# DIAGNOSTIC EFFICACY OF PROCALCITONIN, C-REACTIVE PROTEIN AND BILIRUBIN IN ACUTE APPENDICITIS AND ITS COMPLICATIONS

**Submitted by**

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**In**

**GENERAL SURGERY**

**UNDER THE GUIDENCE OF**

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# ABSTRACT

**Background and Objectives**

Acute appendicitis is the most common abdominal emergency encountered in general surgery. In most of the cases, the diagnosis can be made clinically by assessing the symptoms and physical findings and confirmed by laboratory tests and ultrasonography.

However, diagnosis is difficult sometimes even after all these tests and in such doubtful cases either the diagnosis is missed or patients normal appendix is operated on, leading to increase in mortality and morbidity.

In this study, diagnostic accuracy of Procalcitonin, C-Reactive Protein (CRP), Bilirubin as a biomarker in acute appendicitis and its complications have been analyzed.

**Methodology**

A cross sectional study was conducted in the Department of Surgery, BLDE (Deemed to be University) Shri. B. M. Patil Medical College Vijayapur during the period of October 2016 to May 2018 A total of 82 patients with clinical diagnosis of acute appendicitis or appendiceal perforation were studied. The serum Procalcitonin, C-Reactive Protein (CRP), and Bilirubin were carried out in all the patients.

**Results:**

In the present study of the 82 patients enrolled for the study, 53 patients (64.6%) were males while the remaining 29 patients (35.4%) were females. The mean age in our study population (82 patients) was 25.9 ± 11.5 years. This is consistent with the quoted incidence of Appendicitis in the literature where it is most frequently seen in patients in their second through fourth decades of life. The average age in females 27.8±12.6 years was slightly higher than males 24.9±10.8 years.

In our study population of 82 patients, 65 patients (79.3%) were diagnosed as acute appendicitis pre-operatively while 17 patients (20.7%) were diagnosed with Appendiceal perforation. The diagnosis was confirmed USG reports and intra-operative findings and those differing from the pre-operative diagnosis were excluded from the study. The mean level of procalcitonin, C-Reactive Protein (CRP), Bilirubin were found to have increased in both acute appendicitis and appendiceal perforation.

The mean procalcitonin levels in patients diagnosed with acute appendicitis was 2.2 ±0.9 ng/mL (range, 0.8– 3.4 ng/mL) while in patients diagnosed with Appendiceal perforation was 2.7±0.8 ng/mL (range, 1.5– 4.6 ng/mL).

The mean bilirubin levels in patients diagnosed with acute appendicitis was 0.7 ± 0.4 mg/dL (range, 0.09– 1.6 mg/dL) while in patients diagnosed with Appendiceal perforation was 0.8±0.2 mg/dL (range, 0.5– 1.2 mg/dL). Estrada et al[55] had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean CRP levels in patients diagnosed with acute appendicitis was 1.4 ± 0.5 mg/dL (range, 0.5– 2.2 mg/dL) while in patients diagnosed with Appendiceal perforation was 1.8±1.1 mg/dL (range, 0.9– 6.0 mg/dL).

The Sensitivity, Specificity, Positive predictive value, Negative predictive value and Odds ratio was calculated from a 2x2 table. Sensitivity of Procalcitonin, C-Reactive Protein (CRP) and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis was 64.6%, 41.54% and 16.9% respectively.

**Keywords**

Acute Appendicitis; Appendiceal perforation; Procalcitonin, Hyperbilirubinemia, CRP

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# INTRODUCTION

Acute appendicitis is the most common abdominal emergency encountered in general surgery. The diagnosis of appendicitis can be difficult, occasionally taxing the skills of even the most experienced surgeon. "Addiss and associates[1] estimated the incidence of acute appendicitis in the United States population to be 11 cases per 10,000 populations annually. The disease is slightly more common in males, with a male: female ratio of 1.4:1. In a lifetime, 8.6% of males and 6.7% of females can be expected to develop acute appendicitis. Young age is a risk factor, as nearly 70% of patients with acute appendicitis are less than 30 years of age. The highest incidence of appendicitis in males is in the 10- to 14-year-old age group (27.6 cases per 10,000 population), while the highest female incidence is in the 15- to 19-year-old age group (20.5 cases per 10,000 population). Patients at extremes of age are more likely to develop perforated appendicitis. Overall, perforation was present in 19.2% of cases of acute appendicitis".

This number was significantly higher, however, in patients under 5 and over 65 years of age. Although less common in people over 65 years old, acute appendicitis in the elderly progresses to perforation more than 50% of the time.[1]In most of the cases, the diagnosis can be made clinically by assessing the symptoms and physical findings and confirmed by laboratory tests and ultrasonography. However, diagnosis is difficult sometimes even after all these tests and in such doubtful cases either the diagnosis is missed or patients normal appendix is operated on, leading to increase in mortality and morbidity.[2]No reliably specific marker for acute appendicitis has been identified till now. A raised white cell count is not specific for appendicitis and although C-reactive protein is commonly used in the assessment of suspected appendicitis, its specificity varies markedly between studies and may only

significantly raise once appendiceal perforation takes place.[3]Cases presenting with non-specific abdominal pain and acute appendicitis are extremely common in general surgery, accounting for about 75% of admissions due to acute abdominal complaints. Also, the rate of negative appendectomies in these cases is about 30%, leading to increased morbidity and risk of incisional hernia. Whereas delayed diagnosis and treatment of patients with acute appendicitis may lead to several complications that are potentially life threatening, such as perforation, peritonitis, sepsis, small bowel obstruction, urinary retention and abdominal abscess formation.Recently, elevation in serum bilirubin was reported, but the importance of the raised total has not been stressed in acute appendicitis and appendiceal perforation.

The endotoxin of Escherichia coli has been shown in vivo to affect physiological bile flow, which led to the theory that hyperbilirubinemia may possess inferential potential in the preoperative early diagnosis of appendix perforation[4]Elevated Serum bilirubin level will help in the early and accurate diagnosis of acute appendicitis and in predicting its serious complications, most importantly the perforation.

It is hypothesized that an association exists between Hyperbilirubinemia, CRP and PROCALCITONIN in acute appendicitis and its complications such as appendicular perforation.

Thus the need for the study is to conclude whether the serum BILIRUBIN and CRP and PROCALCITONIN can 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.

## AIM OF THE STUDY:

To determine the diagnostic efficacy of Procalcitonin, C-Reactive Protein (CRP), Bilirubin as a biomarker in acute appendicitis and its complications.

# REVIEW OF LITERATURE

## HISTORICAL PERSPECTIVE:

The first descriptions of the appendix date to the sixteenth century.[5–7] Although first sketched in the anatomic notebooks of Leonardo da Vinci around 1500, the appendix was not formally described until 1524 by da Capri[8] and 1543 by Vesalius.[9]In 1554 the French physician Jean Fernel (1497-1558) reported the first case of perforative appendicitis at autopsy.10

A classical post-mortem description is owed to Lorenz Heister (1683-1758), professor of medicine and also a practising surgeon at the universities of Altdorf-Nürnberg and Helmstedt in Germany (1712). Heister was the first tostudy the pathology of appendicitis (1711).11

The 19th century pathological concept is based on the notion´perityphilitis´, that is inflammation of the cecum (typhlon, blind). The cecumrather than the appendix was considered as the site of the disease; this is easilyexplained by advanced stages of inflammation which were observed in autopsies.Surgery for appendicitis.

The first appendicectomy was performed at St. George's Hospital,London, in 1736 by Claudius Amyand, a surgeon at St. George's Hospital inLondon and Sergeant Surgeon to Queen Ann, King George I, and King GeorgeII. The acutely inflamed appendix, perforated by a pin, and surrounding omentumwas removed through a scrotal wound while dealing with a faecal fistula in achronic scrotal hernia. The patient was 11-year-old boy and patient recovered.12The first published account of appendicectomy for appendicitis was by.

Krönlein in 1886. However, the patient died two days postoperatively.Fergus, in Canada, performed the first elective appendicectomy in1883.13Charles McBurney (1845-1913) was one of the surgeons pioneering thediagnostics and operative treatment of appendicitis. McBurney's classic report onearly operative interference in cases of appendicitis was presented before theNew York Surgical Society in 1889. In it he described the area of greatestabdominal pain in this disease process, now known as McBurney's point.Five years later in 1894, he set forth in another paper the incision that heused in cases of appendicitis, now called McBurney' sincision. However, McBurney later credited McArthur with first describing thisincision.14

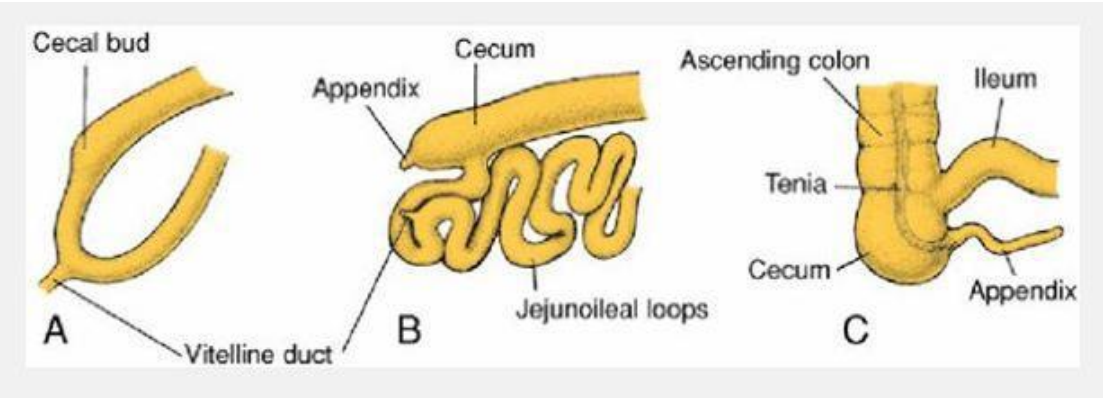
The US surgeon John Benjamin Murphy introduced and popularized earlyremoval of the appendix in all cases of suspected appendicitis. In 1904 hedescribed the triad of pain in abdomen, vomiting and fever, which remains asound basis for diagnosis even today.15

Dawbarn suggested the use of a purse string suture, placed around thebase of the appendix. In 1889, Senn first drew attention to the risks of ligatureslipping off the appendix stump with subsequent peritoneal contamination.On 13 September 1983 the gynaecologist Professor Kurt Semmperformed the world's first laparoscopic appendicectomy at the University of Kielin Germany.16

**EMBRYOLOGY**

Embryologically, the appendix and cecum develop as outpouchings of the caudal limb of the midgut loop in the sixth week of human development. By the fifth month, the appendix elongates into its vermiform shape. At birth, the appendix is located at the tip of the cecum, but due to unequal elongation of the lateral wall of the

cecum, the adult appendix typically originates from the posteromedial wall of the cecum, caudal to the ileocecal valve.




**"Successive stages in development of the caecum and appendix.**

**A. 7 weeks. B. 8 weeks. C. Newborn."**

**"CONGENITAL ABNORMALITIES:**

Congenital abnormalities32 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-

oB1-„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.

oB2- 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 or 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.

**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**

"The appendix averages 9 cm in length,[17] with its outside diameter ranging from 3–8 mm and its lumen ranging from 1–3 mm. The base of the appendix is consistently found by following the teniae coli of the colon to their confluence at the base of the cecum. The appendiceal tip, however, can vary significantly in location. Sir Frederick described the various positions of the appendix comparing the position with the face of a clock33.

1l 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)

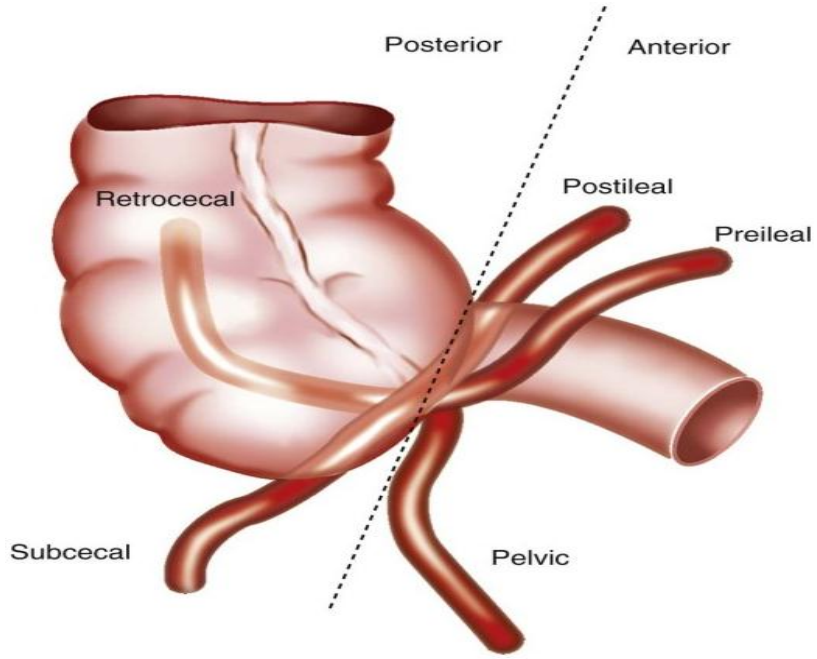
1 O clock(1%)- Pre-ileal

2 O clock(0.2%)- Post ileal

3 O clock(0.05%)- Promonteric (the tip of the organ points towards the promontory of the sacrum).

4 O clock(31.01%)- Pelvic (Appendix dips into the pelvis).

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




**Vascular Supply**

Is byAppendiceal artery, a branch from the lower division of theileocolic artery, runs behind the terminal ileum and enters the mesoappendix ashort distance from the appendiceal base. Here it gives off a recurrent branch,which anastomoses at the base of the appendix with a branch of the posteriorcaecal artery.

