A Combination of Clinical Examination with Specific Biomarkers and Judicious Use of Imaging Modality can Reduce the Rates of Negative Appendicectomy

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Abstract

Background: Acute appendicitis is one of the most common surgical emergencies. Accurate diagnosis of acute appendicitis is based on careful history, physical examination and laboratory and imaging findings.

Objective: The primary aim is the correlation between clinical, biochemical and radiological assessment in patients of appendicitis and also to reduce the rates of negative appendicectomy.

Method: The study was carried out in Department of General Surgery, Sir Sunderlal Hospital, IMS and BHU from September 2015 to July 2017. Total 61 patients of age group 16-65 years and either sex were evaluated on the basis of predetermined proforma, which included a detailed history, clinical examination, laboratory investigations and high resolution sonography or CT and histopathology. Sensitivities, specificities, positive and negative predictive values of TLC, neutrophil percentage, Modified Alvarado Score, CRP, D-dimer, USG and CT scan were calculated in respect to histopathology finding as a gold standard.

Results: Modified Alvarado scoring (MAS 7-9:Appendicitis definitive) was present in 24 (39.3%) patients. Raised leucocyte count was present in 49 (80.32%) patients, while neutrophil count above 75% was present in 47 (77%) patients. Raised CRP was present in 55 (90.16%) patients with cut-off of >3 mg/l (normal range 1-3 mg/l) while D-dimer was elevated in 44 (72.13%) patients with cut-off of >5 mg/l. On ultrasonography,(77%) patients were diagnosed as acute appendicitis whereas (83.3%) had diagnosis of acute appendicitis in CECT abdomen. Histopathological examination was positive in 60 (98.4%) patients.

Conclusion: We concluded that combination of thorough clinical evaluation along with certain routine biochemical & specific markers and ultrasonography as the primary imaging modality is sufficient in establishing a diagnosis of acute appendicitis in more than 90% cases.

Keywords: *Acute appendicitis, Histopathological examination, Rovsing's sign.*

Introduction

Abdominal pain is one of the most common reasons for visits to the emergency room, comprising 7% of all visits[1]. In most of the patients, symptoms are benign and self-limited; a subset will be diagnosed with an "acute abdomen" as a result of serious intra-abdominal pathology necessitating emergency intervention. The incidence of acute appendicitis declines with age[2-4]. The incidence is highest among children aged 10–14 years. A declining incidence has been reported over the last decade[, 5]. Males are more commonly affected with male to female ratio of 1.4:1[6, 7]. A three-fold risk

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of appendicitis has been shown in patients with a family history of appendicitis, which also suggests the presence of genetic factors[8]. While the clinical diagnosis may be straightforward in patients who present with classic signs and symptoms, atypical presentations may result in diagnostic confusion and delay in treatment.

In many cases, the diagnosis of appendicitis is straightforward, however, the diagnosis can be challenging and despite advanced diagnostic imaging, rate of removal of healthy appendices in suspected cases of appendicitis remains high. During the past two decades, imaging techniques like ultrasonography and particularly computed tomography (CT) have allowed preoperative diagnosis of appendicitis to be more reliable[9], related complications to be evaluated, the negative appendectomy rate and costs of caring to be lowered and differential diagnosis to be sought. Identifying perforated clinical appendicitis depends on clinical examination supported by raised inflammatory and biochemical markers. An early diagnosis of perforation improves outcomes, allowing the surgeon to prepare for a relatively difficult procedure[10]. The negative appendectomy and perforated appendicitis rates are both important quality measures of the treatment of acute appendicitis. There is an inverse relationship between these two measures[11].

The primary aim of this study was to establish whether there is a correlation between clinical, biochemical and radiological parameters in patients of appendicitis. Also to explore the role of CT scan as complementary imaging tool in management of these patients.

