“ROLE OF C-REACTIVE PROTEIN, TOTAL LEUCOCYTE COUNT, NEUTROPHIL PERCENTAGE IN PREOPERATIVE DIAGNOSIS OF ACUTE APPENDICITIS - A CROSS SECTIONAL STUDY”

REG.NO. BH0111010

Dissertation

Submitted to the
KLE University, Belgaum, Karnataka

In Partial Fulfillment
of the requirements for the degree of

M. S.
in
GENERAL SURGERY

DEPARTMENT OF SURGERY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELGAUM, KARNATAKA

APRIL - 2014

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ENDORSEMENT BY THE HOD/PRINCIPAL/ HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"ROLE OF C-REACTIVE PROTEIN, TOTAL LEUCOCYTE COUNT, NEUTROPHIL PERCENTAGE IN PREOPERATIVE DIAGNOSIS OF ACUTE APPENDICITIS" A CROSS SECTIONAL STUDY"** is a bonafide research work done by **CANDIDATE REG. NO. BH0111010**.

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LIST OF ABBREVIATIONS USED

AA	-	Acute appendicitis
ALP	-	Alkaline phosphatase
ALT	-	Alanine transaminase
AST	-	Aspartate transaminase
ATP	-	Adenosine triphosphate
Cm	-	Centimeters
Cmm	-	Cubic millimeter
CRP	-	C-reactive protein
CT	-	Computed tomography
dL	-	Deciliters
DLC	-	Differential leukocyte count
DNA	-	Deribonucleic acid
E. Coli	-	Escherichia coli
ELISA	-	Enzyme linked immunosorbent assay
g	-	Grams
HbsAg	-	Hepatitis B surface antigen
HPR	-	Histopathopathological report
IL-6	-	Interleukin-6
IV	-	Intravenous
LFT	-	Liver function tests
mg	-	Milligrams
mL	-	Milliliters
mm	-	Millimeters
MRI	-	Magnetic resonance imaging

n	-	Total number
NC	-	Neutrophil count
NPV	-	Negative predictive value
NSAP	-	Nonspecific abdominal pain
OR	-	Odds ratio
p	-	Probability
PAS	-	Pediatric Appendicitis Score
PMNC	-	Polymorphonuclear cell count
PPV	-	Positive predictive value
RLQ	-	Right lower quadrant
ROC	-	Receiver operating curve
SB	-	Serum bilirubin
SGOT	-	Serum glutamic oxaloacetic transaminase
SGPT	-	Serum glutamic pyruvic transaminase
SMV	-	Superior mesenteric vein
Sr.	-	Serum
TLC	-	Total leukocyte count
TNF	-	Tumor necrosis factor
TSB	-	Total serum bilirubin
USG	-	Ultrasonography
WBC	-	White blood cells

ABSTRACT

Background and Objectives

A common blood analysis including white blood cell counts, neutrophil percentage and serum level of CRP has been demonstrated to be important in the diagnosis for acute appendicitis. The present study was aimed to find out the role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis.

Methodology

This one year hospital based cross-sectional study was done on total of 160 patients admitted with clinical diagnosis of acute appendicitis at the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2012 to December 2012.

Results

In the present study 53.13% patients were females and the male to female ratio was 1:1.13. The commonest age of presentation was 21 to 30 years (38.75%) and the mean age was 27.60±8.43 years. All the patients presented with abdominal pain (100%) while RIF tenderness was commonest sign (100%). Based on HPR findings, 80.62% of patients were diagnosis as having acute appendicitis. HPR findings revealed 80.63% of patients with acute appendicitis.

Conclusion and interpretation

Raised CRP, TLC and direct count were seen in 75%, 63.75% and 66.75% of patients respectively. The sensitivity and specificity of CRP in

predicting acute appendicitis was 96.12% and 90.32% respectively and total leukocyte count showed sensitivity and specificity of 96.90% and 90.32% respectively. The combined CRP, TLC and neutrophil percentage in predicting acute appendicitis showed sensitivity and specificity of 96.90% and 90.32% respectively.

Keywords

Acute appendicitis; C-reactive protein; Neutrophil percentage; Total leucocyte count;

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Chapter 1

Introduction

INTRODUCTION

Acute appendicitis is the most common cause of an 'acute abdomen' in young adults. Appendicitis is defined as an inflammation of the inner lining of the vermiform appendix that spreads to its other parts. This condition is a common and urgent surgical illness with protean manifestations, generous overlap with other clinical syndromes, and significant morbidity, which increases with diagnostic delay.[1]

Obstruction of the lumen is the dominant factor for acute appendicitis and fecoliths are the usual cause of obstruction. Other causes of obstruction could be lymphoid hyperplasia, intestinal worms, tumors, or other conditions.[2] In industrialized countries, individuals have a 7% lifetime risk of developing appendicitis, with the highest frequency occurring at ages from 10 to 30 years. The risk gradually decreases until age 50, when it stabilizes.[3] In the past 30 years, the incidence has fallen dramatically in these countries, such that the individual lifetime risk of appendicectomy is 8.6% and 6.7% among males and females respectively.[4]

Appendectomy in a suspicious case of acute appendicitis is routinely done. The rate of unnecessary normal appendix removal remains high (15%-30%) irrespective of various techniques. Normal appendix during appendectomy is a misdiagnosis whereas delay in diagnosis and treatment can lead to diffuse peritonitis.[5]

The negative exploration itself carries a complication rate not much lower than that after removal of a pathological appendix.

Equally distressing is the fact that perforation may occur in upto 35% of cases.[6] Due to this fact traditionally surgeons have decided to perform negative appendicectomies to reduce incidence of perforation which is being questioned in modern era of evidence based medicine.

This is because of similar signs and symptoms of a wide range of acute abdominal clinical disorders and nonspecific laboratory and conventional radiographic findings.

The diagnosis of acute appendicitis relies on a thorough history and examination.[7] Accurate preoperative diagnosis is always not possible. Typical uncomplicated cases of acute appendicitis are easy to diagnose and treat. Unfortunately, 20-33% of the patients suspected of having acute appendicitis present with atypical findings.[8]

In recent years however with the availability of various cross-sectional imaging techniques viz. Ultrasonography, Spiral CT and MRI, false positive diagnosis of acute appendicitis has reduced. The overall accuracy of cross-sectional imaging techniques in diagnosing acute appendicitis varies from 87%-98%.[9]

To supplement the clinical diagnosis and to reduce the frequency of unnecessary appendicectomy, the importance of laboratory investigations like White Blood Cell (WBC) counts and C-reactive protein (CRP) etc values has been stressed.[10] The use of Ultrasonography (USG) as a diagnostic tool for appendicitis has been widely known and studied.[11] Various scores combining clinical features and laboratory investigations have also been developed and are

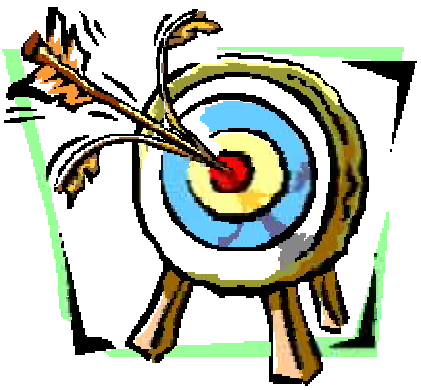
good enough to reach the diagnosis. These are the Alvarado score[12] and the Modified Alvarado score.[13]

In the diagnosis for acute appendicitis a common blood analysis including white blood cell counts, neutrophil percentage and serum level of CRP has been demonstrated to be important.[14-20] Some reports indicated that appendicitis is unlikely, when the white blood cells count and CRP value are normal.[21-23]

However, their values in diagnosing acute appendicitis have been debated by many authors.[14-20,23-26] Also, the data reporting the diagnostic value of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis is scanty especially in Indian context. Hence the present study was undertaken to find out the role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis.

Chapter 2

Objectives



OBJECTIVES

The objectives of the present study were to evaluate the role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis.

Chapter 3

Review of Literature

REVIEW OF LITERATURE

Historical review

Caludius Amyrand in 1736 performed first appendicetomy on a boy of 11 years of age who had right scrotal hernia accompanied by fistula (within the scrotum was found the appendix, perforated by pain).[27]

Heister in 1755 recognized that appendix might be sight of primary inflammation. Hamock in 1848 successfully drained an appendix abscesses in a pregnant female during her eight month of pregnancy. Lawson Tait in 1880 first abdominal appendicectomy.[27]

Reginald Fitz n 1886 first described acute appendicitis. He was also the first to use the term appendicitis. McBurney in 1889 advanced the act of diagnosis sufficiently to remove the first unruptured appendix and also devised the muscle splitting incision named after him.[27]

Two hundred years after its anatomical description, the appendix was observed to be the site of inflammatory disease. This was not widely accepted until the publication by Fitz 120 years later. American surgeons led in demonstrating that early appendectomy was safe and life saving. Perforation of the appendix with peritonitis continues to be a significant problem, but the mortality rate has dramatically declined. Appendiceal disease has clearly affected the course of history.[28]

Anatomy

The vermiform appendix is a narrow, vermian (worm shaped) tube, arising from posteromedial caecal wall, 2 cm or less below the end of the ileum. It can be found in any of the following position:

1. Retrocaecal (12 O'clock) position – directed upwards in the retrocaecal recess. If the length is greater it may be retrocolic on hepatic.
2. Right Paracaecal (11 O'clock) position: lies on right side of caecum.
3. Left Paracaecal (10 O'clock) position: lies on left side of caecum. It may be preileal or postileal.
4. Splenic (2 O'clock) position: directed towards spleen.
5. Promontoric (3 O' clock) position: directed towards sacral promontory.
6. Pelvic (4 to 5 O'clock) position: Crosses the pelvic brim and lies in true pelvis.
7. 6 O'clock position: Appendix in mid inguinal position.

The location of appendix as follows.[29]

Retrocaecal and retrocalic	:	74%
Pelvic	:	21%
Sub caecal	:	1.5%
Preileal	:	1%
Post ileal	:	0.5%

The length varies from 2 to 20 cm with an average of 9 cm. it is longer in children than adults. The diameter is about 5 mm. The lumen is quite narrow and may be obliterated after mid-adult life.

The appendicular orifice is situated at posteromedial aspect of the caecum 2 cms below the ileocaecal orifice. The appendicular orifice is occasionally guared by an indistinct semilunar fold of mucous membrane known as valve of Gerlach.

The appendix is suspended by a small triangular fold of peritoneum, called mesoappendix. The appendicular artery often runs in its free edge, but may run closer to the base of the appendix.

Blood supply

The caecum is supplied by the anterior and posterior caecal branches of the ileocolic artery which is a branch of superior mesenteric artery.

The appendicular artery, a branch of ileocolic artery reaches the appendix through the mesoappendix. There may be an accessory appendicular artery (artery of Seshachalam) arising from the posterior caecal artery. If the mesentery is incomplete, the artery lies on the wall of appendix in its distal part and may be thrombosed in acute appendicitis.[30]

Venous drainage

Venous drainage is brought about by the appendicular, ileocolic and superior mesenteric veins and is to the portal vein.

Lymphatic drainage

The lymph vessels from caecum and appendix terminate in ileocolic nodes situated close to the ileocolic artery. Small appendicular nodes usually lie close to the meso-appendix.

Nerve supply

A plexus of nerves consisting of both sympathetic and parasympathetic fibres accompany the arteries to reach the caecum and appendix. The plexus is an offshoot from the superior mesenteric plexus. The sympathetic fibres are derived from T10 – T11 segment of the cord and the parasympathetic fibres are derived from vagi.

Development

The caecum and appendix develop form the caecal bud of the midgut. Agensis of the appendix is extremely rare. A study reported an incidence of one in 1,00,000 laparotomies for suspected appendicitis.[31]

Histology

The structure of the appendix resembles that of large intestine. The lamina propria is extensively infiltrated with lymphocytes and the details of the mucosa are often obscured by the many lymphatic nodules that may fill the mucosa and submucosa. This profusion of lymph tissue has promoted the description of "abdominal tonsil" for the appendix, and draws attention to this features as relevant to the causes of appendicitis.

Duplication of the appendix

Duplication of the appendix is an anomaly of extreme rarity, classified it into three types.

Type A: Partial duplication of the appendix on a single caecum.

Type B: Single caecum with two completely separate appendices.

B1 : Bird like appendix where there are two appendices symmetrically placed on either side of ileocaecal value.

B2 : Along with the usual appendix another rudimentary appendix arises from the caecum along the line of one of the teniae coli.

Type C: There are two caeca, each of which bears an appendix.

Tinkler described a unique case of a triple appendix, associated with double penis and ectopia vesicae.[32]

Epidemiology

Appendicitis is the most common acute surgical condition of the abdomen. Approximately 7 percent of the population will have appendicitis in their lifetime, with the peak incidence occurring between the ages of 10 and 30 years.[33]

Studies have demonstrated that AA is seen most commonly in western societies, particularly in youths and males.[34,35] Consequently only 5% to 10% of acute appendicitis cases are seen in the elderly.[36] The lower incidence of AA and

the less pronounced gender gap in regions such as Africa and Asia is worth mentioning.[37,38]

Epidemiological and demographic studies report the appendicitis incidence to vary according to age, gender, race, socioeconomic status, food culture, and seasonal changes.[35,37,39,40] Therefore, the frequency of AA is different in each country.

Appendicitis is most frequently seen in patients in their second through fourth decades of life, with a mean age of 31.3 years and a median age of 22 years.[41,42]

The studies performed in the last decade have reported a decrease in the incidence of AA in western countries[43] but an increase in some African[44] and Asian[45] countries is interesting.

In California, the incidence of appendicitis was 137.5 per 100.000 for Caucasian males while this incidence was 162.7 for Hispanics, 98.0 for Asian/others, and 70.7 for blacks. The same was true in female patients with rates per 100,000 of 98.8, 97.5, 64.6, and 49.6 for the above groups respectively.[43]

The effect of better socioeconomic conditions created as a result of improving water supplies and hygienic conditions, has been found to be the reason for this decrease in Western societies. A recent study from Spain found a decrease in appendicitis in the last 10 years.[46] A study from Greece evaluating the last 30 years found the age-standardized appendicitis rate to fall 75% from 652/100.000 to 164/100.000.[47]

Pathogenesis

The appendix is a long diverticulum that extends from the inferior tip of the cecum. Its lining is interspersed with lymphoid follicles. Most of the time, the appendix has an intraperitoneal location (either anterior or retrocecal) and, thus, may come in contact with the anterior parietal peritoneum when it is inflamed. Up to 30 percent of the time, the appendix may be "hidden" from the anterior peritoneum by being in a pelvic, retroileal or retrocolic (retroperitoneal retrocecal) position. The "hidden" position of the appendix notably changes the clinical manifestations of appendicitis.[33]

Obstruction of the narrow appendiceal lumen initiates the clinical illness of acute appendicitis. Obstruction has multiple causes, including lymphoid hyperplasia (related to viral illnesses, including upper respiratory infection, mononucleosis, gastroenteritis), fecaliths, parasites, foreign bodies, Crohn's disease, primary or metastatic cancer and carcinoid syndrome. Lymphoid hyperplasia is more common in children and young adults, accounting for the increased incidence of appendicitis in these age groups.[33]

History and Physical Examination

Abdominal pain is the most common symptom of appendicitis.[48] In multiple studies,[48-50] specific characteristics of the abdominal pain and other associated symptoms have proved to be reliable indicators of acute appendicitis. A thorough review of the history of the abdominal pain and of the patient's recent genitourinary, gynecologic and pulmonary history should be obtained.

Common Symptoms of Appendicitis[48,50]

Common symptoms	Frequency (%)
Abdominal pain	~100
Anorexia	~100
Nausea	90
Vomiting	75
Pain migration	50
Classic symptom sequence (vague periumbilical pain to anorexia/nausea/unsustained vomiting to migration of pain to right lower quadrant to low-grade fever)	50

Onset of symptoms typically within past 24 to 36 hours

Anorexia, nausea and vomiting are symptoms that are commonly associated with acute appendicitis. The classic history of pain beginning in the periumbilical region and migrating to the right lower quadrant occurs in only 50 percent of patients. Duration of symptoms exceeding 24 to 36 hours is uncommon in nonperforated appendicitis.[33]

In a meta-analysis,[51] likelihood ratios were calculated for many of these symptoms. A likelihood ratio is the amount by which the odds of a disease change with new information (e.g., physical examination findings, laboratory results).[52] This change can be positive or negative. Symptoms such as anorexia, nausea and vomiting commonly occur in acute appendicitis; however, the presence of these symptoms does not necessarily increase the likelihood of

appendicitis nor does their absence decrease the likelihood of the diagnosis. Moreover, other symptoms have more notable positive and negative likelihood ratios.