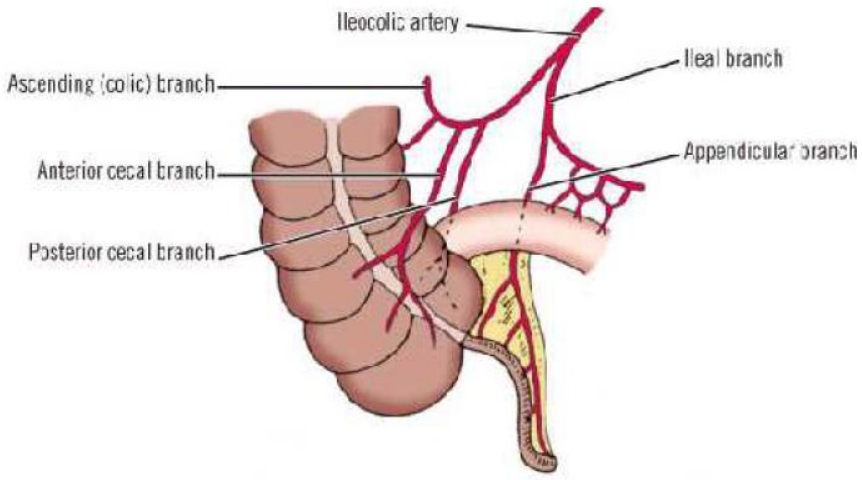



**Figure 2. Blood supply of appendix**

**Appendiceal Veins:**

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

**Lymphatic drainage**:

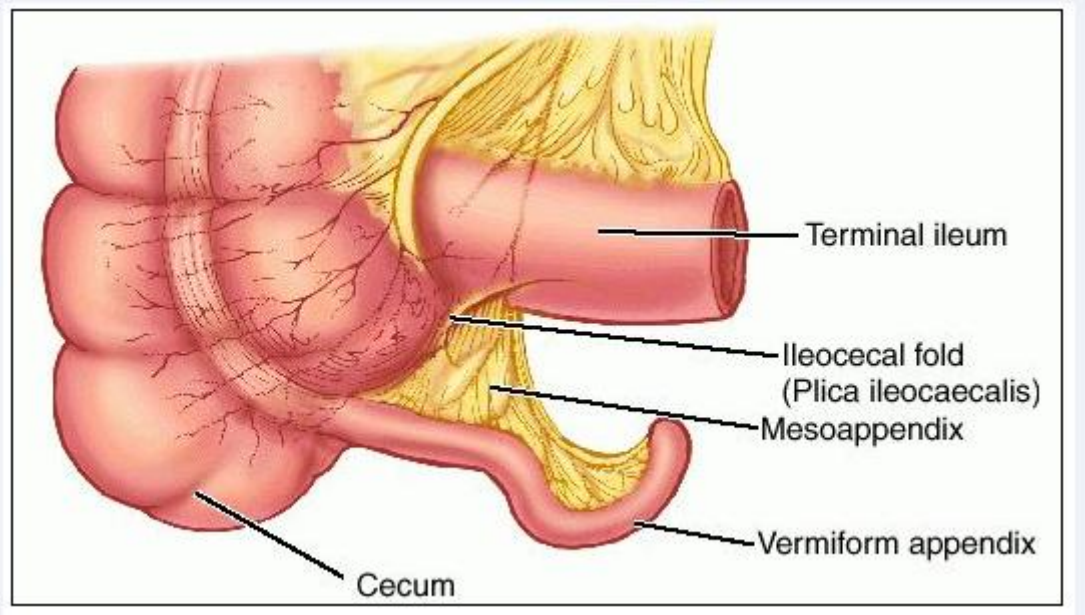
"Lymphatic vessels in the appendix are numerous: there is abundantlymphoid tissue in its walls. From the body and apex of the appendix 8 to 15vessels ascend in the mesoappendix, and are occasionally interrupted by one ormore nodes. They unite to form three or four larger vessels which run into thelymphatic vessels draining the ascending colon, and end in the inferior andsuperior 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 thesymptoms of pain felt during the initial stages of appendiceal inflammation. Inkeeping with other structures derived from the midgut, these sensations arepoorly localized initially, and referred to the central (periumbilical) region of theabdomen.

**Mesoappendix**

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




**Microstructure of the Appendix**

*Mucosa*

The mucosa is covered by a columnar epithelium, and M cells are presentin 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 obscures the muscularis mucosae layer: consequently this becomes discontinuous. These aggregates also cause the mucosa to bulgeinto the lumen of the appendix, so that it narrows irregularly. They are absent atbirth 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 tissueelse where. 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 muscularisexterna 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 thebase of the appendix, the longitudinal muscle thickens to form rudimentarytaeniae that are continuous with those of the caecum and colon. Between thetaeniae coli the longitudinal layer is much thinner, less than half the circular layerin 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 appendix32:

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 wouldnt ideally enter the appendix for processing.

2. Endocrine: The neuroendocrine cells and their secretory products in the appendix have not shown to hav 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

**Pathophysiology**

"Wangensteen extensively studied the structure and function of the appendix and the role of obstruction in appendicitis.[18,19] Based on anatomic studies, he postulated that mucosal folds and a sphincter like orientation of muscle fibers at the appendiceal orifice make the appendix susceptible to obstruction. He proposed the following sequence of events to explain appendicitis:

1. closed loop obstruction is caused by a fecalith and swelling of the mucosal and submucosal lymphoid tissue at the base of the appendix;
2. intraluminal pressure rises as the appendiceal mucosa secretes fluid against the fixed obstruction;
3. increased pressure in the appendiceal wall exceeds capillary pressure and causes mucosal ischemia; and

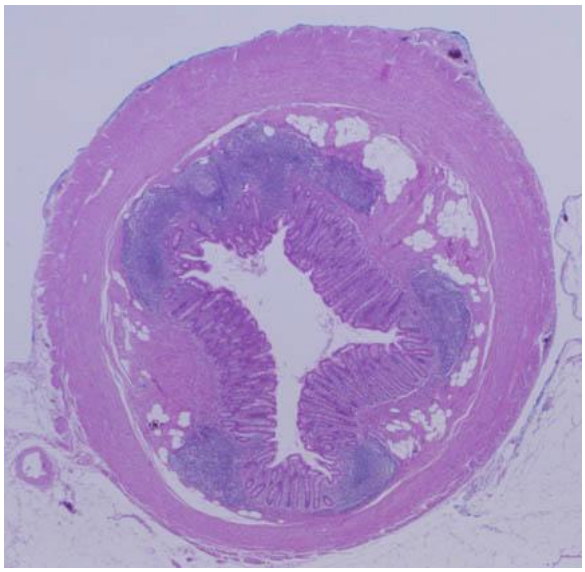
4. Luminal bacterial overgrowth and translocation of bacteria across the appendiceal wall result in inflammation, edema, and ultimately necrosis. If the appendix is not removed, perforation can ensue.

Although appendiceal obstruction is widely accepted as the primary cause of appendicitis, evidence suggests that this may be only one of many possible etiologies. First, some patients with a fecolith have a histologically normal appendix.[20,21,22] Moreover, the majority of patients with appendicitis show no evidence for a fecalith. Arnbjornsson and Bengmark[23] studied at laparotomy the appendixes of patients with suspected appendicitis. They found the intraluminal pressure of the appendix prior to removal to be elevated in only 8 of 27 patients with nonperforated appendicitis. They found no signs of obstruction in the remaining patients with nonperforated appendicitis, as well as all patients with a normal appendix. Taken together, these studies imply that obstruction is but one of the possible etiologies of acute appendicitis".

**Bacteriology**

The principal organisms seen in the normal appendix, in acute appendicitis, and in perforated appendicitis are *Escherichia coli* and *Bacteroides fragilis.*[24–27]Appendicitis is a polymicrobial infection, with some series reporting the culture of up to 14 different organisms in patients with perforation.[24]

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



**Clinical Presentation**:

The classic presentation of acute appendicitis begins with crampy, intermittent abdominal pain, thought to be due to obstruction of the appendiceal lumen. The pain may be either periumbilical or diffuse and difficult to localize. This is typically followed shortly thereafter with nausea; vomiting may or may not be present. If nausea and vomiting precede the pain, patients are likely to have another cause for their abdominal pain, such as gastroenteritis. Classically, the pain migrates to the right lower quadrant as transmural inflammation of the appendix leads to inflammation of the peritoneal lining of the right lower abdomen. This usually occurs within 12–24 hours of the onset of symptoms. The character of the pain also changes from dull and colicky to sharp and constant. Movement or Valsalvamaneuver often worsens this pain, so that the patient typically desires to lie still; some patients describe pain with every bump in the car or ambulance ride to the hospital. Patients may report low-grade fever up to 101°F (38.3°C). Higher temperatures and shaking chills should again alert the surgeon to other diagnoses, including appendiceal perforation or nonappendiceal sources. When questioned, patients who have appendicitis commonly report anorexia; appendicitis is unlikely in those with a normal appetite.

**Perforated Appendicitis**:

"When acute appendicitis has progressed to appendiceal perforation, other symptoms may be present. Patients will often complain of two or more days of abdominal pain, but their duration of symptoms may be shorter, as previously discussed. The pain usually localizes to the right lower quadrant if the perforation has been walled off by surrounding intra-abdominal structures including the omentum, but it may be diffuse if generalized peritonitis ensues. The pain may be so severe that patients do not remember the antecedent colicky pain. Patients with perforation often

have rigors and high fevers to 102°F (38.9°C) or above. A history of poor oral intake and dehydration may also be present.”

**Diagnosis**

**History and Physical Examination**:

“Many patients with acute appendicitis do not have a classic history. Because the differential diagnosis of appendicitis is extensive, patients should be queried about certain symptoms that may suggest an alternative diagnosis. Surgeons must also remember that a previous appendectomy does not definitively exclude the diagnosis of appendicitis, as "stump appendicitis" (appendicitis in the remaining appendiceal stump after appendectomy), although rare, has been described.”[28]

On inspection, patients look mildly ill and may have slightly elevated temperature and pulse. They often lie still to avoid the peritoneal irritation caused by movement. The surgeon should systematically examine the entire abdomen, starting in the left upper quadrant away from the patient's described pain. Maximal tenderness is typically in the right lower quadrant, at or near McBurney's point, located one-third of the way from the anterior superior iliac spine to the umbilicus. This tenderness is often associated with localized muscle rigidity and signs of peritoneal inflammation, including rebound, shake, or tap tenderness. Right lower quadrant tenderness is the most consistent of all signs of acute appendicitis;[29,30] its presence should always raise the specter of appendicitis, even in the absence of other signs and symptoms. Because of the various anatomic locations of the appendix, however, it is possible for the tenderness to be in the right flank or right upper quadrant, the suprapubic region, or the left lower quadrant. Patients with a retrocecal or pelvic appendix may have no abdominal tenderness whatsoever. In such cases, rectal examination can be helpful to elicit right-sided pelvic tenderness

**Physical examination:**

**Various signs:**

1. *The pointing sign:* The patient is then asked to point to where the pain began and where it moved.
2. *Rovsing's sign:* Pain in the right lower quadrant on palpation of the left lower quadrant, is further evidence of localized peritoneal inflammation in the right lower quadrant
3. *Psoas sign:* Pain with flexion of the leg at the right hip, can be seen with aretrocecal appendix due to inflammation adjacent to the psoas muscle.
4. *The obturator sign:* Pain with rotating the flexed right thigh internally, indicates inflammation adjacent to the obturator muscle in the pelvis.

**Laboratory Studies**:

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 inmost patients. A completely normal leukocyte count and differential 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 orperforation.31

The clinician must remember, however, that the WBC count can benormal 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.32

**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 isassociated 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.33-35Multiple studies have been done evaluating the sensitivity of CRP levelalone for the diagnosis of appendicitis in patients selected to undergo appendicectomy. Gurleyik et al noted a CRP sensitivity of 96.6% in 87 of 90patients with histologically proven disease.[36]

**Procalcitonin**

Inactive precursor of caclitonin is a 116 amino acid polypeptide glycoprotein with a molecular weight of 13 kDa. It is found only in the C cells of thyroid gland under normal metabolic conditions. Its levels are relatively low in healthy subjects. Assicot has first reported the increased PCT levels in patients with bacterial and fungal infections and sepsis. Serum PCT concentrations are positively correlated with severity of infection. Adequate antibiotic treatment leads to decreasing PCT levels.

**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 notuncommon in patients with appendicitis. Its presence does not exclude thediagnosis of acute appendicitis, but it should be identified and treated. Althoughpyuria 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.[37]A calcified appendicolith is visible on plain films in only10% to 15% of patients with acute appendicitis.42 Studies show that faecoliths are not pathognomonic for appendicitis, as some patients with abdominal pain and 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 costeffective 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 withappendicitis.38

***Ultrasonography (USG)***

Among patients with abdominal pain, *Abdominal ultrasonography* has asensitivity of about 85% and a specificity of more than 90% for the diagnosis of acute appendicitis.39

**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 sectionreferred to as a *target lesion.*
3. Increased echogenicity of the surrounding fat signifying inflammation, or
4. Presence of an appendicolith
5. In more advanced cases, peri-appendiceal fluid or a mass may be found. Ultrasonography has the advantages of being a noninvasive 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.40

*Pelvic ultrasound* can be especially useful in excluding pelvic pathology, such as tubo-ovarian abscess or ovarian torsion, that may mimic acuteappendicitis.41

***Computed tomography***

Computed tomography (CT) is commonly used in the evaluation of adultpatients with suspected acute appendicitis, especially so in the elderly. CT benefits has a high diagnostic accuracy for appendicitis,42and visualization anddiagnosis of many of the other causes of abdominal pain that can be confusedwith appendicitis. Improved imaging techniques, including the use of 5-mm sections, have resulted in increased accuracy of CT scanning,[43]which has a sensitivity of about90% 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 thedisease. Classic findings include a distended appendix greater than seven mm in diameter and circumferential wall thickening, which may give the appearance ofa halo or target. As inflammation progresses, one may see periappendiceal fatstranding, edema, peritoneal fluid, phlegmon, or a periappendiceal abscess. CTdetects appendicoliths in about 50% of patients with appendicitis and also in asmall percentage of people without appendicitis.Among patients with abdominalpain, the positive predictive value of the finding of an appendicolith on CTremains high at about 75%.

