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Accuracy of Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) for the Diagnosis of Acute Appendicitis, Taking Histopathology as the Confirmatory Standard

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ABSTRACT

Objective: This study was aimed to determine the diagnostic accuracy of ESR and CRP for diagnosis of acute appendicitis, taking histopathology as the gold standard.

Methodology: This cross-sectional study was conducted, at the department of general surgery, Pakistan Institute of Medical Sciences, Islamabad, from September 2024 to March 2025. Patients of either gender, aged 14 to 40 years, presenting within 48 hours onset of right lower quadrant pain, nausea, anorexia, or vomiting, and undergoing appendectomy with Alvarado score ≥4 were included. Venous blood samples were analyzed for CRP (>0.6 mg/L considered raised) and ESR (>20 mm/h considered raised). Histopathological confirmation of appendicitis served as the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were analyzed.

Results: Overall mean age of the patients was 25.97±6.44 years, with male predominance (62.6%). Histopathological evaluation confirmed acute appendicitis in 91.6% cases, along with erythematous type being most frequent (76.8%). Majority of the patients had raised ESR levels (62.1%), and among these, the majority was histopathology-positive (58.4%), whereas considerable proportion with normal ESR was still histopathology-positive (33.2%), whereas the raised CRP levels even more common (79.5%), with the vast majority of these cases confirmed positive on histopathology (76.8%), seemed more closely aligned with confirmed appendicitis than elevated ESR, with overall sensitivity of 83.91%, specificity of 68.75%, PPV (96.69%), NPV 28.21% and diagnostic accuracy around 82.63%.

Conclusion: CRP is a more accurate and reliable biomarker than ESR for diagnosing acute appendicitis, supporting its routine use to improve diagnostic confidence and reduce unnecessary appendectomies.

Keywords: Accuracy, Acute Appendicitis, CRP, ESR, Histopathology

Introduction

Acute appendicitis is one of the most common abdominal surgical emergencies worldwide. It can lead to serious complications such as paralytic ileus, peritonitis, abscess formation, and in rare cases, even death, while also placing significant burden on healthcare systems.[1] Its incidence is reported to be higher in men, with more than 40% cases occurring in patients 10 to 29 years of age.[2] On average, its annual incidence is around 233 cases per one hundred thousand population, with lifetime risk estimated between 6.7% and 8.6%.[3] Although Western countries documented decline in incidence during mid-twentieth century, newly industrialized nations have demonstrated an increasing trend in 20th century.[4] According to local study carried out in Lahore General Hospital, the prevalence of acute appendicitis was reported as 57.1%.[5]

The diagnosis of acute appendicitis is based on classical clinical signs and symptoms,[6] in addition to physical examination, laboratory investigations such as white blood cell count, CRP, and ESR levels are commonly employed as the next step in diagnosis.[7] These inflammatory markers can prevent nearly half of unnecessary surgeries, reduce negative appendectomy rates to about 15.2%, and lower the occurrence of perforated appendices to 11.7%.[8] The literature on the diagnostic utility of these markers is fluctuate, like many studies highlight the usefulness of CRP in confirming appendicitis, while some also report an increase in ESR levels.[9] Conversely, certain research has shown that in small proportion of patients with proven appendicitis both preoperative WBC counts and CRP levels may remain normal.[10]

In the most widely available and cost-effective of these markers are ESR and CRP, both of which reflect the systemic inflammatory response activated by appendiceal inflammation. ESR, a marker of the erythrocyte aggregation rate driven largely by fibrinogen and other acute-phase proteins, rises and falls more slowly than CRP, which is synthesized directly by the liver in response to inflammatory cytokines, primarily interleukin-6, increasing in proportion to the intensity of inflammation and responding sensitively even to understated changes. Such faster kinetics and shorter half-life of

approximately 19 hours allow CRP to fall quickly once inflammation resolutions, making it a preferred marker not only for diagnosis but also for monitoring treatment response.[11]

Although, their comparative performance for diagnosis remains vary and limited across the literature. According to a recent study evaluating inflammatory markers in suspected appendicitis observed CRP with considerably higher sensitivity than ESR, reinforcing its preference as a first-line inflammatory marker,[11] whereas another study of diagnostic markers for appendicitis noted almost similar sensitivity and specificity of ESR as 80% and 48% and CRP 82% and 62%[13] reflecting the two markers' differing kinetics and inflammatory responsiveness. Based on considerable controversy across existing literature, and limited comparable data specifically at local level for directly comparing ESR and CRP against histopathology as the confirmatory gold standard, this study has been carried out to generate clear, locally applicable evidence on the more accurate diagnostic accuracy of ESR and CRP in acute appendicitis.