A careful, systematic examination of the abdomen is essential. While right lower quadrant tenderness to palpation is the most important physical examination finding, other signs may help confirm the diagnosis. The abdominal examination should begin with inspection followed by auscultation, gentle palpation (beginning at a site distant from the pain) and, finally, abdominal percussion. The rebound tenderness that is associated with peritoneal irritation has been shown to be more accurately identified by percussion of the abdomen than by palpation with quick release.[33]

Common Signs of Appendicitis[33]

- Right lower quadrant pain on palpation (the single most important sign)
- Low-grade fever (38°C [or 100.4°F])—absence of fever or high fever can occur.
- Peritoneal signs.
- Localized tenderness to percussion
- Guarding
- Other confirmatory peritoneal signs (absence of these signs does not exclude appendicitis)
- Psoas sign—pain on extension of right thigh (retroperitoneal retrocecal appendix)
- Obturator sign—pain on internal rotation of right thigh (pelvic appendix)

- Rovsing's sign—pain in right lower quadrant with palpation of left lower quadrant
- Dunphy's sign—increased pain with coughing
- Flank tenderness in right lower quadrant (retroperitoneal retrocecal appendix)
- Patient maintains hip flexion with knees drawn up for comfort

When the appendix is hidden from the anterior peritoneum, the usual symptoms and signs of acute appendicitis may not be present. Pain and tenderness can occur in a location other than the right lower quadrant. A retrocecal appendix in a retroperitoneal location may cause flank pain. In this case, stretching the iliopsoas muscle can elicit pain. The psoas sign is elicited in this manner: the patient lies on the left side while the examiner extends the patient's right thigh. In contrast, a patient with a pelvic appendix may show no abdominal signs, but the rectal examination may elicit tenderness in the cul-de-sac. In addition, an obturator sign (pain on passive internal rotation of the flexed right thigh) may be present in a patient with a pelvic appendix.[48]

The differential diagnosis of appendicitis is broad, but the patient's history and the remainder of the physical examination may clarify the diagnosis. Because many gynecologic conditions can mimic appendicitis, a pelvic examination should be performed on all women with abdominal pain. Given the breadth of the differential diagnosis, the pulmonary, genitourinary and rectal examinations are equally important. Studies have shown, however, that the rectal examination provides useful information only when the diagnosis is unclear and, thus, can be reserved for use in such cases.[50]

Diagnosis

Typical uncomplicated cases of acute appendicitis are easy to diagnose and treat. Typical cases present classically with para-umbilical pain (visceral pain) migrating to the right lower quadrant of the abdomen (RLQ). Pain usually is associated with nausea, vomiting and low-grade fever.[3]

Localized irritation and inflammation of the peritoneum results in pain with cough (Dunphy's sign), tenderness and muscle guarding on palpation in the RLQ over McBurney's point and rebound tenderness elicited by deep palpation with quick release (Blumberg sign). Unfortunately, 20-33% of the patients suspected of having acute appendicitis present with atypical findings.[3,8]

If the patient's history and the physical examination do not clarify the diagnosis, laboratory and radiologic evaluations may be helpful. A clear diagnosis of appendicitis obviates the need for further testing and should prompt immediate surgical referral.

Laboratory tests

The white blood cell (WBC) count is elevated (greater than 10,000 per mm3 [100 × 109 per L]) in 80 percent of all cases of acute appendicitis. Unfortunately, the WBC is elevated in up to 70 percent of patients with other causes of right lower quadrant pain.[33] Thus, an elevated WBC has a low predictive value. Serial WBC measurements (over 4 to 8 hours) in suspected cases may increase the specificity, as the WBC count often increases in acute appendicitis (except in cases of perforation, in which it may initially fall).[50]

In addition, 95% of patients have neutrophilia and, in the elderly, an elevated band count greater than 6 percent has been shown to have a high predictive value for appendicitis. In general, however, the WBC count and differential are only moderately helpful in confirming the diagnosis of appendicitis because of their low specificities.[33]

A more recently suggested laboratory evaluation is determination of the C-reactive protein level. An elevated C-reactive protein level (greater than 0.8 mg per dL) is common in appendicitis, but studies disagree on its sensitivity and specificity.[49,50] An elevated C-reactive protein level in combination with an elevated WBC count and neutrophilia are highly sensitive (97 to 100 percent). Therefore, if all three of these findings are absent, the chance of appendicitis is low.[50]

In patients with appendicitis, a urinalysis may demonstrate changes such as mild pyuria, proteinuria and hematuria, but the test serves more to exclude urinary tract causes of abdominal pain than to diagnose appendicitis.[33]

Specialist investigations are rarely needed to make the diagnosis of appendicitis as the diagnosis is predominantly clinical. The judicious use of simple bedside tests and laboratory markers of inflammation can provide additional evidence to support the diagnosis of acute appendicitis and exclude important differentials.

The majority of patients presenting with abdominal pain will have blood drawn for a full blood count and urea and electrolyte analysis. Urine analysis and microscopy can exclude urinary tract infection but may be abnormal in up to 48%

of patients undergoing appendicectomy. The cause for abnormalities often leukocytosis and microscopic haematuria is the underlying inflammatory process irritating the renal tract along the line of the inflamed appendix.[53]

The most commonly used serological markers of inflammation in the diagnosis of acute appendicitis are the leukocyte count and C-reactive protein (CRP). Neither is diagnostic of acute appendicitis and studies have attempted to define potential thresholds values which are predictive of a diagnosis and disease severity.[53]

Repeated tests may also be useful in the context of patients in whom the diagnosis is unclear initially and are observed clinically with two studies suggesting other diagnoses or further tests should be considered if repeat measures are normal. In the presence of normal inflammatory markers CRP, WBC and neutrophil count the diagnosis of acute appendicitis is unlikely.[53,54]

The performance of these tests is clearly related to the population under study and a meta-analysis of studies of reporting results on patients admitted to hospital with acute abdominal pain and those selected for appendicectomy demonstrated that CRP performed better as a diagnostic test in those with an acute abdomen than in those selected already for surgery.[53]

A further meta-analysis of studies reporting on patients with a clinical suspicion of appendicitis concluded that the diagnosis of acute appendicitis was more likely when two or more inflammatory variables [granulocyte count, proportion of polymorphonuclear blood cells, white blood cell count (WBC) and CRP] were elevated.[55]

Studies of inflammatory markers in children notably of CRP and WBC count have concluded that an elevation of both parameters can support the diagnosis of acute appendicitis.[56-58] These studies have all used different cut off levels to determine abnormal results and have generally been small single centre studies.

Therefore, it is suggested that the use of inflammatory variables should be used to support a clinical diagnosis of acute appendicitis and to exclude other pathologies. All women of child bearing age should have a serum or urine beta HCG requested to confirm pregnancy status. Given the differential diagnosis of acute appendicitis other blood tests including amylase, lipase, liver function tests, and clotting studies may be required to confirm or exclude other diagnoses.[53]

Given the limitations of the current inflammatory markers there has been considerable research interest in identifying other potential biomarkers for the diagnosis of acute appendicitis and for predicting perforation.[53]

Hyper-bilirubinaemia has been shown to correlate with a diagnosis of perforated appendicitis[59] but a stronger correlation has been recently reported for CRP.[60]

Interleukin-6 serum levels have not been shown to aid the diagnosis of appendicitis or reduce negative laparotomy rates. The use of plasma D-lactate levels in the diagnosis of appendicitis is unclear with some studies suggesting it may or may not be a useful adjunct.[53]

A recent study of 51 patients with appendicitis suggested plasma concentration of lactoferrin and calprotectin are elevated in those with appendicitis but their role in diagnosis is unclear.[61]

Clearly the use of these markers in routine clinical practice will require much larger validation studies in defined cohorts of patients. Laboratory tests have also been used to try and determine the need for further investigation in patients presenting with abdominal pain. Due to the non specific nature of most inflammatory variables, however, no single specific test has been able to predict the need for further radiological investigation.[62]

Radiologic evaluation

The options for radiologic evaluation of patients with suspected appendicitis have expanded in recent years, enhancing and sometimes replacing previously used radiologic studies.

Plain radiographs, while often revealing abnormalities in acute appendicitis, lack specificity and are more helpful in diagnosing other causes of abdominal pain. Likewise, barium enema is now used infrequently because of the advances in abdominal imaging.[33]

Ultrasound

Graded compression Sonography is relatively inexpensive, rapid, non-invasive, and requires no patient preparation or contrast material administration. Unfortunately, graded compression sonography is operator-dependent and requires a high level of skill and expertise. Sonography is also a dynamic

investigation, and photographs of sonographic images cannot be reliably re-evaluated.[63]

An inflamed appendix appears on ultrasound as a non-compressible tubular structure, more than 6 mm in diameter, with a thickened wall.

Ultrasonography may significantly improve the diagnostic accuracy in patients with suspected acute appendicitis and should be performed in some patients in whom the clinical diagnosis is equivocal. The overall sensitivity, specificity and accuracy of ultrasonography in the diagnosis of acute appendicitis were 78%, 92% and 87%, respectively.[64]

Another limitation of ultrasound in the diagnosis of acute appendicitis is the fact that patients cannot be safely be sent home after a negative result unless there are good clinical grounds for their discharge.[65]

Ultrasound is helpful in young females in diagnosis of some gynecological conditions like torsion of ovarian cyst and ectopic pregnancy which may be confused with acute appendicitis.

Contrast-Enhanced CT

CT is a well-established technique in the study of acute abdominal pain and has shown high sensitivity and specificity for diagnosing and differentiating appendicitis, providing an accurate diagnosis in the early stages of disease.[66]

CT is readily available, is supposed to be operator-independent, is relatively easy to perform, and has results that are easy to interpret. Helical CT

has reported sensitivities of 90-100%, specificities of 91-99%, accuracies of 94-98%, positive predictive values of 92-98%, and negative predictive values of 95-100%.[67-68] Studies have proven that CT without the administration of contrast material in the setting of suspicion of acute appendicitis can be as accurate as those techniques in which oral, rectal, or IV contrast medium is administered.[3]

The typical CT finding of an inflamed appendix is a thickened wall and a non-filling appendix associated with periappendicular inflammatory fluid.[3]

CT scanning of patients with suspected appendicitis may reduce the number of patients admitted for observation and decrease the rate of negative appendectomy.[69]

Diagnostic Laparoscopy

Several authors have advocated the use of laparoscopy as a diagnostic modality in the evaluation of a patient suspected of having acute appendicitis. Diagnostic laparoscopy should be viewed as an invasive procedure requiring general anesthesia and having a risk similar to appendectomy. For this reason, it is not preferred as a diagnostic tool. There is a lot of debate whether to remove a normal-looking appendix during diagnostic laparoscopy or to leave it. Naturally, many surgeons prefer not to come out empty-handed regardless of the gross appearance of the appendix, especially if no other pathology is identified. Many authors advocate removal of appendix regardless of the gross appearance as they believe not all normal-looking appendices are not inflamed and the inflammation may be limited to the mucosa (endo-appendicitis); however, the routine removal of a normal appendix is not a complication-free technique even in laparoscopy.[3]

In a study authors reviewed the literature for the years 1978 to 1998 to analyze the negative appendectomy rates, complication rates, the accuracy of laparoscopic appendix assessment, and the incidence of false negative diagnosis of appendicitis, at surgical and gynaecological laparoscopy. He concluded that, contrary to general opinion, there is no substantial evidence to support the assumption that the macroscopic diagnosis of appendicitis is unreliable. High rates of conflicting diagnoses of excision specimens suggest that endo-appendicitis has little clinical significance. At present, negative appendectomy rates are considerably higher for laparoscopic appendectomy than for the open approach. The role of diagnostic laparoscopy in suspected appendicitis should be reconsidered. It may be useful in particular subgroups of patients, but it is no substitute for good clinical judgement.[70]

Another report stated that, 3.2% of the intra-operatively normal-appearing appendices demonstrated acute inflammation after pathological examination.[71]

Furthermore, a prospective study evaluated 109 diagnostic laparoscopies for suspected appendicitis with normal-looking appendices in 100 cases. After a median follow-up of 4.4 years, only two patients had acute appendicitis and nine had some recurrent pain Study suggested that it is safe to leave a normal-looking appendix in place when a diagnostic laparoscopy for suspected appendicitis is performed, even if another diagnosis cannot be found at laparoscopy.[72]

Diagnostic laparoscopy may be helpful in equivocal cases or in women of childbearing age, while therapeutic laparoscopy may be preferred in certain subsets of patients (e.g., women, obese patients, athletes),[73] but it should not be

advocated as a routine diagnostic procedure to replace the classical pre-operative work-up usually performed for clinically suspected appendicitis, because it has its own morbidity and in most cases requires general anesthesia.[3]

Despite technologic advances, the diagnosis of appendicitis is still based primarily on the patient's history and the physical examination. It has been estimated that the accuracy of the clinical diagnosis of acute appendicitis is lying between 76% and 92%, with values correlating with the surgeon's experience.[3]

Scoring Systems

The diagnosis of acute appendicitis can be difficult and any delay in definitive treatment with surgery can lead to an increase in mortality and morbidity as the disease progresses to appendiceal perforation. This increase in morbidity and mortality has been used to justify the high rates of negative appendicectomy which range from 14 to 75%.[74]

A drive, therefore, has been to improve the diagnosis of appendicitis using clinical scoring systems. These systems have been based on symptoms, signs and laboratory findings. In some instances they have been part of a computer-aided diagnostic algorithm. The most widely cited score in the diagnosis of adults with acute appendicitis is the Alvarado score.[74]

In children the pediatric appendicitis score or Samuel score is most widely used.[75] The scores have now been validated in a wide variety of populations, however, they have not made it into routine clinical practice in all settings.[53]

A number of studies have also used computer aided diagnosis in patients with acute abdominal pain in an attempt to improve the management of patients presenting with acute abdominal pain. These systems have reported a diagnostic accuracy of 97.2% in acute appendicitis, improvement in time to surgery, with a reduction in the number of perforations over a 2 year period. They have, however, not been introduced into routine clinical practice. In an aid to further improve diagnosis artificial neural networks have been suggested as adjuncts to diagnosis but this remains an area of research with only a small number of patients having had diagnoses made in this way.[76,77]

Alvarado Score or MANTRELS Score[74]

	Variable	**Value**
Symptoms	Migration	1
	Anorexia	1
	Nausea – Vomiting	1
Signs	Tenderness in right lower quadrant	2
	Rebound pain	1
	Elevation of temperature > 37.3 ^{0}C	1
Laboratory	Leukocytosis > 10.0 x 10^{9} /L	2
	Shift to the left > 75%	1

The score was originally developed by Alfredo Alvarado in 1986 as an aid to the diagnosis of patients with appendicitis. The score was based on a cohort

of 305 patients based at the Nazareth Hospital in Philadelphia in the United States of America who presented with suspected appendicitis. The charts of these patients were reviewed retrospectively and the sensitivity and specificity of a number of symptoms, signs and laboratory variables were assessed with those with the greatest diagnostic value being used to form a scoring system. This resulted in the formation of a simple score consisting of three symptoms, three signs and two laboratory markers of inflammation weighted as either one or two based on their importance in diagnosis. These variables could be recalled using the pneumonic MANTRELS. The maximum total score achievable is, therefore, 10. A score of 5 or 6 is compatible with a diagnosis of acute appendicitis, with a score of 7 or 8 indicating probable appendicitis and a score of 9 or 10 indicating a very probable acute appendicitis. It has been suggested that score can used as a guide to determine which patients require further observation and which patients require surgery. Those with a score of 5 or 6 required observation while those with a score of 7 or above needed to proceed to surgery as it was likely that they had appendicitis.

The Alvarado score is the best performing of the clinical scoring systems in current use. The score, however, is not based on a formal mathematical model which has accounted for the variables independent ability to predict a diagnosis. It was also based on retrospective data. These factors have resulted in a number of authors proposing multiple other scoring systems including a variety of other clinical, laboratory and imaging findings.[53]

Other Scoring Systems

All of the described clinical scoring systems have attempted to aid the clinician in the diagnosis of the patient with acute appendicitis. The systems use a variety of signs, symptoms and investigations to form their respective scores. None has been adopted into wide spread clinical practice. They remain only as an aid to clinical diagnosis but do alert the clinician to all probable variables that should be considered in making a diagnosis of appendicitis.[53]

The Tzanakis scoring system incorporated ultrasound scanning along with clinical and laboratory findings to predict the diagnosis of appendicitis. Following a multivariate logistic regression analysis four variables formed the scoring system (Ultrasound positive for acute appendicitis, tenderness in the right lower quadrant, rebound tenderness and a leukocyte count[12,000/lL).[53]

The Appendicitis Inflammatory Response Score was constructed from eight independent predictive variables (right lower quadrant pain, rebound tenderness, muscular defense, WBC count, proportion of neutrophils, CRP, body temperature and vomiting) and performed better than the Alvarado score in a sample of 229 patients suspected of appendicitis (Sensitivity 0.97 vs. 0.92, p=0.0027 and Specificity 0.93 vs. 0.88, p=0.0007).

The Ohmann score was developed in Germany and was subject to a before and after intervention study and used computer – aided diagnosis. The variables completing the score are tenderness in the right lower quadrant, rebound tenderness, no micturition difficulties, steady pain, leukocyte count[10.0

9 109/L, age\50 years, relocation of the pain to right lower quadrant and rigidity.[79]

The score was developed using stepwise logistic regression analysis of a German database and confirmed on a Dutch database. Following introduction of the score over a 4 month period the rates of delayed appendicectomy (2 vs. 8%) and delayed discharge (11 vs. 22%) decreased significantly (p\0.02), however, there were no changes in the number of perforations or complications.[53]

The Lintula score was developed from 35 symptoms and signs recorded for 131 Finnish children with abdominal pain which were modeled using logistic regression for their predictive value for a diagnosis of acute appendicitis. The score was then validated on a cohort of prospectively collected children with abdominal pain. The score uses gender, intensity of pain, relocation of pain, vomiting, pain in the right lower quadrant, fever, guarding, bowel sounds and rebound tenderness to form a score which if greater than 21 appendicectomy was advocated.[80]

The Lintula score was developed for use in children but has subsequently been validated in adults.[81] The Fenyo-Lindberg scoring system was developed using a prospectively collected sample of 1,167 patients with suspected appendicitis. The system uses nine clinical and one laboratory variable to form a score. Each variable is given a weight between -15 and +15.[82] The authors initially reported a reduction in the rate of negative laparotomies associated with the use of the score.

