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Triple Assessment of Acute Appendicitis: A Better Diagnostic Modality

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Abstract: ***Introduction: Acute appendicitis is one of the most common surgical emergencies and the most common source of infection in community-acquired intra-abdominal infections. Its diagnosis is usually made depending on the presenting history, clinical evaluation, and physical examination. It is further reinforced by laboratory investigations, such as white blood cells, differential counts (the percentage of neutrophil granulocytes and band neutrophil granulocytes) and C-reactive protein (CRP). Aims and Objectives: To compare the efficacy of clinical impression, biochemical markers (CRP, NLR, TLC) C-reactive protein, and radiological imaging with HPR in the diagnosis of Acute Appendicitis. Results: In the study among 91 subjects with appendicitis by HPE, 75.8% were diagnosed by Biochemistry, 85.7% were diagnosed by Radiology, 68.1% were diagnosed by Clinical and 85.7% were diagnosed by Combined methods. Among 9 subjects without Appendicitis by HPE, 100% were diagnosed as negative by biochemistry, 88.9% were diagnosed as negative by Radiology, 100% were diagnosed as negative by Clinical, 11.1% were diagnosed as negative by combined methods. Combined methods had sensitivity of 85.71%, specificity of 88.89%, PPV of 98.73%, NPV of 38.1% and Diagnostic Accuracy of 86%. Agreement of combined methods with HPE Diagnosis was 0.4661 [Moderate agreement]. Conclusion: The diagnosis of appendicitis in this study showed us No single clinical or laboratory test is able to reliably predict acute appendicitis. USG of the abdomen had an important role in the diagnosis of appendicitis with significant sensitivity, specificity, and PPV. Use of triple assessment for acute appendicitis using laboratory investigations and USG imaging as an adjunct to clinical diagnosis will help to diagnose acute appendicitis in patients with RIF pain.***

Keywords: Acute Appendicitis, Triple assessment, Biochemistry, Radiology

1. Introduction

Acute appendicitis is one of the most common surgical emergencies and the most common source of infection in community-acquired intra-abdominal infections. Its diagnosis is usually made depending on the presenting history, clinical evaluation, and physical examination. It is further reinforced by laboratory investigations, such as white blood cells, differential counts (the percentage of neutrophil granulocytes and band neutrophilgranulocytes) and C-reactive protein (CRP) that were the only diagnostic tools for many years. It has been estimated that the accuracy of the clinical diagnosis of acute appendicitis is only between 76 percent and 92 percent. Thus, accurate diagnosis of acute appendicitis is still difficult. The perforation rate is high, as well as the number of negative appendectomies. Following the introduction of ultrasound scans during the last two decades and computed tomography (CT) in the last decade, the rate of negative appendectomies has decreased, but the perforation rate has remained high (22%-62%). Negative appendectomies are one of the burdens facing not only the general surgeon but also the patient her/himself and society as a whole, since appendectomy, as any other operation, results in socio-economic impacts in the form of lost working days and declinedproductivity.3

A delay in diagnosis can lead to appendicular perforation with increased morbidity, and an appendectomy as soon as the condition is suspected, may increase the number of unnecessary appendectomies. A number of clinical and laboratory-based scoring systems such as the Alvarado score, Tzanakis score, etc., have been devised to assist the diagnosis. Atypical histories require imaging with ultrasound and/or computed tomography scanning. In practice, the diagnosis of Acute Appendicitis is supported by the presence of elevated inflammatory markers, that is, white cell count and CRP. However, some studies have shown that neither of these markers is diagnostic nor specific for Acute appendicitis.7

Acute appendicitis affects 1.5–1.9individuals in a population of 100, 000 and is1.4 times more common in men. The lifetime risk of suffering from acute appendicitis is 7%, with perforation rates being 17%–20%. The mortality risk of this condition is less than 1%in the general population but can rise to 50%among the elderly population [2].

