"ASSESSMENT OF BLOOD C-REACTIVE PROTEIN LEVELS AS A PREDICTOR OF DIFFICULT LAPAROSCOPIC CHOLECYSTECTOMY - A HOSPITAL BASED CROSS-SECTIONAL STUDY"

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This is to certify that the dissertation entitled **"ASSESSMENT OF BLOOD C-REACTIVE PROTEIN LEVELS AS A PREDICTOR OF DIFFICULT LAPAROSCOPIC CHOLECYSTECTOMY - A HOSPITAL BASED CROSS-SECTIONAL STUDY"** is a bonafide research work done by **REG NO. BH0116006.**

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LIST OF ABBREVIATIONS USED

LC	**:**	Laparoscopic cholecystectomy
CBD	**:**	Common bile duct
GB	**:**	Gall bladder
CRP	**:**	C reactive protein
NIH	**:**	National Institutes of Health
SMA	**:**	Superior mesenteric artery
CCK	**:**	Cholecystokinin
BDI	**:**	Bile duct injuries
OC	**:**	Open cholecystectomy
LSTC	**:**	Laparoscopic subtotal cholecystectomy
TLC	**:**	Total leucocyte count
ALP	**:**	Alkaline phosphatase
ERCP	**:**	Endoscopic retrograde cholangiopancreatography
Fcγ	**:**	Fragment crystalline γ
hs-CRP	**:**	High-sensitivity C reactive protein
KAHER	**:**	KLE Academy of higher education and research
BMI	**:**	Body-mass index
ROC	**:**	Receiver's Operating Characteristic

ABSTRACT

INTRODUCTION:

Laparoscopic cholecystectomy is the treatment of choice for symptomatic gall stone disease and for selected cases of acute cholecystitis. Difficult laparoscopic cholecystectomy and conversion to open surgery are known to increase post-operative morbidity. Thus, it is essential to have a simple pre-operative indicator to predict the same.

OBJECTIVE:

To find out if blood CRP levels can predict intra-operative factors that can objectively be used to assess difficulty in laparoscopic cholecystectomy and to evaluate C reactive protein as a predictor for conversion to open surgery.

MATERIALS AND METHODS:

This one-year cross-sectional study was done with the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2017 to December 2017. A total of 100 patients posted for laparoscopic cholecystectomy were studied. Pre-operative hs-CRP (High sensitivity C-reactive protein) levels were analysed with conversion to open procedure and intra-operative difficulty based on findings including adhesions, empyema, wall thickening, difficulty in grasping and perforation.

RESULTS:

Yoden index was calculated using different levels of hs-CRP as cut-off. It was found to be optimum (77.98) at 4mg/L. It was found that patients with hs-CRP>4mg/L had a

higher incidence of intra-operative difficulty that was statistically significant (P<0.001) with a sensitivity of 88.89% and a specificity of 89.09%. Conversion to open surgery had a higher incidence in patients having hs-CRP higher than 10mg/L (P=0.005).

CONCLUSION:

Based on these results, C-reactive protein (by measurement of hs-CRP) can be used as an effective independent predictor of difficult laparoscopic cholecystectomy above 4mg/L and conversion to open procedure above 10mg/L.

Key words: cholelithiasis, C reactive protein, difficult laparoscopic cholecystectomy, conversion.

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INTRODUCTION

Cholecystectomy is currently one of the most commonly performed operative procedures[1]. Laparoscopic cholecystectomy (LC), as we know today, was introduced for the first time in 1987 and has eventually become the preferred method for cholecystectomy[2]. This procedure has changed the face of treatment of gall stones by reducing postoperative pain, risk of surgical site infection and incisional hernia[3]. This surgery is still evolving with time and size and the number of ports is reducing day by day.

Despite vast experience, multiple advances and updates in technique, there are few circumstances in which the surgery becomes difficult leading to prolonged operating time, injury to surrounding structures like the common bile duct (CBD) and vessels. These cause significant morbidity to the patient, may lead to prolonged admission, shock and increased cost of care and increased risk of mortality[4,5]. To avoid these circumstances, many a times, a decision to convert the laparoscopic procedure to an open surgery has to be taken.

There are multiple studies done to evaluate factors that could possibly predict a difficult laparoscopic cholecystectomy and the probability of conversion in such cases. These include male gender, advanced age, co-morbidities, high ASA grade, recurrent attacks of acute cholecystitis, ongoing active infection, thickened gall bladder (GB) walls and pericholecystic collection on pre-operative imaging[5-10]. C-reactive protein has recently come in sight as a factor that could predict difficult laparoscopy in a few studies[11-13].

C-reactive protein (CRP) is a phylogenetically highly conserved plasma protein which is an integral part of the systemic response to inflammation. Its plasma

concentration increases during inflammatory states, a characteristic that has long been employed for clinical purposes. CRP is a pattern recognition molecule, that binds to specific molecular configurations that are typically exposed during cell death or found on the surfaces of pathogens. Its synthesis rapidly increases within hours of tissue injury or infection. This suggests that it contributes to host defense and is a part of the innate immune response[14].

Most of the predictors of difficult laparoscopy mentioned above are directly or indirectly related to the degree of inflammation in and around the gall bladder. As CRP has been proven to be a direct predictor of ongoing inflammation, it shows a correlation between CRP and the probability of a difficult laparoscopic cholecystectomy[15]. There has been considerable evidence pointing towards the predictive value of CRP for conversion to open cholecystectomy[11,12].

It is fairly obvious to note that conversion to open surgery also depends upon the skill and choices of individual surgeons. It is, thus, a subjective criterion for analyzing difficult laparoscopy. In this study we intend to analyze CRP as a predictor of difficult laparoscopic cholecystectomy using intra-operative findings as a parameter for analysis.

OBJECTIVE

Primary- To find out if blood CRP levels can predict intra-operative difficulty in laparoscopic cholecystectomy.

Secondary- To evaluate C-reactive protein as a predictor for conversion to open surgery.

REVIEW OF LITERATURE

Laparoscopic cholecystectomy (LC) has been established as the gold standard for the elective treatment of cholecystolithiasis, and is now being increasingly used for the treatment of acute cholecystitis as well[8]. The advantages of laparoscopic over open cholecystectomy have been well documented which include earlier return of bowel function, less postoperative pain, improved cosmesis, shorter length of hospital stay, earlier return to full activity, and decreased overall cost[16,17].

HISTORICAL REVIEW:

Gallstones have been described since ancient times with even autopsies of Egyptian mummies revealing their presence. There was an improved learning of the anatomy of the gall bladder and biliary system in the 17th and 18th centuries. After initial attempts at treating this condition medically, surgical approaches were applied starting in the second half of the 19th century[18-20].

In the year 1867, John S. Bobbs successfully performed cholecystotomy with extraction of gallstones. For his work he is regarded as the father of gall bladder surgery. After a decade, James Marion Sims, performed the first planned cholecystostomy for the treatment of cholecystitis[21]. In 1882, Carl Langenbuch revolutionised the treatment of gallstone disease by performing the first successful cholecystectomy following his work on animals and cadavers which led to him being convinced that surgical removal of the gall bladder should lead to permanent cure[22].

The treatment of gallstones underwent another revolution in the late twentieth century with Eric Muhe performing the first laparoscopic cholecystectomy in 1985 with his ‘galloscope’, hemoclips and pistol grip scissors, paving the way for a new generation of therapy[23]. Shortly thereafter, laparoscopes coupled with CCD video

cameras came into picture that allowed the entire team to visualise the operative field, giving rise to the current technique of laparoscopic cholecystectomy[24]. In 1992, the National Institutes of Health (NIH) Consensus Development Conference stated that laparoscopic cholecystectomy provides a safe and effective treatment for most patients with symptomatic gallstones[25]. Currently it is estimated that over 80% of cholecystectomies are performed using the laparoscopic approach[26].

SURGICAL ANATOMY:

The classic anatomy of the biliary tree is present in only 30% of individuals. It is therefore said that anomalies are the rule and not the exception in gall bladder surgery. The knowledge of normal anatomy and common variants is critical to the success of surgical intervention like most procedures[26]. The gallbladder is a muscular sac situated beneath the liver. The normal capacity of the gallbladder is 30 mL but it can distend to allow up to 300 mL of fluid in case of chronic distal obstruction. The wall of the gallbladder is composed of the visceral peritoneum (on areas not in direct contact with the liver), sub-serosa, muscularis, lamina propria, and columnar epithelium. The parts of the gallbladder are named as seen in Illustration 1. They are the fundus, body, infundibulum (Hartman pouch), and the neck[27].

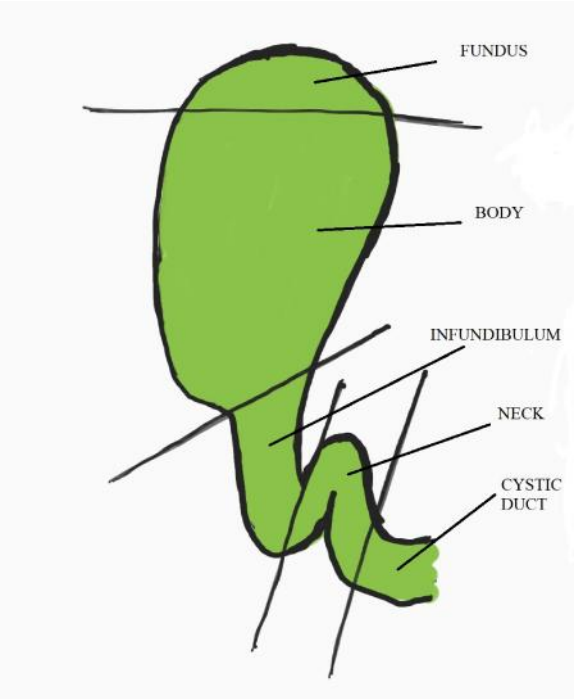


Illustration 1. Parts of the Gall Bladder

The neck of the gall bladder drains into the cystic duct. The lumen of the cystic duct has characteristic mucosal folds called the spiral valves of Heister[28]. The cystic duct can run a very short course draining into the right hepatic duct or it can also course alongside the common hepatic duct for a distance, inserting into it just above the pancreas.

The blood supply to the gallbladder is from the cystic artery, which is usually a branch of the right hepatic artery. Significant variation in the course of the cystic artery has been reported. Rarely, it may branch from the left hepatic artery or hepatic artery proper, running anteriorly to the hepatic duct on its course to the gallbladder. It may also arise from a replaced right hepatic artery from the superior mesenteric artery (SMA)[27].

Venous drainage of the gallbladder includes veins that follow the cystic and hepatic ducts to drain into the liver via the portal system as well as veins draining directly into the liver[27].

LAPAROSCOPIC ANATOMY:

The advent laparoscopy led to a new approach into biliary anatomy especially that of the Calot's triangle and the term 'laparoscopic anatomy' has been developed. The 'laparoscopic view' of the area around the GB especially the Calot's triangle contributes to misidentification of structures[29].

The triangle of Calot was originally described to have the common hepatic duct as the left border, the cystic duct inferiorly and the cystic artery superiorly[30]. The commonly accepted working definition of the triangle of Calot, however, is described as having the inferior surface of the right lobe of the liver as the upper border and the cystic duct as the lower border (Illustration 2)[28]. The content of this triangle is the cystic lymph node of Lund. Dissection of this triangle is of key significance during cholecystectomy, because in this triangle runs the cystic artery, often the right branch of the hepatic artery, and occasionally a bile duct, which should always be displayed before cholecystectomy. In case there is a replaced or accessory common or right hepatic artery, it usually runs behind the cystic duct to enter the triangle of Calot[31].