The Pediatric Appendicitis Score (PAS) was first described by Madan Samuel in 2002. It was based on an analysis of a prospectively collected cohort of 1,170 children aged 4–15 years.[83] The symptoms, signs and laboratory findings were evaluated for sensitivity, specificity, predictive value and joint probability. A diagnostic index/weight for each clinical feature and investigation was calculated. A stepwise multiple linear regression analysis was then performed on the best independent predictors to develop a scoring system based on eight variables. The variables were given a score of one except for physical signs which were assigned a score of 2 to give a total score of 10. The variables in order of diagnostic index are, cough/percussion/hoping tenderness in the right lower quadrant of the abdomen, anorexia, pyrexia, nausea and emesis, tenderness over the right iliac fossa, leukocytosis, polymorphonuclear neutrophilia and migration of pain. The score was then validated on the cases and was found to have a sensitivity of 1, specificity of 0.92, positive predicted value of 0.96 and negative predictive value of 0.99.[53]

The PAS has been evaluated in other cohorts of paediatric patients. It has been suggested that it is useful in stratifying the clinical risk of acute appendicitis in those children presenting to the emergency department with abdominal pain and classifying them as low, medium and high risk of acute appendicitis.[84] A score of less than or equal to 2 was found to have a high validity of ruling out acute appendicitis while a score greater than or equal to 7 was found to have a high validity of predicting acute

Scoring Systems and the Use of Radiological Investigations

None of the scoring systems described have been able to replace the clinical diagnosis of acute appendicitis, however, they do act as an adjunct to diagnosis. Several studies have detailed their possible use in determining the need for further investigation in patients with abdominal pain. The authors of a prospective evaluation of 849 children with abdominal pain suggested that those with a PAS score of between 3 and 6 should go on to have further investigation such as ultrasound or computed tomography or a period of further evaluation.[84]

The accuracy of clinical diagnosis of suspected cases of acute appendicitis can further be improved by repeated clinical examination and adoption of what is called active observation. Patients under active observation are kept fasting and re-evaluated for progression or regression of their symptoms and signs by repeated clinical examination every 2-3 hours (preferably by the same physician) and repeated estimation of white blood count and C-reactive protein.[53]

Active observation confirms intraperitoneal pathology which requires surgical intervention or further investigation in a small group of patients. It also excludes those found to have medical illness, e.g., UTI. In 30-40% of patients, a firm diagnosis is not possible; those patients can benefit from a further period of active observation with or without further investigation depending on whether the symptoms are persisting or improving. Active observation results in a substantial fall in negative appendicectomy rate and is widely considered as safe and effective approach to the management of patients with equivocal features of acute appendicitis.[3]

Diagnostic difficulties

Accurate and timely diagnosis of atypical cases remains clinically challenging and one of the most commonly missed problems in the emergency departments. Precaution appendectomy or misdiagnosis of presumed appendicitis is an adverse outcome that leads to unnecessary surgery, serious interruption of patient's daily activities and considerable waste of hospital resources in addition to the recognized postoperative complications. On the other hand, delay in diagnosis may increase the morbidity and cost.[3]

Statistics reported that 1 of 5 cases of appendicitis is misdiagnosed; however, a normal appendix is found in 15-35% of patients who have emergency appendectomy.[85-87]

Variation in the position of the appendix, age of the patient and degree of inflammation make the clinical presentation of appendicitis inconsistent. Females during childbearing age present diagnostic difficulty and the incidence of misdiagnosis is increased for women of the reproductive age.[88]

Treatment

The standard for management of nonperforated appendicitis remains appendectomy. Because prompt treatment of appendicitis is important in preventing further morbidity and mortality, a margin of error in over-diagnosis is acceptable. Some studies have investigated nonoperative management with parenteral antibiotic treatment, but 40% of these patients eventually required appendectomy.[33]

Appendectomy may be performed by laparotomy (usually through a limited right lower quadrant incision) or laparoscopy. Diagnostic laparoscopy may be helpful in equivocal cases or in women of childbearing age, while therapeutic laparoscopy may be preferred in certain subsets of patients (e.g., women, obese patients, athletes).[33]

While laparoscopic intervention has the advantages of decreased postoperative pain, earlier return to normal activity and better cosmetic results, its disadvantages include greater cost and longer operative time.4 Open appendectomy may remain the primary approach to treatment until further cost and benefit analyses are conducted.

Complications

Appendiceal rupture accounts for a majority of the complications of appendicitis. Factors that increase the rate of perforation are delayed presentation to medical care, age extremes (young and old) and hidden location of appendix. A brief period of in-hospital observation (less than six hours) in equivocal cases does not increase the perforation rate and may improve diagnostic accuracy.[53]

Diagnosis of a perforated appendix is usually easier (although immediately after rupture, the patient's symptoms may temporarily subside). The physical examination findings are more obvious if peritonitis generalizes, with a more generalized right lower quadrant tenderness progressing to complete abdominal tenderness. An ill-defined mass may be felt in the right lower quadrant. Fever is more common with rupture, and the WBC count may elevate

to 20,000 to 30,000 per mm3 (200 to 300 × 109 per L) with a prominent left shift.[48]

A periappendiceal abscess may be treated immediately by surgery or by nonoperative management. Nonoperative management consists of parenteral antibiotics with observation or CT-guided drainage, followed by interval appendectomy six weeks to three months later.[53]

Prompt diagnosis of appendicitis ensures timely treatment and prevents complications. Because abdominal pain is a common presenting symptom in outpatient care, family physicians serve an important role in the diagnosis of appendicitis. Obvious cases of appendicitis require urgent referral, while equivocal cases warrant further evaluation and, many times, surgical consultation.

C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis

Appendicitis has been mainly treated by surgical management. However, non-surgical treatment of appendicitis has also been documented with good success. The traditional practice of an interval appendectomy has been called into question by some, indicating that patients who do not have recurrent episodes of appendicitis within 3 to 6 months may never need an appendectomy. Therefore, the clinician often wonders whether a patient with appendicitis needs to receive surgical treatment or to be managed with antibiotics. After a patient is diagnosed with appendicitis, clinician generally want to determine the severity before they can select the optimal treatment. If a clinician could predict the severity of

appendicitis, one could determine the therapeutic method and the timing of the operation. A surgical indication marker such as the total leucocyte count, neutrophil percentage or CRP would be useful for deciding between treating the patient with surgery or antibiotics.[89]

C-reactive protein

C-reactive protein has been a measure of acute phase reactions to inflammation for the last 15 years. Recently improved highly sensitive and standardized quantitative assays in serum and cerebrospinal fluid have allowed a re-evaluation of its potential as a diagnostic laboratory. C-reactive protein is the first protein to be discovered which behaves as an acute phase reactant. It has been named for its calcium-dependent interaction with the somatic C-polysaccharide of pneumococci. The discovery of C-reactive protein was reported in 1930 by Tillet and Francis.[90]

They were investigating serological reactions in pneumonia with various extracts of pneumococci and observed that a non type specific somatic polysaccharide fraction, which they designated fraction C, was precipitated by the sera of acutely ill patients. After the crisis, the capacity of the patients sera to precipitate C-polysaccharide rapidly disappeared, and the C-reactive material was not found in the sera from normal healthy individuals.

Lofstrom G. in 1944 independently described a non-specific capsular-swelling reaction of some strains of pneumococci when mixed with acute-phase sera and subsequently showed that the substance responsible was C-reactive protein. He detected C-reactive protein in non-infectious as well as infectious

conditions - and the acute-phase reaction, in which the concentration of certain plasma proteins increase, is now recognized as a general and non-specific response to most forms of infective and non-infective inflammatory processes, cellular and /or tissue necrosis and malignant neoplasia.

Structure of C-reactive protein[91]

C-reactive protein is a cyclic pentameric protein composed of five non-covalently bound, identical 23.5 kDa subunits, arranged in a doughnut-shaped polymer. The main function of this pentamer is related to the ability to bind biologically significant ligands in vivo. The human C-reactive protein molecule (Molecular weight - 1,05,500 Da) is composed of five identical nonglycosylated polypeptide subunits (each of mass 23027 Da), with each subunit containing 206 amino acid residues. The promoters are non-covalently associated in an annular configuration with cyclic pentameric symmetry. Each promoter has the characteristic 'lectin fold', composed of a two- layered β-sheet with flattened jelly roll topology. The ligand binding site, composed of loops with two calcium ions bound 4 A^0 apart by protein side-chains, is located on the concave face. The other face carries a single α-helix. The pentraxin family is named for its electron micrographic appearance from the Greek penta (five) ragos (berries).

Functional properties[92-94]

C-reactive protein has calcium interaction with the somatic C-polysaccharide of pneumococci, wherein it recognizes phosphocholine residues.58 It also binds to other substances which contain phosphocoline, including phospholipids, some plasma lipoproteins and plasma membranes of

damaged or apoptotic, but not intact cells. In addition, C-reactive protein binds specifically to small nuclear ribonucleoprotein particles when they are exposed in dead or damaged cells.

The function of CRP is related to its role in the innate immune system. Similar to immunoglobulin IgG, it activates complement, binds to Fc receptors and acts as an opsonin for various pathogens. Interaction of CRP with Fc receptors leads to the generation of proinflammatory cytokines that enhance inflammatory response. Unlike IgG, which specifically recognizes distinct antigenic epitopes, CRP recognizes altered self and foreign molecules based on pattern recognition. Thus, CRP is thought to act as a surveillance molecule for altered self and certain pathogens. This recognition provides an early defence and leads to a proinflammatory signal and activation of the humoral, adaptive immune system.

C-reactive protein binds to molecular groups found on a wide variety of bacteria and act as an opsonin. A number of functions have been ascribed to CRP, including initiation of opsonization and phagocytosis and activation of complement, neutrophils, and monocytemacrophage.

C-reactive protein can also have tissue damaging effects. Complement activation by C-reactive protein exacerbates ischemic injury, the pro-inflammatory actions of C-reactive protein and its binding to phospholipids and lipoproteins may be pro-atherogenic. Also its capacity to stimulate tissue factor production by macrophages may be pro-atherogenic.

C-reactive protein synthesis and its serum concentration

Plasma C-reactive protein is produced only by hepatocytes, predominantly under transcriptional control by the cytokine IL-6.[92,93] In man, the only CRP gene coding sequence is found on Chromosome 1. C-reactive protein is synthesized by the liver. Trace amounts of mRNA for CRP have been found in other cells, it is not known of the importance of locally produced CRP. Synthesis of CRP and other acute phase proteins by hepatocytes is modulated by cytokines.

Interleukins 1b and 6 and tumour necrosis factor are the most important regulators of CRP synthesis. After stimulation with IL-6, IL-1b, TNF and INF, the hepatocytes receive signals to start transcription of DNA coding for CRP.

C-reactive protein begins to rise in bacterial infections within 4-6 hours, peaks at 36-50 hours, closely parallels acute response with 4-7 hour half-life, allowing to normal 3-7 days after the stimulus is withdrawn.

Following an acute-phase stimulus, C-reactive protein values may increase from less than 50µg/L to more than 500mg/L, that is 10,000-fold. De-novo hepatic synthesis starts very rapidly after a single stimulus, serum concentrations rising above 5mg/L by about 6 hours and peaking around 45 hours. The plasma half-life of C-reactive protein is about 19 hours and is constant under all conditions of health and disease, so that the sole determinant of circulating CRP concentration is the synthesis rate, which thus directly reflects the intensity of the pathological process stimulating CRP production.

When the stimulus for increased production completely ceases, the circulating CRP concentration falls rapidly at almost the rate of plasma CRP clearance. Because CRP levels are stable over long period of time, are not affected by food intake and demonstrate almost no circadian variation, there is no need to obtain fasting samples for CRP measurement. The only physical condition which seriously interferes with the capacity to intercept CRP levels is serious hepatocellular impairment, since CRP is synthesized exclusively in the liver. Other factors known to effect CRP are smoking, obesity, patients on HRT and oral contraceptive pills.

Aspirin and Statin therapy is known to reduce CRP levels in the serum probably explaining their direct anti-inflammatory effects. All acute inflammatory processes (infectious and non-infectious) and certain malignant conditions result in rise in serum CRP as a non-specific phenomenon. CRP production is a non-specific response to disease and it can never, on its own, be used as a diagnostic test. However, if CRP results are interpreted in the light of full clinical information on the patient, then it can provide exceptionally useful information.

Further serial measurements important information can be obtained by the resolution or continuation of the inflammation process.

Routine clinical uses of CRP measurement

Screening test for organic disease

Assessment of disease activity in inflammatory conditions:

- Juvenile chronic (rheumatoid) arthritis, Rheumatoid arthritis, Ankylosing spondylitis, Reiter's disease, Psoriatic arthropathy
- Vasculitis - Behcet's syndrome, Wegner's granulomatosis, Polyarteritis Nodosa, Polymyalgia rheumatica
- Crohn's disease, Rheumatic fever, Familial Mediterranean Fever, Acute Pancreatitis

Diagnosis and management of infections:

- Bacterial endocarditis
- Neonatal speticaemia and meningitis
- Intercurrent infection in Systemic Lupus erythematosus
- Intercurrent infection in leukemia and its treatment
- Operative complications including infection and thromboembolism.

Differential diagnosis/classification of inflammatory disease:

- Serum lupus erythematosus Vs rheumatoid arthritis
- Crohn's vs ulcerative colitis
- Predictor of cardiovascular events
- Detection and management of intercurrent infection

- CRP levels are elevated in bacterial and protozoal infections, neonatal sepsis.[95]

C-reactive protein rises up to 50,000-fold in acute inflammation, such as infection. It rises above normal limits within 6 hours, and peaks at 48 hours. Its half-life is constant, and therefore its level is mainly determined by the rate of production (and hence the severity of the precipitating cause).[96]

In surgical diseases CRP levels increase postoperatively and peak at the 3rd postoperative day. In uncomplicated cases serum CRP concentration returns to normal by the 7th-10th postoperative day. Acute surgical diseases are characterized by mild elevation of CRP levels, while significant rise is observed in cases of infectious complications.[96]

In acute appendicitis CRP levels may be within normal limits or slightly elevated during the first hour, but perforated or gangrenous appendix is almost always connected with significant elevation, as shown by our study. Acute appendicitis is a very rare diagnosis when both total leukocyte count and CRP levels are within normal limits.[96]

The first studies concerning the use of CRP in diagnosing acute appendicitis were conducted by Russian surgeons in 1967, in which diagnostic and prognostic role of CRP were evaluated. Since then, several similar studies, many of which concern children, have been conducted, giving varying results.[97]

As far as Greek bibliography is concerned, it seems that there is no well documented record of the importance of CRP in acute surgical diseases, with the

exception of studies concerning children and the work of the authors of this study.[97]

A study 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.[15]

In 1997, a study reviewed 22 eligible articles including 3436 patients on the accuracy of CRP in patients with suspected appendicitis. Sensitivity and specificity varied considerably from 40-99% and 27-90%, respectively. They concluded that CRP is a test of medium accuracy and it was not possible to draw firm conclusion on its usefulness.[98]

Another study reviewed 150 patients who underwent appendectomies and had pathologically confirmed appendicitis, between May 1, 1999 and September 31, 2007, in attempt to clarify the role of CRP as a surgical indication marker for appendicitis. This study showed that the white blood cell counts and neutrophil percentage are not useful for surgical indication, whereas univariate analysis indicated that only CRP was significantly different between the surgery necessary group and unnecessary group, and multivariate analysis showed that only CRP was an independent marker for necrotic appendicitis.[89]

In 2003, a prospective study evaluated patients admitted with nontraumatic, acute, abdominal pain to the surgical department of a large referral hospital over a period of 1 year. Patients were divided into 3 groups: nonspecific abdominal pain (NSAP), surgical non-operative and surgical operative group.

Despite statistically significant differences between the groups, the authors could not identify a useful level of CRP to differentiate between patients with NSAP and those requiring operative and nonoperative management.[99]

The sensitivity and specificity of CRP in diagnosing acute appendicitis was estimated in a study during 2004 at 75,6% and 83,7% respectively.[100] In the same year, another study reviewed 28 different diagnostic variables in the assessment of patients with acute appendicitis in 24 eligible primary articles. The author found that each element of history, examination and laboratory markers of inflammation is of weak discriminatory and predictive capacity. However a combination of more than one variable would make the diagnosis more likely.[101]

A study in 2007 on 110 patients who were operated for acute appendicitis determined the role of TLC, 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.[102]

Several studies have addressed the accuracy of CRP in diagnosing appendicitis and it is agreed that its level increases in appendicitis, which is related to the severity of appendiceal inflammation.[102] The CRP concentration is thus a very useful nonspecific biochemical marker of inflammation, measurement of which contributes importantly to (1) screening for organic disease, (2) monitoring of the response to treatment of inflammation and infection and (3)

detection of intercurrent infection in immunocompromised individuals and in the few specific diseases characterized by modest or absent acute-phase responses.[103]

Total leukocyte count

Total Leukocyte count (TLC) is one of the helpful investigations in diagnosis of acute appendicitis. Mild leukocytosis, ranging from 10,000 to 18,000 is usually present in patients with acute, uncomplicated appendicitis and is often accompanied by a moderate polymorphonuclear predominance. TLC is easily available test and not very expensive. It can be done in almost all laboratories round the clock. Various studies have been published on the evaluation of role of Leukocytosis in the diagnosis of acute appendicitis. The diagnostic accuracy of TLC is increased further if combined with CRP, neutrophil count, shift to the left, sequential leukocyte count and neutrophil **:** lymphocyte ratio.[104]

A raised TLC may be highly sensitive for acute appendicitis but its low specificity has decreased its diagnostic value. Increased leukocyte count is usually the earliest laboratory test to indicate appendicle inflammation, only during protracted inflammation CRP increase. The leukocyte count does not, however, increase any more in appendicle perforation or abscess formation, as reported earlier11 and confirmed in the present study.[105]

The total leukocyte count is widely used to aid the diagnosis of acute appendicitis. Various studies[106,107] have reported that 80% to 85% patients with acute appendicitis will have a total leukocyte count of over 11,000/mm^3. A raised TLC is regarded as a sensitive test for acute appendicitis but is not diagnostic

because of its relatively low specificity and does not add much to the management in patients with un doubtful clinical findings.[108]

Some authors stress a polymorphic leucocytosis as an important feature for diagnosing acute appendicitis. The leukocyte count is raised above 12000 cells/mm6 in three fourths of patients with acute appendicitis. In a study of 493 patients with acute appendicitis, Pieper and associates in 1982 noted that 66.7% had a leukocyte count of 11,000 or more and 5.5% had a raised count of more than 20,000.[109]

A considerable overlap exists between the TLC and neutrophil count of healthy individuals and those with acute appendicitis. Interpretation of these counts together is more significant than either count alone. It is clear that 80-85% patients with acute appendicitis will have a total WBC count of over 10,000/cu mm.[110,111] Neutrophilia of > 75% will occur in 78% patients.[111]

When TLC and neutrophil count are taken together, less than 4% patients with acute appendicitis will have normal values. However, TLC is raised in 20-70% of patients with other causes of acute right iliac fossa pain. Leucocytosis increases with the duration of the disease process, but even a perforated appendix may present with a normal TLC. Of note is the observation of some that if TLC is repeated after a few hours, it tends to remain high in those with acute appendicitis but tends to fall in those without.