Diagnostic scoring systems have been developed in an attempt to improve the diagnostic accuracy of acute appendicitis. Although these scores can help guide clinical thinking, they do not markedly improve diagnostic accuracy. However, these diagnostic adjuncts may be expensive, may involve high radiation exposure, and may not always have accurate and reproducible results.1

Assessment of appendix diameter and complete blood count parameters can be used together to increase the diagnostic value of Acute Appendicitis. The present study was undertaken to reach an accurate diagnosis in the fastest and cheapest way.1[0]

2. Aims and Objectives

To compare the efficacy of clinical impression, biochemical markers (CRP, NLR, TLC) c-reactive Protein, and

radiological imaging with HPR in the diagnosis of Acute Appendicitis

3. Methods and Materials

a) Design of study& number of subjects –Cross Sectional study & 100 subjects
b) Mode of selection of subjects-Any patient presenting to OPD or casualty with symptoms of Acute appendicitis
c) Equipment / procedure and other material to be used-Biochemical markers and Ultrasonography will be done
d) Statistical methods: Softwares such as MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to code and analyse data. P value <0.05 will be considered as statistically significant.

The setting was the department of surgery of a tertiary health care centre in South India. The main objectives were to compare clinical examination, biochemical investigations (CRP, NLR, TLC) and the role of USG in various aetiologies of RIF pain with special reference to appendicitis.

All patients who presented to the casualty with complaints of RIF pain and were referred to the surgery team were studied. Patients who were pregnant, patients with RIF mass/abscess at presentation, patients with history of previous appendicectomy were excluded from this study. Informed consent was obtained from the patients. Detailed history and per abdomen findings were noted. All patients underwent a routine USG. Acute appendicitis was diagnosed on USG when the diameter of the appendix was >6 mm and the appendix was tender and incompressible, associated with hypertrophy of the peri-appendicular fat. Blood samples were collected from all patients for CRP levels, TLC, NLR.

Patients with definitive diagnosis of appendicitis were posted for emergency appendicectomy and postoperative histopathology reports were followed up. Patients with alternative diagnosis based on clinical or USG abdomen findings were treated accordingly or referred to relevant specialities. Patients with equivocal diagnosis were observed and discharged once their pain resolved. Patients with RIF mass formation were managed conservatively and called for interval appendicectomy.

Patients who came with recurrent pain were assessed and subjected to appendicectomy if they had signs suggestive of acute appendicitis.

Postoperative histology reports were classified as having acute uncomplicated appendicitis (simple/resolving), complicated appendicitis (perforated/gangrenous/chronic appendicitis) or as histologically normal appendix.

During the final analysis, the patients were divided into two groups. Group one (appendicitis group) included all proven cases of appendicitis by histology. Group two (non – appendicitis group) included all the patients with an alternative cause for RIF pain, the patients with histologically normal appendix.

The clinical features, biochemical parameters, and USG findings were compared between the two groups. The correlation between patients with simple appendicitis and complicated appendicitis with respect to their clinical features and biochemical parameters were also analysed.

4. Results

In the study among 91 subjects with appendicitis by HPE, 75.8% were diagnosed by Biochemistry, 85.7% were diagnosed by Radiology, 68.1% were diagnosed by Clinical and 85.7% were diagnosed by combined methods. Among 9 subjects without Appendicitis by HPE, 100% were diagnosed as negative by biochemistry, 88.9% were diagnosed as negative by Radiology, 100% were diagnosed as negative by Clinical, 11.1% were diagnosed as negative by Combined methods. Combined methods had sensitivity of 85.71%, specificity of 88.89%, PPV of 98.73%, NPV of 38.1% and Diagnostic Accuracy of 86%. Agreement of combined methods with HPE Diagnosis was 0.4661 [Moderate agreement].

Table 1: General Profile of subjects in the study

		Count	Column, N %
Age	<10 years	4	4.00%
	11 to 20 years	27	27.00%
	21 to 30 years	33	33.00%
	31 to 40 years	18	18.00%
	41 to 50 years	7	7.00%
	51 to 60 years	8	8.00%
	>60 years	3	3.00%
Gender	Female	28	28.00%
	Male	72	72.00%
Diagnosis	Acute Appendicitis	96	96.00%
	Appendicular Perforation	4	4.00%
Anaesthesia	GA	18	18.00%
	SA	82	82.00%
Procedure	Lap	11	11.00%
	Open	89	89.00%

Mean age of subjects was 29.23±14.255 Years. In the study majority of subjects were in the age group 21 to 30 years (33%), 72% were males and 28% were females.96% had acute appendicitis and 4% had Appendicular Perforation.82% were given Spinal anaesthesia and 18% had General anaesthesia.89% underwent Open surgery and 11% underwent Laparoscopic surgery.

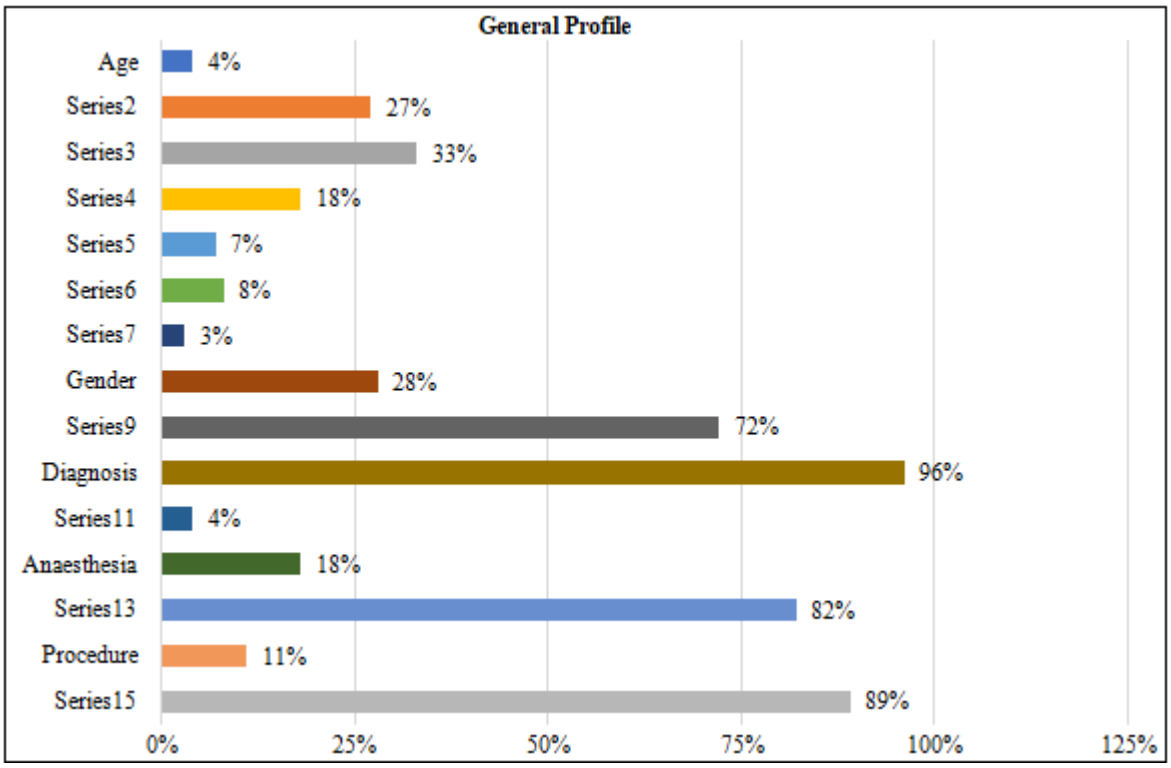

Figure 1: Bar diagram showing General Profile of subjects in the study

Table 2: Diagnosis of Appendicitis by various modalities

	Positive		Negative	
	Count	Row N %	Count	Row N %
Histopathology	91	91.00%	9	9.00%
Biochemistry	69	69.00%	31	31.00%
Radiology	79	79.00%	21	21.00%
Clinical	62	62.00%	38	38.00%
Combined	79	79.00%	21	21.00%

In the study on HPE, 91% were diagnosed as acute appendicitis. From Biochemistry, 69% were diagnosed as acute appendicitis, from Radiology, 79% were diagnosed as acute appendicitis, from clinical methods, 62% were diagnosed as acute appendicitis and from combined methods, 79% were diagnosed as acute appendicitis.

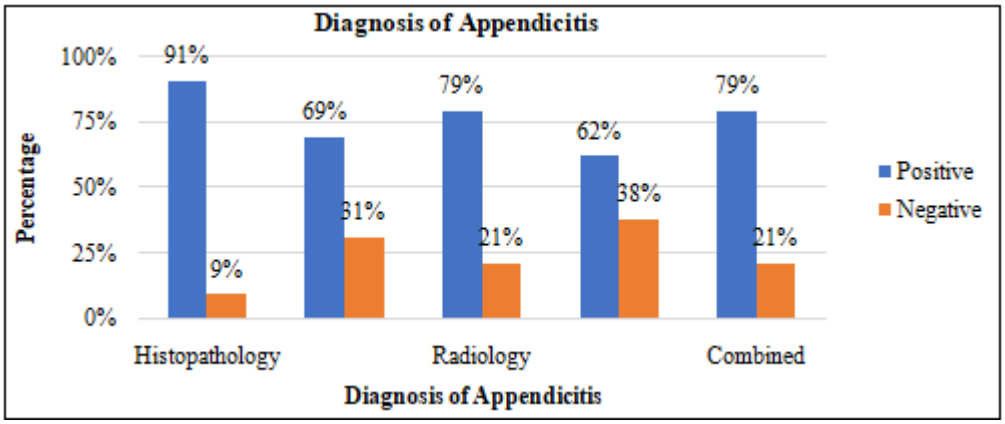

Figure 2: Bar diagram showing Diagnosis of Appendicitis by various modalities

Table 3: Association of Biochemistry, Radiology, Clinical and combined methods in diagnosis of Acute appendicitis in comparison with Gold standard Histopathological examination

		Histopathology				P value
		Positive		Negative		
		Count	Column N %	Count	Column N %	
Biochemistry	Positive	69	75.80%	0	0.00%	<0.001*
	Negative	22	24.20%	9	100.00%	
Radiology	Positive	78	85.70%	0	0.00%	<0.001*
	Negative	13	14.30%	9	100.00%	
Clinical	Positive	62	68.10%	0	0.00%	<0.001*
	Negative	29	31.90%	9	100.00%	
Combined	Positive	78	85.70%	0	0.00%	<0.001*
	Negative	13	14.30%	9	100.00%	

In the study among 91 subjects with appendicitis by HPE, 75.8% were diagnosed by Biochemistry and among 9 subjects without Appendicitis by HPE, 100% were diagnosed as negative by biochemistry. There was significant association between Biochemistry diagnosis and HPE diagnosis.

In the study among 91 subjects with appendicitis by HPE, 85.7% were diagnosed by Radiology and among 9 subjects without Appendicitis by HPE, 100% were diagnosed as negative by Radiology. There was significant association between Radiology diagnosis and HPE diagnosis.

In the study among 91 subjects with appendicitis by HPE, 68.1% were diagnosed by Clinical and among 9 subjects without Appendicitis by HPE, 100% were diagnosed as negative by Clinical. There was significant association between Clinical diagnosis and HPE diagnosis.

In the study among 91 subjects with appendicitis by HPE, 85.7% were diagnosed by Combined methods and among 9 subjects without Appendicitis by HPE, 100% were diagnosed as negative by Combined methods. There was significant association between combined methods and HPE diagnosis.

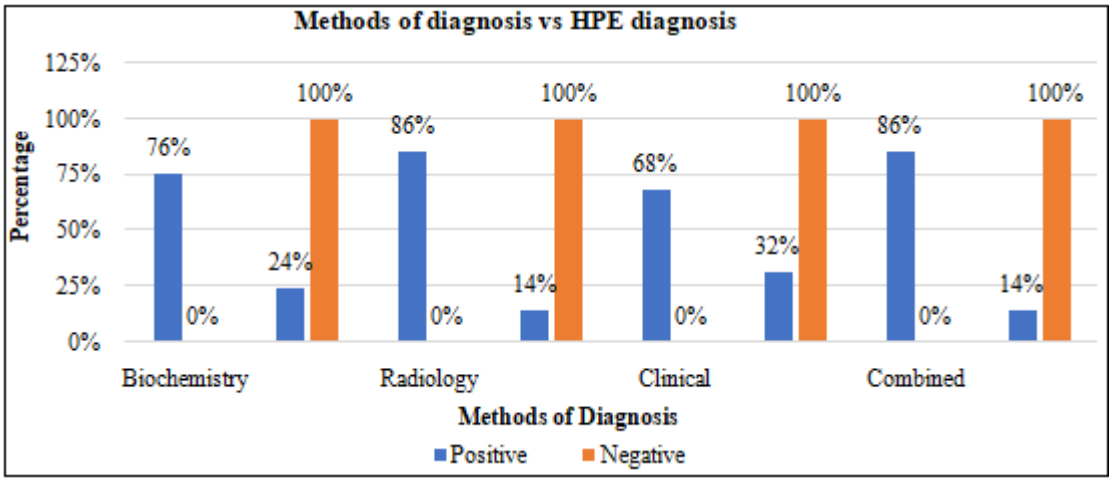

Figure 3: Bar diagram showing Association of Biochemistry, Radiology, Clinical and combined methods in diagnosis of Acute appendicitis in comparison with Gold standard Histopathological examination

Table 4: Validity of Biochemistry diagnosis of acute appendicitis in comparison with HPE

Parameter	Estimate	Lower-Upper 95% CIs
Sensitivity	75.82%	66.1, 83.46
Specificity	100%	70.08, 100
Positive Predictive Value	100%	94.73, 100
Negative Predictive Value	29.03%	16.1, 46.59
Diagnostic Accuracy	78%	68.93, 85
Cohen's kappa (Unweighted)	0.3608	0.2101-0.5116

In the study Biochemistry had sensitivity of 75.82%, specificity of 100%, PPV of 100%, NPV of 29.03% and Diagnostic Accuracy of 78%. Agreement of Biochemistry with HPE Diagnosis was 0.3608 [Fair agreement].

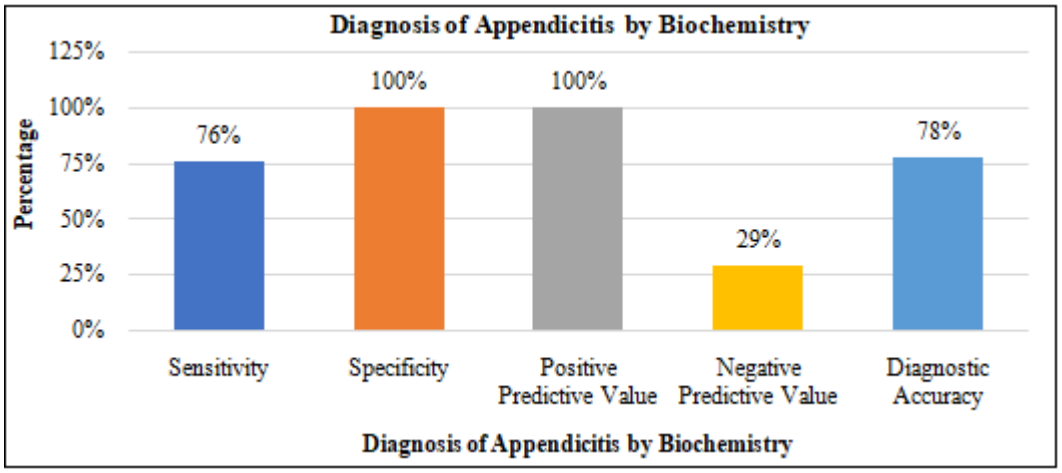

Figure 4: Bar diagram showing Validity of Biochemistry diagnosis of acute appendicitis in comparison with HPE

Table 5: Validity of Radiological diagnosis of acute appendicitis in comparison with HPE

Parameter	Estimate	Lower-Upper 95% CIs
Sensitivity	85.71%	77.08, 91.46
Specificity	100%	70.08, 100
Positive Predictive Value	100%	95.31, 100
Negative Predictive Value	40.91%	23.26, 61.27
Diagnostic Accuracy	87%	79.02, 92.24
Cohen's kappa (Unweighted)	0.5192	0.3474-0.6911

In the study Radiological methods had sensitivity of 85.71%, specificity of 100%, PPV of 100%, NPV of 40.91% and Diagnostic Accuracy of 87%. Agreement of Radiological methods with HPE Diagnosis was 0.519 [Moderate agreement].

