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Acute Appendicitis in the Presence of Normal Inflammatory Markers: A Single Centre Retrospective Cohort Analysis

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Abstract

Purpose: This study aims to explore the incidence of normal inflammatory markers in patients undergoing appendectomy for acute appendicitis.

Materials and Methods: This study presents a single-centre retrospective cohort analysis conducted at Sheikh Khalifa Medical City in Ajman, UAE, examining patients who underwent appendectomy for acute appendicitis between January 1, 2019, and December 31, 2023. The study cohort comprised 500 patients aged 4 to 60 years. Data were systematically extracted from electronic medical records using a standardised data extraction sheet, ensuring both consistency and accuracy in the analysis.

Findings: Out of 500 patients, 368 were included in the study. The majority were male (66.8%), while females comprised 33.2%. The mean age of the patients was 23.6 years, with a standard deviation of 13 years. The sensitivity, or true positive rate, for white blood cell (WBC) counts in patients with appendicitis was found to be 71.5% (95% confidence interval: 66.8%–76.1%). In comparison, the sensitivity of C-reactive protein (CRP) was 69.8% (95% CI: 65.1%–74.5%), which is consistent with findings from previous studies. The overall sensitivity for all biomarkers, combining the true positive rates of CRP and WBC, was established at 49.2% (95% CI: 44.1%–54.3%). Conversely, the false-negative rate for WBC counts in appendicitis patients was determined to be 28.5% (95% CI: 24%–33.2%), while the false-negative rate for CRP was 30.2% (95% CI: 25.4%–34.8%). Notably, a total of **7.8%** (95% CI: 5.1%–10.6%) of patients with confirmed appendicitis exhibited normal (false negative) preoperative levels of both WBC and CRP.

Unique Contribution to Theory, Practice and Policy: we recommend that clinicians remain cautious regarding normal inflammatory markers in patients with a high clinical suspicion of appendicitis.

Key Words: *Acute appendicitis, Normal Inflammatory Markers, Retrospective Cohort*

INTRODUCTION

Acute appendicitis (AA) represents one of the most prevalent causes of abdominal pain, necessitating emergency surgical intervention. The lifetime incidence has been estimated to be 8.6% in males and 6.7% in females(1,2) Although it is effectively treatable, acute appendicitis can lead to serious complications, including perforation, peri-appendiceal abscess, peritonitis, and in rare cases, fatalities. The incidence of perforation has been estimated to range between 17% and 20% (3)

Historically, the diagnosis of appendicitis was made based on clinical evaluation, frequently using elevated inflammatory markers to support decision-making [4]. In contemporary practice, ultrasonography and, more recently, computed tomography (CT) scans [5] are increasingly employed to facilitate diagnosis and to minimise unnecessary surgical interventions.

In the past, a negative appendectomy rate of up to 20% has been deemed acceptable to reduce the incidence of perforation and peritonitis associated with delays in treatment.[6] Nevertheless, a growing sentiment is that such rates may now be unacceptable. The increased availability of computed tomography (CT) imaging has led to a decrease in the negative appendectomy rate. Some medical centres in the United States have reported rates of less than 2%.[7]

In situations where computed tomography (CT) is not readily accessible or where there are concerns regarding radiation exposure, clinicians must rely on patient history, clinical examination, and laboratory tests to establish a diagnosis and assess the necessity for surgical intervention. This methodology forms the foundation of the Alvarado score, which has been demonstrated to predict appendicitis with a relatively high degree of sensitivity and specificity.8-10. The white blood cell (WBC) count and C-reactive protein (CRP) are widely recognized as key markers of inflammation in cases of acute appendicitis (AA).[13-14] The utilization of inflammatory markers for the diagnosis of appendicitis has prompted significant discussion within the medical community. Existing literature indicates that the sensitivity and specificity of CRP can vary considerably, with reported values ranging from 40% to 95%. Additionally, there remains a lack of consensus on whether the white blood cell count (WCC) is a more sensitive or specific diagnostic indicator compared to CRP.

