"EVALUATION OF HYPERBILIRUBINEMIA AS A DIAGNOSTIC MARKER FOR ACUTE APPENDICITIS"

By

Dr. MADHU S N

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In partial fulfillment of the requirements for the degree of

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IN

GENERAL SURGERY

Under the Guidance of

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Signature of the candidate

Dr. MADHU S N

LIST OF ABBREVIATIONS USED

ALP	-	Alkaline phosphatase
ALT	-	Alanine transaminase
AST	-	Aspartate transaminase
ATP	-	Adenosine triphosphate
cm	-	Centimeter(s)
CRP	-	C-reactive protein
CT	-	Computed tomography
dL	-	Deciliter(s)
DLC	-	Differential leukocyte count
E. Coli	-	Escherichia coli
ELISA	-	Enzyme linked immunosorbent assay
g	-	Gram(s)
HbsAg	-	Hepatitis B surface antigen
IL-6	-	Interleukin-6
LFT	-	Liver function tests
mg	-	Milligram(s)
mL	-	Milliliter(s)
mm	-	Millimeter(s)
n	-	Total number
NPV	-	Negative predictive value
OR	-	Odds ratio
PPV	-	Positive predictive value
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

ABSTRACT

Background and Objectives

Acute Appendicitis is the commonest general surgical emergency, which needs early surgical intervention, to improve the outcome. The rate of misdiagnosis of appendicitis and the rate of appendicular perforation has remained constant, inspite of increased use of ultrasonography, computed tomography scanning and laparoscopy. For early and accurate preoperative diagnosis, acute appendicitis still remains an enigmatic challenge and is a reminder for the art of surgical diagnosis.

Our study was done to find if the Serum Bilirubin could be considered as a new laboratory marker to aid in the diagnosis of Acute appendicitis and if so, does it have the predictive capacity to warn us about Appendicular perforation.

Materials & Methods

Patients reported to R L Jalappa Hospital and Research centre constituent, of Sri Devraj Urs Medical college, surgery department with acute abdomen, was considered for our study. The Study group included 100 patients. Maximum in the age group of 21-40 years. Clinically proven cases of acute appendicitis and perforation was considered. All the cases were evaluated biochemically to find if any association of serum bilirubin existed/present with clinically proven acute appendicitis.

Results

In our study, males were (51%) and females (49%) with overall mean age was 25.41 ± 11.44 years. Of the 100 patients, on HPR 82% were confirmed as acute appendicitis while 11% were diagnosed with Appendicular perforation and 7% were diagnosed as recurrent appendicitis. Of 82 patients with acute appendicitis, 69.5% had elevated bilirubin levels, while 30.5% had normal levels. 11 patients were diagnosed as Appendicular perforation, all patients had elevated bilirubin levels. Of 7 patient with recurrent appendicitis 28.6% patient had elevated bilirubin levels, while 71.4% had normal levels. The Sensitivity and Specificity of serum bilirubin as a marker in predicting Acute appendicitis was 69.51% and 27.78 % respectively. Similarly the Positive predictive value and Negative predictive value was 81.43 % and 16.67% respectively with diagnostic accuracy was 62%. ROC curve showing area under curve for acute appendicitis was 0.26 , and it was highest for appendicular perforation 0.98 with cut off bilirubin 1.85 mg/dl had 100% sensitivity and 92% specificity in diagnosis of appendicular perforation.

Conclusion

- Serum bilirubin levels comes out to be a favorable laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis remains static - clinical. Its level appears to be a useful marker in diagnosis of appendicitis and would be helpful in managing acute cases.

- Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia more than the normal range should be considered as having a higher chance of Appendicular perforation suggesting, serum bilirubin levels have a promising predictive potential for the early diagnosis of Appendicular perforation.

Keywords

Acute Appendicitis; Appendicular perforation; Hyperbilirubinemia; Serum Bilirubin, Recurrent appendicitis.

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INTRODUCTION

INTRODUCTION

Acute appendicitis is the most common cause of "Acute Surgical abdomen"[1,2]. Appendicectomy is the commonest emergency abdominal surgery, performed by a surgeon,[1]

Diagnosis of Appendicitis still remains a puzzle in spite of advances in the radiological and laboratory investigations. Diagnosis of appendicitis could be accurately made only with a combination of history, physical examination and laboratory studies, as per a clinician has experienced [3]. Although most patients with Acute Appendicitis can be easily diagnosed, a firm diagnosis still remains difficult as the sign and symptoms are variable in some cases. This is particularly true where the appendix is retrocaecal or retroileal. Following appendicectomies the percentage of appendix found to be normal varies 15- 50% and postoperative complications can occur in up to 50% of these patients.[4,5.] Hence, a delay in diagnosis of Acute Appendicitis leads to perforation and peritonitis and increased mortality. Perforation ranges from 50-90% in various cases.[6,7.]

It is documented that clinical diagnosis is often biased and needs an adjuvant which shall substantiate the confirmation. This could prevent unnecessary surgical intervention. In such case, laboratory investigations such as White Blood Cell (WBC) counts and C-reactive protein (CRP) etc needs to be stressed upon.[8] The use of Ultrasonography (USG) as a diagnostic tool for appendicitis has been well known .[9-12] To clinch an accurate diagnosis various scores combining clinical features and laboratory investigations have also been developed . These are the Alvarado score[13] and the Modified Alvarado score.[14]

However till date there is no confirmatory laboratory marker for the pre-operative diagnosis of acute appendicitis and/ or appendicular perforation or recurrent appendicitis , moreover those which are done are neither clear nor conclusive.

Although, the significance of serum bilirubin was reported recently, the importance of the elevated total bilirubin has not been stressed in acute appendicitis and appendicular perforation.[15] It is well established that when microbes invade the body, leukocytes defend it. This leads to increase in the leukocyte count and further leads to release of pro-inflammatory cytokines such as TNF-alpha, IL6 and other cytokine which occurs due to Bacterial invasion in the appendix and transmigration of bacteria .These inflammatory cytokines reach the liver via Superior mesenteric vein (SMV) and may produce inflammation, abscess or dysfunction of liver either directly or indirectly by altering the hepatic blood flow resulting in alteration of liver function tests particularly the bilirubin values. [16-22.]

This created an interest in us to find any relationship between hyperbilirubinemia and acute appendicitis and to evaluate its credibility as a diagnostic marker for acute appendicitis and also, to find if any correlation level of elevated bilirubin levels do have a predictive potential role in the diagnosis of appendicular perforation.

OBJECTIVES

OBJECTIVES

1. To estimate serum bilirubin in patients with acute appendicitis
2. To correlate serum bilirubin level in appendicitis , appendicular perforation and recurrent appendicitis.
3. To study the relationship between hyperbilirubinemia and acute appendicitis and to evaluate its usefulness as a diagnostic marker for acute appendicitis.
4. To evaluate whether elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY

For many years, the appendix was considered as a vestigial organ with no known function. As appendix actively participates in the secretion of immunoglobulins, particularly immunoglobulin A (IgA), it is considered now a well recognized immunologic organ.

The history of the appendicitis is referred back since the history of medicine when the disease of appendix existed in ancient times with fibrous adhesions in the right lower portion of the abdominal cavity being found in an Egyptian mummy from the Byzantine era .

In ancient times, the appendix was probably observed by both Egyptian and Arabic anatomists. To describe the vermiform appendix of the caecum. Da Vinci used the Arabic term “Orecchio” (Literally means ear)

Sushrutha mentions of “Affliction of Appendix”, in his “Samhita” approximately 2500 years ago (P. Kutumbaiah, Ancient IndianMedicine).

The first description of appendix vermiformis as an anatomical structure was done in 1521 by Jacopo Berengario da Carpi (1470-1530), professor of anatomy at Bologna. The first case of perforated appendicitis was reported by the French physician Jean Fernel in 1554 (1497-1558) at autopsy.

Lorenz Heister (1683-1758), professor of medicine and also a practicing surgeon at the universities of Altdorf-Nürnberg and Helmstedt in Germany (1712)gave a classical postmortem description and the first to study the pathology of appendicitis (1711) was done by Heister.[25]

´Perityphilitis´, which is inflammation of the caecum (typhlon, blind) was the initial pathological concept of appendix where the caecum rather than the appendix was considered as the site of the disease; and can be easily explained by advanced stages of inflammation which were observed in autopsies.

The condition became a surgical problem which is now called appendicitis, once the point of initiation of disease is obvious as the appendix vermiformis. The famous Pathologist Reginald Webber Fitz (1843-1913) was the first man to establish acute appendicitis as a definitive lesion, he also explained the relationship of peritonitis as a result of acute appendicitis was explained by him which was ill-understood initially.[26]

The frequent abscesses in the right iliac fossa were not due to typhilitis, perityphilitis or epityphlitis but due to perforation of the vermiform appendix ,which was pointed out by Fitz in his publication. Hence to avoid the possibility of misunderstanding and to localize the disease in its usual place of origin, he named it as Appendicitis.[26]

A study stated that the lymphocytes are normally found in considerable numbers in the submucosa. In 1928 Menon of India considered that a definite relationship existed between the lymphoid hyperplasia of the appendix and the colic like pain

in the abdomen

Surgery for appendicitis

The appendicectomy was first performed in 1736 at St. George‟s Hospital, London, by Claudius Amyand, a surgeon at St. George's Hospital in London and Sergeant Surgeon to Queen Ann, King George I, and King George II.

The acutely inflamed appendix, perforated by a pin, and surrounding omentum was removed in 11-year-old boy through a scrotal wound while dealing with a faecal fistula in a chronic scrotal hernia and patient recovered.[2,23,27]

The account of appendicectomy for appendicitis was first published by Krönlein in 1886. However, the patient died on second postoperative day.

Charles McBurney (1845-1913) was one of the surgeons pioneering the diagnosis and operative treatment of appendicitis. His classic report on early operative interference in cases of appendicitis was presented before the New York Surgical Society in 1889. In it he described the area of greatest abdominal pain in this disease process, now known as McBurney‟s point.[28]

Five years later in 1894, he set forward in another paper the incision that he used in cases of appendicitis, now called McBurney‟s incision.[28]

Later , McBurney credited McArthur with first describing this incision.[28]

The early removal of the appendix in all cases of suspected appendicitis was introduced and popularized by the US surgeon John Benjamin Murphy . In 1904, he advanced the well known statement “in case of acute appendicitis open the abdomen as quickly as possible and close it, more quickly”. He described the

triad of pain abdomen, vomiting and fever, which remains a gold standard for diagnosis even today.[29]

The use of a purse string suture, placed around the base of the appendix was first suggested by Dawbarn. In 1889, Senn first drew attention to the risks of ligature slipping off the appendix stump with subsequent peritoneal contamination.

The world's first laparoscopic appendicectomy was performed at the University of Kiel in Germany by a gynaecologist Professor Kurt Semm in 1983.[30]

Laparoscopic appendicectomy is now as widely used as Open appendicectomy and their comparison has been a matter of great debate.

Liver Function Tests

The significance of serum bilirubin was reported recently, the importance of the elevated total bilirubin has not been stressed in acute appendicitis and appendicular perforation.

It is hypothesized that an association exists between hyperbilirubinemia and acute appenditics and its complications such as appendicular perforation.[55]

Bilirubin

Bilirubin (a tetrapyrrole, formerly referred to as hematoidin) is the end product of the metabolic degradation of haem (prosthetic group of haemoglobin), myoglobin, the cytochrome P450's and various other haemo-proteins.[55] The serum level of bilirubin represents the balance between production and excretion (destruction) of these breakdown products. Laboratory evaluation of serum bilirubin allows detection in two forms:

1. Indirect or Unconjugated bilirubin (i.e. before hepatic metabolism)

2. Direct or Conjugated (i.e. after hepatic metabolism)[56]

Since bilirubin is a most significant toxic waste product, hepatic handling is designed to eliminate it from the body via biliary tract. There are various steps involved in this process namely

I. Hepatocellular uptake

II. Intracellular binding,

III. Conjugation and

IV. Excretion.[55]

Modern analytical methods document that normal plasma contains virtually no bilirubin conjugate. The 10 to 20% of the bilirubin in normal plasma that gives rise to prompt (Diazo) reaction is an artifact of kinetic of the Van Den Berg reaction which along with various modifications is the method most commonly used to quantitate bilirubin in clinical laboratories. Indeed, when direct reacting fraction is less than 15% of total bilirubin at virtually any total bilirubin concentration, the bilirubin in the sample can be considered as essentially all unconjugated.[55]

Conjugated bilirubin (mono- and di-glucronide) is excreted across canalicular plasma membrane by an ATP dependant transport process mediated by multi-drug resistant- associated-protein-2(Canalicular membrane protein).

The excretion of conjugated bilirubin by the canalicular transport mechanism is highly sensitive to injury. Accordingly, in hepatocellular disease as well as with other cholestatic or mechanical obstruction to the bile duct, bilirubin conjugates within the hepatocytes that is prevented from taking their normal pathway into the canaliculi and down the bile duct and may reflux into blood stream, resulting in mixed or less often a truly conjugated hyperbilirubinemia.[55]

Hyperbilirubinemia occurs either due to haemolytic, hepatocellular or cholestatic diseases. Cholestatic and hepatocellular hyperbilirubinemia are associated with a rise in liver enzymes. In these cases the bilirubin is predominantly direct in type (mixed type). An isolated serum bilirubin elevation (without enzyme elevation) may be familial or due to hemolysis.[57]

Cholestasis is the failure of normal bile to reach duodenum. This may be due to pathology anywhere between the hepatocyte and ampulla of Vater. Intrahepatic cholestasis includes those conditions where there is no demonstrable obstruction to major bile duct. The causes are drugs, hormones, primary biliary cirrhosis and sepsis.[57] Sepsis reaches to the liver through portal vein

from the gastrointestinal tract as one of the most common route of the various routes. Any inflammatory condition may cause transmigration/translocation of bacteria; its toxin or cytokines may cause suppression of hepatocellular function and reduced excretion of bile from biliary canaliculi.[58]

Hyperbilirubinemia and appendicitis

Hyperbilirubinemia, defined as an elevated level of serum bilirubin in the blood, either because of increased bilirubin production or alteration of bilirubin clearance. Serum bilirubin is not a well recognized significant laboratory marker for aiding preoperative diagnosis of acute appendicitis and appendicular perforation. Both mechanisms i.e increased production and alteration of bilirubin clearance, lead to an accumulation of bilirubin and might play a role in elevation of serum bilirubin in patients with appendicular perforation.

Bacterial infections leading to hepatic dysfunction may be due of abnormalities in bile acid formation and bile flow. This ultimately can result in hyperbilirubinemia, which is a well-known side effect in the setting of bacterial infection and especially in septic patients.[59] Septic patients those with extrahepatic bacterial infection, such as in perforated appendicitis, show a proinflammatory cytokine and nitric oxide – triggered cholestasis by impairing hepatocellular and bile duct function.[60]

Further, *Escherichia coli* and *Bacteroides fragilis are* the most common bacterial species cultured from appendicular wall of patients with acute appendicitis, both of which have been shown to interfere with hepatocyte microcirculation, including sinusoidal damage as shown in a rat liver model.[61,62]

E. Coli associated lipopolysaccharides have been shown to have an effect on

hepatocyte uptake and excretion of bile acids.[63] Endotoxin secreted from *E. Coli* leads to a dose-dependent impairment of choleresis(production of bile from the liver), which has been shown in a rat model.[64] In addition, *E. Coli* infection has been shown to induce hemolysis of regular erythrocytes.[65] This leads to an increased bilirubin load in infected individuals, which likely promotes hyperbilirubinemia.

In Summarising the patho-physiology behind the elevation of Sr. Bilirubin in Acute Appendicitis/Appendicular perforation:[15,54]

Acute Appendicitis/Appendicular perforation

Inflammatory response causes appendix to become more oedematous and ischaemic

Causes transmigration/translocation of bacteria/toxins/cytokines

Leading to endotoxemia / bacteremia

Bacterial invasion into the hepatic parenchyma alter the physiology of biliary excretion.

Hyperbilirubinemia.

The mechanism of hepatic injury in sepsis could be because of bacteria, its toxin or cytokines. In early sepsis bacteria and its toxin or cytokines are involved , where as in late sepsis, ischemia is common mechanism of hepatic injury due to decreased hepatic blood flow. In both above situations the hepatic injury leads to dysfunction of hepatocyte and tubule leading to mixed type of hyperbilirubinemia (hepatocellular and intra hepatic cholestasis).[22]

Cholestasis in chronic bacterial infection, particularly in childhood or post operatively, is presumably hepatocellular in nature. It can be due to cholestatic effect of endotoxin on sodium-potassium-ATPase.[57]

All the constituents of bile show an increased level in serum. Conjugation of biliary substance is intact but excretion is defective. Serum alkaline phosphatase is raised. The rise is due to increased synthesis or release of enzymes from liver or biliary plasma membrane. The minimal elevation in transaminase value and sometimes serum bilirubin, are the markers for hepatocellular damage

A few case reports describe hyperbilirubinemia and jaundice as a clinical observation in patients with appendicitis.[66,67] However there is a lack of studies with a larger group of patients.

It is inconclusive evidence that an association exists between hyperbilirubinemia and acute appendicitis and its complications.[54] There are only a few case reports in the available literature that describe the finding of hyperbilirubinemia in patients of acute appendicitis.[54]

A retrospective study was done at The Department of General and Visceral Surgery, Augusta Krankenanstalt, Academic Teaching Hospital of the Ruhr University, Bochum, Germany involving 538 patients (306 females: 232 males, mean age, 35.6 years) by Sand M et al, with histologically confirmed acute appendicitis who underwent conventional or laparoscopic

appendicectomy between January 2004 to December 2007 found the mean bilirubin level of all patients was 0.9mg/dl . Patients with Appendicular perforation, had a mean bilirubin level of 1.5mg/dl which was significantly higher than those with a non perforated appendicitis *($p<0.05$)*. The Specificity of hyperbilirubinemia for appendicular perforation was 0.86 compared with 0.55 for white blood count and 0.96 for C-reactive protein.[69] The study concluded that the Patients with clinical symptoms of appendicitis with hyperbilirubinemia should be identified as having probability of appendicular perforation than those with normal bilirubin levels.[68]

A retrospective study done by Emmanuel A et al at Department of Surgery, St. Luke's Hospital Kilkenny Ireland, whereby retrospective analysis of appendicectomies performed in two hospitals (n=472) was done. They collected included laboratory and histological results. Patients were grouped according to histology findings and comparisons were made between the groups.[69] They found that the mean bilirubin levels were higher for patients with simple appendicitis compared to those with a non-inflamed appendix ($p<0.001$). More patients with simple appendicitis had hyperbilirubinemia on admission (30% vs 12%) and the odds of these patients having appendicitis were over three times higher (odds ratio: 3.25, $p<0.001$). Hyperbilirubinemia had a specificity of 88% and a

positive predictive value of 91% for acute appendicitis.

Patients with appendicitis who had a perforated or gangrenous appendix had higher mean bilirubin levels ($p=0.01$) and were more likely to have hyperbilirubinemia ($p<0.001$). The specificity of hyperbilirubinemia for perforation or gangrene was 70%. The specificities of white cell count and C-reactive protein were less than hyperbilirubinemia for simple appendicitis (60% and 72%) and perforated or gangrenous appendicitis (19% and 36 %).

