Original Research Article

A clinical study on acute appendicitis with special reffrence to TLC, DLC, C-reactive protein and plain x-ray abdomen

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Abstract

Objective: To diagnose the case of acute appendicitis accurately on basis of a combined criteria including TLC,DLC,CRP and plain X ray abdomen so that timely intervention can be performed and avoiding negative laparatomies in term of better management of patient in patient with acute right lower quadrant of abdominal pain. **Methods** During the study period of 18 months, 60 patients between the ages of 11 and 65 years operated upon for suspected acute appendicitis were included in this prospective study. Both open as well as laparoscopic appendectomies were included in the study. On admission, note was made of the symptoms and signs relevant to the study. Venous blood was routinely taken on admission and was sent to the emergency laboratory for testing. **Results** The present study revealed that males were affected more than females and the commonest age group affected was 11 – 20 year age group. Pain, anorexia, vomiting and fever seems to be the reliable symptoms and one should deeply inquire about these symptoms. RLQ tenderness and rebound tenderness along with tachycardia were the commonest signs and presence of all three should highly suggest the diagnosis of acute appendicitis. An increase in C-reactive protein level is highly sensitive in diagnosing inflammatory condition like acute appendicitis, but again it has low specificity and results should be interpreted along with valid clinical picture. Plain x-ray abdomen can serve as an important adjunct in the diagnosis of acute appendicitis, with RLQ 'sentinel loop' being the commonest finding. **Conclusion** If all the investigations such as TLC, DLC, CRP and PLAIN X-RAY ABDOMEN are combined, it can highly increase the sensitivity and positive predictive value in diagnosing acute appendicitis.

Keywords: acute appendicitis, 'lily-white' appendectomy, X-Ray abdomen, sensitivity and positive predictive value, ultrasonography, computed tomography, and laparoscopy.

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Introduction

Acute appendicitis is an acute inflammation of the appendix. It is not an easy diagnosis to make. This is particularly true in early stages of the disease. A failure of early diagnosis can lead to progression of the disease with its attendant morbidity and occasional mortality[1]. Acute appendicitis is one of the most common surgical emergencies. Surgery for acute appendicitis is the most frequent operation performed[2]. A certain diagnosis can only be obtained at surgery and after pathological examination of surgical specimen. Despite the increased use of ultrasonography, computed tomography, and laparoscopy, the rate of misdiagnosis of acute appendicitis has remained constant (15.3%), as has the rate of appendiccal rupture.

The percentage of misdiagnosed cases of acute appendicitis is significantly higher among women than among men (22.2% vs. 9.3%)[3]. A decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 30 % of cases (negative appendectomy rate)[4].

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For many years, the appendix was erroneously viewed as a vestigial organ with no known function. It is now well recognized that the appendix is an immunologic organ that actively participates in the secretion of immunoglobulins, particularly immunoglobulin A. Data suggest that appendectomy may protect against the subsequent development of inflammatory bowel disease; however, the mechanism is unclear[5]. Appendix is useful in reconstructive urological surgery[6]. Negative appendectomy therefore robs the patient of a useful asset and also has a morbidity of 15%. Among the diseases that can cause acute abdominal pain in RLQ, acute appendicitis is the most common pathological condition. This disease is diagnosed on the basis of clinical examination, white blood cell count, abdominal ultrasound, CT scan and radiographic studies of the abdomen. Additional tests that would improve the diagnostic accuracy and reduce the number of unnecessary operations are needed. This is particularly important in these days where health planning is driven by cost containment. C-reactive protein (CRP), together with other acute-phase proteins, increases in response to tissue injury[8]. Many reports have investigated the value of raised serum CRP measurement, alone or in combination with WBC count, in improving the diagnosis of acute appendicitis. The majority of patients with acute appendicitis have WBC count more than 10000/mm3. But it also rises in other inflammatory conditions which can mimic acute appendicitis. Overall, the WBC should not be used alone to rule in or rule out the disease. In acute abdomen, plain abdominal radiographs are of great importance. But somehow with the advent of USG and CT scan this