In prospective studies, CT demonstrated a sensitivity of 0.94 and aspecificity of 0.95.44CT thus has a high negative predictive value, making itparticularly useful in excluding appendicitis in patients for whom the diagnosis isin doubt. Appendicitis is highly unlikely if enteric contrast fills the lumen of the appendix and no surrounding inflammation is present. The clinician mustremember, however, that a CT performed

early in the course of appendicitis might not show the typical radiographic findings. 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.45

***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.

| 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 |

**Liver Function Tests**

Importance of hyperbilirubinemia or elevated Serum Bilirubin (serumbilirubin) and its association in acute appendicitis has being postulated recently. It is hypothesized that an association exists between hyperbilirubinemia and acuteappenditics and its complications such as appendiceal perforation.46

***Bilirubin***

Bilirubin (a tetrapyrrole, formerly referred to as hematoidin) is the endproduct of the metabolic degradation of haem, prosthetic group of haemoglobin, myoglobin, the cytochrome P450s and various other haemo-proteins.47The serumlevel of bilirubin represents the balance between production and excretion(destruction) of this

breakdown product. Laboratory evaluation of serum bilirubinallows detection in two forms

1. Indirect or Unconjugated bilirubin (i.e. before hepatic metabolism)
2. Direct or Conjugated (i.e. after hepatic metabolism)48

Since bilirubin is potentially 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; hepatocellular uptake, intracellular binding, conjugation and excretion

Conjugated bilirubin (mono- and di-glucronide) is excreted acrosscanalicular plasma membrane into the canaliculus by an ATP dependant transport process mediated by a canalicular membrane protein called multi-drug resistantassociated-protein-2. The canalicular transport mechanism of excretion of bilirubin conjugate is very sensitive to injury. Accordingly, in hepatocellular disease, as well as with either cholestasis or mechanical obstruction to the bileduct, bilirubin conjugates within the hepatocytes, prevented from taking the irnormal pathway into the canaliculi and down the bile duct, may reflux into bloodstream, resulting in mixed or less often a truly conjugated hyperbilirubinemia.49

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

- Bulent K, Baris S, Koray K, Orhan B (2012) conducted a study of The Diagnostic Value of D-dimer, Procalcitonin and C-Reactive protein in Acute Appendicitis concluded that An increase in CRP levels alone is not sufficient to make the diagnosis of acute appendicitis, CRP levels may differentiate between acute appendicitis and perforated appendicitis, PCT and D-dimer are not better markers then CRP for the diagnosis of Acute appendicitis. (50)

- I G Panagiotopouloup, et al (2013) conducted a study of The diagnostic value of White Cell Count, C-reactive protein and bilirubin in acute appendicitis concluded that CRP had the highest diagnostic accuracy in perforated appendicitis(PA) and this was increased when it was combined with White cell count Bilirubin added no diagnostic value in PA. Normal levels of WCC, CRP, bilirubin could not rule out appendicitis.(51)

- Mohammad Vazir, et al (2014) conducted a study of Evaluation of procalcitonin as a biomarker of diagnosis, severity and post operative complications in patients with acute appendicitis concluded that The sensitivity and specificity of PCT level measurement for acute appendicitis diagnosis were 44% and 100% respectively. The value of PCT level increased with severity of appendicitis and also with the presence of perotonitis and infection.(52)

- Maru K, Sung Jeep K, Hang Joo C (2016) conducted a study of international normalized ratio and serum C-reactive protein are feasible markers to predict complicated appendicitis concluded that INR and CRP increased significantly in patients with complicated appendicitis.(53)

- Prkno A, Wacker C, Brunkhorst FM,Schalttmann P(2013) conducted a study of Procalcitonin-guided therapy in intensive care unit patients with severe sepsis and septic shock –a systemic review and meta-analysis and concluded that procalcitonin therapy is a helpful approach to guide antibiotic therapy and surgical interventions without a beneficial effect on mortality.(54)

- Akcay I et al(2014) conducted study of The prognostic value of pro-CALCITONIN, CRP, and thyroid hormones in secondary peritonitis and concluded that procalcitonin is a better predictor of outcome than CRP in secondary peritonitis and low thyroid hormone level can serve as an important prognostic parameter of disease severity in secondary peritonitis.(55)

# MATERIAL AND METHODS

**SAMPLINE SIZE CALCULATION:** A study conducted by Bulent kaya, Baris Sana, Cengiz eris, Koray Karabulut, Orhan Bat, Riza Kutanis titled the diagnostic value of d-dimer pro calcitonin and crp in acute appendicitis in 2012 was taken as reference study.

Type of study - Prospective cross sectional study.

Time period of study - September 2016 to August 2018

With anticipated incidence of acute appendicitis as 10% and anticipated sensitivity as 91.5% and anticipated specificity as 91% and desired precision as 20% the minimum Sample size 81.

Formula for estimating sample size

$$n = \frac{z^2 p(1-p)}{d^2}$$

where

Z= z statistic at 5% level of significance

d is margin of error

p is expected prevalence rate

This sample size will give for precision of 20% or less for both sensitivity and specificity.

## STATISTICAL ANALYSIS

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean ± standard deviation (SD) were used. Chi-square ($\chi^2$) test was used for association between two categorical variables.

The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value.

C= (number of rows-1)* (number of columns-1)

In cases of more than 30% cell frequency <5, Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t test.

The t statistic to test whether the means are different can be calculated as follows:

$$t = \frac{(\overline{x_1} - \overline{x_2}) - (\mu_1 - \mu_2)}{\sqrt{\frac{{s_1}^2}{n_1} + \frac{{s_2}^2}{n_2}}}$$

where $\bar{x}_1$ = mean of sample 1

$\bar{x}_2$ = mean of sample 2

$n_1$ = number of subjects in sample 1

$n_2$ = number of subjects in sample 2

$$s_1^2 = \text{variance of sample 1} = \frac{\Sigma(x_1 - \bar{x}_1)^2}{n_1}$$

$$s_2^2 = \text{variance of sample 2} = \frac{\Sigma(x_2 - \bar{x}_2)^2}{n_2}$$

ROC analysis for Sensitivity- specificity was done to check relative efficiency.

**sensitivity or true positive rate (TPR)**

eqv. with hit rate, recall

$$TPR = TP/P = TP/(TP + FN)$$

**specificity (SPC) or true negative rate**

$$SPC = TN/N = TN/(FP + TN)$$

**precision or positive predictive value (PPV)**

$$PPV = TP/(TP + FP)$$

**negative predictive value (NPV)**

$$NPV = TN/(TN + FN)$$

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

**SOURCE OF DATA:**

All patients admitted in BLDE (Deemed to be University) Shri. B. M. Patil Medical College Hospital and Research Centre, Vijayapur diagnosed with acute appendicitis during the period of September 2016 to August 2018 will be taken for the study.

Patient suspected clinically to have acute appendicitis and its complications like Perforated appendicitis, Appendicular abscess are evaluated with Procalcitonin,

C-reactive protein, bilirubin levels and their diagnostic accuracy is evaluated.

**METHOD OF COLLECTION OF DATA:** The following tests were carried out for patients diagnosed as acute appendicitis or perforation under general surgery and admitted to BLDE (Deemed to be University) Shri. B. M. Patil Medical College, Hospital And Research Centre, Vijayapur.

INVESTIGATION

1 COMPLETE BLOOD COUNT
2 SERUM BILIRUBIN
3 C-REACTIVE PROTEIN
4 SEROPOSITIVITY FOR HbsAG and HCV
5 ULTRASONOGRAPHY OF ABDOMENAND PELVIS
6 PROCALCITONIN

**INCLUSION CRITERIA:** All patients presenting with acute appendicitis clinically on admission

- Cases of complicated appendicitis
- appendicular abscess
- appendicular perforation

**EXCLUSION CRITERIA :**

- All patients documented to have a past history of jaundice or liver disease
- All patients with acquired or congenital biliary diseases
- All patients who are HbsAg and HCV positive

# RESULTS

The present one year cross sectional study was conducted in the Department of Surgery, BLDE (Deemed to be University) Shri. B. M. Patil Medical College Vijayapur during the period of October 2016 to May 2018.

A total of 82 patients with clinical diagnosis of acute appendicitis or appendiceal perforation were enrolled in the study and studied.

**TABLE 2: AGE DISTRIBUTION**

| AGE (yrs) | N | % |
|---|---|---|
| ≤10 | 1 | 1.2 |
| 11-20 | 30 | 36.6 |
| 21-30 | 31 | 37.8 |
| 31-40 | 11 | 13.4 |
| >40 | 9 | 11 |
| Total | 82 | 100 |

| PARAMETER | Mean | SD |
|---|---|---|
| AGE | 25.9 | 11.5 |

**FIGURE 1: AGE DISTRIBUTION**

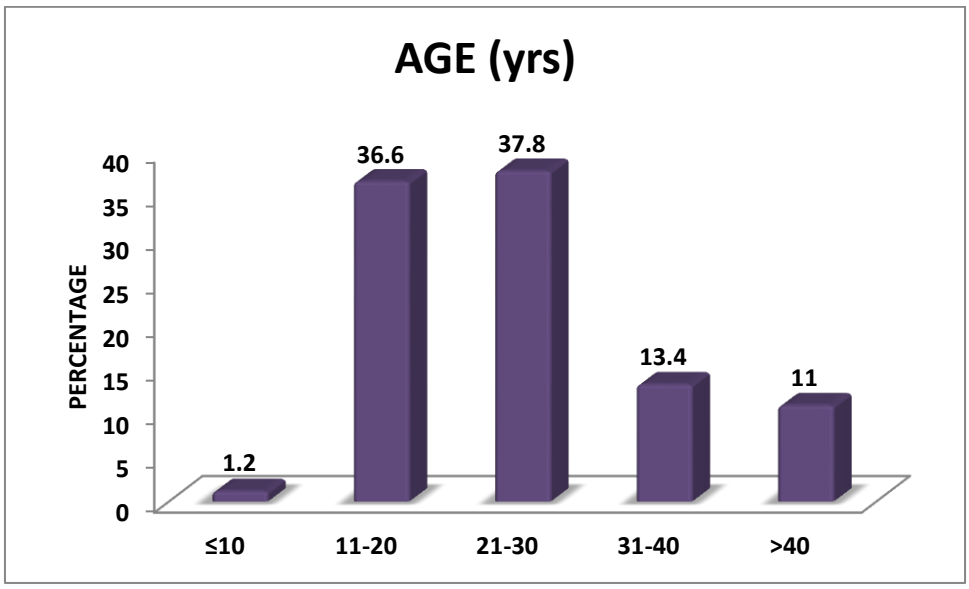


**TABLE 3: SEX DISTRIBUTION**

| SEX | N | % |
|---|---|---|
| Male | 53 | 64.6 |
| Female | 29 | 35.4 |
| Total | 82 | 100 |

**FIGURE 2: SEX DISTRIBUTION**

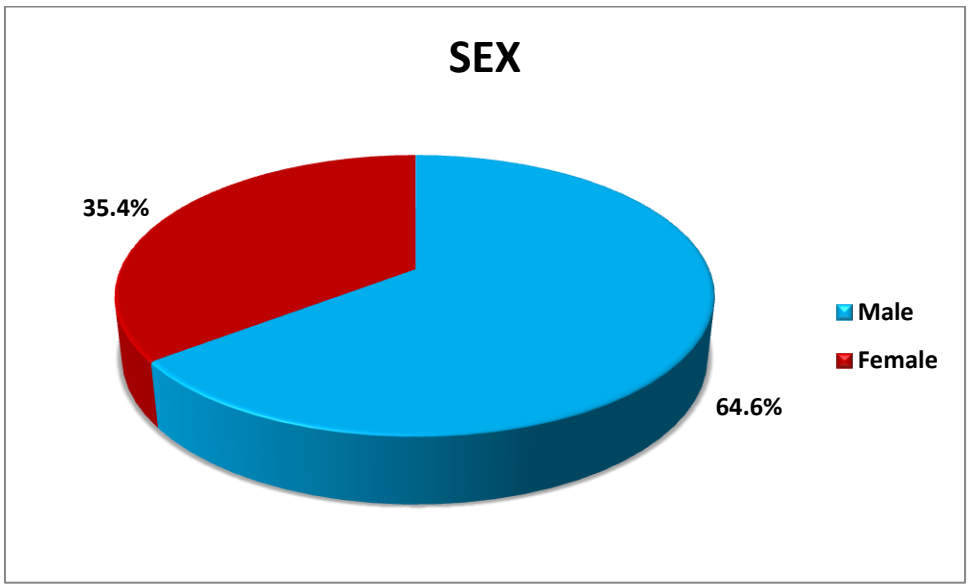


**TABLE 4: MEAN AGE DISTRIBUTION BY SEX**

| AGE | Male | | Female | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| | 24.9 | 10.8 | 27.8 | 12.6 | 0.29 |

**FIGURE 3: MEAN AGE DISTRIBUTION BY SEX**

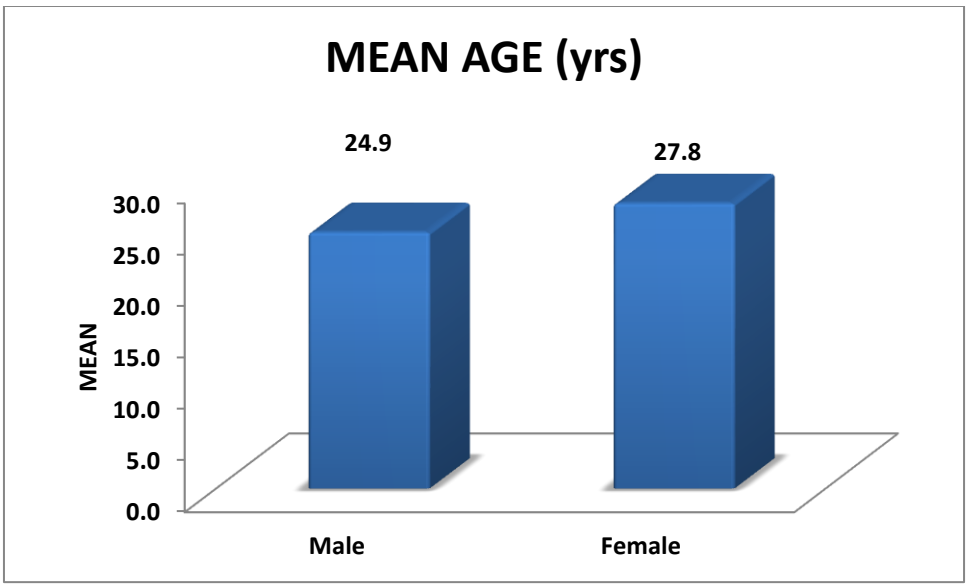


**TABLE 5: DISTRIBUTION OF CASES BY CLINICAL DIAGNOSIS**

| CLINICAL DIAGNOSIS | N | % |
|---|---|---|
| ACUTE APPENDICITIS | 65 | 79.3 |
| APPENDICEAL PERFORATION | 17 | 20.7 |
| Total | 82 | 100 |

