

Acute appendicitis; clinical features, haematological parameters, biochemical markers, histopathological diagnoses and associations

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ABSTRACT

Introduction: Acute appendicitis is a global problem requiring timely surgical intervention to prevent serious complications. Correct diagnosis of appendicitis remains a challenge as clinical features, and laboratory findings vary in majority of patients. The aim of the study was to determine the association of clinical features, biochemical markers and haematological parameters with histopathological diagnosis in patients with acute appendicitis in National Hospital Galle.

Methods: This is a descriptive, cross-sectional study carried out among 380 patients selected using convenient sampling method. The data were obtained by the retrospective review of medical records of the patients who were diagnosed with acute appendicitis and underwent appendicectomy in all five surgical units in National Hospital Galle from June 2022 to June 2024. Association of clinical features, biochemical markers and haematological parameters with histopathological diagnoses were assessed using standard statistical tests.

Results: Among the 380 patients, 95% (n=361) had histopathologically confirmed acute appendicitis. Significant associations were found between histopathological diagnosis and typical abdominal pain ($p=0.042$), anorexia ($p=0.032$), nausea ($p=0.007$), rebound tenderness ($p=0.004$), elevated CRP ($p=0.039$), WBC ($p=0.045$), and neutrophil counts ($p=0.049$). CRP, WBC, and neutrophil count had very high positive predictive values for acute appendicitis; 97.63%, 96.87% and 95.63% respectively. There were significant differences in mean values of CRP, WBC and neutrophil counts between uncomplicated and complicated cases of acute appendicitis; ($p=0.001$), ($p=0.003$) and ($p=0.002$) respectively.

Conclusions and Recommendations: Certain clinical features, elevated CRP, WBC, and neutrophil counts were significantly associated with acute appendicitis. Integrating these laboratory markers with clinical symptoms enhances diagnostic accuracy, helping to identify high-risk cases. Elevated CRP level, WBC and neutrophil counts were helpful to distinguish complicated cases from uncomplicated. This approach can reduce misdiagnosis and unnecessary surgical procedures, improving patient outcomes and clinical decision-making in acute appendicitis management.

Keywords: Acute appendicitis. Association, Clinical features, Biochemical markers, Haematological parameters, Histopathological diagnosis.

Introduction

Acute appendicitis is the inflammation of the appendix. It is one of the commonest causes of acute abdominal pain among young adults requiring emergency surgery (1). Appendicitis occurs due to obstruction of the appendicular lumen resulting in local infection. As the appendix is blind ended it is unable to drain and this led to swelling of the appendix. It causes local ischemia, necrosis, and bacterial translocation and ultimately perforation and subsequent generalized peritonitis or abscess formation.

The diagnosis is often done in combination of clinical, biochemical, histopathological and radiological guidance which help in the possible subsequent management (2). Patients with acute appendicitis typically present with a para-umbilical colicky pain which eventually localizes to the right iliac fossa and becomes constant. Examination will reveal tenderness, guarding and rigidity at the McBurney's point. Rovsing's sign, Cope's obturator sign and Iliopsoas sign may also be positive (3). Delay in diagnosis could result in increased morbidity and mortality and complications like perforation, peritonitis or sepsis may complicate it with septic shock (4).

The diagnosis is supported by haematological parameters including full blood count (FBC) and biochemical markers such as C reactive protein (CRP) level. The gold standard for diagnosing acute appendicitis is histopathological examination of the surgically removed appendix (5).

The acute appendicitis patients are initially treated conservatively using multi-modal analgesia, fluid resuscitation and intravenous antibiotics. Appendectomy is the last resort of treatment, and routine histopathological assessment is done to correlate the findings with the clinical diagnosis.

According to literature, correct diagnosis of appendicitis remains a challenge as clinical signs or positive laboratory parameters can be absent in almost half of the patients (6). A delay or misdiagnosis of appendicitis can result in severe complications such as perforation, abscess formation, sepsis and intra-abdominal adhesions.