Methodology

This cross-sectional validation study was conducted in the Department of General Surgery, Pakistan Institute of Medical Sciences, Islamabad, over a period of six months from September 2024 to March 2025 following approval of synopsis from CPSP and Ethical approval from Ethical Review Board (ERB) (Dated 24-06-2024 i.e. F-5-2/2024(ERRC)/PIMS]. A total of 184 patients undergoing appendectomy were enrolled through non-probability consecutive sampling after obtaining written informed consent from patients or parents/guardians. Sample size was calculated as 190, assuming expected sensitivity and specificity of CRP at cut off >0.6 mg/L to be 90% and 71% respectively.[14] absolute precision 10%, confidence level 95%, and prevalence of acute appendicitis 57.1%.[5]. Patients of either gender aged between 14 to 40 years, presenting within 48 hours onset of right lower quadrant pain, nausea, anorexia, or vomiting, and undergoing appendectomy with Alvarado score greater than four were included. Patients presenting after 48 hours of symptoms onset, undergoing interval appendectomy, having other systemic infections, known autoimmune diseases, active malignancy, chronic liver, kidney or lung disease, those receiving immunosuppressive therapy, or patients with uncontrolled comorbid conditions (BSL > 200 mg/dl or blood pressure > 140/90mmHg) were excluded from the study.

For each enrolled patient, demographic details including age, gender, and BMI were recorded. Clinical history and physical examination were performed, time of symptom onset noted. Alvarado score was categorized as 5 – 6, 7 – 8 or 9 – 10. Baseline investigations including complete blood count, liver and renal function tests, serum electrolytes, and coagulation profile were performed. Leukocytosis was considered if white blood cell count exceeded 11 x 10^9/L. Ultrasound abdomen and pelvis were also carried out. Venous blood samples were collected within 6 hours of admission, for C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), which were analyzed in chemical pathology laboratory of PIMS. CRP value >0.6 mg/L and ESR value >20 mm/h were considered raised. All patients subsequently underwent routine appendectomy, either laparoscopic or open. The excised appendix was preserved in formalin-filled jar, appropriately labeled, and sent to histopathology laboratory of PIMS. Histopathology was considered as the confirmatory gold standard for acute appendicitis. Histological features consistent with appendicitis included neutrophilic infiltration, mucosal ulceration, sub-mucosal edema, serosal inflammation, fibrinopurulent exudate, and vascular congestion. Patients with raised CRP or ESR and histological evidence of appendicitis were classified as true positive, those with normal CRP or ESR and normal histology as true negative, those with normal CRP or ESR but histological evidence of appendicitis as false negative, and those with raised CRP or ESR but normal histology as false positive. Data were collected using predesigned proforma. Statistical analysis was performed using SPSS version 26. Mean and standard deviation were calculated for continuous variables. Frequencies and percentages were computed for categorical variables. Diagnostic accuracy was assessed in terms of sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy by constructing two-by-two contingency tables, taking histopathology as the confirmatory gold standard.

Results

A total of 190 patients undergoing appendectomy were included with mean age calculated was 25.97 ± 6.44 years (range 14–40), among them majority were males 62.6% vs 37.4% females. The mean BMI and duration of symptoms calculated were 23.05 ± 1.91kg/m2, and 17.38 ± 10.38 hours, respectively. Based on Alvarado score, 23.2% patients scored 5–6, 47.9% scored 7–8, and 28.9% scored 9–10. Leukocytosis was present in 94.2% patients, raised ESR was found in 62.1% and raised CRP was in 79.5% of then cases. Histopathological evaluation confirmed acute appendicitis in 91.6% cases, while 8.4% had normal appendix. In the inflamed appendices, the erythematous type was by far the most frequent (76.8%), followed by purulent (9.5%),

perforated (3.7%), and necrotic (1.6%) types, whereas a small proportion of appendices (8.4%) were found to be histologically normal. Table I

According to ESR, majority of the patients had raised levels (62.1%), and among these, the majority was histopathology-positive (58.4%), whereas a considerable proportion with normal ESR were still histopathology-positive (33.2%). According to CRP, raised levels were even more common (79.5%), with the vast majority of these cases confirmed positive on histopathology (76.8%), in contrast too only 14.7% among those with normal CRP. The overall, elevated CRP seemed more closely aligned with confirmed appendicitis than elevated ESR. Table II.