Atypical presentations of acute appendicitis may display characteristic features, but the inflammatory markers might not be significantly elevated. This can complicate the diagnosis. Such atypical presentations are particularly worrisome, as they can lead to delayed or incorrect diagnoses and inappropriate management. These delays may result in serious complications, such as perforation, peritonitis, and abscess formation, which can worsen the patient's condition and increase treatment costs [3,11-15] The reasons why some patients with AA do not show elevated inflammatory markers are still not fully understood. This variation may be due to differences in disease progression, individual immune responses, or the possibility that these cases are in the early stages of the disease.

A meta-analysis by Andersson[11] found that inflammatory markers alone are weak indicators of appendicitis without clinical findings. However, a recent study by Sengupta et al.[16] reviewed 98 patients with lower abdominal pain and claimed a 100% negative predictive value and sensitivity when combining CRP and WCC. They suggested that patients with a 'normal' WCC (≤11 × 10^9/l) and CRP (≤10 mg/l) are unlikely to have appendicitis and can be safely discharged. This finding could reduce unnecessary admissions and procedures. This paper analyzes preoperative levels of CRP, WCC, and neutrophil count in patients undergoing appendicectomy at two hospitals to validate Sengupta et al.'s approach.

This study presents a retrospective cohort analysis of acute appendicitis cases at a single center, specifically focusing on those with normal inflammatory markers. The primary objective is to assess the prevalence of this uncommon presentation and to characterize the associated clinical, radiological, operative, and pathological findings. By analyzing these cases, the study aims to identify potential factors that may contribute to the presence of normal inflammatory markers and to evaluate their impact on diagnostic accuracy, clinical management, and patient outcomes.

MATERIALS AND METHODS

Study Design and Setting

This retrospective cohort study was carried out at Sheikh Khalifa Medical City in Ajman, UAE, from November 2023 to November 2024.

Participants

A total of 500 patient medical records were reviewed, among which 368 were identified as fulfilling the specified inclusion criteria for the study.

Inclusion Criteria

All patients aged 4 to 60 years who underwent laparoscopic or open appendectomy for acute appendicitis. They had inflammatory blood test results available in the hospital medical records and had histopathologically confirmed appendicitis.

Exclusion Criteria

Patients who have undergone surgical procedures other than appendectomy and those with incomplete data regarding inflammatory parameters, such as preoperative white blood cell (WBC) counts or C-reactive protein (CRP) levels, will be excluded from consideration.

Participants were identified through convenience sampling, utilising the medical records of all eligible patients during the designated study period**.**

Data Collection

Data were collected retrospectively from electronic medical records using a standardised data extraction sheet. The following key variables were recorded:

Demographic Data: Medical record number (MRN), sex, age, nationality, and ethnicity.

Clinical Presentation: Admission date and time, duration of symptoms, presence of symptom migration, fever, nausea or vomiting, and the nature of peritonitis (localised or generalised).

Preoperative Laboratory Parameters: White blood cell (WBC) count (cells/µL) and C-reactive protein (CRP) levels (mg/dL).

Imaging: The type of imaging modality used (CT and ultrasound) and the classification of appendicitis based on imaging findings (uncomplicated or complicated appendicitis).

Surgical Details: The type of surgical procedure performed (open or laparoscopic appendectomy).

Postoperative Data: Length of hospital stay, histopathology results, and findings from culture and sensitivity tests.

To ensure the security and confidentiality of the data, all extracted information was stored in a password-protected Microsoft Excel file, accessible solely to the research team.

Ethical Considerations

Throughout the study, participants' privacy and confidentiality were rigorously maintained. Identifiable information, such as MRNs, was de-identified and replaced with unique study codes for analysis. Data handling practices adhered to the data protection policies established by MOHAP(Ministry of Health and Prevention) and the institution, reinforcing a commitment to ethical standards in analysis.

