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RESEARCH ARTICLE

EVALUATING C-REACTIVE PROTEIN AND TOTAL LEUKOCYTE COUNT AS PREDICTIVE MARKERS FOR COMPLICATED APPENDICITIS

Dr. Kundrapu Veera Venkata Siva, Dr. Avanish Kumar Saxena, Dr. Anam Fatima, Dr. Abhishek Yadav, Dr. Khadeeja Tanveer and Dr. Parkar Zainuddin Liyakat

Department of General Surgery, F.H. Medical College and Hospital (FHMCH), Agra, U.P., India.

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Abstract

Background and Aims: Appendicitis is a common surgical emergency, yet it's still difficult to tell the difference between simple and complex cases. More severe forms of appendicitis, such as gangrenous or perforated instances, have worse consequences and need prompt medical attention. In order to distinguish between simple and complex appendicitis, this study sought to assess the diagnostic accuracy of total leukocyte count (TLC) and C-reactive protein (CRP).

Methods: This hospital-based observational research was undertaken at F.H. Medical College, Agra, from September 2022 to March 2024. After obtaining informed permission, 88 patients, ages 18 to 60, who were scheduled for appendectomy were included. To quantify CRP (>60 mg/L) and TLC (>11,000/cumm), blood samples were obtained. For diagnosis, histopathological results constituted the gold standard. SPSS version 25.0 was used to analyze the data, and chi-square and ANOVA tests were used for statistical comparisons. To evaluate the diagnostic performance, Receiver Operating Characteristic (ROC) curves were created, with a significance threshold of $p < 0.05$.

Results: CRP demonstrated superior diagnostic accuracy with an AUC of 0.95 ($p < 0.001$), sensitivity of 85.7%, and specificity of 90.9%. TLC showed an AUC of 0.66 ($p = 0.046$), with 94.4% sensitivity but lower specificity at 37.1%. The projected cut-off for CRP was >94 mg/L and for TLC, >12,222/cumm. CRP also had a higher accuracy (90%) compared to TLC (48.9%).

Conclusion: CRP emerged as a more reliable marker than TLC in predicting complicated appendicitis, with greater diagnostic accuracy and specificity. Larger multi-center studies are recommended to further validate these findings and establish universal cut-off values.

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Introduction:-

Appendicitis is one of the most common surgical emergencies worldwide, characterized by inflammation of the vermiform appendix.¹ While acute appendicitis can be effectively treated, distinguishing between uncomplicated and complicated appendicitis remains a challenge for clinicians.² Complicated appendicitis, which includes conditions like gangrenous or perforated appendicitis, often leads to worse outcomes and requires urgent surgical

Corresponding Author:- Dr. Avanish Kumar Saxena

Address:- Department of General Surgery, F.H. Medical College and Hospital (FHMCH), Agra, U.P., India.

intervention.³ Complications such as appendicular abscess or perforation occur in a significant number of untreated cases, contributing to increased morbidity and mortality rates.⁴

Despite advances in imaging and clinical evaluation techniques, reliable differentiation between uncomplicated and complicated appendicitis remains a dilemma, particularly in vulnerable populations such as children and the elderly.⁵ Over the years, non-invasive preoperative methods, including laboratory investigations and imaging, have been utilized to assess the severity of appendicitis.⁶ Among these, C-reactive protein (CRP) and total leukocyte count (TLC) have emerged as key markers due to their accessibility, ease of interpretation, and cost-effectiveness. Elevated levels of CRP and TLC are commonly associated with complicated cases, highlighting their role in predicting severe inflammation, necrosis, and perforation.⁷

The aim of the study is to compare the diagnostic accuracy of TLC and CRP in differentiating between simple and complex appendicitis. The study aims to improve clinical decision-making, lower diagnostic ambiguity, and eventually improve patient outcomes by concentrating on these commonly available and utilized laboratory markers. The results of this study might help determine a safe, non-invasive method for estimating the degree of appendicitis, which would facilitate prompt and suitable surgical surgery.