The study suggested that hyperbilirubinemia is a valuable marker for acute appendicitis. Patient with hyperbilirubinemia are also more likely to have appendicular perforation or gangrene. Bilirubin should be included in the assessment of patients with suspected appendicitis.[69]

A prospective study conducted by Khan S during Oct.2004-Oct.2005 at Department of Surgery, Nepalgunj Medical College, Teaching Hospital Nepalgunj, Nepal in which 45 Consecutive cases of acute appendicitis admitted in surgical unit III were recruited for the study. Clinically suspected cases were subjected to investigations to confirm the diagnosis. These cases were also subjected to routine liver function tests. Subsequently these cases were operated and clinical diagnosis was confirmed per-operatively and post operatively by histopathological examination of the specimen. Of 45 cases, 25 were males and 20 were females. Their age ranged from 11years to 60 years with an average of 27.2 years. Duration of symptoms ranged from five hours to maximum nine days. Among 45 cases diagnosed as acute appendicitis clinically (preoperatively), 36 cases had inflamed appendix per operatively, while three cases had gangrene, five cases had perforation with peritonitis (four localized and one generalized peritonitis) and only a single case was noted to be of normal appendix. Liver

function tests (LFT) revealed serum bilirubin to be raised in 39 cases where as six cases had normal serum bilirubin level. The raised serum bilirubin ranged from 1.2 mg/dL to 8.4 mg/dL. The meanlevel of serum bilirubin was 2.38 mg/dL. All the cases had indirect fraction of serum bilirubin above 15%. The eleavted in serum bilirubin was without concomitant much rise in liver enzymes.[15] The study arrived at the following conclusions, Firstly there was Hyperbilirubinemia in 86.6% of the patients of acute inflammation of appendix (that is, acute appendicitis and its complications). Secondly elevated serum bilirubin ranged from 1.2 mg/dL - 8.4 mg/dL. Thirdly, the elevated in serum bilirubin was mixed in type (both indirect and direct).

Finally, the hyperbiliubinemia was intra hepatic cholestatic in type either due to abnormality in permeability of hepatocyte or ductular membrane enzyme inhibition as the liver enzymes were not much elevated.[15]

A retrospective review by Estrada J et al done at the Department of Surgery, Keck School of Medicine of the University of Southern California and Los Angeles County, USC Medical Center, Los Angeles, CA, USA between January 2005 to December 2005 , studied the relationship between hyperbilirubinemia and appendicitis. Patients with liver function tests on admission and pathologically confirmed appendicitis were included in the study. Age, duration of symptoms, temperature, white blood cell counts, systemic inflammatory response score, and bilirubin levels were independent variables in a logistic regression analysis assessing factors predicting the presence or absence of appendicular gangrene/perforation.[56] Elevated total bilirubin levels (>1mg/dl) were found in 59(38%) of 157 patients. Patients with gangrene/perforation were significantly *(p=0.004)* more likely to have hyperbilirubinemia than those with acute suppurative appendicitis. No statistical differences were observed for any of

the other variables. On logistic regression the only significant relationship between the presence or absence of appendicular gangrene and perforation was the presence of hyperbilirubinemia (p=0.031, 95% confidence interval 1.11–7.6). The odds of appendicular perforation are three times higher (odds ratio 2.96) for patients with hyperbilirubinemia compared to those with normal bilirubin levels. Hyperbilirubinemia is frequently associated with appendicitis. Elevated bilirubin levels have a predictive potential for the diagnosis of appendicular perforation.[54]

Another study conducted at Department of surgery, Nepalgunj Medical College, Nepalgunj, Nepal by Khan S to determine the role and predictive value of elevated total serum bilirubin (total serum bilirubin) in the diagnosis of acute appendicitis. In this study all patients admitted with clinical diagnosis of acute appendicitis were tested by laboratory investigations and ultrasonography of the abdomen. Preoperatively patient's blood was also collected for serum bilirubin and other liver enzymes estimation. Cases that underwent emergency appendicectomy from January 2004-May 2007 were included in present study.[70]

It found that all the patients presented within five hours to seven days of onset of pain. Out of 110 patients studied, 71 (64.54%) were males and 39(35.45%) were females. Age distribution was between six years to 73 years with a mean of 29.5 years. Out of 110 cases, 106 cases had acute appendicitis (positive cases). Among 106 positive cases, total serum bilirubin was elevated in 87 (82.07%) cases. The mean of elevated total serum bilirubin was 2.26 mg/dL, ranged 1.2 to 11.5 mg/dL. An interesting finding was observed that patients in whom the appendix was gangrenous or perforated; elevation of total serum bilirubin was found to be

higher as compared to simple suppurative acute appendicitis. The specificity and sensitivity was 100% and 82.07% respectively with predictive value of positive test 100% and predictive value of negative test 17.3%. The liver enzymes were either normal or marginally elevated (<1 time) in most of the cases. The Study concluded that elevated total serum bilirubin (without severe abnormalities in the value of liver enzymes) is good indicator of acute appendicitis. The specificity and sensitivity of elevated total serum bilirubin was 100% and 82.07% respectively with a predictive value for positive test 100%.

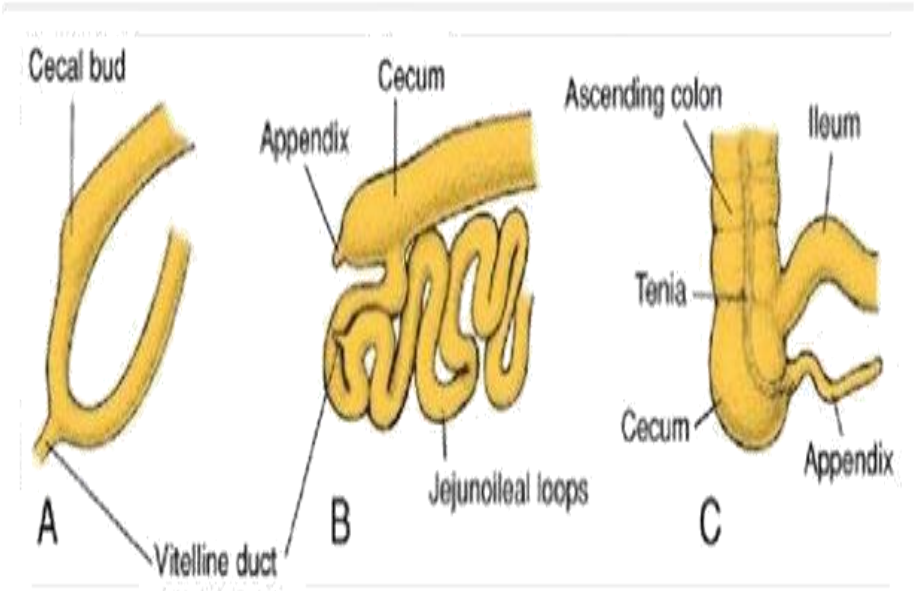
If total serum bilirubin is added to already existing laboratory tests, then the diagnosis of acute appendicitis in clinically suspected cases can be made with fair degree of accuracy and unnecessary / delay in appendicectomy can be avoided.[70]

EMBRYOLOGY AND DEVELOPMENT

At the beginning of the 6th week of development of embryo, the vermiform appendix and the Caecum develops from the caecal bud which arises from the antimesenteric borders of the caudal limb of the mid gut loop[2]. At this stage definite identification of the small and large intestine as separate entities occur. The out pouching maintains a conical shape until the fifth month of fetal growth, after which proximal portion expands to form the Caecum and the tip begins to elongate and develops into the vermiform appendix[31]

About two weeks after birth, lymphoid tissue first appears in human appendix. The number of lymph follicles gradually increases to a peak of about 200 between the ages of twelve and twenty. After thirty there is an abrupt reduction to less than half and then to trace or total absence of lymphoid tissue after sixty.

Figure 1: Successive stages in development of the caecum and appendix.
A. 7 weeks. B. 8 weeks. C. Newborn



CONGENITAL ABNORMALITIES:

Congenital abnormalities[32] of the appendix are:

1. Congenital absence
2. Duplication or triplication
3. Variation in positions
4. Congenital diverticulum / band of appendix.

1. Congenital absence:

Robinson (1952) in reporting a case of congenital absence of the appendix was able to collect only 68 other examples, a figure sufficiently indicative of the greater rarity of this condition.

2. Duplication / Triplication of Appendix:

It is extremely rare anomaly reviewed by Khanna, fewer than 100 cases have been reported.

Wall bride (1962) classified duplication into three types-

- Type A- Partial duplication of single caecum
- Type B- Single caecum with two completely separate appendices. This is further subdivided into-

  - B1-"Bird like appendix" because of its resemblance to the normal arrangement in birds where there are two appendices symmetrically placed on either side of the ileocaecal valve.
  - B2- One appendix arises from the usual site on the Caecum, with another

rudimentary appendix arising from caecum along the line of one of the taenia coli.

- TYPE C- There are two caeci each bearing one appendix.

Tincker described an unique case of a triple appendix, associated with a double penis and ectopia vesicae..

3. Variation in position:

Due to the developmental changes in caecum, midgut loop and caecal mesentery the following different variations may be seen.

- Incomplete downward descent of Caecum may cause appendix in subhepatic position. Over growth of the ascending colon may cause appendix down to pelvic position with Caecum

- Incomplete or non-rotation of the midgut loop may cause the appendix on the left side of the abdomen. It may be associated with transposition of the viscera.

Caecum may have a mesentery and be mobile. Because of its mobility appendix may take variable positions in abdomen.

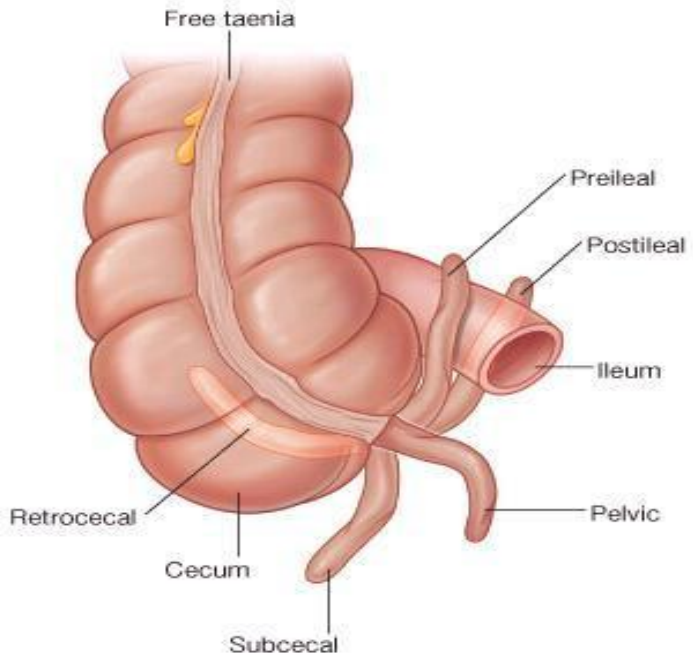


Figure 2. Various positions of appendix

4. Congenital diverticulum / band of appendix:

Congenital diverticulum differs from acquired one, by having a muscular coat in its wall. Some diverticulae originate from the vitellointestinal duct and caecum develops at the point of attachment of the duct. In such cases the diverticulum is attached to the umbilicus by a fibrous band.

Apart from the band, a ring may be found upto the umbilicus called the "appendiculo ovarian ligament".

ANATOMY OF VERMIFORM APPENDIX[32]

The vermiform appendix is a narrow, vermian (worm-shaped) tube which arises from the posteromedial caecal wall, 2 cm below the end of the ileum. It may occupy one of several positions.

The various positions of the appendix comparing the position with the face of a clock was described by Sir Frederick .[33]

- 11 O‟ clock (0.2%)- Para colic (lies in the sulcus on the lateral aspect of the caecum).
- 12 O‟ clock (65.28%)- Retrocaecal (lies behind the caecum and may be totally or partially retroperitoneal)
- 1 O‟ clock (1%)- Pre-ileal
- 2 O‟ clock (0.2%)- Post ileal
- O‟ clock (0.05%)- Promonteric (the tip of the organ points towards the promontory of the sacrum).
- 5 O‟ clock (31.01%)- Pelvic (Appendix dips into the pelvis).

6 O‟ clock (2.26%)- Subcaecal or midinguinal or mid Poupart

The three taeniae coli on the ascending colon and caecum converge on the base of the appendix, and merge into its longitudinal muscle. The anterior caecal taenia is usually distinct and can be traced to the appendix, which affords a guide to its location in clinical practice.

The appendix varies from 2 to 20 cm in length: it is often relatively longer in children and may atrophy and shorten after mid-adult life. It is connected by a short mesoappendix to lie in lower part of the ileal mesentery. This fold is usually triangular, extending almost to the appendicular tip along the whole viscus.

The lumen of the appendix is small, not more than 6 mm in diameter and opens into the caecum by an orifice lying below and slightly posterior to the ileocaecal opening. The orifice is sometimes guarded by a semilunar mucosal fold forming a valve. The lumen may be widely patent in early childhood and is Often partially or complete obliterated in the later decades of life.

The appendix usually contains numerous patches of lymphoid tissue although these tend to decrease in size from early adulthood.

Vascular Supply

The main appendicular artery, a branch from the lower division of the ileocolic artery, runs behind the terminal ileum and enters the mesoappendix a short distance from the appendicular base. Here it gives off a recurrent branch, which anastomoses at the base of the appendix with a branch of the posterior caecal

artery: the anastomosis is sometimes extensive. The main appendicular artery approaches the tip of the organ, at first near to, and then in the edge of the mesoappendix. The terminal part of the artery lies on the wall of the appendix and may be thrombosed in appendicitis, which results in distal gangrene or

necrosis. Accessory arteries are common, and many individuals possess two or more arteries of supply.

Appendicular Veins

The appendix is drained via one or more appendicular veins into the posterior caecal or ileocolic vein and thence into the superior mesenteric vein.

Lymphatic drainage

Lymphatic vessels in the appendix are numerous: there is abundant lymphoid tissue in its walls. From the body and apex of the appendix 8 to 15 vessels ascend in the mesoappendix, and are occasionally interrupted by one or more nodes. They unite to form three or four larger vessels which run into the lymphatic vessels draining the ascending colon, and end in the inferior and superior nodes of the ileocolic chain.

Innervation

The appendix and overlying visceral peritoneum are innervated by sympathetic and parasympathetic nerves from the superior mesenteric plexus. Visceral afferent fibres carrying sensation of distension and pressure mediate the symptoms of pain felt during the initial stages of appendicular inflammation. In

camparsion with other structures derived from the midgut, these sensations are poorly localized initially, and referred to the central (periumbilical) region of the abdomen. It is not until parietal tissues adjacent to the appendix become involved in any inflammatory process that somatic nociceptors are stimulated, and there is an associated change in the nature and localization of pain.

Mesoappendix

The mesentery of the appendix is a triangular fold of peritoneum around the vermiform appendix. It is attached to the posterior surface of the lower end of the mesentery of the small intestine close to the ileocaecal junction. It usually reaches the tip of the appendix but some times fails to reach the distal third, in which case a vestigial low peritoneal ridge containing fat is present over the distal third. It encloses the blood vessels, nerves and lymph vessels of the vermiform appendix, and usually contains a lymph node.

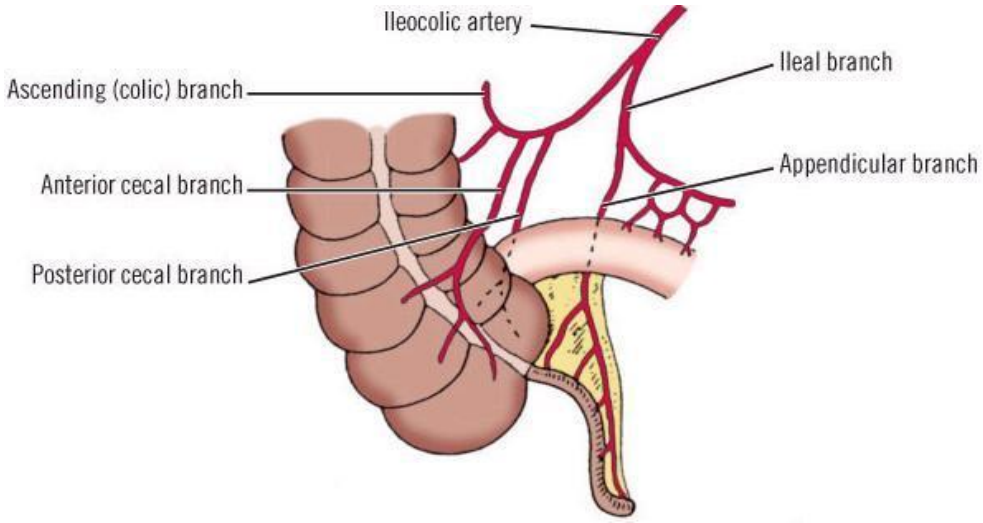


Figure 3. Blood supply of appendix

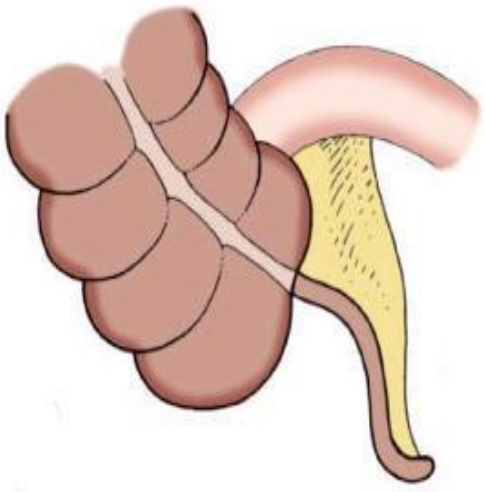


Figure 4. Mesoappendix

Caecal recesses

Several folds of peritoneum may exist around the caecum and form recesses. Paracaecal recesses are common sites for abscess formation following acute appendicitis.

Others include, Superior ileocaecal recess, Inferior ileocaecal recess and Retrocaecal recess.

The usual surface marking of appendicular base is the junction of the lateral and middle thirds of the line joining the right anterior superior iliac spine to the umbilicus (**Mc Burney's point**), but this is merely a useful surgical approximation with considerable variation. The three-taenia coli on the ascending colon and caecum converge on the base of the appendix merging in to its longitudinal muscle. The anterior caecal taenia is usually distinct and traceable to the appendix affording a clue to it.

Microstructure of The Appendix

Mucosa

The mucosa is lined by a columnar epithelium, and M cells are present in the epithelium that overlies the mucosal lymphoid tissue. Glands (crypts) are fewer in number and thus less densely packed. They penetrate deep into the lymphoid tissue of the mucosal lamina propria.

Sub-Mucosa

The submucosa typically contains many large lymphoid aggregates that extend from the mucosa and obscure the muscularis mucosae layer: consequently this becomes discontinuous. These aggregates also cause the mucosa to bulge into the

lumen of the appendix, so that it narrows irregularly . They are absent at birth but accumulate over the first 10 years of life to become a prominent feature. The submucosal lymphoid tissue frequently exhibits germinal centres within its follicles, indicative of B-cell activation, as it is in secondary lymphoid tissue elsewhere . In adults, the normal layered structure of the appendix is lost and the lymphoid follicles atrophy and are replaced by collagenous tissue. In the elderly, the appendix may be filled with fibrous scar tissue.

Muscularis Externa

The muscularis externa has outer longitudinal and inner circular layers of smooth muscle. The longitudinal fibres form a continuous layer but, with the exception of the uniform outer muscle layer of most of the appendix, macroscopically these are aggregated as longitudinal bands or taeniae coli. At the base of the appendix, the longitudinal muscle thickens to form rudimentary taeniae that are continuous with those of the caecum and colon. Between the taeniae coli the longitudinal layer is much thinner, less than half the circular layer in thickness.

Serosa

The serosa forms a complete covering, except along the mesenteric attachment. The longitudinal muscular fibres form a complete layer of uniform thickness, except over a few small areas where both muscular layers are deficient, leaving the serosa and submucosa in contact.

