A COMPARATIVE STUDY BETWEEN BISAP AND APACHE II SCORE IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS

A DISSERTATION SUBMITTED TO

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APRIL 2013

CERTIFICATE

This is to certify that the dissertation entitled ***"A COMPARATIVE STUDY BETWEEN BISAP AND APACHE II SCORE IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS"*** is the bonafide work done by ***Dr. M. SIVAKUMAR,*** Post Graduate student (2010 – 2013) in the Department of General Surgery, Government Stanley Medical College and Hospital, Chennai under my direct guidance and supervision, in partial fulfillment of the regulations of The Tamil Nadu Dr. M.G.R Medical University, Chennai for the award of M.S., Degree (General Surgery) Branch - I, Examination to be held in April 2013.

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DECLARATION

I, **DR. M. SIVAKUMAR** solemnly declare that this dissertation titled "**A COMPARATIVE STUDY BETWEEN BISAP AND APACHE II SCORE IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS**" is a bonafide work done by me in the Department of General Surgery, Government Stanley Medical College and Hospital, Chennai under the guidance and supervision of my unit chief **Prof. A. RAJENDRAN, M.S.,** and my Head of the Department **Prof. P. DARWIN, M.S.**

This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the university regulations for the award of M.S., Degree (General Surgery) Branch - I, Examination to be held in April 2013.

Place: Chennai.
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CONTENTS

INTRODUCTION

Acute pancreatitis is a common disorder with substantial burden on the healthcare system[1]. Acute pancreatitis includes wide spectrum of disease varying from mild self-limiting symptoms to fulminant multi organ failure and high mortality. The overall mortality rate is 3-10%, wherein 11-30% of cases are with severe disease manifested as pancreatic necrosis.

`1n 1889, Reginald Fitz described the classic clinico-pathological features of acute pancreatitis and opined about the ineffectiveness and hazards of early operative intervention.

The rationale behind the assessment of severity is mainly for practical purpose, where mild pancreatitis responds to supportive measures well but severe pancreatitis requires intensive monitoring of various parameters, specific therapeutic interventions and it has guarded prognosis.

Since 1974, several scoring systems have been developed clinically and radiologically for this purpose, including Ranson's criteria, the acute physiology and chronic health evaluation (APACHE II) score, Medical Research Council Sepsis Scoring (MRCS) and Bedside Index for Severity in Acute Pancreatitis (BISAP).

Current methods of stratification of risk factors in acute pancreatitis have much important limitations. The Ranson's and Modified Glasgow score (IMRIE's) contains data which are not routinely collected during hospitalization. Both these study require 48 hrs. to complete, thereby minimizing the most precious early therapeutic window period.

The most commonly used APACHE II scoring system however was originally formulated as an intensive care instrument, which required a large number of parameters to be collected, some of them may not be relevant to prognosis[1].

An ideal prognostic method should be able to differentiate between patients with mild & severe disease, easy to use, and widely available and should be accurate, and should have low interobserver variability. It should also be able to apply early in disease process so that patient who could prone to develop potential complications will be closely monitored and treated if possible empirically.

REVIEW OF LITERATURE

HISTORY OF THE PANCREAS

The pancreas was generally ignored in antiquity, both as an organ and as a seat of disease.

The pancreas was ***first discovered by Herophilus***, a Greek anatomist cum surgeon, born in 336 BC on the Asiatic side of the Bosporus in Chalcedon[2].

The word pancreas first mentioned in the writings of Eristratos (310-250 B.C.). The Four hundred years later, ***Rufus,***(1st or 2nd Century AD), an anatomist cum surgeon of Ephesus, **gave the name "pancreas".** Written in Greek language, the word meant **"pan: all, kreas: flesh"[2].**

Galen (Claudius Galenus 138-201 AD), "Physician to the Gladiators" of Rome& the Roman Emperor, taught that the pancreas serves as a cushion to protect the large blood vessels lying behind it[2].

In March 2, 1642, a German émigré, Johann Georg Wirsüng, discovered the pancreatic duct at San Francisco Monastery in Padua, Italy. But it was named by his colleague as "The Duct of Wirsüng"[2].Whereas papilla, the enlargement of that duct at its junction with the common bile duct (CBD) which projects into the

second part of duodenum, were first described by Vater in 1720. Santorini, in 1734, described the accessory duct that bears his name.

In 1869, Paul Langerhans (“Junior”), a student of the famous Berlin Institute of Pathology, headed by the eminent Professor Rudolph Virchow, described the islets of the pancreas that was subsequently known as the “islets of Langerhans”, an endocrine system which lies within the pancreas[2]. This was the first good histologic description of the pancreas.

In 1893, Laguesse suggested that the islet cells produce a hormone. In 1909 Jean de Meyer suggested the name 'insulin' for this hormone.

Eugene Lindsay Opie (1873-1971) was able to show the association between diabetes and failure of the islet cells and in 1901, proposed his "common channel" hypothesis[3].

In 1908, Julius Wohlgemuth, of Berlin, devised a method for measuring the concentration of serum amylase (“diastase”), which was found to be most useful for diagnosing the acute pancreatitis prior to laparotomy or autopsy[2].

Since 1898, many surgeons undertook various steps for the resection of tumors of ampulla and head of the pancreas. ***Allen O. Whipple*** (1881-1963), son of

American missionaries in Persia, was recognized as the ***"Father of Pancreatic Surgery"*** for his successful single stage surgery in pancreatic head tumors[2].

In 1963, the first Marseilles Symposium favored the development of classification system for pancreatitis. This was revised in 1984; at the second Marseilles Symposium.

Finally, at the Atlanta Symposium, in 1992, clinically oriented classification system was established for acute pancreatitis.

In the upcoming years, we may expect further refinements in classification systems with the availability of MRI and other newer innovative technologies.

Although the disease now classified as acute pancreatitis has been known from antiquity, not until the mid-19th century did the importance of pancreas and its severity became evident. In 1889, Fitz presented a succinct clinical and pathologic feature of acute pancreatitis. Moynihan in 1925 described "the most terrible of all the calamities which occur in relation with the abdominal viscera" as acute pancreatitis[4, 5].

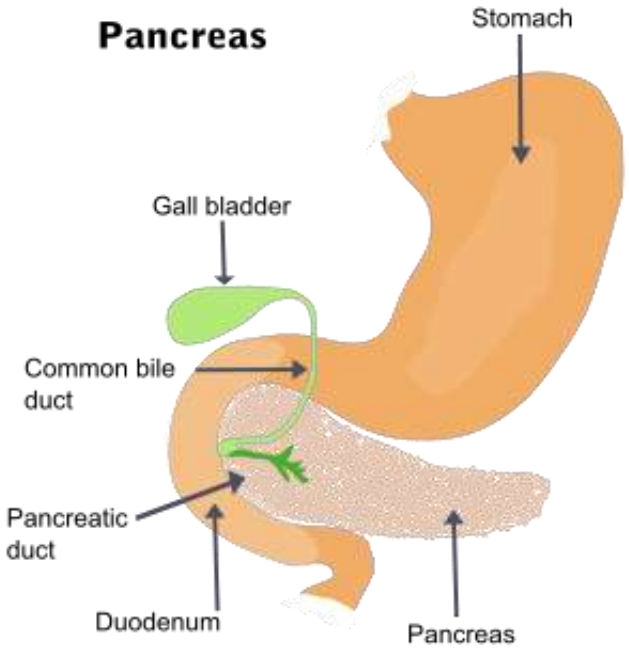
Gross Anatomy

The pancreas perhaps considered as the most unforgivable organ in the human body, which threatens most surgeons to even palpating it unnecessarily[6]. This is a retroperitoneal organ which lies obliquely from the C-loop of the duodenum to the hilum of spleen[7].

The pancreas lies posterior to the stomach, roughly in the Trans pyloric plane. The gland weighs approximately 80 g, varying from 75 – 125g and measures 15 to 22 cm length in adults[7].

The pancreas has four parts[7, 8]:

- The head (which includes the uncinate process),
- The neck,
- The body and
- The tail.



The head lies in the C- loop of the duodenum overlying the body of second lumbar vertebra and the inferior vena cava, with the aorta beneath the neck of the gland, more medially and lies posterior to transverse mesocolon. The right renal artery and both renal veins lie posterior to the head. Coming off the side of the pancreatic head and passing to the left and behind the superior mesenteric vein is the pancreatic uncinate process.