A study reported that the WBC and neutrophils count had higher power in discriminating for advanced appendicitis than for all appendicitis. Appendicitis was unlikely at lowest level of the WBC and neutrophils count and rate (LR0.16-

0.28 at WBC count <8000/cmm, neutrophils count<7000/cmm, or rate <70%) and likely at the highest WBC count.[111]

Another study reported that WBC is a poor predictor of the severity of the disease.[112] The white cell and neutrophil count are especially sensitive in children and elderly patients.

A study pointed that the combination of a raised leukocyte count and neutrophilia is useful in the diagnosis of acute appendicitis in children.[113] The study found that in 225 children with acute appendicitis, 96% had neutrophilia and 42% had a raised leukocyte count.

Another study after evaluating 221 adult patients admitted with right lower abdominal pain have concluded that the white cell count did not significantly influence surgical decision-making in cases of suspected acute appendicits.[114]

In a series 20 of patients of acute appendicitis, sensitivity and specificity of leucocyte count was 76.5% and 73.7%. Thus although raised white cell count may be highly sensitive test for acute appendicitis, it has low specificity and has little diagnostic value. Even a perforated appendics may be associated with a normal white cell count.[107]

A study reported that, TLC, neutrophils and CRP are helpful in diagnosis of acute appendicitis and patients with normal values in all the three tests are highly unlikely to have acute appendicitis.[22] Another study showed that, TLC

may serve as predictive parameter for early diagnosis of acute appendicitis in children.[115]

Various studies evaluating TLC in diagnosis of acute appendicitis have variable results. 80–85% patients with acute appendicitis will have TLC count of more than 10,000/cmm.[106] A raised TLC is regarded as sensitive test for diagnosis of acute appendicitis but is not diagnostic because of its lower specificity.[107]

The diagnostic value of TLC is increased when combined with neutrophilia and C-reactive proteins. Neutrophilia of more than 75% occurs in 78% of patients with acute appendicitis. When neutrophil count and TLC are considered together about 4% of the patients will have normal values. Leukocyte count by itself is not completely preventive against negative appendectomy, a finding consistent with results of the current study.[104]

Neutrophil percentage

Neutrophil count (Differential leukocyte count)has been evaluated in many studies and was found helpful in increasing the diagnostic accuracy in patients with suspected acute appendicitis. Neutrophilia has high sensitivity but it is a less specific test. A patient with perforated appendix may have normal neutrophils count.[104]

Neutrophilia with deviation to the left is frequently associated to lymphopenia and can be presented along with monocytosis, characteristic of acute infection.[104]

A study showed that, the presence of lymphopenia associated to clinic history can have an accuracy superior to the count of leukocytes or CRP in diagnosis of acute appendicitis. Although no relevant data was found in literature comparing lymphopenia and evolution stage of appendix infection, these results show lower quantities of lymphocytes in the advanced stages related to the initial ones (9,3% e 14,8%, respectively), with value of $p<0,05$.[116]

Literature

A prospective study involving 496 patients was done to assess the diagnostic value of elements of the laboratory examination for patients with suspected appendicitis. They found that appendicitis was likely at the highest WBC count and polymorphonuclear cell count (PMNC) and rate (WBC count greater than 15 x 10 -9 cells/L, PMNC count greater than 13 x 10 -9 cells/L or PMNC rate greater than 85 % with positive LR values of 5.96 to 8.27). On the other hand, appendicitis was unlikely at the lowest levels of WBC count and the PMNC count and rate (WBC count less than 8.0 x 10-9 cells/L, PMNC count less than 7.0 x 10 -9 cells/L or PMNC rate less than 70 % with positive LR values of 0.16 to 0.28). The authors found that the inflammatory variables had power for discriminating for appendicitis similar to that of the clinical findings and were especially important discriminators for complicated appendicitis. Using multiple logistic regression, three of the six independent predictors of appendicitis were laboratory examinations, namely the WBC count, the PMNC rate and the CRP concentration. After combining these three laboratory examinations with the other three independent predictors of appendicitis (patients' gender, rebound

tenderness and abdominal rigidity), the ROC for this model was 0.93 for all appendicitis and 0.95 for complicated appendicitis.[117]

Although CRP concentration was found to be one of the independent predictors of appendicitis, it is deemed unnecessary because it only had a high power in discriminating for complicated appendicitis (ROC area 0.81) but not for all cases of appendicitis (ROC area 0.70). This is probably because CRP is a late 18 marker of inflammation so that significant increases in CRP concentration are noted only in complicated appendicitis.[117]

A prospective study involving 1,032 patients was done to determine the value of the total leukocyte count and neutrophil percentage in the diagnosis of acute appendicitis. The upper limit of normal for the total leukocyte count was 10 x 109/L. The upper limit of normal for the neutrophil percentage was 75 % for all patients above 15 years of age while for children below 15 years of age, the total lymphocyte and neutrophil percentage varied with age and the upper limits used were those reported by Mann. A raised total lymphocyte count had a sensitivity of 81.4 % and specificity of 77.3%. With a raised total lymphocyte count and neutrophil percentage, the sensitivity decreased to 65.7% but the specificity increased to 81.4%. The authors concluded that a raised total lymphocyte count, preferably combined with a raised neutrophil percentage, are useful as diagnostic aids in acute appendicitis especially in patients 15-65 years of age. It must however be emphasized that the total lymphocyte count and neutrophil percentage should only be interpreted in the light of the physical findings in patients with suspected appendicitis.[118]

A retrospective study involving 300 patients was done to determine the value of the leukocyte count and the C-reactive protein (CRP) in the diagnosis of appendicitis. The authors found that all 200 patients with acute appendicitis had either a leukocyte count or CRP value, or both, above the normal limits. The authors concluded that the leukocyte count was a better laboratory test than CRP in diagnosing uncomplicated appendicitis because it is a very early marker of inflammation. On the other hand, the CRP value was superior to the leukocyte count in reflecting appendiceal perforation or abscess formation.[119]

A retrospective study involving 124 pediatric patients was done to determine the diagnostic accuracy of C-reactive protein and its possible advantage, if any, over the leukocyte count in children with acute appendicitis. Correlating the CRP and the leukocyte count with the pathologic diagnosis of acute appendicitis, the mean CRP values were found to increase as the pathologic inflammation type progressed. The CRP receiver operating characteristic curve showed that the CRP value with the highest accuracy was 1.7 mg/dl. CRP had a sensitivity of 58 %, specificity of 80 %, accuracy of 83.8 %, PPV of 94 % and NPV of 26 %. A comparison of the respective receiver operating characteristic curves demonstrates that CRP, leukocyte count, and the combination of both tests all have a good diagnostic value but without any significant difference. The authors concluded that although the serum CRP has adequate diagnostic accuracy, it is neither individually nor in combination with the WBC count better than the WBC count alone.[120]

A double blind trial was conducted in 78 patients to study the impact of a normal (rather than raised) serum C-reactive protein in reducing the rate of

negative explorations. White blood count (WBC), CRP and the histopathology findings were correlated. Results: In patients with histopathologically proven acute appendicitis both the WBC count and serum CRP level were significantly raised ($p=0.025$ and $p<0.000$ respectively). Serum CRP level was normal in 13 out of 15 negative explorations (normal appendix on histopathology). The specificity and sensitivity of serum CRP was 86.6% and 93.6%, respectively. They concluded that a normal pre-operative serum CRP measurement in patients with suspected acute appendicitis is most likely associated with a normal appendix. Deferring surgery in this group of patients would probably reduce the rate of unnecessary appendicectomies.[121]

In a study the diagnostic value of C-reactive protein (CRP), total white blood cell (WBC) count, total neutrophil count, and neutrophil differential count were evaluated in a prospective blinded study of 204 patients submitted with the tentative diagnosis of acute appendicitis. WBC count demonstrated the best sensitivity (83 percent) and predictive value of a negative result (88 percent). Combining the tests by an "or" rule enhanced the sensitivity to 100 percent. It was concluded that both single tests and combined tests are of limited value in predicting acute appendicitis. However, the triple test combination proved a predictive value of a negative result at 100 percent (95 percent confidence limits 92 to100 percent), indicating that acute appendicitis is unlikely when these tests are simultaneously negative. Therefore, the triple test is recommended as a help in reducing the significant rate of negative laparotomies in patients suspected of having acute appendicitis.[15]

In another study, authors studied the role of leukocyte count, neutrophil percentage and C-reactive protein in the diagnosis of acute appendicitis in the elderly. In conclusion, patients with normal results in all these tests were highly unlikely to have acute appendicitis and should be evaluated with extra caution before surgery.[22]

A study conducted in 209 patients, to find out if the C reactive protein concentration is of any value in the diagnosis of acute appendicitis, either alone or in combination with other laboratory test concluded that, C reactive protein concentration of ≥ 6 mg/1 alone had a sensitivity of 87% and a specificity of 50%, measurement of the C reactive protein concentration can increase the accuracy in the diagnosis of acute appendicitis.[122]

In another study was carried out to find out the specificity and sensitivity of WCC and CRP in diagnosing appendicitis in 259 patients presenting with right iliac fossa pain. A total of 259 patients were included in this study and out of them 37 had a normal appendix giving an over all negative appendicectomy rate of 14.3%. Out of these 11 were male and 26 were female, male to female ratio being 1:2.3. The sensitivity and specificity of WCC in this study was 83% and 62.1 % and that for CRP was 75.6% and 83.7 %. : Both theinflammatory markers i.e. WCC and C-reactive protein can be helpful in the diagnosis, when measured together as this increases their positive predictive value.[100]

In another study, authors measured serum CRP level and WBC count every four hours in a cohort of 227 patients with suspected acute appendicitis and reported that it was unusual to find a normal CRP level after 8 hours of

observation in the presence of acute appendicitis. If these test results are normal, the surgeon should preferably refrain from operating and consider other differential diagnosis. The positive and negative predictive values (96.7% and 76.5%, respectively) of serum CRP was reported in the current study.[124]

In a study serum C-reactive protein was measured in 56 patients hospitalized with a suspected diagnosis of acute appendicitis. Based on these determinations, it is concluded that an increase in C-reactive protein levels to more than 2.5 mg/dl is not a definite indicator of acute appendicitis. However, if the C- reactive protein level in blood drawn 12 hours after the onset of symptoms is less than 2.5 mg/ dl, acute appendicitis can be excluded.[125]

In another study on 70 suspected cases of acute appendicitis authors concluded that a normal CRP value in a patient presenting with symptoms for more than 12 hours, does not have acute appendicitis and can be followed in an outpatient setting.[126]

A multivariate analysis showed that serial CRP measurement can improve the accuracy of diagnosing acute appendicitis. Other reports did not support this view.[127]

According to a study when used individually, both the absolute and categorical WCC and NC distinguish normal appendices from acute appendicitis, though they do not distinguish uncomplicated from complicated appendices. Neither do they individually predict abscess when used as absolute or categorical variables. CRP has no definite value for predicting acute appendicitis in either its absolute or categorical forms, though a significantly elevated level is strongly

suggestive of abscess. In terms of excluding appendicitis in the patient felt clinically to require laparotomy, the inflammatory markers were less effective. Normal values for WCC, NC and CRP excluded appendicitis with a 71%. Laboratory tests of the white cell count, neutrophil count and C-reactive protein are more effective in supporting a clinical diagnosis of acute appendicitis in patients with typical clinical features than in excluding the diagnosis.[128]

In a meta analysis of 22 articles with the aim to review the literature on the accuracy of C-reactive protein (CRP) in diagnosing acute appendicitis, the sensitivity ranged from 0.40 to 0.99, and the specificity from 0.27 to 0.90. The cut-off values for a positive test varied from 5 to 25 mg 1-1. The diagnostic accuracy of CRP tended to be a little inferior to that of total leukocyte count (13 studies). CRP is a test of medium accuracy in diagnosing acute appendicitis. However, definitive conclusions on the clinical usefulness of the test could not be drawn.[129]

A study conducted in Jammu and Kashmir State of India found that CRP demonstrated the best sensitivity (89%) followed by ultrasonography (78%), though the best specificity (90.47%) was observed in the latter test. The sensitivity decreased when raised TLC, NP, CRP and suggestive USG were used together to predict appendicitis but the specificity increased markedly (95%) indicating the fact that acute appendicitis is unlikely when all these tests are simultaneously negative.[130]

A study conducted in Karachi found that, Positive Predictive Value of total leucocyte count was 90.6% and negative predictive value was 44.4% with

accuracy of diagnosis of 74%., PPV of C-reactive protein was 97.1% and NPV was 62.5% with accuracy of diagnosis of 86%.[131]

A study done in Srinagar, India found that TLC had a sensitivity, specificity and positive predictive value of 97.82%, 55.55% and 91.8%, respectively. CRP had a sensitivity, specificity and positive predictive value of 95.6%, 77.77% and 95.6% respectively. Percentage of neutrophil count had a sensitivity, specificity and positive predictive value of 98.9%, 38.88% and 89.21%, respectively.[102]

A study conducted in Nepal found that the sensitivity and specificity of CRP estimation in diagnosing appendicitis was 74.8% and 66.7% respectively and the sensitivity and specificity for total WBC count was 78.6 and 54.8% respectively. The present study suggests that we cannot rely wholly on CRP or on WBC count for operative decision.[132]

A study conducted in Rawalpindi found that Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and Diagnostic efficacy of CRP and TLC were 93.42 %, 79.17 %, 93.42 %, 79.17%, 90 % and 53.95 %, 75 %, 87 %, 34 %, 59 % respectively. CRP and TLC together had Sensitivity 92.86 %, Specificity 88.24 %, PPV 95.12 %, NPV 83.33 % and Diagnostic efficacy 91.53 %.[133]

A study conducted in Lahore, Pakistan showed that, CRP level within normal limits (6 ugm/dl) which was associated with normal appendices in most of the times. Very high levels, up to six times normal of CRP were found in complicated acute appendicitis. Positive predictive value of CRP and TLC both

(100%) were as good as CRP (100%) alone as compared to TLC, (93%). Negative predictive value of TLC and CRP (66%) was better than TLC (50%) and CRP (50%). So both CRP and TLC are better than either TLC or CRP alone.[105]

Avoidance of negative appendecectomies and at the same time deciding for mandatory explorations remains the final goal. In this context, the reliability and clinical usefulness of these inexpensive blood tests TLC and CRP is sorted out.

Chapter 4

Methodology

METHODOLOGY

The present study was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum over a period, from January 2012 to December 2012.

Study design

The study design was hospital based cross-sectional study.

Study period and duration

The present study was conducted for one year from January 2012 to December 2013.

Place

The present study was carried done in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum a teaching hospital attached to KLE University's Jawaharlal Nehru Medical College, Belgaum.

Source of Data

All patients admitted with clinical diagnosis of acute appendicitis under Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were studied.

Sample size

A total of 160 patients with acute appendicitis were included in the study.

Sampling procedure

The sample size was calculated based on the formula as below.

$n = 4Z^2 \times p \times q / d^2$

Where, n: Sample size

Z: 1.96 ~ 2 (taking confidence as 95%)

p: Sensitivity (sensitivity is taken as 80%).

q: 100 – p i. e., 20% (specificity is taken as 20%)

d: Relative error which is 15%

Selection criteria

Inclusion

- All patients with clinical diagnosis of acute appendicitis on admission.

Exclusion

- Pregnancy
- Extremes of age that is, less than 10 or more than 50 years.
- Patients with;
    - Diabetes mellitus
    - Immunodeficiency disease
    - Bleeding disorders
    - Pre-existing systemic infection
    - Appendicular lump
- Patient on steroids

Ethical clearance

Prior to the commencement, the study was approved from the Ethical and Research Committee, Jawaharlal Nehru Medical College, Belgaum.

Informed Consent

The patients fulfilling selection criteria were informed in detail about the nature of the study and a written informed consent was obtained before enrollment (Annexure I).

Method of collection of data

Patients were interviewed and demographic data such as age, sex and the presenting symptoms were noted. Further these patients were subjected to thorough clinical examination and the findings such as signs were recorded. These findings were recorded on a predesigned and pretested proforma (Annexure II).

Investigations

The following tests were subjected to the following investigations.

- Routine blood investigations including:
    - Complete blood count.
        - Hemoglobin.
        - Total leucocyte count.
        - Differential count.
        - Platelet count.

        - Reticulocyte count
    - Urine examination (routine and microscopy)
    - Peripheral smear to rule out hemolytic anaemia
- Serum C-reactive protein
- Mini renal profile
- Liver function test

The interpretation of C-reactive protein, total leukocyte count and neutrophil percentage was done as below.

C-reactive protein

The estimation of C-reactive protein was done based on immunoturbidometry assay method and value of less than 0.6 mg/dL was considered as normal.