**FIGURE 4: DISTRIBUTION OF CASES BY CLINICAL DIAGNOSIS**

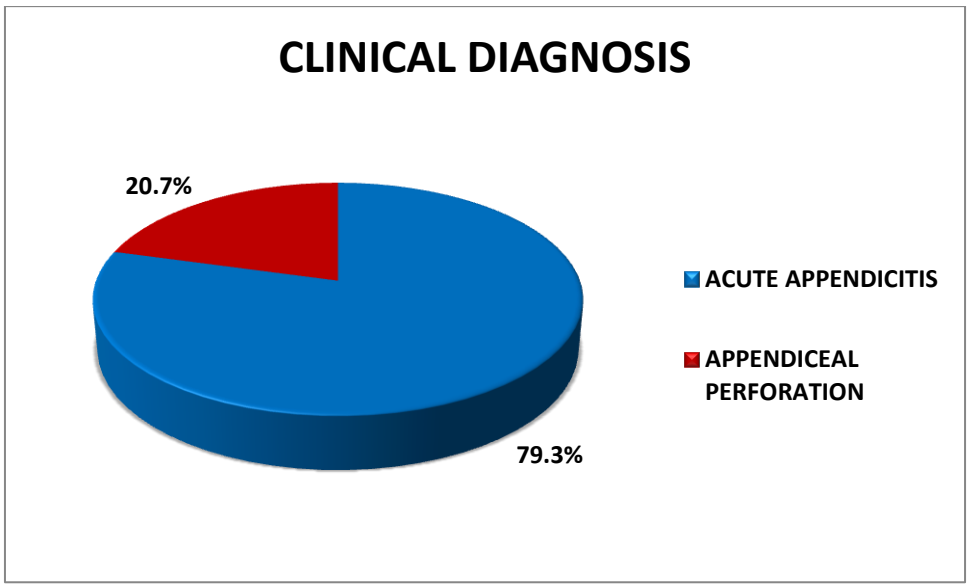


**TABLE 6: DISTRIBUTION OF CASES BY ULTRASOUND FINDING**

| ULTRASOUND FINDING | N | % |
|---|---|---|
| ACUTE APPENDICITIS | 68 | 82.9 |
| NORMAL | 14 | 17.1 |
| Total | 82 | 100 |

**FIGURE 5: DISTRIBUTION OF CASES BY ULTRASOUND FINDING**

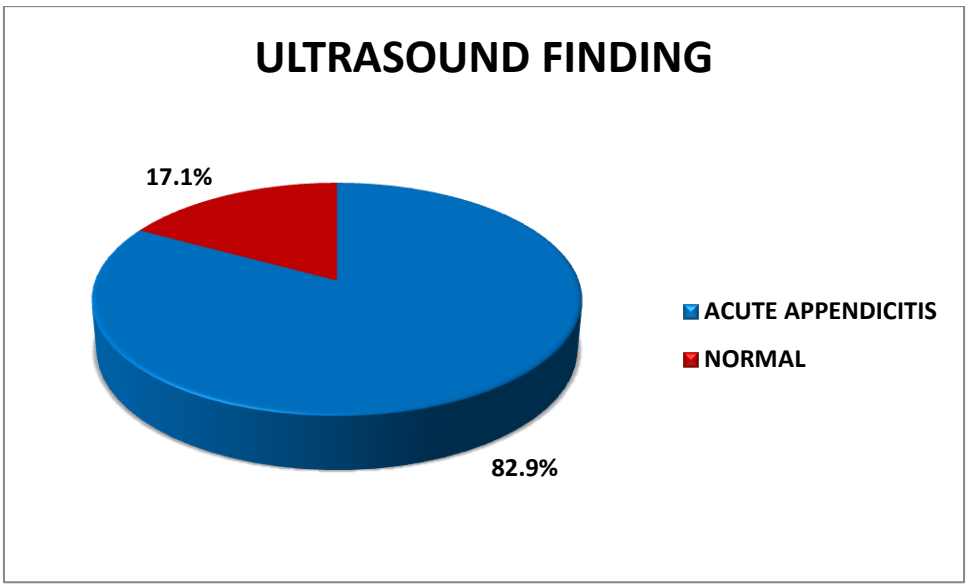


**TABLE 7: DISTRIBUTION OF CASES BY INTRAOPERATIVE DIAGNOSIS**

| INTRAOPERATIVE DIAGNOSIS | N | % |
|---|---|---|
| ACUTE APPENDICITIS | 59 | 72 |
| APPENDICEAL PERFORATION | 23 | 28 |
| Total | 82 | 100 |

**FIGURE 6: DISTRIBUTION OF CASES BY INTRAOPERATIVE DIAGNOSIS**

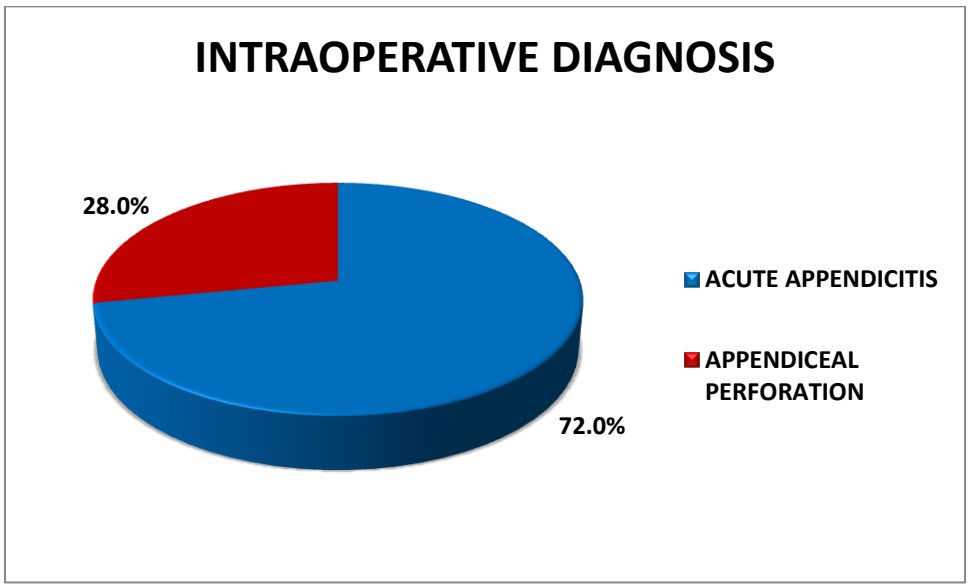


**TABLE 8: DISTRIBUTION OF CASES BY TC**

| TC | N | % |
|---|---|---|
| ≤11000 | 33 | 40.2 |
| >11000 | 49 | 59.8 |
| Total | 82 | 100 |

**FIGURE 7: DISTRIBUTION OF CASES BY TC**

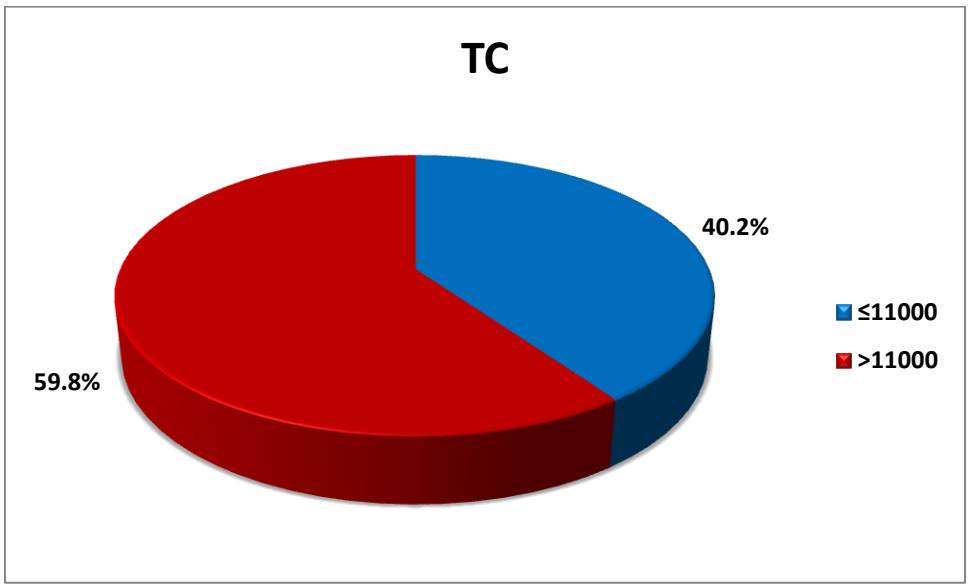


**TABLE 9: MEAN STUDY PARAMATERS**

| PARAMETER | Mean | SD |
|---|---|---|
| PROCACLITONIN | 2.3 | 1.9 |
| TOTAL BILIRUBIN | 0.7 | 0.3 |
| CRP | 1.5 | 0.7 |

**DIFFERENTIAL LEUKOCYTE COUNT**

| PARAMETER | Mean | SD |
|---|---|---|
| NEUTROPHIL | 85.5 | 3.2 |
| EOSINOPHILS | 2.3 | 0.5 |
| MONOCYTES | 3.4 | 0.9 |
| BASOPHILS | 0.0 | 0.2 |
| LYMPHOCYTE | 8.9 | 2.5 |

**TABLE 10: MEAN STUDY PARAMATERS BY CLINICAL DIAGNOSIS**

| PARAMETERS | ACUTE APPENDICITIS | | APPENDICEAL PERFORATION | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| PROCACLITONIN | 2.2 | 0.9 | 2.7 | 0.8 | 0.317 |
| TOTAL BILIRUBIN | 0.7 | 0.4 | 0.8 | 0.2 | 0.238 |
| CRP | 1.4 | 0.5 | 1.8 | 1.1 | 0.078 |

**FIGURE 8: MEAN STUDY PARAMATERS BY CLINICAL DIAGNOSIS**

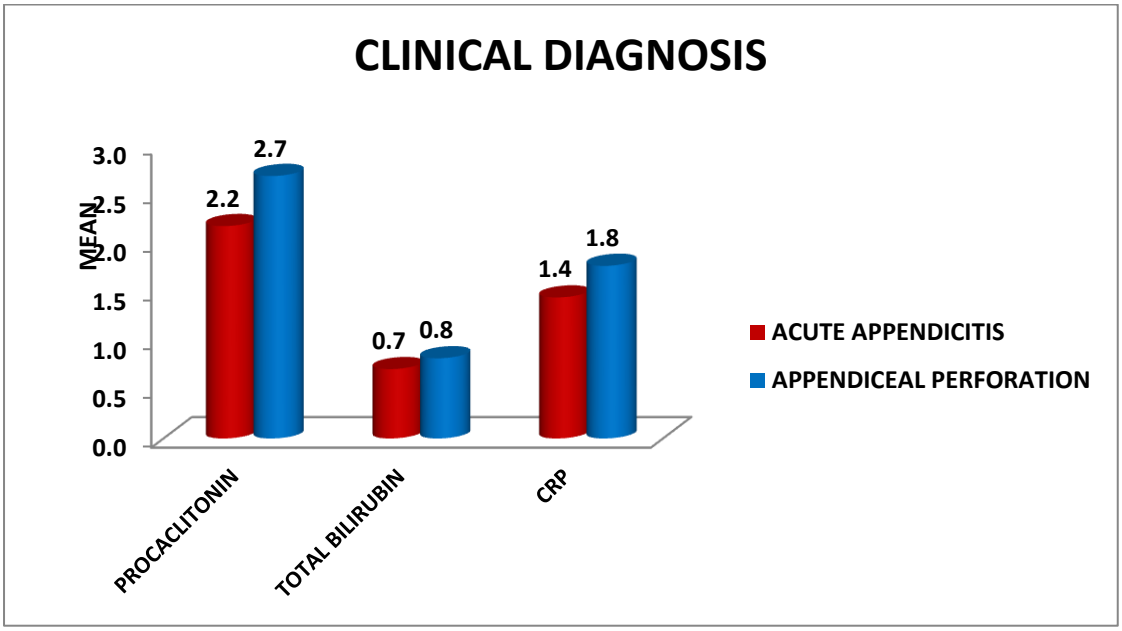


**TABLE 11: PROCACLITONIN LEVEL IN CLINICALLY DIAGNOSED PATIENTS**

| PROCACLITONIN | ACUTE APPENDICITIS | | APPENDICEAL PERFORATION | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.5 | 23 | 35.4 | 1 | 5.9 | 0.017 * |
| >1.5 | 42 | 64.6 | 16 | 94.1 | |
| Total | 65 | 100.0 | 17 | 100.0 | |

Note: * significant at 5% level of significance (p<0.05)

**FIGURE 9: PROCACLITONIN LEVEL IN CLINICALLY DIAGNOSED PATIENTS**

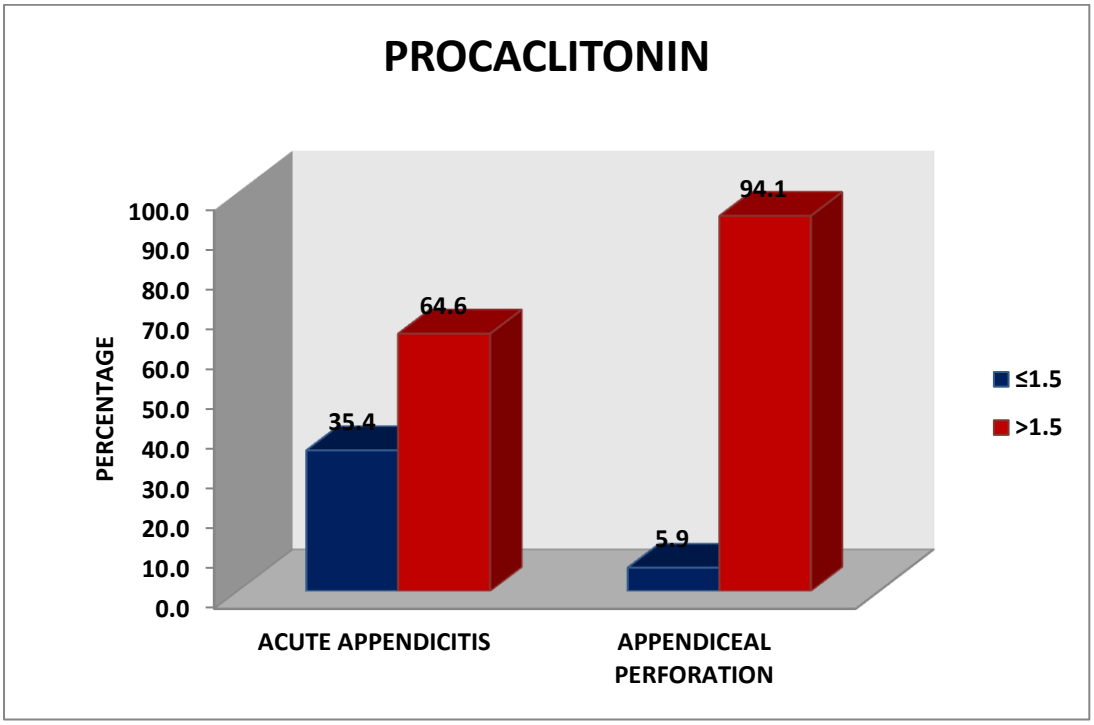


**TABLE 12: PROCACLITONIN LEVEL IN USG DIAGNOSED PATIENTS**

| PROCACLITONIN | ACUTE APPENDICITIS | | NORMAL | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.5 | 22 | 32.4 | 2 | 14.3 | 0.176 |
| >1.5 | 46 | 67.6 | 12 | 85.7 | |
| Total | 68 | 100.0 | 14 | 100.0 | |