Outcome parameters and definitions:

The primary outcomes of this study included the number and percentage of patients with normal preoperative inflammatory markers who were diagnosed with histopathologically confirmed acute appendicitis after undergoing an appendectomy. Inflammatory markers were deemed normal if the white blood cell (WBC) count was ≤ 11 × 10^9/L and the C-reactive protein (CRP) level was ≤ 5 mg/L. Hospital guidelines established these threshold values.

The secondary outcomes included the results of preoperative imaging and the intraoperative assessment of the appendix's inflammatory state, which was classified as uncomplicated, gangrenous, or perforated appendicitis. Additionally, the associated histopathological findings were analysed.

Statistical analysis

Data analysis was conducted using SPSS version 26. Categorical demographic variables were reported as frequencies and percentages, while continuous variables that followed a normal distribution were summarised as means with standard deviations (SD). The chi-square test and Fisher's Exact tests were employed to summarise and compare the false-negative findings of white blood cell counts and C-reactive protein levels in patients with appendicitis. Additionally, univariate logistic regression analysis was performed to identify the factors that significantly influence false-negative results for white blood cell counts and C-reactive protein. Statistical significance was established for p-values below 0.05.

FINDINGS

A total of 500 patients' medical records were retrieved. Of these, 368 patients met the inclusion criteria. The majority of patients were male (66.8%), while females comprised 33.2%. The mean age of patients was 23.6 years (±13). In terms of ethnicity, Arabs represented the largest group at 62.8%, followed by South Asians (22.6%), Southeast Asians (3.3%), Central Asians (2.4%), and smaller proportions of Caucasians and others (1.1% each). Most patients presented with symptoms lasting less than two days (67.9%), whereas 31.5% reported symptoms lasting longer. The sensitivity (true positive rate) for white blood cell counts in appendicitis patients was 71.5% (95% CI: 66.8%–76.1%), compared to 69.8% (95% CI: 65.1%–74.5%) for C-reactive protein. The overall sensitivity across all markers—combining the true positive rates of both CRP and WBC—was 49.2% (95% CI: 44.1%–54.3%). Conversely, the false-negative rate for white blood cell counts in appendicitis patients was 28.5% (95% CI: 24%–33.2%), compared to 30.2% (95% CI: 25.4%–34.8%) for C-reactive protein. Overall, a total of **7.8%** (95% CI: 5.1%–10.6%) of patients with confirmed appendicitis had normal (false negative) preoperative WBC and CRP.

Demographics, Signs, and Symptoms of Patients with Acute Appendicitis.

Table 1: Demographics, Signs and Symptoms of Acute Appendicitis Patients

Variables	Groups	Frequency	Percentage
Gender	Female	122	33.2
	Male	246	66.8
Age (Years), mean ± SD	23.6 ± 13	------	------
Ethnicity	Southeast Asian	12	3.3
	South Asian	83	22.6
	Central Asian	9	2.4
	Arab	231	62.8
	African	25	6.8
	Other	8	2.2
Duration of symptoms	Less than 2 days	252	68.5
	More than 2 days	116	31.5
Migration of pain	Yes	128	34.8
	No	240	65.2
Nausea and vomiting	Yes	286	77.7
	No	82	22.3
Fever	Yes	44	12
	No	324	88
Peritonitis	Diffused	45	12.2
	Localized	323	87.8

Table 1 provides an overview of the demographics, signs, and symptoms of patients with appendicitis within a study cohort. Most patients were male (66.8%), while females accounted for 33.2%. The average age of the patients was 23.6 years (±13). In terms of ethnicity, Arabs represented the largest group at 62.8%, followed by South Asians (22.6%), Africans (6.8%), Southeast Asians (3.3%), Central Asians (2.4%), and a smaller proportion of others (1.1%). Most patients presented with symptoms lasting less than two days (68.5%), whereas 31.5% reported symptoms persisting for longer. Pain migration was observed in 34.8% of cases, while 65.2% did not experience it. Nausea and vomiting were prevalent among 77.7% of patients, whereas 22.3% reported no such symptoms. Fever was noted in only 12% of cases, with 88% of patients remaining afebrile. Peritonitis was predominantly localized (87.8%), with only 12.2% presenting with diffuse peritonitis. These findings highlight key demographic and clinical features within this cohort of patients with appendicitis patients.