FUNCTIONS OF THE APPENDIX

The human vermiform appendix is usually referred to as a vestigial organ with no known function. On the contrary currently available evidences suggest that the appendix is highly specialized part of alimentary tract.

Postulated functions of the appendix[32]:

1. Exocrine: There have been suggestions that the appendix in human has an exocrine function, assisting in digestion of plant foods. However the 2 ml of clear fluid secreted containing mucin, amylase and proteolytic enzymes per day in low concentrations cannot have any effect on food stuffs in the caecum and food stuffs wouldn‟t ideally enter the appendix for processing.

2. Endocrine: The neuroendocrine cells and their secretory products in the appendix have not shown to have any selective endocrine functions.

3. Neuromuscular: It has been suggested that, the appendix may be the pacemaker for synchronized contraction and emptying that side of the bowel.

4. Lymphoid: The amount of the lymphoid tissue in the appendix is equal to that in the ascending, transverse and descending colon. There is a relative increases in IgM, IgA and IgG containing lymphocytes in the lamina propria of the appendix.

Stowens claims that the appendix is not a vestigial organ but has the same function as the thymus and possible function as a mammalian equivalent of the bursa of fabricus has been suggested.

Epidemiology of Appendicitis

Acute appendicitis is the most common general surgical emergency, and early surgical intervention improves outcomes. In Western countries About 8% of people have appendicitis at some time during their lifetime.[3]

The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately seven percent of all people undergoing appendicectomy for acute appendicitis during their lifetime. The overall appendicectomy rate decreased in parallel with a decrease in incidental appendicectomy over the 10 year period from 1987 to 1997.[33,34] However, the rate of appendicectomy for appendicitis has remained constant at 10 per 10,000 patients per year.[35] Despite the increased use of ultrasonography, computed tomography (CT) and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15.3%) and the rate of appendicular rupture. The percentage of misdiagnosed cases of appendicitis is significantly higher among women than among men (22.2 vs. 9.3%).

The negative appendicectomy rate for women of reproductive age is 23.2%, with the highest rates in women aged 40 to 49 years. The highest negative appendicectomy rate is reported for women >80 years of age.[34,35]

In the United States, 250,000 cases of appendicitis are reported annually, representing one million patient-days of admission. The incidence of acute appendicitis has been declining steadily since the late 1940s, and the current annual incidence is 10 cases per 100,000 population. Appendicitis occurs in seven percent of the US population, with an incidence of 1.1 cases per 1000 people per year. Some familial predisposition exists.

In Asian and African countries, the incidence of acute appendicitis is probably lower because of the dietary habits of the inhabitants of these geographic areas. The incidence of appendicitis is lower in cultures with a higher intake of dietary fiber. Dietary fiber is thought to decrease the viscosity of feces, decrease bowel transit time, and less formation of faecaliths, which predispose individuals to obstructions of the appendicular lumen.

In the last few years, a decrease in frequency of appendicitis has also been reported in Western countries, which may be related to changes in dietary fiber intake. In fact, the higher incidence of appendicitis is believed to be related to poor fiber intake in such countries.

AETIOLOGY[36]

The etiological factors still remain unknown and obscure although appendicitis is a common disease. It is or has been, universally rare prior to the adoption of western standards of living. The riddle of appendicitis, its actual causes and its meteoric rise from an insignificant disease to the most common serious intra-abdominal inflammatory affection of western civilized areas-has been a matter of much speculation. It is rare in rural communities in economically less developed countries and its incidence is rising with economic development, migration to urban area and emigration to western countries. No individual with an appendix seems immune from the risk of developing appendicitis, but many contributory factors may be responsible.

1. **Age and Sex**:

No age is immune from the risk of developing appendicitis, which has been reported in new born (Shinaberger JH-1957) and also at the extremes of age. It is rare under the age of four year and after the age of 50 yrs. About 65% of the patients are under the age of 30 yrs and only 2% are 60 yrs and above. The appendicitis incidence is maximum between 20 to 30yrs.[3]

In teenagers and young adults - there is a slight male preponderance of 3:2. While in adults, the incidence of appendicitis is approximately 1.4 times greater in men than in women.

2. **Familial susceptibility**:

There are instances of appendicitis occurring in families, suggesting an inherited susceptibility. Downs (1942) operated 16 cases out of 22 closely related individuals for appendicitis. In each case appendix was sharply kinked at the base by a fibrous band, binding it to the lateral aspect of the caecum. Males and females in direct inheritance shared the anomaly equally.

3. **Seasonal factors**:

There is, particularly in children, a possible association between seasonal respiratory tract infection and acute appendicitis. The lymphoid tissue in the appendix and tonsils may be simultaneously affected. A blood born origin of such cases may be supported by observation of such cases.

4.Race and Diet:

In general, appendicitis is associated with non- roughage diet and with the consumption of a high proportion of meat. Racial distribution may be related to

diet, as many of those races said to escape appendicitis may develop the disease of civilization. The national distribution of the disease is interesting. It is common in highly industrialized countries, such as Great Britain, United States, France and Germany. In Denmark and Sweden it is low. In Spain, Greece, Italy and the rural parts of Rumania it is very low. Mc Carrison[37] states that during the early years of his practice in North -West India, he never saw a case of appendicitis, but we find that in Indians it is not uncommon.

5. **Faecaliths**:

Non-calcified inspissated faecal masses are a common finding in a large proportion of appendices removed for acute disease. Ulceration or perforation usually occurs at or near a faecaliths may turn diffuse inflammatory lesion into gangrene.

6.Constipation and Purgation:

Constant and frequent use of purgation for constipation leads to violent peristaltic action, which results, favours and determines the perforation of inflamed appendix.

7. **Parasites**:

Blackadder (1824) reported a case in which a man died suddenly after a very severe bout of pain in the abdomen and who was found at autopsy to have a round worm impacted at the appendicaecal junction. Other parasites like thread worm injures mucus membrane or at times cause obstruction of the lumen of the appendix and cause acute inflammation of the appendix.

8. **Bacterial factors**:

The bacterial population of the normal appendix is similar to that of the normal colon. The appendicular flora remains constant throughout life with the exception of *Porphyromonas gingivalis.* This bacterium is seen only in adults.[40] The bacteria cultured in cases of appendicitis are therefore similar to those seen in other colonic infections such as diverticulitis. The principal organisms seen in the normal appendix, in acute appendicitis, and in perforated appendicitis are *Escherichia coli* and *Bacteroides fragilis.*[38-41]

However, a wide variety of both facultative and anaerobic bacteria and mycobacteria may be present (Table 1). Appendicitis is a polymicrobial infection, with some series reporting the culture of up to 14 different organisms in patients with perforation[38].

Aerobic and Facultative	Anaerobic
Gram-negative bacilli *Escherichia coli* *Pseudomonas aeruginosa* *Klebsiella* species	**Gram-negative bacilli** Other *Bacteroide*s species *Bacteroides fragilis* *Fusobacterium* species
Gram-positive cocci *Streptococcus anginosus*	**Gram-positive cocci** *Peptostreptococcus* species
Other *Streptococcu*s species *Enterococcus* species	**Gram-positive bacilli** *Clostridium* species

Table 1. Common Organisms seen in Patients with Acute appendicitis

9. **Bands and Adhesions**:

Various abnormal peritoneal attachments of congenital origin have been described and if these cause kinking of the appendix, it results into obstruction. Inflammatory or acquired adhesions due to repeated attacks of appendicitis may induce final acute obstructive picture.

10. **Strangulation within a hernial Sac**:

Strangulation or trauma of the appendix, which lies in an internal or external hernial sac, may induce progressive changes similar to strangulated small bowel.

Diffuse inflammation of an appendix in hernial sac may be aggravated by the obstructive effect at the neck of the sac. Amyand removed the first gangrenous appendix from the inguinal hernia[2]. Chatter (1966) removed the inflamed appendix from the femoral hernial sac.

11. **Trauma**:

This is a very rare cause of acute appendicitis, if the attack of acute appendicitis follows within 24 hrs after a blunt injury to right iliac region the probable cause of appendicitis is due to the displacement of faecaliths by trauma to the abdomen i.e. to the right iliac region and causing sudden obstruction. Birrel (1928) described four cases of this type, while Black (1948) reported 2 cases and Bhaje Kar (1953) 1 case[42].

12. **Acute appendicitis secondary to metastatic carcinoma**:

Kenneth (1966)[43] reviewed total 13 cases from the literature, of these 7 cases have presented as acute appendicitis and in 5 of them, the cases showed appendicular perforation at operation. In 5 cases, breast was the site of primary Carcinoma metastatic carcinoma of the appendix due to the encroachment of the growth presents as acute obstructive appendicitis leading to perforation and other complications.

13. Epidemic Form:

Acute appendicitis may occur as an epidemic and the portal of entry for the infection is the nasopharynx and the organisms are usually streptococci.

14. **Amoebic appendicitis**:

The acute appendicitis due to amoebic infection a case was reported by De S. N.,

and Sengupta[44] .

15. **Vascular factors**:

The appendicular artery is an end artery. It is possible that extramural ischemia may play a role in this disorder. Any thing that compromises the external blood supply could therefore contribute to ischemia, inflammation and hence secondary infection in the appendix.

Pathogenesis[23]

Obstruction of the lumen is the dominant etiologic factor in acute appendicitis. Faecoliths are the most common cause of appendicular obstruction. Less common causes are hypertrophy of lymphoid tissue, inspissated barium from previous x-ray studies, tumours, vegetable and fruit seeds, and intestinal parasites. The frequency of obstruction rises with the severity of the inflammatory process. Faecoliths are found in 40% of cases of simple acute appendicitis, in 65% of cases of gangrenous appendicitis without rupture, and in nearly 90% of cases of gangrenous appendicitis with rupture.

Traditionally the belief has been that there is a predictable sequence of events leading to eventual appendicular rupture. The proximal obstruction of the appendicular lumen produces a closed-loop obstruction, and continuing normal secretion by the appendicular mucosa rapidly produces distension. The luminal capacity of the normal appendix is only 0.1 mL. Secretion of as little as 0.5 mL of fluid distal to an obstruction raises the intraluminal pressure to 60 cm H_2O. Distension of the appendix stimulates the nerve endings of visceral afferent stretch fibres, producing vague, dull, diffuse pain in the mid abdomen or lower

epigastrium. Peristalsis also is stimulated by the sudden distension, so that some cramping may be superimposed on the visceral pain early in the course of appendicitis. Distension increases from continued mucosal secretion and from rapid multiplication of the resident bacteria of the appendix. Distension of this magnitude usually causes reflex nausea and vomiting, and the diffuse visceral pain becomes more severe. As pressure in the organ increases, venous pressure is exceeded. Capillaries and venules are occluded, but arteriolar inflow continues, resulting in engorgement and vascular congestion. The inflammatory process soon involves the serosa of the appendix and in turn parietal peritoneum in the region, which produces the characteristic shift in pain to the right lower quadrant.

The mucosa of the GI tract, including the appendix, is susceptible to impairment of blood supply; thus its integrity is compromised early in the process, which allows bacterial invasion. As progressive distension encroaches on, first the venous return and subsequently the arteriolar inflow, the area with the poorest blood supply suffers most: ellipsoidal infarcts develop in the antimesenteric border. As distension, bacterial invasion, compromise of vascular supply, and infarction progress, perforation occurs, usually through one of the infarcted areas on the antimesenteric border. Perforation generally occurs just beyond the point of obstruction rather than at the tip because of the effect of diameter on intraluminal tension.

This sequence is not inevitable, however, and some episodes of acute appendicitis apparently subside spontaneously. Many patients who are found to have acute appendicitis at operation give a history of previous similar, but less severe, attacks of right lower quadrant pain. Pathological examination of the appendices removed from these patients often reveals thickening and scarring, suggesting

old, healed acute inflammation.[36,45]

The strong association between delay in presentation and appendicular perforation supported the proposition that appendicular perforation is the advanced stage of acute appendicitis; however, recent epidemiologic studies have suggested that non perforated and perforated appendicitis may, in fact, be different diseases.[45]

Pathology[23]

Morphology

Appendicular inflammation is associated with obstruction in 50% to 80% of cases, usually in the form of a faecalith and, less commonly, a gallstone, tumor, or ball of worms (oxyuriasis vermicularis).

Continued secretion of mucinous fluid in the obstructed viscus presumably leads to a progressive increase in intraluminal pressure sufficient to cause eventual collapse of the draining veins. Ischemic injury then favors bacterial proliferation with additional inflammatory edema and exudation, further embarrassing the blood supply. Nevertheless, a significant minority of inflamed appendices have no demonstrable luminal obstruction, and the pathogenesis of the inflammation remains unknown.

At the earliest stages, only a scanty neutrophilic exudate may be found throughout the mucosa, submucosa, and muscularis propria. Subserosal vessels are congested, and often there is a modest perivascular neutrophilic infiltrate. The inflammatory reaction transforms the normal glistening serosa into a dull, granular, red membrane; this transformation signifies early acute appendicitis for the operating surgeon. At a later stage, a prominent neutrophilic exudate

generates a fibrinopurulent reaction over the serosa.

As the inflammatory process worsens, there is abscess formation within the wall, along with ulcerations and foci of suppurative necrosis in the mucosa. This state constitutes acute suppurative appendicitis.

Further vascular compromise leads to large areas of hemorrhagic green ulceration of the mucosa and green-black gangrenous necrosis through the wall, extending to the serosa, creating acute gangrenous appendicitis, which is quickly followed by rupture and suppurative peritonitis.

The histological criterion for the diagnosis of acute appendicitis is neutrophilic infiltration of the muscularis propria. Usually, neutrophils and ulcerations are also present within the mucosa. Since drainage of an exudate into the appendix from alimentary tract infection may also induce a mucosal neutrophilic infiltrate, evidence of muscular wall inflammation is requisite for the diagnosis.

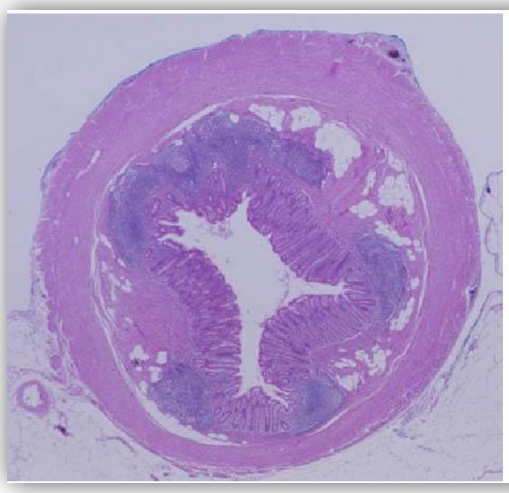


Figure 5:

Normal histology of appendix.

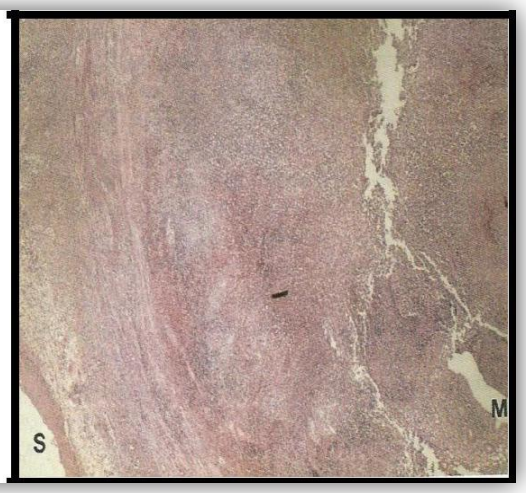
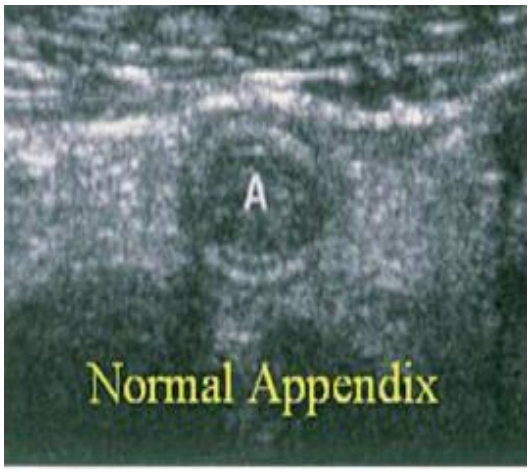


Figure-6:

Histology of inflamed appendicitis



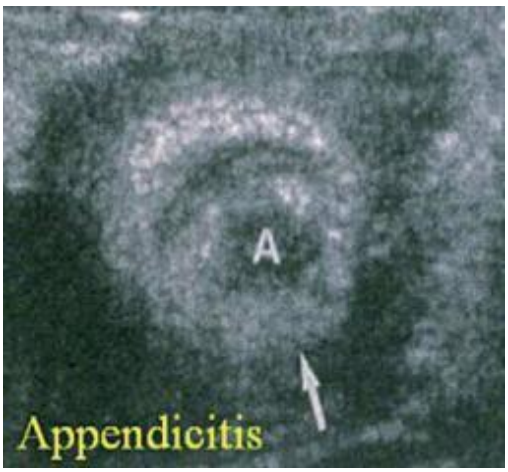


Figure 7. USG finding of a normal appendix and inflammed appendix (Appendicitis)

DIAGNOSIS

History[1]

The classical features of acute appendicitis begin with poorly localised colicky abdominal pain. This is due to mid-gut visceral discomfort in response to appendicular inflammation and obstruction. The pain is frequently, first, noticed in the peri-umbilical region and is similar to, but less intense than, the colic of small bowel obstruction. Central abdominal pain is associated with anorexia, nausea and usually one or two episodes of vomiting that follow the onset of pain (Murphy‟s triad). Anorexia is a useful and constant clinical feature, particularly in children. The patient often gives a history of similar discomfort that settled spontaneously. A family history is also useful as up to one-third of children with appendicitis have a first-degree relative with a similar history.

With progressive inflammation of the appendix, the parietal peritoneum in the right iliac fossa becomes irritated, producing more intense, constant and localised somatic pain that begins to predominate. Patients often report this as an abdominal pain that has shifted and changed in character. Typically, coughing or sudden movement exacerbates the right iliac fossa pain. The classic visceral–somatic sequence of pain is present in only about half of those patients subsequently proven to have acute appendicitis.

Atypical presentations include pain that is predominantly somatic or visceral and poorly localised. Atypical pain is more common in the elderly, in whom localisation to the right iliac fossa is unusual. An inflamed appendix in the pelvis may never produce somatic pain involving the anterior abdominal wall, but may instead cause suprapubic discomfort and tenesmus. In this circumstance, tenderness may be elicited only on rectal examination and is the basis for the recommendation that a rectal examination should be performed on every patient who presents with acute lower abdominal pain. During the first six hours, there is rarely any alteration in temperature or pulse rate. After that time, slight pyrexia (37.2 to 37.7°C) with a corresponding increase in the pulse rate to 80 or 90 is usual. However, in 20% of patients, there is no pyrexia or tachycardia in the early stages. In children, a temperature greater than 38.5°C suggests other causes, for example mesenteric lymphadenitis.

Because appendicitis is so common, a high index of suspicion for appendicitis is warranted in all patients with abdominal pain.[46]

Physical examination[1]

The diagnosis of appendicitis rests more on thorough clinical examination of the abdomen than on any aspect of the history or laboratory investigation. The cardinal features are those of an unwell patient with low-grade pyrexia, localised abdominal tenderness, muscle guarding and rebound tenderness. Inspection of the abdomen may show limitation of respiratory movement in the lower abdomen.