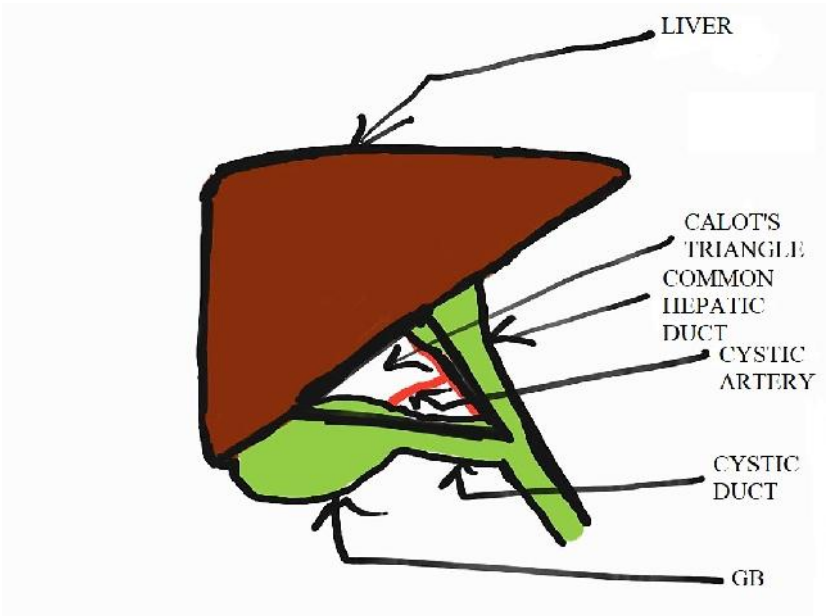


Illustration 2. Calot's triangle

The Rouviere's sulcus is a fissure on the liver between the right lobe and caudate process and is clearly seen during a LC during the posterior dissection in a majority of patients. It corresponds to the level of the porta hepatis where the right pedicle enters the liver. It has hence been recommended that all dissection be kept to a level above (or anterior) to this sulcus to avoid injury to the bile duct. Also, this being an 'extra biliary' reference point it does not get affected by distortion due to pathology.

A clear delineation of the junction of the cystic duct with the GB along with the demonstration of a space between the GB and the liver clear of any other structure other than the cystic artery is also recommended as an essential step to prevent bile duct injury. This is called safety window or critical view of safety[32]. A difficulty in achieving this critical view of safety mainly arises due to adhesions or difficulty in grasping the gall bladder.

PHYSIOLOGY:

Bile flowing from the liver drains to the CBD. The resting tone in the sphincter of Oddi prevents the flow of bile into the duodenum and allows the bile to fill the duct followed by retrograde filling of the cystic duct and gallbladder. The bile is concentrated by the gallbladder epithelium, which contains channels that actively transport sodium chloride. Water follows along with sodium chloride, thereby concentrating the bile[27].

Contraction of the gallbladder is under the control of multiple signals. The major positive mediators of contraction are cholecystokinin (CCK) and parasympathetic innervation. CCK is a hormone secreted by the epithelium in the duodenum in response to intraluminal nutrients. Its secretion results in contraction of the gallbladder in the post-prandial period to move bile into the duodenum for

digestion. The hepatic branch of the vagus nerve supplies parasympathetic innervation, which also promotes contraction. Like the rest of the intestinal tract, the gallbladder is innervated by the enteric nervous system, promoting coordination with the migratory motor complex[27].

There are also multiple modulators of gallbladder contraction. The sympathetic innervation to gallbladder is via the celiac plexus. It promotes relaxation of the gallbladder smooth muscle. Recent literature also supports that components of bile itself dampen gallbladder contractions through G-protein coupled receptors[33]. Stasis of bile in the gallbladder is thought to contribute to the formation of cholelithiasis.

PATHOGENESIS OF CHOLELITHIASIS:

Gallstones are divided into the 3 following types: cholesterol stones, black and brown pigment stones. Cholesterol stones (>50% cholesterol content) are the most common in the Western world and account for approximately 70% of all stones. Black pigment stones account for the remainder of stone carriers in the Western world and can be caused by haemolytic disorders or cirrhosis. Brown pigment stones are seen most commonly in East Asia and are associated with infection of the biliary tree[34]. The prevalence of cholesterol gallstones seems to be increasing worldwide nowadays as a result of socioeconomic and lifestyle changes associated with an increase in a more Western diet[35]. The formation of cholesterol gallstones has been illustrated since the 1960s with variations of Admirand's triangle, which is essentially an equilibrium diagram of bile salt, cholesterol, and lecithin. Supersaturation with cholesterol, a decrease in the quantity of bile salt or lecithin, or a combination of these factors promotes gallstone formation (Illustration 3)[36]. Many of the previously mentioned risk factors like female gender, increasing age and body mass index, rapid

weight loss, pregnancy, sex steroids, comorbidities such as diabetes mellitus, cirrhosis, hypertriglyceridemia, Crohn's disease and conditions that lead to bile stasis alter the composition of bile, thus leading to the formation of gallstones[37-42].

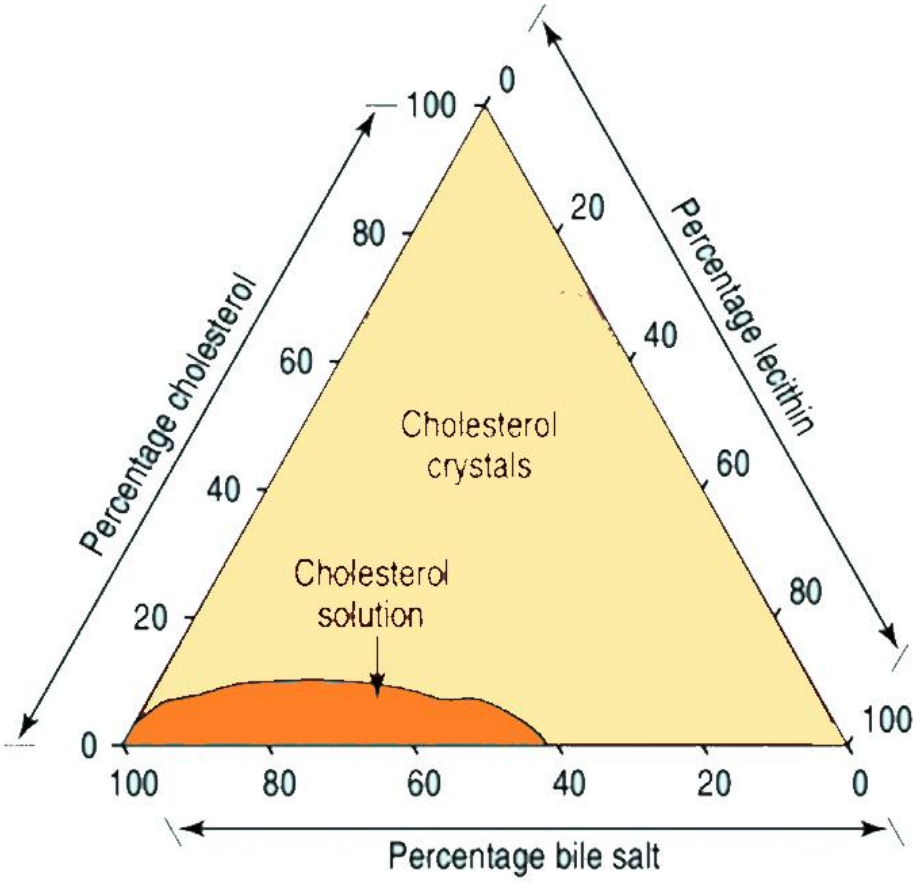


Illustration 3. Admirand's triangle

MANAGEMENT:

Asymptomatic gall bladder (GB) stone is treated conservatively in majority of cases because complications develop in only 1% to 2% of patients annually[43]. The current standard for management of uncomplicated gallstone disease, or symptomatic cholelithiasis, is laparoscopic cholecystectomy. Medical management consists of oral dissolution therapy with oral bile acids and is reserved for patients who are not

candidates for surgery and have small (equal to or less than 5 mm in size), uncalcified, cholesterol stones in a functioning gallbladder with a patent cystic duct.

Oral litholysis involves use of oral hydrophilic bile acids for dissolution therapy for cholesterol gallstones. Ursodeoxycholic acid is currently used as it leads to decreased biliary cholesterol secretion, increased solubility of cholesterol by forming liquid crystals, and reduced intestinal absorption. However, this approach is successful only in a small subset of patients; as recurrence is common (30%–50% at 5 years) and the cost-benefit ratio is unfavourable[44]. A variety of other medications and pathways have been studied in their effect on gallstone formation, including statins, aspirin, ezetimibe, and nuclear receptors that drive lipid homeostasis in the hepatobiliary and gastrointestinal systems[45-48].

Studies have reported that nutritional modifications, such as increased dietary polyunsaturated or monounsaturated fatty acids, fibre, caffeine, vegetable protein, and a diet low in refined carbohydrates, may aid in reduction of symptoms[49]. Overall, most patients will undergo laparoscopic cholecystectomy as a definitive and effective management for symptomatic cholelithiasis[50].

LAPAROSCOPIC CHOLECYSTECTOMY:

Laparoscopic cholecystectomy has been described as the ‘gold standard’ for the treatment of symptomatic gallstones presenting as chronic cholecystitis[24]. However, the laparoscopic approach was initially considered to be relatively contraindicated or unsafe in acute cases. It was believed that inflammation of the tissues makes the dissection difficult, thus increasing the risk of serious complications as well as the rate of conversion to open surgery[51]. In 1990s, the feasibility, safety and benefits of early laparoscopic surgery in acute cholecystitis were proved by several studies and it soon became the treatment of choice for acute cholecystitis as well[52]. In

1990, 10% of cholecystectomies were being performed laparoscopically in the United States. This figure has risen dramatically over the past two decades and stands at 90.5% in 2010. Never before had a surgical revolution occurred so quickly[53].

The major advantage of the laparoscopic approach was improved recovery, which allowed patients to have better quality of life in the immediate postoperative period[53]. Even in cases of acute cholecystitis patients undergoing laparoscopic cholecystectomy had a significantly lower rate of complications, shorter hospital stays and more comfortable postoperative period when compared to those undergoing open cholecystectomy[54].

A few disadvantages have been pointed out against laparoscopic cholecystectomy. Three-dimensional depth perception is limited by the two-dimensional monocular image of the videoscope. In case of significant haemorrhage there is more difficulty in control using laparoscopic technology than in an open surgical field. Also, there is less haptic discrimination of structures with laparoscopic instruments as opposed to manual palpation during open cholecystectomy. Carbon dioxide insufflation to create the pneumoperitoneum is associated with numerous potential risks, including reduction of vena caval flow and systemic hypercarbia with acidosis[26].

The major indication for elective LC is symptomatic cholelithiasis, also known as “biliary colic.” In one of the large studies from Europe published recently, the indications for LC were cholelithiasis in 75.5%, pancreatitis in 13.3%, cholecystitis in 6.3%, choledocholithiasis in 3.05%, and other complications in 1.2% of cases[55].

Absolute contraindication for laparoscopic cholecystectomy is the inability to tolerate abdominal insufflation with carbon dioxide.

Relative contraindications include:

- Suspicion of gallbladder cancer
- Cirrhosis, portal hypertension, or bleeding disorders
- Previous abdominal operations precluding minimal invasive approach
- Pregnancy (first or third trimester)[56]

Pregnancy is not an absolute contraindication to LC and can be performed safely with a few modifications such as the Hasson technique for abdominal access, a left-sided bed tilt, and appropriate placement of trocars to accommodate the size of the gravid uterus. LC is considered the preferred technique for the pregnant patient as it offers a faster postoperative recovery, reduced opioid usage, and fewer wound complications[53].

DIFFICULT LAPAROSCOPY AND CONVERSION:

Laparoscopic cholecystectomy (LC) can be the easiest or the most difficult laparoscopic operation. A traditional marker of difficult LC has been conversion to open surgery and anticipation of conversion can help in counselling patients and preparing them for longer stay and complications. Difficult LC can also have similar implications in terms of operating time, expertise required and training of juniors[11].

Bile duct injuries (BDI) can be a complication in selected cases of LC and their importance cannot be underestimated[57,58]. The incidence of such injuries ranges between 0% to 6%[59,60]. Many times, these injuries are attributed to intra-operative difficulty which can be termed as difficult laparoscopic cholecystectomy for further references.

It was previously thought that LC has less morbidity than open cholecystectomy (OC) even if it takes longer time[61]. However, Giger et al. in their analysis from Swiss database have shown that risk of complications of LC is

increased with conversion as well as with longer operating time that is typically seen in difficult LC. They claimed that addition of each 30 min duration increases chances of both local and systemic postoperative complications[62]. This finding demonstrates why predicting difficult LC is as important as predicting conversion.