Materials and Methods:-

The general surgery department of the F.H. Medical College and Hospital (FHMCH), in Agra, was the site of this hospital-based observational research. Serving mostly socioeconomically disadvantaged individuals from suburban and rural areas, FHMCH is a 650-bed tertiary care facility. The study was carried out from September 2022 to March 2024, a period of eighteen months.

Study Population:

The research comprised individuals with appendicitis symptoms who were scheduled for an appendectomy and who were between the ages of 18 and 60 when they visited the emergency room or the department of surgery. The study included 88 patients in all who fulfilled the inclusion criteria.

Inclusion Criteria:

1. Patients scheduled for appendectomy.
2. Age between 18 and 60 years.
3. Both male and female patients.
4. Patients who provided informed consent.

Exclusion Criteria:

1. Patients on corticosteroid therapy.
2. Patients with systemic inflammatory diseases.
3. Patients with recent infections, or positive for HIV, HBsAg, or HCV.
4. Pregnant patients.

Ethical Approval:

The F.H. Medical College, Agra Institutional Ethical Committee provided ethical approval. Before each person was included in the study, their informed permission was obtained.

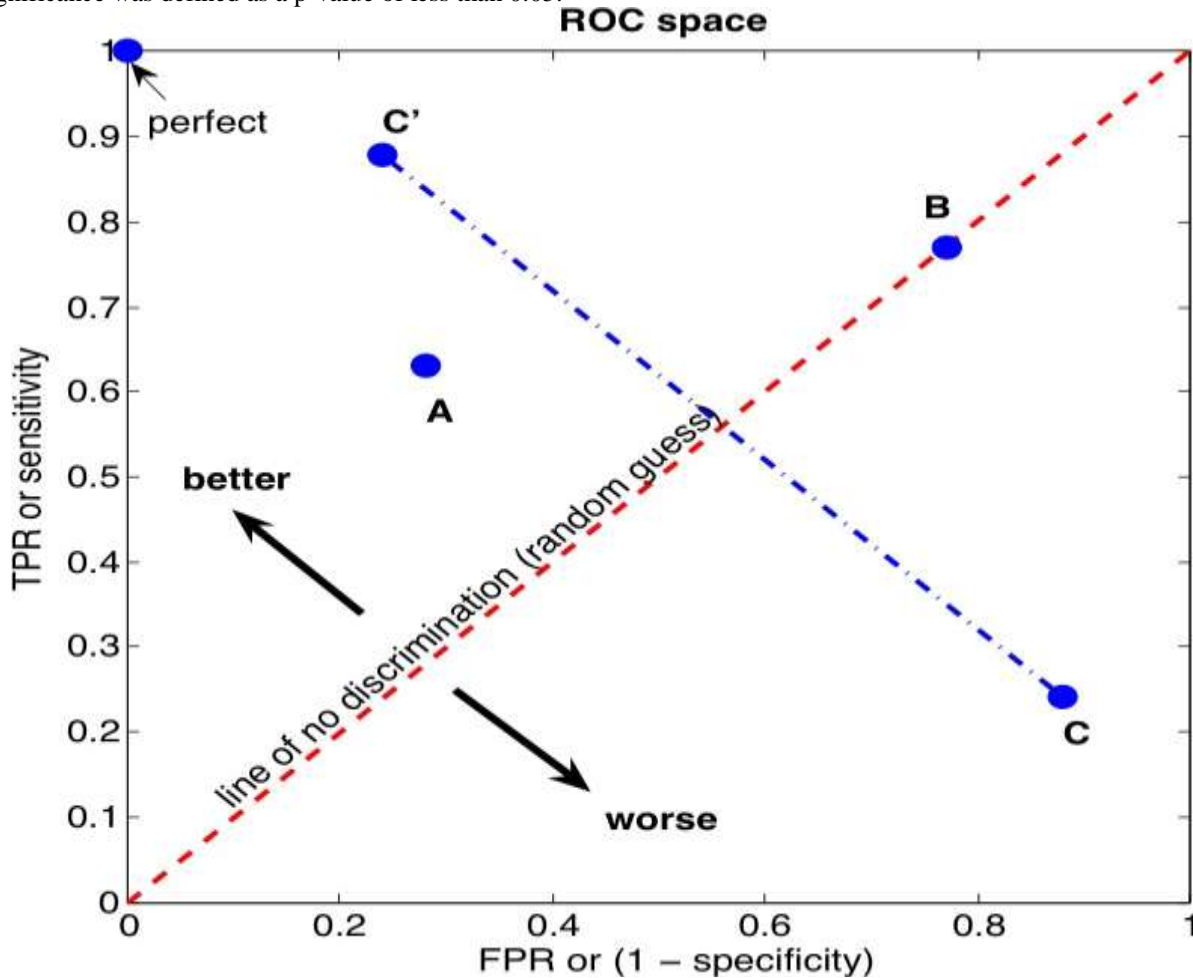
Methodology:-

The patients' clinical history, presenting symptoms, and demographic information were all noted. An abdominal ultrasound was performed on each patient as part of the preoperative evaluation. Prior to surgery, blood samples were taken for the measurement of total leukocyte count (TLC) and C-reactive protein (CRP). TLC was set at $>11,000/\text{cumm}$ and the CRP threshold at $>60 \text{ mg/L}$.

Every patient had an appendectomy, and the results of the procedure were recorded. Histopathological analysis, the gold standard for determining the type of appendicitis—complex or simple—was performed on the excised appendix.