Method

This is a prospective hospital based observational study which was done after obtaining ethical approval from the Ethical Committee of Institute of Medical Sciences, Banaras Hindu University from September 2015 to June 2017. The study includes 61 patients who presented with peri-umbilical pain or pain in right iliac fossa was included in the study. Patients with age group <15 and >65 years, pregnant women and patients having history of previous abdominal surgery or diagnosis of appendicular lump or other abdominal conditions such as perforation peritonitis, ovarian malignancy, pancreatitis etc. where raised value of biochemical markers were excluded from the study.

Patients demographic profile was recorded clinically followed by detailed history related to symptoms and their duration, presence or absence of similar complains in past, any history of diabetes or other co-morbidities, trauma, surgery, drug intake history were taken. A detailed abdominal examination to look for contour of abdomen (flat/distended/visible lump in right iliac fossa), local temperature, direct, indirect and rebound tenderness, lump in right iliac fossa, presence/absence of Rovsing's sign, Obturator sign and Psoas sign, presence of free fluid and bowel sound were also recorded.

Relevant hematological tests like complete blood count (CBC) with special test like serum C-reactive protein (CRP) and D-dimer was carried out. Soon after the report of CBC patients were graded according to Modified Alvarado Score. Further patients were subjected to high resolution sonography (HRS) at a frequency of 7.5 MHz where the points of interest were probe tenderness in RIF, visualization of appendix, mesenteric echogenicity and presence or absence of appendicitis. In case of discordance between clinical finding/scoring and ultrasonography patients were subjected to multidetector 128-slice CT scan abdomen where the points of interest were appendicular perforation, peri-appendigeal collection and presence or absence of dilated inflamed appendix. The patient was then subjected to laparoscopic/ open appendicectomy and the specimen was sent for histopathological examination.

Modified Alvarado scoring was done along with the biochemical, Ultrasound and CT scan findings, finally these were correlated with their histopathology report.

All these data were statistically analyzed using SPSS 16.0 software Windows version.

Results and Discussion

Acute appendicitis the accuracy of the clinical diagnosis is approximately 80%, which corresponds to a negative appendectomy rate of around 20%[12].61 patients were suspected to have acute appendicitis. In 27 patients (44.3%) patients had Modified Alvarado scoring (MAS) 5-6 (Appendicitis possible) followed by MAS 7-9 (Appendicitis definitive) which was present in 24 (39.3%) patients. Raised leucocyte count 49 (80.32%) patients, neutrophil count above 75% was present in 47 (77%) patients. Raised CRP was present in 55 (90.16%) patients, D-dimer was elevated in 44 (72.13%) patients.

CECT abdomen was done in only 12 patients. 4 (33.3%) patients had appendicular perforation and 9

(75%) patients had peri appendigeal lymph node and dilated inflamed appendix **(Figure 1)** on CECT abdomen. Out of 12 patients, 10 (83.3%) had diagnosis of acute appendicitis in CECT abdomen. **(Figure 1)**HPE was positive in 60 (98.4%) patients.**(Table-1)** On correlating modified Alvarado score with TLS, neutrophil (%), lymphocyte (%), CRP (mg/l) and D-dimer (mg/l). Positive significant correlation was observed between MAS with TLC (r=0.514, p<0.001), CRP (r=0.613, p<0.001) and D-dimer (r=0.628, p<0.001) (Fig. 1-3). Negative significant correlation was observed only in MAS with lymphocyte (r= -0.438, p<0.001).**(Table 2)**

All clinically positive patients (n=55) had appendicitis on HPE, while in 6 patients having no clinical features of appendicitis, 5 were positive on histopathology and one had no appendicitis on HPE. So the sensitivity and specificity of clinical evaluation of our study is 91.67% and 100% respectively. The sensitivity of clinical assessment was almost equivalent with the results of the study conducted by MojcaGroselj-Grenc et al[13] which was 93.9%.

In present study, total leucocyte count was raised in 80.3% (n=49) patients while it was normal in the rest 19.7% (n=12). All patients having raised count were found to have appendicitis on HPE, while of 12 patients having normal TLC, 11 patients were positive on HPE and one had no appendicitis in histology. The sensitivity and specificity of total leucocyte count of the study was 81.67% and 100% respectively. This sensitivity was consistent with the study by Lau[14].