Difficult LC has the following predicting factors:[63,64]

- Age greater than 60 years
- Male sex
- Obesity
- Presence of acute cholecystitis
- Chronic cholecystitis and fibrosis
- Liver cirrhosis
- Clinically palpable gall bladder[5]
- Increased wall thickness[65]
- History of prior upper abdominal surgery
- Cystic duct stones
- Large liver and big gall bladder
- Cholangiocarcinoma of gall bladder and biliary tract
- Anatomic variation
- Biliodigestive fistula
- Diabetic patients
- Less experienced surgeon

Surgeon's experience is an important factor in the management of difficult LC. In a study by Gabriel et al, surgeons with high caseload and those who have performed >100 cholecystectomies were more able to do difficult LC[66]. It has also been noted that surgeons who have high caseload, have less complications and

conversion[67]. Huang et al reported 6 bile duct injuries among the first 10 to 15 laparoscopic operations performed by a surgeon. However, these findings were not concurrent with those of a few other investigators who reported no difference in the incidence of complications between the first and the second series of 1500 LCs[69]. Targarona et al have reported that the highest incidence of complications occurs with surgeons who had done >50 operations[70].

A scoring system has also been proposed which takes into consideration the time taken for surgery, bile/stone spillage, injury to cystic duct or cystic artery and conversion to open cholecystectomy and further divides the procedure into 3 grades as per the criteria mentioned[71].

Difficult laparoscopic cholecystectomy has been sub-divided as per the step in which the difficulty is encountered and they are mentioned in the following table with measures to tackle them:[64]

DIFFICULTY	**SOLUTION**
Difficult access and pneumoperitoneum	Hasson technique, optical port, avoiding Veress needle insertion in midline and near previous scars.
Difficult in grasping/retraction of GB	Applying suture at fundus
Difficult dissection of Calot's triangle	Laparoscopic subtotal cholecystectomy, fundus first approach
Short and wide cystic duct	Careful suturing, endolooping
Abnormal anatomy	Open cholecystectomy, finger dissection, stenting of CBD pre-operatively, percutaneous cholecystostomy, intra-operative cholangiogram, intra-operative methylene blue injection technique, intra-operative fluorescence imaging
Difficult retrieval of specimen	Suction, crocodile grasper, retrieval bag

Table 1: Difficulties encountered in laparoscopic cholecystectomy and their suggested solutions

Every surgeon has a different approach towards difficult LC. Diversity of the techniques and methods to manage difficult LC are based on experience of the surgeon. Current evidence from research does not specify if any approach is superior to the other as there is no randomized controlled trial to compare laparoscopic subtotal cholecystectomy (LSTC), fundus first or antegrade or other techniques to manage difficult LC. However, many studies involving large numbers of patients have demonstrated the safety and efficacy of certain techniques. There has been found

no consensus among surgeons to manage difficult GB but there has been a growing interest in LSTC and fundus first techniques.

Currently 5 popular approaches are being practiced for difficult LC. These are in order of preference (based on current conversion rate and complications), LSTC if possible, fundus first or antegrade LC, intraoperative cholangiogram and LC, OC, or stop the procedure and consider another date. Conversion and rescheduling should not be considered as a failure. In many situations rescheduling is helpful as a difficult GB can be removed easily after some time when storming inflammation is under control[64].

The conversion rate has come down in comparison with the previous decade. However, complete avoidance of bile duct injury and conversion is not achievable in the current era of surgical practice. Unfortunately, iatrogenic injuries and other potential difficulties direct the procedure to open cholecystectomy (OC) with definite increase in complications and cost[64]. Occasionally anatomical or physiological considerations cause a hindrance to the minimal access approach, and conversion to open surgery in such cases reflects sound clinical judgment and should not be considered a complication[26]. The conversion rate can be correlated to access problems, abnormal or unusual anatomy due to acute or chronic inflammation, patient comorbidities, bleeding, visceral injuries, and surgical experience[72]. It is reported that approximately 2% to 15% of patients require conversion to open surgery for various reasons[6,73].

Conversion to open surgery is a safe choice in cases of extreme difficulty[74,75]. Surgeons having insufficient laparoscopic experience, also have a high conversion rate as discussed earlier[72]. Despite this, OC is a valuable option in certain cases in which dense adhesions, abnormal anatomy, GB malignancy, choledochal cyst, Mirizzi

syndrome, or enterobiliary fistulas are diagnosed. Performing LC for these patients (except GB cancer) is a secondary consideration; however, intraoperative diagnosis of the unexpected pathologies requires prompt decision-making and change of the operative plan, which often necessitate a complicated operation.

The major causes of conversion are dense adhesions in Calot's triangle or a friable gallbladder[6]. Emergency conversions are usually due to bleeding from the cystic artery and injuries to CBD.

Schrenk et al. have analyzed pre- and perioperative risk factors for conversion to OC in 1300 patients and found that right upper abdominal quadrant rigidity, thickening of the gallbladder wall on ultrasound scans, evidence of dense adhesions, and acute cholecystitis were significant indicators for conversion to OC in 56 (4.3%) converted cases[76]. In another study Fried et al. reported 5.6% conversions to OC. Age above 65, acute cholecystitis, thickened gallbladder wall on ultrasound scans, obesity, and male sex were determining factors for conversion in that study[65]. It was seen in a study by Alponat et al that in addition to acute cholecystitis and thickened gallbladder wall on ultrasound scans elevated total leucocyte counts (TLC) and ALP levels were significant predictors. These biochemical abnormalities commonly accompany acute inflammation of biliary tree and are indicators of a complicated disease[6].

Rattner et al report that patients with acute cholecystitis who had laparoscopic cholecystectomy that required conversion to open cholecystectomy had a higher TLC than those who had an uneventful laparoscopic procedure[77]. Halachmi et al showed that with TLC of more than 18 x 10^9/L or more, the incidence of conversion was three times that of the group with a lower TLC. Additional explanatory factors associated with conversion were empyema or gangrene of the gallbladder, male sex, and age

over 60 years. It was also noted that if the temperature was 38°C or more, the complication rate was twice that of the group with lower temperatures[8].

Rosen et al reported that for elective laparoscopic cholecystectomy, morbidly obese patients with chronic cholecystitis and a thickened gallbladder wall were more likely to require conversion[7].

COMPLICATIONS:

There are various complications encountered during LC. Some are specific to this technique while some are common to laparoscopic surgery in general. It should be emphasized that LC is a surgical procedure that should have a low incidence of complications and efforts should be concentrated on prevention rather than treatment of these complications[56]. A few of them are discussed here.

- Hollow viscus injury should be recognized early and repaired.
- Bile leak may be from the cystic duct stump, an aberrant Luschka duct, or a bile duct injury (BDI). Its management depends on the presence of abdominal drainage and if intraoperative cholangiography was performed. Ultrasonography or computed tomography scan of the abdomen is required for evaluation of free fluid and collection the abdomen. ERCP with stenting, sphincterotomy, or both should be considered early. Placement of a percutaneous abdominal drain should be done for drainage of bilomas[56].
- BDI most frequently results from a failure to recognize the anatomy of the triangle of Calot (e.g., common bile duct or right hepatic duct are at times mistaken for the cystic duct), but may also result from excessive use of electrocautery or clips to control bleeding in the porta hepatis, or excessive traction on the cystic duct and common bile duct during dissection. (Deziel)

Its management depends on the timing of recognition (intraoperative vs postoperative), nature, and severity of the injury.

- Retained spilled stones: every effort should be made to profusely irrigate the operative area and to recover spilled stones when they occur.
- Retained CBD stones can usually be managed endoscopically if identified in the postoperative period[56].

C-REACTIVE PROTEIN:

C-reactive protein (CRP) is an acute-phase protein with a half-life of 19 hours[79]. It synthesised and secreted by the liver, mainly in response to interleukin-6 and other pro-inflammatory cytokines. It is a member of pentraxin family of proteins[79,80]. It is also produced by certain cells present in the vascular wall such as endothelial cells, smooth muscle cells, and adipose tissue[81,82]. It was discovered by Tillett and Francis in 1930[83]. CRP is a 224-residue protein with a molecular weight of 25106 Da. The CRP gene is located on chromosome 1[84]. The protein was named C-reactive protein because of its capacity to precipitate the somatic C-polysaccharide of Streptococcus pneumonia[79]. It has no relationship with protein C or C-peptide.

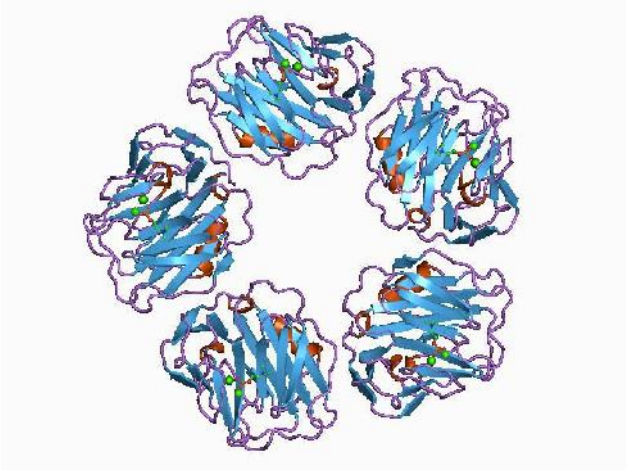


Illustration 4 Image depicting C-reactive protein

CRP binds to numerous ligands including phospholipids exposed on bacterial surfaces, damaged or dying eukaryotic cells, and cellular nuclear debris. Once bound, it activates the classical complement cascade, binds to the Fcγ receptors and stimulates phagocytosis[14]. High CRP concentrations in serum may be seen in cases of infection, inflammation, trauma, malignancy and tissue infarction. It is, therefore, not specific for a particular disease. A rise in CRP may be seen earlier in a disease process when compared to other non-specific markers (e.g. fever), and falls rapidly on resolution of inflammation[85]. Therefore, CRP may be useful as a screening test to detect an inflammatory response early in its course, and also for monitoring disease activity and response to therapy in conditions where CRP is raised[15].

The reference range for C-reactive protein is as follows:

- CRP: 0-10mg/L
- High-sensitivity CRP (hs-CRP): < 3 mg/L[83]

CRP is known to increase in acute or chronic inflammatory conditions, tissue necrosis or tissue injury, ischemia or infarction of issues, infection, inflammation, metabolic syndrome, malignant tumours especially of breast, lung and gastrointestinal tract, acute pancreatitis, post-surgery, burn, leukaemia, tobacco smoking, hormone replacement therapy, obesity. It is known to decrease in states of exercise, weight loss and moderate alcohol consumption, medications like statins, niacin and fibrates[81].

Schäfer et al. reported that, CRP levels on admission were found to be determinants of surgical approach-laparoscopic or open along with American Society of Anaesthesiology grade, duration of symptoms, age and TLC on admission in a study for acute cholecystitis[9]. Another study done for acute cholecystitis by Gurbulak et al concluded that CRP can be accepted as a strong predictor in classifying the

disease into different grades and treatment can be reliably planned according to this classification.

Another study found that CRP level at admission and male gender were strongly related to conversion of emergency LC in patients with acute cholecystitis[10]. Wevers et al also concluded in their study of acute cholecystitis that higher age and elevated CRP level were independent predictors for conversion. Surgery for acute cholecystitis in patients with age >65 years and/or CRP level >165 mg/L should be considered as high risk for conversion[12].

Mok et al studied CRP level of patients during their index admission for acute cholecystitis. They then correlated the conversion rates to these values and concluded that patients with high index CRP values were at an increased risk of difficult LC and conversion irrespective of timing of operation[11].

METHODOLOGY

The present study was conducted in the Department of General Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, from January 2017 to December 2017 on 100 patients undergoing laparoscopic cholecystectomy.

Study design

The study design was a cross-sectional study.

Study period and duration

The present study was carried out for a period of one year from January 2017 to December 2017

Place

This study was done under the Department of General Surgery of a tertiary care teaching hospital attached to KAHER's Jawaharlal Nehru Medical College, Belagavi.

Source of Data

All patients undergoing laparoscopic cholecystectomy were included in the study.

Sample size

The study sample was comprised of 100 patients.