In Sri Lankan literature, this field is barely touched in the hospital setting. Therefore, the aim of this study was to analyse the association of clinical

features, biochemical markers and haematological parameters with histopathological diagnosis in a selected group of patients with acute appendicitis in National Hospital Galle.

Methods

This study was a descriptive cross-sectional study, carried out in National Hospital Galle. The study population consisted of patients aged above 18 years, who were diagnosed with acute appendicitis and underwent appendectomy in National Hospital Galle from June 2022 to June 2024. As our study setting, we choose surgical wards in National Hospital Galle. Although appendicitis is more prevalent among children, our study population consists patients aged above 18 years, as the majority of admissions to our surgical wards consist of adult patients. In order to minimize the bias, known patients with neutropenic conditions, patients with coexisting septic foci, patients who underwent interval appendectomy where histopathological findings are not evident and patients on whom the CRP, FBC and ESR were not done before appendectomy were excluded from the study.

The data was obtained from the medical records including bed head tickets and the clinic records of the patients who were diagnosed with acute appendicitis and underwent appendectomy, with prior permission of the Director of National Hospital Galle and all the relevant consultant surgeons. The records with non-legible handwriting were excluded. Relevant data including demographic details, clinical symptoms and signs, highest pre surgical values of biochemical and haematological parameters and histopathological findings were recorded in a data extraction sheet.

To study the association between clinical features and histopathological diagnosis, the clinical features selected were; typical abdominal pain, atypical abdominal pain, anorexia, nausea, vomiting, fever, abdominal tenderness, rebound phenomenon, guarding, Rovsing's sign, Cope's obturator sign, and Iliopsoas sign.

In order to determine the association between biochemical markers and histopathological diagnosis C Reactive Protein (CRP) level was selected as the biochemical marker. Reference

values used were based on a study conducted by Msolli, *et al.*, (7). A CRP level of <6 mg/L was considered as normal and values >6 mg/L was considered as being high.

For haematological parameters, White Blood Cell (WBC) count and neutrophil count were considered. According to previous research, the normal range of WBC is 3,500 - 12,000 cells/ μ L, and therefore values above 12,000 cells/ μ L were considered high (8). The normal neutrophil count is generally accepted as $1.5 - 7.5 \times 10^9/L$ (1,500 - 7,500 cells/ μ L), and levels above this range were considered elevated (9).

Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Ruhuna. Data was analysed using SPSSTM (Statistical Package for Social Sciences) 24.

Results

The study sample consisted of 380 patients who were clinically diagnosed as having acute appendicitis and underwent appendicectomy. Among them majority 235 (61.84%) were females. Our study sample consisted of patients who were above 18 years of age and the mean age of the sample was 28 year (Table 1).

Table 1: Socio-demographic profile of the sample

		Frequency (n)	Percentage (%)
Age	18 - 30	208	54.74%
	31 - 45	112	29.47%
	46 - 60	45	11.85%
	>60	15	3.94%
Gender	Male	145	38.16%
	Female	235	61.84%

The association between clinical features and histopathological diagnosis

In our study sample, out of the 380 patients who were clinically diagnosed with acute appendicitis, 361(95%) patients were histopathologically

diagnosed with acute appendicitis. The remaining 19(5%) cases who had features suggestive of acute appendicitis clinically, were histopathologically negative. Among patients who were histopathologically diagnosed with acute appendicitis the most prevalent clinical feature was abdominal tenderness which was observed in 343(95%) patients. Abdominal tenderness is closely followed by typical abdominal pain 325 (90.02%). Obturator sign was the least common clinical feature which was positive in 7 (1.93%) patients. Out of the clinical features assessed, only typical abdominal pain ($p=0.042$), anorexia ($p=0.032$), nausea ($p=0.007$), abdominal tenderness ($p=0.012$) and rebound phenomenon ($p=0.004$) demonstrated significant associations with the histopathological diagnosis (Table 2).