The neck of pancreas lies directly anterior to the portal vein. Behind the neck of the pancreas, near its upper border, the superior mesenteric vein joins the splenic vein and continues toward the portahepatis as the portal vein. The inferior mesenteric vein often drains into the splenic vein near its confluence with portal vein. Sometimes, the inferior mesenteric vein drains into the superior mesenteric vein or merges with the superior mesenteric portal venous junction and forms a trifurcation. The common bile duct lies within a groove in head of the gland or embedded within it, until joining the main pancreatic duct at ampulla of Vater and opens into the 2^{nd} part of the duodenum.

The body and tail of the pancreas related posteriorly to splenic artery and its vein. The splenic vein lies in a groove on the posterior surface of the pancreas and draining multiple fragile pancreatic venous branches. These vessels must be ligated to perform a spleen-sparing distal pancreatectomy. The splenic artery runs parallel

and just superior to the vein along the postero superior edge of the body and tail of pancreas. The splenic artery often has tortuous course. The peritoneum covers the anterior surface of the pancreatic body. Once the gastrocolic omentum was divided, the body and tail of pancreas can be visualized along the floor of the lesser sac, just posterior to the stomach. Pancreatic pseudocysts commonly develop in this area, and the posterior aspect of the stomach can form the anterior wall of the pseudocyst, allowing drainage into the stomach. The transverse mesocolon base attaches to the inferior margin of the body and tail of pancreas.

The body of pancreas overlies the aorta at origin of the superior mesenteric artery. The neck of the pancreas overlies the vertebral body of L1 and L2, and blunt antero-posterior trauma can compress the neck of the pancreas against the spine, causing parenchymal and ductal injury. The neck divides the pancreas into approximately two equal halves.

The tail is referred to as the small portion of the pancreas that lies in front of the left kidney and was nested in the splenic hilum near the splenic flexure of colon.

Pancreatic Ductal Anatomy:

The common variations in pancreatic duct anatomy can be appreciated by understanding the embryology. The pancreas is formed by the fusion of a ventral and dorsal bud[9].

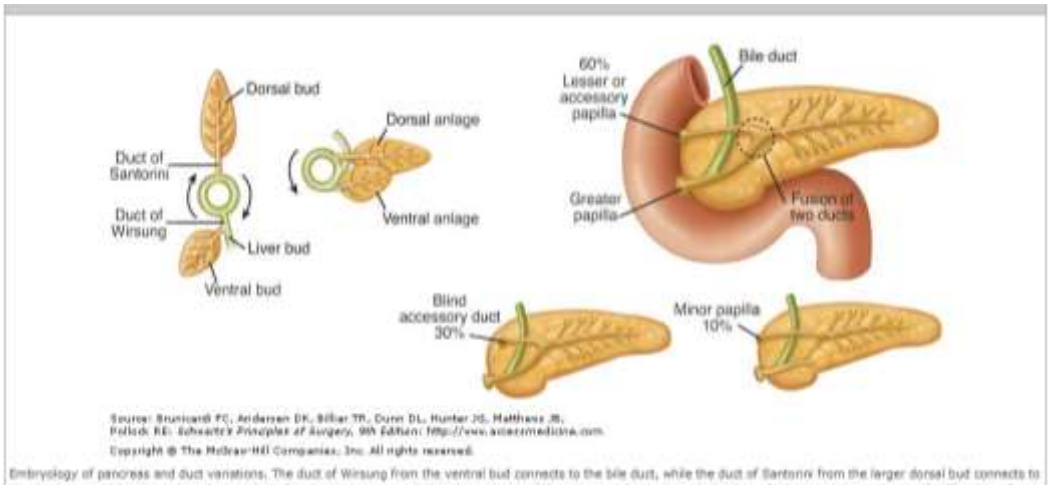
- The duct from the smaller ventral bud, which arises from the hepatic diverticulum, connects directly to the CBD.

- The duct from larger dorsal bud, which arises from the duodenum, drains directly into the duodenum.

The duct of the ventral anlage becomes the duct of Wirsung, and from the dorsal anlage becomes the duct of Santorini. The ducts from each anlage usually fuse together in the pancreatic head such that most of the pancreas drains through the Wirsung, or main pancreatic duct (MPD), into the common channel formed from the CBD and MPD.

The length of common channel is often variable. In about one third of patients, the CBD and MPD remains distinct from the papilla; the two ducts may merge at the papilla in another third, and in the remaining third a true common channels will be there for few millimeters.

Commonly, the duct from the dorsal anlage, the duct of Santorini, persist as the lesser pancreatic duct, and sometimes drains directly into the duodenum through the lesser papilla just proximal to the major papilla. In approximately 30% of patients, the duct of Santorini ends as a blind accessory duct and does not empty into the duodenum. In 10% of patients, the ducts of Wirsung and Santorini fail to fuse with each other. This ends up with the majority of drainage via the duct of Santorini and lesser papilla, while the inferior part of the pancreatic head and uncinate drains via the duct of Wirsung and major papilla. This normal anatomic variant, which occurs in 10% of patients, is referred to as *pancreas divisum*. In a minority of these patients, the lesser papilla can't be to handle the flow of pancreatic juices from the majority of the gland. This relative outflow obstruction can result in pancreatitis and is sometimes treated by sphincteroplasty of the minor papilla.



Embryology of pancreas and duct variations. The duct of Wirsung from the ventral bud connects to the bile duct, while the duct of Santorini from the larger dorsal bud connects to the duodenum. With gut rotation, the two ducts fuse in most cases such that the majority of the pancreas drains through the duct of Wirsung to the major papilla. The duct of Santorini can persist as a blind accessory duct or drain through the lesser papilla. In a minority of patients, the ducts remain separate, and the majority of the pancreas drains through the duct of Santorini, a condition referred to as pancreas divisum.

The MPD is normally 2 to 3 mm in diameter and lies between the superior and inferior borders and closer to the posterior surface. The MPD pressure inside is about twice that of in the CBD, thus said to prevent bile reflux into the pancreatic duct.