Formula:

$n = 4pq/d^2$

where,

p= incidence of difficult laparoscopy in patients with high CRP

q= (100-p),

d= permissible error

Statistical analysis: Pearson's Chi Square test

Sampling procedure

Systematic Random Sampling

SELECTION CRITERIA

Inclusion criteria

- Patients with symptomatic cholelithiasis/acute cholecystitis requiring LC.
- Patients aged 16 years and above.
- Patients of either sex.

Exclusion criteria

- Uncooperative and unwilling patients.
- Patients with history of anaphylaxis to opioids.
- High BMI (>35)
- Previous upper abdominal surgery
- Those who refuse surgery

As the study aims to look at the association between CRP and difficult cholecystectomy/conversion due to GB pathology only, the following patients are excluded to avoid confounding effect of these factors on difficulty/conversion as these co morbidities could cause derangement of CRP levels:

- Lymphoma
- Known malignancy of breast, lung, gastrointestinal tract
- Acute pancreatitis
- Concurrent appendicitis
- Hormone replacement therapy
- Autoimmune disorders (e.g.-Systemic lupus erythematosus, Behcets, Rheumatoid arthritis)

- Inflammatory bowel disease
- Bacterial infections at sites apart from the biliary tract
- Tuberculosis
- Pregnant women
- Hepatic failure

Ethical clearance

The Ethical Clearance was obtained from the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belagavi prior to the commencement.

Informed Consent

Those patients who fulfilled selection criteria were briefed about the nature of study and a written informed consent regarding the study, investigations sent and procedure involved was obtained (Annexure I) prior to the enrolment.

Method of collection of data

Patients satisfying selection criteria were interviewed and the demographic data such as age and sex, presenting complaints were noted. Further the patients were subjected to clinical and systemic examination and the findings were noted on a predesigned and pretested proforma (Annexure II). Blood samples were sent for all the included patients for analysis of hs-CRP by immunoturbidometric analysis.

Procedure of laparoscopic cholecystectomy

Position

Patient was placed in classical supine position with surgeon standing at the patient's left side. Nasogastric tube was used to ensure complete gastric deflation during the procedure, since a distended stomach and duodenal cap can obscure the operative field. The urinary bladder was emptied by a catheter prior to creation of pneumo-peritoneum. If catheterization was not done, percussion the suprapubic

region to exclude a distended urinary bladder was done before inserting the Veress needle. The nasogastric tube was removed at the end of the operation. Part preparation and draping was done in the standard manner.

Access to peritoneal cavity

Open technique using the modified Hasson's cannula or closed technique using Veress needle.

Insufflation of the peritoneal cavity was done with carbon dioxide through the supraumbilical/ infraumbilical/ transumbilical trocar if open technique was adopted, or following insertion of Veress needle if closed technique was adopted to a pressure of approximately 10 to 15 mmHg. During the insufflation all quadrants of the abdomen were percussed to confirm uniform distension. Once pneumoperitoneum was established, a 10mm port was inserted at the transumbilical/ supraumbilical/ infraumbilical region, through which the camera (30 degree) was introduced.

Following this the abdomen was inspected for the following;

a. To detect any injury to organs or vessels caused during insufflations and insertion of main trocar.

b. Exclusion of additional unsuspected intra abdominal pathology.

c. Assessment of the feasibility of LC.

After inspection, three more ports were inserted under vision. A 10-mm port was placed in the epigastrium, a 5-mm port in the middle of the clavicular line, and a 5-mm port in the right flank, in line with the gallbladder fundus. Through the lateral-most port, a grasper was used to grasp the gallbladder fundus. It was retracted over the liver edge upward and toward the patient's right shoulder to expose the proximal gallbladder and the hilar area. Exposure of the hilar area may be facilitated by placing

the patient in reverse Trendelenburg position with slight tilting of the table to bring the right side up.

The presence of adhesions, pus in gall bladder (empyema), gangrene, increased wall thickness, difficulty in grasping the gall bladder, perforation were looked for:

Through the midclavicular port a second grasper was used to grasp the gallbladder infundibulum and retract it laterally to expose the triangle of Calot. Before this, any adhesions between the omentum, duodenum, or colon, and the gallbladder were taken down. Most of the dissection was carried out through the epigastric port using a dissector, hook cautery, or scissors. The dissection started at the junction of the gallbladder and the cystic duct. A helpful anatomic landmark was the cystic lymph node of Lund.

The peritoneum, fat, and loose areolar tissue around the gallbladder and the cystic duct–gall bladder junction were dissected off toward the bile duct. This was continued until the gallbladder neck and the proximal cystic duct were clearly identified. The next step was the identification of the cystic artery, which usually runs parallel to and somewhat behind the cystic duct. Once the cystic duct and artery were well exposed, the cystic duct was clipped and cut between the two clippings. A wide cystic duct that was too big for clips, required the placement of a pre-tied loop ligature to close. The cystic artery was then clipped and divided. Finally, the gallbladder was dissected out of the gallbladder fossa, using either a hook or scissors with electrocautery. Before the gallbladder was removed from the liver edge, the operative field was carefully searched for bleeding points, and the placement of the clips on the cystic duct and cystic artery was inspected. The gallbladder was removed through the

umbilical or epigastric incision. The fascial defect and skin incision were enlarged if the stones were large.

If the gallbladder was acutely inflamed or gangrenous, or if the gallbladder was perforated, it was placed in a retrieval bag before it was removed from the abdomen. Any bile or blood that has accumulated during the procedure was sucked away, and if stones were spilled, they were retrieved, placed inside a retrieval bag, and removed. If the gallbladder was severely inflamed or gangrenous or if any bile or blood was expected to accumulate, a closed-suction drain was placed through one of the 5-mm ports and left underneath the right liver lobe close to the gallbladder fossa.

After this final inspection was done to look for any oozing, if present, haemostasis was achieved. All ports were removed under vision after decompressing the abdominal cavity to evacuate the carbon dioxide. Ports were closed using 1 no. Polyglactin (Vicryl) port closure for the rectus sheath and skin using 3-0 Nylon (Ethilon). Sterile dressing was applied.

In case of difficult dissection methods like subtotal cholecystectomy and conversion to open cholecystectomy were used at the surgeon's discretion.

ANALYSIS OF OUTCOMES

Demographics

Patients' age, sex, site of pain abdomen, mean weight, vitals, co- morbidities like hypertension and diabetes were assessed.

Difficult laparoscopic cholecystectomy

Intra-operative findings were noted. The presence of following intra-operative findings were considered as a case of difficult laparoscopy and a predesigned, pretested and pre-validated proforma was filled. (Annexure II)

- Adhesions
- Pus in gall bladder (empyema)
- Gangrene
- Increased wall thickness
- Difficulty in grasping the gall bladder
- Perforation

Modification of the procedure due to difficulty (like subtotal cholecystectomy was also noted.

Conversion

The conversion of laparoscopic to open procedure and the reason for conversion was also be noted.

Statistical analysis

All the relevant data was tabulated. Mean hs-CRP level was calculated. The hs-CRP levels were compared to the difficulty encountered and sensitivity, specificity and Yoden's index was calculated at various levels of hs-CRP to get the most desirable cut-off value. Pearson's chi square test was applied using that cut-off value and P value was calculated. A P-value of <0.05 was considered significant. An arbitrary cut-off of 10mg/L was used to determine significance of relationship of hs-CRP with conversion.

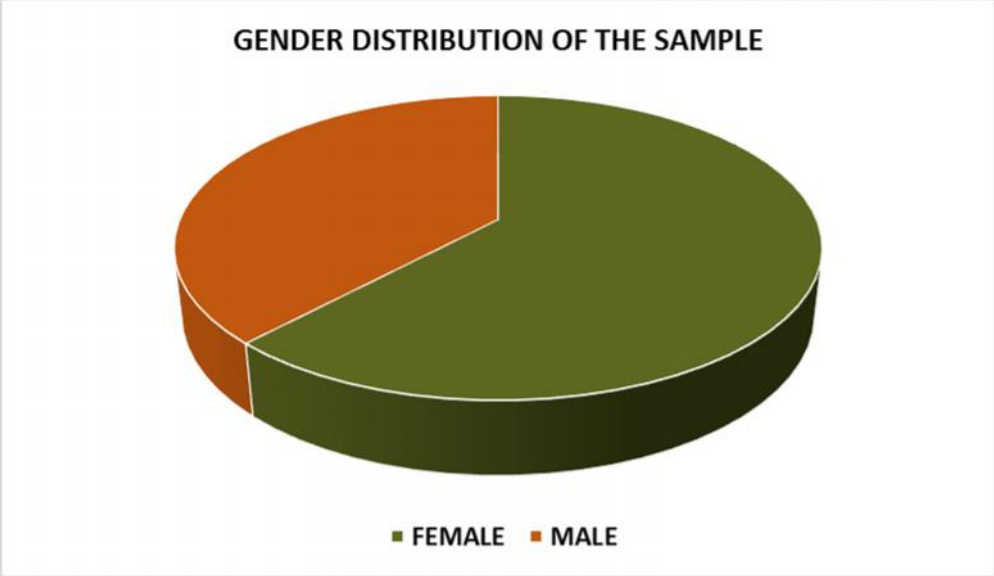
RESULT

The data obtained was tabulated and analysed using Pearson's Chi square test. The final results and observations were tabulated as below

TABLE 2: GENDER DISTRIBUTION

GENDER	NUMBER
FEMALE	62
MALE	38
TOTAL	100

GRAPH 1: GENDER DISTRIBUTION

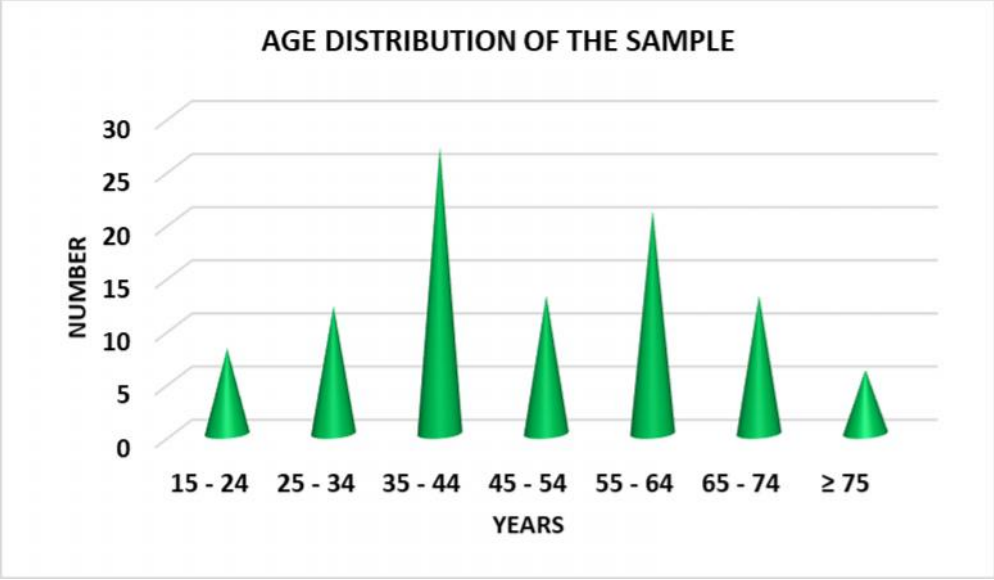


In the present study 38% of the patients were males and 62% were females. The male to female ratio was 1:1.63. The sex distribution in group A and B was comparable

TABLE 3: AGE DISTRIBUTION

AGE	NUMBER
15 – 24	8
25 – 34	12
35 – 44	27
45 – 54	13
55 – 64	21
65 – 74	13
≥ 75	6
TOTAL	100

GRAPH 2: AGE DISTRIBUTION

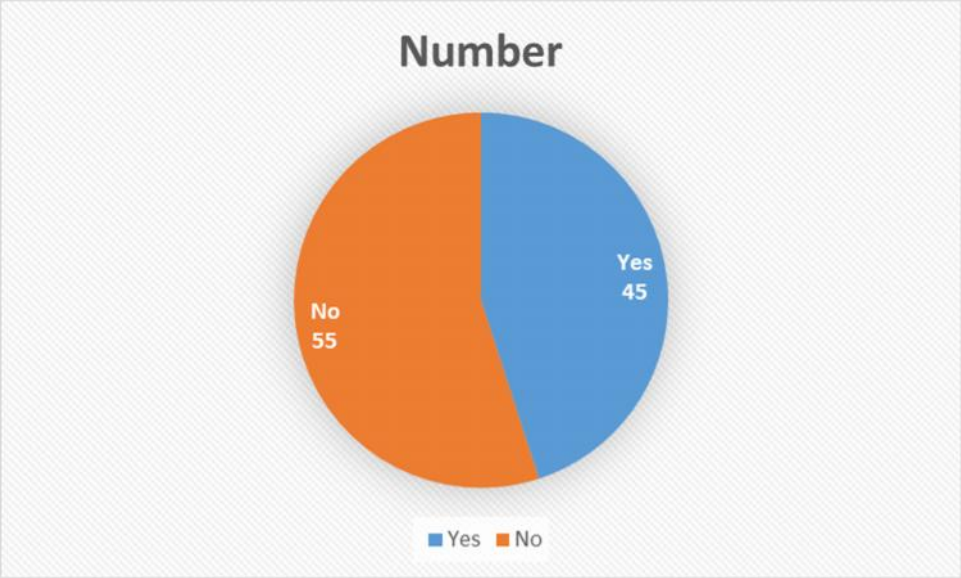


In this study the commonest age group in patients was 35 to 44 years (27%) followed by 55-64 years (21%).