Total leukocyte count

The leukocyte count was considered to be normal when the values were between 4000 to 11000 /mm^3.

Neutrophil percentage

The neutrophil percentage between 40 to 70% was considered as normal.

Procedure

Based on the signs and symptoms the clinical diagnosis was established among the patients. These patients were evaluated for C-reactive protein, total

leukocyte count and neutrophil percentage. Further the diagnosis of acute appendicitis was confirmed by HPR.

Statistical analysis

The data obtained was coded and entered in Microsoft Excel Spreadsheet. The categorical data was expressed as rates, ratios and percentages and comparison was done using chi-square test. Continuous data was expressed as mean ± standard deviation. The diagnostic accuracy of C-reactive protein, total leukocyte count and neutrophil percentage in predicting acute appendicitis was determined by sensitivity, specificity, positive predictive value and negative predictive value. Kappa agreement was used to correlate the agreements between diagnosis of acute appendicitis and C-reactive protein, total leukocyte count and neutrophil percentage. A ‘p’ value of less than or equal to 0.05 was considered as statistically significant.

Chapter 5

Results

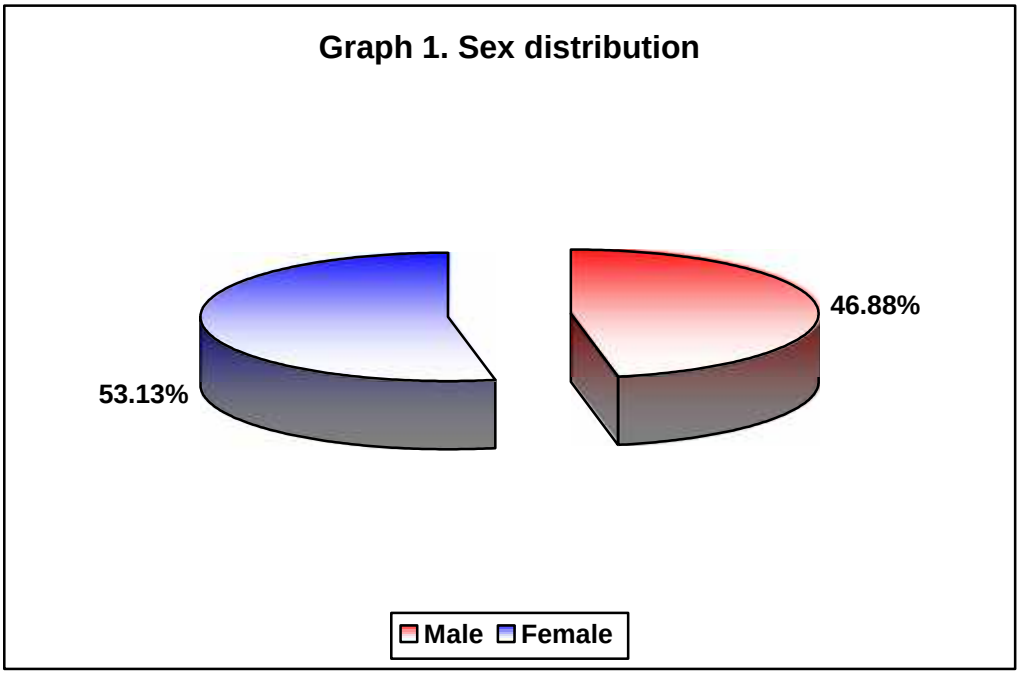
RESULTS

This one year hospital based cross-sectional study was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum over a period, from January 2012 to December 2012. A total of 160 patients admitted with clinical diagnosis of acute appendicitis were studied.

The data obtained was tabulated on Microsoft Excel spreadsheet (Annexure III). The data was analysed and the final observations and results were tabulated as below.

Table 1. Sex distribution

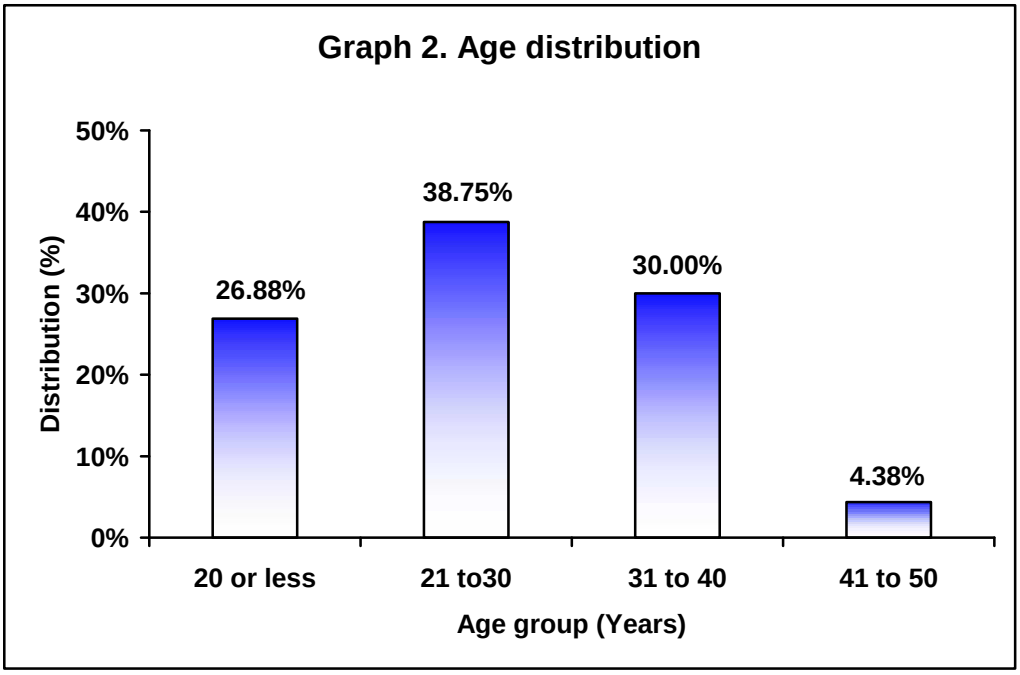
Sex	Distribution (n=160)	
	Number	**Percentage**
Male	75	46.88
Female	85	53.13
Total	**160**	**100.00**



In the present study 53.13% patients were females and 46.88% were males. The male to female ratio was almost comparable (1:1.13).

Table 2. Age distribution

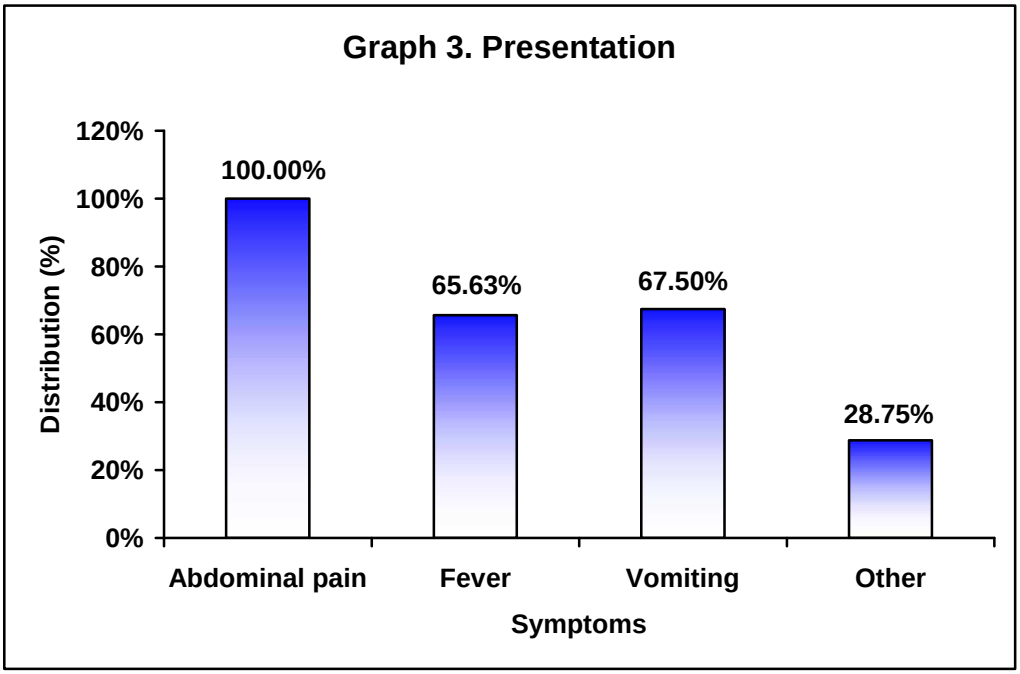
Age group (Years)	Distribution (n=160)	
	Number	**Percentage**
20 or less	43	26.88
21 to 30	62	38.75
31 to 40	48	30.00
41 to 50	7	4.38
Total	**160**	**100.00**



In this study the commonest age of presentation was 21 to 30 years (38.75%) followed by 31 to 40 years (30%) and less than 20 years (26.88%). Few patients (4.38%) were aged 41 to 50 years. The mean age of the study population was 27.60 ± 8.43 years.

Table 3. Presentation

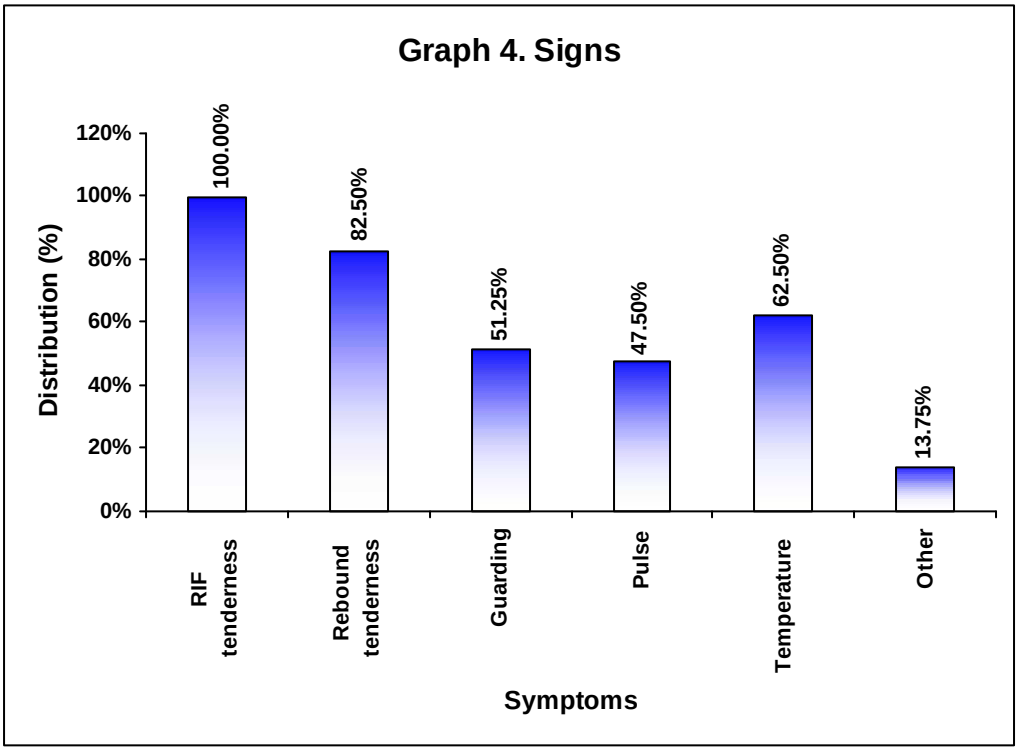
Symptoms	Distribution (n=160)	
	Number	**Percentage**
Abdominal pain	160	100.00
Fever	105	65.63
Vomiting	108	67.50
Other	46	28.75



In the present study, all the patients presented with abdominal pain (100%). Fever and vomiting was seen in 65.63% and 67.5% of patients respectively.

Table 4. Signs

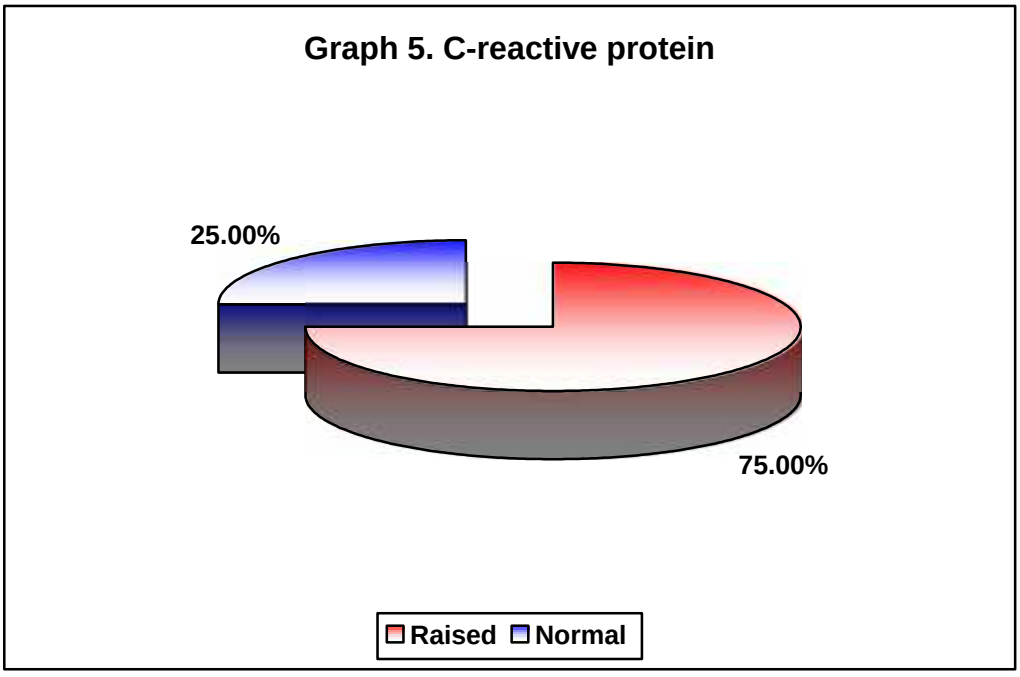
Symptoms	Distribution (n=160)	
	Number	**Percentage**
RIF tenderness	160	100.00
Rebound tenderness	132	82.50
Guarding	82	51.25
Pulse	76	47.50
Temperature	100	62.50
Other	22	13.75



In this study, RIF tenderness was commonest sign present among all the patients (100%). Rebound tenderness and temperature was observed in 82.5% and 47.5% of patients respectively. The other signs included guarding (51.25%) and pulse (47.5%).

Table 5. C-reactive protein

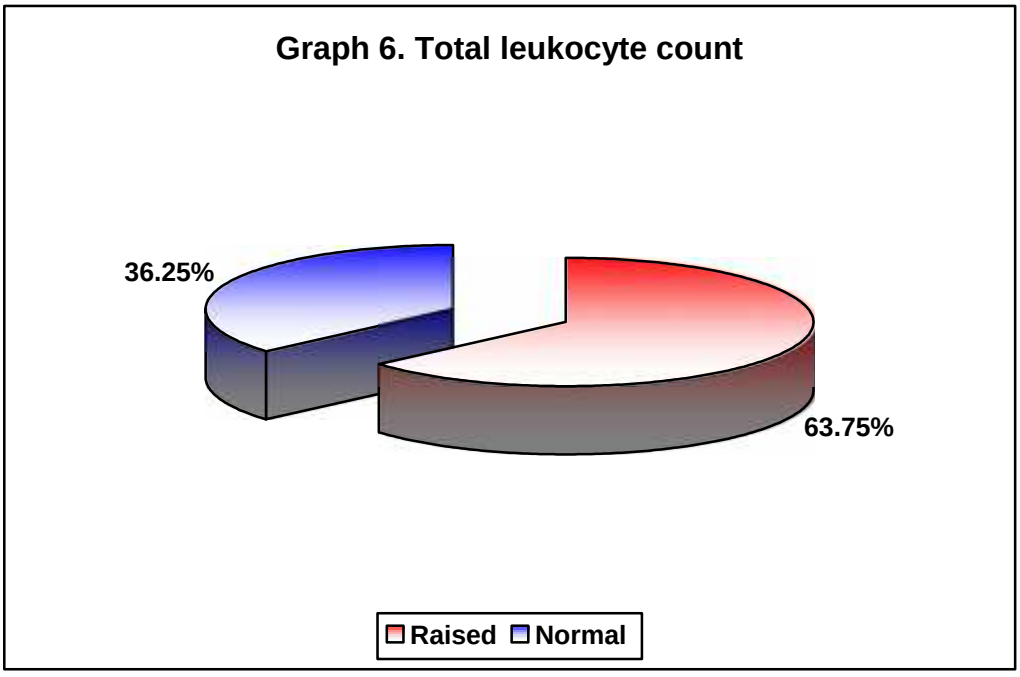
Findings	Distribution (n=160)	
	Number	**Percentage**
Raised	120	75.00
Normal	40	25.00
Total	**160**	**100.00**



In the present study CRP value was found to be raised in 75% of patients and normal among 25%.