Association between biochemical markers and histopathological diagnosis

The analysis of CRP levels (high vs. normal) versus the results of histopathological diagnosis (positive vs. negative) is showed in Table 3. According to the analysis out of the 380 cases, 289 patients with elevated CRP levels had a positive histopathological diagnosis, whereas 72 patients had normal CRP levels. Our study shows that there is a significant association between CRP level and histopathological diagnosis ($p=0.039$).

The sensitivity, specificity, positive and negative predictive values of CRP in diagnosing acute appendicitis were 80.05%, 63.15%, 97.63% and 14.28% respectively.

Association between haematological parameters and histopathological diagnosis

Based on our results, 279 (96.87%) patients with a high WBC count were diagnosed as histopathologically positive for acute appendicitis, whereas only 9 (3.13%) cases fell under the negative category. Conversely, among individuals with a normal WBC count, 82 (89.13%) were histopathologically positive, while 10 (10.87%) were histopathologically negative. The total count for WBC category sums to 288 (high) and 92 (normal), respectively. The statistical significance for this comparison yielded a p -value of 0.045,

indicating a potential association between elevated WBC counts and positive histological diagnosis (Table 4).

A high neutrophil count was observed in 306 (98.07%) histopathologically positive cases and in 6 (1.93%) histopathologically negative cases. In contrast, among individuals with a normal neutrophil count 55 (80.88%) were positive and 13 (19.12%) were negative, summing up to a total of 68 cases with normal neutrophil count. This association resulted in a p -value of 0.049, suggesting a statistically significant association between increased neutrophil counts and a positive histological diagnosis (Table 4)

The sensitivity, specificity, positive and negative predictive values of WBC count in diagnosing acute appendicitis were 77.28%, 52.63%, 96.87% and 10.86% respectively.

The sensitivity, specificity, positive and negative predictive values of neutrophil count in diagnosing acute appendicitis were 95.63%, 68.42%, 98.07% and 19.11% respectively.

Both high WBC and neutrophil counts exhibit a very high positive predictive value of histopathological diagnosis. These findings suggest that elevated levels of WBC and neutrophils may serve as potential haematological biomarkers for predicting histopathological outcomes in acute appendicitis.

Potential biochemical marker/ haematological parameter that can be used to predict the complications of acute appendicitis

The patients were categorised into complicated appendicitis based on the presence of complications such as perforations, appendicular abscess, suppurations and gangrenes appendicitis. Table 5 provides a detailed analysis of association between biochemical marker; CRP and hematological parameters; WBC, and neutrophil count and complicated appendicitis.

Table 2: Association between clinical features and histopathological diagnosis in patients with acute appendicitis

		Histopathological Diagnosis			p
		Positive	Negative	Total	
Typical Abdominal pain	Yes	325 (95.02%)	17 (4.97%)	342 (100%)	0.042
	No	36 (94.73%)	2 (5.27%)	38 (100%)	
	Total	361	19	380	
Anorexia	Yes	292 (96.05%)	12 (3.95%)	304 (100%)	0.032
	No	69 (90.79%)	7 (9.21%)	76 (100%)	
	Total	361	19	380	
Nausea	Yes	289 (93.83%)	19 (6.16%)	308 (100%)	0.007
	No	72 (100%)	0	72 (100%)	
	Total	361	19	380	
Abdominal Tenderness	Yes	343 (95.01%)	18 (4.99%)	361 (100%)	0.012
	No	18 (94.73%)	1 (5.27%)	19 (100%)	
	Total	361	19	380	
Rebound phenomenon	Yes	297 (95.49%)	14 (4.50%)	311 (100%)	0.004
	No	64 (92.75%)	5 (7.24%)	69 (100%)	
	Total	361	19	380	

Table 3: Association between biochemical markers and histopathological diagnosis in patients with acute appendicitis.

