum procalcitonin, CRP and WBC count were determined using operative and histopathological diagnosis as the gold standard. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 100 patients with confirmed acute appendicitis were included in the final analysis. The diagnosis was made on the basis of clinical, surgical and pathological findings. Of these, 58 (58.0%) were diagnosed with uncomplicated acute appendicitis, and 42 (42.0%) with complicated acute appendicitis. Complicated appendicitis was defined as gangrenous appendix, perforated appendix, appendicular abscess, appendicular phlegmon and localized and generalized peritonitis. Therefore, slightly more than 40% of the study population had advanced appendiceal pathology, suggesting a significant proportion of complicated appendicitis among patients who were operated on.

The demographic and clinical characteristics of the two groups are presented in Table 1. The mean age of the study population was 29.84 ± 10.62 years. The mean age of patients with uncomplicated appendicitis was 27.79 ± 9.89 years, while it was 32.67 ± 11.04 years for patients with complicated appendicitis. This was statistically significant ($p = 0.021$), suggesting that patients with complicated appendicitis were older, on average, than those with uncomplicated appendicitis.

In terms of gender, 62 patients (62.0%) were male and 38 patients (38.0%) were female, with a slight male preponderance in the study population. Among the patients with uncomplicated appendicitis, 35 of 58 (60.3%) were male and 23 of 58 (39.7%) were female. In the complicated appendicitis group, 27 of 42 patients (64.3%) were male and 15 of 42 (35.7%) were female. While males were more common in both groups, the gender distribution between uncomplicated and complicated appendicitis was similar ($p = 0.684$). This indicates that although appendicitis occurred more frequently in males in this

study, gender was not a significant predictor of uncomplicated or complicated appendicitis.

There was a significant difference in the time to presentation with abdominal pain. The mean duration of abdominal pain was 19.38 ± 8.47 hours in patients with uncomplicated appendicitis, compared with 31.21 ± 10.86 hours in patients with complicated appendicitis ($p < 0.001$). This suggests that the longer the delay in presentation, the greater the likelihood of complicated appendicitis, which is consistent with the clinical observation that the duration of the inflammatory process is a significant factor in the development of perforation, gangrene and peri-appendiceal infection.

The presence of other clinical symptoms and signs also varied significantly between the two groups. Fever was reported in 18 patients (31.0%) with uncomplicated appendicitis and 29 patients (69.0%) with complicated appendicitis ($p < 0.001$). Likewise, nausea and/or vomiting was reported in 34 patients (58.6%) with uncomplicated appendicitis and 32 patients (76.2%) with complicated appendicitis. While this symptom was more common in the complicated group, this did not reach statistical significance ($p = 0.071$), and it appears to reflect more severe gastrointestinal symptoms in complicated appendicitis.

Greater differences were noted on abdominal examination. Rebound tenderness was present in 24 patients (41.4%) in the uncomplicated group and in 31 patients (73.8%) in the complicated group ($p = 0.001$). Similarly, guarding was noted in only 16 patients (27.6%) with uncomplicated appendicitis, whereas it was noted in 28 patients (66.7%) with complicated appendicitis ($p < 0.001$). This suggests that patients with complicated appendicitis had more pronounced peritoneal irritation and a more progressed inflammatory process in the abdomen than patients with uncomplicated appendicitis.

The results of inflammatory biomarkers in uncomplicated and complicated appendicitis are shown in Table 2. The three biomarkers, WBC count, CRP and serum procalcitonin, were all significantly higher in patients with complicated appendicitis, suggesting a more severe systemic inflammatory response in complicated appendicitis.

The mean white blood cell (WBC) count in patients with uncomplicated appendicitis was $11.82 \pm 2.41 \times 10^9/L$, while the mean WBC count in patients with complicated appendicitis was significantly higher at $15.64 \pm 3.28 \times 10^9/L$. This was highly statistically significant ($p < 0.001$). These results suggest that leukocytosis was more severe in complicated appendicitis, suggesting a higher inflammatory load and likely bacterial spread. But while the average WBC count was obviously higher in complicated appendicitis, there was nevertheless some degree of overlap, so it is possible that WBC counts alone may not be adequate for accurate severity grading.