Table 2: Clinical and Procedural Characteristics of Patients with Acute Appendicitis

Variables	Groups	Frequency	Percentage
Preoperative WBC mean ± SD	13.67 ± 4.5	-------	-------
Preoperative CRP mean ± SD	49.89 ± 77.1	-------	-------
US/CT imaging results	Complicated	175	47.6
	Uncomplicated	159	43.2
	Not visualized	12	3.3
	No imaging	22	6
Histopathology findings	Complicated	100	27.2
	Uncomplicated	268	72.8
Actual Procedure	Laparoscopic appendicectomy	336	91.3
	Open Appendectomy	32	8.7

Abbreviations: WBC; white blood cell, CRP; C-reactive protein, US; ultrasound, CT; Computed Tomography

Table 2 summarizes the clinical and procedural characteristics of appendicitis patients. The mean preoperative white blood cell (WBC) count was 13.67 ± 4.5, and the mean preoperative C-reactive protein (CRP) level was 49.89 ± 77.1. Imaging results showed that 47.6% of cases were classified as complicated, 43.2% as uncomplicated, 3.3% were not visualized, and 6% had no imaging performed. Histopathological findings revealed that 27.2% of cases were complicated, while 72.8% were uncomplicated. Most patients (91.3%) underwent laparoscopic appendectomy, with 8.7% requiring open appendectomy.

Comparison of Factors Associated with False-Negative (Normal) White Blood Cell Counts in Acute Appendicitis Patients

The sensitivity of white blood cell (WBC) counts in patients with appendicitis was 71.5% (95% CI: 66.8%–76.1%), while the sensitivity for C-reactive protein (CRP) was 69.8% (95% CI: 65.1%–74.5%). The overall sensitivity, when combining both markers, was 49.2% (95% CI: 44.1%–54.3%). The false-negative rate for WBC counts stood at 28.5% (95% CI: 24%–33.2%), compared to 30.2% (95% CI: 25.4%–34.8%) for CRP. The combined false-negative rate for both markers was significantly lower at 7.8% (95% CI: 5.1%–10.6%).

Table 3: Diagnostic Characteristics of False-Negative WBC (Normal) Values in Acute Appendicitis Cases

Variables	Groups	False negative (n=105)	P-value
Gender	Female	34 (27.9%)	0.472
	Male	71 (28.9%)	
Ethnicity	Southeast Asian	2 (16.7%)	
	South Asian	19 (22.9%)	
	Central Asian	0	**0.001**
	Arab	65 (28.1%)	
	African	16 (16%)	
	Other	3 (37.5%)	
Duration of symptoms	Less than 2 days	65 (62%)	**0.013**
	More than 2 days	40 (38%)	
Migration of pain	Yes	32 (25%)	0.165
	No	73 (30.4%)	
Nausea and vomiting	Yes	74 (25.9%)	**0.035**
	No	31 (37.8%)	
Fever	Yes	14 (31.8%)	0.362
	No	91 (28.1%)	
Peritonitis	Diffused	17 (37.8%)	0.143
	Localized	88 (27.2%)	
US/CT imaging results	Complicated	52 (29.7%)	0.156
	Uncomplicated	46 (28.9%)	
	Not visualized	5 (41.7%)	
	No imaging	2 (9.1%)	
Histopathology findings	Complicated	23 (23%)	0.151
	Uncomplicated	82 (20.6%)	
Actual Procedure	Laparoscopic appendicectomy	96 (28.6%)	0.569
	Open Appendectomy	9 (28.1%)	