Table I: Clinico-demographic characteristics of study population (n=190)

Age (years)	Mean ± SD	25.97 ± 6.44
	Minimum	14
	Maximum	40
Gender frequency (%)	Male	119 (62.6%)
	Female	71 (37.4%)
BMI		23.05 ± 1.91
Symptoms Duration (hours)		17.38 ± 10.38
ALAVARADO Score N (%)	5-6	44 (23.2%)
	7-8	91 (47.9%)
	9-10	55 (28.9%)
WBC	Mean ± SD	16.93 ± 3.24
	Leukocytosis frequency (%)	179 (94.2%)
ESR	Mean ± SD	20.38 ± 4.02
	Raised ESR frequency (%)	105 (55.3%)
CRP	Mean ± SD	0.87 ± 0.33
	Raised CRP frequency (%)	130 (68.4%)
Acute Appendicitis on Histopathology		174 (91.6%)
Type of inflamed appendix	Erythematous	112 (76.8%)
	Purulent	18 (9.5%)
	Perforated	7 (3.7%)
	Necrotic	3 (1.6%)
	Normal	16(8.4%)

Moreover the CRP showed considerably better diagnostic accuracy with sensitivity of 83.91% and specificity of 68.75%, with an overall diagnostic accuracy of around 82.63%, along with PPV (96.69%) and NPV 28.21%, whereas ESR showed sensitivity around 63.79%, specificity 56.25%, and overall accuracy of 63.16%, with PPV (94.07%) and NPV (12.50%), indicating CRP as considerably more reliable diagnostic marker compared to ESR for acute appendicitis, as presented in table III.

Table II: Histopathological findings as per raised ESR and CRP . (n=190)

ESR and CRP findings		Histopathology Result		Total
		Negative	Positive	
ESR	Normal	9	63	72
		4.7%	33.2%	37.9%
	Raised	7	111	118
		3.7%	58.4%	62.1%
Total		16	174	190
		8.4%	91.6%	100.0%
CRP	Normal	11	28	39
		5.8%	14.7%	20.5%
	Raised	5	146	151
		2.6%	76.8%	79.5%
Total		16	174	190
		8.4%	91.6%	100.0%

Discussion

Since acute appendicitis is a most frequent abdominal emergency and a leading cause of hospitalization. However, the, non-invasive markers like as white blood cell count, C-reactive protein, and ESR play an important diagnostic role with varying sensitivity. This study was conducted to prove the better diagnostic accuracy of ESR and CRP for acute appendicitis, taking reference of histopathology. In this study, histopathology confirmed acute appendicitis was in 91.6% patients. he findings of the present study are concordant with those reported by Chaochankit et al, reported lower rates of unnecessary appendectomies (8.6%) in adults.[15] The prevalence reported in our study was some higher than that reported by Khan J et al[16], where histopathology-confirmed acute appendicitis was around 89%, with gangrenous appendicitis 6% and normal appendix was in 5% of the cases. Likewise Khan ZA et al[17] reported a more diverse histopathological spectrum, with acute appendicitis as the leading finding around 51.66%, followed by follicular lymphoid hyperplasia (18.45%), acute appendicitis with periappendicitis (16.61%),

Table III: Diagnostic Accuracy of ESR and CRP for diagnosing acute appendicitis (n=190)