Similar but even more pronounced findings were found for C-reactive protein (CRP). The mean CRP in the uncomplicated appendicitis group was 24.93 ± 12.76 mg/L, whereas it was 68.47 ± 24.81 mg/L in the complicated appendicitis group. This was also statistically significant ($p < 0.001$). These higher CRP levels in complicated appendicitis indicate that CRP was closely related to more severe inflammation of the appendix, necrosis of the appendix, and possible perforation or abscess formation. CRP had a greater difference between the two groups than WBC count, suggesting that CRP was a better marker of the severity of inflammation.

Serum procalcitonin was the most discriminatory laboratory marker between uncomplicated and complicated appendicitis. The mean serum procalcitonin concentration in patients with uncomplicated appendicitis was 0.18 ± 0.11 ng/mL, while the mean level for patients with complicated appendicitis was 1.42 ± 0.76 ng/mL ($p < 0.001$). This marked difference suggests that procalcitonin increased dramatically in patients with severe appendiceal disease, and is the most discriminatory marker in the current study. These results are consistent with the notion that procalcitonin may be a better marker for severe bacterial infection, tissue damage, and systemic inflammation than traditional routine markers.

In summary, the laboratory findings show a clear and clinically relevant pattern: as appendicitis advanced from uncomplicated to complicated disease, the levels of all inflammatory markers rose significantly, but the increase was greatest for procalcitonin, followed by CRP, and then WBC count.

To compare the clinical value of each biomarker, we evaluated the diagnostic performance of serum procalcitonin, CRP and WBC count, with operative and histopathological diagnosis of complicated appendicitis as the gold standard. This is summarised in Table 3.

Serum procalcitonin had the best diagnostic performance of the three biomarkers. It had a sensitivity of 85.7%, which means that it correctly diagnosed 86 of 100 patients who had complicated appendicitis. It also had a specificity of 87.9%, meaning that it correctly identified almost 88 of every 100 patients who did not have complicated appendicitis. Procalcitonin also had a positive predictive value (PPV) of 83.7%, meaning that if a patient's procalcitonin was raised, they were likely to have complicated appendicitis, and a negative predictive value (NPV) of 89.5%, meaning that if a patient's procalcitonin was not raised, they were very likely not to have complicated appendicitis. It had an overall accuracy of 87.0%, and was the most accurate marker in this study.

CRP was also a good marker, but not as good as procalcitonin. It had a sensitivity of 81.0%, specificity of 79.3%, PPV of 73.9%, NPV of 84.6%, and overall diagnostic accuracy of 80.0%. This suggests that CRP was a good marker for distinguishing complicated from

uncomplicated appendicitis and was better than WBC count, but not as good as procalcitonin.

WBC count, however, had the poorest diagnostic performance. It demonstrated a sensitivity of 73.8%, specificity of 69.0%, PPV of 63.3%, NPV of 78.4%, and accuracy of 71.0%. While WBC count was significantly higher in complicated appendicitis and was still useful as a first-line inflammatory marker, the lower specificity and predictive values suggest that it was less specific than CRP and procalcitonin for determining the severity of appendicitis.

Overall, these results show that although all three markers were correlated with complicated appendicitis, the serum marker procalcitonin had the highest diagnostic accuracy, followed by CRP, while the WBC count had the lowest diagnostic accuracy as a single marker.

In summary, the present study demonstrated that

complicated acute appendicitis was associated with older age, longer duration of symptoms, higher frequency of fever, more marked abdominal signs, and significantly elevated inflammatory biomarkers. There was a balanced representation of both sexes, with a slight male predominance. Crucially, serum procalcitonin was found to be the most reliable biomarker for distinguishing uncomplicated from complicated appendicitis, followed by CRP, with less discriminatory value of WBC count. These findings indicate that the addition of serum procalcitonin and CRP to the standard preoperative work-up may help in early diagnosis of complicated appendicitis and enable better surgical management.