		Histopathological Diagnosis			<i>p</i>
		Positive	Negative	Total	
CRP	High	289 (97.63%)	7 (2.37%)	296 (100%)	0.039
	Normal	72 (85.71%)	12 (14.29%)	84 (100%)	
	Total	361	19	380	

Table 4: Association between haematological parameters and histopathological diagnosis in patients with acute appendicitis

		Histopathological Diagnosis			<i>p</i>
		Positive	Negative	Total	
WBC count	High	279 (96.87%)	9 (3.13%)	288 (100%)	0.045
	Normal	82 (89.13%)	10 (10.87%)	92 (100%)	
	Total	361 (95%)	19 (5%)	380 (100%)	
Neutrophil count	High	306 (98.07%)	6 (1.93%)	312 (100%)	0.049
	Normal	55 (80.88%)	13 (19.12%)	68 (100%)	
	Total	361 (95%)	19 (5%)	380 (100%)	

Table 5: Identify potential biochemical marker or haematological parameter that can be used to predict the complications of acute appendicitis

Acute appendicitis	Biochemical marker / haematological parameter			
	High (n, %)	Normal (n, %)	Total (n, %)	Mean
CRP(mg/L)				
Complicated	33 (82.5%)	7 (17.5%)	40 (100%)	126
Uncomplicated	256 (79.7%)	65 (20.2%)	321 (100%)	64
Total	289 (80.05%)	72 (19.94%)	361 (100%)	
WBC (cells/ μ L)				
Complicated	31 (77.5%)	9 (22.5%)	40 (100%)	16,580
Uncomplicated	248 (77.25%)	73 (22.75%)	321 (100%)	11,300
Total	279 (77.28%)	82 (22.72%)	361 (100%)	
Neutrophil count (cells/ μ L)				
Complicated	29 (72.5%)	11 (27.5%)	40 (100%)	13,280
Uncomplicated	277 (86.29%)	44 (13.71%)	321 (100%)	8,900
Total	306 (84.76%)	55 (15.24%)	361 (100%)	

When considering CRP levels, complicated cases showed a markedly higher mean value (126 mg/L) compared to uncomplicated cases (64 mg/L), demonstrating a statistically significant difference ($p=0.001$). Similarly, the mean WBC count was significantly elevated in complicated cases (16,580 cells/ μ L) compared to uncomplicated cases (11,300 cells/ μ L) ($p=0.003$). Comparable findings were observed in neutrophil counts, where complicated cases exhibited a higher mean (13,280 cells/ μ L) than uncomplicated cases (8,900 cells/ μ L), also reaching statistical significance ($p=0.002$).

These results indicate that elevated CRP, WBC, and neutrophil counts are strongly associated with complicated appendicitis. Therefore, CRP can be identified as a potential biochemical marker, while WBC and neutrophil counts serve as haematological markers useful in predicting complications of acute appendicitis.

Discussion

Our study findings align with and expand upon the existing body of literature regarding the diagnostic value of clinical features, biochemical markers, and haematological parameters in acute appendicitis. Clinical signs like nausea, anorexia and the right iliac fossa pain have been repeatedly emphasized in prior research as being important in the diagnosis of acute appendicitis (10). These findings are supported by our findings, which show that histopathological diagnosis is significantly associated with typical abdominal pain, anorexia, nausea and rebound tenderness. This shows the continuing relevance of the clinical examination in the diagnosis of acute appendicitis.

The importance of inflammatory markers in predicting acute appendicitis has been highlighted in several studies. According to Msolli, *et al.*, (7), CRP levels above 10 mg/L demonstrated a sensitivity range of 65 - 85% and a specificity of 59 - 73%. The values obtained in our study for CRP fall within a similar range, showing a sensitivity of 80.5% and a specificity of 63.15% in diagnosing acute appendicitis, although our reference threshold was slightly lower at 6 mg/L. In our analysis, there was a statistically significant association between elevated CRP levels and positive histopathological

findings ($p=0.039$). Furthermore, the mean CRP value was markedly higher in complicated cases (126 mg/L) compared with uncomplicated cases (64 mg/L), a difference that was statistically significant ($p=0.001$). These findings suggest that CRP is not only valuable in diagnosing acute appendicitis but also serves as a useful biochemical marker in differentiating complicated from uncomplicated disease.

