



Role of Inflammatory markers in acute appendicitis

Dr Ankur Sharma

Associate Professor, Dept of General Surgery, IIMS&R, Integral University, Lucknow.

Dr Saurabh Agrawal

Associate Professor, Dept of General Surgery, Himalayan Institute of Medical Sciences, Dehradun.

ABSTRACT

Acute appendicitis is a common surgical problem encountered by surgeons all over the world. Also, appendicectomy accounts for a large number of emergency cases operated worldwide. Although the diagnosis essentially remains clinical, however in some cases with ambiguity, support from blood investigations and radiology is sought to promptly diagnose cases and provide surgical care. Appendicectomy is a procedure often done in emergency setting when senior clinicians are not available for opinion. Ancillary tests which can predict the likelihood of appendicitis will amount to better evaluate a patient with acute onset right iliac fossa pain. Negative appendicectomy rates range from 30 to 50% in some studies. That is why it is essential to increase sensitivity and specificity of the diagnosis with ancillary investigations.

KEYWORDS

Introduction:

Acute appendicitis remains one of the most common surgical emergencies and one of the leading causes of acute abdominal pain across all ages. Appendicectomy accounts for upto 10% of all abdominal surgeries. (1) Accurate diagnosis of acute appendicitis remains a challenging dilemma and at times, can confuse even the senior most and experienced clinicians. The scenario can be even more challenging in paediatric patients. Also, at times, when the patients are referred to higher centre with loading dose of antibiotics and analgesics, the signs and symptoms can often be masked and subtle.

Treatment for acute appendicitis has come a long way since the recognition of the entity.

From almost 100 % mortality without surgery to mortality rates less than 1% with prompt care and diagnosis. However, delay in diagnosis can still have profound effect on mortality and morbidity due to risk of perforation and subsequent generalised peritonitis. Such risk is more troublesome in extremes of ages. However, at the same time, the chances of having a negative laparotomy reaches almost to 1 in two, in young children, elderly patients and adolescent girls. Many attempts have been made to decrease the negative appendicectomy rate.

Diagnosis of acute appendicitis essentially remains a clinical diagnosis and role of investigations was only ancillary to rule out other conditions which can mimic appendicitis. However, certain investigations can help in accurately diagnosing the condition in certain situations.

Of these, there are two kinds of investigations available. The first set of investigations is blood investigations and the other set is radiological investigations: Ultrasound and CT of the abdomen.

When a blind tubular structure can be demonstrated in right iliac fossa with probe tenderness on Ultrasound of the abdomen, the diagnosis can almost be sure. However, such a scenario is not always possible. Despite the high specificity of both Ultrasound and CT Abdomen, the issues with radiological investigations are lack of widespread availability at remote areas and during emergency hours, which restricts their use.

Leucocytosis is an important hallmark feature of acute inflammation. C-reactive protein (CRP), an acute phase protein is also an important feature of inflammation and serves as a marker for infection or tissue injury.

The focus of this article is to stress upon the blood investigations that can help in diagnosing acute appendicitis

Materials and Methods:

This prospective study was conducted at IIMSR, Integral University, Lucknow.

All patients who underwent appendicectomy for acute appendicitis were included in this study.

Exclusion criteria:

1. Patients who underwent interval appendicectomy after the acute attack had subsided.
2. Patients who underwent appendicectomy in addition to some other surgical procedure.
3. Patients who had received antibiotics elsewhere before admission to current hospital.

The study period was from Jan 2015 to December 2016.

In all patients, white blood cell counts and CRP levels were measured. Normal values for WBC and CRP were accepted as $4-11 \times 10^3/\mu\text{L}$ and $<0.6\text{mg/dL}$, respectively.

Results:

Total of 249 patients were considered and after exclusion 170 patients were included in the study. The study population consisted 74 males and 96 females.

The patients were divided into following groups :

- Group 1: Patients with histologically normal appendices.
- Group 2: Patients with histologically confirmed appendicitis.
- Group 3: Patients with complicated appendicitis.

Complicated appendicitis included perforation of appendix, empyaema or phlegmon formation.

Since the study was only designed as an observational study, decision for appendicectomy was taken as per treating surgeon's choice and results of leucocytosis and CRP levels did not direct the decision to plan for appendicectomy.

Use of radiological investigations like Ultrasound and CT of the abdomen were based on the treating surgeon's discretion.

Treatment in the form of open appendicectomy or Diagnostic Laparoscopy and appendicectomy were also left to the treating

surgeon.