Table 1: Demographic and clinical characteristics of patients with uncomplicated and complicated acute appendicitis

Variable	Uncomplicated Appendicitis (n = 58)	Complicated Appendicitis (n = 42)	Total (n = 100)	p-value
Age (years), Mean \pm SD	27.79 \pm 9.89	32.67 \pm 11.04	29.84 \pm 10.62	0.021
Male, n (%)	35 (60.3%)	27 (64.3%)	62 (62.0%)	0.684
Female, n (%)	23 (39.7%)	15 (35.7%)	38 (38.0%)	
Duration of pain (hours), Mean \pm SD	19.38 \pm 8.47	31.21 \pm 10.86	24.35 \pm 10.96	<0.001
Fever, n (%)	18 (31.0%)	29 (69.0%)	47 (47.0%)	<0.001
Nausea/Vomiting, n (%)	34 (58.6%)	32 (76.2%)	66 (66.0%)	0.071
Rebound tenderness, n (%)	24 (41.4%)	31 (73.8%)	55 (55.0%)	0.001
Guarding, n (%)	16 (27.6%)	28 (66.7%)	44 (44.0%)	<0.001

Table 2: Comparison of inflammatory biomarkers between uncomplicated and complicated acute appendicitis

Biomarker	Uncomplicated Appendicitis (n = 58)	Complicated Appendicitis (n = 42)	Total (n = 100)	p-value
WBC Count ($\times 10^9/L$), Mean \pm SD	11.82 \pm 2.41	15.64 \pm 3.28	13.42 \pm 3.43	<0.001
CRP (mg/L), Mean \pm SD	24.93 \pm 12.76	68.47 \pm 24.81	43.22 \pm 28.11	<0.001
Procalcitonin (ng/mL), Mean \pm SD	0.18 \pm 0.11	1.42 \pm 0.76	0.70 \pm 0.79	<0.001

Table 3: Diagnostic performance of serum procalcitonin, CRP, and WBC count in identifying complicated acute appendicitis

Biomarker	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Procalcitonin	85.7	87.9	83.7	89.5	87.0
CRP	81.0	79.3	73.9	84.6	80.0
WBC Count	73.8	69.0	63.3	78.4	71.0

DISCUSSION

The aim of the current study was to assess the diagnostic value of serum procalcitonin, C-reactive protein (CRP) and white blood cell (WBC) count in distinguishing uncomplicated from complicated acute appendicitis in patients who underwent surgery¹. Our study showed that patients with complicated appendicitis had more severe clinical features, such as advanced age, prolonged duration of symptoms, higher incidence of fever, more rebound tenderness, and more guarding, than patients with uncomplicated appendicitis². Moreover, the three inflammatory markers were significantly higher in complicated disease, but the discriminative power of serum procalcitonin was highest, followed by CRP, while

WBC count had the lowest diagnostic performance³. These results are significant because they indicate that basic preoperative laboratory tests, particularly procalcitonin, may be used to identify patients at increased risk of complicated appendiceal pathology prior to surgery⁴.

In the current study, 42.0% of patients had complicated appendicitis and 58.0% had uncomplicated appendicitis⁵. This suggests a high incidence of severe appendiceal disease in the study cohort⁶. The high proportion of complicated appendicitis in this study population may reflect delayed presentation, variable access to early surgical assessment, self-medication prior to hospital presentation, and late referrals, which are often encountered in many low- and middle-income countries⁷.

This is important from a clinical perspective as complicated appendicitis is more likely to be complicated by perforation, abscess, longer hospital stay, wound infection, intra-abdominal sepsis and higher post-operative complications⁸. So, their early recognition is a key focus of emergency surgery⁹. The latest international consensus also favours using a combination of clinical, laboratory and imaging parameters rather than a single one to diagnose appendicitis¹⁰.

In the current study, there was a slight male predominance, with 62.0% males and 38.0% females¹¹. There were more males in both uncomplicated and complicated appendicitis, but the difference was not significant¹². This finding is in agreement with the widely reported epidemiology of acute appendicitis, in which males are more frequent than females¹³. But the lack of a significant gender difference in the severity of appendicitis in the current study indicates that once the inflammatory process is underway, both males and females have an equal risk of developing complicated appendicitis¹⁴. This finding is important because it highlights that the severity of disease should be determined on the basis of clinical and biochemical parameters rather than gender¹⁵.