Numerous studies have investigated the predictive value of WBC and neutrophil counts in cases of acute appendicitis. We discovered that 96.87% of histopathologically confirmed patients had increased WBC counts. Ulukent, *et al.*, had shown that WBC counts $>10,000$ cells/ mm^3 had a sensitivity between 32% to 82% (11) while in our study WBC counts $>12,000$ cells/ mm^3 had a sensitivity of 77.28% in diagnosing acute appendicitis. Our analysis found that 98.07% of histopathologically confirmed cases had high neutrophil counts and neutrophil count revealed a very high sensitivity of 95.63% in diagnosing acute appendicitis supporting earlier work by Sengupta, *et al.*, that emphasized the diagnostic value of neutrophil ratios (12). Furthermore, the mean WBC count was significantly higher in complicated cases (16,580 cells/ μ L) compared to uncomplicated cases (11,300 cells/ μ L) ($p=0.003$). Similarly, the mean neutrophil count was significantly higher in complicated cases (13,280 cells/ μ L) compared to uncomplicated cases (8,900 cells/ μ L) ($p=0.002$).

One of the important findings of our study was that 5% of patients exhibiting clinical features of acute appendicitis lacked histopathological evidence of acute appendicitis. De Jonge, *et al.*, found that 1.8% of patients with suspected appendicitis had normal histopathological findings; a lower value compared to our study (13). Our findings suggest that reliance solely on clinical and laboratory markers may lead to unnecessary surgical procedures in some cases, underscoring the role of imaging techniques such as ultrasound and CT scans in equivocal presentations (14).

Our analysis confirms earlier research showing that haematological and biochemical markers can predict complicated appendicitis. According to our analysis, CRP, WBC and neutrophil count

had very much higher mean values in complicated acute appendicitis compared to uncomplicated cases; 126 vs. 64, 16,580 vs 113 and 13,280 vs 8,900 respectively.

The findings of Humes and Simpson have shown that leukocytosis and neutrophilia associated with appendiceal perforation risk are supported by the noticeably higher mean WBC count (16,580 cells/ μ L) and neutrophil count (13,280 cells/ μ L) in complicated cases (3). These findings suggest a potential role for dynamic monitoring of inflammatory markers in risk stratification.

Conclusions and recommendations

In conclusion this study offers valuable insights about the relationship between the histopathological diagnosis of acute appendicitis and clinical features, biochemical markers, and hematological parameters. Our results show that histopathological diagnosis of acute appendicitis is significantly associated with certain clinical symptoms, including typical abdominal pain, anorexia, nausea, abdominal tenderness, and rebound tenderness. Furthermore, our findings suggest that higher CRP, WBC, and neutrophil counts are significantly associated with histopathological diagnosis of acute appendicitis. Elevated CRP, WBC, and neutrophil counts are reliable markers for predicting complications of acute appendicitis according to our analysis.

A small percentage of patients with clinical features of acute appendicitis did not have histopathological confirmation, which is notable and emphasizes the necessity of adjunct imaging methods like ultrasound scans in instances that are unclear. High-risk patients who may have difficulties can be identified with the aid of routine evaluations of CRP, WBC, and neutrophil levels. Standardized procedures with verified hematological and biochemical markers should be implemented by hospitals to facilitate decision-making.

Strengths and Limitations

The identification of important predictors for key inflammatory markers, such as CRP, WBC count, and neutrophil count, supports their incorporation into standard diagnostic procedures. With a large

sample size (n=380) and a retrospective design, the study ensures practical application by reflecting real-world clinical settings. The results of this single-centre investigation, which was carried out at National Hospital Galle in Sri Lanka, may not be very generalizable. Concerns about missing data and possible selection bias are introduced by the retrospective nature. Furthermore, the study's wider relevance is limited by the lack of imaging data and the omission of pediatric cases. The scope is further limited by lack of surgical follow-up. Notwithstanding these limitations, the study helps clinical decision-making by offering insightful information about laboratory-based diagnosis of acute appendicitis.

Authors declare no competing interests.

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