TABLE 4: DIFFICULT LC

Difficult	Number
Yes	**45**
No	**55**
Total	**100**

GRAPH 3: DIFFICULT LC

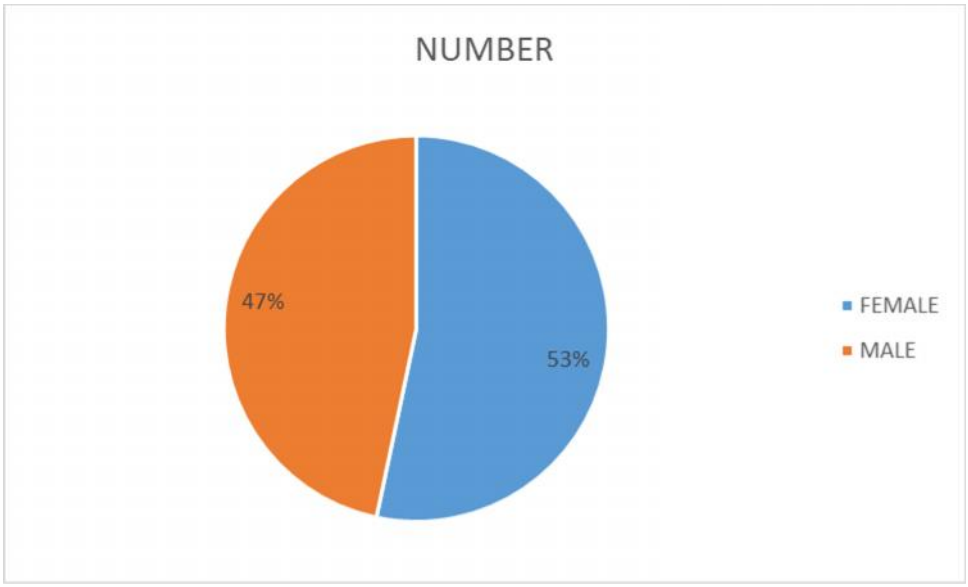


According to the mentioned criteria, 45% of the laparoscopic cholecystectomies were classified as difficult and 55% were not difficult.

TABLE 5: GENDER DISTRIBUTION OF DIFFICULT LC

GENDER	NUMBER
FEMALE	24
MALE	21
TOTAL	45

GRAPH 4: GENDER DISTRIBUTION OF DIFFICULT LC

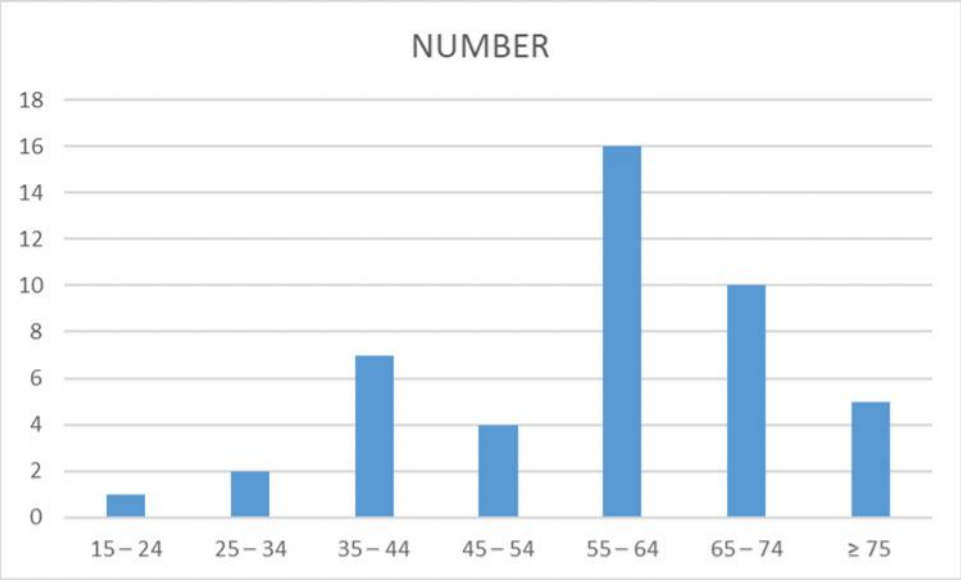


47% of the difficult cholecystectomies were in males and 53% in females. The chi-square statistic was 2.6084. The p-value was 0.106297. This result is not significant at $p < 0.05$

TABLE 6: AGE DISTRIBUTION OF DIFFICULT LC

AGE	NUMBER
15 – 24	1
25 – 34	2
35 – 44	7
45 – 54	4
55 – 64	16
65 – 74	10
≥ 75	5
TOTAL	45

GRAPH 4: AGE DISTRIBUTION OF DIFFICULT LC

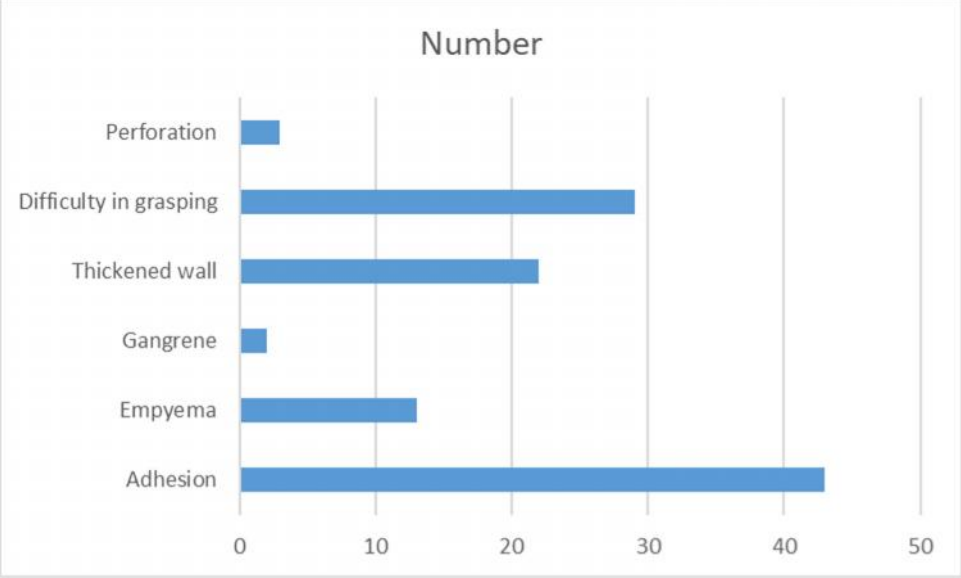


Majority of the difficult cases were in the age-group of 55-64years followed by 65-74 years.

TABLE 7: DIFFICULTIES ENCOUNTERED IN LC

Difficulty	Number
Adhesion	**43**
Empyema	**13**
Gangrene	**2**
Thickened wall	**22**
Difficulty in grasping	**29**
Perforation	**3**

GRAPH 5: DIFFICULTIES ENCOUNTERED IN LC



Adhesions were the most commonly encountered difficulty seen in 43(95.56%) of the difficult cases followed by difficulty in grasping seen in 29(64.44%).

The mean hs-CRP levels were 6.57mg/L.

A table was constructed using "Receiver's Operating Characteristic" (ROC) curve technique using continuous variable values of hs-CRP and sensitivity, specificity and Yoden's index was calculated taking each value as cut-off. An hs-CRP of 4mg/L was found to be optimum to predict a difficult LC as per its results.

TABLE 8: DIFFICULT LC AT CUT-OFF 4mg/L

	Difficult	**Not difficult**	**Total**
hsCRP>4	**40**	**6**	**46**
hsCRP<4	**5**	**49**	**54**
Total	**45**	**55**	**100**

Sensitivity= 88.89%

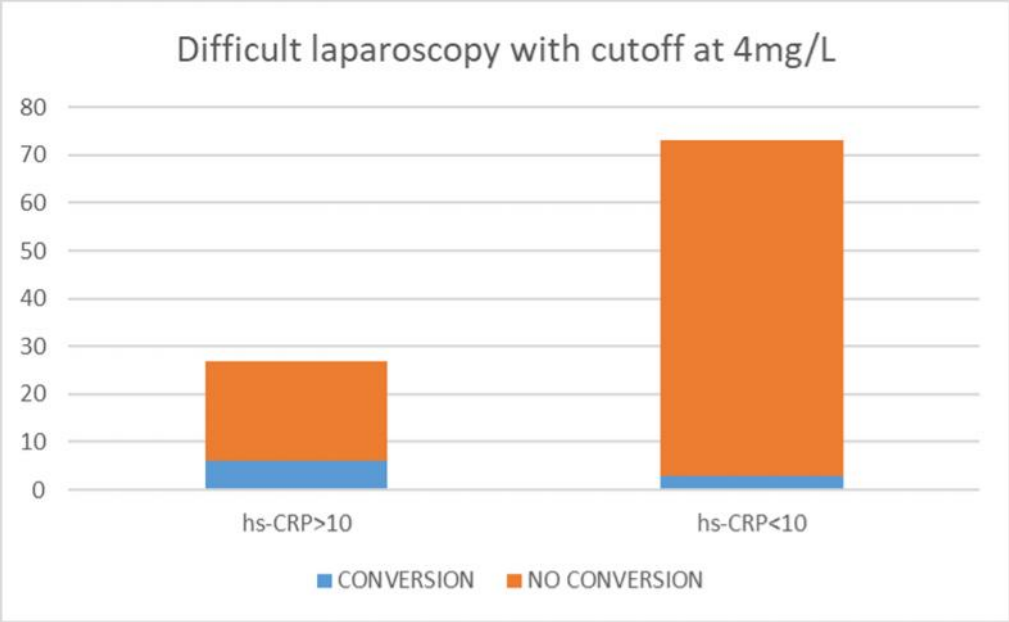
Specificity= 89.09%

Positive predictive value= 86.96%

Negative predictive value= 90.74%

Yoden index= 77.98%

GRAPH 6: DIFFICULT LC AT CUT-OFF 4mg/L



The chi-square statistic is 60.5882. The p-value is <0.001. This result is significant at $p < 0.05$.