Table 6. Total leukocyte count

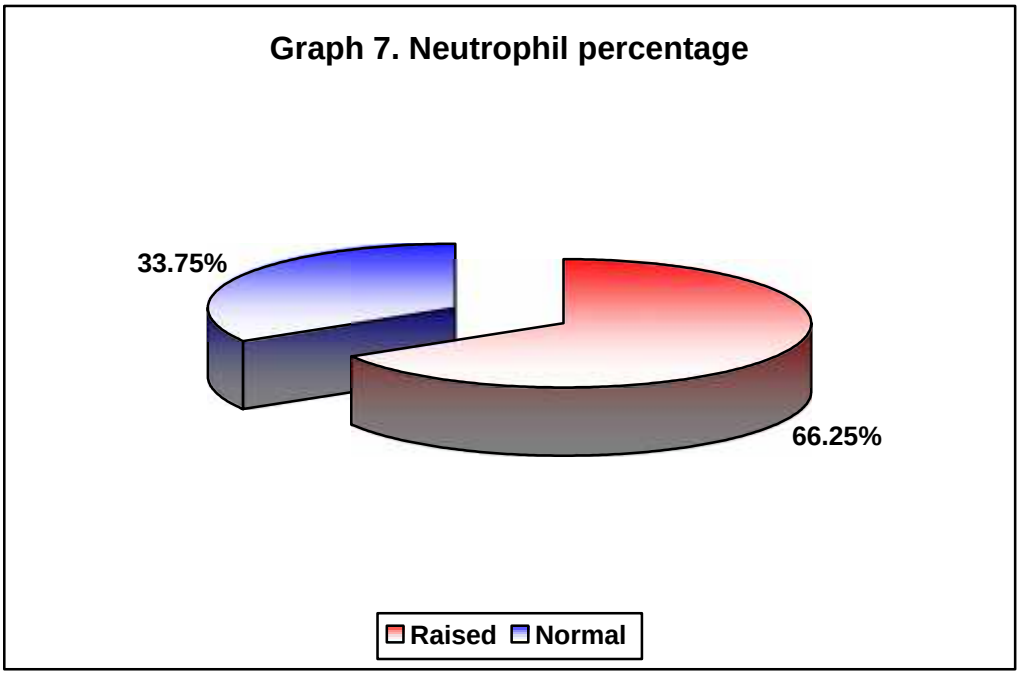
Findings	Distribution (n=160)	
	Number	**Percentage**
Raised	102	63.75
Normal	58	36.25
Total	**160**	**100.00**



In this study TLC was raised in 63.75% of patients whereas normal in 36.25% of patients.

Table 7. Neutrophil percentage

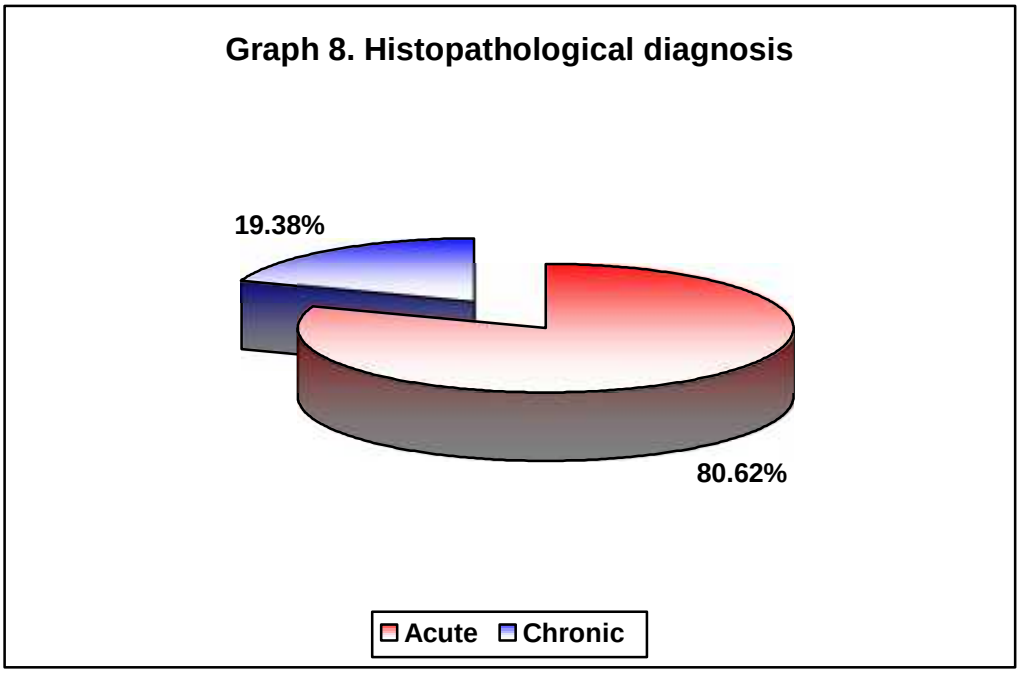
Findings	Distribution (n=160)	
	Number	**Percentage**
Raised	106	66.25
Normal	54	33.75
Total	**160**	**100.00**



In the present study DLC was raised among 66.75% of patients whereas normal in 33.75% patients.

Table 8. Histopathological diagnosis

Diagnosis		Distribution (n=160)	
		Number	**Percentage**
Acute appendicitis	Inflammed	125	78.13
	Gangrenous	3	1.88
	Perforated	1	0.63
	Total	*129*	*80.62*
Chronic appendicitis		31	19.38
Total		**160**	**100.00**



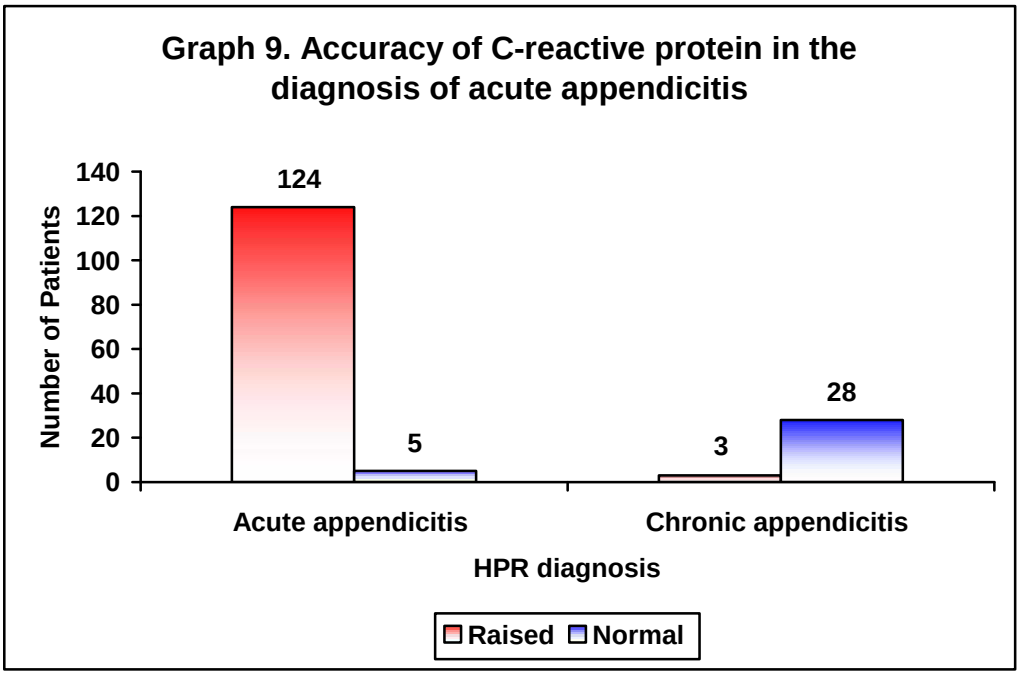
In the present study on HPR, majority of the patients (78.13%) had acute appendicitis and other findings included gangrenous (1.88%) and perforated appendicitis (0.63%) summing up the diagnosis of acute appenditicitis to 80.62%.

Table 9. Accuracy of C-reactive protein in diagnosis of acute appendicitis

C reactive protein	HPR findings (n=160)		Total
	Acute	Chronic	
Raised	124	3	127
Normal	5	28	33
Total	129	31	160

Kappa= 0.844; p<0.001; strength of agreement is considered to be 'very good'.

Sensitivity	Specificity	PPV	NPV
96.12%	90.32%	97.64%	84.85%



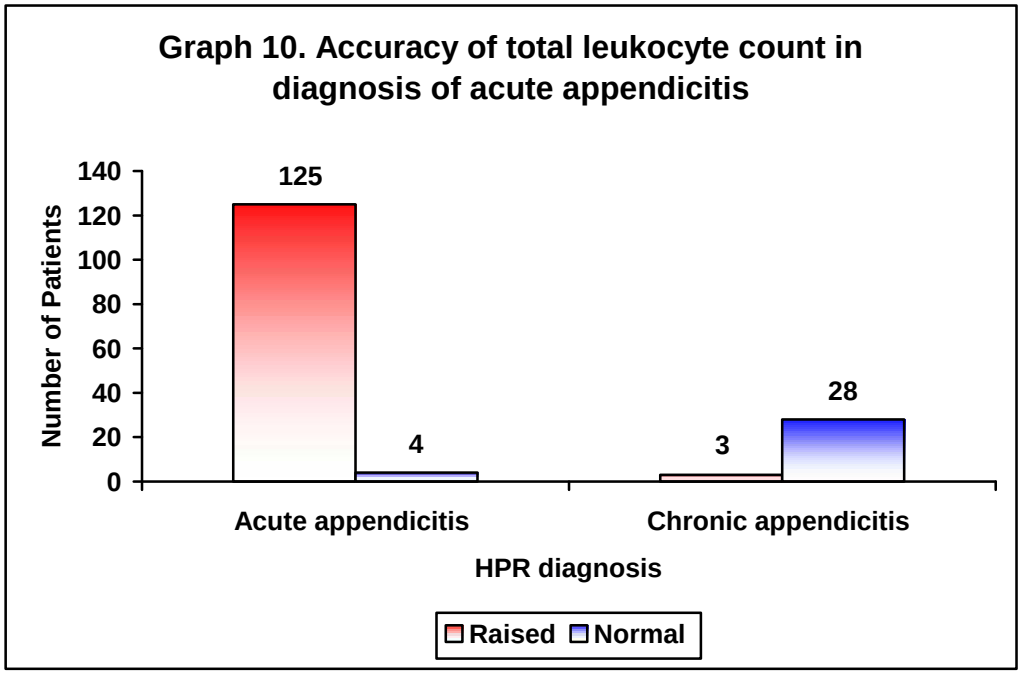
In this study HPR diagnosis showed acute appendicitis in 129 patients. Of these, 124 patients had raised CRP levels. The sensitivity and specificity of CRP in predicting acute appendicitis was 96.12% and 90.32% respectively.

Table 10. Accuracy of total leukocyte count in the diagnosis of acute appendicitis

Total leukocyte count	HPR findings (n=160)		Total
	Acute	Chronic	
Raised	125	3	128
Normal	4	28	32
Total	129	31	160

Kappa= 0.862; p<0.001; strength of agreement is considered to be 'very good'.

Sensitivity	Specificity	PPV	NPV
96.90%	90.32%	97.66%	87.50%



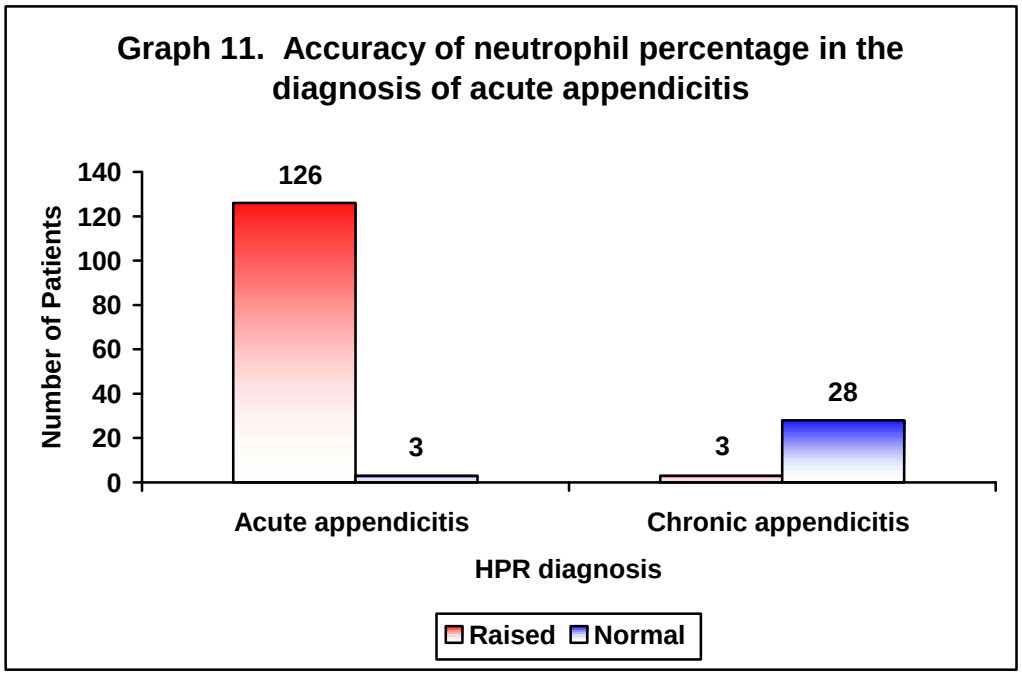
In the present study 129 patients had acute appendicitis on HPR. Among them, 125 had raised total leukocyte count. The sensitivity and specificity of total leukocyte count in predicting acute appendicitis was 96.90% and 90.32% respectively.

Table 11. Accuracy of neutrophil percentage in the diagnosis of acute appendicitis

Neutrophil percentage	HPR findings (n=160)		Total
	Acute	Chronic	
Raised	126	3	129
Normal	3	28	31
Total	129	31	160

Kappa= 0.880; p<0.001; strength of agreement is considered to be 'very good'.

Sensitivity	Specificity	PPV	NPV
97.67%	90.32%	97.67%	90.32%



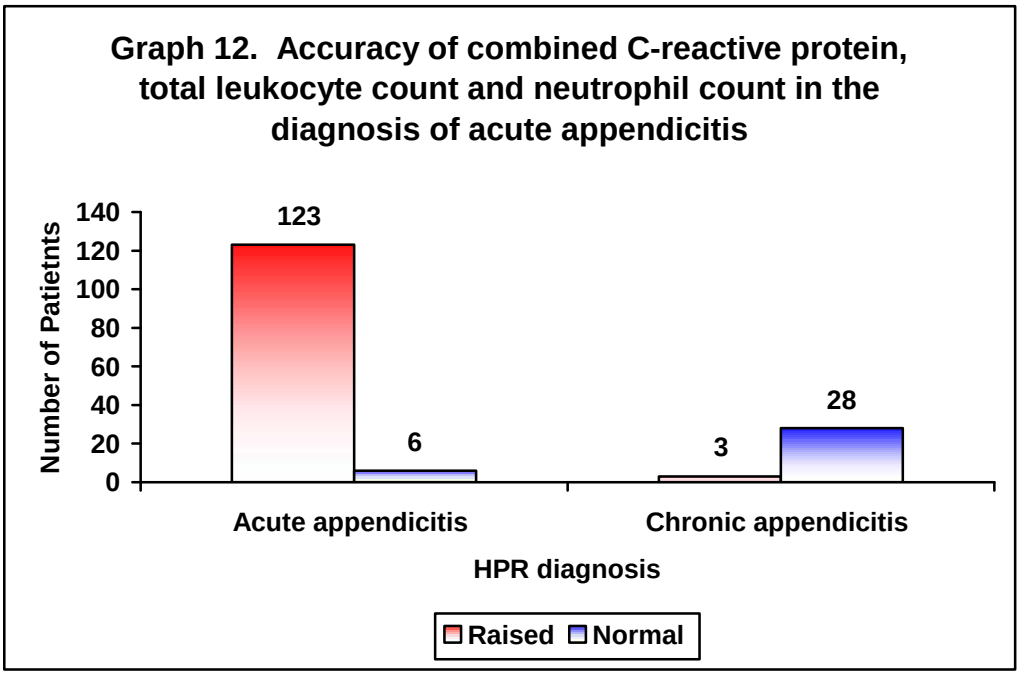
In this study acute appendicitis was seen on HPR in 129 patients of which, 126 had raised neutrophil percentage. The sensitivity and specificity of total leukocyte count in predicting acute appendicitis was 96.90% and 90.32% respectively.

Table 12. Accuracy of combined C-reactive protein, total leukocyte count and neutrophil count in the diagnosis of acute appendicitis

Neutrophil percentage	HPR findings (n=160)		Total
	Acute	Chronic	
Raised	123	3	126
Normal	6	28	34
Total	129	31	160

Kappa= 0.826; p<0.001; strength of agreement is considered to be 'very good'.

Sensitivity	Specificity	PPV	NPV
95.35%	90.32%	97.62%	82.35%



In the present study HPR findings revealed 129 patients with acute appendicitis. Among them, 123 had raised CRP, TLC and neutrophil percentage. The sensitivity and specificity of total leukocyte count in predicting acute appendicitis was 95.35% and 90.32% respectively.

Chapter 6

Discussion

DISCUSSION

The diagnosis of acute appendicitis relies on a thorough history and examination. Accurate preoperative diagnosis is always not possible. Typical uncomplicated cases of acute appendicitis are easy to diagnose and treat.

Availability of various cross-sectional imaging techniques viz. Ultrasonography, Spiral CT and MRI, false positive diagnosis of acute appendicitis has reduced.

To supplement the clinical diagnosis and to reduce the frequency of unnecessary appendicectomy, the importance of laboratory investigations like WBC counts and CRP etc values has been stressed.[10] The use of USG as a diagnostic tool for appendicitis has been widely known and studied.[11] Various scores combining clinical features and laboratory investigations have also been developed and are good enough to reach the diagnosis.

However, the data reporting the diagnostic value of CRP, TLC and neutrophil percentage in preoperative diagnosis of acute appendicitis is scanty especially in Indian context. The present study was an attempt to find out the role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis.

The present one year hospital based cross-sectional study was done at the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2012 to December 2012. A total of 160 patients admitted with clinical diagnosis of acute appendicitis were studied.

In the present study the incidence of acute appendicitis was equally seen in males and females that is, 53.13% patients were females and 46.88% were males with male to female ratio of 1:1.13. Epidemiological and demographic studies reported the appendicitis incidence to vary according to gender. [35,37,39,40] Several studies have reported male preponderance,[134] however in this study equal distribution of sex was noted which could be attributed to the regional variations. Similar findings were observed in studies from Africa[43] and Asia[44] which have shown the less pronounced gender gap similar to the present study.