**FIGURE 10: PROCACLITONIN LEVEL IN USG DIAGNOSED PATIENTS**

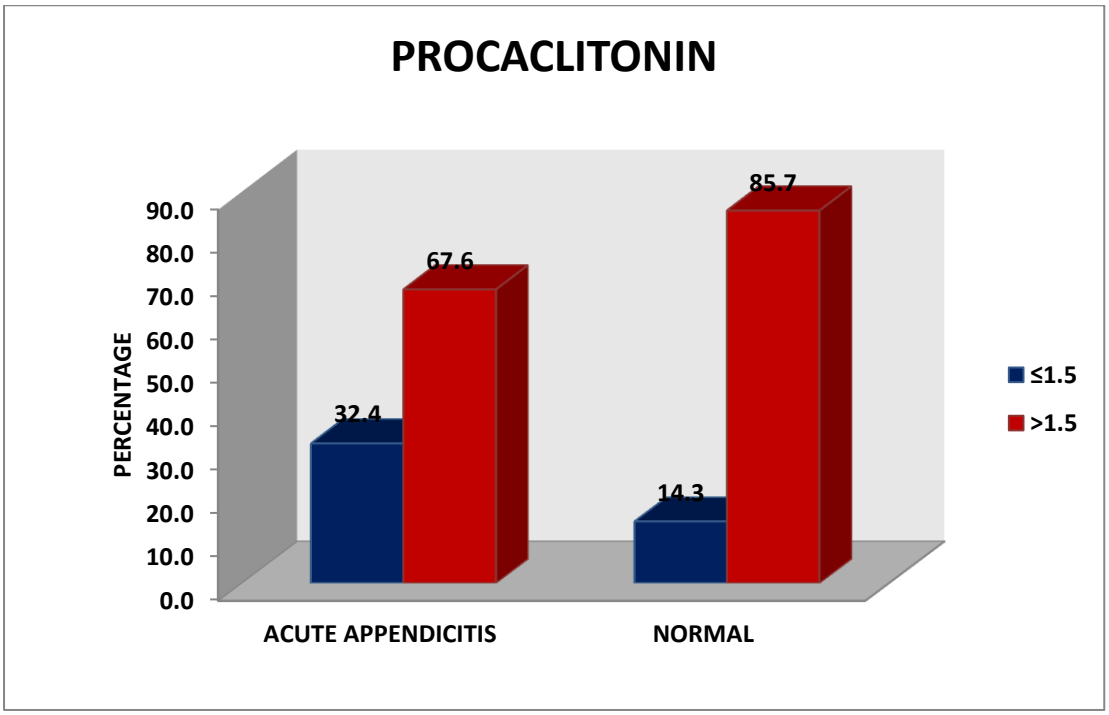


**TABLE 13: PROCACLITONIN LEVEL IN INTRAOPERATIVELY DIAGNOSED PATIENTS**

| PROCACLITONIN | ACUTE APPENDICITIS | | APPENDICEAL PERFORATION | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.5 | 23 | 39.0 | 1 | 4.3 | 0.002 * |
| >1.5 | 36 | 61.0 | 22 | 95.7 | |
| Total | 59 | 100.0 | 23 | 100.0 | |

Note: * significant at 5% level of significance ($p<0.05$)

**FIGURE 11: PROCACLITONIN LEVEL IN INTRAOPERATIVELY DIAGNOSED PATIENTS**

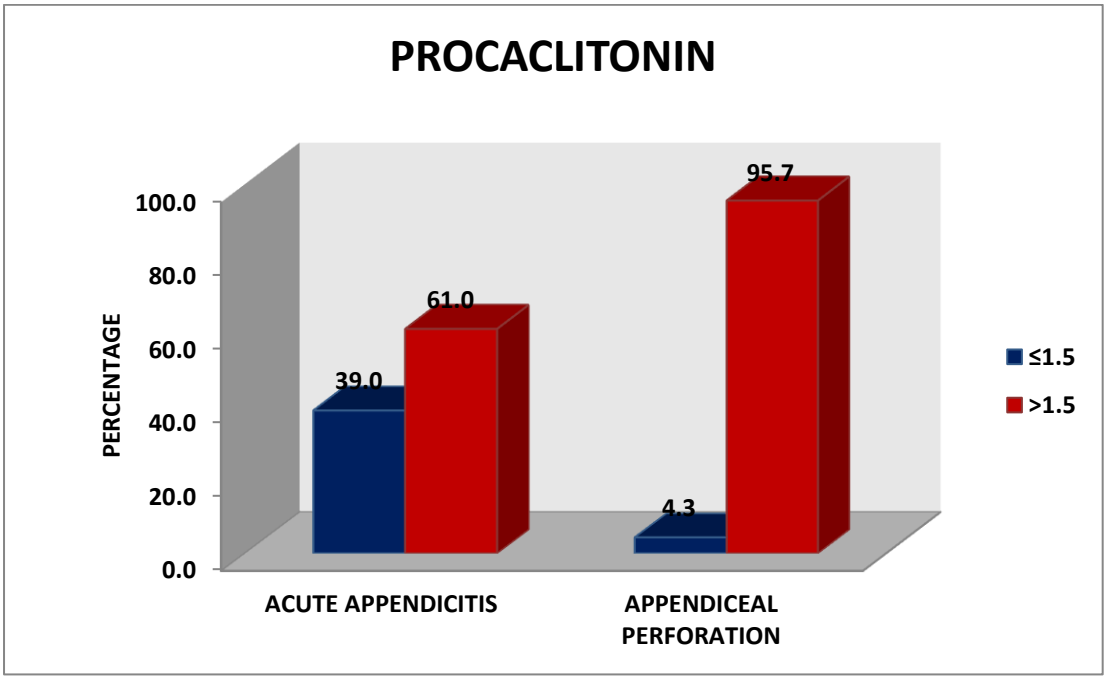


**TABLE 14: TOTAL BILIRUBIN LEVEL IN CLINICALLY DIAGNOSED PATIENTS**

| TOTAL BILIRUBIN | ACUTE APPENDICITIS | | APPENDICEAL PERFORATION | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.0 | 54 | 83.1 | 15 | 88.2 | 0.604 |
| >1.0 | 11 | 16.9 | 2 | 11.8 | |
| Total | 65 | 100.0 | 17 | 100.0 | |

**FIGURE 12: TOTAL BILIRUBIN LEVEL IN CLINICALLY DIAGNOSED PATIENTS**

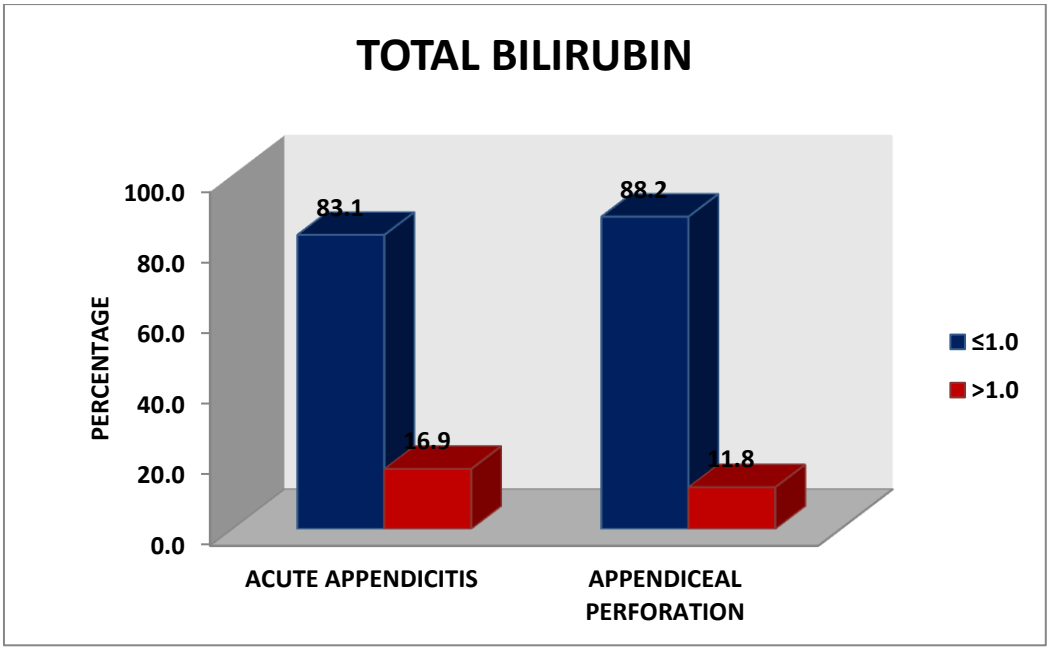


**TABLE 15: TOTAL BILIRUBIN LEVEL IN USG DIAGNOSED PATIENTS**

| TOTAL BILIRUBIN | ACUTE APPENDICITIS | | NORMAL | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.0 | 55 | 80.9 | 14 | 100.0 | 0.075 |
| >1.0 | 13 | 19.1 | 0 | 0.0 | |
| Total | 68 | 100.0 | 14 | 100.0 | |

**FIGURE 13: TOTAL BILIRUBIN LEVEL IN USG DIAGNOSED PATIENTS**

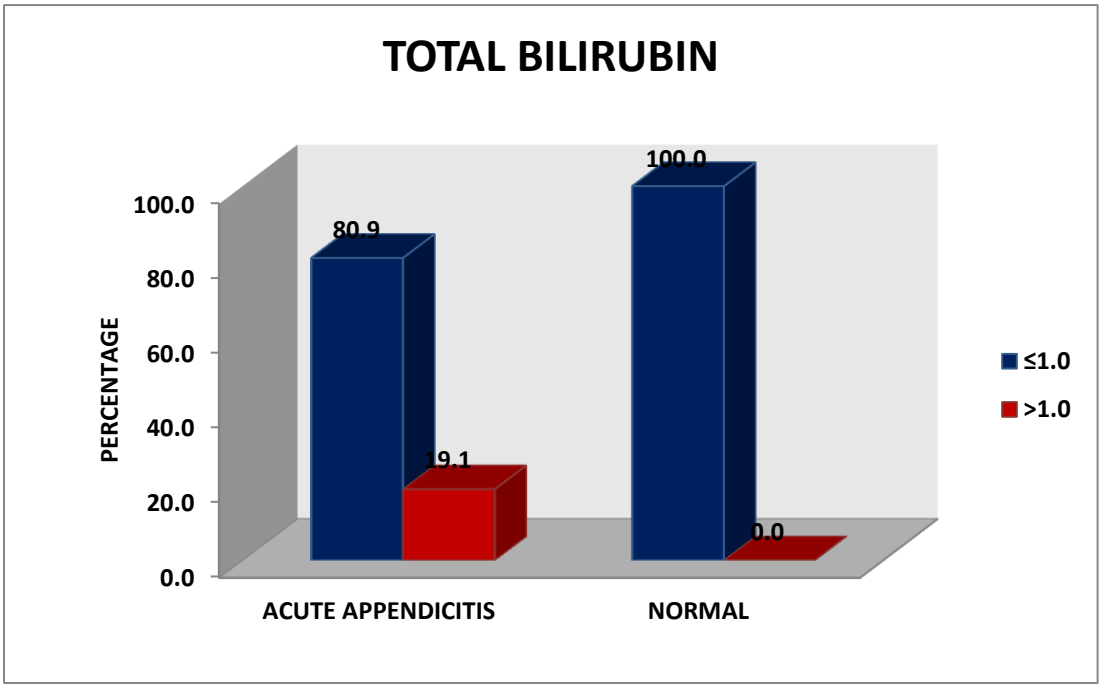


**TABLE 16: TOTAL BILIRUBIN LEVEL IN INTRAOPERATIVELY DIAGNOSED PATIENTS**

| TOTAL BILIRUBIN | ACUTE APPENDICITIS | | APPENDICEAL PERFORATION | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.0 | 48 | 81.4 | 21 | 91.3 | 0.268 |
| >1.0 | 11 | 18.6 | 2 | 8.7 | |
| Total | 59 | 100.0 | 23 | 100.0 | |