TABLE 9: CONVERSION TO OPEN SURGERY AT CUT-OFF 10mg/L

	CONVERSION		
hs-CRP>10	**Y**	**N**	**TOTAL**
Y	6	21	27
N	3	70	73
TOTAL	9	91	100

Sensitivity = 66.67%

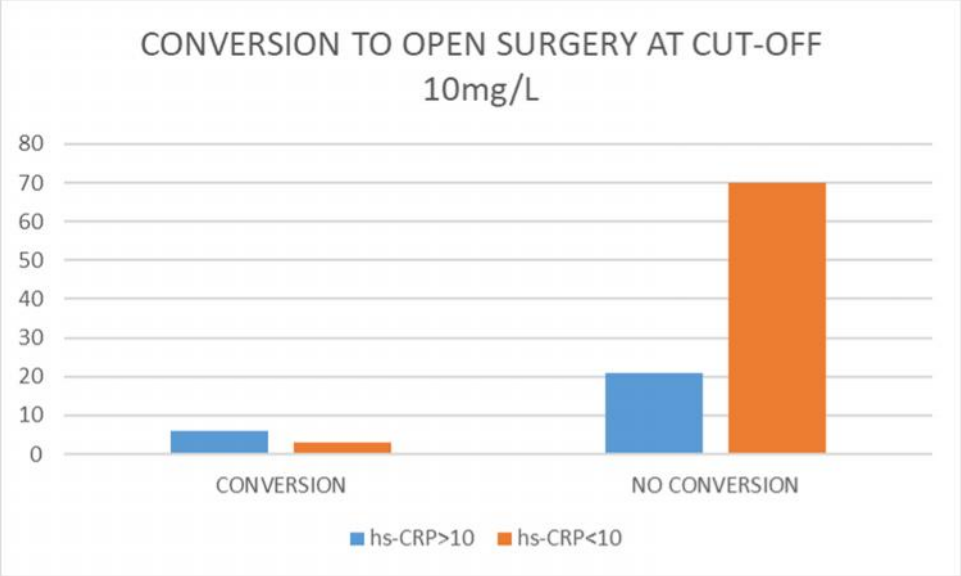
Specificity = 76.92%

Positive predictive value= 22.22%

Negative predictive value= 95.89%

Yoden index= 43.59%

GRAPH 7: CONVERSION TO OPEN SURGERY AT CUT-OFF 10mg/L



The chi-square statistic was 7.8953. The p-value was 0.004956. This result is significant at $p < 0.05$.

DISCUSSION

The undisputed benefits of laparoscopic cholecystectomy make it the procedure of choice for symptomatic cholelithiasis. With growing experience, laparoscopic cholecystectomy is becoming increasingly safe and cost-efficient in an ambulatory setting[86,87].

At times LC becomes difficult. It takes longer time even with bile/stone spillage and occasionally it requires conversion to open cholecystectomy. It is very difficult to say preoperatively whether it is going to be easy or difficult. The degree of difficulty is again impossible to predict clinically.

Difficult LC is a hot issue; it creates arguments and debates among surgeons till date. There has been a constant search for the factors that predict this difficulty and many studies have been carried out with this mindset. There is cumulative evidence, based on retrospective studies, that identifies certain factors predicting difficult LC[64]. Randhawa et al even developed a scoring system for evaluating the same[5].

Halachmi et al reported in their study that raised TLC and fever correlated with difficult LC. As both manifestations are definite results of ongoing inflammation, there was an increased interest in evaluation of a universal inflammatory marker as a predictor of difficult LC[8]. C-reactive protein is a sensitive serum marker of inflammation which has been used previously for varying purposes in the peri-operative period[15]. Schafer et al demonstrated that CRP was a strong predictor of severity of inflammation in cases of acute cholecystitis. In their study, patients with LC were significantly younger, in better condition, with a shorter duration of symptoms and lower CRP levels and TLC compared with primary open cholecystectomy and conversions ($P<0.001$)[9].

Another study by Gurbulak et al found CRP levels to be highly and significantly correlated with the grade of acute cholecystitis as per Tokyo guidelines ($P < 0.0001$). A CRP level of 198.95mg/L as cut-off was found to have a sensitivity of 75.5%, in predicting patients with grade 3 acute cholecystitis[13].

Tekchandani et al also reported that high serum C-reactive protein levels in acute cholecystitis were found to be strongly associated with failure of early laparoscopic cholecystectomy and could significantly predict the intraoperative and histopathological severity of acute cholecystitis. Serum C-reactive protein level of >3.6 mg/dl at admission was found to be strongly related to failure of early laparoscopic cholecystectomy in acute cholecystitis[10].

In a study by Wevers et al, an increase in CRP of 50 mg/L resulted in an Odd's ratio of 1.64. This association is likely to reflect the inflammatory response associated with more acute disease and its related changes to the gallbladder. In contrast to the findings in previous literature the TLC did not show significant predictive value for conversion[12].

Mok et al analysed CRP as the sole predictor of conversion and successfully demonstrated it as an independent predictor for difficult LC and for conversion to open procedure. 3.2% cases were converted to open surgery if CRP was ≤220mg/L whereas 61.9% patients who had CRP >220 mg/L during their index admission were converted irrespective of the nature of operation (emergency or delayed), thus proving its value as a predictor. Here index admission was considered as the one for acute cholecystitis[11]. In this study we have sent CRP levels on admission when surgical intervention by laparoscopic cholecystectomy was planned and not exclusively during acute episodes.

All of the aforementioned studies except the last only compared conversion to open procedure as a marker of difficulty. As previously mentioned, surgeon expertise plays an important role in labelling the procedure as difficult and thus, becomes a very subjective way of analysing. In our study, analysis was done by classifying into 2 groups of difficult (45%) or not (55%) using a checklist of intra-operative findings which were marked by a blinded observer and not the surgeon himself. Thus, this was an unbiased analysis of stating intra-operative difficulty.

Majority of the cases seen in our study were elective unlike previous studies which comprised of CRP values in acute cholecystitis, which has led to an overall low mean CRP levels (6.57mg/L). Also, the laboratory parameter used was hs-CRP which has lower cut-offs when compared to CRP.

Using "Receiver's Operating Characteristic" (ROC) curve technique, an optimum cut-off of 4mg/L was calculated and used for analysis. At 4mg/L, the sensitivity and specificity were at 88.89% and 89.09% respectively. The Yoden's index at that value was optimum in comparison to all other values as seen by the ROC curve technique (77.98%). *P* value of predicting difficult LC with that cut-off was <0.001, confirming the strong relation between CRP and difficult LC.

The procedure was converted to open in 9% of the patients out of which 6% had a hs-CRP of >10mg/L and 3% having lesser which was statistically significant, confirming the predictive value of conversion. *P* values for difficulty and conversion do not match as it was not a single surgeon study and thus, conversion rates may vary as per expertise.

It can be argued that conversion is an objective criterion and is a definite marker for difficulty but there cannot be a cut-off decided for the same as the decision to convert to an open procedure depends on the surgeon's judgement, skill, expertise

and experience with laparoscopy. Even then, most studies with CRP have compared conversion rates and have consistently shown that there is a definite correlation between CRP levels and conversion to open surgery, indirectly making it an indicator of difficult laparoscopy.

In our study important to note was the approach of subtotal cholecystectomy used in 7% of the patients. This method is used at the discretion of the surgeon and is useful in avoiding the complications of open surgery, though it needs considerable skill. For practical purposes, an analysis should ideally include a combination of procedures converted and modified (e.g. subtotal, fundus first). It poses the technical difficulty of finding a suitable cut-off to compare the efficacy of CRP in predicting the type of procedure.

This is only the second study of its kind and the first in India within the limits of our knowledge that was not exclusively done for cases of acute cholecystitis but also included cases of chronic symptomatic cholelithiasis which formed the major chunk of the patient population. The promising significance, sensitivity and specificity of hs-CRP at cut-off of 4mg/L provides an increased scope for counselling even in cold cases.

A limitation of using CRP can be the number of conditions that can interfere with the values leading to false positive cases. Though these cases were eliminated during case selection, the presence of a latent condition cannot be eliminated.

A large-scale prospective study analysing the effect of CRP during admission for surgery in presence of these conditions will be desirable to further confirm the findings of this study and for a larger application of this investigation for routine usage pre-operatively for both elective and emergency cases of laparoscopic

cholecystectomy. A large-scale study with a greater number of conversions and modifications will also lead to the calculation of a cut-off value for those procedures.

CONCLUSION

Based on the findings of this study, it may be concluded that C-reactive protein by measurement of hs-CRP is an effective independent predictor of difficult laparoscopic cholecystectomy above 4mg/L and conversion to open procedure above 10mg/L.

Multi centric studies with larger sample size are required to support this hypothesis

SUMMARY

The present study aimed to find out if blood C-reactive protein (CRP) levels can predict intra-operative difficulty in laparoscopic cholecystectomy and to evaluate it as a predictor for conversion to open surgery.

This one-year cross-sectional study was done with the Department of Surgery, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2017 to December 2017. A total of 100 patients posted for laparoscopic cholecystectomy were studied. Pre-operative hs-CRP (High sensitivity C-reactive protein) levels were analysed with conversion to open procedure and intra-operative difficulty based on findings including adhesions, empyema, wall thickening, difficulty in grasping and perforation.

In the present study, Yoden index was calculated using different levels of hs-CRP as cut-off. It was found to be optimum (77.98) at 4mg/L. It was found that patients with hs-CRP>4mg/L had a higher incidence of intra-operative difficulty that was statistically significant ($P<0.001$) with a sensitivity of 88.89% and a specificity of 89.09%. Conversion to open surgery had a higher incidence in patients having hs-CRP higher than 10mg/L ($P=0.005$).

C-reactive protein (by measurement of hs-CRP) is, thus, an effective independent predictor of difficult laparoscopic cholecystectomy above 4mg/L and conversion to open procedure above 10mg/L.

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ANNEXURES I: CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____ we are requesting you to enroll yourself in study titled "Assessment of blood c-reactive protein levels as a predictor of difficult laparoscopic cholecystectomy - a hospital based cross-sectional study" in KLES HOSPITAL & MRC, BELAGAVI conducted by Dr. _____, Post Graduate in M.S. General Surgery under the guidance of Dr. _____, Department of General Surgery, J.N. Medical College, Belagavi under KAHER, Belagavi.

Respected Sir/Madam, We request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study your clinical presentation, need for pre-operative investigations and operative outcome will be accessed by some questions which will be answered by your operating surgeon.

Purpose of the study:

In this study we are assessing **the role of raised C-reactive protein on admission as a predictor of difficult laparoscopic cholecystectomy in patients undergoing elective laparoscopic cholecystectomy and for conversion to open surgery.**

Procedure Involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history then you will be clinically examined in detail and investigated routinely.

On admission, regular pre-operative care and treatment shall be given. Routine investigations shall be sent along with blood for CRP levels on admission itself. The

planned surgery shall be carried out uninterrupted in the most ideal way possible. The findings of laparoscopy will be assessed and noted. The proforma shall be filled accordingly.

In the event of the procedure being converted to open surgery (if separate consent given for the same), the conversion shall be accounted and reason for conversion will be noted.

No further intervention or follow-up will be required.

Risks and Benefits:

Risk-There is no risk involved. Benefits- Any co existing upper gi pathologies which could be the true of of your symptoms will be identified and treated accordingly, thus reducing the incidence of post operative persistence of symptoms.

Alternatives:

Even if you decline the participation in the study, your operative outcomes will not be documented. Your participation in this research is voluntary. You may choose not to enrol yourself in this study. If you decide to withdraw from the study at any time, you will still receive the standard heath care by the treating doctors. If you decide to participate you are free to withdraw at any time.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Institutional/sponsors policy:

There is no possibility of any harm or injury during your participation in this study.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with your identity remaining confidential.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr. _____, Department of General Surgery, KLES Hospital and MRC, Belagavi, phone number _____or Dr. _____, Dept of General Surgery, KLES Hospital and MRC, Belagavi, phone number _____.

If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli, Professor, Department of Pathology and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number- 9448863866, or extension 1529 at J.N. Medical College, Belagavi.