Gentle superficial palpation of the abdomen, beginning in the left iliac fossa moving anticlockwise to the right iliac fossa will detect muscle guarding over the point of maximum tenderness, classically McBurney‟s point. Asking the patient to cough or gentle percussion over the site of maximum tenderness will elicit rebound tenderness. Cutaneous hyperaesthesia may be demonstrable in the right iliac fossa, but is rarely of diagnostic value.

Multiple signs can be detected on physical examination to contribute to the diagnosis of appendicitis.

1. ***Mc Burney's sign:*** Maximum tenderness at Mc Burney‟s point.

2. ***Blumberg's sign:*** A hand kept in the right iliac fossa is progressively pressed with each movement of expiration. It is then removed suddenly; the patient will wince or cry with pain, if the sign is positive, this indicates inflammation of the parietal peritoneum. It is useful sign in the absence of guarding or rigidity.

3. ***The pointing sign:*** The patient is asked to point where the pain began and where it moved.

4. ***Rovsing's sign:*** This sign is positive as a result of pressure on the left side of the colon, forcing the gas into the caecum distending the caecum and surrounding of the inflamed focus resulting in pain.

5. ***Psoas sign:*** Pain with flexion of the leg at the right hip, can be seen with a retrocecal appendix due to inflammation adjacent to the psoas muscle

6. ***The Cope's(obturator) sign:*** Pain with rotating the flexed right thigh internally, indicates inflammation adjacent to the obturator muscle in the pelvis.

7. ***Sherren's sign:*** Sherren in 1925, pointed out this Sherren‟s triangle and is defined as the triangle bounded by lines joining umbilicus, right anterior superior iliac spine and pubic symphysis. Hyperesthesia is elicited by gently striking the skin. It is compared with left side. If hyperesthesia is present it indicates the perforation of the appendix.

   This sign is although classic, it is not reliable. It depends upon the discrimination capacity of the patient.

8. ***Baldwin's test for retrocaecal appendix****:* After identifying the tender spot in the right flank, light pressure is maintained over the spot and the patient is asked to lift the right lower limb keeping the knee in straight position. This produces increased pain in the loin and the patient drops the leg with pain. This is a positive sign of retrocaecal appendicitis. Sometimes there may be irritation of the ureters with pain shooting around flank. Sometimes red blood corpuscle may be found in the urine.

9.Shifting Tenderness (Alder's): The most tender spot is marked first, the patient is put in left lateral position and point of maximum tenderness is marked again. If the tender spot shifts probably it is not a case of appendicitis. This sign is useful to differentiate appendicitis from mesenteric lymphadenitis and painful uterine conditions in pregnancy.

Rectal examination[2]:

Digital per rectal examination should be done in all cases of acute abdomen. Tenderness on right side is significant. As digital examination itself produces discomfort, by palpating left lateral and posterior wall of rectum is compared with that produced on right side. It may be the only positive sign in pelvic appendicitis. It is positive in one-third cases; perfect examination can also detect a pelvic abscess.

Investigations

The diagnosis of acute appendicitis is essentially clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of a normal appendix in 15 to 30% of cases. The premise that it is better to remove a normal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly.[1]

A number of Laboratory and Imaging studies have been devised to assist diagnosis.

Laboratory Tests

Laboratory studies can be helpful in the diagnosis of appendicitis, but no single test is definitive.

White Blood Cell Count (WBC)

A White Blood Cell count (WBC) is perhaps the most useful laboratory test. The white blood cell count is elevated with more than 75% neutrophils in most patients.A completely normal leukocyte count and differential count is found in

about 10% of patients with acute appendicitis. A high white blood cell count (>20,000/mL) suggests complicated appendicitis with either gangrene or perforation.[3]

The clinician must remember, however, that the WBC count can be normal in patients with acute appendicitis, particularly in early cases. Serial WBC measurements improve the diagnostic accuracy, with a rising value over time commonly seen in patients with appendicitis.[46]

C-reactive protein

C-reactive protein (CRP) is an acute-phase reactant synthesized by the liver in response to infection or inflammation and rapidly increases within the first 12 hours. CRP has been reported to be useful in the diagnosis of appendicitis; however, it lacks specificity and cannot be used to distinguish between sites of infection. CRP levels of greater than 1 mg/dl are commonly reported in patients with appendicitis, but very high levels of CRP in patients with appendicitis indicate gangrenous evolution of the disease, especially if it is associated with leukocytosis and neutrophilia.

However, CRP normalization is known to occur 12 hours after onset of symptoms. Several prospective studies have shown that in adults who have had symptoms for longer than 24 hours, a normal CRP level has a negative predictive value of 97-100% for appendicitis.

Multiple studies have been done evaluating the sensitivity of CRP level alone for the diagnosis of appendicitis in patients selected to undergo appendicectomy. Gurleyik et al noted a CRP sensitivity of 96.6% in 87 of 90 patients with histologically proven disease.[50]

Urinalysis

Urinalysis is performed to diagnose other potential causes for abdominal pain, specifically urinary tract infection and ureteral stone. Significant hematuria with colicky abdominal pain suggests ureterolithiasis, and testing directed at this diagnosis is indicated. A urinary tract infection, on the other hand, is not uncommon in patients with appendicitis. Its presence does not exclude the diagnosis of acute appendicitis, but it should be identified and treated. Although pyuria suggests urinary tract infection, it is not uncommon for the urinalysis in a patient with appendicitis to show a few white blood cells solely due to inflammation of the ureter by the adjacent appendix.

In certain patient populations, other laboratory tests are indicated. In women of childbearing age, the urine human chorionic gonadotropin should be checked to alert the clinician to the possibility of ectopic or concurrent pregnancy. Ectopic pregnancy is another cause of right lower quadrant pain that demands emergent diagnosis and treatment.

Imaging Studies

The potential imaging modalities for diagnosis of acute appendicitis include plain radiographs, ultrasound and computed tomography

Plain radiographs

Prior to the wide-spread use of modern imaging techniques, plain abdominal films were often obtained in patients with abdominal pain, and a right lower

quadrant faecolith (or appendicolith) was considered pathognomonic for acute appendicitis.[2] A calcified appendicolith is visible on plain films in only 10% to 15% of patients with acute appendicitis.[3] Studies show that faecaliths are not pathognomonic for appendicitis, as some patients with abdominal pain and a faecolith have a normal appendix. In addition, faecoliths are not common enough in patients with appendicitis to be used as a reliable sign.

As a result, plain abdominal radiographs are neither helpful nor cost effective and are not recommended for the diagnosis of acute appendicitis. Plain abdominal films may be useful for the detection of ureteral calculi, small bowel obstruction or perforated ulcer, but such conditions are rarely confused with appendicitis.[3]

Ultrasonography (USG)

Among patients with abdominal pain, *Abdominal ultrasonography* has a sensitivity of about 85% and a specificity of more than 90% for the diagnosis of acute appendicitis.[3]

Sonographic findings consistent with acute appendicitis include:

1. Appendix of seven mm or more in antero-posterior diameter,
2. A thick-walled, noncompressible luminal structure seen in cross section referred to as a *target lesion,*
3. Increased echogenicity of the surrounding fat signifying inflammation ,
4. Presence of an appendicolith
5. In more advanced cases, peri-appendicular fluid or a mass may be found.

Ultrasonography has the advantages of being a non-invasive modality requiring no patient preparation that also avoids exposure to ionizing radiation. For these

reasons, it is commonly used in children and in pregnant patients with equivocal clinical findings suggestive of acute appendicitis. Disadvantage of ultrasonography is that it is highly operator-dependent, and it is frequently unable to visualize the normal appendix.[51]

Pelvic ultrasound can be especially useful in excluding pelvic pathology, such as tubo-ovarian abscess or ovarian torsion, which may mimic acute appendicitis.[42]

Computed tomography

Computed tomography (CT) is commonly used in the evaluation of adult patients with suspected acute appendicitis, especially so in the elderly.[3] CT has a high diagnostic accuracy for appendicitis,[52] and visualization and diagnosis of many of the other causes of abdominal pain that can be confused with appendicitis.

Improved imaging techniques, including the use of 5-mm sections, have resulted in increased accuracy of CT scanning,[53] which has a sensitivity of about 90% and a specificity of 80% to 90% for the diagnosis of acute appendicitis among patients with abdominal pain.
Controversy remains as to the importance of intravenous, oral gastrointestinal, and rectal contrast in improving diagnostic accuracy.

In general, CT findings of appendicitis increase with the severity of the disease. Classic findings include a distended appendix greater than seven mm in diameter and circumferential wall thickening, which may give the appearance of a halo or target. As inflammation progresses, one may see periappendicular fat stranding, edema, peritoneal fluid, phlegmon, or a periappendicular abscess. CT detects appendicoliths in about 50% of patients with appendicitis and also in a small percentage of people without appendicitis. Among patients with abdominal pain,

the positive predictive value of the finding of an appendicolith on CT remains high at about 75%.

In prospective studies, CT demonstrated a sensitivity of 0.94 and a specificity of 0.95.[52] CT thus has a high negative predictive value, making it particularly useful in excluding appendicitis in patients for whom the diagnosis is in doubt. Appendicitis is highly unlikely if enteric contrast fills the lumen of the appendix and no surrounding inflammation is present. The clinician must remember, however, that a CT performed early in the course of appendicitis might not show the typical radiographic findings.[1]

The rational approach is – the selective use of CT scanning.

Laparoscopy

Although most patients with appendicitis will be accurately diagnosed based on history, physical exam, laboratory studies, and if necessary, imaging techniques, there are a small number in whom the diagnosis remains elusive. For these patients, diagnostic laparoscopy can provide both a direct examination of the appendix and a survey of the abdominal cavity for other possible causes of pain.

Laparoscopy can serve as both a diagnostic and therapeutic maneuver for patients with acute abdominal pain and suspected acute appendicitis.

Laparoscopy is probably most useful in the evaluation of females with lower abdominal complaints, because appendicectomy is performed on a normal appendix in as many as 30 to 40% of these patients. Differentiating acute gynecologic pathology from acute appendicitis can be effectively accomplished using the laparoscope.[23]

Barium enema studies

In the past, barium enema examination was used to diagnose appendicitis. However in the era of ultrasonography and CT scanning, barium enema study has absolutely no role in the diagnosis of acute appendicitis.

Scoring Systems

A number of clinical and laboratory-based scoring systems have been devised to assist diagnosis. The most widely used is the Alvarado score. A score of seven or more is strongly predictive of acute appendicitis.[1]

Features	Score
Symptoms	
• Migratory RIF pain	1
• Anorexia	1
• Nausea and vomiting	1
Signs	
• Tenderness (RIF)	2
• Rebound tenderness	1
• Elevated temperature	1
Laboratory	
• Leucocytosis	2
• Shift to left	1

Table 2: The Alvarado score

MATERIALS & METHODS

MATERIALS AND METHODS

Patients reported to R L Jalappa Hospital and Research centre constituent of sri Devraj Urs Medical college, surgery department with acute abdomen, was considered for our study. The Study group included 100 patients. Maximum in the age group of 21-40 years. Clinically proven cases of acute appendicitis and perforation was considered. All the cases were evaluated biochemically to find if any association of serum bilirubin with clinically proven acute appendicitis.

Study design

Prospective study.

Study place

Our study was conducted in the Department of Surgery, in R.L. JALAPPA HOSPITAL TAMAKA .

Study period

December 2014 to 2016.

Source of data

Patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation or recurrent appendicitis under the Department of Surgery, in R.L. JALAPPA HOSPITAL TAMAKA during the study period.

Sample size

A total of 100 patients with clinical diagnosis of acute appendicitis or appendicular perforation or recurrent appendicitis were studied.

Sampling method

Sample size = 100 was estimated based on the mean bilirubin level of 1.5 +/- 0.65 in a study.

Alpha error at 1% , power at 99%

n=92 expecting 10 % of non response n = 100

Selection criteria

Inclusion criteria.

- All patients diagnosed as acute appendicitis clinically on admission.
- All patients diagnosed as appendicular perforation clinically on admission.
- All patients diagnosed as recurrent appendicitis clinically on admission.

For these groups, only patients with histopathological report suggestive of acute appendicitis or appendicular perforation or recurrent appendicitis were included.

Exclusion criteria.

- All patients documented to have a past history of
  - Jaundice or Liver disease.
  - Chronic alcoholism (that is intake of alcohol of > 40 g/day for Men and > 20 g/day in Women for 10 years).[71]
  - Hemolytic disease.
  - Congenital or Acquired biliary disease.
- All patients with positive HBsAg.
- All patients with cholelithiasis.
- All patients with hepato-biliary system malignancy.

Procedure

Ethical clearance has been obtained from "Ethical Clearance Committee" of the institution for the study. It is in the form of signature from Head of Dept. Surgery and Dean of SDUMC, TAMAKA ,KOLAR. Based on the selection criteria patients admitted with clinical diagnosis of acute appendicitis or appendicular perforation under Department of Surgery in R.L. JALAPPA HOSPITAL TAMAKA during the study period were screened for eligibility. The eligible patients were briefed about the nature of the study and a written informed consent (Annexure I) was obtained from the consented patients. Thorough history was taken and clinical examination was done for all patients and findings were recorded on predesigned and pretested proforma (Annexure II) .

The following tests were carried out on admission.

- Routine blood investigations (Complete blood count, platelet count, reticulocyte count).
- Peripheral smear to rule out hemolytic anemia.
- Serum haptoglobulin if peripheral smear and blood tests indicate features of hemolytic anemia.
- Serum Bilirubin (Total and Direct bilirubin).
- Liver Function Tests (LFTs) which include;
  - SGPT (Alanine transaminase).
  - SGOT (Aspartate transaminase).
  - ALP (Alkaline phosphatase).
- Seropositivity for HbsAg
- Urine analysis (routine and microscopy).

The serum bilirubin and LFTs were carried out using the Auto Analyser (cobas c 111) machine available in the hospital and HbsAg was tested by ELISA / Spot technique using HEPALISA© or HEPACARD© kit.

Reference Range of Serum Bilirubin and Liver Enzymes[23]

Test	Normal Range
Serum Bilirubin	
Total	0.3 - 1.2 mg/dl
Direct	0.4– 0.6 mg/dl
Liver Enzymes	
SGOT	– 40 U/L
SGPT	– 35 U/L
ALP	– 290 U/L

The results were grouped as „Normal" or „Raised" (hyperbilirubinemia) as per the above reference values

Statistical analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. p value <0.05 was considered as statistically significant.

Screening of Disease:

Screening test results	Diagnosis		Total
	Diseased	Healthy	
Positive	a (True postive)	b (False Postive)	a+b
Negative	c (False Negative)	d (True Negative)	c+d
Total	a + c	b + d	a+b+c+d

- Sensitivity = a/(a+c) x 100 = True positive / True positive + False Negative
- Specificity = d/(b+d) x 100 = True Negative / True Negative + False Postive
- Positive predictive value = a/ (a+b) x 100 = True Postive / True positive + False Postive
- Negative predictive value = d/ (c+d) x 100 = True Negative / True Negative + False Negative
- Diagnostic accuracy = a + d / a + b + c + d = True postive + True Negative / Total

Sensitivity: Defined as ability of a test to identify correctly all those who have the disease i.e. true positive

Specificity: It is the ability of test to identify correctly those who do not have the disease i.e. true negative.

Positive predictive value (PPV): The proportion of patients who test positive who actually have the disease.

Negative predictive value (NPV): The proportion of patients who test negative who are actually free of the disease.

Diagnostic accuracy: Is the ability of screening test to detect true positives and true negatives in the total population studied.

RESULTS

RESULTS:

Table 1: Gender distribution of subjects

		Count	%
Gender	Female	49	49.0%
	Male	51	51.0%
	Total	100	100.0%

In the study majority of subjects i.e. 51% were males and 49% were females.

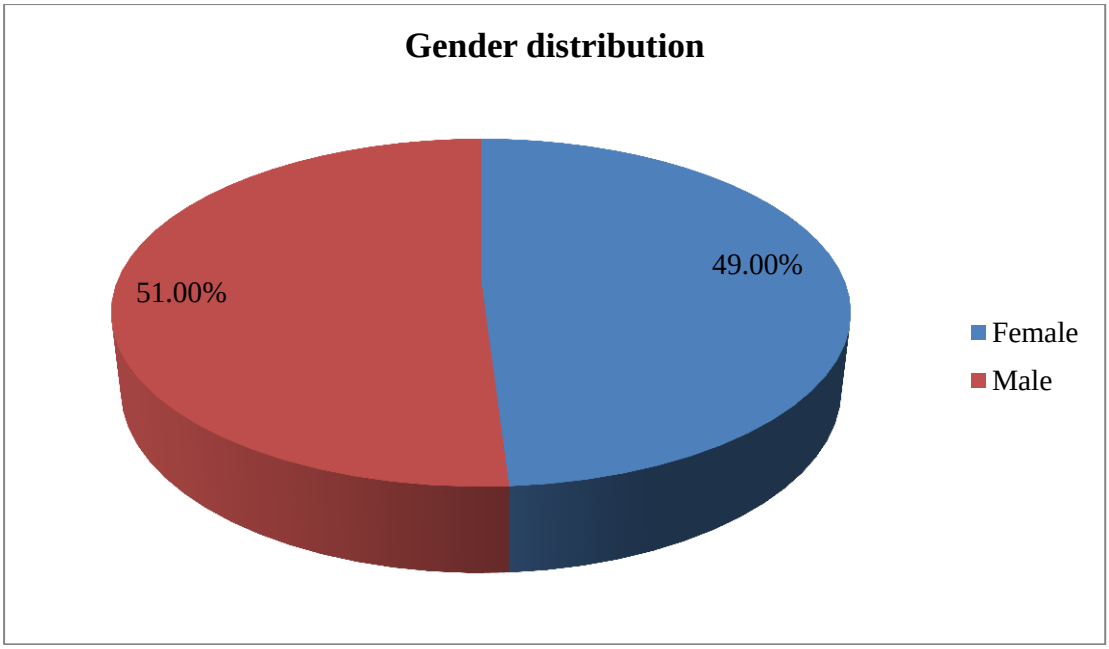


Figure 1: Pie diagram showing Gender distribution of subjects

Table 2: Age distribution of subjects with appendicitis

		Count	%
Age	<20 years	40	40.0%
	21 to 40 years	50	50.0%
	> 40 years	10	10.0%
	Total	100	100.0%

In the study 90% of subjects were below 40 years and 10% of them were above 40 years of age.

Mean age of subjects was 25.41 ± 11.14 years.