In this study, 21 to 30 years was the commonest age of presentation observed in 38.75% patients followed by 31 to 40 years in 30% of patients. However, 26.88% patients were less than 20 years and few (4.38%) were aged 41 to 50 years. The mean age of the study population was 27.60 ± 8.43 years. These findings were consistent with the previous literature which has reported that, the incidence of appendicitis gradually rises from birth, peaks in the late teen years, and gradually declines in the geriatric years. Similar pattern of age was reported in a study from Spain.[135]

In the present study, pain abdomen was the commonest clinical symptoms at presentation seen in all the patients (100%). Fever and vomiting were seen in 65.63% and 67.5% of patients respectively. Abdominal pain is the most common symptom of appendicitis. Anorexia, nausea and vomiting are symptoms that are commonly associated with acute appendicitis.[48-50]

It is reported that, a careful, systematic examination of the abdomen is essential for the diagnosis of acute appendicitis. While right lower quadrant

tenderness to palpation is the most important physical examination finding, other signs may help confirm the diagnosis. The abdominal examination should begin with inspection followed by auscultation, gentle palpation (beginning at a site distant from the pain) and, finally, abdominal percussion.[33] In this study, the commonest sign at presentation was RIF tenderness present among all the patients (100%). Rebound tenderness and temperature was observed in 82.5% and 47.5% of patients respectively. However, guarding and other pulse were seen in 51.25% and 47.5% of patients respectively. The rebound tenderness that is associated with peritoneal irritation has been shown to be more accurately identified by percussion of the abdomen than by palpation with quick release.[33] In multiple studies,[48-50] specific characteristics of the abdominal pain and other associated symptoms have proved to be reliable indicators of acute appendicitis. The classic history of pain beginning in the periumbilical region and migrating to the right lower quadrant occurs in only 50% of patients.[33] The RIF tenderness present among all the patients (100%) in this study was in agreement with a study from India[136] whereas, another study from Wales observed rebound tenderness in 60% of patients which was less compared to the present study (82.5%).

In this study, HPR findings revealed majority of the patients (78.13%) with acute appendicitis and other findings on HPR included gangrenous (1.88%) and perforated appendicitis (0.63%) and hence the diagnosis of acute appendicitis was noted in 80.62% These findings were in agreement with a study done in India.[136]

In the present study CRP was raised in 75% of patients and normal among 25%. Of the 129 patients with acute appendicitis on HPR, 124 patients had raised

CRP levels. The sensitivity and specificity of CRP in predicting acute appendicitis was 96.12% and 90.32% respectively.

C-reactive protein was first found in the serum of patients suffering from pneumonia caused by Streptococcus pneumoniae. Together with their acute phase-proteins, the serum level of CRP rises in response to any tissue injury. It also increases in response to infections (bacterial and viral) and in non-infectious conditions like myocardial infarction, malignancies and rheumatic disorders.[7] CRP concentration increases within 8 hours of the onset of tissue injury, peaks in 24-48 hours and remains high as long as there is continuing infection or tissue destruction. Due to its short half-life (4-7 hours) serum CRP concentration rapidly declines as the acute inflammatory process subsides.[138]

Earlier reports showed that, in surgical diseases CRP levels increase postoperatively and peak at the third postoperative day. In uncomplicated cases serum CRP concentration returns to normal by the seventh to tenth postoperative day. Acute surgical diseases are characterized by mild elevation of CRP levels, while significant rise is observed in cases of infectious complications.[4]

Many reports have investigated the value of CRP in improving the diagnostic accuracy of acute appendicitis with conflicting results. A multivariate analysis[122] showed that serial CRP measurement can improve the accuracy of diagnosing acute appendicitis. Another study[89] reviewed 150 patients who underwent appendectomies and had pathologically confirmed appendicitis in attempt to clarify the role of CRP as a surgical indication marker for appendicitis. This study showed that only CRP was significantly different between the surgery

necessary group and unnecessary group, and multivariate analysis showed that only CRP was an independent marker for necrotic appendicitis. In addition, during 2003, a prospective study evaluated patients admitted with nontraumatic, acute, abdominal pain and the study was not able to identify a useful level of CRP to differentiate between patients with NSAP and those requiring operative and nonoperative management.[99] Another review[98] of 22 eligible articles including 3436 patients on the accuracy of CRP in patients with suspected appendicitis. They concluded that CRP is a test of medium accuracy and it was not possible to draw firm conclusion on its usefulness.

The sensitivity and specificity of CRP in diagnosing acute appendicitis was estimated in a study during 2004 at 75,6% and 83,7% respectively.[100]

Another study,[101] showed CRP had a sensitivity, specificity and positive predictive value of 95.6%, 77.77% and 95.6% respectively.

A study[102] done in Srinagar, India found that CRP had a sensitivity, specificity and positive predictive value of 95.6%, 77.77% and 95.6% respectively.

A study[132] conducted in Nepal found that the sensitivity and specificity of CRP estimation in diagnosing appendicitis was 74.8% and 66.7% respectively.

A study[133] conducted in Rawalpindi found that Sensitivity, Specificity, PPV, NPV and Diagnostic efficacy of CRP were 93.42%, 79.17%, 93.42%, 79.17%, 90% respectively. The sensitivity of the present study was comparable with a study done from Srinagar, India and Rawalpindi.

In this study TLC was raised in 63.75% of patients whereas normal in 36.25% of patients. Of the 129 patients with acute appendicitis on HPR, 125 had raised total leukocyte count. The sensitivity and specificity of total leukocyte count in predicting acute appendicitis was 96.90% and 90.32% respectively.

Total Leukocyte count (TLC) is one of the helpful investigations in diagnosis of acute appendicitis. Mild leukocytosis, ranging from 10,000 to 18,000 is usually present in patients with acute, uncomplicated appendicitis and is often accompanied by a moderate polymorphonuclear predominance. A raised TLC may be highly sensitive for acute appendicitis but its low specificity has decreased its diagnostic value. Increased leukocyte count is usually the earliest laboratory test to indicate appendicle inflammation, only during protracted inflammation CRP increase.[50]

In a study of 493 patients with acute appendicitis, Pieper and associates in 1982 noted that 66.7% had a leukocyte count of 11,000 or more and 5.5% had a raised count of more than 20,000.[109]

A study[102] from Srinagar, India found that TLC had a sensitivity, specificity and positive predictive value of 97.82%, 55.55% and 91.8%, respectively.

A study[133] conducted in Rawalpindi found that sensitivity, specificity, PPV, NPV and Diagnostic efficacy of TLC were 53.95%, 75%, 87%, 34% and 59% respectively. The findings of the present study were comparable with these reports whereas a study conducted in Nepal found that the sensitivity and specificity of CRP estimation in diagnosing appendicitis was 74.8% and 66.7%

respectively and the sensitivity and specificity for total WBC count was 78.6 and 54.8% respectively.

In the present study DLC was raised among 66.75% of patients whereas normal in 33.75% patients. Acute appendicitis was seen on HPR in 129 patients of which, 126 had raised neutrophil percentage. The sensitivity and specificity of total leukocyte count in predicting acute appendicitis was 96.90% and 90.32% respectively.

Neutrophil count (DLC) has been evaluated in many studies and was found helpful in increasing the diagnostic accuracy in patients with suspected acute appendicitis. Neutrophilia has high sensitivity but it is a less specific test. A patient with perforated appendix may have normal neutrophils count. Neutrophilia with deviation to the left is frequently associated to lymphopenia and can be presented along with monocytosis, characteristic of acute infection.[104]

According a study the presence of lymphopenia associated to history can have an accuracy superior to the count of leukocytes or CRP in diagnosis of acute appendicitis. Although no relevant data was found in literature comparing lymphopenia and evolution stage of appendix infection, these results show lower quantities of lymphocytes in the advanced stages related to the initial ones (9,3% e 14,8%, respectively), with value of $p<0,05$.[116]

A study[102] done in Srinagar, India found that percentage of neutrophil count had a sensitivity, specificity and positive predictive value of 98.9%, 38.88% and 89.21%, respectively[8] which were comparable to the present study.

In general, it is postulated that acute appendicitis is unlikely in patients with normal DLC, leukocyte count and CRP value, even if clinical symptoms and signs indicate acute appendicitis. Furthermore several studies have shown that combining total leukocyte count with CRP value enhances the accuracy of both tests. In the present study HPR findings revealed 129 patients with acute appendicitis. Among them, 123 had raised CRP, TLC and neutrophil percentage. The sensitivity and specificity of total leukocyte count in predicting acute appendicitis was 95.35% and 90.32% respectively.

A prospective study[117] involving 496 patients found that the inflammatory variables had power for discriminating for appendicitis similar to that of the clinical findings and were especially important discriminators for complicated appendicitis.

In another study[15] the diagnostic value of CRP, WBC count, total neutrophil count, and neutrophil differential count were evaluated in a prospective blinded study of 204 patients with the tentative diagnosis of acute appendicitis. The triple test combination proved a predictive value of a negative result at 100% (95% confidence limits 92 to100%), indicating that acute appendicitis is unlikely when these tests are simultaneously negative.

A study[22] assessed the role of leukocyte count, neutrophil percentage and C-reactive protein in the diagnosis of acute appendicitis in the elderly. In conclusion, patients with normal results in all these tests were highly unlikely to have acute appendicitis and should be evaluated with extra caution before surgery.

Comparison of sensitivity, specificity, PPV and NPV using individual markers and combined

Markers	Sensitivity	Specificity	PPV	NPV
CRP	96.12%	90.32%	97.64%	84.85%
TLC	96.90%	90.32%	97.66%	87.50%
DLC	97.67%	90.32%	97.67%	90.32%
Combined	95.35%	90.32%	97.62%	82.35%

Avoidance of negative appendecectomies and at the same time deciding for mandatory explorations remains the final goal. In this context, the study showed usefulness of CRP, TLC and neutrophil percentage individually and when combined in predicting acute appendicectomy. However, though the sensitivity and specificity of CRP, TLC and neutrophil percentage individually and combined was very high further studies with large sample are required to confirm these observations.

Chapter 7

Conclusion

CONCLUSION

In the present study CRP, TLC and direct count was raised in 75%, 63.75% and 66.75% of patients respectively. The sensitivity and specificity of CRP in predicting acute appendicitis was 96.12% and 90.32% respectively. The sensitivity and specificity of total leukocyte count in predicting acute appendicitis was 96.90% and 90.32% respectively. Raised leukocyte levels had sensitivity and specificity of 96.90% and 90.32% in predicting acute appendicitis respectively.

Of the 129 patients with acute appendicitis on HPR 123 had raised CRP, TLC and neutrophil percentage. The sensitivity and specificity of combined CRP, TLC and neutrophil percentage in predicting acute appendicitis was 95.35% and 90.32% respectively.

Chapter 8

Summary

SUMMARY

The present study was an aimed to find out the role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis.

This one year hospital based cross-sectional study was done at the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2012 to December 2012. A total of 160 patients admitted with clinical diagnosis of acute appendicitis were studied.

In the present study 53.13% patients were females and the male to female ratio was 1:1.13. The commonest age of presentation was 21 to 30 years (38.75%) and the mean age was 27.60 ± 8.43 years. All the patients presented with abdominal pain (100%). RIF tenderness was commonest sign present among all the patients (100%). Based on HPR findings 80.62% of patients were diagnosed to have acute appendicitis and chronic in 19.38%.

Raised CRP, TLC and direct count were seen in 75%, 63.75% and 66.75% of patients respectively. The sensitivity and specificity of CRP in predicting acute appendicitis was 96.12% and 90.32% respectively and total leukocyte count showed sensitivity and specificity of 96.90% and 90.32% respectively. The combined CRP, TLC and neutrophil percentage in predicting acute appendicitis showed sensitivity and specificity of 96.90% and 90.32% respectively.

Chapter 9

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Annexures

Annexure I

ANNEXURE I – CONSENT FORM

Dear Mr/Mrs/Dr_____, you are kindly requested to participate in a research study titled "Role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis" a cross sectional study conducted by Dr. *** **** ******, a post graduate student in M.S. General Surgery in Jawaharlal Nehru Medical College, Belgaum.

You have been requested to participate in this as you fit into the laid out criteria for a study 'subject'/ participant. The important elements of this study have been explained below in a question-answer format to help clear your queries/doubts.

During the study you will be asked some questions and you are supposed to answer to the best of your knowledge. Your participation in this research is voluntary. Your decision whether or not to participate in the study will not affect your treatment in any form during your hospital stay. If you decide to participate you are free to withdraw at any time.

Title of the Study: "Role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis" a cross sectional study.

Objective/purpose of the study: To Study the role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis.

Why am I being asked to participate in this research? You are being asked to participate in this research as you find all the criteria laid by the author of the study as 'subjects'

Who is being recruited or selected? Patients being selected are those diagnosed as Acute Appendicitis clinically on admission

Who are the investigators? The investigator/author of this study is Dr. **** ***** *****, a postgraduate student in Department of General Surgery, Jawaharlal Nehru Medical College.

Who is funding the study? The study is self funded by the author the study.

Procedures

What procedures are involved? Procedure(s) involved would be a prick on the skin to collect blood sample.

Will they cause pain or discomfort? It may cause slight/minimal pain.

Will they cause any temporary or lasting problems to me? None

How many times I need to undergo the procedure? Ideally only one prick would be involved, however two or more pricks may be needed if vein is not accessible.

Risks and benefits

What are the potential risks and discomforts? There are no potential risks involved with the procedure. However, if there is h/o any bleeding disorder, then the duration on bleed from the prick site would be a little longer than usual, but not to an extent where it could be lethal to the patient.

Are the benefits to taking part in this research? None

Alternatives

What other options are there? What happens if I decline participation? You would be simply be excluded from the study and all your details shall be kept confidential.

Will I be told about new information that may affect my decision to participate? Yes, you would be informed as when there is any information that may affect your decision to participate in this study.

Withdrawing / removal from the study

Can I withdraw from the study any time I want? You would be always having the voluntary will to withdraw from participation from the study anytime during the study.

Will I be penalized for that in anyway? No.

Can I be removed from the study? Yes, you can be removed from the study anytime as the author wishes to, if at any stage the author concludes that you may not continue to be an appropriate 'subject' for the study.

Privacy and confidentiality

What about privacy and confidentiality? All data collected or disclosed by you during the course of participation of study, will be kept fully confidential.

Will my identity be disclosed? No. If however during the course it becomes necessary for the progress of the course to disclose the identity, it would be done so only after your informed & written consent.

Financial incentives for participation

What are the costs for participating in this research? e.g., for services, etc No additional costs shall be incurred upon you for the purpose of this study.

Will be reimbursed for any of my expenses for participation in this research? No

Contact details:

Whom should I contact if I need my clarification or help at any time during the study period? You shall be free to contact the below mentioned name & addresses anytime during the study period for any clarification or help as you may desire for.

Dr. **** *********
Chairman, College Ethical Dissertation & Research Committee,
Jawaharlal Nehru Medical College,
Nehru Nagar,
Belgaum 590 010

Dr. *** ********
Professor of Surgery,

Dr. ***** ****** ********
Post Graduate Student,
Department of Surgery,
Jawaharlal Nehru Medical College,
Nehru Nagar, Belgaum 590 010
Mobile No.: **** *******

Will they be available all the time? Yes.

Will I be given the contact numbers & addresses of these persons? Yes. If desired by you, contact numbers and addresses will be provided to you separately.

Authorization to publish results

How will the results of the study be used? The results of the study may be used to publish an article.

Consent statement

I the undersigned Mr/Mrs/Dr_____ do hereby give consent for my participation in this research study after being explained in-depth about the important elements of this study in own my vernacular language.

I give this consent voluntarily in my sound mind knowing very well the risks involved and been given enough time to clear my doubts and other queries to participate as a 'subject' in this study. I do hereby also give consent for publication of this article in any media / journal and have no objections whatsoever.

Did you read the contents or were the contents read out to you? Tick one as appropriate:

- ☐ Read the contents by myself
- ☐ The contents were read out to me in English/Marathi/Kannada/Vernacular Language.