Consent for participation in prospective study

I, Mr/Ms/Mrs. _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name :

Signature or the Left Thumb Print of Subject :

Date:

Witness Name: _____

Signature:_____

Date:

Investigators Name: _____

Signature:_____

Date :

Place : _____

ANNEXURES II: PROFORMA

PROFORMA

ASSESSMENT OF BLOOD C-REACTIVE PROTEIN LEVELS AS A PREDICTOR OF DIFFICULT LAPAROSCOPIC CHOLECYSTECTOMY - A HOSPITAL BASED CROSS-SECTIONAL STUDY

PATIENT DETAILS:

I.P.D/O.P.D NO.: **D.O.A:**

NAME: **D.O.D:**

SEX:

AGE:

ADDRESS:

Chief Complaints:

Co-morbid illness:

GENERAL EXAMINATION:

Built and Nourishment:

Weight: ***kg***

BMI: ***kg/m^2***

PULSE: ***/min***

BP : ***mmHg***

R/R : ***/min***

TEMPERATURE: ***^oF***

INVESTIGATIONS:

hsC-reactive protein:

Cholecystitis diagnosed by:

(Name of investigation)

Finding:

Intra-operative findings:

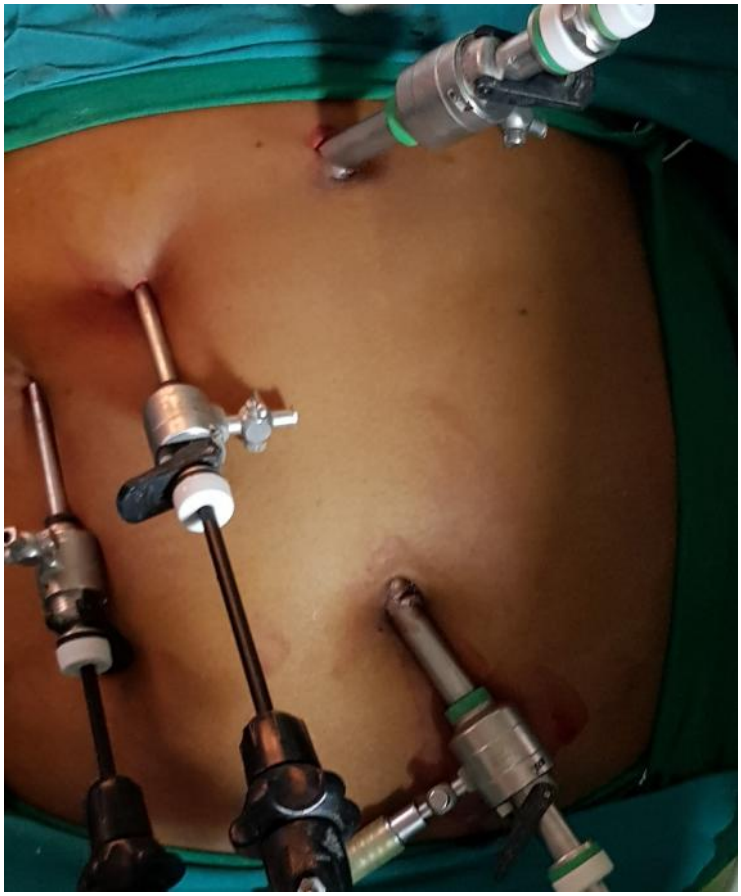
Adhesions	
Pus in gall bladder (empyema)	
Gangrene	
Increased wall thickness	
Difficulty in grasping the gall bladder	
Perforation	

Subtotal cholecystectomy/Converted to open surgery?

If yes, reason:

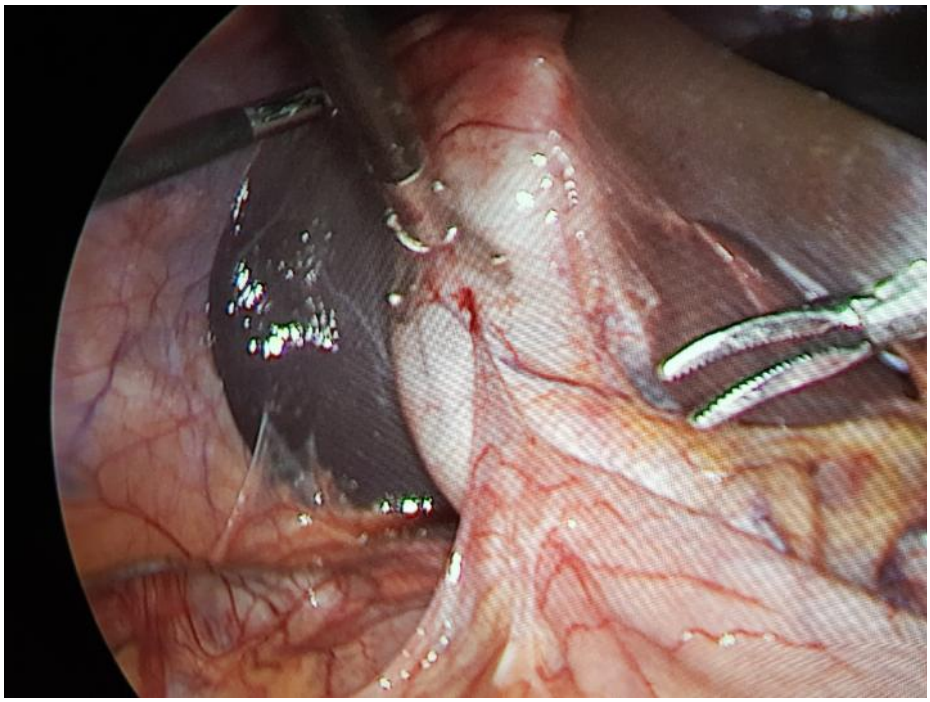
ANNEXURES III: PHOTOGRAPHS

Port placement for laparoscopic cholecystectomy

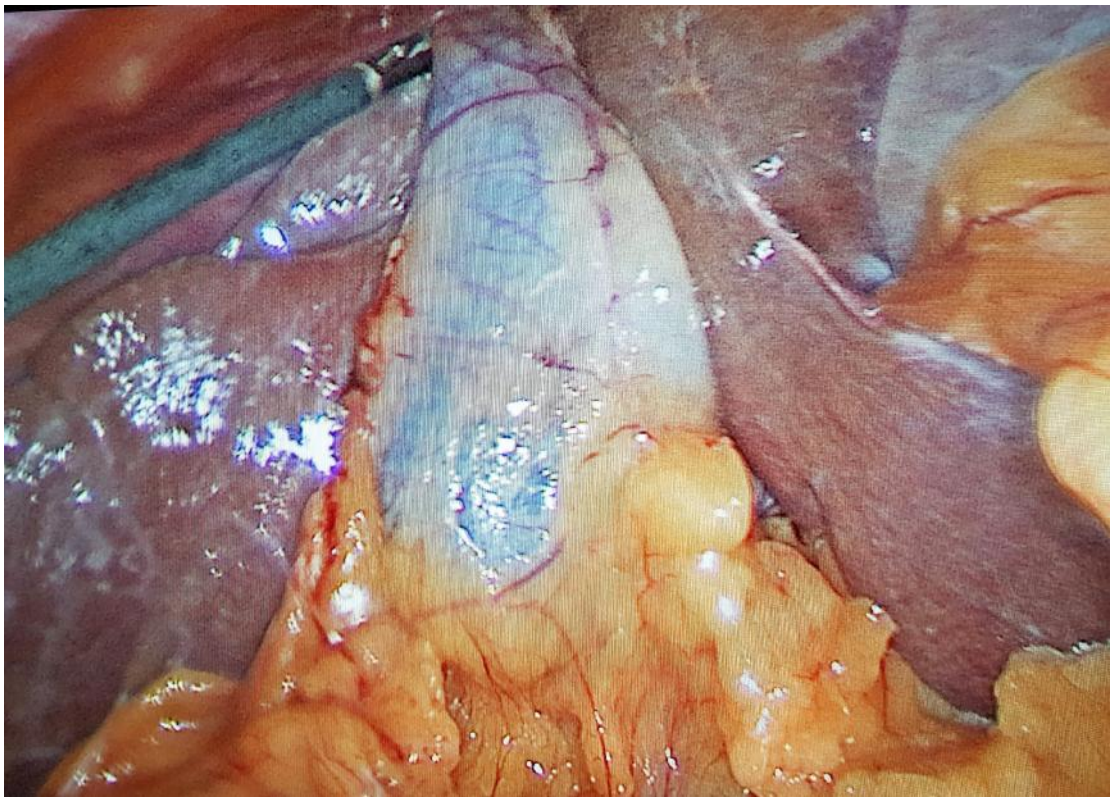


Dense adhesions over the gall bladder

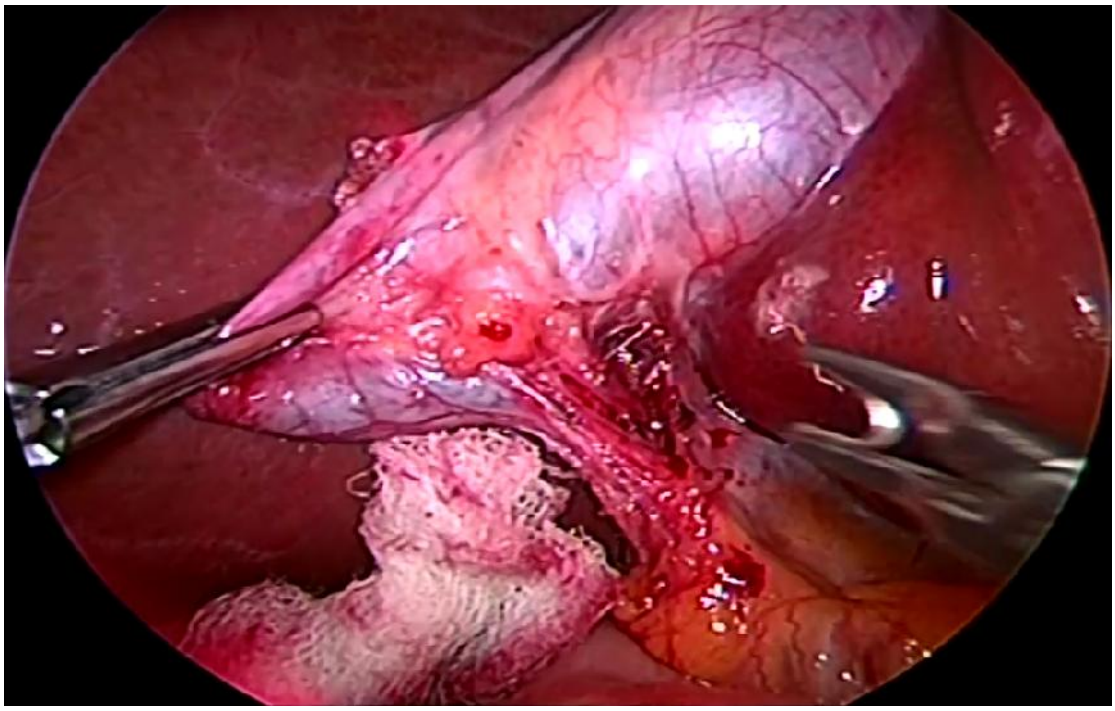
Retraction of gall bladder towards the right shoulder