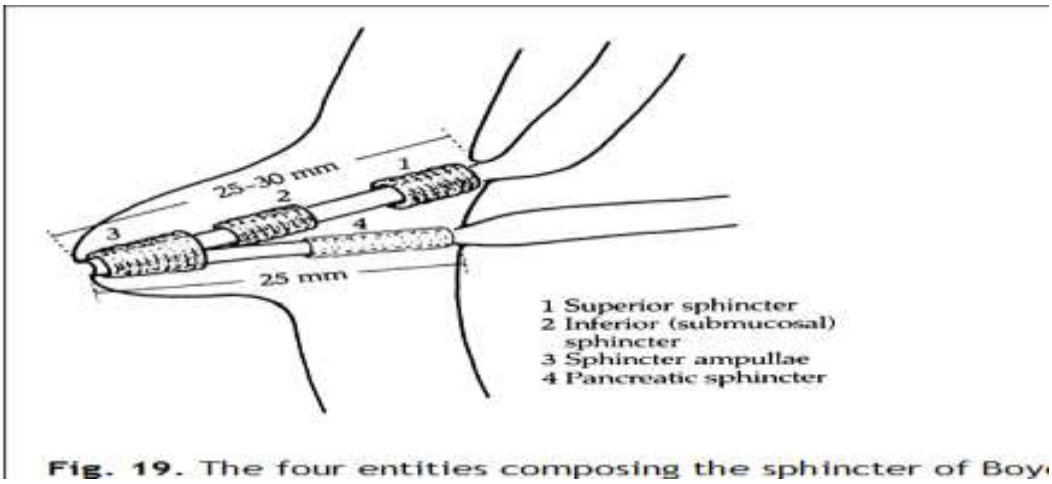


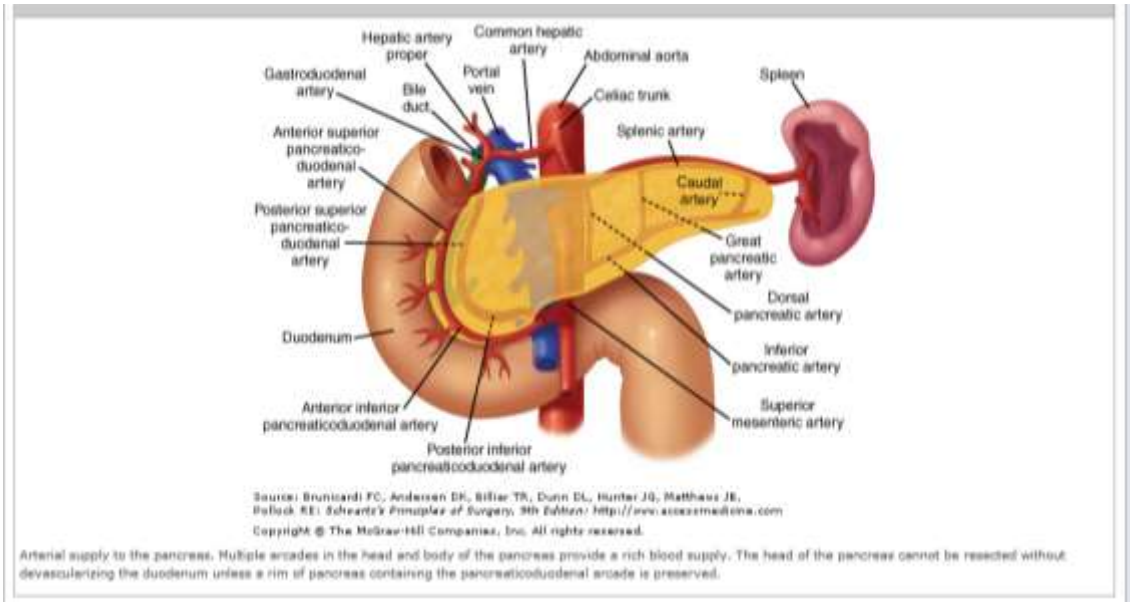
Fig. 19. The four entities composing the sphincter of Boy

The muscle fiber which lies around the ampulla forms the sphincter of Oddi that controls the flow of biliary and pancreatic secretions into the 2nd part of duodenum. Contraction and relaxation of this sphincter is regulated by both hormonal and neural factors. When the accessory pancreatic duct or lesser duct drains into the duodenum, a lesser papilla can be identified 2 cm proximal to the major papilla.

Arterial supply

The pancreatic blood supply comes mainly from the celiac axis and the superior mesenteric artery[7, 8].

The coeliac axis gives the common hepatic artery which in turn gives rise to the gastroduodenal artery before continuing toward the porta hepatis as the hepatic artery proper. The gastroduodenal trunk becomes the superior pancreaticoduodenal artery as it passes behind the first portion of the duodenum and branches into the anterior and posterior divisions.



Arterial supply to the pancreas. Multiple arcades in the head and body of the pancreas provide a rich blood supply. The head of the pancreas cannot be resected without devascularizing the duodenum unless a rim of pancreas containing the pancreaticoduodenal arcade is preserved.

The superior mesenteric artery while passing behind the neck of pancreas, it gives off the inferior pancreaticoduodenal artery, this quickly divides into the anterior and posterior divisions. The superior and inferior pancreaticoduodenal

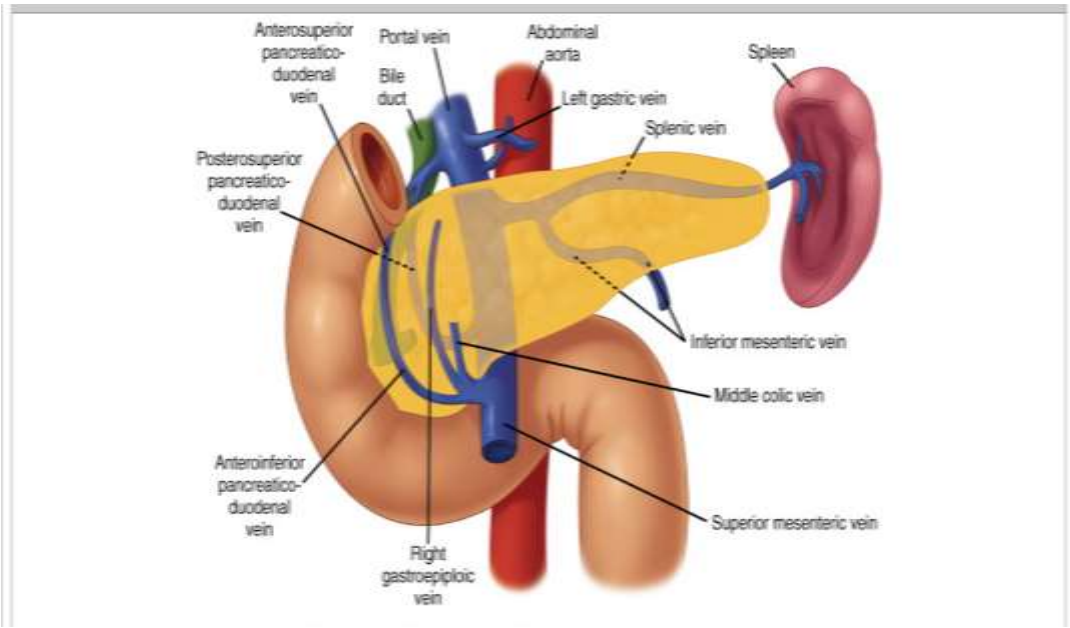
arteries anastomose within the parenchyma of the head of pancreas along the medial aspect of the C-loop of duodenum to form arcades that give off numerous branches to duodenum and head of pancreas. Therefore, it is impossible to resect the pancreatic head without devascularizing blood supply to the duodenum, unless a rim of pancreas containing the pancreaticoduodenal arcade is preserved.

The body and tail are supplied by multiple branches from splenic artery. Three vessels run perpendicular to the long axis of the pancreatic body and tail and connect the splenic artery and inferior pancreatic artery. They are, from medial to lateral, the dorsal (AKA the transverse pancreatic artery), great, and caudal pancreatic arteries. These arteries form arcades within the body and tail of pancreas, and account for rich blood supply to the organ.

Venous drainage

The venous drainage of the pancreas follows the arterial supply[7, 8]. The veins are usually superficial to the arteries within the parenchyma of the pancreas. There is an anterior and posterior venous arcade within the pancreatic head. The superior vein drains directly into the portal vein and the posterior inferior arcade drains directly into inferior mesenteric vein. The anterior inferior pancreaticoduodenal vein joins the right gastro-epiploic vein and the middle colic vein and forms a common venous trunk that drains into the (SMV) superior mesenteric vein.

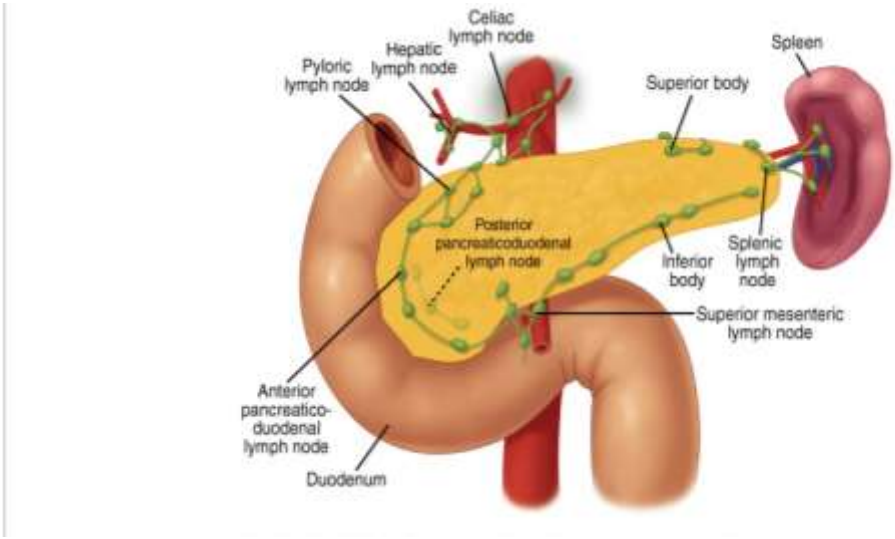
Traction on the transverse colon during colectomy can tear these fragile veins, which then retract into the parenchyma of the pancreas, making control tedious. There also are numerous small venous branches coming from the pancreatic parenchyma directly into the lateral and posterior aspect of the portal vein. Venous return from the body and tail of the pancreas drains into the splenic vein.