In the present study, 77% (n=47) patients had neutrophil percentage above 75% and all these patients were positive on HPE. of 23% (n=14) cases having normal neutrophil percentage, 21.3% (n=13) had appendicitis on HPE while one was negative on histology. This gives sensitivity, specificity and accuracy of 78.33%, 100% and 78.69% respectively. This sensitivity was comparable to study by Sasso et al[15] In present study raised value of MAS (>4) was present in 83.6% (n=51) cases while in other 16.4% (n=10) MAS value was <4. In patients having raised MAS value, 50 cases were positive on HPE and one patient had no appendicitis on HPE. All the remaining 16.4% (n=10) cases having MAS<4 were histologically positive which makes sensitivity of 98% and specificity 0%. The sensitivity of studies by Ohle et al[16] and Musharraf Husain et al[17] had concordance to our study.

The preoperative serum C-reactive protein (CRP) levels were correlated with the histopathology. Out of 61 patients, 90.2% (n=55) cases had raised C-reactive protein level and all these patients were histologically found to have appendicitis. CRP level was normal in 9.8% (n=6) of which 8.2% (n=5) cases were having appendicitis while one patient had no features of appendicitis on HPE. In our study, sensitivity and specificity of C-reactive protein was 91.67% and 100% respectively.This result of Presentstudy is in concordance with the study done by Wu et al[18].

In our study D-Dimer was raised in 72.1% (n=44) patients while it was normal in 27.9% (n=17). All patients having raised value of D-Dimer had appendicitis on HPE while of the remaining 17 patients one had normal appendix and 26.23% (n=16) had appendicitis on histology. The sensitivity, specificity & accuracy in diagnosing appendicitis was 73.33%, 100% and 73.77% respectively which is much more than previous studies and is due to low cut-off D-dimer (>5mg/L taken as raised level). Our study was in concordance to Cayrol et al[19]which took D-dimer cut-off point of 0.230 mg/L. Combining the results of CRP and D-dimer improves the sensitivity value for diagnosing appendicitis. If we use both inflammatory marker (CRP & D-Dimer) we get a higher sensitivity value as 97%. The use of these biochemical tests is limited and so should only be used as a guide, with the wider clinical picture being of greatest importance rather than solely relying on the biochemical markers for a diagnosis.

In present study, USG suggested appendicitis in 80.33% (n=49) patients and all these patients had appendicitis on histopathological examination also. In other 19.7% (n=12) cases having no appendicitis on USG, 18% (n=11) had appendicitis on HPE while one patient was found to be negative on histology. Sensitivity, specificity and accuracy of High-resolution ultrasonography came out to be 81.67%, 100% and 81.97% respectively. Present study was also consistent with the study done by MojcaGroselj-Grenc et al[12] having sensitivity of 91% and specificity of 95% respectively. Accuracy of CT scan is higher as compared to USG for diagnosing acute appendicitis[20] but till today still there is utility of USG for the diagnosis of acute appendicitis particularly in pediatric cases[21]. CECT was not performed routinely in all patients but done only when there was discordance between clinical findings and Ultrasonography. In present study done in

only 12 cases out of 12 cases 83.33% (n=10) had acute appendicitis on CECT and HPE, one case was negative on CECT but positive in HPE and one had appendicitis neither on CECT nor in HPE. Sensitivity of CECT was 92.86%, while specificity 100% and accuracy 93.33%, positive predictive values of 100%. Similarly Lazarus et al[22] had sensitivity and specificity values in concordance to our study.

Conclusion

The diagnosis of acute appendicitis is generally made on clinical grounds but on many occasions especially in children and female clinical findings alone cannot be used unequivocally for making treatment decisions. In our study we have shown that the combination of CRP & D-Dimer is a better predictor of acute appendicitis and complimentary to clinical diagnosis. A combination of thorough clinical evaluation along with routine biochemical & specific biomarkers and ultrasonography as the primary imaging modality is sufficient in establishing a diagnosis of acute appendicitis and reduce the rates of negative appendicectomy. Limited CECT abdomen can help in patients with discordant clinical and USG findings.