vital investigation has lost its charm, particularly in case of acute appendicitis. Many radiographic signs have been related to appendicitis Till date, numerous studies have been done to highlight the importance of each of the above modalities to aid in the clinical diagnosis of acute appendicitis. But to our knowledge and after exhaustive search of medical database, we could not find a study where combined predictive value of total & differential count, Creactive protein & plain x-ray abdomen were evaluated in the diagnosis of acute appendicitis. Hence, we wish to study the role of TLC/DLC, CRP & Plain X-ray abdomen, in combination to improve on the clinical diagnosis of acute appendicitis and diminish the rate of *'lily-white'* appendectomy.

Materials and methods

This study was conducted in the Department of Surgery, People's College of Medical Sciences & Research Centre, Bhopal. The necessary approval was taken from the Institute's Research Advisory Committee and Ethical Committee before commencing the study.

Population under study		All the patients with right lower quadrant abdominal pain admitted in the	
		Department of Surgery, Peoples Hospital, Bhopal.	
8	Place of Study Department of Surgery, Peoples Hospital associated with People's College		
		Medical Sciences & Research Centre, Bhopal.	
≻	Study design	Cross-sectional study.	
\triangleright	Study period	18 months period, 1st January 2014 to 30th June 2015	
≻	Sample size 60 cases.		
\checkmark	Source of data	Pre-designed pro forma containing the details of patient's demographic	
		information, symptoms & signs, investigative data, operative records, and	
	histopathology reports.		

Inclusion Criteria

Patients of either gender, aged between 11 - 65 years, with pain in right lower quadrant of abdomen who were subsequently operated either by open or laparoscopic method with the presumptive diagnosis of acute appendicitis, and were willing to participate in the study. **Exclusion criteria**

- 1. Patients who did not undergo surgery.
- Patients who did not undergo surgery.
 Patients having appendicular phlegmon or appendicular abscess.
- Patients with signs of generalized peritonitis.

Methodology

During the study period of 18 months, 60 patients between the ages of 11 and 65 years operated upon for suspected acute appendicitis were included in this prospective study. Both open as well as laparoscopic appendectomies were included in the study. On admission, note was made of the symptoms and signs relevant to the study. Venous blood was routinely taken on admission and was sent to the emergency laboratory for testing.

TLC and DLC both were done by cell counter mindray bc-2800 auto hematology analyzer. DLC was further cross-checked by manual peripheral smear. The upper limit of TLC and that of NP were defined.CRP estimation was done by biosystems c-reactive protein latex agglutination test. Again the reference values were defined.Erect Plain X-Ray abdomen was done in all the cases using Allengers – 525 X-Ray machine.USG was also performed on all these patients by 5-8 MHz-linear probe with graded compression. Other abdominal and pelvic pathologies were also looked for.

The diagnosis was finally confirmed when transmural acute inflammatory changes were seen on histopathological examination, which has been considered as the 'gold standard' in this study. The distinctions between gangrenous and perforated appendices were made on the operative appearance by the surgeon. The study variables like TLC, DLC, C-reactive protein, and X-ray Abdomen were analyzed for their diagnostic accuracy, both alone and in combination, by means of sensitivity, specificity, positive predictive value (PPV), and accuracy. In addition the data was matched with the results of USG, so as to have a comparative analysis.

Observation chart

We included total 60 patients in our study who presented with right lower quadrant abdominal pain and were subsequently operated with the presumptive diagnosis of acute appendicitis based on clinical signs & symptoms, and investigative data.

Out of these patients, 53 patients were found to have a final diagnosis of acute appendicitis as confirmed by histopathological examination – the 'gold standard' in our study. In 03 cases appendix was not removed due to alternative operative diagnosis while in another 04, removed appendix did not show any inflammatory features.