Lymphatic drainage

The pancreas has rich lymphatic drainage and follows venous drainage in all directions[7]. This diffuse lymphatic drainage contributes to the fact that pancreatic cancer often presents with positive lymph nodes and a high incidence of local recurrence after resection. Lymph nodes can be palpated along the posterior aspect of pancreatic head in the pancreaticoduodenal groove, where the mesenteric vein

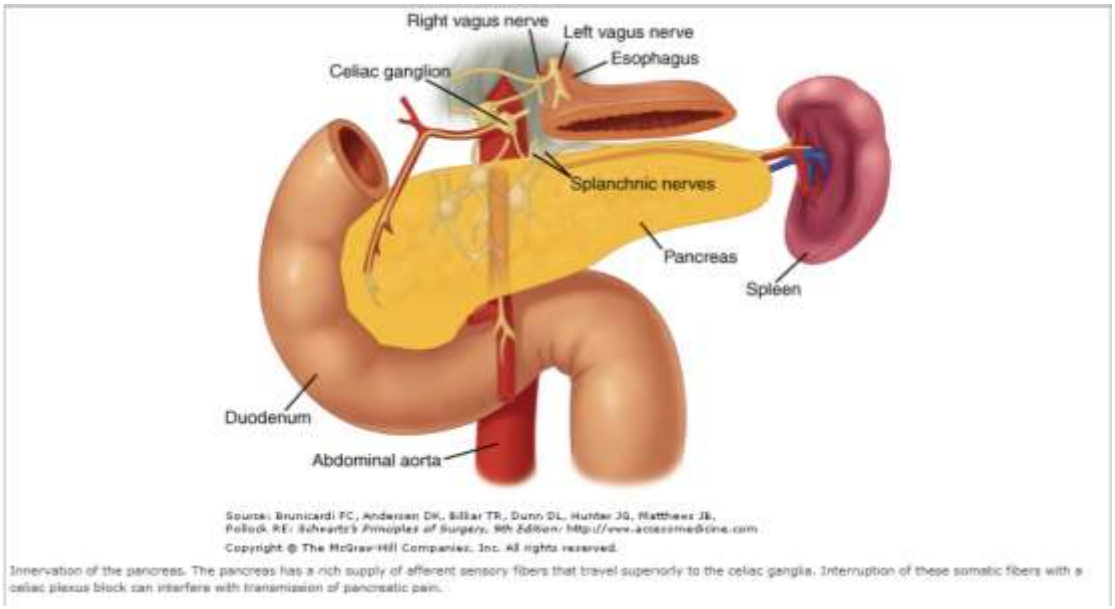
passes under the pancreatic neck, along inferior border of the pancreas, along the hepatic artery ascending into the portahepatis, and along the splenic artery and vein. The pancreatic lymphatics also communicate with lymph nodes in the transverse mesocolon and mesentery of the proximal jejunum. Tumors in the body and tail often metastasize to these nodes and lymph nodes along the splenic vein and in the hilum of the spleen.



Nerve supply

The pancreas is innervated by both sympathetic via splanchnic nerve & parasympathetic via vagus nerve[7, 8]. The acinar cells responsible for exocrine secretion, the islet cells responsible for endocrine secretion, and the islet vasculature are innervated by both systems. The parasympathetic system stimulates endocrine and exocrine secretion and the sympathetic system inhibits secretion. The pancreas is also innervated by neurons that secrete amines and peptides, such

as somatostatin, calcitonin gene-related peptide (CGRP), vasoactive intestinal peptide (VIP), and galanin. The exact physiological role of these neurons is not certain, may appear to affect both exocrine and endocrine function. The pancreas also has a rich supply of afferent sensory fibers, which are responsible for the intense pain associated with advanced pancreatic cancer, as well as acute and chronic pancreatitis. These somatic fibers travel superiorly to the celiac ganglia. Interruption of these somatic fibers can stop transmission of pain sensation in pancreatic disease.



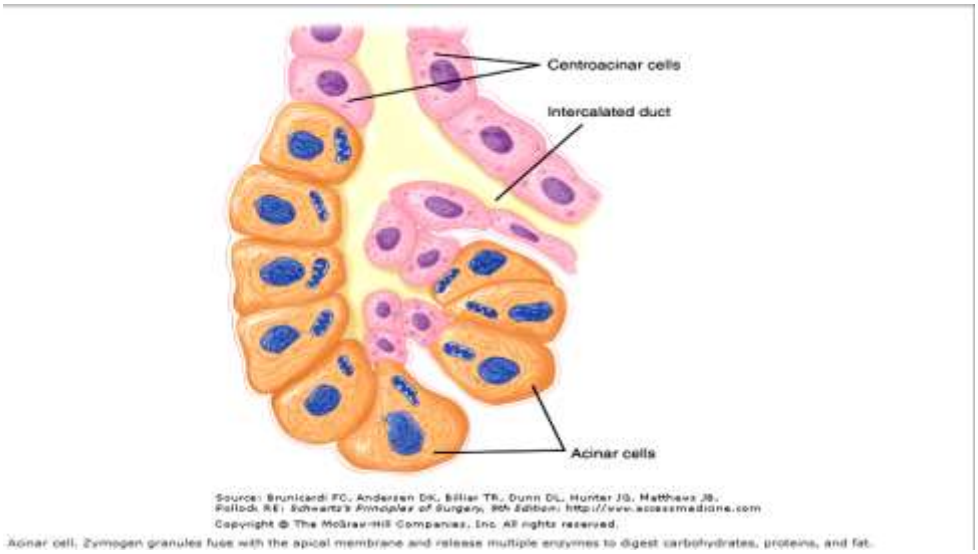
Innervation of the pancreas. The pancreas has a rich supply of afferent sensory fibers that travel superiorly to the celiac ganglia. Interruption of these somatic fibers with a celiac plexus block can interfere with transmission of pancreatic pain.

Histology

Pancreas has exocrine and the endocrine glandular tissues. The exocrine pancreas consists of acinar glands whereas the endocrine part consists of islets of Langerhans[10].

The pancreas contains 85% exocrine gland, 10% extracellular matrix, and 4% blood vessels & the major ducts, and only 2% of endocrine tissue[11]. Thus the endocrine and exocrine pancreas is thought to be functioning separately, but coordinated well for regulating the feedback system of digestive enzyme and hormone secretion.

The acinar cells, so named because they are clustered like grapes on the stem of a vine, are organised into lobules. The main duct ramifies into intralobular and interlobular ducts, ductules and finally acini, that secretes into a centrally located acinar space that communicates with the main pancreatic duct. Histologically, acinar cells have a high content of endoplasmic reticulum and an abundance of apically located eosinophilic zymogen granules. The cells lining the main pancreatic duct are tall columnar cells, and many contain mucin granules. With progression from the large ducts to the smaller intralobular and interlobular ducts, the lining cells become flatter, assuming a cuboidal configuration, and mucin granules are no longer seen. Centroacinar cells, located at the junction between ducts and acini, resemble acinar cells in size and shape but lack zymogen granules[7].



The islets of Langerhans are distributed throughout the pancreas. Within an islet, the B cells form an inner core surrounded by the other cells. Capillaries draining the islet cells drain into the portal vein forming a pancreatic portal system.

Surgical physiology

In response to a meal, the pancreas secretes digestive enzymes in an alkaline (pH 8.4) bicarbonate-rich fluid. The duodenal mucosa releases the hormone secretin which evokes a bicarbonate-rich fluid. Cholecystokinin-pancreozymin (CCK) is released from the duodenal mucosa in response to food: CCK produces no increase in the volume of secretion, but is responsible for enzyme secretion. Vagal stimulation increases volume. Approximately 6 - 20 g of digestive enzymes enters the duodenum each day[7, 8].

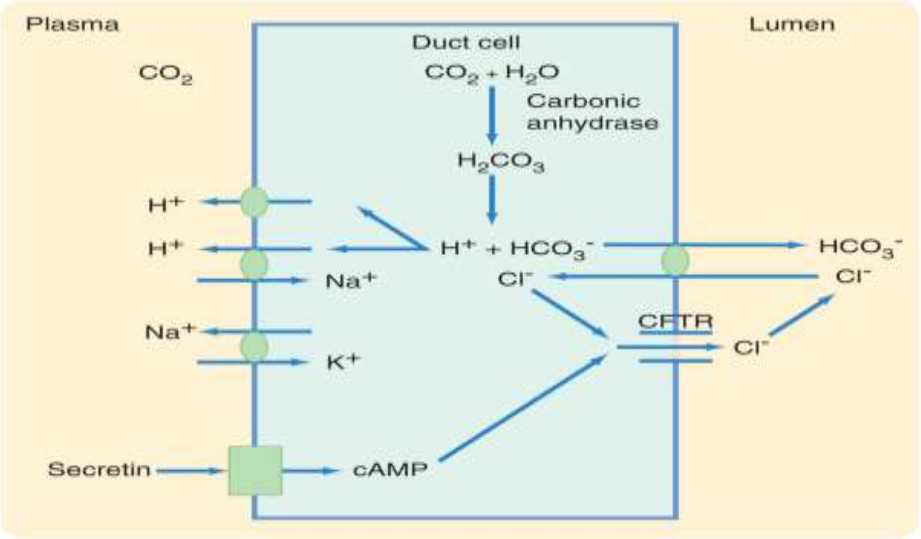
Exocrine Pancreas

The pancreas secretes about 500 to 800 mL of colourless, odourless, isosmotic, alkaline, pancreatic juice daily[7]. Pancreatic juice is made up secretions from ductal and acinar cells. The acinar cells secrete the enzymes that are responsible for digestion of carbohydrate, protein, and fatty foods.

Pancreatic amylase is the only enzyme secreted in active form and all other enzymes are secreted in proenzymes form which requires further activation for their action.Familial pancreatitis is a condition, where there is no expression of normal trypsinogen inhibitors, like *SPINK1 or* pancreatic secretory trypsin inhibitor (PSTI). Trypsinogen is expressed in several isoforms and a missense mutation on the cationic trypsinogen, or *PRSS1*, results in premature, intrapancreatic activation of trypsinogen[12]. This accounts for the basis of hereditary pancreatitis.

Table 33-1 Pancreatic Enzymes

Enzyme	Substrate	Product
Carbohydrate		
Amylase (active)	Starch, glycogen	Glucose, maltose, maltotriose, dextrins
Protein		
Endopeptidases	Cleave bonds between amino acids	Amino acids, dipeptides
Trypsinogen (inactive) $\xrightarrow{\text{Enterokinase}}$ Trypsin (active)		
Chymotrypsinogen (inactive) $\xrightarrow[\text{Trypsin}]{\text{Enterokinase}}$ Chymotrypsin (active)		
Proelastase (inactive) $\xrightarrow[\text{Trypsin}]{\text{Enterokinase}}$ Elastase (active)		
Exopeptidases	Cleave amino acids from end of peptide chains	—
Procarboxy peptidase A&B (inactive) $\xrightarrow{\text{Enterokinase}}$ Carboxypeptidase		
A&B (active)		
Fat		
Pancreatic lipase (active)	Triglycerides	2-Monoglycerides fatty acids
Phospholipase A2 (inactive) $\xrightarrow{\text{Trypsin}}$ Phospholipase A2 (active)	Phospholipase	—
Cholesterol esterase	Neutral lipids	—



At the time of secretion from the pancreatic acini, the proteolytic enzymes are in an inactive form, the maintenance of which is important in preventing pancreatitis.

Endocrine Pancreas

There are about 1 million pancreatic islet cells present in adults normally. The size varies from 40 – 900 µm. largest cells lie close to major arterioles and smaller cells are embedded more deeply in the parenchyma. Most islets contain five major types of cells:

1. α cells - secretes glucagon(20%)
2. β cells - secretes insulin(75%)
3. δ cells - secretes somatostatin
4. ε cells - secretes ghrelin and
5. PP cells - secretes pancreatic polypeptide.

Table 33-2 Pancreatic Islet Peptide Products		
Hormones	**Islet Cell**	**Functions**
Insulin	β (beta cell)	Decreased gluconeogenesis, glycogenolysis, fatty acid breakdown, and ketogenesis
		Increased glycogenesis, protein synthesis
Glucagon	α (alpha cell)	Opposite effects of insulin; increased hepatic glycogenolysis and gluconeogenesis
Somatostatin	γ (delta cell)	Inhibits GI secretion
		Inhibits secretion and action of all GI endocrine peptides
		Inhibits cell growth
Pancreatic polypeptide	PP (PP cell)	Inhibits pancreatic exocrine secretion and section of insulin
		Facilitates hepatic effect of insulin
Amylin (IAPP)	β (beta cell)	Counterregulates insulin secretion and function
Pancreastatin	β (beta cell)	Decreases insulin and somatostatin release
		Increases glucagon release
		Decreases pancreatic exocrine secretion
Ghrelin	ε (epsilon cell)	Decreases insulin release and insulin action

IAPP = islet amyloid polypeptide.

ACUTE PANCREATITIS

Definition:

Acute pancreatitis is "an inflammatory disease, associated with little or no fibrosis of the pancreas". There are several initiating factors, which include gallstones, alcohol, trauma, and infections, and, rarely hereditary[7].

Etiology of acute pancreatitis:

There are so many different factors have been implicated in the causation of this disease. On the basis of worldwide data, the most common cause are gallstones, account for about 45 percent of cases. Alcoholism is the second

common cause**,** in about 35 percent of cases. In a study done in New Delhi, India, gall stones and alcoholism were found to be the cause in 49% and 23.6% cases, respectively[13].

The disease occurs at higher rate in young men and older women. Females are more prone to have gall stone pancreatitis and males are more prone to have alcohol induced pancreatitis[14].

CAUSES OF ACUTE PANCREATITIS[7]:

Alcohol

Biliary tract disease

Obstructive causes:

- Choledocholithiasis
- Ampullary carcinoma or pancreatic malignancy
- Papillary obstruction by worms/foreign bodies
- Pancreas divisum with minor duct obstruction
- Choledochocele
- Duodenal diverticula at periampullary region
- Spasm sphincter of Oddi

Toxins or drugs:

- Toxins:- ethanol/methanol, scorpion sting, organo phosphorous compounds
- Drugs:- **Definite Cause**

- 5-Aminosalicylate (ASA)
- 6-Mercaptopurine (6-MP)
- Azathioprine
- Cytosine arabinoside (cytarabine)
- Didanosine
- Diuretic agents
- Estrogens, etc.

Probable Cause

- Acetaminophen
- α-Methyl-DOPA
- L-Asparaginase
- Isoniazid (INH)
- Phenformin, etc.

Trauma:

- External / surgical traumatic injury to the abdomen.
- Iatrogenic injury- postoperative trauma, post ERCP, post endoscopic sphincterotomy and manometry of sphincter of Oddi

Metabolic abnormalities:

- Hypercalcemia
- Hypertriglyceridemia

Inherited conditions

Infection:

- Parasitic:- ascariasis, Clonorchis sinensis
- Viral:- mumps, rubella, hepatitis A, B, non-A, non-B, coxsackie B, echo virus, adenovirus, CMV, varicella, EBV, HIV.
- Bacterial: - mycoplasma pneumoniae, Campylobacter jejuni, Myco. tuberculosis, MAC, legionella pnemophila, leptospiral infection

Vascular causes:

- hypo perfusion causing ischemia (e.g., after major cardiac vascular surgery)
- Athero-embolism
- Vasculitis-SLE, PAN, malignant hypertension

Miscellaneous causes:

- Peptic ulcer penetration
- Cystic fibrosis
- Crohn's disease
- Reye's syndrome
- Hypothermia

Idiopathic causes

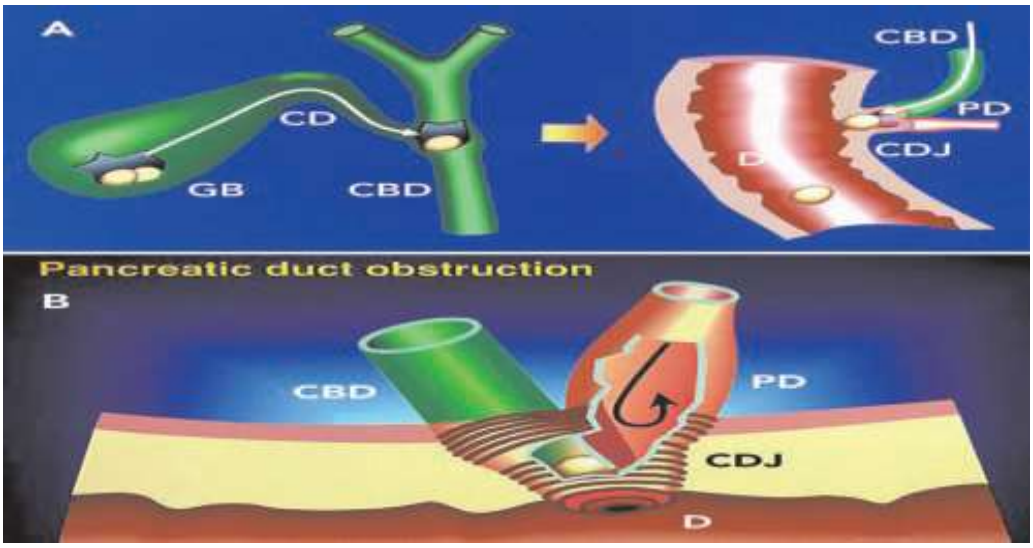
Gall stones

Gall stones are the leading cause of acute pancreatitis in most series (30-60%). Women are more commonly affected than men, and the peak incidence is between 50 to 60 yrs of age[14].

In 1901, Opie, at the Johns Hopkins Hospital in Baltimore, documented impaction of gallstone in the ampulla of Vater during the autopsy of a patient (operated on by Halsted) who had died due to gallstone pancreatitis and thereby first to describe the pathogenic mechanism of gallstone induced pancreatitis[3].He suggested that the stone might have caused outflow obstruction from a common 'biliopancreatic channel'. This led him to propose the "common-channel hypothesis[3]" in which a blockage below the junction of the biliary and pancreatic ducts would cause bile to flow into the pancreas, which could then be damaged by the detergent action of bile salts. Although this bile reflux theory was originally favored, most observers now believe that it is stone-induced pancreatic duct obstruction and ductal hypertension, rather than bile reflux that triggers acute pancreatitis.

Opie's hypothesis regarding the pathogenesis of pancreatitis has dominated much of the twentieth century, but it's regarded as a myth today. By experiments in opossum animal model with easily accessible long common channel, Lerch et al. have demonstrated that pancreatic duct obstruction alone causes necrotizing pancreatitis which can't be distinguishable from that occurred when CBD also occluded simultaneously. On commenting the demise of the Opie's theory, Fitzgerald remarked, 'never in medical history have so many owed so much to a single stone'.

Another proposed mechanism of causation postulates that passage of a gallstone through the sphincter of Oddi renders it momentarily incompetent, permitting the reflux of duodenal juice containing activated digestive enzymes into the pancreatic ductal system.



Microlithiasis (occult gall stones/biliary sludge) is a well-known cause of acute pancreatitis. The diagnosis of microlithiasis should be ruled out before labeling the disease as idiopathic pancreatitis. Biliary microscopy & endosonogaraphy are recommended nowadays to diagnose the microlithiasis.

Alcohol

The second most common etiological agent, alcohol is responsible for about 30% of all cases. In a patient with history of exposure to alcohol with absence of

other possible causes, even the first attack of pancreatitis is considered to be related to alcoholic pancreatitis. However, it is possible that a first attack of alcohol-related pancreatitis in the typical longstanding alcohol user is really the first manifestation of chronic pancreatitis. The disease can recur with continuous abuse of alcoholism. The nature of alcohol that was consumed (i.e., beer, wine, or hard liquor) is less significant than a daily intake of between 100 and 150 g of ethanol[7].

Various theories have been put forward[7, 8]:

1. Alcohol consumption can alter lipid metabolism, and a transient hyperlipidemic state that causes hypertriglyceridemia and the generation of fatty acids as well as their ethyl ester metabolites, that can injure the pancreas.

2. Alcohol consumption causes intra pancreatic generation of oxygen free radicals, which can injure the pancreas.

3. It promotes secretion of pancreatic juice that is high in proteolytic enzyme content but low in enzyme inhibitor content. Enzyme activation can theoretically occur in these conditions and cause pancreatic injury.

4. The "***secretion with blockage***" mechanism is possible because ethanol causes spasm of the sphincter of Oddi, leading to ductal hypertension and, more important, ethanol is a metabolic toxin to pancreatic acinar cells, where it can interfere with enzyme synthesis and secretion.

5. Secretion of enzyme-rich fluid, deficient in enzyme inhibitors could also lead to precipitation of protein and calcium within this protein matrix, causing multiple ductal obstructions, while continued secretion can cause pressure to buildup and the formation of intra-ductal plugs, which cause ductal obstruction and ductal hypertension.
6. Ethanol causes focal ischemic injury to the gland, thereby transiently decreases pancreatic blood flow.

Hyperlipidemia

It is responsible in 1.5-4 % of cases. Triglyceride level > 1000 mg/dl increases the likelihood of developing pancreatitis. It is hyperlipidemia type I, IV or V that causes pancreatitis. It has been suggested that lipase can liberate large amounts of toxic fatty acids into the pancreatic microcirculation[8]. This could lead to endothelial injury, sludging of blood cells, and consequent ischemic states.

Hypercalcemia

Hypercalcemia secondary to hyperparathyroidism or any other cause can cause acute pancreatitis. The mechanism most likely involves hyper secretion and the formation of calcified stones intra ductally.

Iatrogenic Pancreatitis

Acute pancreatitis can be associated with a number of surgical procedures[7], most commonly those performed on or close to the pancreas, such as pancreatic biopsy, biliary duct exploration, distal gastrectomy and splenectomy. Acute pancreatitis is associated postoperatively with Bill Roth II gastrectomy and jejunostomy, in which increased intraduodenal pressure can cause backflow of activated enzymes into the pancreas. However, pancreatitis also can occur in association with surgery that uses low systemic perfusion, such as cardiopulmonary bypass and cardiac transplantation. Acute pancreatitis has been reported to be associated with severe hypothermia, and the hypothermia associated with cardiopulmonary bypass may be similarly causative. It also is possible that atheromatous emboli or ischemia may cause pancreatic injury. Most commonly, endoscopic retrograde cholangio pancreatography (ERCP) results in pancreatitis in 2 to 10% of patients, due to direct injury and/or intraductal hypertension. Similarly manometry of sphincter of Oddi is associated with increased risk for AP.

Tumours

About 1 to 2% of patients with acute pancreatitis may have pancreatic malignancy, in which an episode of acute pancreatitis could be the first clinical sign of a periampullary tumor. In both conditions, the pancreatitis occurs probably due to blockade of pancreatic secretion and its upcoming consequences.

Drugs

For practical reasons, it often is difficult to implicate a drug as the cause of pancreatitis. Many drugs can produce hyperamylasemia and/or abdominal pain, and a drug is considered to be a cause if the pancreatitis-like illness resolves with its discontinuation.

Infections

Though mumps, coxsackievirus, and *Mycoplasma pneumoniae* are believed to be capable of inducing acute pancreatitis by infecting the acinar cells, none of these agents has been isolated from a diseased pancreas. The antibody titres to mumps and coxsackievirus are elevated in about 30% of cases with acute pancreatitis with no other identified cause. However, this elevation may be an anamnestic or nonspecific response to pancreatitis.

Miscellaneous Causes

The infestations by Ascaris lumbricoides and the liver fluke Clonorchis sinensis, which is endemic to China, Japan, and Southeast Asia, cause Oriental cholangitis, which is associated with cholangiocarcinoma obstructing the pancreatic duct.

A dominant gene mutation following Mendelian inheritance is known to result in hereditary pancreatitis. Whitcomb and associates described several families from various parts of the world were found to have mutations in the cationic trypsinogen gene *PRSS1*, which results in acute pancreatitis.

20 to 45% of patients with pancreas divisum (unfused ducts of Wirsung and Santorini) develop pancreatitis, but the failure of procedures to improve drainage of the lesser papilla in reducing attacks of pancreatitis, as well as the observed lack of ductal dilatation in such patients, contradicts pancreas divisum as an etiologic factor, rendering the role of this condition as yet unclear[12].

Other implicated factors include azotaemia, vasculitis, and the sting of the Trinidadian scorpion Tityus trinitatis. This scorpion's venom has been shown to cause neurotransmitter discharge from cholinergic nerve terminals, leading to massive production of pancreatic juice. Poisoning with anti-acetyl cholinesterase insecticides has a similar effect.

Finally, no apparent cause can be ascribed to some episodes of acute pancreatitis, and these constitute the group referred to as *idiopathic pancreatitis*, which is the third most common cause of acute pancreatitis[15].

Pathophysiology

Acute pancreatitis occurs in varying degrees of severity, the determinants of which are multifactorial**.** It is generally believed that acute pancreatitis is triggered by digestive enzymes which got activated inside acinar cells. This was thought to be counter acted by endogenously secreted pancreatic enzyme inhibitor. The ultimate severity depends upon the event that subsequently occurs following the acinar cell injury. The events are activation and recruitment of inflammatory cell, synthesis and release of cytokines and other chemical mediators of inflammation. Large amounts of liberated digestive enzymes however overwhelm the system as a whole.