**FIGURE 14: TOTAL BILIRUBIN LEVEL IN INTRAOPERATIVELY DIAGNOSED PATIENTS**

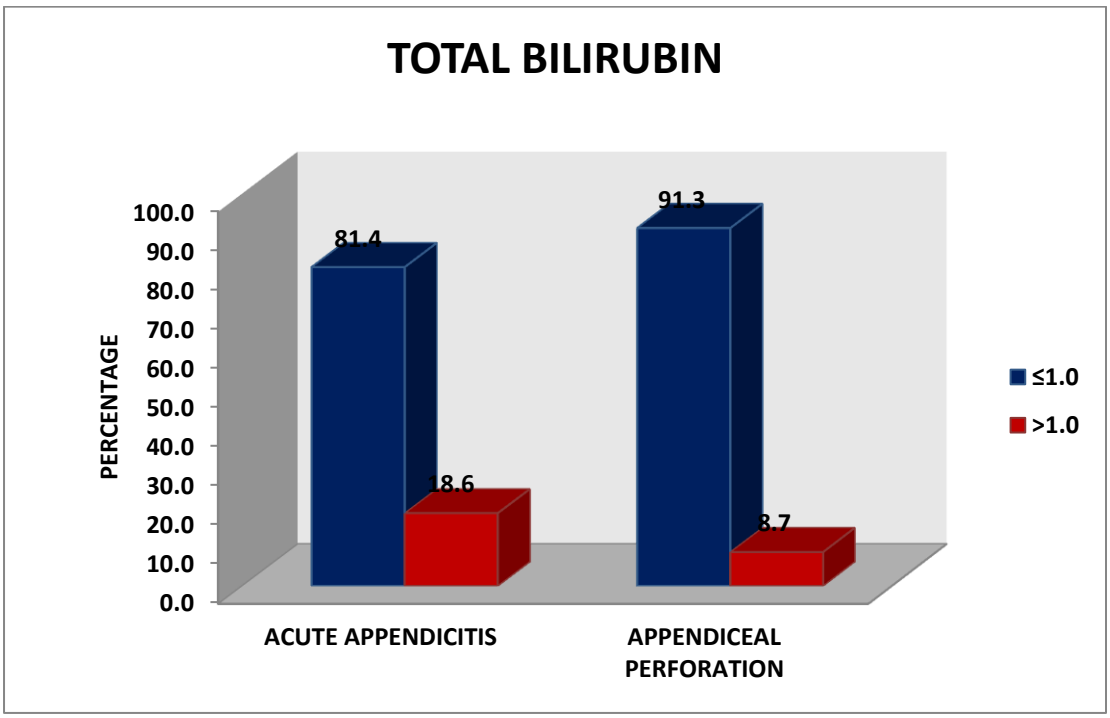


**TABLE 17: CRP LEVEL IN CLINICALLY DIAGNOSED PATIENTS**

| CRP | ACUTE APPENDICITIS | | APPENDICEAL PERFORATION | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.5 | 38 | 58.5 | 7 | 41.2 | 0.202 |
| >1.5 | 27 | 41.5 | 10 | 58.8 | |
| Total | 65 | 100.0 | 17 | 100.0 | |

**FIGURE 15: CRP LEVEL IN CLINICALLY DIAGNOSED PATIENTS**

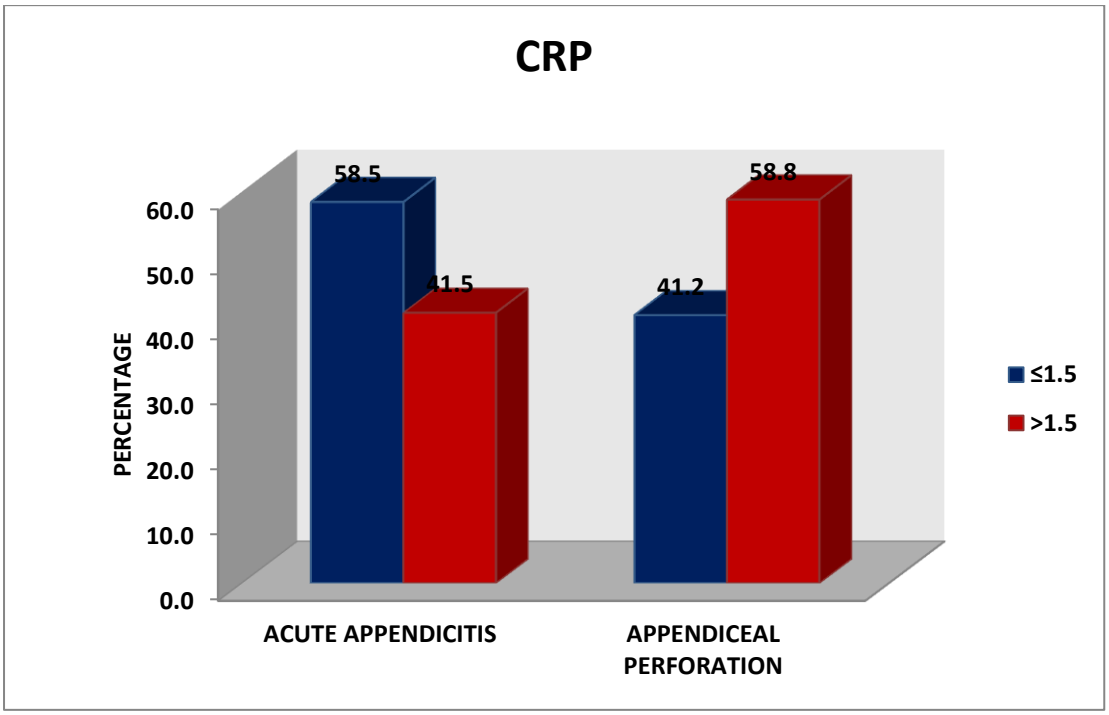


**TABLE 18: CRP LEVEL IN USG DIAGNOSED PATIENTS**

| CRP | ACUTE APPENDICITIS | | NORMAL | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.5 | 40 | 58.8 | 5 | 35.7 | 0.114 |
| >1.5 | 28 | 41.2 | 9 | 64.3 | |
| Total | 68 | 100.0 | 14 | 100.0 | |

**FIGURE 16: CRP LEVEL IN USG DIAGNOSED PATIENTS**

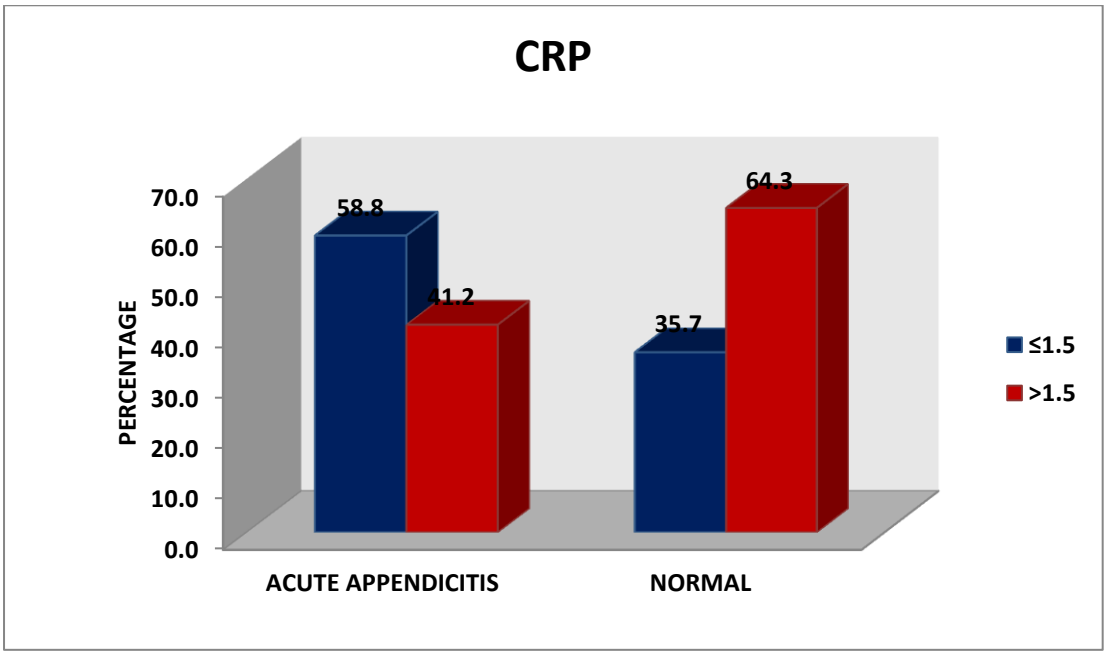


**TABLE 19: CRP LEVEL IN INTRAOPERATIVELY DIAGNOSED PATIENTS**

| CRP | ACUTE APPENDICITIS | | APPENDICEAL PERFORATION | | p value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| ≤1.5 | 34 | 57.6 | 11 | 47.8 | 0.423 |
| >1.5 | 25 | 42.4 | 12 | 52.2 | |
| Total | 59 | 100.0 | 23 | 100.0 | |

**FIGURE 17: CRP LEVEL IN INTRAOPERATIVELY DIAGNOSED PATIENTS**

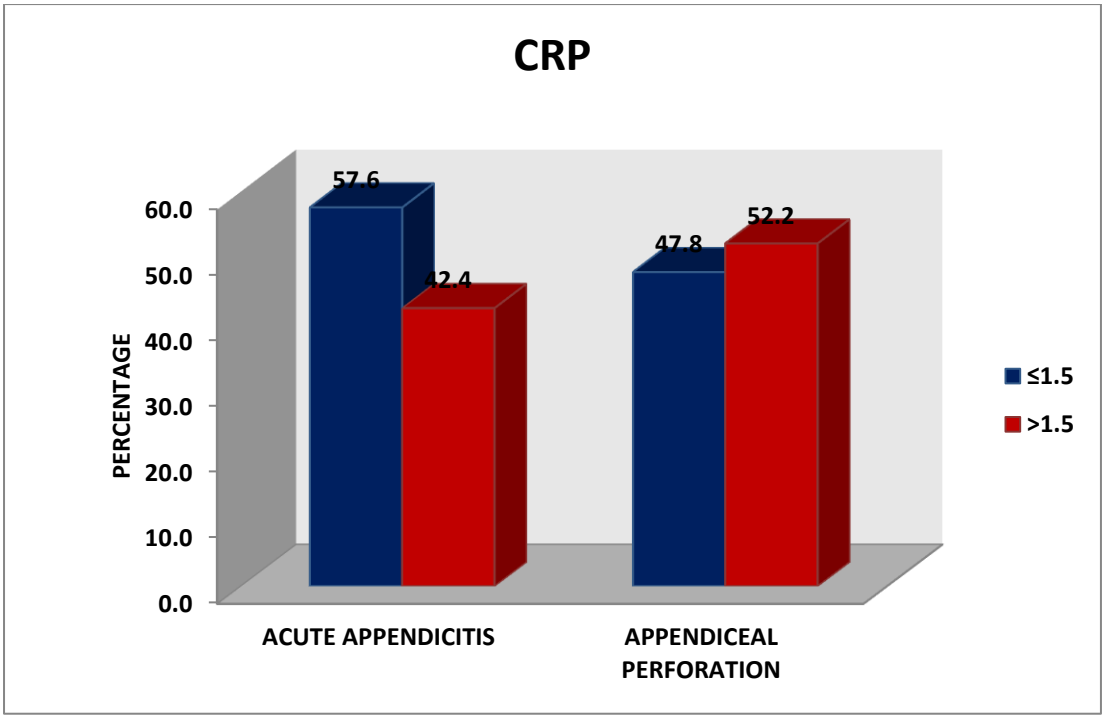
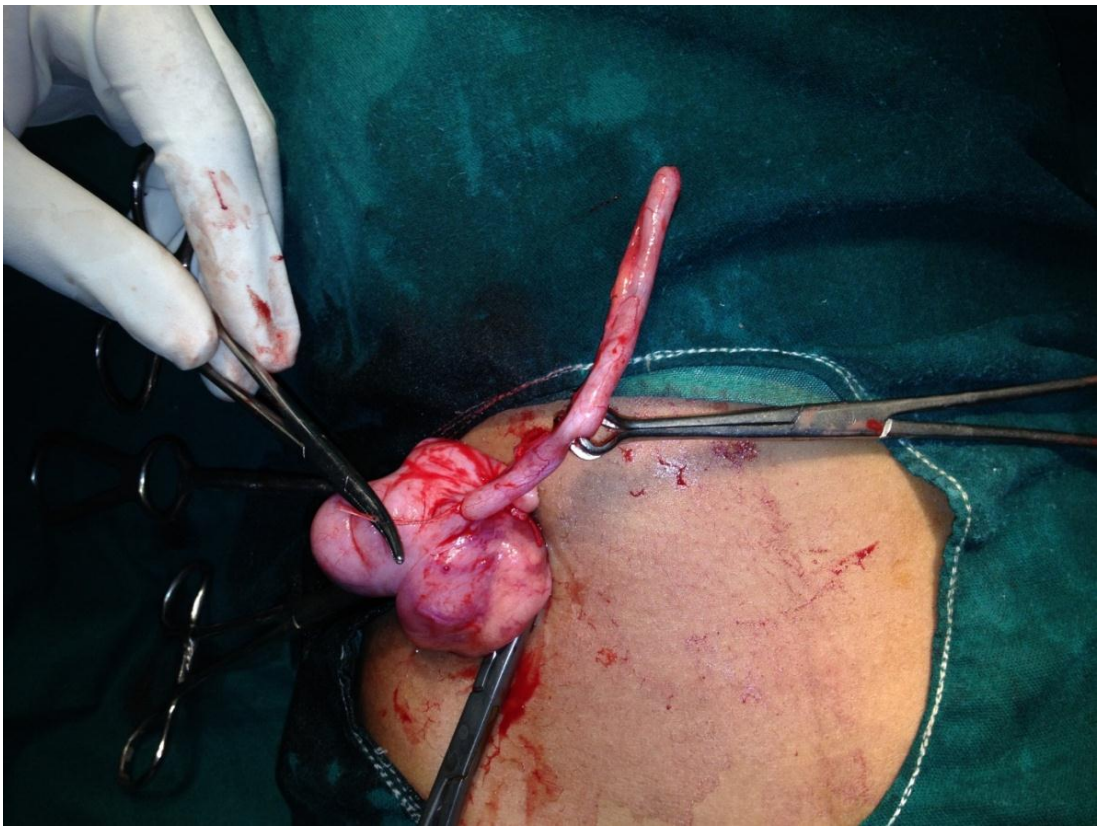