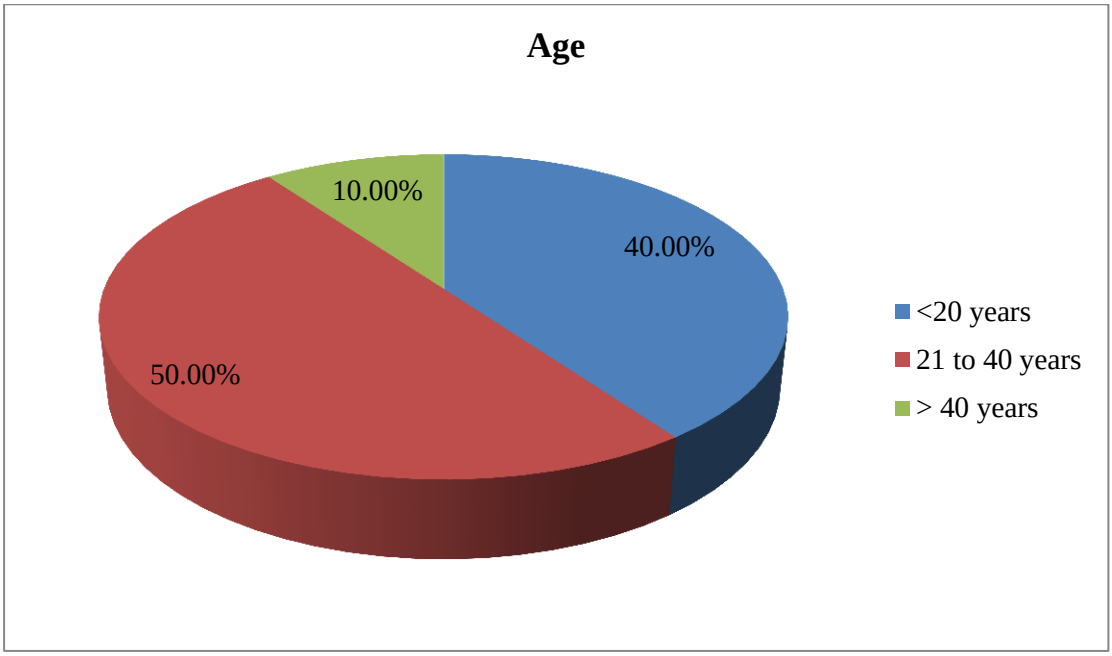


Figure 2: Pie diagram showing Age distribution of subjects in the study

Table 3: Distribution of Liver function parameters and Total Leukocyte count in subjects

	Mean	Standard Deviation
Total Bilirubin	1.3	0.6
Direct Bilirubin	0.5	0.3
SGOT	36.2	15.8
SGPT	32.0	12.7
ALP	164.6	97.6
TLC	10.8	4.2

Mean Total Bilirubin in subjects was 1.3 ± 0.6 mg/dl, Direct Bilirubin was 0.5 ± 0.3 mg/dl, SGOT was 36.2 ± 15.8, SGPT was 32 ± 12.7, ALP was 164.6 ± 97.6 and TLC was 10.8 ± 4.2.

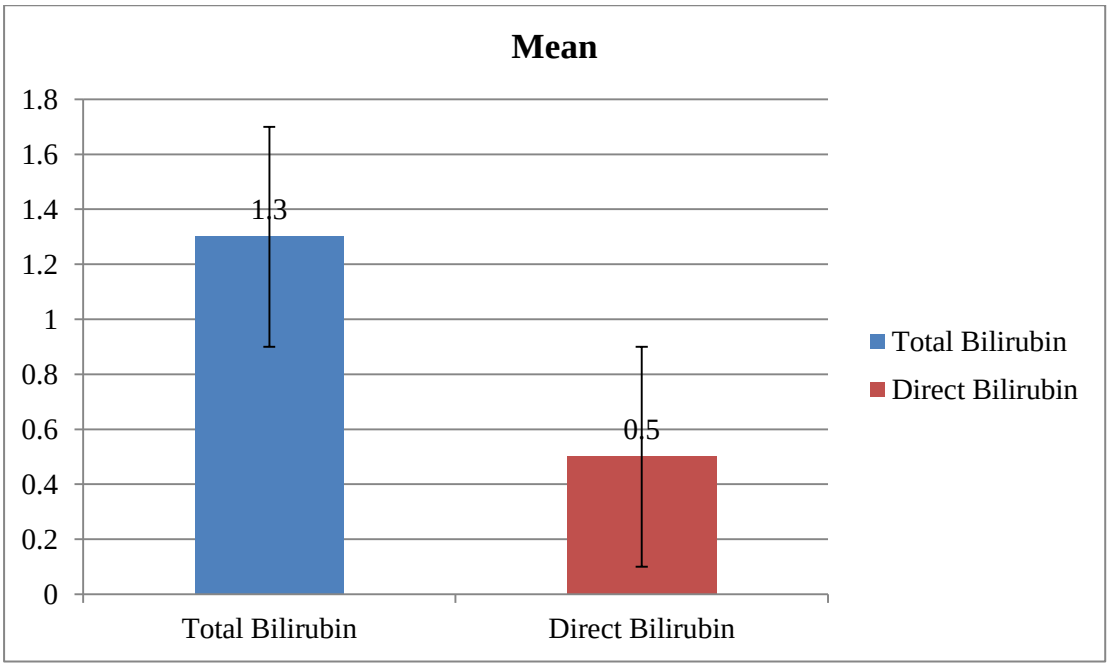


Figure 3: Bar diagram showing Mean Bilirubin levels

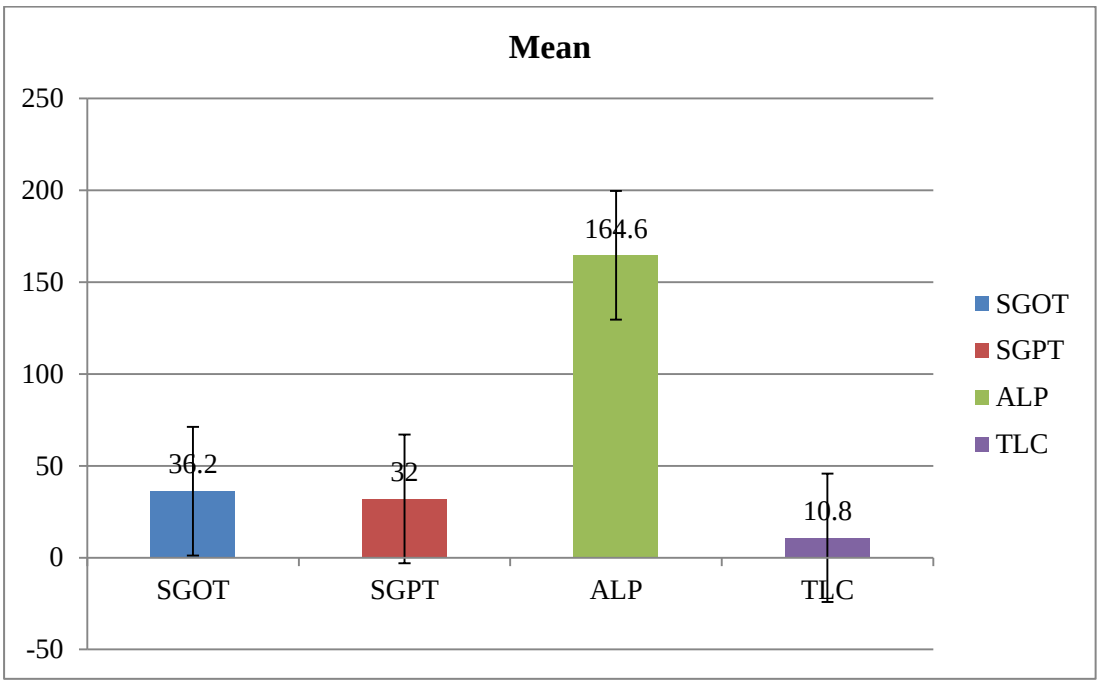


Figure 4: Bar diagram showing Liver function parameters and Total Leukocyte count

Table:4 Mean Total Bilirubin and Direct Bilirubin in Acute appendicitis and Appendicular perforation

	Acute Appendicitis		Appendicular Perforation	
	Mean	SD	Mean	SD
Total Bilirubin	1.2	0.5	2.2	0.3
Direct Bilirubin	0.4	0.3	0.9	0.4

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.2 ± 0.5 mg/dl , while in patients diagnosed with Appendicular perforation was 2.2±0.3 mg/dL.

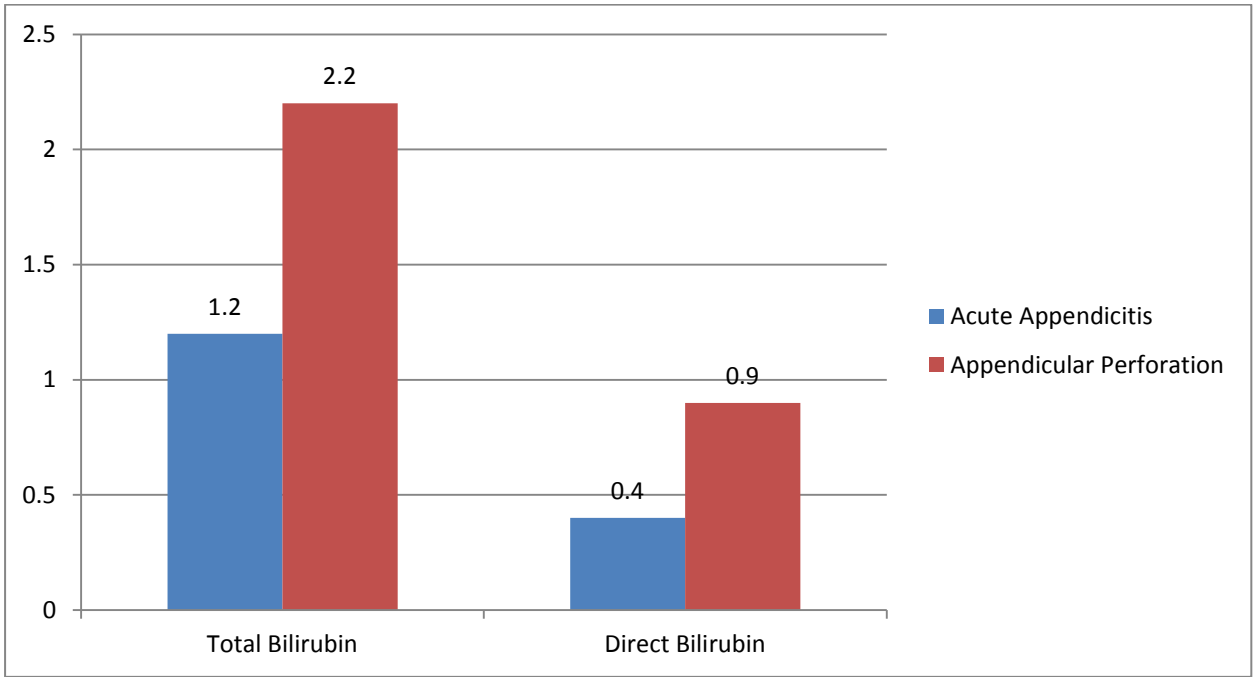


Figure 5: Bar diagram showing Mean Total Bilirubin and Direct Bilirubin in Acute appendicitis and Appendicular perforation.

Table 5: Diagnosis in subjects at different period and methods

		Count	%
Clinical Diagnosis	AA	87	87.0%
	AP	5	5.0%
	RA	8	8.0%
Per operative Diagnosis	AA	86	86.0%
	AP	11	11.0%
	RA	3	3.0%
HPR	AA	82	82.0%
	AGA&P	11	11.0%
	RA	7	7.0%

In the study clinically 87% were diagnosed to have acute appendicitis, 5% as appendicular perforation and 8% as recurrent appendicitis.

Per operatively 86% were diagnosed as acute appendicitis, 11% as appendicular perforation and 3% as recurrent appendicitis.

Histopathologically 82% were diagnosed as acute appendicitis, 11% as appendicular perforation with gangrene and 7% as recurrent appendicitis.

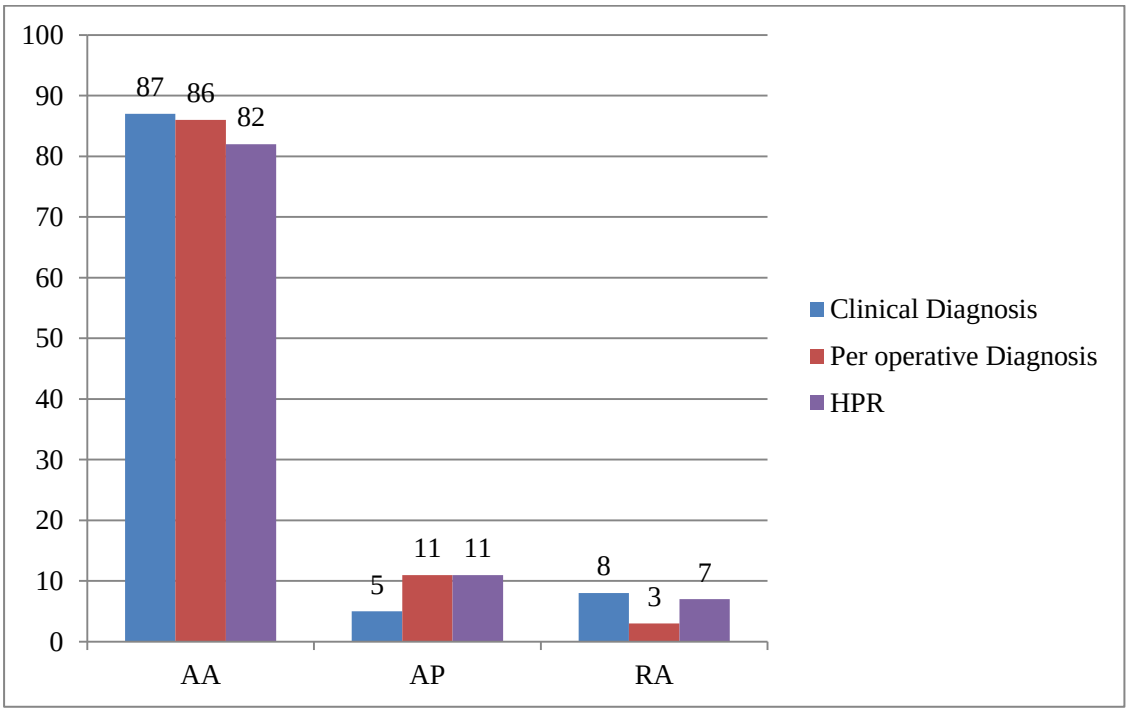


Figure 6: Bar diagram showing Diagnosis in subjects at various periods

Table 6: Bilirubin levels and Hyperbilirubinemia in subjects

		Count	%
Total Bilirubin	Normal	37	37.0%
	Raised	63	63.0%
Direct Bilirubin	Normal	76	76.0%
	Raised	24	24.0%
Hyperbilirubinemia	Absent	30	30.0%
	Present	70	70.0%

In the study Total Bilirubin was raised in 63% of subjects, Direct Bilirubin levels were raised in 24% and Hyperbilirubinemia was present in 70% of subjects based on raised total Bilirubin or raised direct Bilirubin.

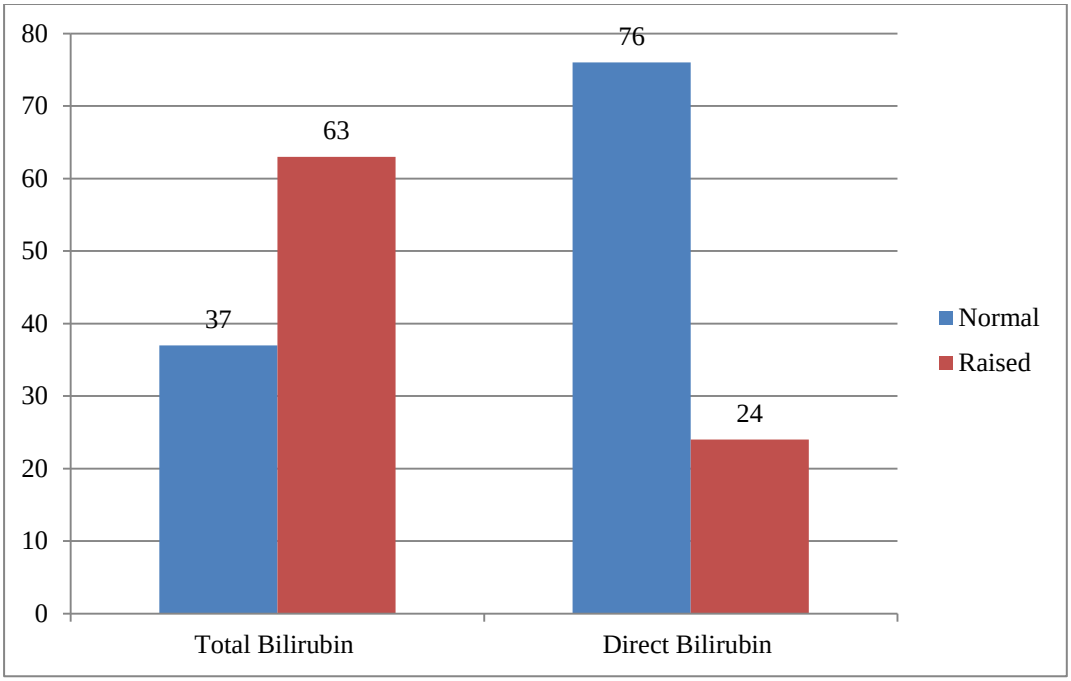


Figure 7: Bar diagram showing Bilirubin levels in subjects

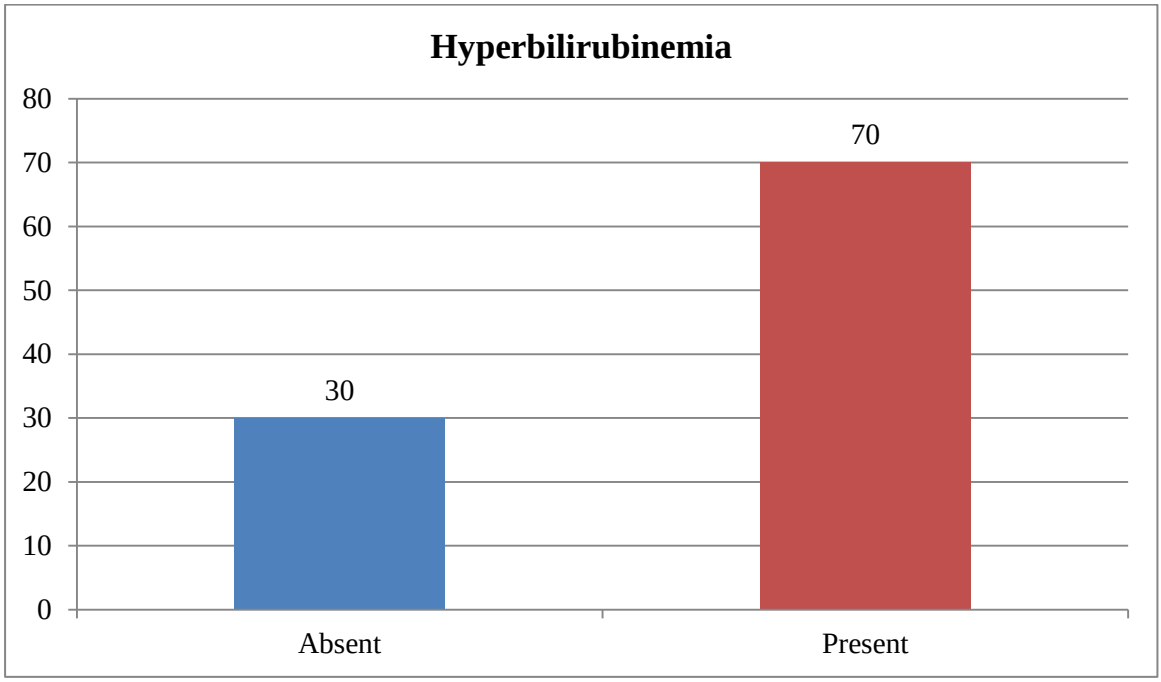


Figure 8: Bar diagram showing Bilirubin levels in subjects

Table 7: Association between Hyperbilirubinemia and clinical diagnosis

		Clinical Diagnosis					
		Acute Appendicitis		Appendicular Perforation		Recurrent Appendicitis	
		Count	%	Count	%	Count	%
Hyperbilirubinemia	Present	63	72.4%	5	100.0%	2	25.0%
	Absent	24	27.6%	0	0.0%	6	75.0%

$\chi 2 = 10.099$, df = 2, p = 0.006*

Out of 87 subjects who were clinically diagnosed as acute appendicitis 72% had Hyperbilirubinemia, out of 5 subjects who were clinically diagnosed as Appendicular Perforation 100% had Hyperbilirubinemia and 25%with recurrent appendicitis had Hyperbilirubinemia.