Table 1: Demographic characteristics of the patients:

	Number	Age, Mean, Range	Males	Females
Group 1	35	25.4 (12-45)	12	23
Group 2	120	23.2 (13-56)	65	55
Group 3	15	33.2 (8- 70)	9	6

Mean age was comparable in Group 1 and Group 2, however mean age was higher in the Group 3, suggesting a increased chances of complications with increasing age.

Table 2: Laboratory values of various groups

	WBC Count x 1000	CRP
Group 1	11.2	0.4
Group 2	13.4	3.2
Group 3	16.5	6.5

Mean WBC count and CRP values were statistically significant between the groups ($p < 0.05$).

Discussion:

Acute appendicitis is a common surgical emergency and appendicectomy is one of the most common surgical procedures performed worldwide, with around 7% of population having undergone appendicectomy. (2)

It also happens to be one of the earliest surgical procedures performed by surgical residents during their training.(3)

The first description of the appendix was given by Jacopo Carpi in 1522. Claudius Amyand was the first surgeon to perform appendicectomy in 1735, during the repair of scrotal hernia.

Appendicectomy even came fashionable in United Kingdom after a surgeon names Treves performed appendicectomy on King Edward VII. The mortality of appendicitis fell considerably after the discovery of antibiotics. (4)

Inflammation is a complex physiological response of body tissues to noxious agents. It primarily serves as a protective mechanism to remove the offending agent and help in healing of the body.

The symptoms of acute appendicitis can at times be very subtle and non specific. It can easily mimic any other surgical conditions. Role of leucocytosis has been extensively studied in making a diagnosis of appendicitis. (5)

Acute phase reactants are a class of protein whose plasma concentrations vary in response to inflammation. They are classified as positive acute phase reactants, whose levels increase due to inflammation and negative acute phase reactants, for whom the concentration will decrease with inflammation.

C- reactive protein (CRP) was discovered by Tillet and Francis in 1930. Initially thought as a pathogenic secretion, it was later discovered to be a native protein. (6) CRP belongs to pentraxin family of proteins. It is a 224 residue protein with a molar mass of around 25 kDa. The CRP gene is located on the first chromosome. It binds to phosphocholine expressed on cells to activate the complement system and enhances phagocytosis and also plays a role in innate immunity. (7)

CRP levels can rise many folds in acute inflammation and infection. Levels rise above normal limits within six hours and peaks around 48 hours. CRP is known to rise in post-operative period too. It peaks around third post-op day and returns to normal by around tenth post-op day. Uncomplicated surgical diseases witness mild increase in the levels but levels are markedly increased in event of surgical complications. (8)

Uncomplicated appendicitis is associated with levels increasing above the baseline, however significant rise is seen in complicated appendicitis like perforated or gangrenous appendicitis. (6)

Normal levels of CRP and absence of leucocytosis makes the diagnosis of appendicitis unlikely. (9)

Role of total leucocyte count, neutrophil and CRP was studied by Yang et al and concluded that with normal values of all these three, the diagnosis of appendicitis is highly unlikely. (10)

Raised TLC of more than 10×10^3 is seen in around 80–85% patients with acute appendicitis. f more than 10,000/cmm.(11) A raised TLC is regarded as sensitive test for diagnosis of acute appendicitis but is not diagnostic because of its lower specificity.(12)

Evaluation of clinical and biochemical variables was suggested by Hallan et al. They suggested that the use of leucocytosis, neutrophil count and C reactive protein reduced the rate of complications in acute appendicitis. Andersson et al also suggested that repeated physical examination, body temperature charting and laboratory tests was beneficial in setting of patients with equivocal signs of appendicitis. (14)

However, not all studies have found a favourable role for CRP in acute abdominal pain. Salem et al evaluated acute abdominal pain over a period of one year, in which the patients were divided into three groups: nonspecific abdominal pain, surgical non-operative and surgical operative group. Statistical significance was found between the groups but no useful cut off level was found between patients in these groups. (15)

Conclusion:

Appendicitis is a common surgical problem and appendicectomy accounts for a large volume of cases operated worldwide. Mortality from appendicitis has considerable decreased over last two centuries due to early intervention in the form of appendicectomy. In order to decrease the negative appendicectomy rates and in cases with doubtful diagnosis, it is advisable to seek radiological help when possible and also use blood inflammatory markers to help the treating doctors make a better decision. Leucocytosis in combination with elevated CRP levels can help in establishing the diagnosis.

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