Table 1: Ultasonography, CECT abdomen and Histopathological finding

Findings	Number (%)
USG Finding (n=61)	
Probe tenderness RIF	54 (88.5)
Appendix Visualisation	34 (55.7)
Periappendiceal Echogenicity	41 (67.2)
Acute appendicitis	47 (77.0)
Chronic appendicitis	1 (1.6)
Resolving appendicitis	2 (3.3)
CECT Abdomen (n=12)	
Appendicular perforation	4 (33.3)
Periapendiceal collection	9 (75.0)
Appendicitis	10 (83.3)
Histopathology	
No Appendicitis	1 (1.6)
Appendicitis	60 (98.4)
Reactive appendix	6 (9.8)
Acute aapendicitis	12 (19.7)
Acute on chronic appendicitis	7 (11.5)
Chronic appendicitis	31 (50.8)
Resolving appendicitis	4 (6.6)

Table 2: The sensitivity, specificity, PPV, NPV and diagnostic accuracy of diagnostic variables with histopathological finding as gold standard

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
TLC	81.67	100	100	8.33	81.97
Neutrophil	78.33	100	100	7.14	78.69
MAS	98.04	0	83.33	0	81.97
CRP	91.67	100	100	16.67	91.8
D-dimer	73.33	100	100	5.88	73.77
USG	81.67	100	100	8.33	81.97
CECT	92.86	100	100	50	93.33
CRP plus D-Dimer	97.73	0	71.67	0	70.49

Figure 1: Axial CECT abdomen shows dilated appendix with periappebdigeal fluid s/o acute appendicitis.

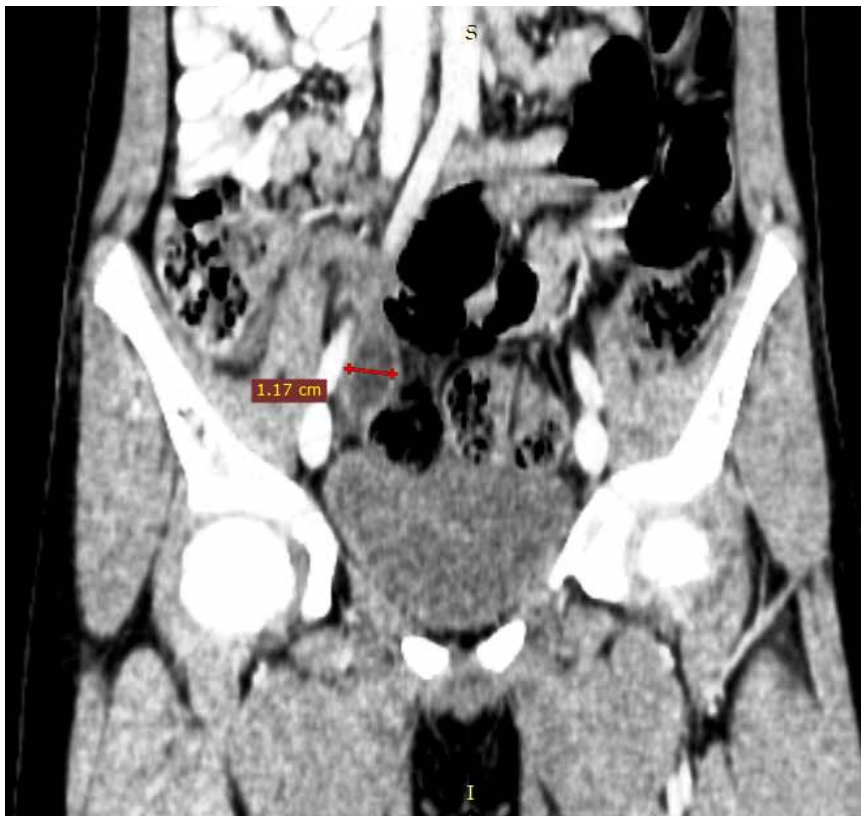

Figure 2: Coronal CECT image showing features of acute appendicitis in right iliac fossa.

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