Table 1: Histopathological Diagnosis		
Histopathological Diagnosis	No. of cases	
Acute Appendicitis	53	
Normal Appendix	04	
Not available	03	
Total	60	



Fig 1: Age and Gender wise distribution of the study group

Table 2: Distribution of symtoms			
SYMPTOMS	PRESENT	ABSENT	
PAIN	60	0	
ANOREXIA	52	8	
VOMITING	49	11	
FEVER	47	13	

Table 3: Distribution of Clinical Signs

	_	
CLINICAL SIGN	PRESENT	ABSENT
TACHYCARDIA	51	9
TENDERNESS	56	4
REBOUND TENDERNESS	52	8

Table 4: Erect X-ray Abdomen findings		
X-ray Abdomen finding	No. of patients #	
Caecal fluid level	30	
Obliteration of psoas shadow	08	
ight lower quadrant mass density	05	
urring of the pro-peritoneal fat line	02	
Extra-luminal gas shadow	02	
No apparent finding	22	

Results of TLC, DLC & CRP Cases with either TLC, DLC or CRP raised Results

In the present study, 60 cases of right lower quadrant pain were operated with presumptive diagnosis of acute appendicitis, the results were analyzed and compared with data in literature and following conclusions were made:-

Table 5: TLC or DLC or CRP			
TLC or DLC or CRP	Appendicitis	o-appendicitis	Total
Positive	50	04	54
Negative	03	03	06
Total	53	07	60

- The present study revealed that males were affected more than females and the commonest age group affected was 11 20 year age group.
- Pain, anorexia, vomiting and fever seems to be the reliable symptoms and one should deeply inquire about these symptoms.
- RLQ tenderness and rebound tenderness along with tachycardia were the commonest signs and presence of all three should highly suggest the diagnosis of acute appendicitis.
- A raised TLC/DLC is regarded as a sensitive test for acute appendicitis but is of limited diagnostic value by itself in doubtful clinical picture because of low specificity. Its significance is in its use with clinical examination and other investigations, not as a separate entity.
- An increase in C-reactive protein level is highly sensitive in diagnosing inflammatory condition like acute appendicitis, but

again it has low specificity and results should be interpreted along with valid clinical picture.

- Plain x-ray abdomen can serve as an important adjunct in the diagnosis of acute appendicitis, with RLQ 'sentinel loop' being the commonest finding.
- If all the investigations such as TLC, DLC, CRP and PLAIN X-RAY ABDOMEN are combined, it can highly increase the sensitivity and positive predictive value in diagnosing acute appendicitis.

Statistical analysis

The diagnostic validity (accuracy) of various tests has been assessed using 2×2 table, calculating the sensitivity, specificity, positive predictive value (PPV), and accuracy.

cc	condition like acute appendicitis, but				
	Teat Degult	Diagnosis		T-4-1	
	Test Result	Diseased	Not diseased	Total	
	Positive	a (true positive)	b (false positive)	a + b	
	Negative	c (false negative)	d (true negative)	c + d	
	Total	a + c	b + d	a + b + c + d	

Discussion

Acute appendicitis is one of the most common surgical emergencies and appendectomy is one of the most frequent operations performed. It is a condition which is diagnosed clinically, and imaging modalities and laboratory tests are a useful adjunct to such diagnosis. Decision making in cases of acute appendicitis poses a clinical challenge especially in developing countries where advanced radiological investigations do not appear cost effective and so clinical parameters remain the mainstay of diagnosis.Though history and clinical examination still remains the mainstay for the diagnosis, misdiagnosis and negative appendectomy still do occur at quite a high rate. In the past few years, various scores have been developed to aid in the diagnosis of acute appendicitis. Although many diagnostic scores have been advocated, most are complex and difficult to implement in the clinical situations. The accurate clinical diagnosis of acute right iliac fossa pain remains a difficult clinical problem as the differential diagnosis of such pain is not always straightforward. The diagnosis is made purely based on history, clinical examination and some laboratory investigations. New diagnostic techniques such as peritoneal aspiration cytology, scoring and computer analysis, graded compression ultrasonography, computed tomography, non-contrast helical computed tomography and laparoscopy have been introduced in recent years. The drawback with these techniques is involvement of additional costs and lack of free availability. Due to these factors, these modalities have not gained wide acceptance as routine diagnostic investigations of acute appendicitis. Imaging techniques have been shown to add very little. A certain diagnosis can only be obtained at surgery and after pathological examination of surgical specimen. The "difficulty" alluded to by Cope relates to our inability to reliably diagnose appendicitis on clinical grounds.