There was significant association between Hyperbilirubinemia and clinical diagnosis.

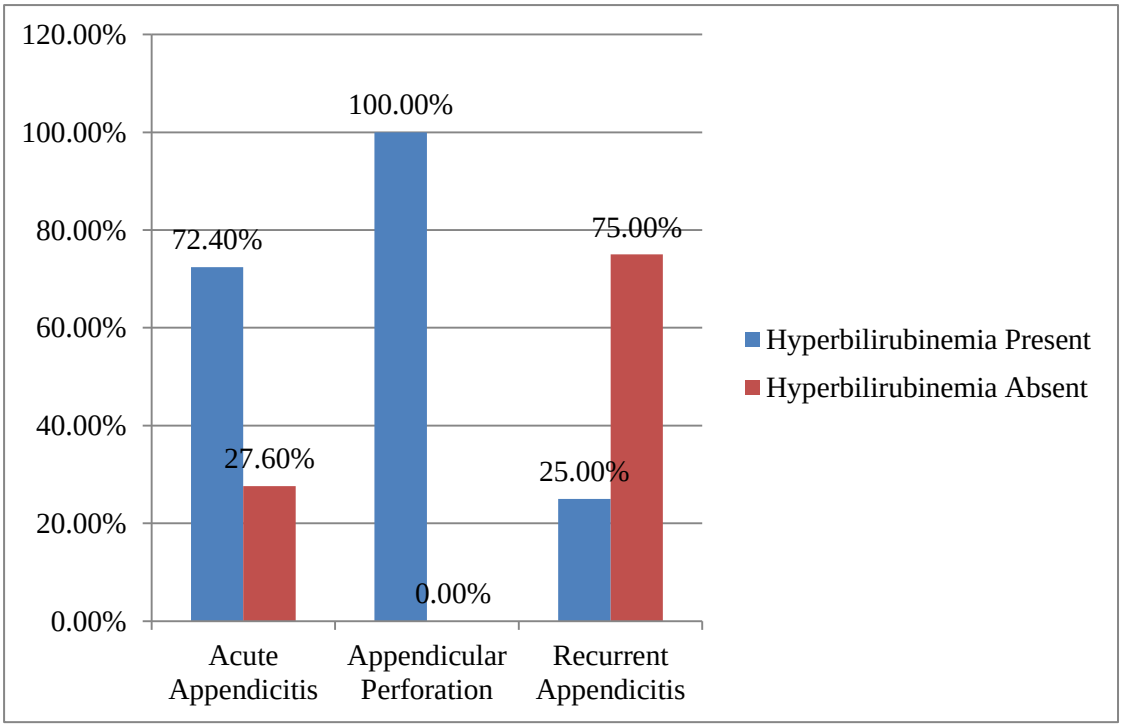


Figure 9: Bar diagram showing Association between Hyperbilirubinemia and clinical diagnosis

Table 8: Association between Hyperbilirubinemia and per operative Diagnosis

		Per operative Diagnosis					
		Acute Appendicitis		Appendicular Perforation		Recurrent Appendicitis	
		Count	%	Count	%	Count	%
Hyperbilirubinemia	Present	58	67.4%	11	100.0%	1	33.3%
	Absent	28	32.6%	0	0.0%	2	66.7%

$\chi 2 = 6.903$, df = 2, p = 0.032*

Out of 86 subjects who were diagnosed as acute appendicitis per operatively 67.4% had Hyperbilirubinemia, out of 11 subjects who were per operatively diagnosed as Appendicular Perforation 100% had Hyperbilirubinemia and 33.3% with recurrent appendicitis had Hyperbilirubinemia.

There was significant association between Hyperbilirubinemia and per operative diagnosis.

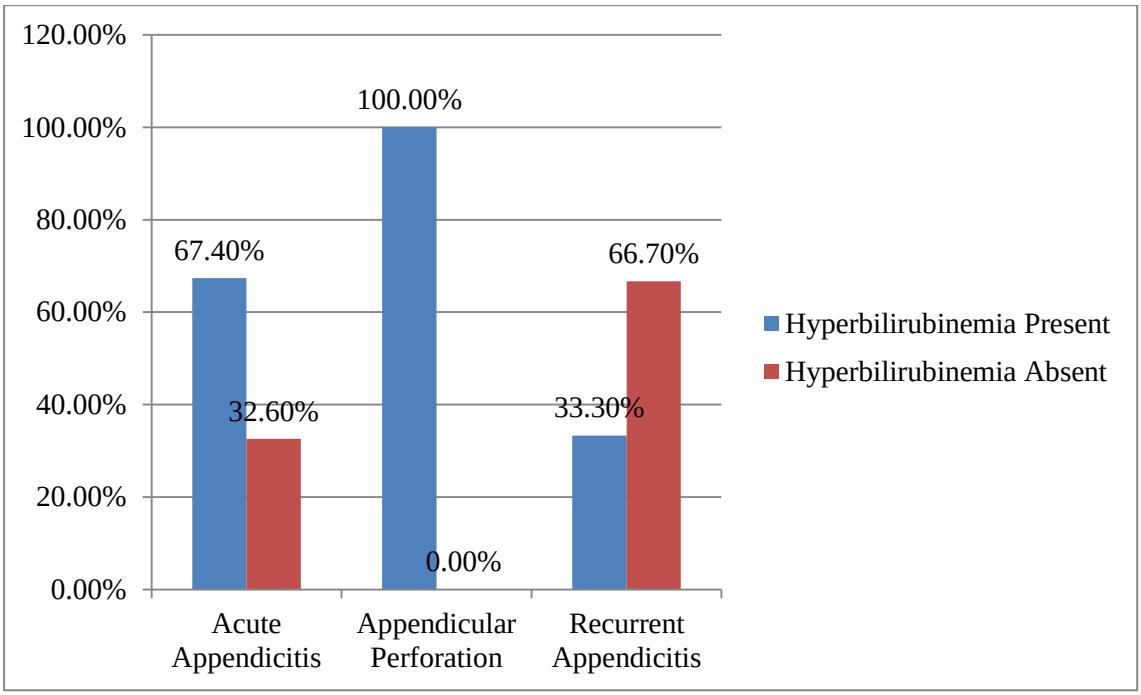


Figure10: Bar diagram showing Association between Hyperbilirubinemia and pre operative diagnosis

Table 9: Association between Hyperbilirubinemia and Histopathological Diagnosis

		HPR					
		Acute Appendicitis		Appendicular Perforation		Recurrent Appendicitis	
		Count	%	Count	%	Count	%
Hyperbilirubinemia	Present	57	69.5%	11	100.0%	2	28.6%
	Absent	25	30.5%	0	0.0%	5	71.4%

$\chi 2 = 10.44$, df = 2, p = 0.005*

Out of 82 subjects who were diagnosed as acute appendicitis histopathologically 69.5% had Hyperbilirubinemia, out of 11 subjects who were histopathologically diagnosed as Appendicular Perforation 100% had Hyperbilirubinemia and 20% with recurrent appendicitis had Hyperbilirubinemia.

There was significant association between Hyperbilirubinemia and Histopathologically diagnosis.

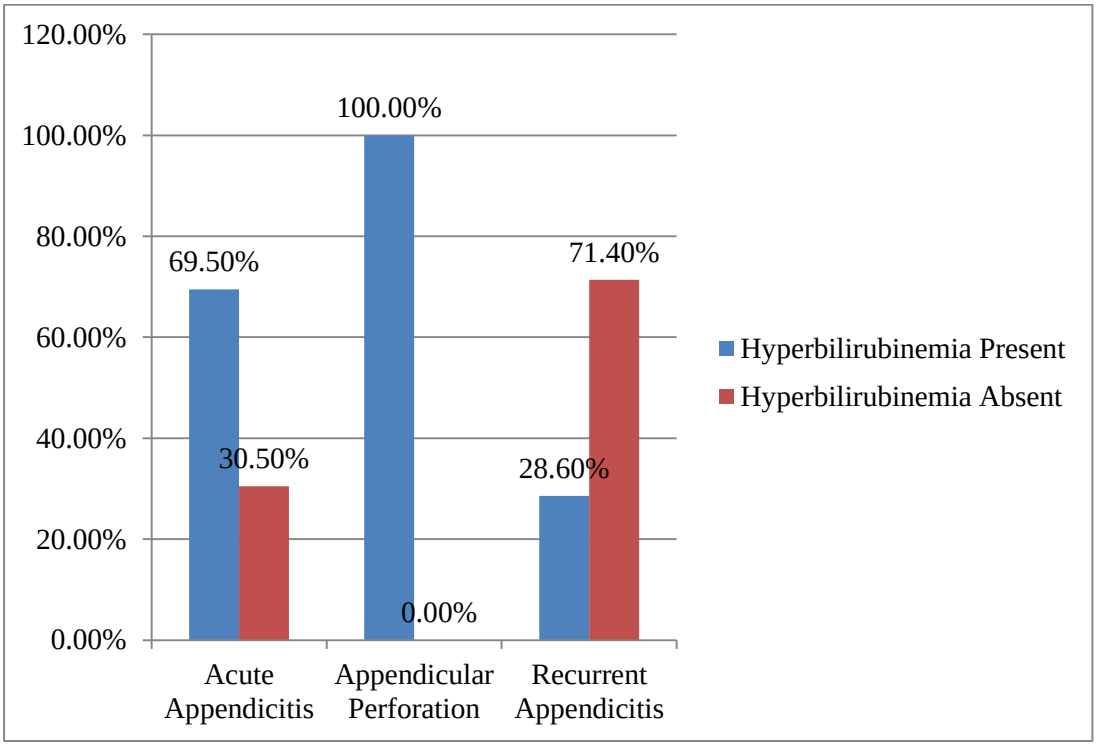


Figure 11: Bar diagram showing Association between Hyperbilirubinemia and clinical Histopathological diagnosis

Table 10: Validity of Hyperbilirubinemia in diagnosis if Acute appendicitis

		HPR			
		Acute Appendicitis Present		Acute Appendicitis Absent	
		Count	%	Count	%
Hyperbilirubinemia	Present	57	69.5%	13	72.2%
	Absent	25	30.5%	5	27.8%

Parameter	Acute Appendicitis
Sensitivity	69.51%
Specificity	27.78%
Positive Predictive Value	81.43%
Negative Predictive Value	16.67%
Diagnostic Accuracy	62%

Hyperbilirubinemia had a diagnostic accuracy of 62% in diagnosis of acute appendicitis.

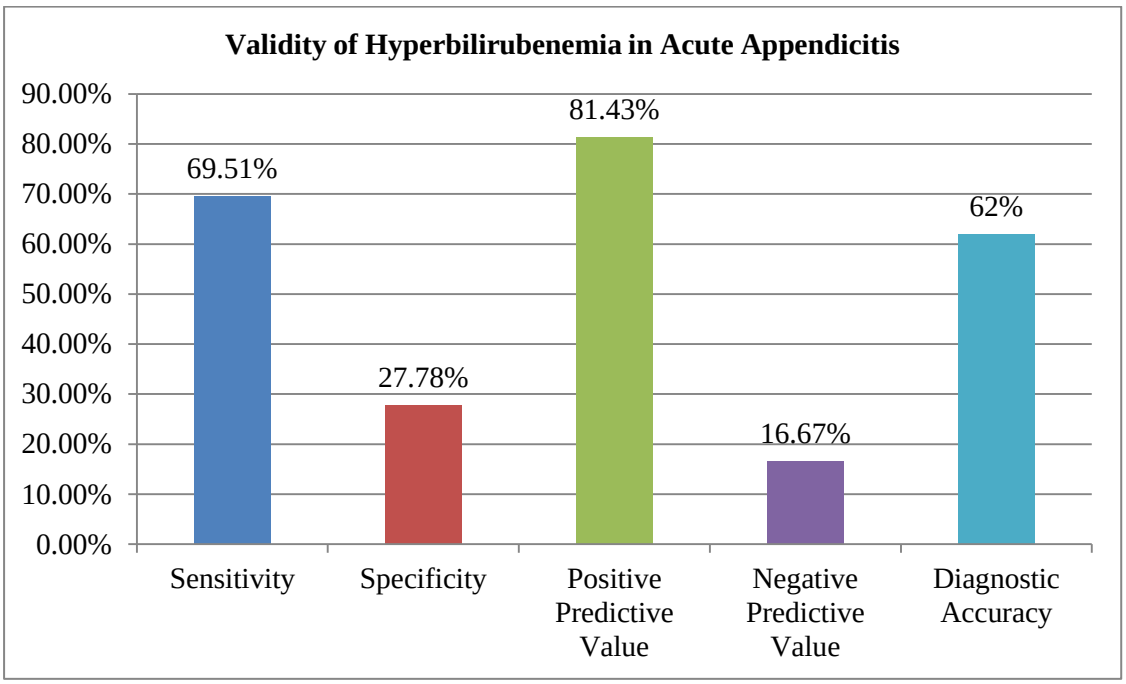


Figure12: Bar diagram showing Validity of Hyperbilirubinemia in Acute Appendicitis

Table 11: Validity of Hyperbilirubinemia in diagnosis of Appendicular Perforation

		HPR			
		AGA &Appendicular Perforation Present		AGA & Appendicular Perforation Absent	
		Count	%	Count	%
Hyperbilirubinemia	Present	11	100.0%	59	66.3%
	Absent	0	0.0%	30	34.7%

Parameter	Appendicular Perforation
Sensitivity	100%
Specificity	33.71%
Positive Predictive Value	15.71%
Negative Predictive Value	100%
Diagnostic Accuracy	41%

Hyperbilirubinemia had a diagnostic accuracy of 41% in diagnosis of appendicular perforation. Were as 100% sensitivity and Negative predictive value was observed.

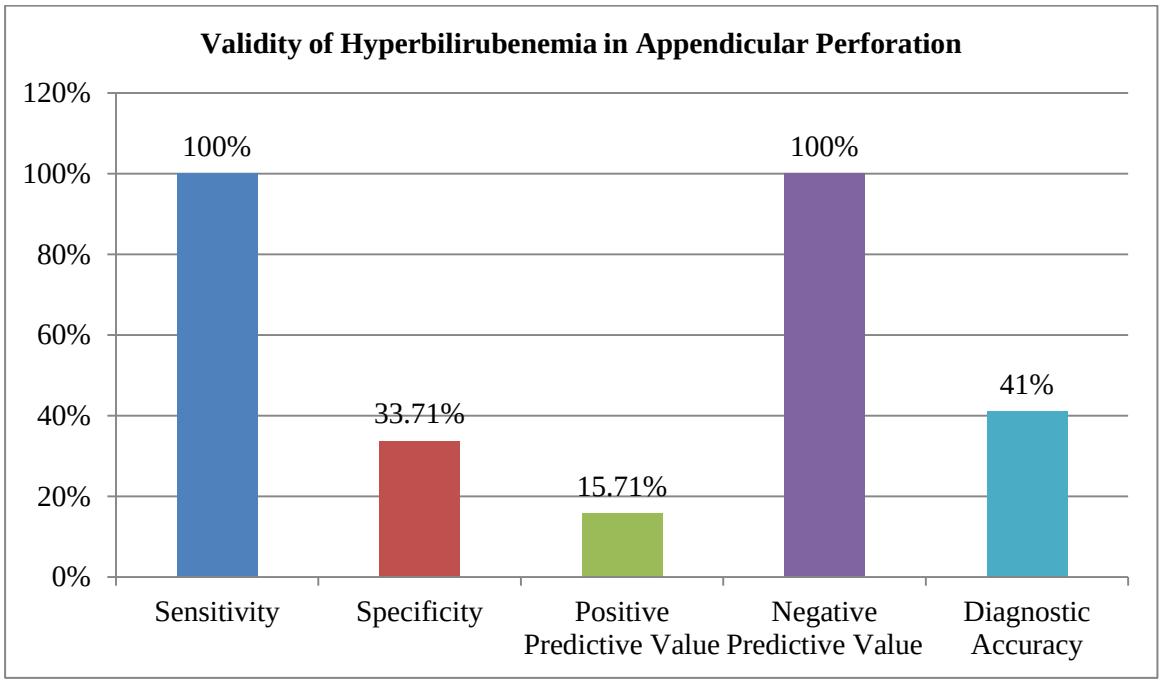


Figure 13: Bar diagram showing Validity of Hyperbilirubinemia in diagnosis of Appendicular Perforation

Table 12: Validity of Hyperbilirubinemia in diagnosis of Recurrent Appendicitis

		HPR			
		Recurrent Appendicitis Present		Recurrent Appendicitis Absent	
		Count	%	Count	%
Hyperbilirubinemia	Present	2	28.6%	68	73.11
	Absent	5	71.4%	25	26.89

Parameter	Recurrent appendicitis
Sensitivity	28.57%
Specificity	26.88%
Positive Predictive Value	2.85%
Negative Predictive Value	83.33%
Diagnostic Accuracy	27%

Hyperbilirubinemia had a diagnostic accuracy of 27% in diagnosis of Recurrent appendicitis.

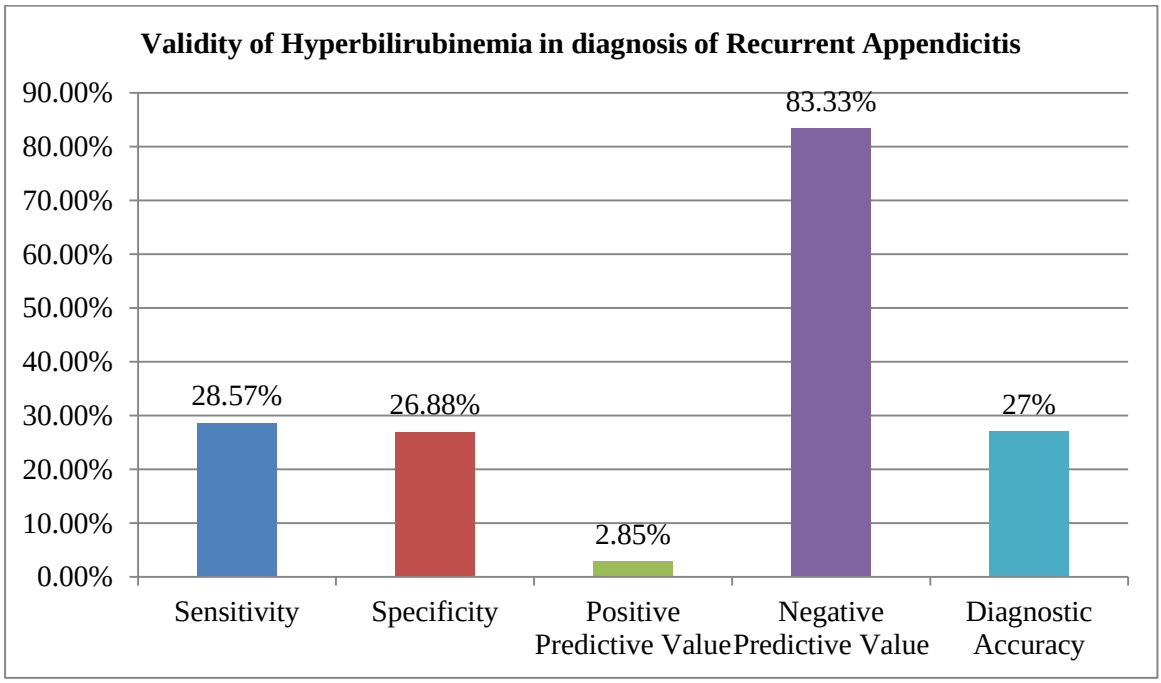


Figure 14: Bar diagram showing Validity of Hyperbilirubinemia in diagnosis of Recurrent Appendicitis

Table 13: Area under the Curve for Diagnosis of Various types of Appendicitis

Area Under the Curve							
Diagnosis	Test Result Variable (s): Total Bilirubin						
	Area	P value	95% Confidence Interval		Bilirubin Cutoff Value	Sensitivity	Specificity
			Lower	Upper			
Acute Appendicitis	0.268	0.002*	0.108	0.428	1.150	0.671	0.222
Appendicular Perforation	**0.987**	**<0.001***	**0.968**	**1.000**	**1.850**	**1.000**	**0.921**
Recurrent Appendicitis	0.294	0.070	0.152	0.436	1.250	0.286	0.344

Area under the curve was highest for appendicular perforation with respect to Total Bilirubin levels. Total Bilirubin of 1.85 cut off had 100% sensitivity and 92% specificity in diagnosis of appendicular perforation.