Chi-squared ($\chi 2$) and Fisher exact test was used, with P-values <0.05 considered statistically significant

Table 3 presents the diagnostic characteristics of normal (false negative) white blood cell (WBC) counts in appendicitis cases (n=105), categorised by demographic, clinical, and procedural variables. Gender showed no significant difference (P=0.472), while ethnicity exhibited significant variation (P=0.001), with the highest false-negative rates in the "Other" group (37.5%) and the lowest in Africans (16%). A symptom duration of less than two days was associated with higher false-negative rates (62%) compared to more than two days (38%), thus proving statistically significant (P=0.013). Among clinical symptoms, the absence of nausea and vomiting was significantly associated with higher false-negative rates (37.8%, P=0.035), while fever, pain migration, and peritonitis showed no significant associations. Imaging results revealed no significant differences (P=0.156). Histopathology showed no significant associations, with false-negative rates slightly lower in complicated appendicitis cases. The procedural approach (laparoscopic vs. open appendectomy) also revealed no significant differences.

Comparison of Factors Associated with False-Negative C-Reactive Protein (CRP) Values in Acute Appendicitis Patients

Table 4 outlines the diagnostic characteristics of normal (false negative) C-reactive protein (CRP) in appendicitis cases among 111 patients, exploring the association of demographic, clinical, and procedural variables. Although gender differences were not statistically significant (P=0.054), females exhibited higher false-negative rates (36.1%) than males (27.2%). Ethnicity analysis revealed no significant differences (P=0.438). Duration of symptoms was highly significant (P<0.001), with higher false-negative rates in patients presenting symptoms for less than two days (36.1%) compared to more than two days (17.2%). Fever significantly influenced false-negative rates (P=0.004), showing a lower likelihood in febrile patients (11.4%) versus afebrile ones (32.7%). Histopathology findings were also significantly associated (P<0.001), with higher false-negative rates in uncomplicated cases (35.4%) compared to complicated cases (16%). Other factors, including pain migration, nausea and vomiting, peritonitis and imaging results did not show statistically significant associations. Statistical significance was set at P<0.05.

Table 4: Diagnostic Characteristics of False-Negative CRP Value in Appendicitis Cases.

Variables	Groups	False negative (n=111)	P-value
Gender	Female	44 (36.1%)	0.054
	Male	67 (27.2%)	
Ethnicity	Southeast Asian	2 (16.7%)	
	South Asian	20 (24.1%)	
	Central Asian	4 (44.4%)	0.438
	Arab	72 (31.2%)	
	African	10 (40%)	
	Other	3 (37.5%)	
Duration of symptoms	Less than 2 days	91 (36.1%)	**< 0.001***
	More than 2 days	20 (17.2%)	
Migration of pain	Yes	32 (25%)	0.115
	No	79 (32.9%)	
Nausea and vomiting	Yes	83 (29%)	0.373
	No	28 (34.1%)	
Fever	Yes	5 (11.4%)	**0.004***
	No	106 (32.7%)	
Peritonitis	Diffused	10 (22.2%)	0.215
	Localized	101 (31.3%)	
US/CT imaging results	Complicated	50 (28.6%)	0.399
	Uncomplicated	54 (34%)	
	Not visualized	3 (25%)	
	No imaging	4 (18.2%)	
Histopathology findings	Complicated	16 (16%)	**< 0.001***
	Uncomplicated	95 (35.4%)	
Actual Procedure	Laparoscopic appendicectomy	102 (30.4%)	0.793
	Open Appendectomy	9 (28.1%)	

Chi-squared ($\chi 2$) and Fisher exact test was used, with P-values <0.05 considered statistically significant

Regression Analysis of Factors Influencing False-Negative Inflammatory Markers in Acute Appendicitis.