Were you informed that participation is voluntary? Tick one as appropriate:

☐ Yes

☐ No

Did you have adequate time to clarify any doubts about the study or your rights as a study participant? Tick one as appropriate:

☐ Yes

☐ No

Signature or left thumb print of participant or legally authorized representative

Participant' name_____

Signature_____

Experimenter's name_____

Signature_____

Witness' name_____

Signature_____

Guardian's name_____

Signature_____ Date_____

(If the participant are Minors (under 18), the parents sign the form, rather than the participants)

Annexures

Annexure II

ANNEXURE II – PROFORMA / QUESTIONNAIRE TO BE USED FOR DATA COLLECION

The proposed proforma / questionnaire to be used for data collection for the study titled "Role of C-reactive protein, total leucocyte count and neutrophil percentage in preoperative diagnosis of acute appendicitis" a cross sectional study is as:

Personal Details:		
	Name:	Age / Sex:
	Address:	
	Educational Status:	Occupation:
	IP No.	Date of Admission:
	Ward:	Date of Discharge:

History:

Chief Complaints:

When did the patient notice the pain :

Nature and site of pain :

Associated features : Fever / Vomiting / Other

Past history:

Any p/h/o Jaundice or Liver disease ☐ Yes ☐ No

Hemolytic disease ☐ Yes ☐ No

Acquired or congenital biliary disease ☐ Yes ☐ No

Previous history of use of antibiotics/steroids :

Any other significant p/h:

Personal history:

Family history (if significant) :	
General examination:	
	Built : Pulse : BP : Respiratory rate : Jaundice : Pallor / Clubbing / Cyanosis / Lymphadenopathy
Systemic Examination:	
	CNS: CVS: RS: P/A:
Clinical Diagnosis:	

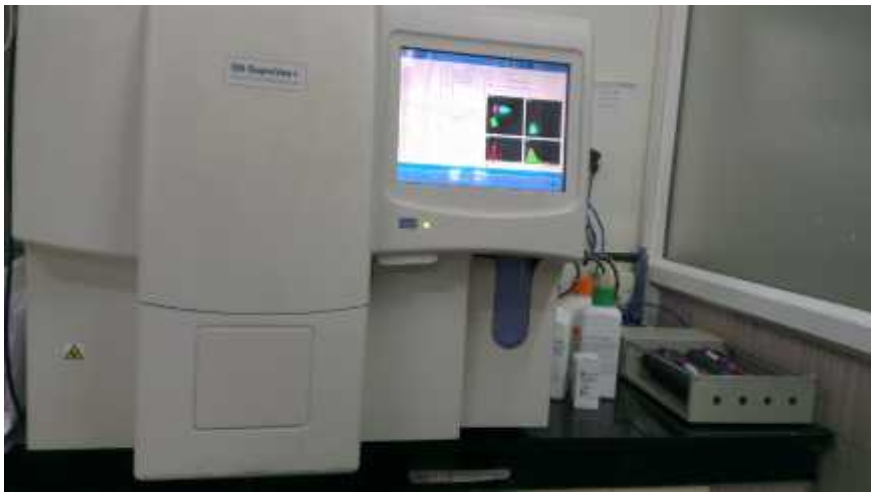
Investigations			
	Serological Investigations		Normal Range
	1.	C- reactive protein: .....mg/dl	< 0.6mg/dl.
	2.	Total Leucocytes Count: .....mg/dl	4000-11000/cmm.
	3.	Neutrophil Count: .....%	40-70%
	USG – Abdomen (if done):		
	Histopathology report (post-operatively):		

Annexures

Annexure III

ANNEXURE III – PHOTOGRAPHS

Photograph 1. CRP kit used for test



Photograph 2. D5 Supreme plus machine used for the estimation total leucocyte count and neutrophil percentage

Photograph 3. Operative picture showing acute appendicitis

Photograph 4. Inflamed appendicectomy specimen

Photograph 5. Surgical picture showing perforated appendicitis

Annexures

Annexure IV

ANNEXURE IV – MASTER CHART

Serial number	In patient number	Age (Year)	Sex	Symptoms				Signs						C-reactive protein	TLC	DLC - N%	Clinical diagnosis	Histopathological report
				Abdominal pain	Vomiting	Fever	Others	RIF Tenderness	Rebound tenderness	Guarding	Pulse	Temperature	Others					
1	454624	28	M	+	+	+	+	+	+	+	-	+	-	+	+	+	AA	AA
2	454702	29	F	+	+	-	-	+	+	+	+	-	-	+	+	+	AA	AA
3	455167	40	M	+	+	-	-	+	+	+	-	-	-	+	+	+	AA	AA
4	455349	20	F	+	-	+	-	+	+	-	-	-	-	-	-	-	AA	CA
5	455660	18	F	+	+	-	-	+	+	-	+	+	+	+	+	+	AA	AA
6	456059	24	F	+	-	-	-	+	+	+	-	-	-	+	+	+	AA	AA
7	456223	27	F	+	-	+	-	+	+	-	-	-	-	+	+	+	AA	AA
8	456626	35	F	+	+	+	-	+	+	+	-	-	-	+	+	+	AA	AA
9	457042	16	F	+	-	+	-	+	-	-	+	-	-	+	+	+	AA	AA
10	457113	40	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
11	457434	38	M	+	+	+	+	+	+	-	-	+	-	-	-	-	AA	CA
12	458301	38	F	+	+	+	-	+	+	-	-	-	-	+	+	+	AA	AA
13	458746	24	M	+	-	-	+	+	+	-	+	+	-	+	+	+	AA	AA
14	459829	20	F	+	+	-	-	+	+	-	+	-	-	+	+	+	AA	AA
15	460258	14	M	+	+	+	+	+	+	+	-	-	-	-	-	-	AA	CA
16	461708	36	M	+	+	+	-	+	-	-	-	-	-	-	-	-	AA	CA
17	462093	19	M	+	+	-	-	+	+	-	-	-	-	-	-	-	AA	CA
18	462467	28	M	+	-	+	-	+	+	+	+	+	+	+	+	+	AA	AA
19	462634	20	F	+	-	-	-	+	-	-	-	-	-	+	+	+	AA	AA
20	462635	38	M	+	+	-	-	+	+	-	-	+	-	+	+	+	AA	AA
21	462720	38	M	+	+	+	-	+	+	+	-	+	+	+	+	+	AA	AA
22	462800	31	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
23	463037	22	F	+	+	-	-	+	+	-	-	+	-	+	+	+	AA	AA
24	463148	26	M	+	-	-	+	+	+	+	-	+	-	+	+	+	AA	AA
25	463449	21	M	+	+	+	-	+	+	+	-	+	-	+	+	+	AA	AA
26	463456	24	M	+	-	-	+	+	+	-	+	+	-	+	+	+	AA	AA
27	463704	40	M	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
28	464583	36	M	+	+	+	+	+	-	-	-	-	-	-	-	-	AA	CA
29	464923	16	M	+	+	+	-	+	+	+	+	+	-	-	-	-	AA	CA
30	464934	34	M	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
31	464958	15	M	+	+	+	-	+	-	+	+	+	+	+	+	+	AA	AA
32	465508	29	F	+	+	-	+	+	+	+	+	+	-	+	+	+	AA	AA
33	465517	19	M	+	+	-	+	+	+	+	+	-	+	+	+	+	AA	AA
34	465986	16	M	+	-	+	-	+	+	+	+	-	-	+	+	+	AA	AA

35	466237	20	F	+	-	-	-	+	+	-	-	+	-	+	+	+	AA	AA
36	467021	16	M	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
37	467035	26	M	+	+	+	-	+	+	+	-	-	-	+	+	+	AA	AA
38	467135	20	F	+	-	-	+	+	+	-	+	-	-	+	+	+	AA	AA
39	467481	28	F	+	+	-	-	+	+	-	+	+	-	+	+	+	AA	AA
40	468224	19	M	+	+	+	-	+	+	-	-	+	-	+	+	+	AA	AA
41	468517	36	F	+	+	-	-	+	+	-	-	+	-	+	+	+	AA	AA
42	468524	16	M	+	+	+	-	+	-	-	+	+	-	+	+	+	AA	AA
43	468694	40	F	+	+	+	-	+	+	+	-	+	+	+	+	+	AA	AA
44	468755	19	M	+	+	-	-	+	+	+	-	-	-	+	+	+	AA	AA
45	468776	36	F	+	-	+	-	+	+	+	+	+	-	+	+	+	AA	AA
46	469659	39	F	+	+	+	-	+	+	-	-	+	-	-	-	-	AA	CA
47	469818	35	F	+	-	+	-	+	+	-	-	+	-	+	+	+	AA	CA
48	470407	37	M	+	+	+	+	+	+	+	-	+	-	+	+	+	AA	AA
49	470456	15	F	+	+	-	-	+	+	-	+	-	-	+	+	+	AA	AA
50	470478	42	F	+	-	+	-	+	+	+	+	+	+	+	+	+	AA	AA
51	470715	16	F	+	+	+	-	+	+	-	+	-	-	+	+	+	AA	AA
52	470887	27	F	+	+	+	-	+	+	-	-	+	-	+	+	+	AA	AA
53	471197	28	F	+	+	+	+	+	+	+	+	+	-	+	+	+	AA	AA
54	471627	28	F	+	+	+	+	+	-	-	-	+	+	-	-	-	AA	CA
55	471684	38	M	+	-	-	+	+	+	+	+	-	-	+	+	+	AA	AA
56	471715	48	M	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
57	472105	35	F	+	-	+	-	+	-	-	+	+	-	+	+	+	AA	AA
58	472269	25	F	+	-	+	-	+	+	-	-	+	-	+	+	+	AA	AA
59	472422	36	M	+	+	+	-	+	-	-	+	-	-	-	-	-	AA	CA
60	472641	17	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
61	472815	29	F	+	+	+	+	+	+	+	-	+	-	+	+	+	AA	AA
62	472862	18	F	+	+	+	-	+	-	-	+	+	-	+	+	+	AA	AA
63	473155	17	F	+	+	-	-	+	+	+	-	+	-	+	+	+	AA	AA
64	473242	23	F	+	-	-	-	+	+	+	+	+	-	+	+	+	AA	AA
65	473676	16	F	+	-	+	-	+	+	-	+	+	-	-	-	-	AA	AA
66	474877	25	F	+	+	-	-	+	+	-	-	+	-	+	+	+	AA	AA
67	475041	26	F	+	+	-	-	+	+	+	+	-	-	-	+	+	AA	AA
68	475347	36	F	+	-	-	-	+	+	+	-	+	-	+	+	+	AA	AA
69	475475	18	F	+	+	-	-	+	+	-	+	+	+	+	+	+	AA	AA
70	475814	29	M	+	-	+	-	+	+	+	-	+	-	+	+	+	AA	AA
71	475859	23	F	+	-	+	+	+	+	+	-	+	-	+	+	+	AA	AA
72	476220	34	F	+	-	-	+	+	-	-	-	+	-	-	-	-	AA	CA
73	476232	38	M	+	+	-	-	+	+	-	-	+	-	+	+	+	AA	AA
74	476333	32	M	+	+	+	-	+	+	+	+	-	-	+	+	+	AA	AA
75	476427	36	M	+	+	+	-	+	+	-	-	-	-	-	-	-	AA	CA
76	476440	16	M	+	+	+	-	+	-	-	-	-	-	-	-	-	AA	CA
77	476661	17	F	+	+	-	+	+	+	-	-	+	-	+	+	+	AA	AA

78	476790	18	M	+	+	-	+	+	+	+	+	+	-	+	+	+	AA	AA
79	476888	27	M	+	+	+	-	+	+	-	-	+	+	+	+	+	AA	AA
80	476893	17	F	+	+	+	-	+	+	-	-	-	-	+	+	+	AA	AA
81	476992	20	F	+	+	+	-	+	+	-	+	+	+	+	+	+	AA	AA
82	477340	40	F	+	-	+	-	+	+	+	-	+	-	+	+	+	AA	AA
83	477389	32	F	+	+	+	-	+	-	-	-	-	-	-	-	-	AA	CA
84	477402	29	M	+	+	+	+	+	+	+	+	+	-	+	+	+	AA	AA
85	477494	38	M	+	+	-	+	+	-	-	-	-	-	+	+	+	AA	AA
86	477508	28	M	+	-	+	-	+	+	+	-	+	-	+	+	+	AA	AA
87	477644	40	M	+	-	+	+	+	-	-	-	-	-	-	-	-	AA	CA
88	477741	18	M	+	-	+	-	+	-	-	-	-	-	-	-	-	AA	CA
89	477897	27	F	+	-	+	-	+	+	+	+	-	-	+	+	+	AA	AA
90	478035	28	M	+	-	-	+	+	+	-	-	-	-	-	-	-	AA	CA
91	478051	42	F	+	+	+	+	+	+	-	+	+	-	+	+	+	AA	AA
92	478060	28	M	+	+	-	-	+	+	+	+	+	-	+	+	+	AA	AA
93	478697	17	M	+	+	+	+	+	+	+	+	+	-	+	+	+	AA	AA
94	479517	39	F	+	+	-	-	+	+	+	+	-	-	+	+	+	AA	AA
95	479597	38	F	+	+	-	-	+	+	+	+	-	-	+	+	+	AA	AA
96	479627	25	F	+	-	+	-	+	+	-	+	+	-	+	+	+	AA	AA
97	479634	24	F	+	+	-	-	+	+	-	-	-	-	-	-	-	AA	CA
98	480000	15	F	+	+	+	-	+	-	-	-	-	-	-	-	-	AA	CA
99	480246	19	F	+	-	+	+	+	-	-	-	-	-	-	-	-	AA	CA
100	481090	27	F	+	+	+	-	+	+	+	-	+	-	+	+	+	AA	AA
101	481493	40	M	+	+	-	-	+	-	+	-	-	+	+	+	+	AA	AA
102	481656	36	M	+	+	-	-	+	+	+	+	-	-	+	+	+	AA	AA
103	481889	25	M	+	+	-	-	+	-	+	-	+	-	+	+	+	AA	AA
104	482691	29	M	+	+	+	+	+	+	+	-	-	-	+	+	+	AA	AA
105	482946	22	M	+	-	+	-	+	+	-	+	+	-	+	+	+	AA	AA
106	483321	24	M	+	-	-	-	+	-	-	-	-	-	-	-	-	AA	CA
107	483354	23	M	+	-	-	-	+	+	-	-	+	-	+	+	+	AA	AA
108	483546	26	F	+	+	-	-	+	+	+	+	-	-	+	+	+	AA	AA
109	483650	26	M	+	+	+	-	+	+	+	-	+	-	+	+	+	AA	AA
110	484590	32	M	+	+	+	-	+	+	+	-	+	-	+	+	+	AA	AA
111	484598	21	M	+	-	-	-	+	+	+	-	-	-	-	+	+	AA	AA
112	484873	38	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
113	484903	25	M	+	+	+	-	+	+	-	-	+	+	+	+	+	AA	AA
114	484914	32	M	+	-	-	+	+	-	+	-	-	-	+	+	+	AA	AA
115	485313	24	M	+	+	+	-	+	+	-	-	+	-	+	+	+	AA	AA
116	485506	23	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
117	486019	46	M	+	-	+	+	+	+	-	+	+	-	+	+	+	AA	AA
118	486311	25	F	+	+	-	+	+	+	+	-	+	-	+	+	+	AA	AA
119	486574	30	M	+	+	-	-	+	-	+	-	+	-	+	+	+	AA	AA
120	486684	38	M	+	+	+	-	+	+	-	+	+	-	+	+	+	AA	AA

121	486690	38	M	+	-	+	-	+	+	-	-	+	-	+	+	+	AA	AA
122	487213	44	M	+	+	+	+	+	+	+	-	+	-	+	+	+	AA	AA
123	494321	37	M	+	+	+	+	+	-	-	+	-	-	+	+	+	AA	AA
124	494401	18	F	+	-	-	-	+	+	-	-	-	-	+	+	+	AA	CA
125	494572	24	M	+	+	+	+	+	+	-	-	+	-	+	+	+	AA	AA
126	494837	40	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
127	494871	20	F	+	+	+	-	+	+	-	+	+	+	+	+	+	AA	GA
128	494903	27	F	+	+	-	+	+	+	-	+	-	-	+	-	+	AA	AA
129	494915	32	M	+	-	+	-	+	+	+	+	+	-	+	+	+	AA	AA
130	494990	22	M	+	+	+	-	+	+	+	-	+	+	+	+	+	AA	AA
131	495005	18	F	+	-	-	+	+	+	-	-	-	+	+	+	+	AA	AA
132	495384	14	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
133	495846	25	F	+	+	+	-	+	+	+	+	+	-	+	-	+	AA	AA
134	496367	35	F	+	+	+	-	+	+	-	-	-	+	+	+	+	AA	AA
135	496655	23	F	+	-	+	-	+	+	-	-	-	-	+	+	+	AA	AA
136	496732	28	F	+	-	+	+	+	+	+	+	+	+	-	-	-	AA	CA
137	497927	22	F	+	-	+	+	+	+	+	+	-	-	-	+	+	AA	AA
138	498171	21	M	+	-	+	+	+	-	-	-	+	-	+	+	+	AA	AA
139	498215	31	F	+	-	+	-	+	+	+	+	-	-	+	+	+	AA	AA
140	498830	38	M	+	+	-	+	+	+	-	-	-	-	-	-	-	AA	CA
141	499074	23	F	+	+	+	+	+	+	-	-	+	-	+	+	+	AA	AA
142	499119	17	F	+	-	-	-	+	-	-	-	+	-	+	+	+	AA	AA
143	499468	25	F	+	+	-	+	+	+	-	-	-	-	-	-	-	AA	CA
144	499500	20	F	+	+	+	+	+	+	+	+	+	+	+	-	+	AA	GA
145	499658	30	F	+	+	+	+	+	+	+	+	+	-	+	+	+	AA	PA
146	499665	29	F	+	+	+	-	+	+	+	+	+	+	+	+	-	AA	GA
147	499922	40	M	+	+	+	-	+	+	+	+	+	-	-	-	-	AA	CA
148	500274	16	M	+	+	+	+	+	+	+	-	-	-	+	+	+	AA	AA
149	500336	45	F	+	+	+	-	+	+	-	+	+	-	+	+	+	AA	AA
150	500339	20	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	CA
151	500341	45	M	+	+	+	-	+	+	-	+	+	-	+	+	+	AA	AA
152	500344	20	M	+	-	+	-	+	+	+	+	+	+	+	+	+	AA	AA
153	500412	30	F	+	-	+	-	+	+	+	+	+	-	-	+	-	AA	AA
154	500591	17	M	+	+	+	-	+	+	+	+	+	-	-	-	-	AA	CA
155	500918	30	F	+	+	+	-	+	+	+	+	+	-	+	+	+	AA	AA
156	503351	22	F	+	+	+	-	+	+	+	+	+	+	+	+	+	AA	AA
157	503437	30	M	+	+	-	+	+	+	+	-	-	-	+	+	+	AA	AA
158	503826	32	F	+	-	+	-	+	+	-	+	-	-	+	+	+	AA	AA
159	504403	23	F	+	-	+	-	+	-	-	-	+	-	-	-	-	AA	CA
160	505005	35	M	+	+	-	+	+	-	-	-	-	-	-	-	-	AA	CA

KEY TO MASTER CHART

-	-	Absent
+	-	Present
AA	-	Acute appendicitis
CA	-	Chronic appendicitis
GA	-	Gangrenous appendicitis
F	-	Female
M	-	Male
PA	-	Perforated appendicitis