Statistical Analysis:

Version 25.0 of SPSS was used to analyze the data. To describe the data, descriptive statistics like mean, standard deviation (SD), and percentages were employed. The Chi-square test for categorical data and independent t-tests for comparing means were examples of inferential statistics. To compare variations between groups, an ANOVA was employed. The diagnostic efficacy of TLC and CRP in predicting complex appendicitis was evaluated by the creation of Receiver Operating Characteristic (ROC) curves. We computed accuracy, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and negative predictive value. Statistical significance was defined as a p-value of less than 0.05.



Results:-

Table 1:- Comparison of Age, Sex, Haematological, and Biochemical Parameters Among Histopathological Categories.

Characteristic	Normal (n=8)	Uncomplicated (n=62)	Complicated (n=18)	Statistical Significance (ANOVA/Chi-square)
Mean Age ± SD (Years)	29.13 ± 5.82	32.02 ± 8.79	28.28 ± 5.89	F=1.731; p=0.183
Sex (Male)	5 (62.5%)	31 (50.0%)	14 (77.8%)	$\chi^2=4.503$; p=0.105
Sex (Female)	3 (37.5%)	31 (50.0%)	4 (22.2%)	
Mean Hb ± SD (g/dl)	11.05 ± 2.06	10.75 ± 2.00	10.22 ± 1.80	F=0.679; p=0.510
Mean TLC ± SD (thousands/cumm)	10.5 ± 2.78	13.67 ± 2.96	14.94 ± 2.49	F=6.72; p=0.002
Mean Platelet Count ± SD (Lakhs/cumm)	2.24 ± 0.60	2.19 ± 0.52	2.12 ± 0.56	F=0.141; p=0.858

Mean CRP ± SD (mg/L)	36.63 ± 13.62	68.73 ± 20.00	125.3 ± 40.73	F=46.71; p<0.001
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This table compares the age, sex, and various haematological and biochemical parameters among different histopathological categories. Notably, mean TLC and CRP levels show statistically significant differences across groups, with the highest levels observed in the complicated cases.