**TABLE 20: DIAGNOSTIC EFFICACY OF PROCACLITONIN TOTAL BILIRUBIN AND CRP**

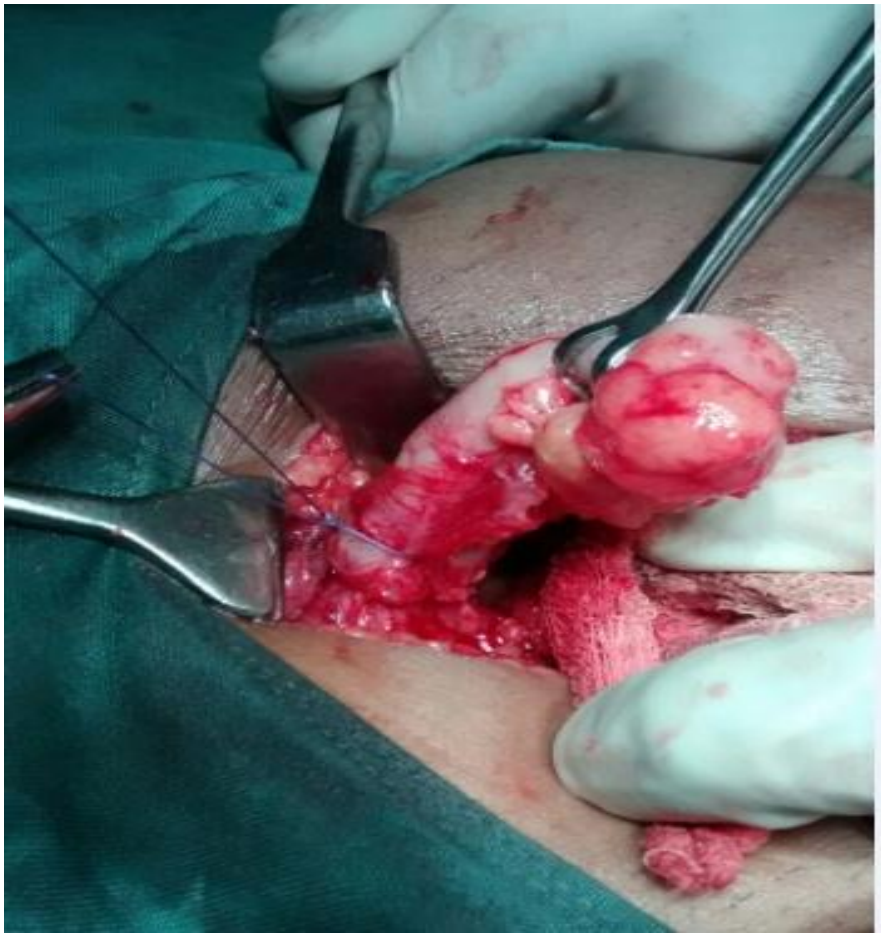
| | PROCACLITONIN | TOTAL BILIRUBIN | CRP |
|---|---|---|---|
| TP (true positive) | 42 | 11 | 27 |
| FN (false negative) | 23 | 54 | 38 |
| FP (false positive) | 16 | 2 | 10 |
| TN (true negative) | 1 | 15 | 7 |

| | PROCACLITONIN | TOTAL BILIRUBIN | CRP |
|---|---|---|---|
| Sensitivity | 64.62% | 16.92% | 41.54% |
| Specificity | 5.88% | 88.24% | 41.18% |
| PPV | 72.41% | 84.62% | 72.97% |
| NPV | 4.17% | 21.74% | 15.56% |
| Accuracy | 52.44% | 31.71% | 41.46% |
| Odds Ratio | 0.11 | 1.53 | 0.50 |

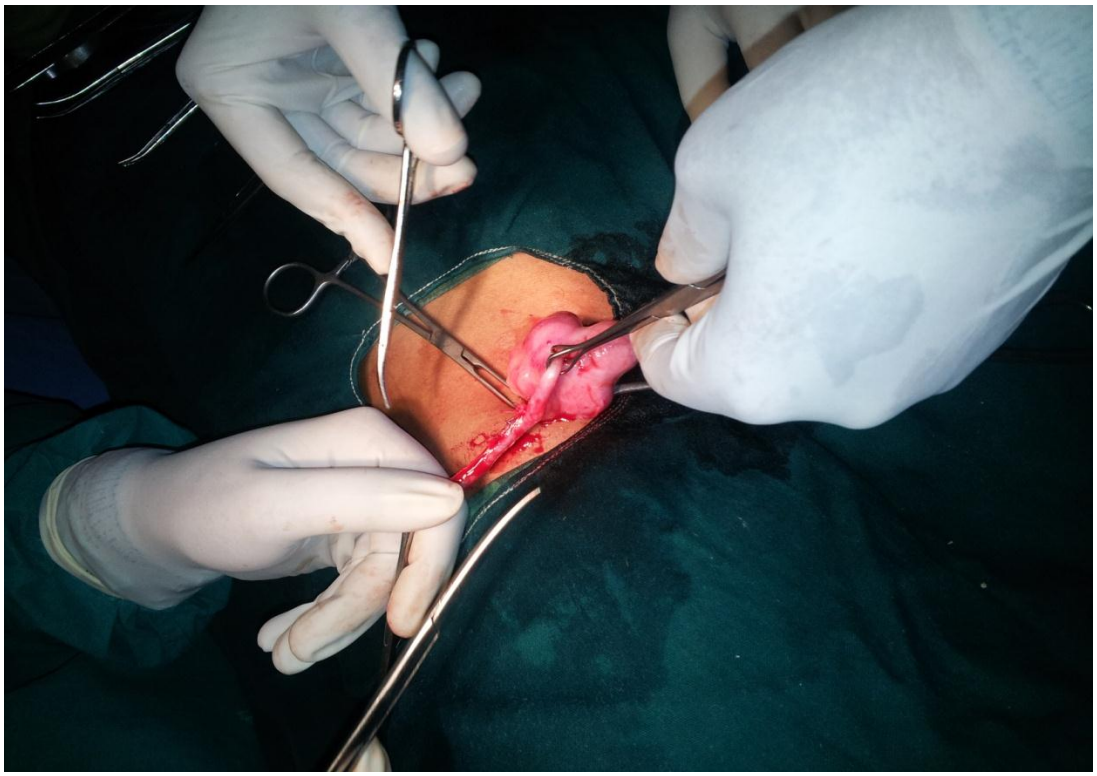
# PHOTOGRAPHS



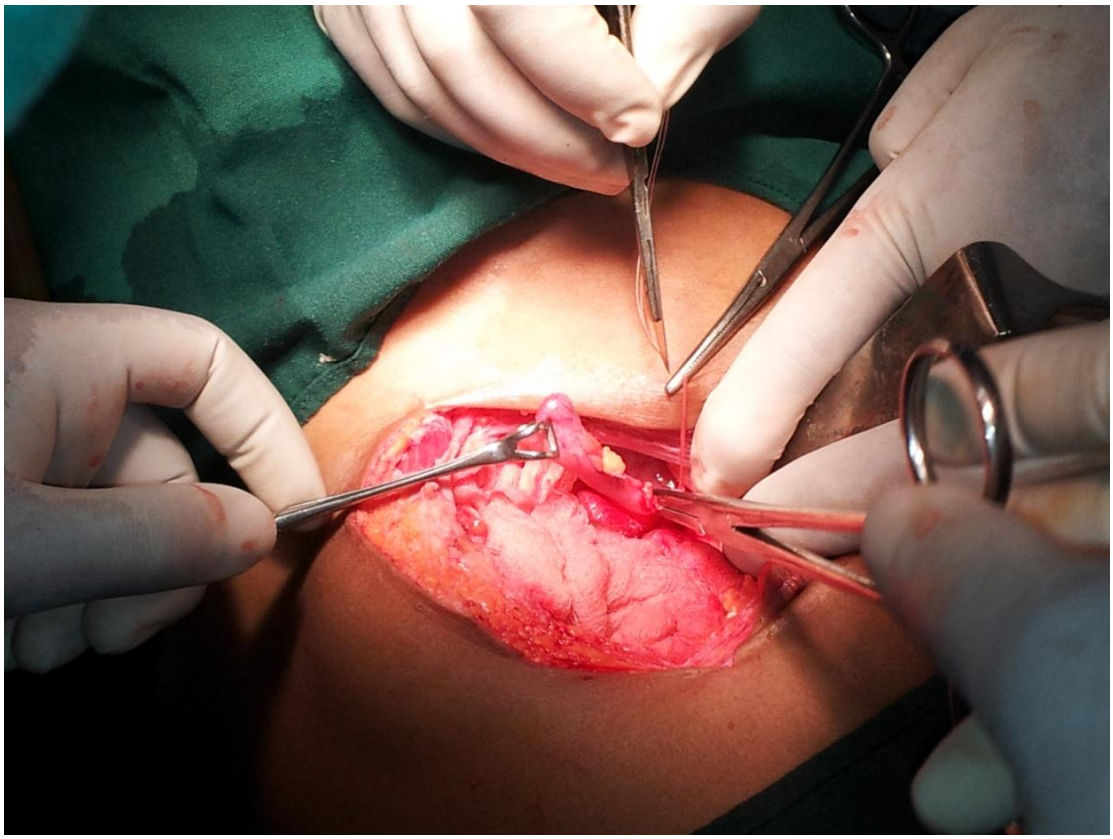
**Photograph 1. Acute appendicitis**



**Photograph 2.Appendiceal perforation**



**Photograph 3. Acute appendicitis**



**Photograph 4.Appendiceal perforation**

# DISCUSSION

Acute appendicitis is the most common cause of 'acute abdomen' in young adults. Appendicectomy is the most frequently performed urgent abdominal operation and is often the first major procedure performed by a surgeon in training. About 8% of people in Western countries have appendicitis at some time in their lifetime.[53]

The peak incidence of acute appendicitis is in the second and third decade of life. It is relatively rare in infants, and becomes increasingly common in childhood and early adult life. The incidence of appendicitis is equal in males and females before puberty. In teenagers and young adults, the male – female ratio increases to 3:2 at age. The lifetime rate of appendicectomy is 12% for men and 25% for women, with approximately 7% of all people undergoing appendectomy for acute appendicitis during their lifetime.[54,55] Obstruction of the lumen is believed to the major cause of acuteappendicitis. Faecoliths are the usual cause of obstruction. Less- common causes are hypertrophy of lymphoid tissue, tumors, intestinal parasites.[56] Thebacteriology of normal appendix is similar to that of normal colon. The principal organism seen in normal appendix, in acute appendicitis and in perforated appendicitis are *Escherichia Coli* and *Bacteroides fragilis*. However a wide variety of both the diagnosis of acute appendicitis is essentially clinical; however, a decision to operate based on clinical suspicion alone can lead to the removal of normal appendix in 15 to 30% of cases. The premise that it is better to remove anormal appendix than to delay diagnosis does not stand up to close scrutiny, particularly in the elderly. Hence, the diagnosis of Appendicitis still remains a dilemma in spite of the advances in various laboratory and radiological investigations. A new tool to help in the diagnosis of acute appendicitis would thus be welcome.

Serum PCT concentrations are positively correlated with severity of infection. Adequate antibiotic treatment leads to decreasing PCT levels.

Serum PCT level elevation will help in the accuracy of clinical diagnosis of acute appendicitis and more importantly help in foreseeing and preventing impeding complications of acute appendicitis.

In this study, diagnostic accuracy of Procalcitonin, C-Reactive Protein (CRP), Bilirubin as a biomarker in acute appendicitis and its complications have been analyzed.

This study was taken up with this thought – that is it possible to add serum PCT as a new laboratory marker to aid in the diagnosis of acute appendicitis and if so, does it have the credibility to help us foresee an impending complication of acute appendicitis? Importance of hyper procalcitonin level and its association in acute appendicitis has being postulated recently. There are only a few case reports in the available literature that describe the finding of hyper procalcitonin in patients of acuteappendicitis.[54] It is hypothesized that an association exists between hyper procalcitonin and acute appenditics and its complications. The present study was undertaken to study the diagnostic accuracy of Procalcitonin, C-Reactive Protein (CRP), Bilirubin as a biomarker in the diagnosis of acute appendicitis and to evaluate its credibility as diagnostic marker for acute appendicitis and also, to evaluate whether elevated procalcitonin levels have a predictive potential for the diagnosis of acute appendicitis.

This study was conducted in the Department of General Surgery, BLDE (Deemed to be University) Shri B. M. Patil Medical College, Vijayapur over a period

from October 2016 to May 2018 on 82 patients with clinical diagnosis of Acute appendicitis and Appendiceal perforation.

In the present study of the 82 patients enrolled for the study, 53 patients (64.6%) were males while the remaining 29 patients (35.4%) were females. The mean age in our study population (82 patients) was 25.9 ± 11.5 years. This is consistent with the quoted incidence of Appendicitis in the literature where it is most frequently seen in patients in their second through fourth decades of life. The average age in females 27.8±12.6 years was slightly higher than males 24.9±10.8 years.

In our study population of 82 patients, 65 patients (79.3%) were diagnosed as acute appendicitis pre-operatively while 17 patients (20.7%) were diagnosed with Appendiceal perforation. The diagnosis was confirmed post-operatively by USG reports and those differing from the pre-operative diagnosis were excluded from the study. The mean level of procalcitonin, C-Reactive Protein (CRP), Bilirubin were found to have increased in both acute appendicitis and appendiceal perforation.

Amongst the patients diagnosed with Acute appendicitis pre-operatively (n=65), 42 patients (64.6%) were found to have elevated procalcitonin (>1.5 ng/mL) while only 23 patients (35.4%) had normal procalcitonin levels (≤1.5 ng/mL). In patients diagnosed with Appendiceal perforation (n=17), 16 patients (94.1%) had elevated procalcitonin (>1.5 ng/mL). Thus, Hyper procalcitonin was found in most of the patients diagnosed with acute appendicitis (64.6%) or appendiceal perforation (94.1%).

Amongst the patients diagnosed with Acute appendicitis pre-operatively (n=82), 11 patients (16.9%) were found to have elevated bilirubin (>1.0 mg/dL) while

only 54 patients (83.1%) had normal bilirubin levels (≤1.0 mg/dL). In patients diagnosed with Appendiceal perforation (n=17), 2 patients (11.8%) had bilirubin elevated (>1.0 mg/dL). Thus, Hyper bilirubinemia was found in less number of the patients diagnosed with acute appendicitis (16.9%) or appendiceal perforation (11.8%).

Amongst the patients diagnosed with Acute appendicitis pre-operatively (n=82), 27 patients (41.5%) were found to have elevated CRP (>1.5 mg/dL) while only 38 patients (58.5%) had normal CRP levels (≤1.5 mg/dL). In patients diagnosed with Appendiceal perforation (n=17), 10 patients (58.8%) had CRP elevated (>1.5 mg/dL). Thus, Hyper CRP was found in most of the patients diagnosed with acute appendicitis (41.5%) or appendiceal perforation (58.8%).

The total leukocyte count was found elevated in just 49 patients (59.8%) of the total 82 patients. The mean of TLC count in all patients was 11922.6±2572.8/mm3 (range, 7692- 12380.79/mm3), in which the highest percentage constituted Neutrophils with 82.65% followed by 10.92% by Lymphocytes.