ESR	Formula	Calculation	Result
Sensitivity	TP / (TP + FN)	111 / (111 + 63) = 111/174	63.79%
Specificity	TN / (TN + FP)	9 / (9 + 7) = 9/16	56.25%
PPV	TP / (TP + FP)	111 / (111 + 7) = 111/118	94.07%
NPV	TN / (TN + FN)	9 / (9 + 63) = 9/72	12.50%
Diagnostic Accuracy	(TP + TN) / Total	(111 + 9) / 190	63.16%
CRP			
Sensitivity	TP / (TP + FN)	146 / (146 + 28) = 146/174	83.91%
Specificity	TN / (TN + FP)	11 / (11 + 5) = 11/16	68.75%
PPV	TP / (TP + FP)	146 / (146 + 5) = 146/151	96.69%
NPV	TN / (TN + FN)	11 / (11 + 28) = 11/39	28.21%
Diagnostic Accuracy	(TP + TN) / Total	(146 + 11) / 190	82.63%

acute suppurative appendicitis (4.43%), fibrosis (3.69%), and perforated appendix (2.95%), whereas the normal appendix was only (1.11%). However, inconsistently Donald et al[18] found notable increase in negative appendectomies (up to 38%) in pediatric patients, and thus inconsistency and a substantial higher rate of negative appendectomy, reflect that it was conducted specifically in a pediatric population, a demographic well known to pose a higher diagnostic challenges due to atypical clinical presentations, difficulty in history-taking, and overlapping symptoms with other common illnesses in children.

In line with previously published literature, this study demonstrated that CRP is superior to ESR in diagnosis of acute appendicitis, with CRP to have a sensitivity of 83.91% and specificity of 68.75%, with an overall diagnostic accuracy of around 82.63%, along with PPV (96.69%) and NPV 28.21%**,** whereas ESR showed sensitivity around 63.79%, specificity 56.25%, and overall accuracy of 63.16%, with PPV (94.07%) and NPV (12.50%). These findings are consistent with Kumari et al, who reported CRP sensitivity and specificity of 94.1% and 73.3%, respectively, with diagnostic accuracy of 91%.[19] In contrast, Baig et al reported lower CRP sensitivity (81.63%), specificity (73.58%), and accuracy 79.5% at similar cut off values used in current study.[20] While Khalid et al. demonstrated enhanced diagnostic accuracy when CRP was used in conjunction with Modified Alvarado Score (sensitivity 91.2%, specificity 88.5%).[21] Blok et

al, have studied CRP at different cutoff values and found sensitivity and specificity of CRP at cutoff >0.6/mg/L 90% and 71%, respectively.[14] On the other hand, our results reaffirm the limited diagnostic role of ESR, which showed lower performance across all indices. Comparable findings were reported by Abedi et al, who found ESR sensitivity and specificity 57.1% and 79.4%, and also found CRP has better predictive role accurately diagnosing appendicitis.[22] Paul et al, in contrast found that elevated ESR had high diagnostic accuracy as confirmed by histopathology finding (96.81%).[23] Azadnajafabad et al, found both ESR and CRP, equally effective in predicting complicated appendicitis.[24] Taken together, the evidence suggests that CRP is a more valuable biomarker in the diagnostic workup of suspected acute appendicitis, both in our study and other relevant studies. Its superior sensitivity and specificity make it an important adjunct to clinical scoring systems and imaging modalities, contributing to reduced rates of unnecessary appendectomy and improved patient outcomes. This study has several limitations like diagnostic accuracy of ESR and CRP was not assessed separately in complicated versus non-complicated cases of acute appendicitis, which could have provided more insight into their role across different clinical severities along with the combined diagnostic role of CRP and ESR was not evaluated, nor was their utility assessed at higher Alvarado score cut-off values, where predictive strength might be greater. Hence further studies with larger sample sizes and broader clinical stratification are recommended to address these aspects and to better define the integrated role of inflammatory markers alongside clinical scoring systems in improving diagnostic accuracy and guiding surgical decision-making.

Conclusion

The CRP noted to be a considerably more reliable diagnostic marker compared to ESR for acute appendicitis, with a favorable balance of sensitivity, specificity, and overall accuracy. Whereas the ESR retains some value in ruling in the disease when strongly elevated, its limited ability to rule out appendicitis limits its standalone clinical utility. Overall findings support the incorporation of CRP, as a preferred adjunct inflammatory marker along with clinical assessment and scoring systems in the workup of diagnosis of suspected acute appendicitis, rather than ESR.

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