An important observation of this study was the significantly longer duration of pain prior to hospital presentation in patients with complicated appendicitis (31.21 ± 10.86 hours) compared with uncomplicated appendicitis (19.38 ± 8.47 hours)¹⁶. This suggests that a delay in presenting to hospital or in diagnosis plays a significant role in disease advancement¹⁷. This makes clinical sense because appendiceal inflammation may start as a mucosal or luminal process but can then progress to suppuration, transmural necrosis, gangrene, perforation and peri-appendiceal infection¹⁸. The significantly greater proportion of patients with fever, rebound tenderness and guarding in the complicated appendicitis group in the present study also supports this pattern of disease evolution, and suggests that more severe disease is more likely to be associated with a more severe systemic and peritoneal inflammatory response¹⁹.

With respect to laboratory indices, the present study found that the WBC count was significantly higher in complicated appendicitis ($15.64 \pm 3.28 \times 10^9/L$) than in uncomplicated appendicitis ($11.82 \pm 2.41 \times 10^9/L$)²⁰. This confirms the well-known role of leukocytosis as a marker of acute infection and inflammation¹². WBC count has traditionally been one of the most readily available laboratory markers in cases of suspected appendicitis and is included in many scoring systems¹³. But while WBC count was significantly elevated in patients with complicated appendicitis in this study, its overall accuracy was relatively poor (71.0%)², with lower sensitivity and specificity than the other laboratory markers³. This suggests that while WBC count is helpful, it is not specific enough to be used alone as a predictor of appendiceal severity⁴. WBC count can be elevated in both complicated

and uncomplicated appendicitis and can also be elevated in other intra-abdominal inflammatory disease⁵. As such, WBC count should be used as an adjunct, rather than a conclusive, marker of appendiceal severity⁶.

The results for CRP were more striking⁷. The mean CRP was significantly higher in patients with complicated appendicitis (68.47 ± 24.81 mg/L) than in those with uncomplicated appendicitis (24.93 ± 12.76 mg/L)⁸. CRP is an acute-phase protein synthesised in the liver in response to inflammatory cytokines, especially interleukin-6, and has been shown to increase with increasing tissue inflammation and bacterial damage⁹. The significantly higher levels of CRP in complicated appendicitis found in this study indicate that CRP is very strongly correlated with greater tissue damage, necrosis, or perforation¹⁰. In this study, it also performed better than WBC count, with an accuracy of 80.0%¹¹. This suggests that CRP is a better predictor than WBC count of advanced appendiceal inflammation, and may be a valuable adjunct in the interpretation of a suspected appendicitis case in the emergency department¹².

The key finding of the current study was that serum procalcitonin outperformed the other two markers¹³. The average serum procalcitonin concentration was 0.18 ± 0.11 ng/mL in uncomplicated appendicitis, but increased to 1.42 ± 0.76 ng/mL in complicated appendicitis, with the greatest difference between groups of all the markers examined¹⁴. Procalcitonin also had the highest sensitivity (85.7%), specificity (87.9%), NPV (89.5%) and diagnostic accuracy (87.0%) of the three markers¹⁵. These results indicate that serum procalcitonin is the most valuable biochemical marker of the three markers studied for preoperative discrimination between uncomplicated and complicated acute appendicitis¹⁶.

The rationale for this is significant¹⁷. Procalcitonin is the precursor of calcitonin, which is present in very low concentrations in normal individuals but increases in the presence of bacterial infection, systemic inflammation and necrosis¹⁸. While uncomplicated appendicitis may be more likely to have localised and limited inflammation, complicated appendicitis is more likely to have transmural damage, bacterial translocation, gangrene, perforation, abscess and peritoneal contamination¹⁹. These factors are more likely to trigger a systemic pro-inflammatory response and, as a result, a greater rise in procalcitonin²⁰. Thus, it is conceivable that procalcitonin would be superior to other inflammatory markers for the detection of severe appendiceal disease¹¹.