The varieties of presentation and the variability of signs are such that even the most experienced surgeons may remove normal appendix or "sit on" those that have perforated. The squeal of delayed diagnosis may result from late presentation by the patient but are sometimes due to the initial failure of the clinician to make the correct diagnosis. The sequelae of delayed treatment include a higher incidence of postoperative sepsis and longer hospital stay. Therefore, misdiagnosis and delay in surgery can lead to complications like perforation and finally peritonitis.

Difficulty in diagnosis arises in very young, elderly patients and females of reproductive age because they usually have atypical presentation and many other conditions also present like appendicitis. Literature shows that 2-7% of all adults on exploration have diseases other than appendicitis. In our study we found in 03 cases, diagnosis other than acute appendicitis. Against this, it is generally accepted that unnecessary surgery should be avoided, and this aspect of care is usually measured by the proportion of appendix that are normal on histology. A negative appendectomy rate of 20-40% has been reported in literature and many surgeons would accept rate of 30% as inevitable. In our study normal appendix were removed in 04 cases, or negative exploration rate was 6.67%. Removing normal appendix is an economic burden both on patients and health resources.

In the present study, we have emphasized on the importance of clinical examination and utilization of simple investigation such as TLC, DLC, and Plain X–RAY abdomen in making a correct diagnosis of acute appendicitis and thereby decreasing the negative appendectomy rate. Total 60 patients with the complaints of right lower quadrant abdominal pain who were ill enough to warrant surgery for suspected acute appendicitis were evaluated. The incidence of acute appendicitis was more common in males than in females. The male to female ratio is 3.3:1 and the age distribution ranged from 11-60 years, mean being 29 years. The incidence of acute appendicitis is variable in both sexes

In Lewis et al series of 1000 cases, the incidence of acute appendicitis was found to occur most commonly in the age group of 20-30 years in both males and females, while we found it to be commonest in 11-20

years of age group. It can be seen from the given statistics, that there are no set patterns for incidence of the disease in both sexes and it is highly variable. Hence in all the above series including the present series appendicitis is more common in males than in females, and in younger age group[5,6].

In this study, it was observed that pain was present in all the cases (100%) and was a major presenting symptom, which coincides with other studies like who have also mentioned that pain was present in all cases. Majority of the patients had aching type of pain and colicky pain was noted in 60 patients. The site of pain, most often complained of was in the right iliac fossa. This is similar to the study of Adesunkanmi AR, who reported lower abdominal pain in all cases of appendicitis.

Anorexia was the second commonest symptom after pain in this study. It was found in 87% of the patients. This figure more or less compares with the literature. According to two studies, anorexia was present in 82% and 77.7% patients respectively. In our study 81.6% had vomiting once or twice usually in the early part of disease. This complaint always followed the pain. Vomiting is more common among teenagers and the younger age group. Review of literature shows that 51-69% of patients with appendicitis had vomiting. It seems that this symptom has high sensitivity rate but less specificity, as quite a large group of patients (30-50%) with normal appendix also had this symptom.

In comparative study by Selvan et al, right lower quadrant pain was present in more than 95% of cases and in more than 65% of cases, there was history of nausea/vomiting and anorexia. If none of these three symptoms are present, the diagnosis should be seriously questioned. In the present series, fever was complained of by 78.3% of the cases and there was a corresponding rise in the pulse rate, whereas in Prabhu et al tachycardia and rise in temperature were noticed in all the cases. Jaiswal et al showed that only 60% of the patients had a rise in temperature. This difference may be due to delay in coming to the hospital and treatment outside the hospital by antibiotics and analgesics[7,8].

Physical signs in diagnosis of Acute Appendicitis			
Signs	Present Series (percentage)	Rajendra Bhatnagar et al (percentage)	
Tenderness in RIF	93	98	
Rebound tenderness	86.6	21	

The degree of tenderness was different in each individual patient, but in obese patients and in older age groups tenderness was elicited on deep palpation. These patients had relatively mild tenderness. Degree of tenderness also depends on difference in sensitivity to pain in different individuals. Incidence of tenderness in our study compares well with other series where tenderness could be elicited in 96-100% patients with appendicitis. After a review of different studies, it has been concluded that the importance of right iliac fossa tenderness is, that in the absence of tenderness acute appendicitis is unlikely.

On clinical examination of the patient, tenderness in the right iliac fossa was the most consistent feature in 93% of cases whereas in Goel K S series it was present in 98% of the patients, which coincides with present series. In the present study rebound tenderness was found in 86.6% cases and tachycardia was found in 85% and it was helpful in diagnosis[9,10].

The total leucocyte count is widely used to aid the diagnosis of acute appendicitis. Its diagnostic value varies from useful to misleading. A raised TLC is regarded as a sensitive test for acute appendicitis but is of limited diagnostic value because of its relatively low specificity and does not add much to the management in patients with urreliable clinical findings. Various studies have reported that 80% to 85% patients with acute appendicitis will have a total white cell count of over 10,000/mm³. The present study also shows that 81.13% cases of acute appendicitis had TLC > 10,000/mm³ which is almost similar to the findings of a series that reported a raised TLC > 10,000/mm³. The sensitivity (81.3%), specificity (57.4%) with PPV (93.48%) of the

raised white cell count in the present study correlated with other study where it showed sensitivity 88.7% and 70% specificity. Thus although raised white cell count may be highly sensitive test for acute appendicitis, it has low specificity and other inflammatory conditions may cause the leucocyte count to rise[10-14].

It was observed in this study that raised Neutrophilia (NP) was less sensitive (73.58%) and specific (57.14%) with higher positive predictive value. The sensitivity of raised NP ranges from 60 to 84% in various studies. The sensitivity improved to 88.68% while the specificity continued to be low when raised TLC and raised NP was combined by the 'or' rule. Similarly, comparable results of 90.5% (sensitivity) and 58.8% (specificity) were observed by Jaiswal et al. In a series of 248 patients of acute appendicitis by Pipal et al, sensitivity and specificity of combined leucocyte count and neutrophilia was 95.7% and 61.5%. Many previous studies have observed that an increased CRP reveals acute appendicitis and claim it to be a highly sensitive investigation. Dueholm observed that CRP had a sensitivity of 75% and specificity of 56%, while Thompson et al. reported a sensitivity of 69% and specificity of 75% in acute appendicitis. The present study depicted a high sensitivity of 90.57% with a specificity of 71.43%. Similar values were observed by Anwar MM (sensitivity of 94% and specificity of 75%) as well as Vaidya VP et al. Adding CRP to the TLC and NP makes it a highly sensitive combination. As in present study combination of TLC, DLC, and CRP gives a high sensitivity of 94.34%[15,16,17].

Plain X-ray abdomen was taken in erect posture. In present study according to the positive finding in x-ray abdomen the sensitivity was 62.26% whereas specificity was 28.57% with PPV of 86.84%. Sentinel loop in right iliac fossa was the commonest finding, seen in 30 cases (50%). Obliteration of psoas shadow was second commonest, seen in 08 cases (13.33%). We could not find any case with free air under diaphragm in cases of perforated appendix, whereas Saeho (1978) reported three examples of pneumo-peritoneum associated with perforated appendix. Thus plain X-ray can have important corroboratory role in few of the doubtful cases, but more importantly it can serve to rule out other gastro-intestinal pathologies like perforations or obstruction[19].In the present series ultrasound scanning of the abdomen was done in all the patients. It showed evidence of appendicitis in 44 patients, though only 42 patients really had appendicitis giving a PPV of 95.45%. Sensitivity and specificity seen are 79.25 % and 71.43% respectively. Accuracy was 78.33% whereas Chen S.C et al (1998) series reported an accuracy of 91.6% for detecting acute appendicitis. Probably this difference may be due to resolution power of equipment, presence of ileus, inadequate preparation of patient and experience of the radiologist. USG was able to diagnose fully inflammed cases of appendicitis easily, however in acute simple appendicitis it missed out on 11 cases (20.75%) cases. So it can be concluded that although USG is good in detecting grossly inflammed appendicitis, it can miss out on cases of acute simple appendicitis or early appendicitis.If we combine all the tests result under study and 'either' of them is positive, the sensitivity of the combined criteria rises highly to 96.23% but with a low specificity of 28.57%. The diagnostic accuracy though remains high at 88.33%. In patients whom all the tests are positive, the specificity is high at 85.71% while sensitivity dips to 54.71%. The PPV remains high at 96.67%. Hence if all the tests are positive, we can effectively rule out patients not suffering from acute appendicitis at least, and avoid surgery.Numerous previous studies have shown that the CRP level enhances the precision of diagnosis of acute appendicitis, but not surgical indication. A large retrospective study has documented that the sensitivity of CRP in these patients is greater than 90%. Furthermore, the negative appendectomy rate is reduced by approximately 8% if surgery is cancelled in patients with CRP levels and white blood cell counts within the reference range. Another prospective study has shown that it is important to measure serial CRP levels and white blood cell counts in patients with suspected appendicitis. The sensitivity of CRP levels in predicting appendicitis was 60% on admission and increased to 100% by the fourth blood specimen. Conversely, white blood cell counts exhibited a sensitivity of 95% on admission, but dropped to 75% by the fourth specimen. Other studies confirm that an elevated CRP serves as a systemic marker of focal inflammation and infection. In this background, CRP and white blood cell counts are important for the diagnosis for appendicitis. After the diagnosis of appendicitis, the clinician must decide surgery or antibiotics. Some reports indicated that appendicitis is unlikely, when the white blood cells count and CRP value are normal.Dueholm et al, in 1989, suggested that only the triple combination of CRP, total white blood cell count and total neutrophil count is of diagnostic value in acute appendicitis, indicating that acute appendicitis is unlikely when these three tests are simultaneously negative. Shafi et al conducted a study in 2007 on 110 patients, who were operated for acute appendicitis to determine the role of total leucocyte count (TLC), C-reactive protein (CRP) and percentage of neutrophil count in the diagnosis of acute appendicitis. According to the results, CRP had a sensitivity, specificity and positive predictive value of 95.6%, 77.77% and 95.6% respectively. The authors concluded that the above inflammatory markers, (TLC, CRP and neutrophil count) can be helpful in the diagnosis when measured together as this increases their specificity and positive predictive value[17,18].In general, most authors agree that acute appendicitis is unlikely in adult patients with normal leukocyte count and CRP value, even if clinical symptoms and signs indicate acute appendicitis. Consequently these patients should not undergo surgery. Furthermore, several studies have shown that combining total leukocyte count with CRP value enhances the accuracy of both tests. Both these results are in agreement with those of our study[15-17].Hence, the present study clearly shows that in presence of definite clinical features suggesting the diagnosis of acute appendicitis, simple blood investigations like TLC, DLC, and CRP can add to the diagnostic accuracy and minimize negative explorations. A plain X-ray of the abdomen can further serve as an important adjunct in arriving at a final diagnosis, most importantly the 'sentinel loop' sign. We are in no way under estimating the role of USG in evaluation of RLQ pain, but these simple investigations as discussed in our study,1 can help in situations where facility of a good USG might not be available in emergency hours or its results are equivocal.

Conclusion

In conclusion we would like to say that the main stay of diagnosis is thorough clinical evaluation by eliciting different signs & symptoms. In addition, simple investigations such as TLC, DLC, CRP, and Plain X-ray Abdomen can add to the diagnostic accuracy and reduce the negative appendectomy rate. Acute appendicitis is highly unlikely with normal TLC, DLC and CRP level, and without positive X-ray Abdomen findings.

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