On Ultrasonography, 68 patients (82.9%) were diagnosed as acute appendicits while 14 patients (17.1%) were reported as normal ultrasonographic findings. None however were diagnosed as Appendiceal perforation on ultrasonography. Ultrasonography per-se was not helpful as a useful investigation for appendicitis or appendiceal perforation in our study as none of the USG findings reported Appendiceal perforation, hence belief that the diagnosis of appendicitis still remains essentially clinical, still hold true.

The mean procalcitonin levels in patients diagnosed with acute appendicitis was 2.2 ±0.9 ng/mL (range, 0.8– 3.4 ng/mL) while in patients diagnosed with Appendiceal perforation was 2.7±0.8 ng/mL (range, 1.5– 4.6 ng/mL).

The mean bilirubin levels in patients diagnosed with acute appendicitis was 0.7 ± 0.4 mg/dL (range, 0.09– 1.6 mg/dL) while in patients diagnosed with Appendiceal perforation was 0.8±0.2 mg/dL (range, 0.5– 1.2 mg/dL). Estrada et al[55] had foundhyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean CRP levels in patients diagnosed with acute appendicitis was 1.4 ± 0.5 mg/dL (range, 0.5– 2.2 mg/dL) while in patients diagnosed with Appendiceal perforation was 1.8±1.1 mg/dL (range, 0.9– 6.0 mg/dL).

Hence, we see that patients with appendiceal perforation had high levels of procalcitonin, C-Reactive Protein (CRP) and bilirubin as compared to that of acute appendicitis. So we infer that, patients with features suggestive of appendicitis with high range of procalcitonin, are more susceptible of having appendiceal perforation than those with normal or slightly elevated level. Sand et al in his study found the mean bilirubin levels in patients with appendiceal perforation to be significantly higher than those with a nonperforated appendicitis.

The Sensitivity, Specificity, Positive predictive value, Negative predictive value and Odds ratio was calculated from a 2x2 table. Sensitivity of Procalcitonin, C-Reactive Protein (CRP) and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis was 64.6%, 41.54% and 16.9% respectively. Less specificity for Procalcitonin was found due to less number of appendicitis cases with normal level.

Similarly Positive predictive value, Negative predicative value and accuracy of Procalcitonin, C-Reactive Protein (CRP) and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis was highest for Procalcitonin, followed by C-Reactive Protein (CRP) and bilirubin.

The Odds ratio was calculated to be 0.11 for Procalcitonin, 0.5 for CRP and 1.53 for bilirubin. The sensitivity in our study was at par with Kafetzis[56] et al in which, he found the sensitivity and specificity in his study of hyper Procalcitonin for predicting appendiceal perforation to be 73.4% and 94.6% respectively.

# CONCLUSION

Finding of the present study suggest:

- These findings indicate that procalcitonin is a useful marker of acute appendicitis with abscess and/or perforation than CRP and Serum bilirubin.
- Serum procalcitonin levels appears to be a promising new laboratory marker for diagnosing acute appendicitis, however diagnosis of appendicitis remains essentially still - clinical. Its levels come out to be a credible *aid* in diagnosis of acute appendicitis and would be helpful investigation in decision making.
- Patients with clinical signs and symptoms of appendicitis and with hyper procalcitonin should be identified as having a higher probability of appendiceal perforation suggesting, serum procalcitonin levels have a predictive potential for the diagnosis of acute appendicitis and appendiceal perforation.

# SUMMARY


**Background and Objectives**

Acute appendicitis is the most common abdominal emergency encountered in general surgery. In most of the cases, the diagnosis can be made clinically by assessing the symptoms and physical findings and confirmed by laboratory tests and ultrasonography.

However, diagnosis is difficult sometimes even after all these tests and in such doubtful cases either the diagnosis is missed or patients normal appendix is operated on, leading to increase in mortality and morbidity.

In this study, diagnostic accuracy of Procalcitonin, C-Reactive Protein (CRP), Bilirubin as a biomarker in acute appendicitis and its complications have been analyzed.

**Methodology**

A cross sectional study was conducted in the Department of Surgery, BLDE (Deemed to be University) Shri. B. M. Patil Medical College Vijayapur during the period of October 2016 to May 2018 A total of 82 patients with clinical diagnosis of acute appendicitis or appendiceal perforation were studied. The serum Procalcitonin, C-Reactive Protein (CRP), and Bilirubin were carried out in all the patients.

**Results:**

In the present study of the 82 patients enrolled for the study, 53 patients (64.6%) were males while the remaining 29 patients (35.4%) were females. The mean age in our study population (82 patients) was 25.9 ± 11.5 years. This is consistent

with the quoted incidence of Appendicitis in the literature where it is most frequently seen in patients in their second through fourth decades of life. The average age in females 27.8±12.6 years was slightly higher than males 24.9±10.8 years.

In our study population of 82 patients, 65 patients (79.3%) were diagnosed as acute appendicitis pre-operatively while 17 patients (20.7%) were diagnosed with Appendiceal perforation. The diagnosis was confirmed by USG reports and intra-operative findings and those differing from the pre-operative diagnosis were excluded from the study. The mean level of procalcitonin, C-Reactive Protein (CRP), Bilirubin were found to have increased in both acute appendicitis and appendiceal perforation.

The mean procalcitonin levels in patients diagnosed with acute appendicitis was 2.2 ±0.9 ng/mL (range, 0.8– 3.4 ng/mL) while in patients diagnosed with Appendiceal perforation was 2.7±0.8 ng/mL (range, 1.5– 4.6 ng/mL).

The mean bilirubin levels in patients diagnosed with acute appendicitis was 0.7 ± 0.4 mg/dL (range, 0.09– 1.6 mg/dL) while in patients diagnosed with Appendiceal perforation was 0.8±0.2 mg/dL (range, 0.5– 1.2 mg/dL). Estrada et al[55] had found hyperbilirubinemia in 59 (38%) of 157 patients studied with acute appendicitis.

The mean CRP levels in patients diagnosed with acute appendicitis was 1.4 ± 0.5 mg/dL (range, 0.5– 2.2 mg/dL) while in patients diagnosed with Appendiceal perforation was 1.8±1.1 mg/dL (range, 0.9– 6.0 mg/dL).

The Sensitivity, Specificity, Positive predictive value, Negative predictive value and Odds ratio was calculated from a 2x2 table. Sensitivity of Procalcitonin, C-Reactive Protein (CRP) and bilirubin in predicting acute appendicitis and appendiceal perforation diagnosis was 64.6%, 41.54% and 16.9% respectively.

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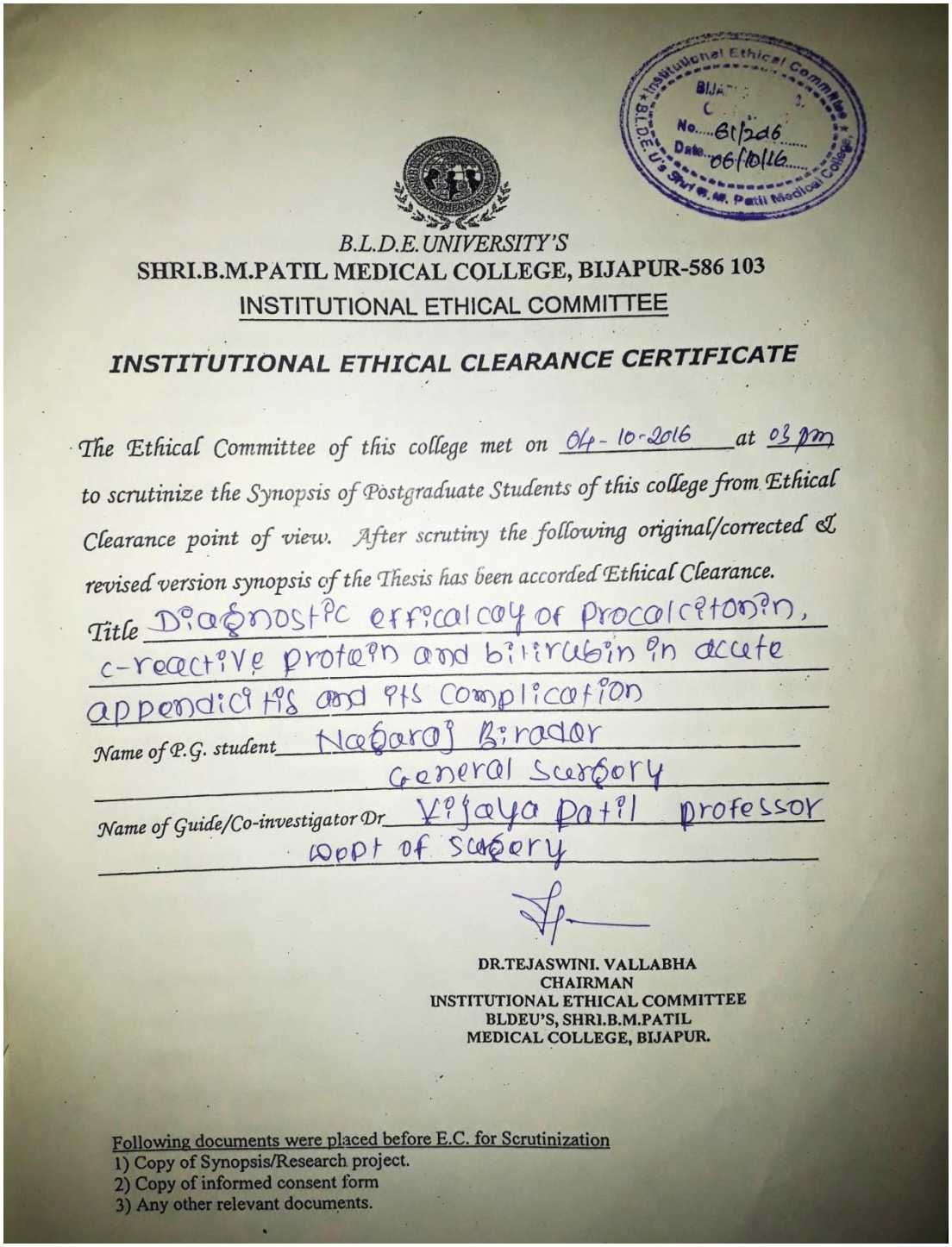
# ANNEXURES

## ETHICAL CLEARANCE CERTIFICATE



Institutional Ethical Committee
BLDE U's Shri B. M. Patil Medical College
No. 81/246
Date 06/10/16

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

**INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE**

The Ethical Committee of this college met on 04-10-2016 at 03 pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title Diagnostic efficacy of procalcitonin, c-reactive protein and bilirubin in acute appendicitis and its complication

Name of P.G. student Nagaraj Birader
General Surgery

Name of Guide/Co-investigator Dr Vijaya Patil professor
dept of surgery

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

## SAMPLE INFORMED CONSENT FORM

## B.L.D.E. (DEEMED TO BE UNIVERSITY) SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR-586 103

**TITLE OF THE PROJECT** : **DIAGNOSTIC EFFICACY OF PROCALCITONIN, C-REACTIVE PROTEIN AND BILIRUBIN IN ACUTE APPENDICITIS AND ITS COMPLICATIONS**

**PRINCIPAL INVESTIGATOR**: **Dr. NAGARAJ BIRADAR**
**DEPARTMENT OF GENERAL SURGERY**

**PG GUIDE** : **Dr. VIJAYA PATIL**
**M.S. GENERAL SURGERY**
**PROFESSOR**
**DEPARTMENT OF GENERAL SURGERY**

**PURPOSE OF RESEARCH:**

I have been informed that this study will analyse the diagnostic efficacy of procalcitonin, c-reactive protein and bilirubin in acute appendicitis and its complications.

I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

**PROCEDURE:**

I have been explained that depending upon the group allocated to me/my ward, I'll/my ward will be subjected to certain blood investigations like procalcitonin, c-reactive protein and bilirubin levels, total leucocyte count and urine investigations, and USG.

**RISKS AND DISCOMFORTS:**

I understand that I/my ward may experience some complications during drawing blood for investigations like injection site infection, bleeding etc, and I understand that necessary measures will be taken to reduce these complications as and when they arise.

**BENEFITS:**

I understand that my/my wards participation in this study will help to analyse the effectiveness of procalcitonin, c-reactive protein and bilirubin in diagnosis of acute appendicitis and its role in early prediction of appendicular perforation.

**CONFIDENTIALITY:**

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

**REQUEST FOR MORE INFORMATION:**

I understand that I may askmore questions about the study at any time. Dr. Nagaraj Biradar will be available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

And that a copy of this consent form will be given to me for keep for careful reading.

**REFUSAL OR WITHDRAWAL OF PARTICIPATION:**

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. Nagaraj Biradar will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

**INJURY STATEMENT:**

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date: Dr. Vijaya Patil (Guide) Dr. Nagaraj Biradar (Investigator)

**STUDY SUBJECT CONSENT STATEMENT:**

I confirm that Dr. Nagaraj Biradar has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

# SCHEME OF CASE TAKING:

1) Name: CASE NO:

2) Age: IP NO:

3) Sex: DOA:

4) Religion: DOS:

5) Occupation: DOD:

6) Residence:

7) CHIEF COMPLAINTS:

8) HISTORY OF PRESENTING ILLNESS:

9) PAST HISTORY:

- Diabetes mellitus
- Hypertension
- History of any drug intake
- Renal disease
- Jaundice

10) FAMILY HISTORY:

11) GENERAL PHYSICAL EXAMINATION:

| | |
|---|---|
| Pallor: | present/absent |
| Icterus: | present/absent |
| Clubbing: | present/absent |
| Generalized Lymphadenopathy: | present/absent |
| Build: | Poor/Middle /Well |
| Nourishment: | Poor / Middle / Well |

12) VITALS

PR:

BP:

RR:

Temp:

Weight:

13) OTHER SYSTEMIC EXAMINATION:

- Per Abdomen examination
- Respiratory System
- Cardiovascular System
- Central Nervous System

14) INVESTIGATION:

BLOOD: Hb :

URINE:

Albumin:

Sugar:

Microscopy:

TC :

DC:

ESR: BT, CT:

HIV:

HbsAG

HCV

PROCALCITONIN

SERUM BILIRUBIN:

C-REACTIVE PROTEIN:

BLOOD UREA:

SERUM CREATININE:

RBS:

USG ABDOMEN:

16) FINAL DIAGNOSIS: