"ASSOCIATION OF SERUM LIPID PROFILE WITH SEVERITY OF ACUTE PANCREATITIS: AN ONE YEAR PROSPECTIVE OBSERVATIONAL STUDY

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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"ASSOCIATION OF SERUM LIPID PROFILE WITH SEVERITY OF ACUTE PANCREATITIS, AN ONE YEAR PROSPECTIVE OBSERVATIONAL STUDY ",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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ABBREVIATIONS

SIRS	: Systemic Inflammatory Response Syndrome
CRP	: C - Reactive Protein
CT	: Computed Tomography
SAA	: Serum Amyloid A
PTX3	: Pentraxin 3
LBP	: Lipopolysachharide Binding Protein
LPS	: Lipopolysachharidases
VLDL	: Very Low Density Lipoproteins
LDL	: Low Density Lipoproteins
HDL	: High Density Lipoproteins
TG	: Triglycerides
LTA	: Lipoteichoic Acid
IFN γ	: Interferon Gamma
IL #	: Interleukin #
AP	: Acute pancreatitis
SAP	: Severe Acute pancreatitis
ERCP	: Endoscopic Retrograde Cholangio Pancreatography
IL 10	: Interleukin 10
NEP	: Neutral Endopeptodase
sTNFR	: Soluble Tumor Necrosis Factors

PAF : Platelet Activating Factor

ICAM : Intercellular Adhesion Molecule

GRO - α : Growth regulated protein - α

CINC : Cytokine induced neutrophil chemoattractant

MIP-1α : Macrophage inflammatory protein

NF-κB : Nuclear factor **κ** B

TNF-α : Tumor necrosis Factor - α

MCP-1 : Monocyte Chemoattractant Protein -1

MODS : Multiple Organ Dysfunction Syndrome

SIRS : Systemic Inflammatory Response Syndrome

PCT : Pro Calcitonin

PAF AH :Platelet Activating Factor - acetyl hydrolase

LCAT : Lecithin–cholesterol acyltransferase

PON1 : Paroxanase 1

TLR : Toll Like Receptor

ABSTRACT

AIMS AND OBJECTIVES

In this study we seek to evaluate the association between the changes in serum lipid profile and the severity of the disease. Various studies have investigated the changes in lipid profiles paramerters in various states of infections and inflammation but the association between serum lipid profile and the severity of acute pancreatitis has not been well discussed in the literature.

METHODS

A prospective observational study conducted from January 2021 to December 2021 among patients admitted to KLE Dr. Prabhakar Kore Hospital and MRC Belagavi.

INCLUSION CRITERIA:

Diagnosed cases of acute pancreatitis: h/o acute epigastric pain, elevated serum inflammatory markers, elevated serum amylase and lipase. Abdominal ultrasound to confirm the diagnosis.

If diagnosis is uncertain, CT abdomen is done to confirm the diagnosis

EXCLUSION CRITERIA:

- Known cases of Diabetes Mellitus
- Known cases of Hyperlipidemia
- Patients on Statin medications.
- Malignancy

Sample Size: 106

RESULTS:

In our study, alcohol induced pancreatitis was 54.72%, Biliary pancreatitis 17.92% and Idiopathic Pancreatitis 27.36%. Lower values of serum lipid profile parameters were associated with severity of acute pancreatitis. Lower HDL values were also associated with higher hospital stay and ICU stay.

CONCLUSION:

Lower values of Serum lipid profile parameters have been found to be associated with the severity of acute pancreatitis.

Key Words: Serum Lipid Profile, Acute Pancreatitis, Severity of Acute Pancreatitis

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INTRODUCTION

Acute pancreatitis is a common clinical condition, with its incidence steadily rising over the past few years [1]. Mild forms of the disease may be self limiting needing only supportive treatment while upto 25% develop the severe form of the disease and among the latter mortality between 30 to 50 % has been recorded [2-6]. Alcoholic and biliary pancreatitis are the 2 most common etiological factors with various studies pointing out increasing incidence of one over the other depending on time, place and context of the study.

Acute pancreatitis manifests as a systemic inflammatory dysfunction which evolves into a cascade of immune response which decides the course of the disease. One of the theories that is recognised widely is the premature activation of pancreatic enzymes leading to auto digestion of pancreas[4-6]. But no matter what the initiating event is the pathogenesis can be described in three phases: pancreatic inflammation, generalised systemic inflammation and multi organ dysfunction[4-6].

Patient who succumb to severe acute pancreatitis fall into two groups [4-6]: Around half the cases lead to mortality in the first week: This stems from an initial severe attack which leads to an exaggerated SIRS (systemic inflammatory response syndrome) thus leading to death. Patients who survive this severe attack often develop extensive retroperitoneal pancreatic necrosis.

This necrosis gets infected leading to sepsis which aggravates the already existing systemic inflammatory response and then finally multi organ dysfunction that leads to mortality eventually [7]

Patients who survive the initial attack of severe pancreatitis often succumb to a relatively milder insult that otherwise is only a trivial injury. This two hit hypothesis states that the first exaggerated SIRS sensitises the inflammatory system following

which even a relatively minor insult (like Lower respiratory tract infection, Cannula site infection) will end up in a severe secondary inflammatory response and possibly mortality[4-6]. Severe acute pancreatitis, as defined by revised Atlanta classification, is an attack of pancreatitis with persistent organ failure. The mortality associated with cases involving sterile necrosis 12% while that of infected necrosis is 30% rising up to 47% in cases with multi organ failure. Thus early diagnosis and management of acute pancreatitis is paramount as it significantly improves mortality and morbidity.

A study conducted by Wilson et al (1990), shows that just relying on clinical judgement in prediction of severe acute pancreatitis is only 34% in sensitivity while specificity is comparatively quite high at 98% [7]. Thus in order to predict severe acute pancreatitis various attempts have been made to evaluate laboratory parameters, imaging findings and other modalities in their utility in predicting severity of acute pancreatitis. Yet these studies have not proved to be fruitful as these modalities have not shown their value during the early course of the disease as well as being low on reliability. This lack of reliability mainly stems from low specificity with increased false positive rates. Considering the lower prevalence of severe acute pancreatitis this results in a reduced positive predictive value. Some scores like Ransons score can be completed only after 48 hrs thus not allowing prognostication during admission

Serum markers have increasingly seen as a tool to prognosticate cases of acute pancreatitis and throughout the course of the disease. C Reactive protein (CRP) is one frequently used serum parameter (with cut off level > 150mg/ml) but still has not been as significant during presentation as its reliability has been proved beyond doubt only 48 hrs after admission [8]. Fine needle aspiration and Contrast enhanced CT imaging have been useful in prognostication and for deciding management decisions during the course of the disease. CT scan can analyse and delineate changes such as fat stranding

in the peri pancreatic region, gland enlargement and anatomic delineation of pancreatic necrosis if present. But these modalities are expensive, not easily available and while the former comes with the caveat of exposure radiation the latter could lead to complications such as haemorrhage and infection [9-11]

Thus finding reliable cost effective serum markers that prognosticate the disease accurately during the initial 24 hr period of symptomatic onset would prove to be extremely useful and will aid in initiating appropriate treatment and in required patients, aggressive treatment could be started in the precious initial time period that could essentially reduce mortality and morbidity associated with severe pancreatitis.

Various studies have evaluated acute phase proteins like CRP, Serum amyloid A (SAA), pentraxin 3 (PTX 3) and lipopolysachharide binding protein (LBP) but other than CRP, the other proteins have not been fruitful in this endeavour [12]. Rau et al conducted a multi center trial including patients with severe acute pancreatitis, which showed that there was no statistically significant difference in CRP levels in patients with infected necrosis and those with sterile necrosis. The same lack of statistical difference was seen in patients who survived and in cases of mortality [13]. It has been found that CRP is neither useful in predicting complications such as infected necrosis, organ failure or mortality nor is it disease specific as its raised in numerous other conditions.

Lipid profile parameters have been frequently implicated in various states of infection and inflammation. Various studies have demonstrated a significant role of HDL in the acute phases of inflammation. By interacting with and neutralising LPS, attenuating the expression of adhesion factors and pro-inflammatory cytokines, increasing the release of anti-inflammatory enzymes and proteins, and stimulating the release of nitric oxide, HDLs reduce the pro-inflammatory response during the acute

phase response [14]. Rise in VLDL and plasma triglyceride levels, which result from both an elevated synthesis and a reduced clearance, are the most distinctive findings noted in lipoprotein metabolism during the acute phase response[15-17]. VLDL and triglyceride metabolism appear to be impacted by LPS and LTA in a major way via cytokines. TNF, IFNγ, IL-1 and IL-6 are among the stimuli that quickly accelerate the synthesis of fatty acids in the liver, increasing the production of VLDL and triglycerides in rats [18-22]

OBJECTIVES

In this study we aim to evaluate the association between the various parameters constituting lipid profile with the severity of acute pancreatitis and whether the values of the above mentioned parameters can prognosticate the disease on admission

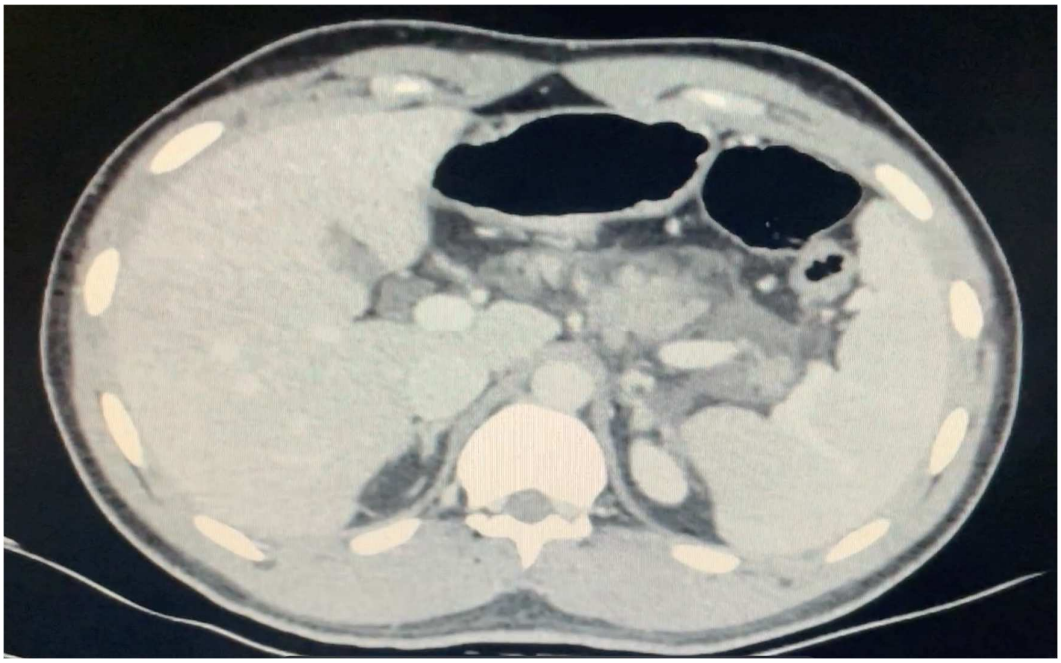
REVIEW OF LITERATURE

An inflammatory condition with a wide range of severity, acute pancreatitis (AP) can range from mild cases which get discharged with an uneventful course to severe cases which lead to mortality. Severe acute pancreatitis (SAP) leads to considerable morbidity and mortality.

Alcohol abuse and biliary tract disorders are the primary causes of AP. Other possible reasons include medications, viral infections, metabolic diseases, post-endoscopic retrograde cholangio-pancreatography (ERCP), trauma to the abdomen and some idiopathic. The diagnosis of AP is made using a combination of clinical indicators, imaging, and laboratory results. Abdominal discomfort, peritonitis symptoms, and more specifically although infrequent indicators of retroperitoneal necrosis including ecchymosis around umbilical region and over the flanks (Cullen's sign and Grey turner sign respectively) constitute typical signs and symptoms. Elevated pancreatic amylase and lipase levels, as well as increased inflammatory markers, are typically seen in acute pancreatitis. Most guidelines consider lipase to be more reliable than amylase [23]. Among imaging studies, Abdominal X-rays are of low value to diagnose pancreatitis per se but can be essential in ruling out other differential diagnoses of acute pain abdomen such has hollow viscus perforation.

Ultrasonography can be an useful modality to image the pancreas. It can report useful information such as pancreatic gland enlargement, peri pancreatic fluid collection and other inflammatory changes around pancreas and ascites. It has been seen that the pancreas visualisation rate in ultrasound imaging is 62 to 90% while the visualisation rate for pancreatic inflammation and inflammation around surrounding regions is 62 to 90% for anterior para-phrenic cavity, 90% for the lesser omentum and

65% for the mesentery[123,124]. Ultrasound can also detect biliary lithiasis, a major case of acute pancreatitis and can also help rule out other abdominal pathologies. CT imaging should be performed aggressively when a definitive diagnosis cannot be reached by other modalities [125,126]. It can also accurately describe pancreatic necrosis and its extent when present. It can also detect enlargement of the pancreas, fat stranding in peri pancreatic and retroperitoneal regions, fluid collection, pseudocyst formation, heterogeneity of pancreatic parenchyma, hepatoma and fissure associated with trauma.



CECT abdomen pelvis with pancreas with peri pancreatic fluid collection with fat stranding

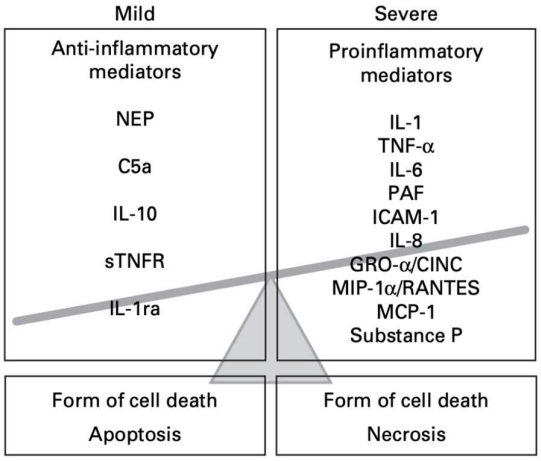
Two categories of patients succumb from acute pancreatitis can be considered[89-91]. In the first week, around 50% of patients face mortality; they have a severe first attack, an aggressive SIRS, leading to multiple organ dysfunction syndrome, and eventually mortality. Patients who develop SAP who live through this point frequently end up in an extensive retroperitoneal pancreatic necrosis. Patients who face mortality at later period typically have sepsis, a persistent systemic inflammatory response, and multiple organ dysfunction syndrome due to infected necrosis.

Patients who experience a severe attack and survive the first inflammatory insult frequently pass away after a relatively mild second incident that wouldn't ordinarily be life threatening. The initial hyperactive SIRS leads to the priming of the inflammatory response, according to the two-hit hypothesis. If there are no further insults, recovery is possible. However, a relatively trivial secondary incident, like a line or chest infection, will result in a heightened secondary inflammatory reaction and maybe even death.

ROLE OF INFLAMMATORY MEDIATORS IN ACUTE PANCREATITIS

The increased leukocyte recruitment associated with pancreatic inflammation is a key hallmark of acute pancreatitis. The pathophysiology of pancreatitis and, more specifically, the inflammatory response that follows, appear to be significantly influenced by inflammatory mediators[92]. In 1988, Rinderknecht H et al originally proposed that cytokines might be crucial in acute pancreatitis and improper immune system activation might worsen both the pancreatic pathology as well as its systemic manifestations[93].

Various pro inflammatory mediators and anti-inflammatory mediators implicated in acute pancreatitis. Transcription factors such as NF-κB regulate the expression of several of these mediators NF-κB.



Pro Inflammatory mediators	Anti inflammatory mediators
TNFα	IL 10
IL 1	Complement component c5a
IL 6	Soluble TNF receptors (sTNFR)
Platelet activating factor (PAF)	IL1 receptor antagonist
ICAM 1	Neural Endopeptidase
IL8	
Growth related oncogene/ cytokine induced neutrophil chemoattractant (GRO/ CINC)	
Monocyte chemoattractant protein1 (MCP 1)	
Substance P	

Though it has been found that NF-κB activity is dictated by the translocation and activation of NF-κB hetero- and homodimers into the nucleus, the precise mechanism by which NF-κB activates cytokines is not fully understood [94.95]. Upon activation, inhibitory element of NF-κB gets degraded releasing NF-κB, resulting in the transportation of NF-κB into the nucleus, thus initiating gene transcription. In cerulein induced rats it has been found that there is a significantly reduced expression of inhibitory element of NF-κB [96-98]. Considering the significant role of pro inflammatory cytokines like NF-κB in the evolution of pancreatitis various studies have evaluated the role of NF-κB. A study by Steinle et al[99] showed that, NF-κB inhibition increased tissue injury and inflammation, while in some studies it was shown that it reduced severity or in some instances even increased survival in various animal models of acute pancreatitis [100-102.] In a recent work, Chen et al. [103] used intraductal injection of the active subunit RelA/p65 using an adenoviral vector to directly activate NF-κB within the pancreas. In this study, pancreatic NF-κB activation was sufficient to trigger an inflammatory response. Despite conflicting findings about this transcription factor, NF-κB is still a crucial eukaryotic transcription factor which warrants future research to identify its significance in the pathogenesis of acute pancreatitis

TNF α and IL1 Beta

TNF α and IL1Beta are pro inflammatory factors frequently implicated in the pathogenesis of acute pancreatitis. Both of these proinflammatory mediators are present in higher concentrations at the beginning and later stages of acute pancreatitis. By inhibiting the activities of TNF- α and IL-1, respectively, naturally produced sTNFR and IL-1ra function as anti-inflammatory mediators[104-106]. TNF-α is demonstrated to be produced and released by pancreatic acinar cells. Mice lacking IL-1 or/and TNF-α receptors have a considerably higher survival rate following the development of acute pancreatitis compared to wild-type mice[107]. Additionally, it has been demonstrated in various animal models of acute pancreatitis that inhibiting IL-1 and TNF-α lessens the occurrence of SAP. Pancreatitis severity and the damage in pancreas gland are both reduced when the IL-1 receptor is blocked prior to or soon after pancreatitis is induced. Additionally, as seen in studies done in rats acute pancreatitis is considerably less severe when TNF-α is neutralised using a polyclonal antibody. In experimental models, strategies that inhibit translation and release of TNF-α or IL-1 reduce the intensity of an attack. The simultaneous expression of serum TNF-α and IL-1 has synergistic pro-inflammatory effects in clinical acute pancreatitis.108 When stimulated by, IL-1, TNF-α and endotoxin, a variety of cells, including monocytes/macrophages, endothelial cells, fibroblasts, and smooth muscle cells, create the pro inflammatory cytokine IL-6[109-112]. In reaction to TNF-α and IL1, periacinar myofibroblasts also create it. Burns, major surgery, and sepsis are a few acute diseases where elevated levels of IL-6 are seen. In an experiment done on rabbits with acute pancreatitis, plasma levels of IL-6 are correlated with cardiovascular phenomena (like left ventricular filling, cardiac output abnormalities) usually associated with the disease[113]. Patients with acute pancreatitis have elevated IL-6 levels, which are correlated with the severity of the

condition. IL6 over expression induced in transgenic mice make them more vulnerable to acute pancreatitis and in these, a mono clonal antibody against IL6 was found to confer a significant level of protection[114].

IL-10

IL-10 is one of the portent anti-inflammatory cytokines. Seitz et al demonstrated in monocyte culture that IL-1ra and sTNFR production is upregulated by IL-10. IL-10 also reduces IL-8 and MCP-1 levels[115]. Dembinski et al and Rongione et al demonstrated experimentally that both the extent of inflammation as well as the mortality associated with acute pancreatitis were reduced by IL-10. In experimental models of acute pancreatitis, the animals were conferred a significant protection when employing recombinant IL-10 [116,117]. The level of pulmonary involvement and resultant from SAP were significantly reduced in rabbits pretreated with synthetic IL-10. In an experimental model involving mice, deletion of the IL-10 gene or anti-IL-10 monoclonal antibody administration makes them more susceptible to acute pancreatitis[118]. In a study conducted by Pizzelli et al, of clinical acute pancreatitis, it was discovered that mild acute pancreatitis had higher serum IL-10 levels than severe acute pancreatitis[119]. IL-10 levels, however, were found to be correlated with SAP in three other trials (Wereszczynska-Siemiatkowska et al, Chen et al, Berney et al)[120-122]

Patients with post-endoscopic retrograde cholangiopancreatography pancreatitis participated in two IL-10 clinical trials. Prior to endoscopic retrograde cholangiopancreatography in both trials, patients either received recombinant IL-10 or a placebo. One study found no discernible difference between the two groups' clinical outcomes [123] during the duration of the illness, but another found that IL-10 provided a significant level of protection[124]. Even in the study by Deviere et al [124] the number of individuals found to have SAP was only 2, with SAP defined as hospital stay longer

than 10 days or organ failure . Thus it is still doubtful if IL-10 will inhibit the disease progression to SAP .

Staubli et al reviewed many existing serum markers that were used to prognisticate acute pancreatitis. Hepatocytes are stimulated by inflammatory stimuli like IL-6 and IL-1 to synthesise CRP which takes upto 72 hours. Rau et al. demonstrated that in a multicenter trial involving SAP patients CRP values did not show statistical difference between who lived and those who died and between those who had infected necrosis or sterile necrosis. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) at the time of presentation we variable as varied cut off values were used, which ranged from 110 to 150mg/l, and were when CRP measurements were taken after 24 or 48h the statistical parameters improved [24]., Accuracy can increase (up to 80%) after 48 hours and at a cut-off level higher than 200 mg/l[25]. Most infectious and inflammatory conditions are associated with an elevated CRP level, hence in conclusion, CRP is neither disease-specific nor especially helpful in predicting complications such as organ failure, infected necrosis, or death. Therefore, none of the current management guidelines for acute pancreatitis take the absolute value of CRP into account. CRP, however, is regarded as the gold standard for determining the severity of an illness in several textbooks.

Another acute-phase reactant, SAA, has a 1000-fold rise in concentration in inflammatory disorders. It is made up of several apolipoproteins, which are proteins that attach to lipoproteins and affect how cholesterol is metabolised. The liver makes a lot of these apo-lipoproteins throughout diverse immunological responses. T lymphocytes, Polymorphonuclear (PMN) cells, monocytes can all be attracted to and activated by SAA, and it also causes chemokine release including IL-1b, tumour necrosis factor-a (TNF-a) and IL-8. In contrast to CRP, a study by Mayer et al

discovered that SAA readings significantly differed between moderate and severe pancreatitis but these were not reproduced by further studies who tried to verify the validity of the same [26]. Thus SAA hasn't proved itself to be useful in assessing the progression to SAP.

Lipopolysaccharide (LPS), a component of Gram-negative bacteria's outer membrane, activates immune-competent cells and causes them to release pro-inflammatory cytokines such TNF-alpha, IL-1b, and IL-6. LPS specifically activates macrophages and monocytes, which are responsible for the majority of cytokine production. The presence of numerous other chemicals in human plasma interfere with the ability to determine LPS in a clinical setting. LBP is instead measured[27]. The liver produces LBP, which both increases the toxicity of LPS and neutralises it by attaching to high-density lipoproteins. 71 patients with Acute Pancreatitis had their LPB and CRP values examined by Rau et al. They discovered that the aforementioned variables followed a similar path, with considerably higher levels seen in cases with pancreatic necrosis, and in cases with organ failure (whether isolated organ failure or multiple organ failure), and cases with mortality. However, it was found that CRP was comparatively more effective at distinguishing between edematous and necrotizing pancreatitis[28]. The association between LPB and severity of the disease in a study by Erwin et al., was not statistically significant possibly because there were only 17 patients in the study. Another sign of the low clinical importance of LPB at the moment is the dearth of studies evaluating its significance [29].

PTX 3 protein is a reactant which plays a crucial role in the acute-phase, just like CRP and SAA. When stimulated by LPS or pro-inflammatory cytokines, macrophages, monocytes, and dentritic cells directly produce and release it (like IL-1b or TNF-a). According to a study by Hill et al., PTX 3 concentration is correlated with

acute respiratory distress syndrome fever, fever and mortality in sepsis[30]. In a study by Kusnierz-Cabala et al. in 2013 PTX3 levels were compared with other biomarkers used in Acute pancreatitis [31]. They discovered that serum levels of PTX3 were considerably greater when compared to that of control group, reaching their maximum levels on the first day following presentation. In comparison to PTX 3, the levels of CRP reached its maximum levels at a later period. Patients with severe AP exhibited PTX 3 levels that were noticeably greater than patients with mild AP. Additionally, there were significant connections between PTX 3 and PMN, IL-6 and SAA elastase. Nevertheless, in spite of the encouraging outcomes, PTX 3 is not suitable for implementing it practically since its concentration can only be measured by the relatively time demanding and costly enzyme-linked immunosorbent assay (ELISA). PTX 3 shows potential to play an important role if measurement of the same becomes more accessible.

The peripheral monocytes, hepatocytes, and thyroid gland all secrete procalcitonin (PCT), the precursor to calcitonin [32]. Its serum content is linked to sepsis, bacterial, and fungal infections[33,34]. Unlike inflammatory cytokines (such as IL-2, IL-6, IL-1b, and TNF-a), PCT is produced and released in response to LPS stimulation [35]. In distinguishing bacterial from non-infectious sources of inflammation, PCT shows more sensitivity (88% vs. 75%) and specific (81% vs. 67%) than CRP [34]. PCT is one of the entities widely studied with regards to acute pancreatitis. In a European multi center trial involving 104 patients, in patients with infected pancreatic necrosis with related MODS or mortality significantly higher PCT levels were discovered. A pancreatic necrosis was indicated by a PCT value of 3.8 ng/ml or greater within 96 hours of the onset of symptoms, with sensitivity and specificity of 93% and 79%, respectively[33]. the systematic review by Mofidi et al. of similar studies confirm the

above findings[32]. Numerous authors have investigated the function of PCT in the prediction of the severity of AP, with somewhat mixed results[33,36,37]. On the one hand, it was discovered that PCT (but not CRP or SAA) varied significantly between mild and severe AP cases. A PCT level of 0.5 ng/l or above showed 81% sensitivity and 86% specificity for SAP within 36 hours of the onset of symptoms. These findings were supported by a recent study by Bezmarevic et al. who measured PCT 24 hours after admission [38]. In contrast to the above findings, in a study consisting of 75 patients, Modrau et al. showed no significant value of PCT [37]. More precisely than PCT, the APACHE II score, the CRP level after 48 hours, and the Ranson score diagnosed severe AP[37]. The variable cut-off values and measurement time periods after the onset of symptoms utilised in each study may be responsible for the vast range of results. As PCT can be measured easily and quickly it still remains an invaluable tool in assessing severity and deciding treatment.

Numerous cytokines have been investigated in relation to AP severity categorization, however most of them have shown to have more of a pathophysiological interest than a clinical one.

Lipid Profile parameters in states of acute inflammation:

Various studies have described the dynamic nature of plasma lipids and lipoproteins in states of acute inflammation. The cytokine induced response to endotoxin results in "Lipemia of sepsis" and a fall in plasma cholesterol, mainly HDL cholesterol, which is proportional to the severity of the disease, mortality and susceptibility to infection [39]. Activity of enzymes associated with HDL like LCAT, PON-1 and PAF-AH is altered in the vascular endothelium [40.] One of the most significant changes in lipid composition during acute inflammation are elevations in

VLDL and Triglyceride levels which are due to both increased production and decreased clearance [41-43.]

LPS and LTA seem to mediate through cytokines to effect on VLDL and Triglyceride metabolism. A variety of factors like TNF-alpha, IL-1, IFN-alpha and IL-6 stimulate synthesis of fatty acids by hepatocytes leading to hyper-triglyceridemia and increased VLDL levels [(44-48).] At the same time, plasma LDL levels are reduced due to increased oxidation of the same in a setting of infection as seen in animal studies [49].

Changes	Effects
VLDL	
Raised VLDL levels	Provides PON1 and PAF-AH lipid substrates to maintain sufficient antioxidant potential [80].
Reduced Hepatic Lipase and Lipoprotein Lipase	Reduced clearance of lipoproteins rich in triglycerides [81]
Elevated Sphingolipid content	Reduced clearance of lipoproteins rich in triglycerides [82]
Reduced expression of Tissue ApoE	Inhibits clearance of lipoproteins [83].
LDL	
Raised levels of Small dense LDLs	increases LDL penetration via endothelium and accumulation in arterial wall, as well as increases sensitivity to oxidation [84].
Reduced PAF-AH activity	Reduces the synthesis of lysophosphatidylcholine (LPC) and its capacity to prevent oxidation of LDL [85]
Elevated Sphingolipid content	Promotes LDL aggregation and macrophage uptake [86]
HDL	
Reduced HDL and apoA-1 Levels	Lowers LPS neutralisation and binding [63]
Reduced levels of LCAT	Inhibits maturation of HDL and attenuates cholesterol ester formation
Elevated levels of SAA	Removes apoA-1 from acute phase HDL leading to a fall in normal HDLs even as the total HDL level remains same [52]
Elevated levels of sPLA2	Leads to fall in HDL cholesterol levels resulting from increased HDL apolipoproteins catabolism and breakdown of cholesterol esters [50]
Fall in Transferrin levels Reduced activity of PON1 (PON/aryleterase)	Inhibits capacity of HDL to protect LDL against oxidation [87,88]

Role of HDL in acute phase reaction:

Various studies have demonstrated the remarkable fall in serum HDL levels in inflammation and acute phase of infection even though the exact mechanism is not established definitely. Various mechanisms have been put forth: A protein which plays a significant role in the acute phase reaction, Secretory phospholipase A2 (sPLA2) has seen to show a predominantly phospholipase activity. Varied tissue sources like vascular smooth muscle cells, neutrophils, and the liver have seen to produce the above mentioned protein. During the initial phase of inflammation the levels of sPLA2 increases which in turn increases HDL catabolism resulting decreased HDL levels[50]. In vitro studies have shown that cytokines inhibit the expression of apoliporoteins leading to low apoA-1 during inflammation Reduced HDL levels may also stem from the inhibition of HDL maturation and cholesteryl ester formation due to reduced LCAT activity [51]. Serum amyloid A (SAA) is another acute phase reactant being investigated in acute inflammatory states. During states of inflammation, apo A1 is displaced by SAA resulting in acute phase HDL (SAA becomes the apo lipoprotein of HDL), resulting in a fall in levels of normal HDL while serum levels of total HDL remains the same[52] ·Catabolism of HDL is increased by enrichment with SAA[53.] The potential of SAA to activate sPLA2 in vitro [54] but not in vivo [50] might also be responsible for the changes in HDL levels although the aforementioned has not been established firmly.

HDLs during phases of acute inflammation and infection known as acute phase HDL lose their cholesterol ester but sphingolipids, free cholesterol, triglyceride are added [55]. LBP and SAA levels get elevated while HDL associated enzymes and apoproteins decrease [56,57]. There are also marked fall in plasma proteins that are significant in HDL metabolism while serum levels of sPLA2 are increased[58].

As a consequence of above changes its hypothesised that HDL induced anti inflammatory effect might be inhibited during acute phase response. One major anti inflammatory effect of HDL stems from the fact that it protects LDL from oxidation[59].This anti oxidant effect is catalysed by various HDL associated proteins with, ceruloplasmin, PAF-AH, PON1, LCAT and transferrin being the most significant ones[40].

During the acute phase reaction, serum PAF-AH and PON1 activity is reduced thus rendering HDL unable to safeguard LDL from oxidation. On the other hand, acute phase HDL itself promotes oxidation and inflammation (as seen by its tendency to enhance migration of monocytes into endothelial smooth muscle cells)[6]

Neutralisation of LPS and acute phase HDL:

LBP (LPS binding protein) is a glycoprotein that has great affinity towards LPS. A potent acute phase reactant, its serum levels surge upto 50 microg/ml (normal <0.5microg/ml) during acute phase response [61]. LBP circulates in association with lipoproteins, helps in neutralisation of LPS as a cofactor and enhances binding of lipopolysachharides to the lipoproteins [62,63]. LBP might also exhibit pro inflammatory effects as plays a significant role in binding of LPS to CD 14 (LPS receptor seen on neutrophils, macrophages and monocytes) which results in increased activation of CD14 TLR 14 complexes [61]. At the same time, the expression of scavenger receptors is increased which eliminate excess microorganims or components preventing the binding of CD 14 receptor which leads to septic shock, thus acting as a protective mechanism [64]. Thus the delicate balance between immune activation and LPS neutralisation is mediated by LBP, CD14, TLR and HDL.

One of the important HDL related acute phase proteins is Serum amyloid A (SAA) [65] . Cytokines released during sepsis (IL 1, IL 6 and TNF alpha) act as stimulus

for the hepatic production of SAA [66]. The serum levels may reach 1000 fold normal during the acute phase response (normal: 1-5 mg/ml), thus demonstrating its significance in host defence. SAA readily binds with HDL, increasing affinity for macrophages 3 to 4 times and decreasing affinity for hepatocytes 2 to 3 times [67]. There is elevation in the number of binding site for SAA/HDL on macrophages while the same in hepatocytes are decreased. This implies that LPS neutralised by HDL is redirected from activating CD14 pathway, towards the scavenger pathway mediated by macrophages [68]. Recent studies point out that biologic activity of LPS can be modulated by SAA and that SAA is suspected to be a LPS binding and neutralising protein [52].

Thus it can be inferred that it is through interactions with HDL that SAA, LBP and other phospholipid binding proteins mediate LPS neutralization. LPS neutralising capacity is significantly affected by the sudden fall in HDL during the acute phase response.

Role of HDL in tissue injury and shock:

The interaction between LPS and macrophages leads to the initiation of cytokine cascade especially TNF alpha and IL 1 that's responsible for the establishment of endotoxin shock[64]. This interaction can be altered by proteins that bind LPS, the most prominent of them being HDL, LDL and LBP. Both in vitro and in vivo it has been demonstrated that native HDL can bind and neutralise LBP thus inhibiting the cytokine response [69]. However it has been demonstrated that its the phospholipid content of HDL that's more significant in this process rather than the cholesterol content. Levine et al demonstrated almost 10 years ago that transgenic mice (where plasma HDL levels were twice that of wild mice) showed highly inhibited levels of TNF alpha as well as attenuation of lethality caused by LPS [70]. They then carried out in vitro studies where rHDL was administered to fasting blood samples obtained from

healthy individuals where it was found that rHDL attenuated the induction of TNF alpha caused by LPS [71]. It has been seen that of rHDL systemically alters the procoagulant state often seen in endotoxemia [72]. It also down regulates cd14 expression by monocytes and inhibits the release of TNF alpha, IL 6 and IL 8. In animal models it has been demonstrated that rHDL leads to decrease in severity of inflammation, organ injury and mortality [73,74,75]. These may be attributed partly to rHDL binding and inactivating LPS, but it has also been demonstrated that its associated with decreased expression of adhesion molecules by endothelial cells , presumably due to alteration in pro inflammatory cytokine expression and this leads to a decrease in polymorphoneutrophils infiltration into tissues and thereby a reduction in oxidative stress. Moreover multiple studies have shown that rHDL is significantly associated with the decrease in MODS associated with haemorrhagic shock and reperfusion of kidney and heart [76,77,78], showing rHDL's anti inflammatory properties which are independent of the LPS scavenger function of HDL

The mechanisms which lead to MODS following acute injury and inflammation and the subsequent shock have not been proved clearly. The expression of adhesion molecules and rapid surge of cytokine levels in the early stages of haemorrhage and trauma and sudden fall in levels of IL-10 in patients who end up in MODS point towards uncontrolled systemic inflammation could be causative in establishment of MODS. It is now evident that rHDL leads to inhibition of inflammation, expression of adhesion molecules, cytokine release, infiltration into tissues and thus in rat models significantly reduced the incidence of MODS associated with acute inflammation[79], haemorrhagic shock [76], endotoxemia [74], and ischemia repercussion injury of certain organs [77].

Khan et al [127] conducted a study to ascertain the association of serum lipid profile with severity of acute pancreatitis. When compared to milder forms of

pancreatitis, those with severe pancreatitis had lower levels of serum total cholesterol, HDL cholesterol, and LDL cholesterol values which were seen to be statistically significant. The fact that these alterations happened early, within 2 days of hospitalisation suggests that they may have a role in estimating the disease severity . These changes continued to persist even later over the course of the disease. When grouped under various ethologies and sub group analysis was done they found that the variations in serum cholesterol concentrations were statistically significant only in alcohol induced pancreatitis which was not seen in other subgroups. This the authors presume to be a consequence of the low sample size.

MATERIALS AND METHODS

Study Design - Prospective Observational Study.

Study Period: January 2021 - December 2021

Study population: Patients admitted to KLE Prabhakar Kore Hospital and MRC, Belagavi

Inclusion criteria:

Diagnosed cases of acute pancreatitis: h/o acute pain over the epigastrium, elevated serum markers for inflammation, serum amylase >= 3 times normal. To confirm the diagnosis imaging modalities like abdominal USG were used. If diagnosis is uncertain, abdominal CT is done to confirm the diagnosis

Exclusion criteria:

- Known cases of Diabetes Mellitus
- Known cases of Hyperlipidemia
- Patients on Statin medications.
- Malignancy

Sample Size:

Formula used for sample size calculation is (With 95% confidence interval , 20% allowable error and 10% attrition)

$$n = \frac{Z^2_{1\text{-alpha}/2} \times SD^2}{(20\% \text{ of } SD)^2} \times 1.1$$

$$n = \frac{1.96^2 \times 1.1}{(0.20)^2}$$

n =105.64

n ~ 106

Procedure:

With institutional consent and written informed consent from patient. The hospitalisation length, acute pancreatitis severity graded according to Ranson score & Glasgow score, the need for surgery or ICU care and mortality rate were noted.

All etiologies of acute pancreatitis will be included including patients of recurrent pancreatitis. When gallstones were implicated as seen in abdominal ultrasound or other imaging modalities, it would be considered gallstone pancreatitis. when the patient reported H/o heavy alcohol consumption (Males : 288 g of ethanol/week ; Females :192 g of ethanol/week) it would be considered as alcohol induced pancreatitis (with other etiologies ruled out).When new or worsening abdominal pain and suggestive laboratory findings are found post endoscopic retrograde cholangiopancreaticography the condition would be considered as Post ERCP pancreatitis, confirmed by abdominal CT imaging when the diagnosis was uncertain, presented shortly after the aforementioned intervention. The patient would be classified under idiopathic pancreatitis when no certain etiology could be identified.

The serum samples are collected immediately after admission to hospital and further samples during the course of hospitalisation and sent for analysis. Serum total cholesterol, serum HDL, serum LDL and serum triglyceride levels were analysed using enzymatic assays.

Statistical analysis:

Descriptive analysis was carried out by frequency, and proportion for categorical variables, mean and standard deviation for quantitative variables. Median and interquartile range (IQR) were used to summarise non normally distributed quantitative variables. Data was depicted using diagrams like bar diagram, pie diagram and box plots wherever appropriate.

Visual inspection of histograms and normality Q-Q plots used to check all Quantitative variables for normal distribution within each category of explanatory variable. Normal distribution was also assessed by Shapiro-Wilk test where p value of >0.05 was considered as normal distribution. The mean values were compared between study groups for normally distributed Quantitative parameters using independent sample t-test (2 groups). Chi square test /Fisher's Exact test was used to compare Categorical outcomes between study groups (Fisher's exact test was used if the overall sample size was < 20 or if the expected number in any one of the cells is < 5.)

Pearson correlation coefficient was used to assess association between quantitative explanatory and outcome variables. P value < 0.05 was considered statistically significant. Statistical analysis done by IBM SPSS version 22.

RESULTS

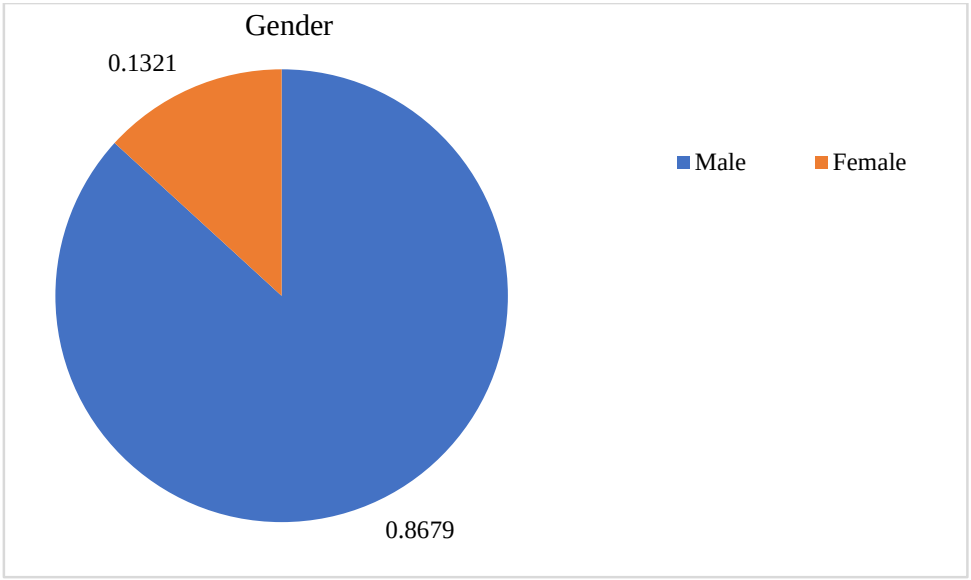
Table 1: Descriptive analysis of age in study population (N=106)

Parameter	Mean ± SD	Median	Minimum	Maximum	95% C.I	
					Lower	Upper
Age	38.53 ± 12.76	36.5	15.0	72.0	36.1	41.0

Table 2: Descriptive analysis of gender in the study population (N=106)

Gender	Frequency	Percentages
Male	92	86.79%
Female	14	13.21%

Graph 1 :Pie chart of gender in the study population (N=106)

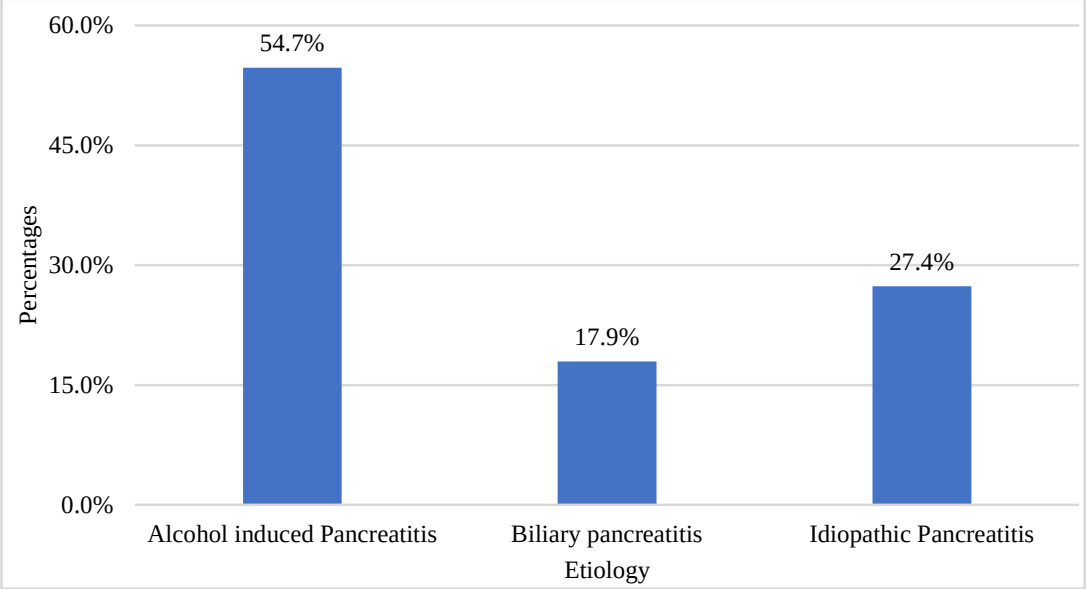


The sample size of the present study was 106. The mean age was found to be 38.53 ± 12.76 years. Most of the study population was males making up 86.79%.

Table 3: Descriptive analysis of Etiology in the study population (N=106)

Etiology	Frequency	Percentages
Alcohol induced Pancreatitis	58	54.72%
Biliary pancreatitis	19	17.92%
Idiopathic Pancreatitis	29	27.36%

Graph 2: Bar chart of Etiology in the study population (N=106)

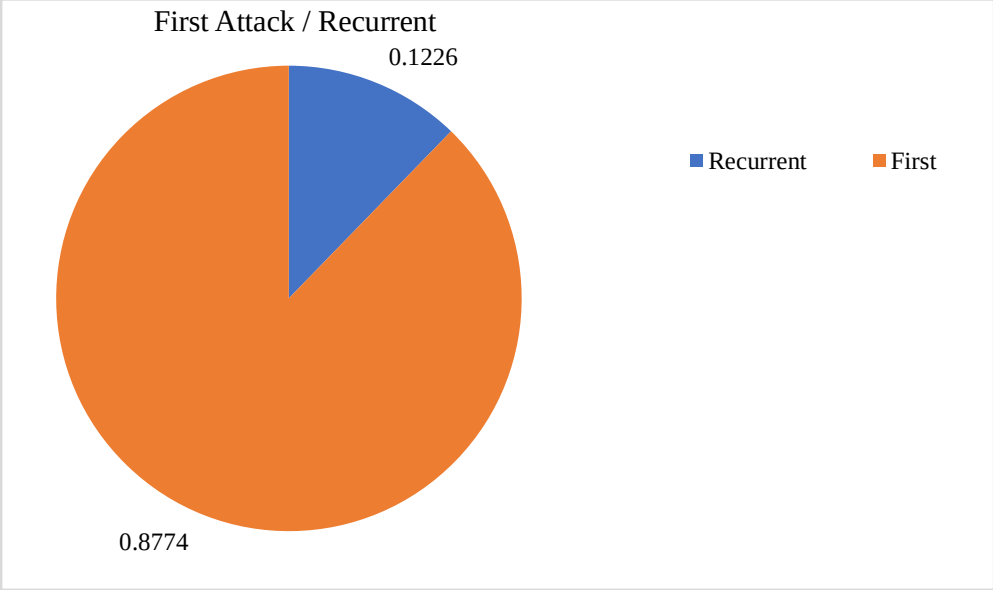


Alcohol induced pancreatitis was the most common aetiology found followed by Biliary pancreatitis and idiopathic pancreatitis

Table 4: **Descriptive analysis of first attack / recurrent in the study population (N=106)**

First Attack / Recurrent	Frequency	Percentages
Recurrent	13	12.26%
First	93	87.74%

Graph 3: Pie chart of first attack / recurrent in the study population (N=106)



Out of 106 patients, 13 (12.26%) experienced recurrent attack of acute pancreatitis while 93 (87.74%) experienced their first attack of acute pancreatitis

Table 5: Descriptive analysis of Lipid profile parameters in study population (N=106)

Serum Lipid Profile Parameter	Mean ± SD	Median	Minimum	Maximum	95% C.I	
					Lower	Upper
Total Cholesterol	148.63 ± 51.42	144.0	49.0	272.0	138.7	158.5
LDL	82.64 ± 45.46	72.0	15.0	282.0	73.9	91.4
HDL	33.69 ± 15.69	32.0	11.0	82.0	30.7	36.7
TG	146.21 ± 63.74	140.0	43.0	414.0	133.9	158.5

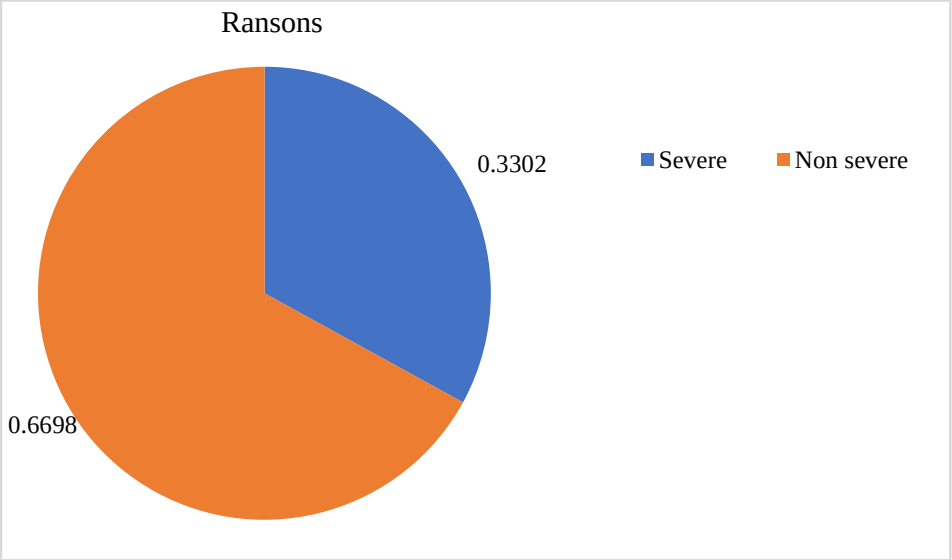
The above table shows Descriptive analysis of Lipid profile parameters in study population

Table 6: Descriptive analysis of Severe and Non severe acute pancreatitis in the study population (N=106)

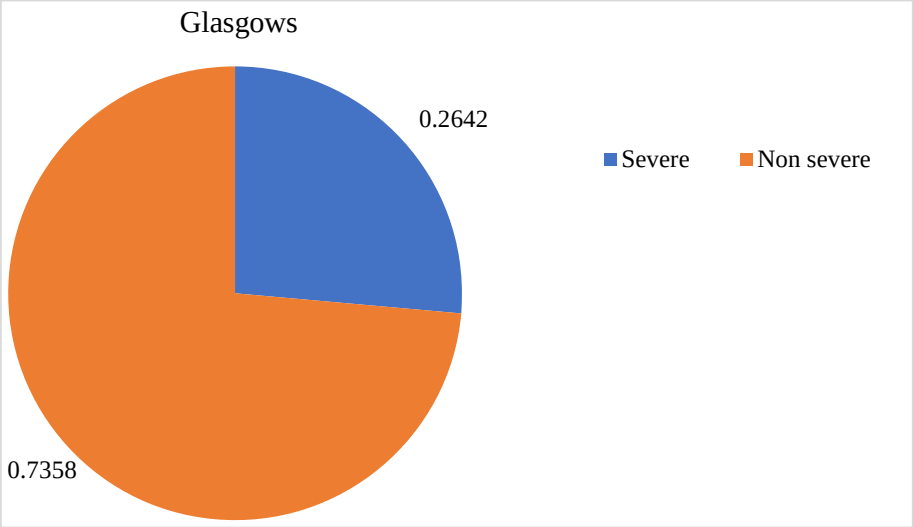
Methods	Frequency	Percentages
Ransons		
Severe	35	33.02%
Non severe	71	66.98%
Glasgows		
Severe	28	26.42%
Non severe	78	73.58%

Out of the 106 patients 35 patients were found to be classified under severe pancreatitis under Ransons criteria while 28 were found to be classified under severe pancreatitis under Glasgows criteria

Graph 4: Pie chart of Severity according to Ransons in the study population (N=106)



Graph 5: Pie chart of Severity according to Glasgows in the study population (N=106)



Out of the 106 patients 35 patients were found to be classified under severe pancreatitis under Ransons criteria while 28 were found to be classified under severe pancreatitis under Glasgows criteria.

Table 7: **Descriptive analysis of Hospital &ICU stay in study population (N=106)**

Parameter	Mean ± SD	Median	Minimum	Maximum	95% C.I	
					Lower	Upper
Hosp Stay	14.89 ± 10.53	10.0	4.0	47.0	12.9	16.9
ICU Stay	2.48 ± 4.26	0.0	0.0	18.0	1.7	3.3

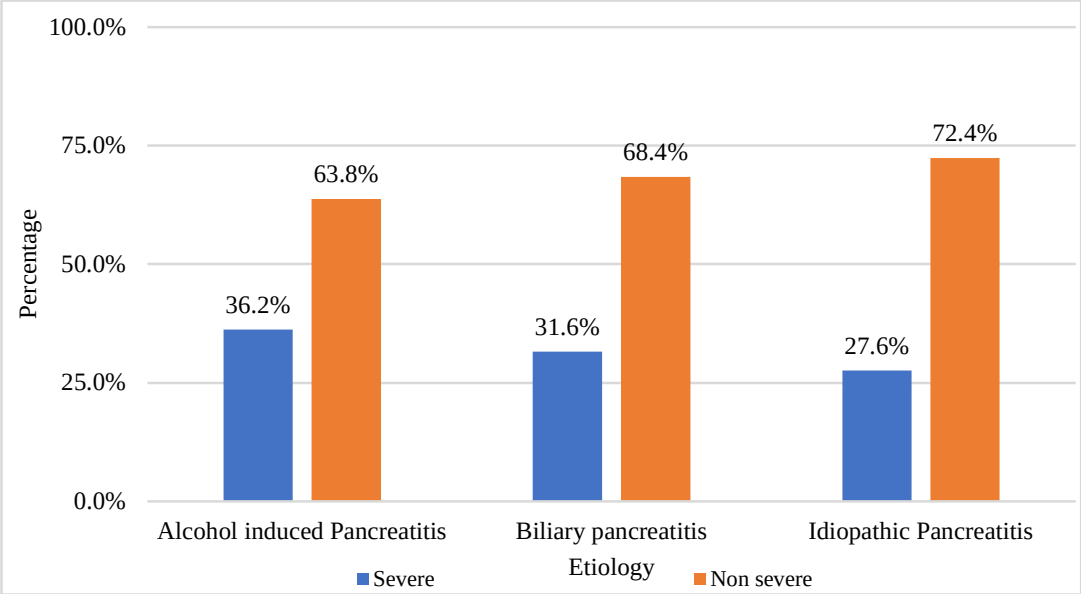
The mean hospital stay was found to be 14.89 ± 10.53 while that of ICU stay was found to be 2.48 days

Table 8: Comparison of Etiology and First / Recurrent attacks with severity of Acute Pancreatitis according to Ransons (N=106)

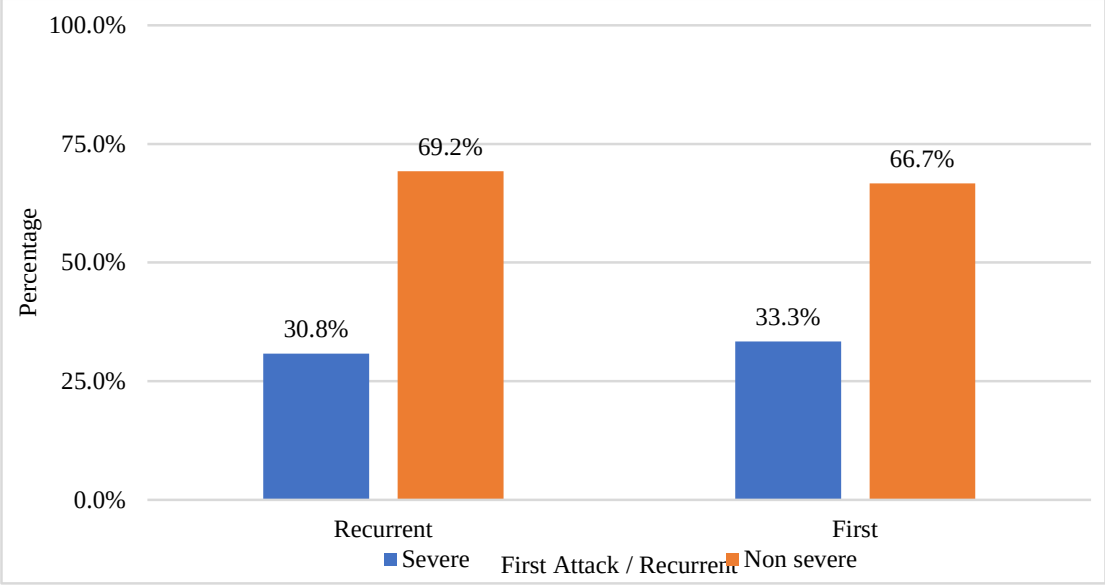
Etiology	Ranson's		Chi square	P value
	Severe	Non-Severe		
Etiology				
Alcohol Induced Pancreatitis (N=58)	21 (36.21%)	37 (63.79%)	0.671	0.715
Biliary Pancreatitis (N=19)	6 (31.58%)	13 (68.42%)		
Idiopathic Pancreatitis (N=29)	8 (27.59%)	21 (72.41%)		
First Attack / Recurrent				
Recurrent (N=13)	4 (30.77%)	9 (69.23%)	0.034	1.000
First (N=93)	31 (33.33%)	62 (66.67%)		

Out of 58 Alcohol induced pancreatitis patients, 21(36.21%) were found to be having severe pancreatitis while 6 (31.58%) and 8 (27.59%) were found to be severe acute pancreatitis in Biliary and Idiopathic Pancreatitis respectively. 4 out of 13 (30.77%) recurrent acute pancreatitis were severe acute pancreatitis while 31 out of 93 (33.33 %) were severe in first attacks of acute pancreatitis. There was no statistically significant associations in the above findings.

Graph 6: Cluster bar chart of comparison of Etiology with severity of Acute Pancreatitis according to Ransons (N=106)



Graph 7 : Cluster bar chart of comparison of first attack / recurrent with severity of Acute Pancreatitis according to Ransons (N=106)



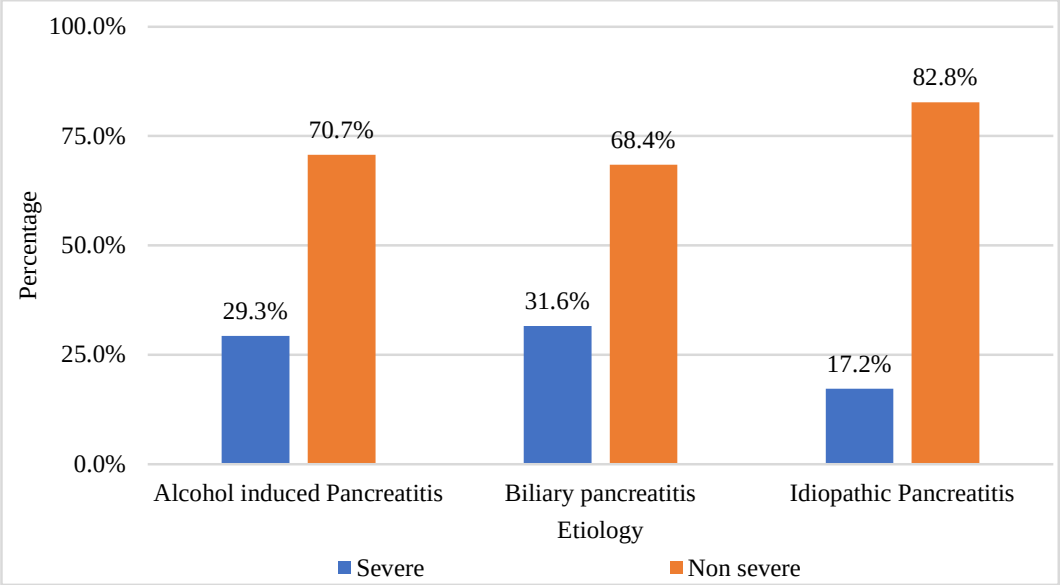
Cluster bar charts showing the distribution of severe and non severe acute pancreatitis according to Ransons with etiologies as well as first/recurrent attacks

Table 9: Comparison of Etiology & First Attack / Recurrent with severity of Acute Pancreatitis according to Glasgow's (N=106)

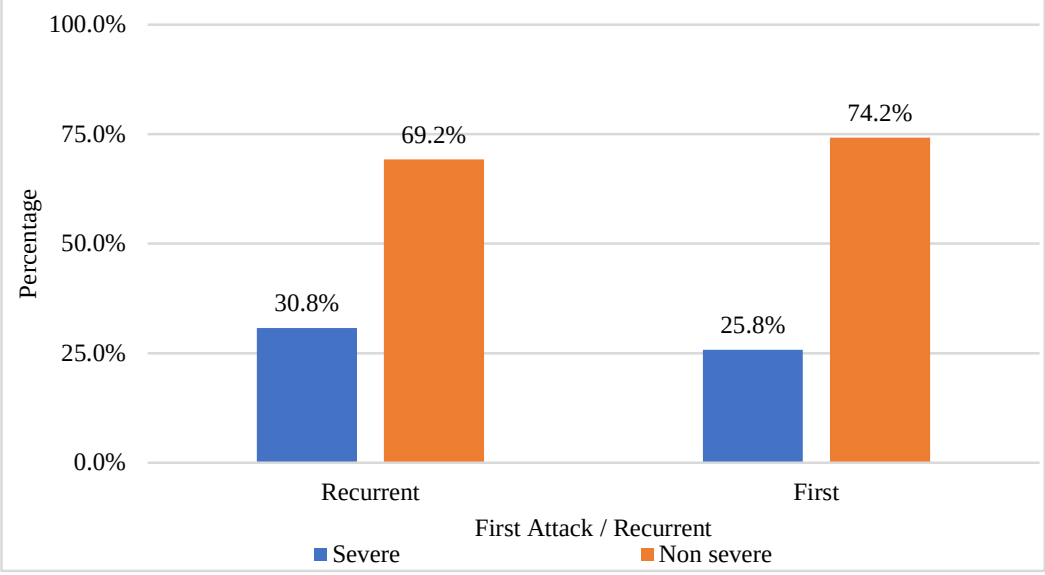
Etiology	Glasgow's		Chi square	P value
	Severe (N=28)	Non-Severe (N=78)		
Etiology				
Alcohol Induced Pancreatitis (N=58)	17 (29.31%)	41 (70.69%)	1.77	0.513
Biliary Pancreatitis (N=19)	6 (31.58%)	13 (68.42%)		
Idiopathic Pancreatitis (N=29)	5 (17.24%)	24 (82.76%)		
First Attack / Recurrent				
Recurrent (N=13)	4 (30.77%)	9 (69.23%)	0.145	0.741
First (N=93)	24 (25.81%)	69 (74.19%)		

Out of 58 Alcohol induced pancreatitis patients, 17(29.31%) were found to be having severe pancreatitis while 6 (31.58%) and 5 (17.24%) were found to be severe acute pancreatitis in Biliary and Idiopathic Pancreatitis respectively. 4 out of 13 (30.77%) recurrent acute pancreatitis were severe acute pancreatitis while 24 out of 93 (25.81%) were severe in first attacks of acute pancreatitis. There was no statistically significant associations in the above findings.

Graph 8: Cluster bar chart of comparison of Etiology with severity of Acute Pancreatitis according to Glasgow's (N=106)



Graph 9: Cluster bar chart of comparison of First Attack / Recurrent with severity of Acute Pancreatitis according to Glasgow's (N=106)



Cluster bar charts showing the distribution of severe and non severe acute pancreatitis according to Glasgows with etiologies as well as first/recurrent attacks

Table 10: Comparison of mean of Serum Lipid profile Parameters with severity of Acute Pancreatitis according to Ransons Criteria (N=106)

Serum Lipid Profile Parameter	Ransons (Mean± SD)		Independent sample t test P value
	Severe (N=35)	Non severe (N=71)	
Total cholesterol	125.43 ± 55.81	160.07 ± 45.29	<0.001
LDL	70.23 ± 50.63	88.76 ± 41.71	0.048
HDL	21.69 ± 12.41	39.61 ± 13.66	<0.001
TG	125.69 ± 55.62	156.32 ± 65.41	0.019

Note: Serum Lipid Profile Parameter are considered approximately normal by histogram & qq-plot for both groups (Severe & Non-Severe)

The above table shows Comparison of mean of Serum Lipid profile Parameters Etiology with severity of Acute Pancreatitis according to Ransons criteria. There was statistically significant association in all parameters.

Table 11:Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Glasgow's Criteria (N=106)

Serum Lipid Profile Parameter	Glasgows (Mean± SD)		Independent sample t test P value
	Severe (N=28)	Non severe (N=78)	
Total cholesterol	121.71 ± 57.05	158.29 ± 45.89	0.001
LDL	71.75 ± 55.09	86.55 ± 41.17	0.140
HDL	21.75 ± 13.41	37.97 ± 14.22	<0.001
TG	116.54 ± 54.15	156.86 ± 63.86	0.004

Note: Serum Lipid Profile Parameter are considered approximately normal by histogram & qq-plot for both groups (Severe & Non-Severe)

The above table shows the Comparison of mean of Serum Lipid Profile Parameter Etiology with severity of Acute Pancreatitis according to Glasgow's Criteria. There was statistically significant association in Total cholesterol, HDL and TG.

Table 12: Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Ransons under each Etiology (N=106)

Serum Lipid Profile Parameter	Ransons (Mean± SD)		Independent sample t test P value
Alcohol Induced Pancreatitis (N=58)			
	Severe (N=21)	**Non severe (N=37)**	
Total cholesterol	133 ± 63.5	173.51 ± 45.53	0.007
LDL	77.05 ± 62.91	99.68 ± 42.04	0.107
HDL	24.76 ± 14.91	39.11 ± 15.63	0.001
TG	133.05 ± 56.09	157.81 ± 54.78	0.107
Biliary Pancreatitis (N=19)			
	Severe (N=6)	**Non severe (N=13)**	
Total cholesterol	91.17 ± 16.08	135.85 ± 32.52	0.006
LDL	44.83 ± 15.7	74.54 ± 38.14	0.087
HDL	17 ± 3.1	41.31 ± 11.73	<0.001
TG	84 ± 17.75	160.54 ± 56.73	0.005
Idiopathic Pancreatitis (N=29)			
	Severe (N=8)	**Non severe (N=21)**	
Total cholesterol	131.25 ± 46.95	151.38 ± 44.91	0.296
LDL	71.38 ± 16.54	78.33 ± 39.61	0.637
HDL	17.13 ± 5.94	39.43 ± 11.35	<0.001
TG	137.63 ± 63.21	151.1 ± 87.16	0.694

The above table shows Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Ransons under each Etiology. Under Alcoholic Pancreatitis, there was statistically significant association in Total cholesterol and HDL. Under Biliary Pancreatitis, there was statistically significant association in Total cholesterol, TG and HDL. Under Idiopathic Pancreatitis, there was statistically significant association in HDL.

Table 13: Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Glasgow's under each etiology (N=106)

Serum Lipid Profile Parameter	Ransons (Mean± SD)		Independent sample t test P value
Alcohol Induced Pancreatitis (N=58)			
	Severe (N=17)	**Non severe (N=41)**	
Total cholesterol	135.94 ± 67.34	168.34 ± 47.98	0.043
LDL	83.29 ± 67.68	94.88 ± 43.22	0.438
HDL	24.65 ± 16.26	37.76 ± 15.58	0.006
TG	131.47 ± 60.97	156.05 ± 53.02	0.130
Biliary Pancreatitis (N=19)			
	Severe (N=6)	**Non severe (N=13)**	
Total cholesterol	91.17 ± 16.08	135.85 ± 32.52	0.006
LDL	44.83 ± 15.7	74.54 ± 38.14	0.087
HDL	17 ± 3.1	41.31 ± 11.73	<0.001
TG	84 ± 17.75	160.54 ± 56.73	0.005
Idiopathic Pancreatitis (N=29)			
	Severe (N=5)	**Non severe (N=24)**	
Total cholesterol	110 ± 32.7	153.29 ± 44.76	0.051
LDL	64.8 ± 11.71	78.83 ± 37.42	0.420
HDL	17.6 ± 7.27	36.54 ± 13.2	0.005
TG	104.8 ± 42.67	156.25 ± 84.11	0.198

The above table shows Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Ransons under each Etiology. Under Alcoholic Pancreatitis, there was statistically significant association in Total cholesterol and HDL. Under Biliary Pancreatitis, there was statistically significant association in Total cholesterol, TG and HDL. Under Idiopathic Pancreatitis, there was statistically significant association in HDL.

Table 14:Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Ransons under Recurrent Pancreatitis (N=106)

Serum Lipid Profile Parameter	Ransons (Mean± SD)		Independent sample t test P value
Recurrent (N=13)			
	Severe (N=4)	**Non severe (N=9)**	
Total cholesterol	125.5 ± 39.61	194.11 ± 46.99	0.028
LDL	68 ± 44.63	119.33 ± 42.41	0.073
HDL	21.75 ± 2.87	33.44 ± 9.34	0.035
TG	135.75 ± 99.61	151 ± 69.46	0.754

The above table shows Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Ransons under Recurrent Pancreatitis. There was statistically significant association in Total Cholesterol and HDL

Table 15: Comparison of mean of Serum Lipid Profile Parameter between Glasgow's method under Recurrent Pancreatitis (N=106)

Serum Lipid Profile Parameter	Glasgow's (Mean± SD)		Independent sample t test P value
Recurrent (N=13)			
	Severe (N=4)	**Non severe (N=9)**	
Total cholesterol	125.5 ± 39.61	194.11 ± 46.99	0.028
LDL	68 ± 44.63	119.33 ± 42.41	0.073
HDL	21.75 ± 2.87	33.44 ± 9.34	0.035
TG	135.75 ± 99.61	151 ± 69.46	0.754

The above table shows Comparison of mean of Serum Lipid Profile Parameter with severity of Acute Pancreatitis according to Ransons under Recurrent Pancreatitis. There was statistically significant association in Total Cholesterol and HDL

Table 16: Correlation of Serum Lipid Profile parameter with Hospital stay (N=106)

Serum Lipid Profile Parameter	Pearson's correlation value (r)	P value
Hospital stay **Vs** Total cholesterol	-0.107	0.274
Hospital stay **Vs** LDL	-0.099	0.313
Hospital stay **Vs** HDL	-0.221	0.023
Hospital stay **Vs** TG	-0.136	0.165

The above table shows Correlation of Serum Lipid Profile parameter with Hospital stay. There was statistical significance in HDL

Table 17: Correlation of Serum Lipid Profile parameter with ICU stay (N=106)

Serum Lipid Profile Parameter	Pearson's correlation value (r)	P value
ICU stay **Vs** Total cholesterol	-0.294	0.002
ICU stay **Vs** LDL	-0.200	0.040
ICU stay **Vs** HDL	-0.391	<0.001
ICU stay **Vs** TG	-0.272	0.005

The above table shows Correlation of Serum Lipid Profile parameter with ICU stay. There was statistical significance in all Serum Lipid Profile Parameters.

DISCUSSION

The sample size of our study was 106. The mean age of the patients was 38.53 ± 12.76. 92 of the study population was male while 14 were female. Various studies report either equal gender distribution in their study population or a male preponderance depending on the geographical location, patient demographics and etiologies associated. Among the etiological factors, the most common was alcohol induced pancreatitis with 58 patients (54.72%) while biliary pancreatitis was seen in 19 patients (17.92%). In 29 patients causative factor could not be discerned and thus classified under idiopathic pancreatitis. It has been seen that the approximately 75% of acute pancreatitis is usually alcohol induced or biliary pancreatitis, with the relative incidence of alcohol induced vs biliary pancreatitis depending on the age distribution of the study population and geographic area. A study conducted by Charles Frey et al[128] of 70,231 patients admitted in the study period of 1994-2001 found that incidence of biliary pancreatitis was the highest at 32.6% followed by alcohol induced pancreatitis at 20.3%. 36.6% were classified to have idiopathic pancreatitis.

Someshekar et al [129]conducted a retrospective survey of patients whose primary diagnosis was acute pancreatitis in two time periods: 2002-2005 and 2009-2012. In 2002-2005 proportion of biliary pancreatitis was found to be 22.19% while that of alcohol induced pancreatitis was 24.72 %. The above mentioned parameters in 2009-2012 was 21.56% and 28.67% respectively. This shows the varying proportions attributed to alcohol induced and biliary pancreatitis. Nevertheless its certain that both of the above mentioned etiologies account for most of the acute pancreatitis cases. Most of the study population experienced their first attack of acute pancreatitis (93, 87.74%) while 13 patients had recurrent pancreatitis (12.26%). In a retrospective study

conducted by Andersson et al [130] the proportion of recurrent pancreatitis was found to be 21% which is comparable to the present study.

Among the study population, percentage of severe pancreatitis was 33.02% according to Ransons criteria, while it was 26.42% according to Glasgows criteria. In a study done by Ajay Khanna et al [131], It was found that the specificity sensitivity and accuracy of Ranson's criteria in predicting severe acute pancreatitis was 78%, 83.9%, and 85% while that of Glasgow criteria was 78%, 71% and 75% respectively which was comparable to a similar study done by Blamey et al[132]. Ransons criteria takes into account more parameters which are taken over the period of 48 hours which may confer the higher sensitivity specificity and accuracy as seen above. The mean hospital stay was found to be 14.89 days while that of ICU stay between 2.38 days.

The percentage of severe pancreatitis in alcohol induced, biliary and idiopathic were 36.21%, 31.58% and 27.59% according to Ranson's criteria (29.31%, 31.58% and 17.24% according to Glasgows) with no statistically significant difference. This was similar to the results found by Jayantha et al[133] where they studied the outcomes of alcohol and biliary pancreatitis. Similarly there was no statistical difference between the proportion of severe cases in first and recurrent attacks.

In our study lower values of all the lipid value parameters were found to be significantly associated with the severe cases of acute pancreatitis. This was similar to the results produced in the study done by Khan et al[127] where they analysed the association between serum lipid profiles with severity of acute pancreatitis as classified by Atlanta criteria. They had reported statistically significant associations between lower values of total cholesterol, HDL and LDL with severe acute pancreatitis. In analysis under individual etiologies lower values of HDL were associated with severe acute pancreatitis in all the categories. Lower values of Total cholesterol was associated

with severity in Alcohol induced and biliary pancreatitis. Under analysis of recurrent cases , lower values of Total cholesterol and HDL were associated with severity. Lower values of serum HDL levels were also associated with prolonged hospital stay.

Bugdaci et al[134] in their study on 122 cases of acute pancreatitis in which they found statistically significant correlation between lower HDL levels and severity in Ransons criteria. They also found statistical association with low HDL levels and prolonged hospital stay. Both of these findings have been observed in our study as well.

It has been shown in numerous studies that various inflammatory and infective conditions as well as acute phase reactions lead to profound alterations in lipid profile parameters. In a study conducted by Stachon et al[135], the lower serum cholesterol values were associated with mortality in patients requiring ICU admission. Various studies have reported a significant fall in HDL levels in states of acute inflammation and infection, but the mechanisms underlying it are not clearly established. Secretory phospholipase A2 (sPLA2) is one of the acute phase reactants and it has a significant phospholipase activity. This reactant is secreted by a variety of tissues like, liver, neutrophils, vascular smooth muscle cells and its levels are raised significantly during inflammation. It has the propensity to up regulate HDL apolipoproteins and cholesteryl ester catabolism this leading to lower HDL cholesterol levels. Another acute phase reactant seen to influence HDL levels is SAA (Serum Amyloid A). SAA displaces apoA-1 from HDL and becomes the primary lipoprotein thus reducing the levels of normal HDL. It also up regulates catabolism of HDL. Numerous more studies have put forth various evidences to show that HDL levels drop during the acute phase reaction. Bugdaci et al in their study mentioned above, propose that the changes in HDL may stem from the effects of TLRs (Toll like Receptors) especially Toll like Receptor 4 expression. Zhang et al[136] in their study provided evidences for the possible role of TLR

4 in the pathogenesis of acute pancreatitis. Similarly in a study done by Liao et al it was found that HDL levels were suppressed by expression of stimulated TLR-4 receptors.

In various studies as done by Khan et al and by Bugdaci et al, an increase in triglyceride levels was associated with severe pancreatitis which was not seen in our study. Bugdaci et al had a study population that included mainly non severe cases and had predominantly biliary pancreatitis. This may be the reason for the disparity.

This study even though brings about the association between lipid parameters and severity of acute pancreatitis, it does not evaluate the mechanisms through which these associations are conceived. Further studies are required to investigate and validate the above finding.

CONCLUSION

In our present study we conclude that lower values of all lipid parameters especially HDL can be used to predict the occurrence of severe pancreatitis and the associated morbidities such as hospital stay and ICU stay.

SUMMARY

Acute pancreatitis is a common clinical condition with severity ranging from mild cases recovering uneventfully to severe cases with high rates of mortality. Clinical judgment alone cannot reliably predict the severity of acute pancreatitis. Various studies have evaluated various laboratory parameters and their association with severe acute pancreatitis.

In our study we aimed to analyse the association between serum lipid profile with severity of acute pancreatitis.

The study was a prospective observational study consisting of 106 patients diagnosed with acute pancreatitis clinically supported with laboratory parameters (serum amylase and lipase) and /or imaging modalities. Their serum lipid profile parameters were compared with severity of acute pancreatitis graded by Ransons and Glasgows criteria.

Lower values of serum lipid profile parameters were associated with severe acute pancreatitis. Sub group analysis revealed lower values of HDL was associated with severe acute pancreatitis in all etiologies and in recurrent acute pancreatitis while that of other parameters varied according to the subgroup. Lower values of HDL was associated with longer hospital and ICU stay.

From our study it may be concluded that lower values of serum lipid profile parameters , especially HDL can predict severe acute pancreatitis.

SCOPE AND LIMITATIONS

Our study has revealed the association between serum lipid profile parameters and the severity of acute pancreatitis but does not reveal the mechanism behind the same. It is possible that the above mentioned changes stem from an exaggerated immune response and attenuated liver function and are simply more pronounced in severe cases. Possibility of unrecognised confounding factors cannot be ruled out. Thus further studies are needed to firmly establish the mechanisms behind this association and to probe into further use of this association in the setting of acute pancreatitis.

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ANNEXURE I: CONSENT

INFORMED CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr./Mrs. _____ we are requesting you to enroll yourself in study titled "ASSOCIATION OF SERUM LIPID PROFILE WITH SEVERITY OF ACUTE PANCREATITIS" conducted by REG NO: BH0120017 Postgraduate in M.S.General Surgery under the guidance of DR. _____, Professor & Unit chief in Department of General Surgery, J.N. MEDICAL COLLEGE, Belgaum under KLE university, Belagavi.

Respected Sir/ Madam,

We request you to participate in our study. Your participation in the research is voluntary. Your decision to participate in the study or otherwise will not affect the relationship with KLES Prabhakar Kore hospital. If you decided not to participate, you are free to withdraw at any time.

Purpose of study:

The purpose of the study is to find out the association between serum lipid profile and severity of acute pancreatitis

Procedure involved:

If you agree to enroll yourself in this study, your detailed history will be taken and you will be clinically examined in detail. Investigations like Serum Lipid Profile, CBC, ESR, CRP, Serum amylase, Serum lipase, USG abdomen, CECT abdomen will be done. The cost of investigations in the above mentioned study will be borne by the principal investigator of the research.

The patient after being diagnosed with acute pancreatitis will be undergoing serum lipid profile test.

The serum samples are collected during hospitalization and stored frozen during the time between their acquisition and analysis. The first sample is obtained immediately after admission, and further follow-up samples will be obtained during the course of the disease. Serum total cholesterol, serum HDL, serum LDL and serum triglyceride levels are measured enzymatically.

Statistical Measures / Tests used. – All the collected datas will be entered in Microsoft Excel Sheet and will be analysed through Chi Square Test.

Risks and Benefits:

There is no increased risk involved when compared with the standard treatment

Type of Study

This study is a prospective observational study

• Alternatives:

Even if you decline your participation in the study, the course of your treatment will not be affected. You are free to withdraw from the study at any point of time. Everything about the study will be explained in detail to you before giving consent for the same.

• 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 policy:

In the event of injury related to the study, treatment will be made available through KLES' Hospital & MRC, Belagavi. There is no compensation or payment for such medical treatment by law.

• Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

• 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.

CONSENT STATEMENT:

Mode of communication of consent form: Verbal / Written

Contents: Self Read/

Read out by Investigator

Participant's awareness regarding voluntary withdrawal from study : Yes / No

Investigators decision to remove participants from study: Yes / No

Awareness regarding voluntary participation: Yes/ No

Adequate time given to clarify any doubts about the study or rights a study participant: Yes/ No

In case they have any questions related to the study, in future or in case of study related injury or illness, they can contact **REG NO: BH0120017**, Department of General Surgery, KLES Hospital and MRC, Belagavi, Phone number-_____ or Dr. _____, M.S., Professor and Unit Chief, Dept. Of General Surgery, KLE'S Hospital and MRC, Belagavi Phone number: _____.

If they have any queries about their rights as a study subject, they may call DR. ROOPA BELLADM.D., Chairman, and Ethical Committee for Human Subjects Research. Professor, Department of Paediatrics, J. N. Medical College, Belagavi, Phone number-9448113403.

Signature or left thumb print of participant or legally authorized representative

Participant's name. _____

Participant's signature/thumb print _____

Experimenters' name _____

Experimenters' signature _____

Witness' name_____

Witness’ signature _____

Date _____

ANNEXURE II: PROFORMA

PROFORMA OF INDIVIDUAL PATIENT

NAME: AGE:

SEX: RELIGION:

IP NO: DATE OF ADMISSION:

OCCUPATION: DATE OF DISCHARGE:

HISTORY :

COMORBIDITIES :

VITALS :

PER ABDOMEN EXAMINATION –

CBC

- HB :
- TLC :

ESR:

CRP:

Serum amylase:

Serum Lipase:

Abdominal USG:

CECT Abdomen:

Lipid Profile:

- TC :
- LDL :
- HDL :

Ranson's Score

ON ADMISSION	
Age > 55 years	
White Blood Cell Count >16 x 10^9 / L	
Blood Glucose > 200mg/dL	
LDH > 350 units /L	
AST > 250 units /L	
WITHIN 48 HOURS	
Hematocrit fall of 10% or greater	
Blood Urea Nitrogen rise > 5 mg/dl despite fluds	
Arterial oxygen saturation (PaO2) < 60 mmhg	
Serum calcium < 2.0mmol / l	
Base deficit >4 mmol/l	
Fluid sequestration >6 litres	

RANSON'S SCORE: ____

SEVERITY OF PANCREATITIS:

GLASGOW SCORE:

Within 48 hours	
Age > 55 years	
WBC count >15 x 10^9/L	
Blood glucose > 10mmol / L (no history of diabetes)	
LDH > 600 units / L	
Serum urea >16mmol/l	
PaO2 <8kPa (60mmhg)	
Serum calcium <2.0mmol/l	
Serum albumin <32 g/l	

GLASGOW'S SCORE: _____

SEVERITY OF PANCREATITIS

- Length of Hospital Stay
- Length of ICU stay (if any)
- Mortality: yes / no

Table 1

IP number	Age	Sex	History	Comorbidities	Etiology	First Attack / Recurrent	Examination	Hb	TC	Lipase	Amylase	Abdominal USG	CECT	Total cholesterol	LDL	HDL	TG	Ransons	Glasgows	Hosp Stay	ICU stay	Mortality
1080451	47	M	Abd pain~ 4 days		Alcohol induced Pancreatitis	R	Soft, tenderness+ @epigastrium	12.4	9600	168	150			213	152	41	102	1 (Non severe)	1 (Non severe)	6	-	-
1070318	21	F	Abd pain ~ 2 days, radiating to back		Idiopathic Pancreatitis	F	Tenderness + epigastrium , L hypochondrium . Guarding +	10.2	18,500	233	303		Edematous head and body of pancreas with peri pancreatic fat stranding	80	68	18	151	3(severe)	3(severe)	28	6	-
1044177	52	M	Abd pain ~ 4 days	HTN	Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium	11.2	13,200	1054	965		Bulky pancreas	190	180	62	240	1 (Non severe)	1 (Non severe)	17	0	-
1045928	33	M	Abd pain ~ 10 days. On and off vomitting +		Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium	12.4	20,800	57	253		Edematous pancreas	202	130	21	152	1 (Non severe)	1 (Non severe)	10	0	-
1051632	39	M	Abd pain radiating to back since 5 days post binge drinking, 2 to 3 episodes of vomiting		Alcohol induced Pancreatitis	F	Soft, tenderness+ @epigastrium, no guarding/rigidity	13.8	9600	2767	1742	Bulky pancreas with ill defined peripancreatic fluid, mild ascitis	Acute interstitial oedematous pancreatitis with peripancreatic collection	164	132	21	272	2 (Non severe)	0 (Non severe)	11	-	-
1034867	20	M	Abd pain ~ 1 week, vomiting +		Alcohol induced Pancreatitis	F	tenderness+ at epigastrium	11.2	8400				Peripherally enhancing intercommunicating cystic collection in the epigastrium extending along lesser & greater curvature of stomach - acute pancreatitis	141	52	62	152	0 (Non severe)	0 (Non severe)	4	-	-
1065415	56	M	Abd pain ~ 2 days, radiating to back, distension +		Biliary pancreatitis	R	Diffuse tenderness+, abd distended, liver dullness+	8.4	21000	1420	1172	Edematous bulky pancreas, Ductal dilatation +		108	48	18	72	6(severe)	5(severe)	23	12	-
1043620	53	M	Abd pain ~ 4 days,distension ~ 1 day	HTN	Idiopathic Pancreatitis	F	Tenderness + epigastrium & umbilical region , no guarding/rigidity	10.6	7300	212	89		Oedematous bulky pancreas with peri pancreatic fat stranding	164	128	17	212	0 (Non severe)	1 (Non severe)	22	-	-
1093959	34	M	Abd pain ~ 3-4 days, generalised weakness +		Alcohol induced Pancreatitis	R	Tenderness + epigastrium & umbilical region , no guarding/rigidity	8.5	16000	54	34		Acute necrotising pancreatitis with necrotic collection	142	78	36	142	0 (Non severe)	0 (Non severe)	9	-	-
1042364	53	F	Abd pain ~ 8 days, on&off fever +	Hypothyroidism	Biliary pancreatitis	F	Mild tenderness + at epigastrium and umbilical region, no guarding/rigidity	7.7	12200	8	15	Pancreas bulky. CBD minimally dilated	Acute pancreatitis with peripherally enhancing hypodense collection	120	82	44	168	0 (Non severe)	0 (Non severe)	4	-	-
1037583	60	M	Abd pain radiating to back ~ 1 week		Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium, no guarding/rigidity	12.4	13200				Necrotising pancreatic with intrapancreatic necrotic collection	246	162	22	202	1 (Non severe)	1 (Non severe)	4	-	-
1071635	18	F	Abd pain ~ 7 days, on&off fever+		Idiopathic Pancreatitis	F	Mild tenderness + at epigastrium, no guarding/rigidity	15.2	7400	158	134			224	149	50	414	1 (Non severe)	1 (Non severe)	12	0	-
1037051	47	M	Abd pain ~ 3 days, decreased urine output,distension+		Alcohol induced Pancreatitis	F	Diffuse tenderness+, distension+	6.9	3500	469	501			62	21	17	51	5(severe)	4(severe)	17	4	-
1054861	52	F	Abd pain ~ 7 days. On and off vomitting +	HTN	Idiopathic Pancreatitis	F	Mild tenderness + at epigastrium	10.4	6176	102	182		Bulky pancreas	151	71	41	102	0 (Non severe)	0 (Non severe)	9	-	-
1039668	51	M	Abd pain, backache, loss of appetite since 15 days		Idiopathic Pancreatitis	F	soft, tenderness+ @epigastrium & L hypochondrium.	11.6	5900	1190	248		Acute interstitial oedematous pancreatitis	78	32	28	82	2 (Non severe)	1 (Non severe)	8	-	no
1049341	54	M	Abd pain since 5 days with vomiting and backache		Alcohol induced Pancreatitis	F	Soft, tenderness + at epigastrium,Abd distension+, no guarding/rigidity	14.9	18800	1168	1264	Features s/o pancreatitis in CBD stenting status,mildly dilated proximal& mid CBD with min IHBRD		170	120	30	101	4(severe)	3(severe)	8	-	-
1033045	30	M	Abd pain ~ 3 days, fever ~ 1 day		Alcohol induced Pancreatitis	F	Tenderness + epigastrium. Localised guarding+	16.2	15600	376	156			122	98	52	133	1 (Non severe)	1 (Non severe)	11	5	-
1043934	35	M	Abd pain ~ 5 days		Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium and umbilical region	13.3	13,700	317	742		Bulky pancreas with peri pancreatic fat stranding	172	92	52	122	1 (Non severe)	1 (Non severe)	14	0	-
1049028	55	M	Abd pain ~ 2 days, radiating to back.	HTN	Idiopathic Pancreatitis	F	Tenderness + around umbilical region, left hypochondrium and left lumbar. Localised guarding +	8.1	20,000	520	429			92	56	14	138	4(severe)	3(severe)	23	8	-
1035729	36	M	Abd pain radiating to back ~ 6 days, on & off vomiting +		Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium and umbilical region	5.9	8600	120	321			249	71	50	119	0 (Non severe)	0 (Non severe)	39	8	-

1039348	41	M	Abd pain since 1 week, hemetemesis and Malena +		Biliary pancreatitis	F	Epigastrium fullness +. Mild tenderness +	13.2	16,200	371	892		-	142	62	38	154	1 (Non severe)	1 (Non severe)	27	-	-
1047661	50	M	Abd pain ~ 7 days		Biliary pancreatitis	F	Soft, Tenderness + epigastrium	10.4	8200	182	204		Acute edematous pancreatitis	224	152	28	274	2 (Non severe)	1 (Non severe)	10	-	-
1041926	46	M	Abd pain ~ 7 days		Alcohol induced Pancreatitis	F	Soft, Tenderness + umbilical region	9.5	11600	88	72		Acute pancreatitis with peripancreatic fat stranding	144	72	60	224	0 (Non severe)	0 (Non severe)	17	-	-
1048694	55	M	Abd pain since 2-3 days, radiating to back and vomiting		Alcohol induced Pancreatitis	F	Soft, Tenderness + epigastrium	14.4	18600	116	107			272	132	17	182	4(severe)	3(severe)	31	5	-
1072835	33	M	Abd pain, loose stools vomitting since 1 week		Alcohol induced Pancreatitis	F	Tenderness + epigastrium and L hypochondriac	14.4	6200	211	130		Bulky head of pancreas with intraparenchymal collection in the head extending in to falciform ligament, anterior subhepatic peri pancreatic collection	171	131	42	152	0 (Non severe)	0 (Non severe)	6	-	-
1060677	50	M	Abd pain with vomiting ~ 3 to 4 days		Alcohol induced Pancreatitis	R	Tenderness + epigastrium, umbilical & L hypochondrium . Guarding +	11.9	19300	26	43		Necrotising pancreatitis with peri pancreatic collection	78	62	24	52	4(severe)	4(severe)	19	8	-
1053558	50	M	Abd pain radiating to back since 10 days, loss of appetite since 10 days		Idiopathic Pancreatitis	F	Soft, tenderness+ @epigastrium & L hypochondirum, no guarding/rigidity	11.4	18800				acute pancreatitis, focal necrosis with ill defined large organising collection	162	104	35	122	2 (Non severe)	1 (Non severe)	8	-	-
1070507	45	F	Abd pain ~ 5 days		Idiopathic Pancreatitis	F	Mild tenderness + at epigastrium and umbilical region	8.4	6000	52	84		Bulky pancreas	232	140	34	220	1 (Non severe)	1 (Non severe)	10	0	-
1039109	48	M	Abd pain ~ 8 days, on&off vomiting+		Alcohol induced Pancreatitis	F	Tenderness + epigastrium.	11.2	12700	103	210		Diffuse peripancreatic fat stranding noted	126	91	21	111	3(severe)	2 (Non severe)	8	-	-
1074983	28	M	Abd pain~ 1 day, vomiting~ 1 day		Alcohol induced Pancreatitis	F	tenderness+ R epigastrium& L hypogastrium, no guarding/rigidity	13.8	8600	620	3192			110	67	16	135	2 (Non severe)	1 (Non severe)	5	-	-
1061413	42	M	Abd pain ~ 4 days, on&off vomiting+		Idiopathic Pancreatitis	F	Soft,tenderness+ at umbilical,R hypochondirum	12.8	11700	150	465			154	110	38	182	0 (Non severe)	0 (Non severe)	7	-	-
1036435	32	M	Abd pain ~ 5 days	HTN	Alcohol induced Pancreatitis	F	Tenderness + around umbilical region, no guarding/rigidity	18.7	13600	1297	513			151	91	42	82	1 (Non severe)	0 (Non severe)	12	-	-
1080448	32	M	Abd pain radiating to back , nausea and vomitting since 5 days		Alcohol induced Pancreatitis	F	Tenderness + epigastrium , L hypochondrium . Guarding +	19.3	10,700	928	738		Acute Necrotising pancreatitis with walled off necrosis in uncinate process	117	102	31	162	0 (Non severe)	0 (Non severe)	10	4	No
1068429	37	M	Abd pain radiating to back since 2 days with nausea & vomiting		Alcohol induced Pancreatitis	F	Soft, mild tenderness+ @epigastrium	16.5	12100	474	910		Acute necrotising pancreatitis with thrombosis of retro-pancreatic portion of splenic vein, hepatomegaly with fatty infiltration	182	32	21	121	3(severe)	1 (Non severe)	9	-	-
1091658	27	M	Abd pain ~ 2 days, radiating to back		Alcohol induced Pancreatitis	F	Tenderness + epigastrium, umbilical & L hypochondrium .	13.7	12000				Multiple communicating intrapancreatic collection in the head & body regions.Ill defined peri pancreatic collection & fat stranding	98	61	19	92	1 (Non severe)	1 (Non severe)	8	-	-
1049274	38	M	Abd pain ~ 10 days. No h/o nausea / vomitting		Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium	11.8	14,260	165	205			140	72	54	142	1 (Non severe)	1 (Non severe)	7	0	-
1076541	39	M	Abd pain~ 6 days, vomiting with multiple episodes~ 3 days		Idiopathic Pancreatitis	F	Tenderness + epigastrium & L hypogastrium . Localized guarding +	13.4	4200	68	34		Peripancreatic fat stranding+	112	68	12	142	3(severe)	2 (Non severe)	6	4	-
1075641	39	M	Abd pain~4 days,vomiting~3 days,fever~3 days		Alcohol induced Pancreatitis	F	Tenderness + epigastrium. No guarding	14.1	25200	102	171		Bulky pancreas	182	71	32	164	1 (Non severe)	1 (Non severe)	15	-	-
1053651	49	M	Abd pain and abd distension since 20 days		Idiopathic Pancreatitis	F	soft,tenderness+ @epigastrium , no guarding/rigidity	11	10100	178	254		Acute pancreatitis with intra parenchymal and peripancreatic collections	152	82	44	184	0 (Non severe)	0 (Non severe)	8	-	-
1093603	28	F	Abd pain ~ 8 days, radiating to back, fever ~ 2 days		Idiopathic Pancreatitis	F	Tenderness + epigastrium & umbilical region, localised guarding +	12.9	8270	928	1247			130	42	58	60	2 (Non severe)	1 (Non severe)	18	-	-
1061794	60	M	On&off abd pain since 3 months,increased since 5-6 days, loss of appetite, giddiness	HTN	Alcohol induced Pancreatitis	F	soft, tenderness+ @epigastrium & L hypochondrium.	8.3	4900	58	50		Acute pancreatitis with pseudocyst	144	42	22	181	0 (Non severe)	0 (Non severe)	7	-	-
1054868	44	F	Abd pain radiating to back ~5 days, distension+		Biliary pancreatitis	F	Tenderness + epigastrium and umbilical region.Localised guarding+	11.4	16200	302	442		Acute interstitial pancreatitis	92	42	18	62	5(severe)	5(severe)	42	14	-
1061739	38	F	Abd pain ~ 10 days. On and off vomitting +		Idiopathic Pancreatitis	F	Mild tenderness + at epigastrium	9.2	5200	114	102		Bulky pancreas	132	51	38	92	0 (Non severe)	0 (Non severe)	6	-	-

1033471	40	M	Abd pain ~8 days, on&off vomiting +	HTN	Biliary pancreatitis	F	Mild tenderness + at epigastrium, no guarding/rigidity	14.8	12500	56	88		Edematous head of pancreas with peri pancreatic fat stranding	111	91	62	141	0 (Non severe)	0 (Non severe)	25	-	-
1091918	22	M	Abd pain ~ 3 days. On and off vomitting +		Idiopathic Pancreatitis	F	Soft, mild tenderness+ @epigastrium	12.4	8200	109	138		Bulky pancreas	132	80	47	111	0 (Non severe)	0 (Non severe)	27	5	-
1088402	30	M	Abd pain with backache and nausea& vomiting ~ 8-10 days		Alcohol induced Pancreatitis	F	Tenderness + epigastrium. No guarding/rigidity	14.3	6900	160	205		Acute pancreatitis with ill defined intra parenchymal and peripancreatic collections	162	70	42	102	0 (Non severe)	0 (Non severe)	8	-	-
1074759	27	M	Abd pain ~5 days, vomiting ~ 1 day		Alcohol induced Pancreatitis	R	Tenderness + epigastrium. No guarding/rigidity	15.4	14600	1927	2258			157	67	31	293	2 (Non severe)	0 (Non severe)	7	-	-
1093442	28	M	Abd pain, breathlessness ~ 4 days		Alcohol induced Pancreatitis	F	Tenderness + epigastrium & umbilical region , distension+	14.2	8600	1889	1300			92	24	18	122	4(severe)	3(severe)	14	5	-
1043233	28	M	Abd pain ~ 2 days,2 episodes of vomiting . On and off fever +		Idiopathic Pancreatitis	F	Tenderness + around umbilical region, left hypochondrium and left lumbar. Localised guarding +	20.4	22,600	1356	597			165	82	14	90	4(severe)	3(severe)	24	5	-
1089373	33	M	Abd pain ~ 5 days		Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium and umbilical region.	19.4	11,300	817	341			189	102	67	140	2 (Non severe)	1 (Non severe)	7	0	-
1061973	24	M	Abd pain ~ 6 days, radiating to back		Alcohol induced Pancreatitis	F	Soft, mild tenderness+ @epigastrium, umbilical region	12.4	6276	144	272			162	102	48	157	0 (Non severe)	0 (Non severe)	10	-	-
1088392	37	M	Abd pain ~ 2 days		Idiopathic Pancreatitis	F	Mild tenderness + at epigastrium and umbilical region, no guarding/rigidity	16.8	13,400	424	271		Bulky pancreas	146	31	55	302	(Non severe) 2	1 (Non severe)	15	0	-
1035009	70	M	Abd pain ~ 4 days, radiating to back, on & off vomiting	HTN	Biliary pancreatitis	F	Tenderness +, distension+,guarding+	8.7	25700	393	199		Necrotising pancreatitis with fluid tracking along L parabolic gutter	71	31	17	82	8(severe)	6(severe)	47	18	-
1068084	72	M	Abd pain~ 7 days, on & off nausea		Biliary pancreatitis	F	Soft,tenderness+ @epigastrium, umbilical region	10.4	11200	192	178		Acute interstitial pancreatitis	138	90	24	172	1 (Non severe)	1 (Non severe)	13	-	-
1035321	35	M	Abd pain~ 6 days with vomiting,non bilious ~ 2 days		Alcohol induced Pancreatitis	F	Tenderness + epigastrium, umbilical & L hypochondrium . Guarding +	13	5700	264	668			82	31	24	95	4(severe)	3(severe)	34	8	-
1035321	38	M	Abd pain ~ 4 days		Biliary pancreatitis	F	Tenderness + epigastrium & umbilical region. No guarding	10.2	16200	342	780			128	41	52	180	2 (Non severe)	2 (Non severe)	34	7	-
1088017	19	M	Abd pain ~ 4 days, on&off vomiting+		Idiopathic Pancreatitis	F	Tenderness + epigastrium , L hypochondrium . No guarding / rigidity	16.7	14,500	547	498		Peripancreatic fluid collection with fat stranding+	108	52	12	102	5(severe)	3(severe)	32	10	-
1049667	16	M	Abd pain radiating to back since 2 to 3 days, vomiting		Idiopathic Pancreatitis	F	Soft,tenderness+ at epigastrium, left hypochondirum	12.5	10400	225	343		Acute necrotising pancreatitis with acute peripancreatic necrotic collection	102	72	48	92	0 (Non severe)	0 (Non severe)	5	-	-
1062888	51	M	Abd pain since 2 days , vomiting ~ 1 day	HTN	Alcohol induced Pancreatitis	F	soft, tenderness+ @epigastrium & L hypochondriac	13.1	14000	304	42		Acute pancreatitis, hepatomegaly with fatty infiltration	212	104	42	152	0 (Non severe)	0 (Non severe)	6	-	-
1060410	34	M	Abd pain ~ 2 days		Alcohol induced Pancreatitis	F	soft,tenderness+ @epigastrium , no guarding/rigidity	12.9	9900	63	112		Acute pancreatitis with peripancreatic fat stranding	194	102	40	162	2 (Non severe)	1 (Non severe)	14	-	-
1056738	28	M	Abd pain~ 4 days, fever ~2 days		Alcohol induced Pancreatitis	F	tenderness+ at epigastrium	19.3	24400	1366	972		peripancreatic collection+	112	48	21	185	4(severe)	2 (Non severe)	8	5	-
1094473	26	M	Abd pain ~ 1 week, vomiting +		Idiopathic Pancreatitis	F	Tenderness + epigastrium and L hypochondrium. Distension +	8.9	10,000	580	600		Acute interstitial pancreatitis	238	122	20	182	0 (Non severe)	0 (Non severe)	12	-	-
1043621	36	M	Abd pain~ 7 days, on&off vomiting +		Alcohol induced Pancreatitis	F	tenderness+ at epigastrium	13.3	11300	92	112		Bulky oedematous pancreas	164	98	30	82	0 (Non severe)	0 (Non severe)	7	-	-
1097855	36	M	Abd pain ~ 4 days		Alcohol induced Pancreatitis	F	Soft, Tenderness + umbilical region	11.2	12200	524	728			162	91	47	82	0 (Non severe)	0 (Non severe)	30	-	-
1041052	26	M	Abd pain~ 4 days		Alcohol induced Pancreatitis	F	tenderness+ in umbilicus,epigastrium & L hypochondrium	11.2	5900	180	175			64	33	13	89	3(severe)	3(severe)	6	-	-

1041523	47	M	Abd pain radiating to back ~ 3 days	HTN	Idiopathic Pancreatitis	F	Tenderness + epigastrium and umbilical region.Localised guarding+	12	8400	27	50		Edematous bulky pancreas,acute pancreatitis	105	66	30	43	4(severe)	3(severe)	18	6	-
1108171	32	M	Abd pain , radiating to back since 1 week, distension +		Alcohol induced Pancreatitis	F	Distended. Diffuse tenderness + . Guarding +	10.7	14,300	173	397		Walled of necrosis present extending along left parabolic gutter	172	102	14	130	4 (severe)	3(severe)	45	15	Yes
1118404	32	M	Abd pain ~ 10 days. On and off vomitting +		Biliary pancreatitis	F	Tenderness + around umbilical region, left hypochondrium and left lumbar. Localised guarding +	14.2	22450	1782	980		Focal walled off necrosis plus in the tail region of pancreas	102	62	11	96	6	5	45	14	-
1036544	46	M	Abd pain ~ 8 days. On and off vomitting +		Alcohol induced Pancreatitis	R	Soft, mild tenderness+ @epigastrium, umbilical region, no guarding/rigidity	11.2	11800	134	266			221	181	11	121	0 (Non severe)	0 (Non severe)	6	-	-
1043838	37	M	Abd pain, abd distension since 1 month aggravated since last 8 days , vomitting since 8 days		Alcohol induced Pancreatitis	R	Soft, Tenderness + epigastrium. Abdomen distended,	13.1	10,800	101	91	Mild bulky pancreas with walled off necrosis in tail of pancreas, dilated CBD with IHBRD	Acute edematous pancreatitis with well defined peri pancreatic collection with IHBRD with pneumobilia	242	121	32	162	1 (Non severe)	0 (Non severe)	24	-	-
1088764	39	M	Abd pain ~ 2 days, radiating to back, distension +	HTN	Alcohol induced Pancreatitis	F	Distended. Diffuse tenderness +	13.8	9100	895	499		Intraparenchymal and peri pancreatic thick walled collection +	90	92	19	132	5(severe)	5(severe)	34	16	-
1078769	35	M	Abd pain~ 3 days, vomiting~ 2 days		Biliary pancreatitis	F	tenderness+, guarding+	9.3	600	73	43		Thick walled peripherally enhancing intraparenchymal collection in distal body of pancreas communicating with a collection anterior to body of pancreas extending to lesser sac with intercommunicating extension	102	62	18	112	5(severe)	3(severe)	32	12	-
1072729	15	F	Recurrent pain abdomen and vomitting since 3 days		Idiopathic Pancreatitis	R	Tenderness + epigastrium.	10.1	13,200	-	-		Features S/o Acute pancreatitis	132	83	40	46	1 (Non severe)	1 (Non severe)	4	-	-
1095264	47	M	Abd pain, distension, breathlessness ~ 3 days		Alcohol induced Pancreatitis	F	Tenderness + epigastrium & umbilical region , distension+, guarding +	11	14400	165	288		Near	224	142	20	188	4(severe)	4(severe)	12	4	-
1066537	52	M	Abd pain ~ 4 days	HTN	Biliary pancreatitis	F	Soft, Tenderness + epigastrium	8.3	12,000	959	841	-	-	144	32	52	82	1 (Non severe)	1 (Non severe)	8	-	-
1090208	70	M	abd pain since 5 days	HTN	Idiopathic Pancreatitis	F	Tenderness + epigastrium &L hypochondrium . No guarding/rigidity	10.9	18200	521	741			212	74	17	182	(severe)4	2 (Non severe)	14	4	-
1041545	36	M	Abd pain ~ 20 days. On and off vomitting +		Alcohol induced Pancreatitis	F	soft, tenderness+ @epigastrium & L hypochondrium.	11.6	4400	129	82		Acute calcific pancreatitis	270	172	30	270	0 (Non severe)	0 (Non severe)	8	-	-
1052050	34	M	Abd pain ~ 3 days, multiple episodes of vomiting ~ 1 day		Alcohol induced Pancreatitis	F	Tenderness + around umbilical region, no guarding/rigidity	9.7	11200	160	300			112	21	42	171	0 (Non severe)	0 (Non severe)	11	-	-
1088291	40	M	Abd pain radiating to back ~ 2 to 4 days, nausea & vomiting+		Biliary pancreatitis	F	Mild tenderness + at epigastrium, no guarding/rigidity	14.7	11000	49	62		Acute calcific pancreatitis	152	121	24	271	0 (Non severe)	0 (Non severe)	5	-	-
1080304	34	M	Abd pain ~ 4 days		Alcohol induced Pancreatitis	F	tenderness+ at epigastrium	12.4	6250	485	305			49	15	14	102	4(severe)	3(severe)	10	-	-
1049354	28	M	Abd pain, back pain since 1 month, vomiting		Alcohol induced Pancreatitis	F	Tenderness + epigastrium , L hypochondrium . Guarding +,distension +	16.1	15700	1764	1310	Walled off necrosis of pancreas	Acute necrotising pancreatitis	62	31	38	142	3(severe)	2 (Non severe)	14	-	-
1091326	27	M	Abd pain ~ 7 days, distension		Alcohol induced Pancreatitis	F	Tenderness + epigastrium, R & L hypochondrium ,umbilical region. Localized guarding +	15.5	21700	1494	1865		Acute pancreatitis with peripancreatic fat stranding & ill defined peri pancreatic exudates	82	34	14	88	5(severe)	4(severe)	16	6	-
1041766	42	M	Abd pain ~ 2 days, vomiting+		Alcohol induced Pancreatitis	R	Diffuse tenderness+, guarding+	8.2	18200	432	688		Acute necrotising pancreatitis	162	30	21	147	5(severe)	4(severe)	26	12	-
1093590	70	M	Abd pain~ 10 days, nausea	HTN	Alcohol induced Pancreatitis	F	Soft, mild tenderness+ @epigastrium, umbilical region	13.2	7200				Bulky pancreas	242	162	82	248	1 (Non severe)	1 (Non severe)	14		-
1045384	25	M	Abd pain ~ 8 days, on&off vomiting+		Idiopathic Pancreatitis	F	Mild tenderness + at epigastrium and umbilical region, no guarding/rigidity	10.3	12,200	21	35		Edematous bulky pancreas s/o acute pancreatitis	102	34	41	132	1 (Non severe)	1 (Non severe)	8	0	-

1077974	40	M	Abd pain~3 days, vomiting~ 1 day		Idiopathic Pancreatitis	F	Abd distension+, tenderness + @epigastrium	12.4	3700	274	731		Edematous pancreas	172	32	17	196	1 (Non severe)	0 (Non severe)	25	-	-
1052173	46	M	Abd pain ~ 2 days		Alcohol induced Pancreatitis	R	Soft, tenderness+ @epigastrium and umbilical region	12.4	10700	202	144			262	172	31	201	0 (Non severe)	0 (Non severe)	23	-	-
1047663	30	F	Abd pain ~ 3 days. On and off vomiting +		Biliary pancreatitis	F	Diffuse tenderness+, guarding+	9.2	21000	1102	542		Acute necrotising pancreatitis	72	24	20	80	5(severe)	4(severe)	37	10	-
1071593	51	M	Abd pain~10 days with nausea&vomiting		Alcohol induced Pancreatitis	R	Tenderness + epigastrium & L hypochondrium . Guarding +,distension +	15.6	17500	63	76		Acute pancreatitis with peripancreatic collection	160	90	40	172	2 (Non severe)	1 (Non severe)	10	2	-
1047949	33	F	Abd pain ~ 2 days, nausea+		Biliary pancreatitis	F	Soft, mild tenderness+ @epigastrium	9.2	4600	88	124		Bulky pancreas	141	81	34	122	0 (Non severe)	0 (Non severe)	12	-	-
1048524	30	M	abd pain~ 7 days, fever~ 2 days		Biliary pancreatitis	F	tenderness+ @ L hypogastrium, no guarding/rigidity	12.6	7000	76	63		Peripancreatic fluid collection+, bulky pancreas	112	64	38	113	1 (Non severe)	1 (Non severe)	10	-	-
1045757	15	M	Abd pain ~ 2 days,3 episodes of vomiting		Idiopathic Pancreatitis	F	Soft, tenderness+ @epigastrium & L hypochondirum, no guarding/rigidity	14.1	8700	58	81		Bulky oedematous pancreas	118	50	42	140	0 (Non severe)	0 (Non severe)	6	-	-
1063926	18	F	Abd pain ~ 7 days, on&off fever+		Idiopathic Pancreatitis	F	Soft, tenderness+ @epigastrium and umbilical region	7.5	5000				Acute pancreatitis with peripancreatic fluid collection	142	30	48	60	2 (Non severe)	1 (Non severe)	9	-	-
1079646	30	F	Abd pain~ 2 days		Biliary pancreatitis	F	soft,tenderness+ @epigastrium , no guarding/rigidity	12.1	6200	77	80		Peripancreatic fat stranding+	82	32	44	112	1 (Non severe)	0 (Non severe)	7	-	-
1145235	33	M	Abd pain ~ 1 week, vomiting + on and off		Alcohol induced Pancreatitis	F	Mild tenderness + at epigastrium and umbilical region.	16.1	12,900	1383	704			144	72	42	92	1 (Non severe)	1 (Non severe)	10	2	-
	24	M	Abd pain, distension, breathlessness since 3 days		Alcohol induced Pancreatitis	F	Abd distended,tenderness+ @epigastrium and L hypochondrie, guarding+	16.1	18800	1083	871			182	102	38	170	6(severe)	4(severe)	10	3	-
1047082	35	M	Abd pain ~ 3 days, 1 episode of low grade fever +		Biliary pancreatitis	F	Soft, tenderness+ @epigastrium and umbilical region	9.5	9100	399	217			128	20	52	152	0 (Non severe)	0 (Non severe)	5	-	-
1074963	41	M	Abd pain ~ 5 days, poor urine stream ~ 2 days		Idiopathic Pancreatitis	F	Soft,tenderness+ around umbilical and epigastrium	17.3	12200	428	309			176	105	20	253	5(severe)	2 (Non severe)	6	-	-
1066780	40	M	Abd pain ~ 1 day post binge drinking,vomiting+		Alcohol induced Pancreatitis	R	Abd distended tenderness+ @epigastrium and L hypochondrium,no guarding/rigidity	13.9	13000		1043	Acute necrotising pancreatitis with intrapancreatic collection	Acute interstitial oedematous pancreatitis	154	132	24	272	3(severe)	3(severe)	25	4	-
1087564	26	F	Abd pain with vomiting ~ 4 days		Idiopathic Pancreatitis	F	Tenderness+ at R hypochondrium, no guarding/rigidity	13.6	9200	1405	2754		Cholelithiasis with thickened enhancing wall & minimal pericholecystic fluid.tiny speck of calcification along distal CBD,bulky pancreas with loss of pancreatic lobulation	98	72	48	122	1 (Non severe)	0 (Non severe)	5	-	-
1042955	28	M	Abd pain ~ 5 days		Alcohol induced Pancreatitis	F	Tenderness + epigastrium & umbilical region , no guarding/rigidity	16	10200	834	176			142	34	21	120	2 (Non severe)	1 (Non severe)	8	-	-
1044149	56	M	Abd pain ~3 days,vomiting ~ 2 days,distension ~ 1 day		Alcohol induced Pancreatitis	F	Tenderness + epigastrium, R & L hypochondrium ,umbilical region. guarding +,distension +	13.1	6700	610	942			144	62	30	82	4(severe)	4(severe)	10	4	-
1034701	41	M	Abd pain radiating to back since 2 days; Nausea vomitting ~ 2 days		Alcohol induced Pancreatitis	F	Mild tenderness + at left hypochondriac	14.9	7300	-	-		Acute pancreatitis with pseudocyst in tail region	125	71	32	142	0 (Non severe)	0 (Non severe)	5	-	-
1035165	31	M	Abd pain ~ 2 days		Biliary pancreatitis	F	Tenderness + epigastrium &L hypochondrium . No guarding/rigidity	12.5	12600	231	167		Peripancreatic fluid collection+ & fat stranding+	144	101	45	146	0 (Non severe)	0 (Non severe)	5	-	-
1066153	70	M	Abd pain ~ 2 days, radiating to back, distension +	HTN	Alcohol induced Pancreatitis	F	Diffuse tenderness+, abd distended, liver dullness+	15.1	23000	2064	1370		Peripherally enhancing intraparenchymal and peri pancreatic fluid collection +. Thick walled	232	282	82	232	5(severe)	4(Severe)	24	5	-
1042873	25	M	Abd pain ~ 4 days, on&off vomiting+		Idiopathic Pancreatitis	R	Tenderness + epigastrium , L hypochondrium . No guarding / rigidity	7.6	36,600	281	179		Peripancreatic fluid collection+ & fat stranding+	218	130	39	120	2 (Non severe)	1 (Non severe)	12	3	-