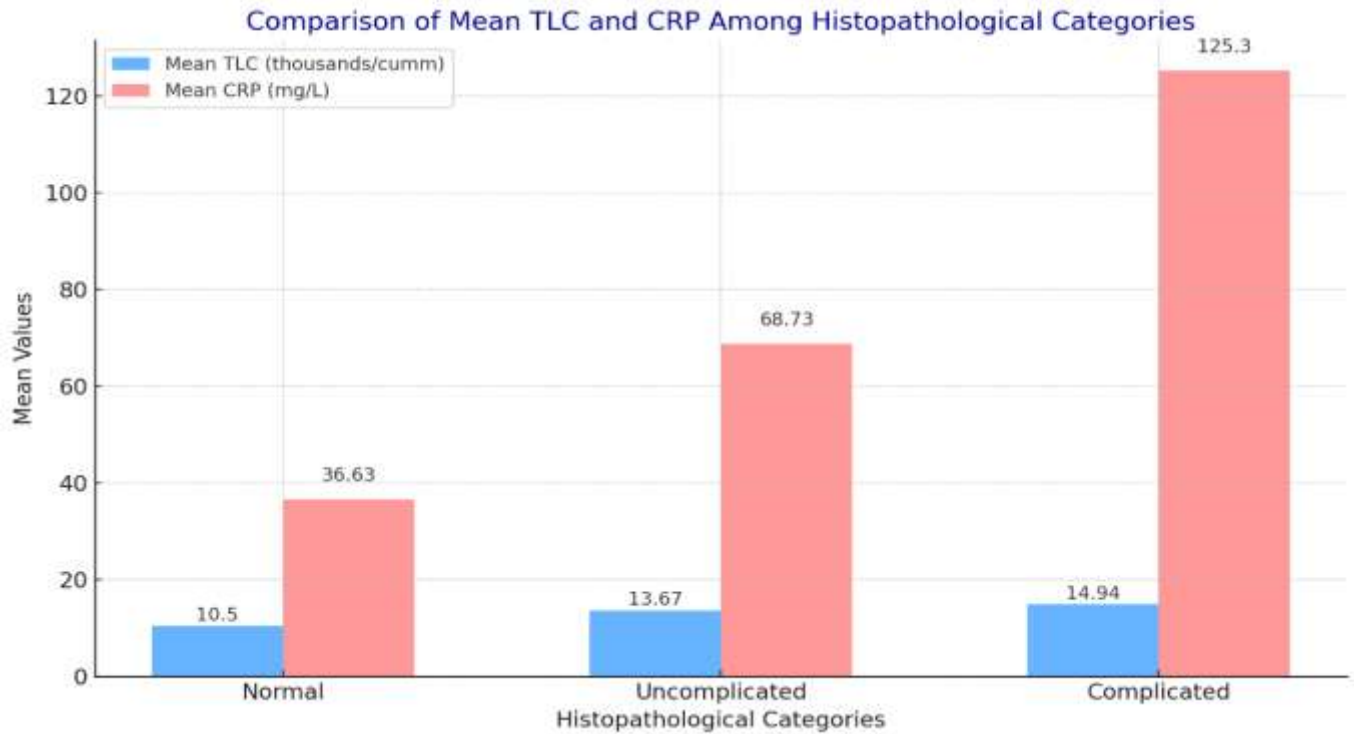


Table 2:- Comparative Distribution of Cases by Sonographic, Intraoperative, and Histopathological Diagnoses.

Diagnosis	Sonographic (%)	Intraoperative (%)	Histopathological (%)
Normal	0.0	5.7	9.1
Uncomplicated	86.3	81.8	70.5
- Inflamed	69.3	64.8	55.7
- Suppurative	17.1	17.0	14.8
Complicated	13.7	12.5	15.9
- Necrotizing	4.6	1.1	4.5
- Gangrenous	2.3	5.7	9.1
- Perforated	4.6	4.5	5.7
- Peritonitis	2.3	1.1	1.1

This table presents a horizontal comparison of the distribution of normal, uncomplicated, and complicated appendicitis cases across sonographic, intraoperative, and histopathological diagnoses. It highlights that uncomplicated cases were most frequently observed across all diagnostic methods, while the detection of complicated cases, particularly necrotizing and gangrenous types, showed variation among the methods.

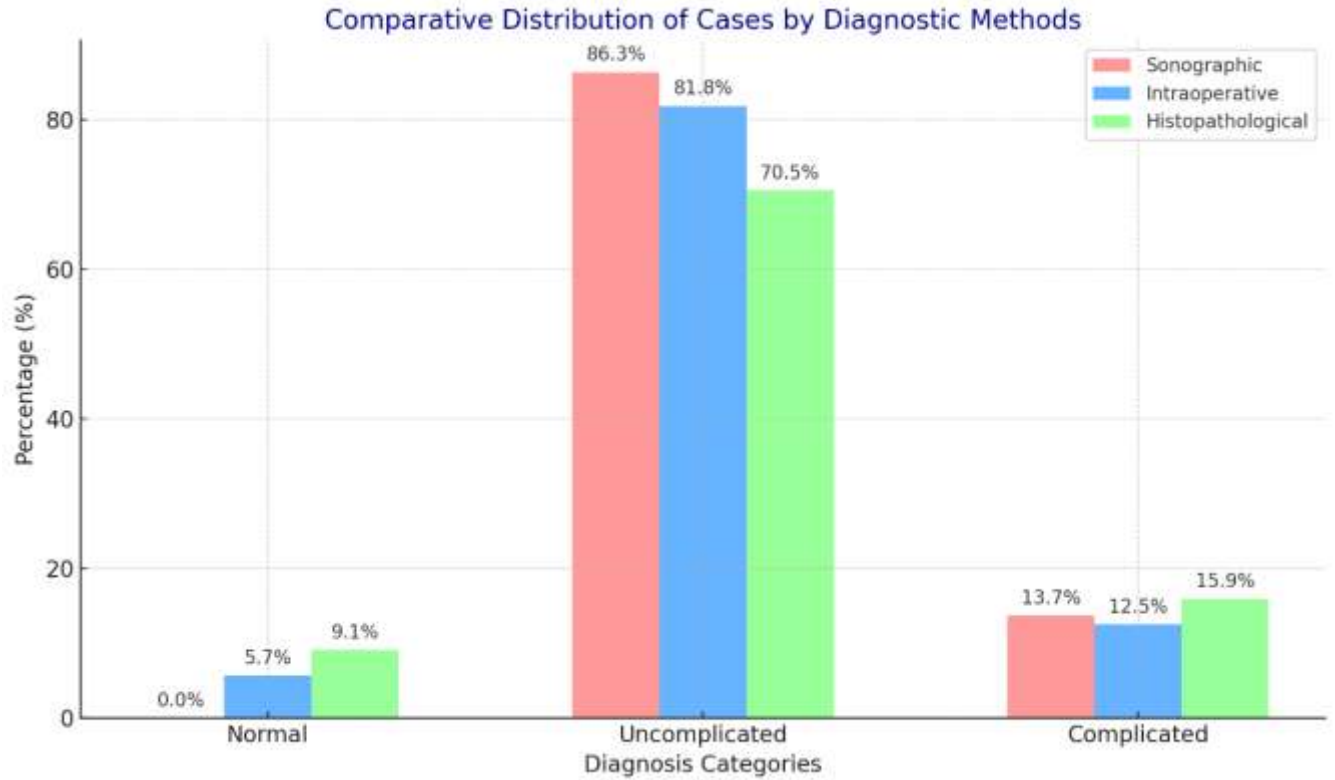


Table 3:- Evaluation of diagnostic efficacy of TLC and CRP in diagnosis ruling out negative appendectomy.

TLC	Histopathological diagnosis		Total	
	Positive	Negative		
>11000/cumm	69	5	74	
<11000/cumm	11	3	14	
	80	8	88	
Sensitivity	Specificity	PPV	NPV	Accuracy
86.3%	37.5%	93.2%	21.4%	81.8%

CRP	Histopathological diagnosis		Total	
	Positive	Negative		
>60 mg/L	57	0	57	
<60 mg/L	23	8	31	
	80	8	88	
Sensitivity	Specificity	PPV	NPV	Accuracy
71.3%	100%	100%	25.8%	73.9%

This table evaluates the diagnostic efficacy of TLC and CRP in ruling out negative appendectomy. TLC showed higher sensitivity but lower specificity compared to CRP. CRP, with 100% specificity, proves to be more effective in ruling out false negatives, while TLC had a higher positive predictive value.

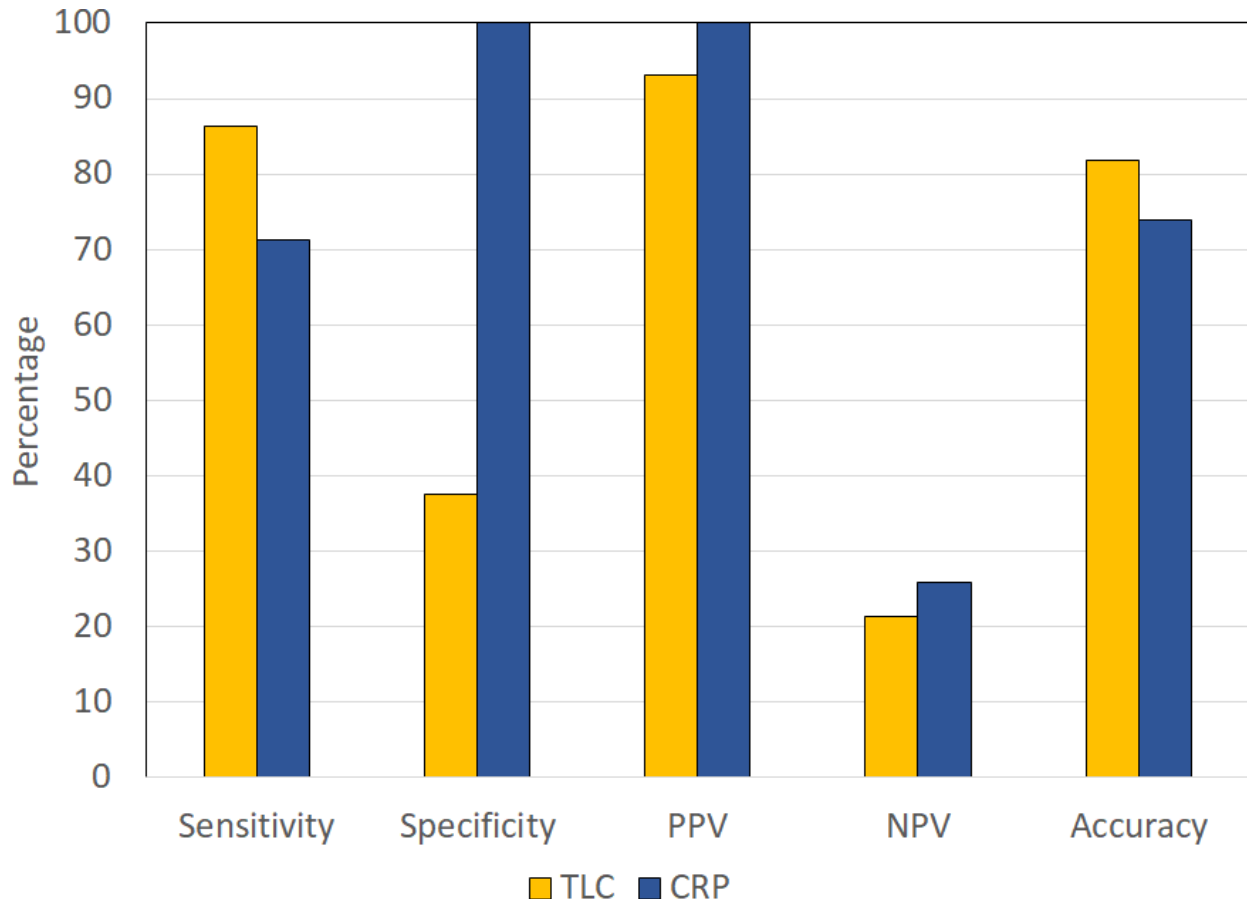
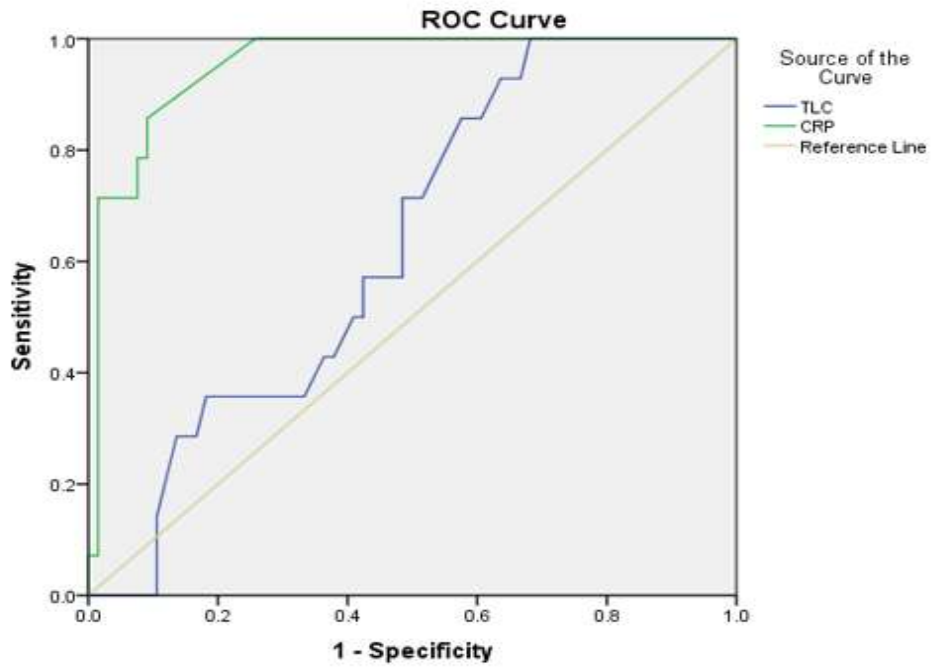