There are three reasons for this theory[7, 15]:

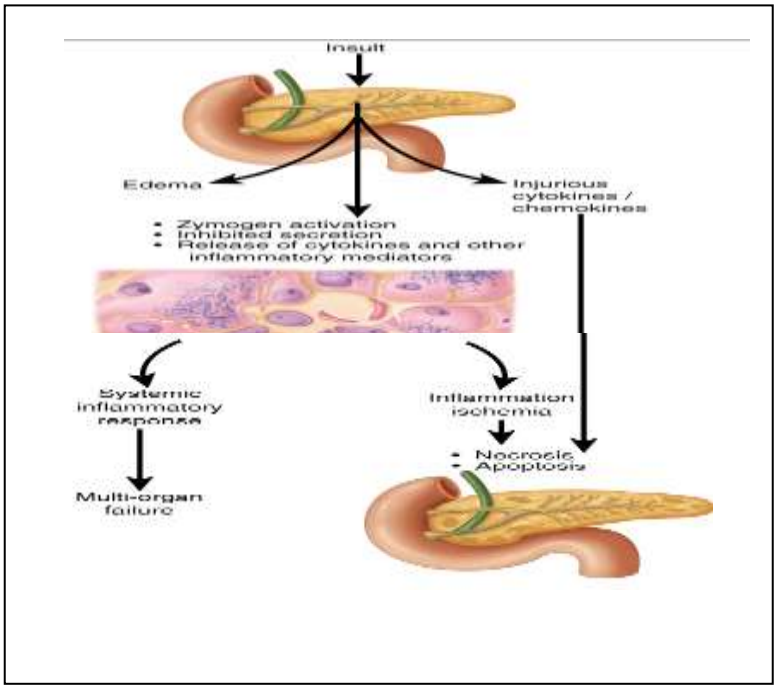
(a) The pancreas is digestible by the activated enzymes of the duodenum.

(b) Activated digestive enzymes are found within the pancreas during pancreatitis.

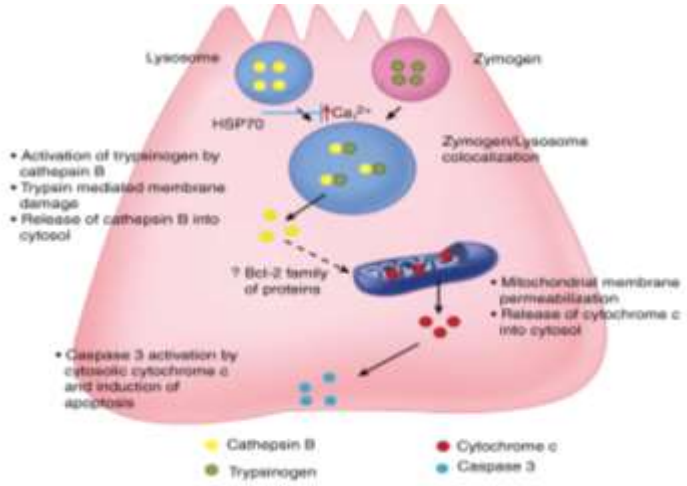
(c) The histology of pancreatitis is suggestive of a coagulative necrosis.

However, the mechanism(s) of erroneous activation are not fully understood.

According to "***colocalization hypothesis***" digestive enzymes are localized in cytoplasmic vacuoles which also contain the lysosomal hydrolase Cathepsin B, which is known to activate trypsinogen[7]. Recent studies suggest that cathepsin B activity inhibition by highly specific inhibitor, CA-074me, protects against intra-acinar cell activation of trypsinogen and hence pancreatitis. These findings suggest that the trypsinogen is activated because it erroneously colocalises in cytoplasmic vacuoles with cathepsin B.



Recent studies suggest that trypsin, once activated inside the colocalized vacuoles (appears similar to autophagic vacuoles), mediates the permeability of these organelles and release of their contents into the cytosol. Cathepsin B is one of the enzymes released into the cytosol



during pancreatitis. Once inside the cytosol, it initiates apoptotic cell death by permeabilizing mitochondrial membranes, which allows cytochrome C to be released into the cytosol. This initiates the apoptotic cascade and ultimately the apoptotic death of the acinar cells.

FACTORS DETERMINING THE SEVERITY OF PANCREATITIS:

The severity of acute pancreatitis varies significantly. Some may have mild form of the disease that is self-limiting, while others suffer a more severe and sometimes lethal attack. The factors determining the severity of pancreatitis are multifactorial, but their identification is of considerable therapeutic importance, because their manipulation may decrease the morbidity and mortality associated with the disease.

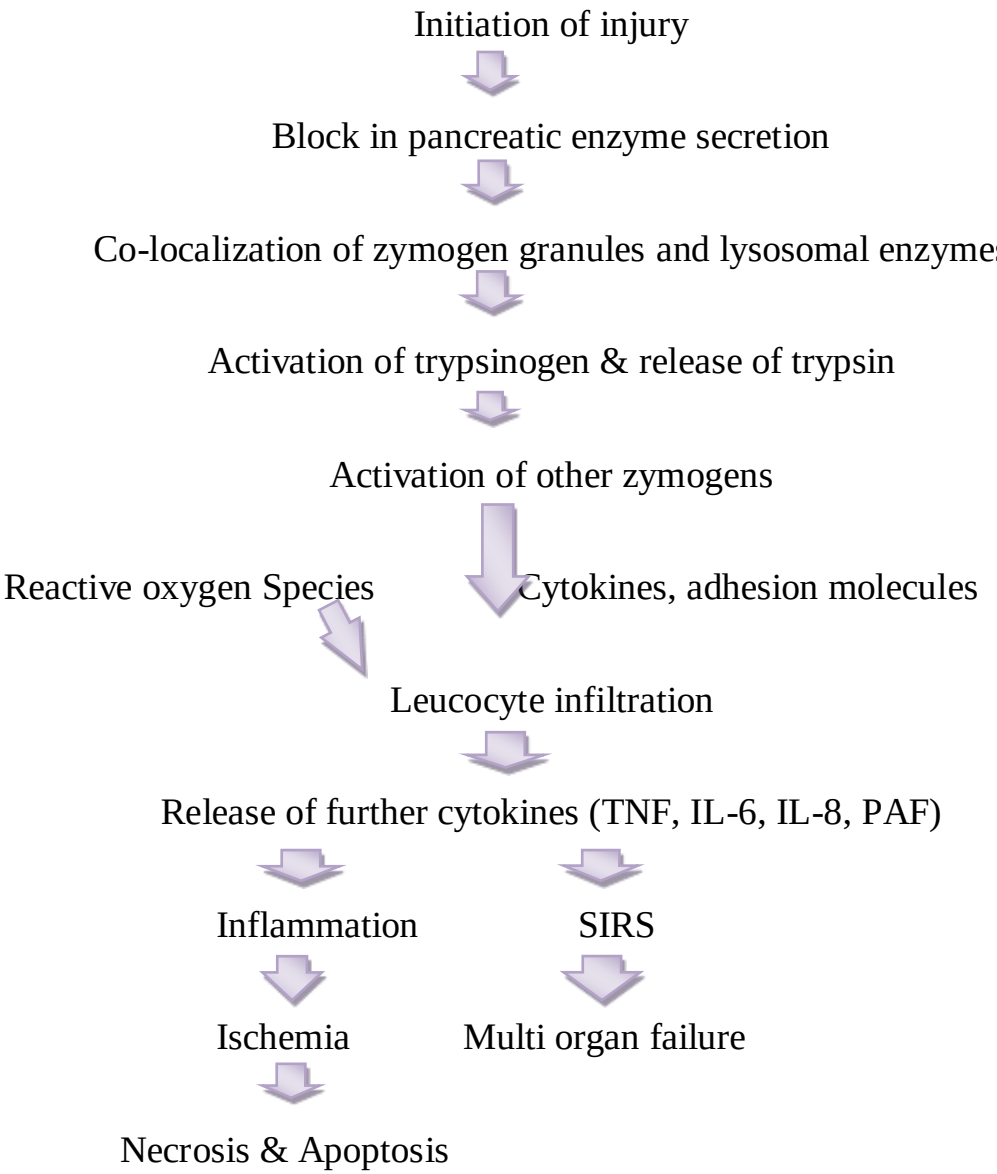
In addition to the cells of the immune system like neutrophils, the pancreatic acinar cells are also a source of inflammatory mediators during pancreatitis. The list of factors associated with pancreatitis and associated lung injury include: tumor necrosis factor alpha, monocyte chemotactic protein-1, Mob1, interleukin-1β (IL-1β), platelet activating factor, substance P, adhesion molecules [intercellular adhesion molecule-1 (ICAM-1) and selectins], IL-6, 8, 10, C5a, the CCR1 receptor and its ligands, granulocyte-macrophage colony-stimulating factor(GMCSF), macrophage migration inhibitory factor, COX-2, prostaglandin E1, nitric oxide (NO) and reactive oxygen species. The heat shock proteins are found to be protective in pancreatitis. The ultimate severity of pancreatitis and associated lung injury depends on the balance between the pro-inflammatory and anti-inflammatory factors[7].