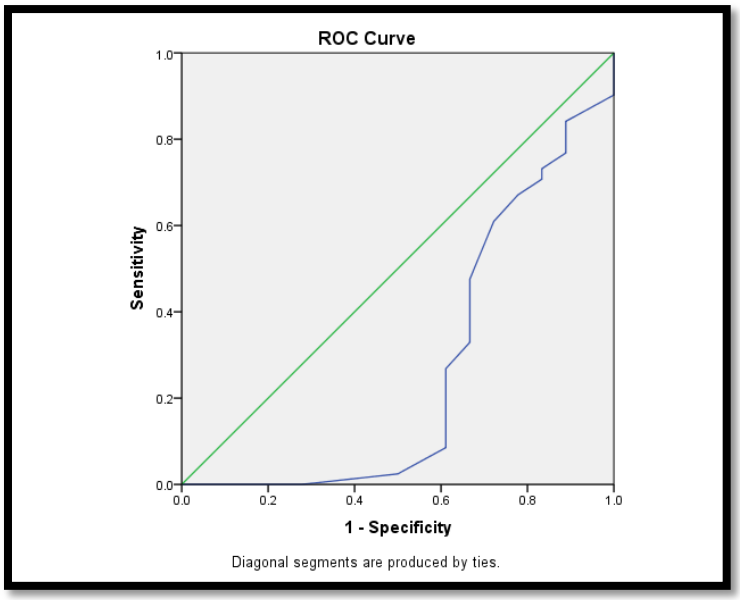


Figure 15: ROC curve showing Area under curve for Acute Appendicitis

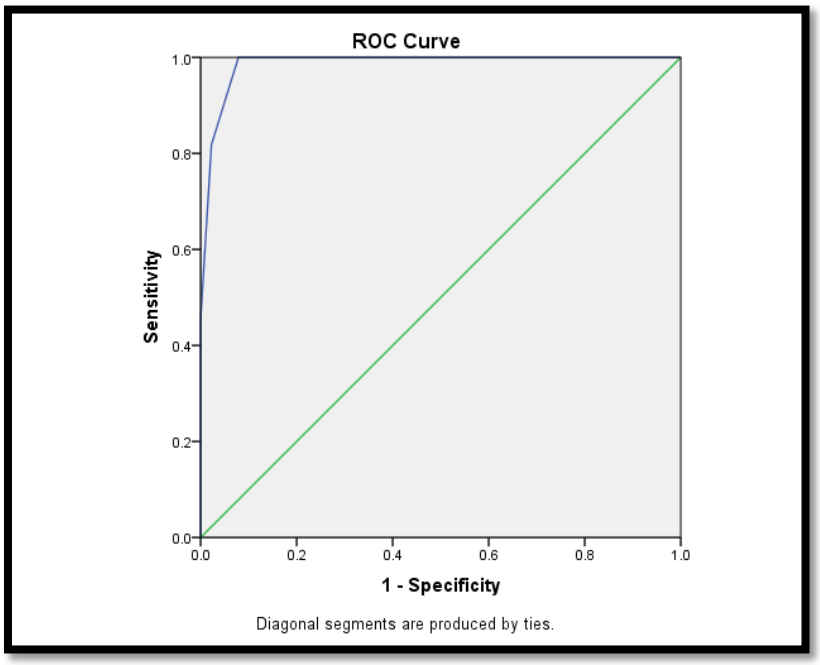


Figure 16: ROC curve showing Area under curve for Appendicular Perforation

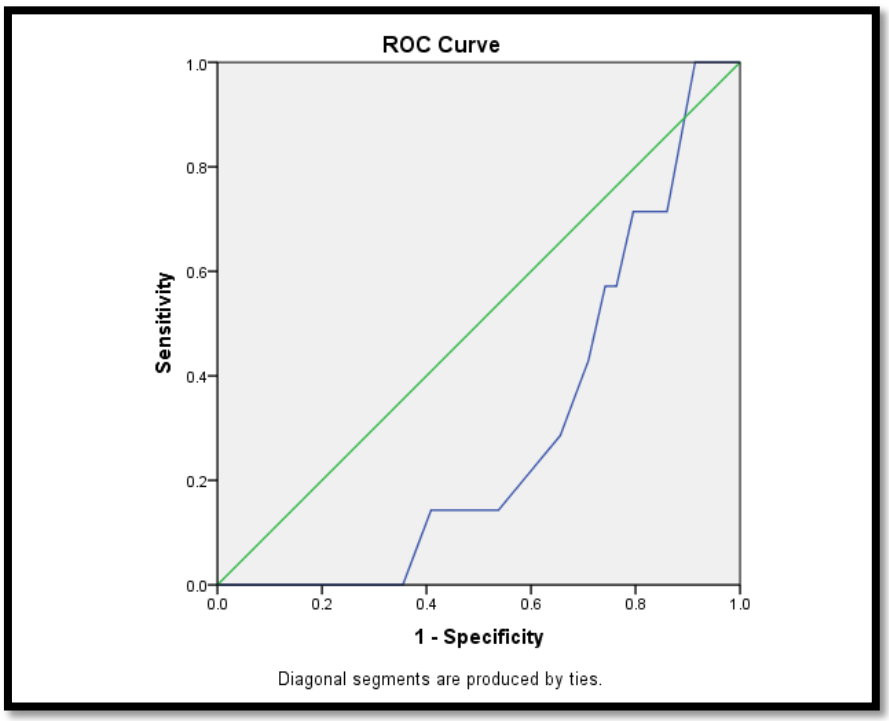


Figure 17: ROC curve showing Area under curve for Recurrent Appendicitis

DISCUSSION

DISCUSSION

Acute appendicitis appears to be the most common cause for "Acute Surgical abdomen"[1,2].Appendicectomy is the commonest emergency abdominal surgery, performed by a surgeon [1]. In Western countries About 8% of people will experience appendicitis in their lifetime.[3]

The incidence of acute appendicitis is maximum in the second and third decade. It is comparitively rare in infants, but becomes more common in childhood and early adult life. The incidence of appendicitis remains equal in both males and females before puberty. By the age of 25, which includes the teenagers and the young adults, where the male – female ratio increases to3:2.[1]

The rate of appendicectomy is 12% for men and 25% for women, where around 7% of all people undergo appendectomy for acute appendicitis during their lifetime.[33,34]

The major cause of acute appendicitis is believed to be due to obstruction of the lumen and Faecoliths are the usual causes for obstruction, Less common causes include hypertrophy of lymphoid tissue, tumors, intestinal parasites.[3,23.] The bacteriology of a normal appendix is similar to normal colon. The major organism commonly seen are *Escherichia Coli* and *Bacteroids fragilis*, in normal appendix, in acute appendicitis, and in perforated appendicitis. However a wide variety of both facultative and anaerobic bacteria may be associated.[23]

The diagnosis of acute appendicitis is mainly clinical; however, a decision to operate based solely on clinical suspicion can lead to the removal of a normal appendix in upto 15 to 50% of cases.[4]

The premise that it is better to remove a normal appendix than to delay diagnosis does not help in improving the condition of the patient, particularly in the elderly, as such procedures are associated with complications in 50% cases.[1,5] Hence, the diagnosis of Appendicitis still remains a dilemma even after many advances in various laboratory and radiological investigations.

Thus, a new tool to help in the diagnosis of acute appendicitis would be welcomed.

Serum Bilirubin level elevation will help in the accurate diagnosis of acute appendicitis and more importantly help in foreseeing and preventing the impending complications of acute appendicitis.

This study was taken up to assess – if it is possible to add serum bilirubin as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have a chance to help us detect early an impending complication of acute appendicitis?

Importance of hyperbilirubinemia and its association in diagnosis of acute appendicitis has been postulated recently.[54] There are very few case reports in the literature that describe the finding of hyperbilirubinemia in patients of acute appendicitis. An association between hyperbilirubinemia and diagnosis acute appendicitis and its complications has been hypothesized.[54]

Our study was considered to know the relationship between hyperbilirubinemia and acute appendicitis and to evaluate it as a diagnostic marker for acute appendicitis and also, to find if any correlation of elevated bilirubin levels have a predictive potential role in the early diagnosis of Appendicular perforation.

Our study of the 100 patients enrolled for the study, 51 patients (51%) were males while the remaining 49 patients (49%) were females. The mean age in our study population (100 patients) was 25.41 ± 11.14 years. In our study 90% of subjects were below 40 years and 10% of them were above 40 years of age.

This is consistent with the quoted incidence of Appendicitis in the literature where it is most commonly seen in patients in their second to fourth decades of life.[33,34]

Total Bilirubin was elevated in 63% of subjects, Direct Bilirubin levels were elevated in 24% and Hyperbilirubinemia was present in 70% of subjects based on elevated total Bilirubin or raised direct Bilirubin. Estrada et al had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.[54]

The mean total serum bilirubin of all 100 patients was 1.3 ± 0.6 mg/dl , which was above the normal range (≤ 1.2 mg/dL) considered for the study, hence indicating the occurrence of hyperbilirubinemia.[15] The mean of Direct bilirubin was 0.5 ± 0.3 mg/dl, Our finding was consistent with hyperbilirubinemia found in a study conducted by Khan S, who found average level of serum bilirubin in his study population to be 2.38 mg/dL.[15]

The mean SGOT was 36.2 ± 15.8, SGPT was 32 ± 12.7, ALP was 164.6 ± 97.6 .

In our study clinically 87% were diagnosed to have acute appendicitis, 5% as appendicular perforation and 8% as recurrent appendicitis. Out of 87 patients who were clinically diagnosed as acute appendicitis 72% (63 patients) had Hyperbilirubinemia, out of 5 patients who were clinically diagnosed as Appendicular Perforation 100% had Hyperbilirubinemia and 25% (2 patients) with recurrent appendicitis had Hyperbilirubinemia. This suggest there was significant association between Hyperbilirubinemia and clinical diagnosis.

Per operatively 86% were diagnosed as acute appendicitis, 11% as appendicular perforation and 3% as recurrent appendicitis. Out of 86 patients who were diagnosed as acute appendicitis per operatively 67.4% had Hyperbilirubinemia, out of 11 patients diagnosed as Appendicular Perforation were per operatively 100% had

Hyperbilirubinemia and 33.3% with recurrent appendicitis had Hyperbilirubinemia. There was significant association between Hyperbilirubinemia and per operative diagnosis.

The diagnosis was confirmed post-operatively by histopathological reports (HPR).

Based on histopathological reports , 82% were diagnosed as acute appendicitis, 11% as acute gangrenous appendicitis with perforation and 7% as recurrent appendicitis. Out of 82 patients were diagnosed as acute appendicitis histopathologically 69.5% had Hyperbilirubinemia, out of 11 patients were diagnosed as acute gangrenous appendicitis with Perforation histopathologically, 100% had Hyperbilirubinemia and 20% with recurrent appendicitis had Hyperbilirubinemia.

There was significant association between Hyperbilirubinemia and Histopathologically diagnosis.

The total leukocyte count was found to be elevated in 52 patients (52 %) of the total 100 patients. The mean of TLC count in all patients was 10.8 ± 4.2 .

The mean bilirubin levels in patients diagnosed with Acute appendicitis was 1.2 ± 0.5 mg/dl , while in patients diagnosed with Appendicular perforation was 2.2±0.3 mg/dL . Hence, we see that patients with Appendicular perforation had higher levels of bilirubin as compared to that of acute appendicitis. So we found that, patients with features suggestive of appendicitis with higher values of bilirubin, are more susceptible to Appendicular perforation than those with normal or slightly elevated total serum bilirubin.

Sand et al in his study found the mean bilirubin levels in patients with Appendicular perforation to be significantly higher than those with a non-perforated appendicitis.[68]

The mean direct bilirubin level in patients with acute appendicitis was 0.4± 0.3 and appendicular perforation 0.9 ± 0.4. The value in appendicular perforation is twice as seen in acute appendicitis. Hence the elevated level of direct bilirubin has a higher prediction for appendicular perforation.

The Sensitivity, Specificity, Positive predictive value, Negative predictive value and diagnostic accuracy was calculated from a 2x2 table. Sensitivity and Specificity of hyperbilirubinemia in predicting acute appendicitis was 69.51% and 27.78 % respectively. Similarly Positive predictive value and Negative predicative value of bilirubin in predicting acute appendicitis was 81.43% and 16.67 % respectively. Hyperbilirubinemia had a diagnostic accuracy of 62% in diagnosis of acute appendicitis.

In appendicular perforation ,Hyperbilirubinemia had a diagnostic accuracy of 41% in diagnosis of appendicular perforation .Where as 100% sensitivity and Negative predictive value was observed.

In recurrent appendicitis , Hyperbilirubinemia had a diagnostic accuracy of 27 % in diagnosis of recurrent appendicitis .where as 29% sensitivity and 83% Negative predictive value was observed.

The sensitivity in our study was more than that by Sand et al in which, he found the sensitivity and specificity in his study of hyperbilirubinemia for predicting Appendicular perforation to be 70% and 86.0% respectively.[68]

Hyperbilirubinemia was found in most of the patients diagnosed with acute appendicitis (70 %) or Appendicular perforation (100 %). Thus Hyperbilirubinemia had a diagnostic accuracy of 62% in diagnosis of acute appendicitis ,41 % in appendicular perforation and 27% in diagnosis of recurrent appendicitis.

CONCLUSION

CONCLUSION

The present study suggests-

- Serum bilirubin levels comes out to be a favorable laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis remains static - clinical. Its level appears to be a useful marker in diagnosis of appendicitis and would be helpful investigation in managing acute cases.

- Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia more than the normal range should be considered as having a higher chance of Appendicular perforation suggesting that serum bilirubin levels have a promising predictive potential for the diagnosis of Appendicular perforation.

SUMMARY

SUMMARY

Acute appendicitis is the most common cause of 'acute abdomen' in young adults. Diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. Importance of hyperbilirubinemia or elevated Serum Bilirubin and its association in acute appendicitis has been postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acute appendicitis and also its complications.

The present study was undertaken to assess relationship between hyperbilirubinemia and acute appendicitis and to evaluate its usefullness as a diagnostic marker for acute appendicitis and also, to see whether elevated bilirubin levels do have a predictive potential for the diagnosis of Appendicular perforation.

Our study was conducted in the department of surgery, in R.L. Jalappa hospital Tamaka , from december 2014 to june 2016. A total of 100 patients with clinical diagnosis of acute appendicitis or Appendicular perforation or recurrent appendicitis were studied. The serum bilirubin and LFTs were carried out in all the patients.

In this study, males (51%) outnumbered females (49%) and overall the mean age was 25.41 ± 11.14 years. Mean total serum bilirubin was noted as 1.3 ± 0.6 mg/dL ,while direct bilirubin was 0.5 ± 0.3 mg/dL. The mean SGOT 36.2 ± 15.8 and SGPT were 32 ± 12.7 U/L . The mean ALP values were 164.6 ± 97.6 U/L .The total leukocyte count was less than 11,000/mm^3 in 48% patients while, 52% patients had counts above 11,000/mm^3.

Normal bilirubin values were seen in 30.5% patients while 69.5% had elevated bilirubin levels (Hyperbilirubinemia). Of 84 patients with acute appendicitis,58(69%) had raised bilirubin levels, while 26(31%) had normal levels. 11 patients were diagnosed as Appendicular perforation, all 11 patients (100%) had elevated bilirubin levels. In Recurrent appendicitis (n = 5), only 1 (20%) patient had elevated bilirubin level (>1.2 mg/dL) , while remaining 4 patients had normal bilirubin levels (≤1.2 mg/dl). Thus, Hyperbilirubinemia was found in most of the patients diagnosed with acute appendicitis (69.5%) or Appendicular perforation (100 %).

Of the 100 patients, 87% were diagnosed as acute appendicitis clinically while 5% were diagnosed with Appendicular perforation and 8% with recurrent appendicitis.

The mean bilirubin levels in patients diagnosed with acute appendicitis was 1.2±0.5 mg/dL,while in patients diagnosed with Appendicular perforation was 2.2±0.3 mg/dL. The total bilirubin and direct bilirubin in patients diagnosed with acute appendicitis was 1.2 ±0.5 mg/dL and 0.4±0.3 respectively. The total bilirubin and direct bilirubin in patients diagnosed with Appendicular perforation was 2.2±0.3 mg/dL and 0.90±0.4 mg/dL respectively.

58 patients (69%) of the total patients diagnosed with acute appendicitis (n=84) were found to have elevated bilirubin levels, while 26 patients (31%) had normal bilirubin levels. Similarly, 11 (100%) of the total patients diagnosed with Appendicular perforation (n=11) were found to have elevated bilirubin levels. The Sensitivity and Specificity of hyperbilirubinemia as a marker in predicting acute appendicitis was 69.51% and 27.78 % respectively. Similarly the Positive predicative value and Negative predicative value for the same was 81.43% and 16.67%

respectively with diagnostic accuracy of 62 %.

The Sensitivity and Specificity of hyperbilirubinemia as a marker in predicting Appendicular perforation was 100 % and 33.71 % respectively. Similarly the Positive predicative value and Negative predicative value for the same was 15.71% and 100 % respectively with diagnostic accuracy of 41%.

Area under the curve(ROC) for diagnosing acute appendicitis was 0.268 and it was highest for appendicular perforation with cut off value of total bilirubin being 1.85mg/dl had 100% sensitivity and 92% specificity in diagnosing appendicular perforation.

Serum bilirubin levels appears to be a favourable laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis depends on clinical findings. Patients with clinical signs and symptoms of appendicitis and with hyperbilirubinemia >1.85 mg/dl should be considerd as having a higher chance of Appendicular perforation suggesting that serum bilirubin levels have a high predictive potential for the diagnosis of Appendicular perforation.