Table 5 presents the regression analysis of factors associated with false-negative white blood cell (WBC) counts in patients with appendicitis. Significant predictors included age, where an increase in age correlated with a higher likelihood of false negatives (OR=1.027, 95% CI=1.009–1.045, P=0.003), as well as the presence of nausea and vomiting, which reduced the odds of false-negative WBC results (OR=0.574, 95% CI=0.342–0.965, P=0.036). Other variables, including gender, ethnicity, duration of symptoms, fever, peritonitis, imaging results, histopathology findings, and procedure type, did not demonstrate statistically significant associations with false-negative WBC counts (P>0.05).

Table 5: Regression Analysis of Factors Associated with False-Negative WBC Results in Acute Appendicitis Patients

	False Negative WBC			
Variables	**OR**	**95% CI**		**P-value**
Age	1.027	1.009	1.045	**0.003**
Gender (Ref. Male)				
Female	0.952	0.588	1.543	0.843
Ethnicity (Ref. Other)				
Southeast Asian	0.333	0.041	2.686	0.302
South Asian	0.495	0.108	2.263	0.364
Central Asian	0.343	0.058	2.036	0.239
Arab	0.653	0.152	2.810	0.567
African	2.963	0.570	15.396	0.196
Duration of symptoms (Ref. More than 2 days)				
Less than 2 days	0.654	0.406	1.053	0.081
Migration of pain (Ref. No)				
Yes	0.758	0.466	1.232	0.263
Nausea and vomiting (Ref. No)				
Yes	0.574	0.342	0.965	**0.036**
Fever (Ref. No)				
Yes	1.190	0.603	2.346	0.616
Peritonitis (Ref. Localized**)**				
Diffused	1.621	0.846	3.107	0.145
US/CT imaging results (Ref. Uncomplicated)				
complicated	1.039	0.648	1.665	0.875
no imaging	0.246	0.055	1.094	0.065
not visualized	1.755	0.530	5.813	0.358
Histopathology findings (Ref. Complicated**)**				
Uncomplicated	1.419	0.831	2.425	0.200
Actual Procedure (Ref. Open Appendectomy)				
Laparoscopic appendicectomy	1.022	0.457	2.289	0.957

Abbreivations: OR; odds ratio, WBC; white blood cell, CRP; C-reactive protein, US; ultrasound, CT; Computed Tomography. P-values <0.05 considered statistically significant

Table 6: This report summarises the regression analysis conducted to identify factors associated with false-negative C-reactive protein (CRP) results in patients diagnosed with appendicitis. The analysis reveals that a shorter duration of symptoms, specifically less than two days, is a significant predictor that increases the odds of obtaining false-negative CRP results (odds ratio [OR]=2.700; 95% confidence interval [CI]=1.563–4.664; P<0.001).

Additionally, the presence of fever is associated with a decreased likelihood of false-negative results (OR=0.262; 95% CI=0.101–0.685; P=0.006). Furthermore, uncomplicated histopathological findings correlate with a higher likelihood of false-negative results (OR=2.889; 95% CI=1.599–5.220; P<0.001). Other examined factors, including age, gender, ethnicity, pain migration, nausea and vomiting, type of peritonitis, and the type of imaging or procedure performed, did not demonstrate statistically significant associations with false-negative CRP results (P>0.

Table 6: Regression Analysis of Factors Associated with False-Negative CRP in Acute Appendicitis Patients.