Table 4:- Receiver-Operator Characteristic (ROC) Analysis for Discriminating Between Uncomplicated and Complicated Appendicitis.

Parameter	AUC ± SE	Youden Index (J)	Projected Cut-off Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
TLC	0.66 ± 0.07 (p=0.046)	0.318	>12,222/cumm	94.4	37.1	27.9	96.3	48.9
CRP	0.95 ± 0.02 (p<0.001)	0.766	>94 mg/L	85.7	90.9	66.7	96.8	90.0

This table represents the ROC analysis for TLC and CRP as diagnostic markers to discriminate between uncomplicated and complicated appendicitis. CRP demonstrates higher accuracy and a larger AUC, making it a more reliable marker compared to TLC in predicting complicated appendicitis.



Diagonal segments are produced by ties.

(a)



Gross appearance of inflamed appendix intra-operatively (IPD NO-23011116)

(b)



Inflamed Appendix (IPDNO-230302021)
(c)



Inflamed Appendix (IPDNO-230614052)
(d)



Laparoscopic procedure showing gross appearance of perforated and gangrenous Appendix (IPDNO-230204009)
(e)



Gangrenous Appendix (IPD NO-221201003)

Discussion:-

The pre-operative assessment of appendicitis is critical for reducing complications, improving outcomes, and enhancing healthcare efficiency. Accurate diagnosis, involving clinical evaluations, imaging, and laboratory markers such as total leukocyte count (TLC) and C-reactive protein (CRP), plays a significant role in detecting the severity of the condition. Early identification of high-risk patients allows timely surgical intervention, which can prevent complications like perforation, abscesses, and sepsis, ensuring better postoperative recovery.

In our study, we evaluated TLC and CRP in distinguishing between complicated and uncomplicated appendicitis. Of the 88 patients studied, 70.5% had uncomplicated appendicitis, and 20.5% had complicated appendicitis. We found that TLC had a sensitivity of 86.3% and a specificity of 37.5% at a predefined cut-off of $>11,000/\text{cumm}$ for diagnosing appendicitis, whereas CRP showed higher accuracy, with 71.3% sensitivity and 100% specificity at $>60 \text{ mg/L}$ for identifying positive appendicectomy. Additionally, CRP had a projected cut-off value of $>94 \text{ mg/L}$ with 85.7% sensitivity and 90.9% specificity for differentiating complicated appendicitis.

Various studies have reported findings in line with our observations. **Dnyanmote et al.⁸ (2018)** found a sensitivity of 76.8% and a specificity of 68.4% for TLC, similar to **Pun et al.⁹ (2020)** and **Alsubaiee and Al-Kinany¹⁰ (2020)**, who reported sensitivities above 80% but varying specificities. However, in our study, TLC showed lower specificity, aligning with studies where TLC was more sensitive than specific for detecting appendicitis. **Rajashekhhar et al.¹¹ (2022)** also reported 100% sensitivity and 44.2% specificity for TLC in differentiating complicated cases, reflecting its limited accuracy in distinguishing complicated from uncomplicated appendicitis.

For CRP, our findings are consistent with earlier studies. **Pun et al.⁹ (2020)** reported a sensitivity of 95.5% and specificity of 75% at a CRP cut-off of $>6 \text{ mg/dl}$, while **Alsubaiee and Al-Kinany¹⁰ (2020)** observed 90.2% sensitivity and 82.3% specificity at a cut-off of $>10 \text{ mg/dl}$. However, our study identified a higher cut-off of $>94 \text{ mg/L}$ for complicated appendicitis, with better specificity, which reflects the need for study-specific cut-off values. **Choudhary et al.¹² (2019)** and **Khatoun et al.¹³ (2020)** also reported lower cut-offs for CRP, resulting in higher sensitivity but lower specificity due to false positives.

In conclusion, while TLC is useful for its sensitivity, CRP proves to be a more reliable marker for diagnosing complicated appendicitis with higher specificity. The need for universal cut-off values, especially for CRP, is evident, and larger studies are recommended to validate these findings.

Strengths and Limitations

This study's strength lies in its use of both TLC and CRP, along with histopathology as a gold standard, providing a reliable diagnostic evaluation. It also offers practical insights for clinical use in appendicitis cases. However,

limitations include a small sample size and single-center design, which may affect the generalizability of the findings. Larger, multi-center studies are needed to validate the results and establish standardized cut-off values.

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Conclusion:-

The study demonstrated that both TLC and CRP were useful markers in diagnosing appendicitis, with CRP proving to be more reliable in distinguishing between uncomplicated and complicated cases. While TLC had a higher sensitivity (86.3%) for ruling out negative appendectomy, its specificity was lower (37.5%), which limited its overall effectiveness. In contrast, CRP showed 100% specificity, making it highly effective in avoiding false negatives, even though its sensitivity was slightly lower at 71.3%. The ROC analysis further reinforced the superior diagnostic performance of CRP, with an AUC of 0.95 compared to 0.66 for TLC, indicating better accuracy in predicting complicated appendicitis. A CRP cut-off of >94 mg/L provided a sensitivity of 85.7% and specificity of 90.9%, while the TLC cut-off of >12,222/cumm, although more sensitive, lacked specificity. The study concluded that CRP was a more dependable marker for identifying complicated cases, offering improved diagnostic accuracy and assisting in more effective treatment planning.

Conflict of Interest:

The authors confirm there are no conflicts of interest.

Funding:

The study did not receive any financial support.

Consent:

Written informed consent was obtained from all participants and securely archived.

Ethical Approval:

The study received ethical clearance, adhering to the required institutional protocols.

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