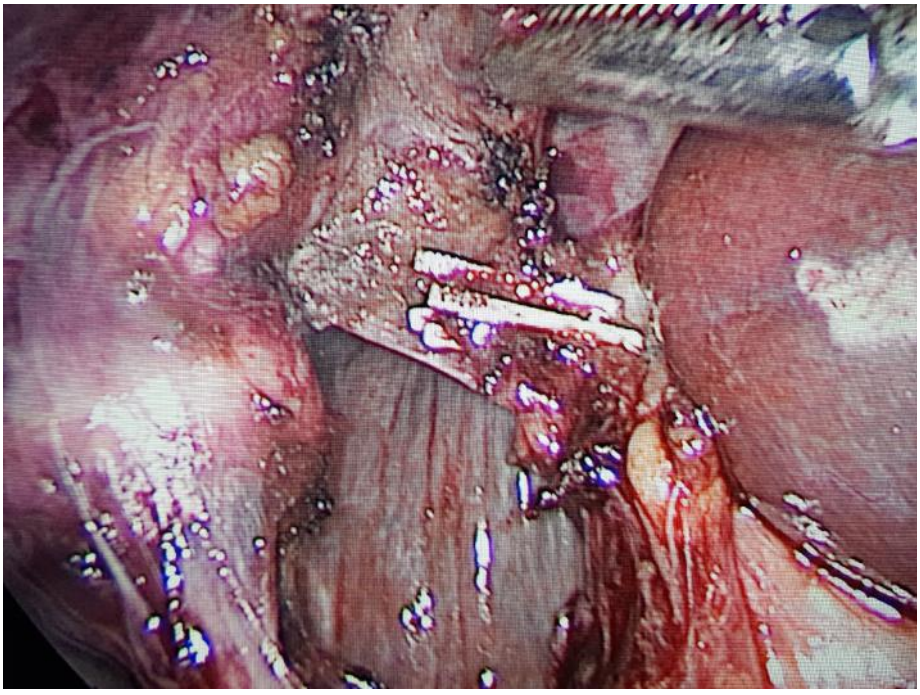
Frozen Calot's triangle



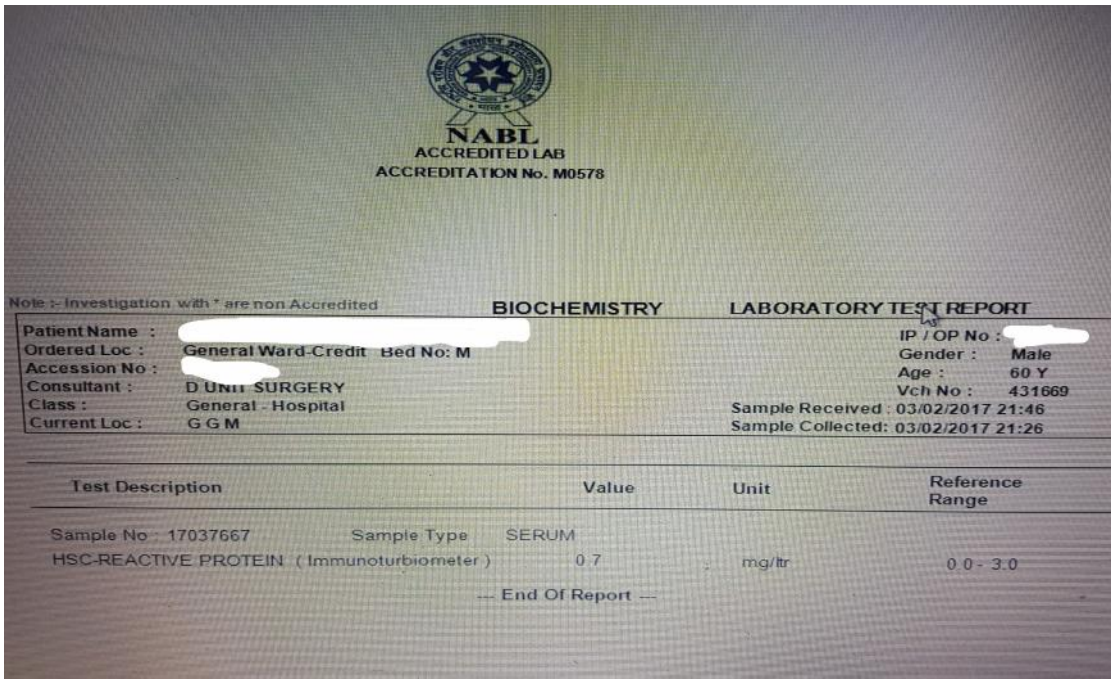
Establishment of critical view of safety



Clip applied over cystic artery



Sample hsCRP report



NABL
ACCREDITED LAB
ACCREDITATION No. M0578

Note :- Investigation with * are non Accredited

BIOCHEMISTRY LABORATORY TEST REPORT

Patient Name : [redacted]
Ordered Loc : General Ward-Credit Bed No: M
Accession No : [redacted]
Consultant : D UNIT SURGERY
Class : General - Hospital
Current Loc : G G M

IP / OP No : [redacted]
Gender : Male
Age : 60 Y
Vch No : 431669
Sample Received : 03/02/2017 21:46
Sample Collected: 03/02/2017 21:26

Test Description	Value	Unit	Reference Range
Sample No : 17037667 Sample Type SERUM			
HSC-REACTIVE PROTEIN (Immunoturbiometer)	0.7	mg/ltr	0.0 - 3.0

--- End Of Report ---

KEY TO MASTERCHART

1. Age- In years
2. Sex-
    - Male- M
    - Female- F
3. hsCRP- High sensitivity C reactive protein (mg/L)
4. 'Difficult?': Difficult laparoscopy (Also applicable for subtotal and conversion)
    - Y: Yes
    - N: No
5. Other findings:
    - Y: Present
    - N: Absent

Serial number	IP Number	Age	Sex	hsCRP	Difficult?	Subtotal	Conversion	Adhesions	Empyema	Gangrene	Thickened wall	Difficulty in grasping	Perforation
1	783811	57	F	8.6	Y	N	N	Y	N	N	Y	N	N
2	785008	64	F	20	Y	Y	Y	Y	N	N	Y	Y	N
3	786770	72	F	1.9	N	N	N	N	N	N	N	N	N
4	786794	43	F	16.4	Y	Y	N	Y	Y	N	Y	Y	N
5	786686	60	M	0.7	N	N	N	N	N	N	N	N	N
6	787862	30	F	1.2	N	N	N	N	N	N	N	N	N
7	791170	56	M	15.8	Y	Y	N	Y	Y	N	Y	Y	N
8	789937	39	M	14.6	Y	N	N	Y	N	N	N	Y	N
9	791455	72	F	1.6	N	N	N	N	N	N	N	N	N
10	791742	56	F	1.3	Y	N	N	Y	N	N	N	N	N
11	792507	63	M	4.2	Y	N	N	Y	N	N	Y	N	N
12	793111	28	F	0.9	N	N	N	N	N	N	N	N	N
13	793346	40	F	1.8	N	N	N	N	N	N	N	N	N
14	795847	65	M	1.8	Y	N	N	Y	N	N	N	N	N
15	796500	40	F	1.3	N	N	N	N	N	N	N	N	N
16	797848	28	F	4.6	Y	N	N	Y	N	N	N	Y	N
17	801064	32	F	0.9	N	N	N	N	N	N	N	N	N
18	802917	40	M	5.2	Y	N	N	N	N	N	Y	Y	N
19	804440	55	F	12.8	Y	N	N	Y	Y	N	Y	Y	N
20	806879	36	F	13.4	Y	Y	N	Y	N	N	N	Y	N
21	806638	62	M	0.5	N	N	N	N	N	N	N	N	N
22	808342	49	M	0.5	N	N	N	N	N	N	N	N	N
23	808069	82	M	0.5	Y	N	Y	Y	Y	N	N	Y	N
24	797843	65	F	5.2	Y	N	Y	Y	N	N	Y	Y	N
25	827938	60	M	4.2	Y	N	Y	N	N	N	N	N	N
26	828051	49	F	1.2	N	N	N	N	N	N	N	N	N
27	811551	42	M	14.2	Y	N	N	Y	N	N	Y	Y	N
28	813357	42	F	1.3	N	N	N	N	N	N	N	N	N
29	814135	30	M	0.6	N	N	N	N	N	N	N	N	N
30	815516	64	M	12.4	Y	N	N	Y	N	N	Y	N	N
31	815855	17	M	0.4	N	N	N	N	N	N	N	N	N
32	815902	47	F	18.3	Y	N	N	Y	N	N	Y	Y	N
33	817912	37	F	1.5	N	N	N	N	N	N	N	N	N
34	818638	30	F	1.9	N	N	N	N	N	N	N	N	N
35	819112	42	F	0.7	N	N	N	N	N	N	N	N	N
36	821300	43	M	1.7	N	N	N	N	N	N	N	N	N
37	820033	65	F	14.5	Y	N	N	Y	N	N	Y	Y	N
38	823177	35	F	1.4	N	N	N	N	N	N	N	N	N
39	823598	60	M	25.6	Y	Y	N	Y	Y	N	N	Y	Y
40	824107	39	M	16.7	Y	Y	N	Y	N	N	N	Y	N
41	821707	81	M	19.5	Y	N	N	Y	Y	N	Y	Y	N
42	826188	40	F	1.6	N	N	N	N	N	N	N	N	N
43	826717	40	M	0.8	N	N	N	N	N	N	N	N	N
44	826928	70	M	24.1	Y	N	Y	Y	Y	N	Y	Y	N
45	828193	17	M	0.9	N	N	N	N	N	N	N	N	N
46	829788	60	M	15.7	Y	N	N	Y	N	N	Y	Y	N
47	794559	26	F	2.3	N	N	N	N	N	N	N	N	N
48	833018	25	M	2.4	N	N	N	N	N	N	N	N	N
49	833785	38	F	4.6	N	N	N	N	N	N	N	N	N
50	834947	36	F	1.2	N	N	N	N	N	N	N	N	N
51	834719	42	F	7.9	N	N	N	N	N	N	N	N	N
52	838040	42	F	3.8	N	N	N	N	N	N	N	N	N
53	838214	47	F	0.6	N	N	N	N	N	N	N	N	N
54	840791	62	F	6.8	Y	N	N	Y	N	N	N	N	N
55	840804	16	M	0.3	N	N	N	N	N	N	N	N	N
56	842317	65	F	11.4	Y	N	N	Y	N	N	N	N	N
57	846989	68	F	5.6	N	N	N	N	N	N	N	N	N
58	847016	40	F	3.1	N	N	N	N	N	N	N	N	N
59	847234	25	M	1	N	N	N	N	N	N	N	N	N
60	847667	40	F	6.1	N	N	N	N	N	N	N	N	N
61	821476	70	M	29.5	Y	N	Y	Y	N	N	Y	Y	Y
62	827654	50	M	13	Y	N	N	Y	N	N	N	Y	N
63	837593	32	N	1.3	N	N	N	N	N	N	N	N	N
64	785131	60	M	10.2	Y	N	N	Y	N	N	N	N	N
65	795826	54	M	2.1	N	N	N	N	N	N	N	N	N
66	799180	45	F	1.6	N	N	N	N	N	N	N	N	N
67	801820	60	F	17.7	Y	N	Y	Y	Y	N	Y	Y	N
68	824332	23	F	14.4	Y	N	Y	Y	Y	N	Y	Y	N
69	838399	25	F	0.4	N	N	N	N	N	N	N	N	N
70	840967	43	M	0.8	N	N	N	N	N	N	N	N	N
71	84384	35	F	1.1	N	N	N	N	N	N	N	N	N
72	794417	38	N	0.9	N	N	N	N	N	N	N	N	N

Serial number	IP Number	Age	Sex	hsCRP	Difficult?	Subtotal	Conversion	Adhesions	Empyema	Gangrene	Thickened wall	Difficulty in grasping	Perforation
73	795399	73	M	23.2	Y	N	Y	Y	N	N	Y	Y	N
74	800948	65	M	15.4	Y	Y	N	Y	N	N	Y	Y	N
75	820405	75	F	36.2	Y	N	N	Y	Y	Y	N	Y	Y
76	823802	70	F	12.2	Y	N	N	Y	Y	N	Y	N	N
77	824415	75	F	17.8	Y	N	N	Y	Y	Y	N	Y	N
78	832716	84	F	8.9	Y	N	N	Y	Y	N	N	Y	N
79	796937	45	F	1.8	N	N	N	N	N	N	N	N	N
80	797625	45	F	9.3	Y	N	N	Y	N	N	Y	Y	N
81	797955	75	F	1.3	N	N	N	N	N	N	N	N	N
82	797421	40	F	2	N	N	N	N	N	N	N	N	N
83	800358	65	F	6.5	Y	N	N	Y	N	N	N	N	N
84	800671	64	F	3.1	Y	N	N	Y	N	N	N	N	N
85	802754	50	M	10.3	Y	N	N	Y	N	N	N	Y	N
86	804051	62	F	5.2	N	N	N	N	N	N	N	N	N
87	803957	22	F	0.6	N	N	N	N	N	N	N	N	N
88	804663	60	F	5.2	Y	N	N	Y	N	N	N	N	N
89	805960	35	F	1.6	N	N	N	N	N	N	N	N	N
90	811868	52	M	0.9	N	N	N	N	N	N	N	N	N
91	814100	20	F	0.4	N	N	N	N	N	N	N	N	N
92	813849	57	F	8.2	Y	N	N	Y	N	N	N	N	N
93	815197	47	F	2.2	N	N	N	N	N	N	N	N	N
94	815371	47	F	1.7	N	N	N	N	N	N	N	N	N
95	817484	29	M	7.4	Y	N	N	Y	N	N	N	N	N
96	819254	60	F	4.8	N	N	N	N	N	N	N	N	N
97	819487	24	F	0.6	N	N	N	N	N	N	N	N	N
98	819829	58	F	1.8	N	N	N	N	N	N	N	N	N
99	821224	39	F	2.3	Y	N	N	Y	N	N	N	N	N
100	822003	24	M	1	N	N	N	N	N	N	N	N	N