	False Negative CRP			
Variables	**OR**	**95% CI**		**P-value**
Age	0.996	0.979	1.013	0.652
Gender (Ref. Male)				
Female	1.507	0.948	2.397	0.083
Ethnicity (Ref. Other)				
Southeast Asian	0.333	0.041	2.686	0.302
South Asian	0.529	0.116	2.412	0.411
Central Asian	1.333	0.191	9.311	0.772
Arab	0.755	0.176	3.244	0.705
African	1.111	0.216	5.727	0.900
Duration of symptoms (Ref. More than 2 days)				
Less than 2 days	2.700	1.563	4.664	< **0.001**
Migration of pain (Ref. No)				
Yes	0.688	0.425	1.115	0.129
Nausea and vomiting (Ref. No)				
Yes	0.789	0.467	1.330	0.373
Fever (Ref. No)				
Yes	0.262	0.101	0.685	**0.006**
Peritonitis (Ref. Localized**)**				
Diffused	0.628	0.299	1.318	**0**.219
US/CT imaging results (Ref. Uncomplicated)				
complicated	0.778	0.489	1.237	0.288
no imaging	0.432	0.139	1.340	0.146
not visualized	0.648	0.168	2.493	0.528
Histopathology findings (Ref. Complicated**)**				
Uncomplicated	2.889	1.599	5.220	< **0.001**
Actual Procedure (Ref. Open Appendectomy)				
Laparoscopic appendicectomy	1.114	0.498	2.491	0.793

Abbreviations: OR odds ratio, WBC; white blood cell, CRP; C-reactive protein, US; ultrasound, CT; Computed Tomography. P-values <0.05 considered statistically significant

Table 7 presents a comprehensive regression analysis examining the factors associated with false-negative results for white blood cell (WBC) counts and C-reactive protein (CRP) levels in patients diagnosed with appendicitis. The data reveal that age is significantly correlated with an increased likelihood of false-negative results, evidenced by an odds ratio (OR) of 1.029 (95% confidence interval [CI]: 1.002–1.057, P=0.037). Additionally, the analysis indicates that South Asian individuals exhibit significantly lower odds of receiving false-negative results compared to the reference group, with an OR of 0.113 (95% CI: 0.016–0.808, P=0.030). The outcomes of

imaging studies suggest that instances where the appendix is "not visualised" are associated with a markedly elevated probability of false negatives, as indicated by an OR of 4.485 (95% CI: 1.059–18.988, P=0.042). Furthermore, the analysis of other factors such as gender, duration of symptoms, migration of pain, nausea and vomiting, fever, peritonitis, histopathological findings, and the type of procedure does not reveal a statistically significant association with false-negative WBC and CRP results (P > 0.05).

Table 7: Regression Analysis for the Factors Associated with the False Negative CRP and WBC in Acute Appendicitis Patients

	False Negative WBC& CRP			
Variables	**OR**	**95% CI**		**P-value**
Age	1.029	1.002	1.057	**0.037**
Gender (Ref. Male)				
Female	1.067	0.480	2.370	0.874
Ethnicity (Ref. Other)				
Southeast Asian	0.715	0.225	2.277	0.571
South Asian	0.113	0.016	0.808	**0.030**
Central Asian	0.675	0.233	1.950	0.448
Arab	0.254	0.048	1.348	0.107
African	0.947	0.150	5.994	0.954
Duration of symptoms (Ref. More than 2 days)				
Less than 2 days	1.769	0.697	4.488	**0**.230
Migration of pain (Ref. No)				
Yes	0.571	0.237	1.374	0.211
Nausea and vomiting (Ref. No)				
Yes	0.610	0.266	1.396	0.242
Fever (Ref. No)				
Yes	0.522	0.120	2.276	**0**.387
Peritonitis (Ref. Localized**)**				
Diffused	0.816	0.237	2.814	**0**.747
US/CT imaging results (Ref. Uncomplicated)				
complicated	1.170	0.515	2.658	0.708
no imaging	0.641	0.079	5.219	0.677
not visualized	4.485	1.059	18.988	**0.042**
Histopathology findings (Ref. Complicated**)**				
Uncomplicated	2.310	0.778	6.855	**0**.132
Actual Procedure (Ref. Open Appendectomy)				
Laparoscopic appendicectomy	0.811	0.231	2.842	0.743

Abbreviations: OR; odds ratio, WBC; white blood cell, CRP; C-reactive protein, US; ultrasound, CT;
Computed Tomography. P-values <0.05 considered statistically significant