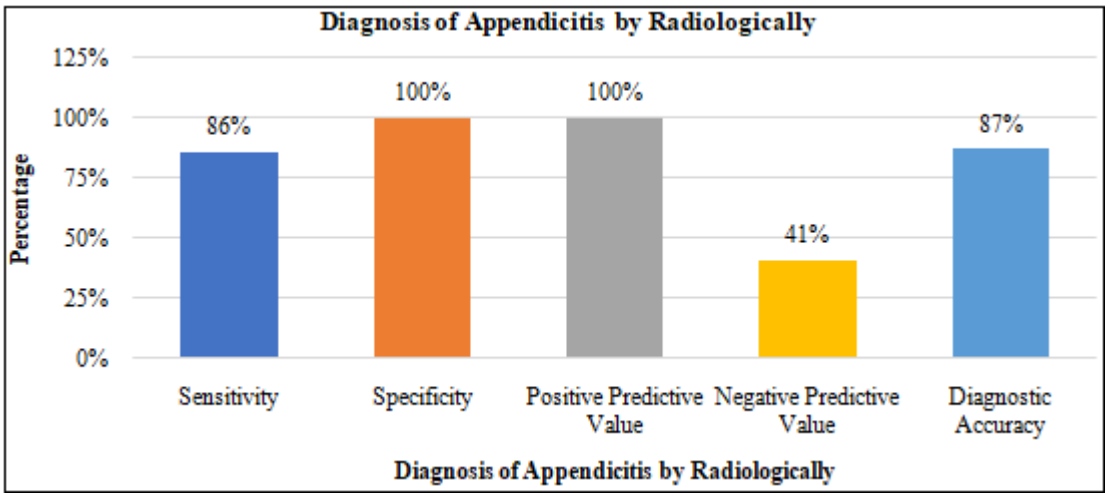

Figure 5: Bar diagram showing Validity of Radiological diagnosis of acute appendicitis in comparison with HPE

Table 6: Validity of Clinical diagnosis of acute appendicitis in comparison with HPE

Parameter	Estimate	Lower-Upper 95% CIs
Sensitivity	68.13%	57.99, 76.8
Specificity	100%	70.08, 100
Positive Predictive Value	100%	94.17, 100
Negative Predictive Value	23.68%	12.99, 39.21
Diagnostic Accuracy	71%	61.46, 78.99
Cohen's kappa (Unweighted)	0.2779	0.1423-0.4135

In the study Clinical methods had sensitivity of 85.71%, specificity of 88.89%, PPV of 98.73%, NPV of 38.1% and Diagnostic Accuracy of 86%. Agreement of Radiological methods with HPE Diagnosis was 0.4661 [Moderate agreement].

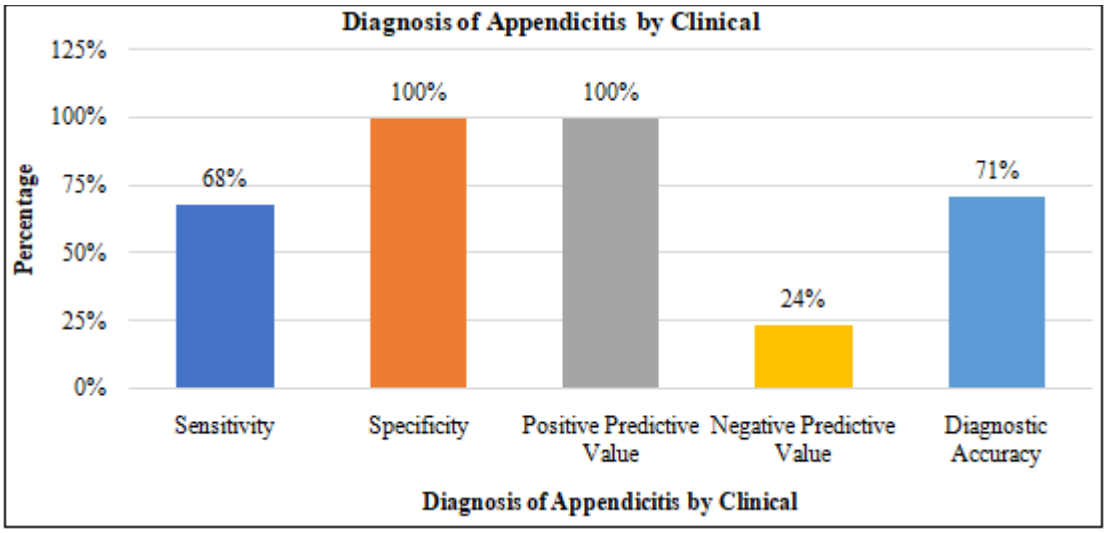

Figure 6: Bar diagram showing Validity of Clinical diagnosis of acute appendicitis in comparison with HPE

Table 7: Validity of Combined diagnosis [Biochemistry, Radiological and Clinical diagnosis] of acute appendicitis in comparison with HPE

Parameter	Estimate	Lower-Upper 95% CIs
Sensitivity	85.71%	77.08, 91.46
Specificity	100%	70.08, 100
Positive Predictive Value	100%	95.31, 100
Negative Predictive Value	40.91%	23.26, 61.27
Diagnostic Accuracy	87%	79.02, 92.24
Cohen's kappa (Unweighted)	0.5192	0.3474-0.6911

In the study combined methods had sensitivity of 85.71%, specificity of 100%, PPV of 100%, NPV of 40.91% and Diagnostic Accuracy of 87%. Agreement of Radiological methods with HPE Diagnosis was 0.519 [Moderate agreement].

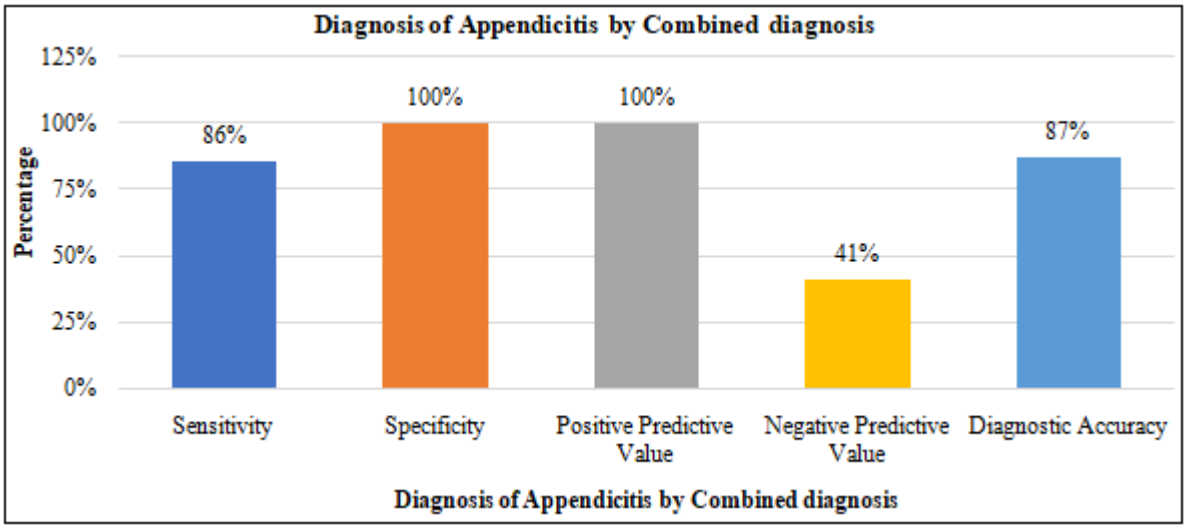

Figure 7: Bar diagram showing Validity of Combined diagnosis [Biochemistry, Radiological and Clinical diagnosis] of acute appendicitis in comparison with HPE

5. Discussion

Though the majority of patients presenting to the hospital with RIF pain had a diagnosis of appendicitis, non-specific RIF pain was also a common cause of RIF pain. The male to female ratio among patients who presented with RIF pain in this study was 18: 7 with a male preponderance. This was similar to the results of the study by Buckius et al. [16]. The rate of appendicular perforation ranged between 18.3 and 34.0% in different studies [17]. In the present study, a perforated/gangrenous appendix was found in 4% of patients with appendicitis.

The Alvarado score has been used commonly as a diagnostic tool for appendicitis, and Chan et al. have also suggested the Alvarado score as a screening method for admission as inpatients [18]. Its high sensitivity (90.3%) supported its value as a screening tool for probable appendicitis and admission. The utility of CRP in diagnosing appendicitis has been evaluated in many studies. Negative CRP levels would most likely be associated with normal appendix [19]. In contrary, Amalesh T et al. showed that the sensitivity, specificity, PPV, and NPV for CRP in appendicitis was 91%, 42%, 88%, and 48%, respectively, and that it may not be a useful tool to surgeons [20].

When CRP was taken alone, the positive predictive value was 94.7%, specificity was 72%, and sensitivity was 85.1% in a study done by Shefki Xharra et al. [21]. A CRP level more than 0.6 mg/dl would show agglutination and the test was considered positive. CRP was not found to be a useful indicator of appendicitis with a sensitivity and specificity of only 44% and 80%. CRP negativity was also not useful to rule out appendicitis in patients with RIF pain as the NPV was only 42%. The specificity, PPV, and NPV for Alvarado score (>4) were 53.6%, 76.9%, and 76.3%, respectively, which were comparable to another similar study [22].

The fairly better sensitivity and PPV with low specificity and NPV indicate that a positive USG favours diagnosis of acute appendicitis but a negative USG was not sufficient to rule out the diagnosis and discharge the patient. This was supported by a meta-analysis by Orr RK et al. in which they found that USG has a high false negative rate when used in patients with classical signs of appendicitis and high false positive rate in patients who are clinically having a low probability of appendicitis [24]. USG becomes the first modality of imaging investigation of choice in our country because of its high accuracy and lower cost.

In a similar study by Xharra S et al., they found that WBC count had a sensitivity of 79.1% and specificity of 68% for a cut off value of 10, 000/mm3 [21]. In another retrospective study by Kim E et al., they found that for the same cut off value WBC had a sensitivity of 81% but poor specificity of only 22%, which is controversial with the results of our study, which showed a better specificity [28]. There was a significantly higher negative predictive value for WBC counts when all causes of RIF pain were included as negative samples. Whether elevated counts help predict complicated appendicitis has been evaluated in different studies.

The Alvarado score (>4) was seen in 50% of patients. Among the patients who were initially discharged as non-appendicitis and who on their subsequent presentations underwent appendicectomy, none of them had complicated appendicitis. This may be due to the early presentation as a result of better patient awareness created during their previous discharge from hospital, as many studies have shown a direct relationship of complicated appendicitis with duration after onset of pain.

The ultimate goal of the present study was to find out the ways to reduce the negative appendicectomy rates and unnecessary admissions for more benign causes of RIF pain. The estimated negative appendicectomies (9%) was lesser compared to different other studies where it ranged from 17% to 23%. It could significantly bring down the health care costs.

In comparison to other studies, the efficacy of biochemical parameters was compared with the non-appendix group in this study. This study group might not actually be a representative of the profile of all patients with RIF pain since some of the patients were partially investigated from other referring hospitals. The CRP levels could only be measured by the semi quantitative agglutination method due to the non-availability of an automated nephlometer. In some patients, CRP and WBC counts could not be carried out due to improper sampling/non availability of test kits

6. Conclusion

The diagnosis of appendicitis in this study showed us No single clinical or laboratory test is able to reliably predict acute appendicitis. USG of the abdomen had an important role in the diagnosis of appendicitis with significant sensitivity, specificity, and PPV. Use of triple assessment for acute appendicitis using laboratory investigations and USG imaging as an adjunct to clinical diagnosis will help to diagnose acute appendicitis in patients with RIF pain.

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