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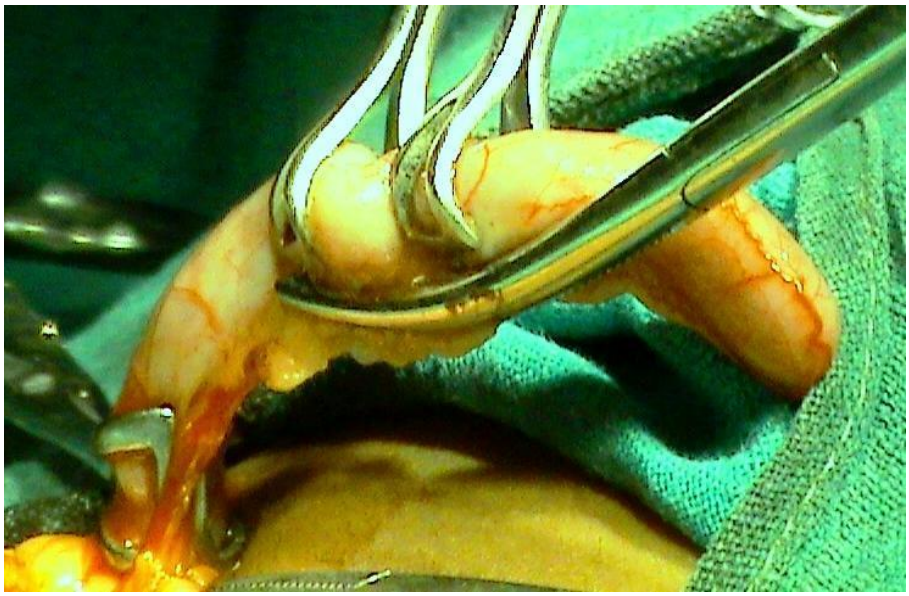
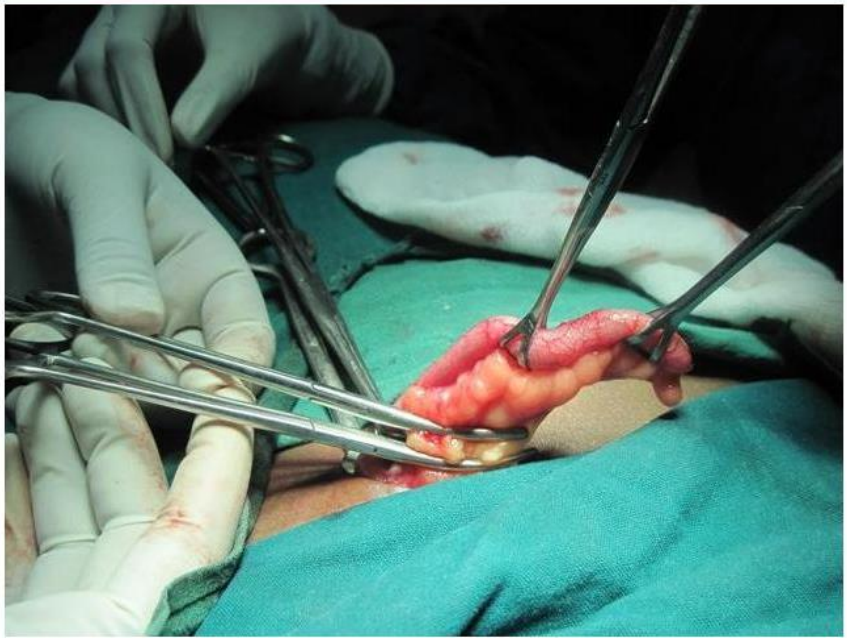
ANNEXURES

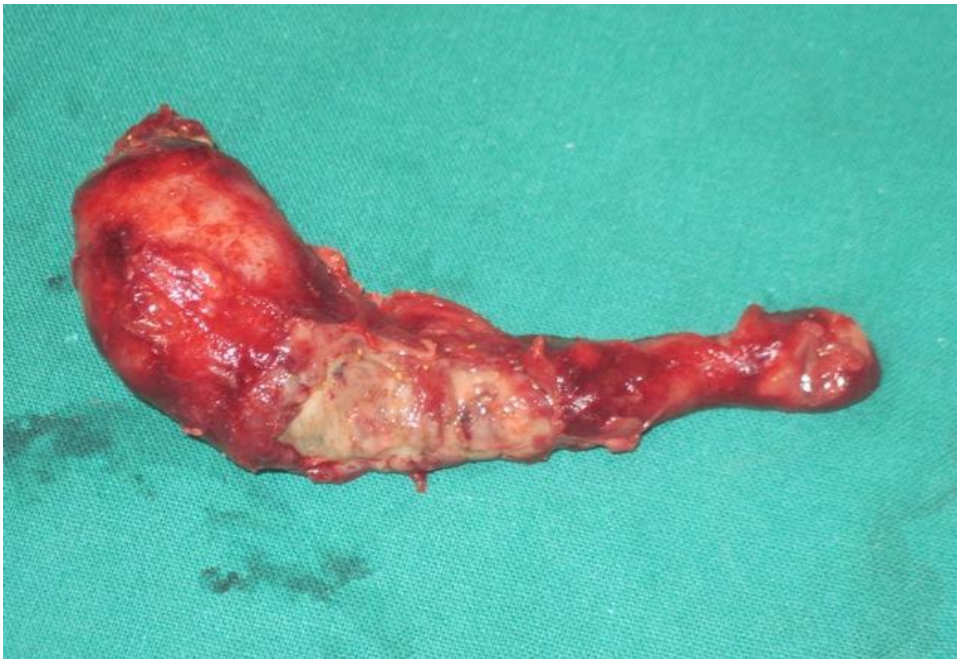
Photograph 1: Acute Appendicitis



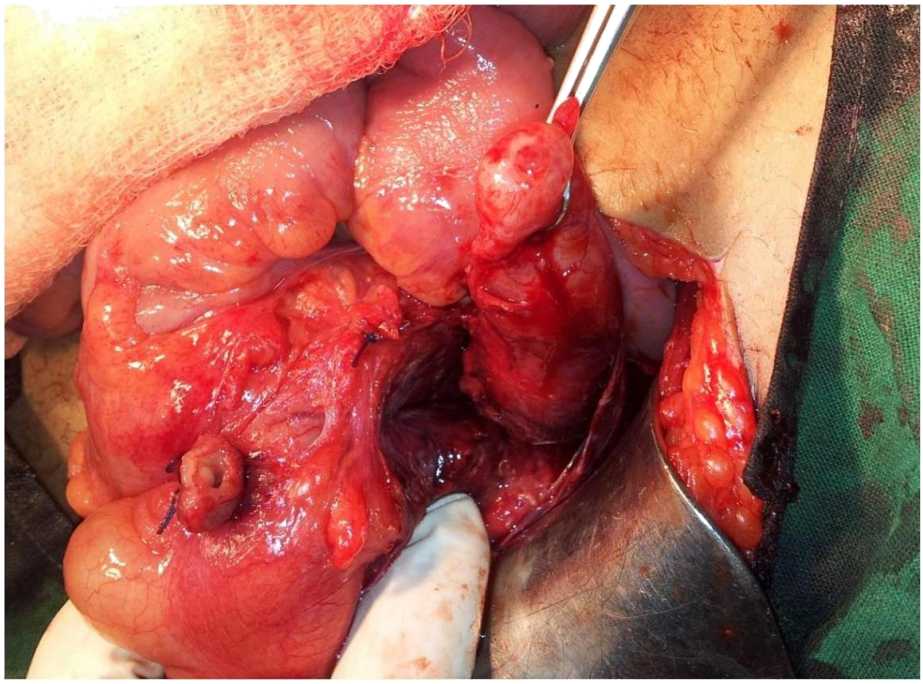
Photograph 2. Acute appendicitis (mesoappendix being ligated)



Photograph 3: Inflamed Appendix with Faecalith



Photograph 4:Appendicular perforation (ligated and cut at base)



INFORMED CONSENT FORM

I, Mr/Mrs have been explained in a language I can understand, that I will be included in a study which is Evaluation of Hyperbilirubinemia as a Diagnostic marker for Acute Appendicitis.

I have been explained that my clinical finding, investigations, intraoperative findings and post-operative specimen will be assessed and documented for the study purpose.

I have been explained that my participation in this study is entirely voluntary and I can withdraw from the study anytime and this will not affect my relation with my doctor or the treatment for my ailment.

I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.

I, in my sound mind give full consent to be added in the part of this study.

Signature of the patient:
Name:

Signature of the witness:
Name:

Date: **Place:**

PROFORMA

Personal Details:	
Name:	Age / Sex:
Address:	
Educational Status:	Occupation:
IP No.	Date of Admission:
Ward:	Date of Discharge:
Chief Complaints:	
Past history: (suggestive of) • Liver disease: • Jaundice: • Hemolytic disease:	
Family history:	
Personal history: • Alcoholism: • Others:	

General examination:	
	Built: Nourishment: Temperature : Pulse: BP : Blood Pressure : Pallor: Icterus : Cyanosis / Clubbing / Edema / Lymphadenopathy :
Systemic Examination:	
	CNS: CVS: RS: P/A:
Clinical Diagnosis:	

Investigations:			
	Serological Investigations		Normal Range
	1. Total Bilirubin:.....	mg/dl	0.2 – 1.3 mg/dl
	2. Direct Bilirubin:.....	mg/dl	0.4 – 0.6 mg/dl
	3. SGOT:.....	U/L	0 – 40 U/L
	4. SGPT:.....	U/L	0 – 35 U/L
	5. ALP:.....	U/L	100 -290U/L
	Blood investigations:		
	USG – Abdomen (if done):		
	Per-operative findings:		
	Histopathology report (post-operatively):		

serial number	Inpatient (IP) Number	Gender	Age (years)	Liver function tests					TLC (/mm3)	Clinical diagnosis (pre operative)	per-operative findings	HPR
				Total bilirubin (mg/dl) N-(0.2-1.3)	Direct Bilirubin (mg/dl) N (0.4-0.6)	SGOT (U/L) (N5-40)	SGPT (U/L) (5-35)	ALP (U/L) N (100-290)				
1	93648	F	16	0.4	0.1	19	15	145	9.3	RA	AA	RA
2	93688	F	23	**1.3**	0.6	18	23	63	11.4	AA	AA	AA
3	29428	F	12	**1.4**	0.4	**83**	**41**	**311**	14.1	AA	AA	AA
4	405458	M	35	**1.6**	0.28	37	34	62	7.3	AA	AA	AA
5	99969	F	28	0.8	0.3	19	25	70	8.2	AA	AA	AA
6	107099	F	21	**1.44**	0.2	20	25	106	9	AA	AA	AA
7	102861	F	13	**1.3**	0.4	**91**	21	120	11.4	AA	AA	AA
8	104394	F	25	0.58	0.2	24	**38**	95	6.1	AA	AA	AA
9	82063	M	20	**2.1**	0.2	19	32	81	18.1	AA	AP	AGA&P
10	1020297	M	35	**1.6**	0.28	37	34	62	4.9	AA	AA	AA
11	1019971	M	10	0.3	0.2	35	35	242	6.4	AA	AA	AA
12	82054	M	20	0.2	0.1	15	24	59	7.8	AA	AA	AA
13	90239	M	23	**1.7**	0.4	**66**	**44**	100	9.7	AA	AA	AA
14	87062	M	43	**1.4**	0.3	25	48	83	14.3	AA	AA	AA
15	85788	M	11	0.16	0.01	**46**	30	220	5.8	AA	AA	AA
16	76398	F	18	0.38	0.15	18	26	65	10.5	AA	AA	AA
17	88317	F	36	**1.21**	**0.8**	13	25	177	15.4	AA	AA	AA
18	124671	F	39	**1.4**	0.44	18	21	45	14.3	AA	AA	AA
19	135657	M	26	**1.99**	0.35	22	26	64	13.4	AA	AP	AGA&P
20	120402	M	25	**2.03**	0.4	23	**45**	64	18.3	AA	AP	AGA&P
21	136509	M	17	1.2	0.1	**45**	3	106	9.4	AA	AA	AA
22	114877	F	38	**1.8**	0.3	**56**	**91**	103	7.3	AA	AA	AA
23	109498	F	36	0.61	0.29	31	26	50	6.5	AA	AA	AA

24	138803	F	28	**1.26**	0.35	27	**31**	52	11.6	AA	AA	AA
25	93648	F	18	0.4	0.1	19	15	145	3.4	AA	AA	AA
26	124447	F	45	**1.71**	0.26	29	**43**	194	10.9	AA	AA	AA
27	124360	M	20	**1.9**	0.58	**59**	**59**	156	12.6	AA	AP	AGA&P
28	135064	F	30	**1.8**	0.25	23	16	41	11.9	AA	AA	AA
29	145988	M	26	0.31	0.28	23	**45**	98	6.5	AA	AA	AA
30	146726	M	8	**1.75**	**0.66**	23	24	98	13.6	AA	AA	AA
31	77707	F	23	**1.58**	0.39	23	24	57	16.2	AA	AA	AA
32	151289	M	26	**1.3**	0.39	24	**36**	72	11.2	AA	AA	AA
33	174144	F	10	0.39	0.01	**45**	**50**	**300**	7.9	AA	AA	AA
34	142999	F	27	0.3	0.03	19	20	60	4.3	AA	AA	AA
35	152041	F	23	0.4	0.03	24	33	50	5.7	AA	AA	AA
36	158019	F	30	0.16	0.02	33	28	128	8.9	AA	AA	AA
37	176302	F	11	**1.3**	0.34	27	28	180	4.9	AA	AA	AA
38	167077	M	26	**1.81**	0.39	24	**39**	66	12.1	AA	AA	AA
39	171195	F	28	**2.5**	**1.2**	**52**	27	39	16.4	AA	AP	AGA&P
40	156189	F	19	0.49	0.1	28	22	84	8.3	AA	AA	AA
41	160146	M	26	**1.6**	0.3	31	**41**	109	10.5	AA	AA	AA
42	158412	F	42	0.26	0.02	27	30	53	4.7	AA	AA	AA
43	172334	M	25	**2.03**	**0.3**	21	18	85	13.8	AA	AA	AA
44	172719	F	49	**1.51**	**0.8**	17	26	163	14.5	AA	AA	AA
45	168791	F	35	0.57	0.43	**47**	35	44	6.7	AA	AA	AA
46	152069	F	45	0.55	0.01	14	27	89	5.6	AA	AA	AA
47	151695	F	28	0.77	0.1	23	33	72	8.3	AA	AA	AA
48	152049	F	36	**1.5**	0.3	20	36	87	8.5	AA	AA	AA
49	113611	F	38	0.2	0.1	**43**	23	71	9.6	AA	AA	AA
50	141634	F	11	**1.6**	0.36	**57**	25	243	11.6	AA	AA	AA
51	228343	M	45	**1.8**	**1**	**60**	**55**	320	16.15	AA	AA	AA
52	236009	F	15	**1.3**	**0.8**	**50**	35	250	16.1	AA	AA	AA

53	194919	M	24	1	**0.9**	**50**	**40**	**300**	6.46	AA	AA	AA
54	236086	M	13	**1.4**	**0.8**	**48**	**50**	**330**	21.95	AA	AA	AA
55	238017	F	18	**2.6**	**1.4**	40	**36**	**400**	10.5	AA	AP	AGA&P
56	198052	F	24	0.4	0.01	21	24	86	10.02	AA	AA	AA
57	239394	M	11	**1.9**	0.6	**55**	35	290	19.1	AA	AA	AA
58	188023	M	23	**2.4**	**1.2**	**42**	**40**	**350**	17.39	AP	AP	AGA&P
59	152188	F	9	1	**0.8**	**42**	**37**	220	17.26	AA	AA	AA
60	201984	M	19	**2.1**	**1.2**	**50**	**55**	**320**	13.79	AP	AP	AGA&P
61	205052	M	11	**1.3**	**1**	**60**	**55**	290	5.74	AA	AA	AA
62	230348	F	50	0.5	0.4	15	34	38	5.31	AA	AA	AA
63	188428	M	13	**1.9**	0.6	**60**	**55**	**350**	16.11	AA	AA	AA
64	205578	M	38	**1.4**	0.5	40	35	290	10.6	AA	AA	AA
65	217885	M	15	1.2	**0.9**	**42**	**40**	200	8.74	AA	AA	AA
66	231607	M	35	**2.3**	**1.2**	**80**	**40**	**330**	13.07	AP	AP	AGA&P
67	196227	F	21	**1.3**	0.6	**45**	35	150	8.39	AA	AA	AA
68	202302	M	33	1.1	**0.7**	35	32	210	10.3	AA	AA	AA
69	194244	M	33	**2.8**	**1**	**60**	**55**	**320**	15.31	AP	AP	AGA&P
70	197179	M	13	0.8	0.6	**45**	**40**	250	6.66	AA	AA	AA
71	223812	M	27	**1.9**	**1**	**50**	**38**	**350**	12.1	AP	AP	AGA&P
72	225501	F	35	**1.7**	0.6	32	**38**	**350**	9.98	AA	AA	AA
73	63574	M	30	**1.5**	0.6	**40**	35	**320**	17.31	AA	AA	AA
74	236036	F	45	**1.4**	**0.8**	**44**	35	250	5.03	AA	AA	AA
75	193497	F	16	**1.3**	0.5	**40**	35	250	17.03	AA	AA	AA
76	187597	M	20	1.2	**0.8**	30	32	200	15.27	AA	AA	AA
77	193478	F	32	**1.7**	0.6	**55**	**48**	**320**	9.34	AA	AA	AA
78	217759	M	26	**1.4**	0.5	**42**	35	220	12.85	AA	AA	AA
79	234186	M	33	**1.3**	0.4	**48**	30	250	11.98	AA	AA	AA
80	240876	M	27	1.2	**0.7**	**44**	**37**	220	5.55	AA	AA	AA
81	279670	F	26	1.3	0.4	36	24	154	5.36	AA	AA	AA

82	278008	M	13	**1.5**	0.4	24	14	190	16.8	AA	AA	AA
83	258736	M	20	1.1	0.4	26	14	114	7.6	RA	AA	AA
84	276643	M	13	**1.9**	**0.8**	**55**	20	230	16.77	AA	AA	AA
85	279219	F	8	**2.1**	**0.7**	**50**	30	214	9.47	AA	AA	AA
86	226950	M	14	**1.4**	0.3	32	35	120	8.44	AA	AA	AA
87	235508	M	13	**1.9**	**0.8**	39	7	221	16.04	AA	AA	AA
88	277409	F	36	**1.6**	0.5	35	27	230	18.1	AA	AA	AA
89	268099	M	28	**1.9**	0.6	**44**	30	210	9.6	AA	AA	AA
90	261052	M	36	**1.5**	0.3	28	15	130	17.34	RA	AA	RA
91	280043	F	20	1.1	0.4	35	20	190	8.7	RA	AA	RA
92	257813	F	32	**1.4**	0.3	35	32	110	12.33	AA	AA	AA
93	298922	M	20	**1.4**	0.5	35	28	180	7	AA	AA	AA
94	301888	M	20	1.2	0.4	28	20	140	8	RA	RA	RA
95	258736	M	20	1.1	0.3	19	10	130	7.46	AA	AA	AA
96	252631	M	18	**1.3**	0.4	**42**	33	110	7.8	RA	RA	RA
97	292967	F	31	0.8	0.3	35	28	90	5.3	RA	RA	RA
98	293305	F	41	0.35	0.02	12	28	74	5.89	RA	AA	RA
99	308317	M	10	**1.5**	0.34	27	15	203	14.3	AA	AA	AA
100	315622	M	65	**1.4**	0.58	35	15	68	9.2	AA	AA	AA

KEY TO MASTER CHART

AA – ACUTE APPENDICITIS

ALP - ALKALINE PHOSPHATASE

AGA&P – ACUTE GANGRENOUS APPENDICITIS WITH PERFORATION

AP – APPENDICULAR PERFORTION

dl - DECILITER

F – FEMALE

HPR – HISTHOPATHOLOGICAL REPORT

M- MALE

MG – MILLIGRAM

RA –RECCURRENT APPENDICITIS

SGOT - SERUM GLUTAMIC OXALOACETIC TRANSAMINASE

SGPT - SERUM GLUTAMIC PYRUVIC TRANSAMINASE

TLC - TOTAL LEUKOCYTE COUNT.