Discussion: Acute appendicitis is characterised by the onset of localised inflammation, which is subsequently followed by a more generalised inflammatory response (17). The rationale for employing laboratory tests in the diagnosis of acute appendicitis lies in their ability to detect signs of systemic inflammation through a widely accessible diagnostic tool that is easy to operate, minimally invasive, cost-effective, and repeatable as necessary (17). The inflammatory markers used in diagnosing acute appendicitis exhibit considerable variability in both sensitivity and specificity. In our study, the sensitivity of white blood cell (WBC)

counts in patients with appendicitis was 71.5% (95% CI: 66.8%–76.1%), while the sensitivity for C-reactive protein (CRP) was 69.8% (95% CI: 65.1%–74.5%) A study conducted by JJY Kim indicates that white blood cell (WBC) count demonstrates lower sensitivity compared to C-reactive protein (CRP)(18). This finding contrasts with our results; however, numerous additional studies have affirmed findings similar to ours, suggesting that WBC count possesses greater sensitivity and specificity(16,19,21).

Regarding the diagnostic characteristics of normal WBC (false negatives), a duration of less than two days was associated with higher false-negative rates (62%) compared to over two days (38%), which is statistically significant (P=0.013). Among clinical symptoms, the absence of nausea and vomiting significantly correlated with higher false-negative rates (37.8%, P=0.035), while fever, pain migration, and peritonitis showed no significant associations. For CRP, the duration of symptoms was highly significant (P<0.001), with higher false-negative rates in patients presenting symptoms for less than two days (36.1%) compared to over two days (17.2%). Fever significantly influenced false-negative rates (P=0.004), showing a lower likelihood in febrile patients (11.4%) versus afebrile ones (32.7%). Histopathology findings were also significantly associated (P<0.001), showing higher false-negative rates in uncomplicated cases (35.4%) compared to complicated cases (16%). In our study, 7.8% of patients with histopathologically confirmed appendicitis had normal inflammatory markers. . While conducting a similar study to ours, PG Vaughan-Shaw et al. [20] and Nalin H. Dayawansa et al. (21) reported normal inflammatory markers in 6.3% and 8.54%, respectively. A 2009 study by Anshuman Sengupta et al. (16) reviewed 98 patients with lower abdominal pain and found that none of the patients with normal white blood cell count (WBC) and C-reactive protein (CRP) had acute appendicitis. This resulted in a sensitivity and negative predictive value of 100%. In their study, the authors concluded that patients exhibiting normal white blood cell count (WBC) and C-reactive protein (CRP) levels are unlikely to have acute appendicitis and can be safely discharged. However, we find their reasoning unconvincing for several reasons. First, the exclusion criteria for the study are not clearly defined, raising concerns about the applicability of the findings. Additionally, there is a lack of follow-up data on patients discharged solely based on normal inflammatory markers. The study does not establish a correlation between symptoms' duration and inflammatory markers' levels. Furthermore, the sample size is notably small, limiting the robustness of the conclusions. Lastly, the study population’s age range or median age was not reported, further complicating the interpretation of the results. Our results and those of Birchley (22) do not support Sengupta et al.'s (16) finding that combined CRP and WBC are 100% sensitive to appendicitis, a finding also reported in 1989 by Dueholm et al. (23).

Conclusion

Appendicitis in the presence of normal inflammatory markers is not uncommon; thus, we recommend that clinicians remain cautious regarding normal inflammatory markers in patients with a high clinical suspicion of appendicitis.

Limitations

Retrospective single-centre study. While this is a single-centre study, the use of only one cut-off value could be questioned. Since there is no national guideline, we chose the range our hospital uses

Ethical approval

The Ministry of Health and Prevention (MOHAP) in the United Arab Emirates has granted ethical approval for this research (Approval Reference No: MOHAP/DXB-REC/F.A.A/No. 46/2024).

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Declaration of competing interest

No conflicts of interest to disclose.

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