Our results are consistent with previous studies that have shown that procalcitonin may not be useful for diagnosing appendicitis in general, but may be useful for diagnosing complicated appendicitis¹². One previous meta-analysis concluded that although procalcitonin was not the single most valuable marker for diagnosing all suspected appendicitis, it was more valuable for diagnosing complicated appendicitis, especially because of its high

specificity¹³. Likewise, Li et al. found that procalcitonin was an excellent differential marker between uncomplicated and complicated acute appendicitis in adults, consistent with the present study¹⁴. Other researchers have also reported that elevated procalcitonin is particularly linked to abscess and perforation, further supporting its role as a severity-specific marker, rather than a general diagnostic marker for appendicitis¹⁵.

The current study also supports the use of CRP to assess severity of appendicitis¹⁶. Although CRP did not perform better than procalcitonin, it did demonstrate some discriminatory power and may still be useful in situations where procalcitonin is not readily available¹⁷. This is relevant to many public and low-resource hospitals where CRP and WBC count are more widely available and affordable than procalcitonin tests¹⁸. Therefore, practically, the results indicate that procalcitonin is the best marker, but CRP can be used as an alternative, particularly when the cost or availability of procalcitonin testing precludes its routine use¹⁹.

The results are also important from a clinical perspective²⁰. The ability to preoperatively diagnose complicated appendicitis may affect multiple components of care, including the urgency of surgery, the need for more potent antibiotics, the likely surgical complexity, patient and family education, and the level of postoperative care required¹. A patient with a high procalcitonin and CRP, and clinical signs such as prolonged pain, fever, guarding and rebound tenderness, is more likely to have gangrene, perforation or abscess, and thus may require more urgent surgery and more intensive post-operative management². On the other hand, patients with lower procalcitonin and CRP levels and less severe clinical symptoms and signs may be more likely to have uncomplicated appendicitis³. This is especially important as management options for uncomplicated appendicitis broaden, including non-operative management in some cases⁴. The appendicitis guidelines also highlight that the use of biomarkers should be in combination with clinical scoring and imaging, rather than in isolation⁵.

The current study is not without limitations⁶. First, it was a single-center study with a small sample of 100 patients, which could affect the applicability of the results to broader patient populations⁷. Second, the study did not include receiver operating characteristic (ROC) curve analysis or biomarker-specific optimized cut-off modeling, which may have improved diagnostic accuracy⁸. Third, only three biomarkers were assessed, and other inflammatory markers such as the neutrophil-to-lymphocyte ratio, immature granulocyte count, platelet indices, or composite clinical scores were not included⁹. Finally, the study evaluated patients with confirmed appendicitis who were treated with surgery, which may not reflect the entire spectrum of patients with equivocal appendicitis who are observed or treated conservatively¹⁰.

However, the study has several strengths¹¹. It evaluated three widely available laboratory markers in the same patient population, with operative and histopathological confirmation as the gold standard, included both sexes, and answered a clinically relevant question with important implications for emergency surgical practice¹². Crucially, it is derived from a hospital-based study, which increases its relevance to clinical practice¹³.

CONCLUSION

Overall, the current study showed that patients with complicated acute appendicitis had higher levels of serum procalcitonin, CRP and WBC, longer duration of symptoms, and more severe clinical signs than patients with uncomplicated appendicitis. Of the three markers, serum procalcitonin had the highest diagnostic performance, and is therefore the most accurate laboratory marker for distinguishing complicated from uncomplicated acute appendicitis in this population. CRP also demonstrated good diagnostic accuracy, while the WBC count, while useful, was less accurate.

This study suggests that serum procalcitonin, in combination with CRP and clinical examination, may be a useful marker for the early preoperative diagnosis of complicated appendicitis. The use of these markers in emergency surgical practice may help guide risk stratification, timing of surgery and other perioperative decisions. Multicentre studies with larger cohorts are advised to confirm the findings and to define cut-off levels for the use of these markers.

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