Several therapeutic regimens aimed at reducing the inflammatory response have been tested and include anti–tumor necrosis factor alpha antibody, IL-1 receptor antagonist, IL-10, anti-ICAM-1 and anti-CD3 Ab, rPAF acetyl hydrolase, and the calcineurin antagonist FK506[8].

Recent studies also indicate that Toll-like receptor 4 (TLR4) is significant in determining the severity of acute pancreatitis. The TLR4 initiates a complex signaling pathway when it interacts with lipopolysaccharides that result in a

proinflammatory response. Mice in which TLR4 is genetically deleted have significantly reduced pancreatitis; this suggests that TLR4 is a significant promoter of proinflammation. However, this effect appears independently of lipopolysaccharides and is probably mediated by a hitherto unknown TLR4 agonist. It is likely that TLR4 antagonists would be a good therapy against pancreatitis[15].

An alternate approach to prevent or reduce the severity of pancreatitis is to inhibit intrapancreatic trypsinogen and NF-κB activation, the two events which occurs early in pancreatitis. Agents that specifically prevent an increase in trypsin activity, either by inhibiting trypsinogen activation and colocalization (e.g., low doses of wortmannin, water immersion, and thermal stress) or inhibiting the cathepsin B activity (E64d or CA074me), are found to be successful in reducing the severity in experimental rodent models. Prior thermal (and arsenite) & water immersion stress, up regulates hsp 70 and 60, respectively, not only prevent cerulein-induced trypsinogen activation, but also inhibit cerulein-induced NF-κB activation within the pancreas, hence protective in pancreatitis[7, 8].



Schematic representation of the mechanisms of pathogenesis of acute pancreatitis[16]

Clinical presentation:

The clinical presentation, diagnosis, and management of an acute attack of pancreatitis are similar regardless of whether that attack is acute or chronic pancreatitis. The acute pancreatitis can mimic like acute abdomen and should never be excluded in differential diagnosis[8].

Abdominal pain, nausea, and vomiting are the predominant symptoms. Each episode begins with severe pain, following a substantial amount of meal. The cardinal symptom is usually epigastric pain, but can occur anywhere in the abdomen or lower chest. The pain was described as "knifing" or "boring through" to the back, and might be relieved by leaning forward(***Mohmadian prayer position***). Pain starts 12-48 hours after a bout of alcohol or after a large meal in case of gall stone pancreatitis. Pain became generalized once peritonitis has been sets in[8, 15].

Peritoneal dialysis, post-operative situations, legionnaire's disease are well known for the occurrence of uncommon painless pancreatitis.

If patient develops generalized paralytic ileus abdominal distension and vomiting can occur. The vomiting may lead to gastro esophageal tears (i.e., Mallory-Weiss syndrome) and upper gastrointestinal bleeding. Vomiting is more

intense in necrotizing pancreatitis than in edematous pancreatitis. Although vomiting and retching may be relieved by passage of a nasogastric tube, the pain usually persists even after gastric decompression.

Fever is an important sign. Fever in the first week is due to acute inflammation mediated by cytokines. Fever in the second or third week is due to infected pancreatic necrosis. Fever in gall-stone induced pancreatitis, may be due to cholangitis and mandates prompt biliary decompression.

Physical Findings:

On examination, the patient may be tachypneic, hypotensive, and hyper thermic, and have tachycardia[7, 8]. The temperature was mildly elevated in uncomplicated pancreatitis. Voluntary and involuntary guarding may present over the epigastric region. The bowel sounds may be decreased or absent. There is usually no palpable swelling or masses. The abdomen may be distended with free intraperitoneal fluid, may associated with pleural effusion, particularly on the left side.

With increasing severity, there are sequestrations of fluid in the retro peritoneum that leads to life threatening intravascular fluid loss. This leads to hemoconcentration. There might be bleeding into the retro peritoneum or

peritoneal cavity which may dissect via the soft tissues and appears as a bluish discoloration around the umbilicus (Cullen's sign) or in the flanks (Grey Turner's sign) and the inguinal region (Fox's sign) [17]. Neither sign is pathognomonic of AP; actually the Cullen's sign was first described with ruptured ectopic gestation.

The severe intravascular fluid loss may lead to acute renal shutdown with elevated BUN and creatinine levels. And also there may be hyperglycemia, hypoalbuminemia, and hypocalcemia that are sufficient enough to produce tetany in few cases.

Diagnosis:

The clinical diagnosis is one of exclusion and diagnosis may be difficult despite the plenty of investigation that are available.

Serum pancreatic enzymes:

Serum pancreatic enzyme estimation is the gold standard for diagnosis[18]. The reason is pancreatic acinar cells synthesize, store, and secrete a large amount of digestive enzymes (e.g., amylase, lipase, trypsinogen, and elastase), the levels of which are elevated in the serum of most patients.

Amylase, lipase, elastase and trypsin were released into the blood stream at the same time, but their clearance varied with different sensitivities, depends on the timing of blood sampling after the onset of disease.

Because of the ease of measurement, serum amylase levels are measured most often. Serum amylase concentration will increase immediately reaches the peak value within several hours after the onset of disease and remains elevated for 3 to 5 days before returns back to normal. There was no significant correlation between the magnitude of serum amylase rise and severity of pancreatitis. But, there are many nonpancreatic causes of hyperamylasemia (e.g., biliary tract disease, intestinal obstruction, mesenteric ischaemia, acute appendicitis, mumps, parotitis, impaired amylase excretion etc.), that make the interpretation of this marker difficult[18]. In contrast, a patient with acute pancreatitis may have a normal serum amylase level, which could be due to several reasons like patients with hyperlipidemia; values might appear to be normal because of interference by lipids with chemical determination of serum amylase. The urinary amylase clearance from the circulation increases during pancreatitis; therefore, the urinary amylase levels might be more sensitive than serum levels. For these reasons, it is recommended to measure the urinary amylase concentrations, which usually remain elevated for several days after serum amylase levels have returned back to normal. In patients with severe pancreatitis associated with significant necrotic

damage, the pancreas may not release large amounts of enzymes into the circulation. It is important to recognize that, in patients with severe pancreatitis, frequent measurement of serum enzymes is not needed. Patients with alcoholic pancreatitis, in general, have a smaller increase in serum amylase levels. Because hyperamylasemia can be observed in many extra pancreatic diseases, measuring pancreatic-specific amylase (p-amylase) rather than total amylase, which also includes salivary amylase, makes the diagnosis more specific (88 to 93%).

The serum lipase estimation has been found to have high sensitivity and specificity in the diagnosis as there are no other sources of lipase[15, 17]. Total amylase is having a sensitivity of 84%, the serum P- amylase has 95% and lipase has 93%. Specificities for amylase, P-amylase and lipase respectively are- 88%, 93% and 96%, respectively. Thus P-amylase is the enzyme with the higher diagnostic value.

The rise of lipase: amylase has been found to differentiate alcoholic from nonalcoholic pancreatitis. The serum (SGPT) alanine aminotransferase level rise of three or more times above the base-line value has great specificity in diagnosing gallstonepancreatitis.

Immunologic assay like serum trypsinogen or immune lipase are generally less specific than the lipase assay. The increased urinary level of activation peptides released during either trypsinogen, procarboxypeptidase, or prophospholipase activation, may aid in predicting the severity of an attack.

Leucocyte migration and activation has considered as major determining factor of local & systemic complications[8, 15].

Although methemalbumin levels sometimes rise during attacks of severe pancreatitis, and methemalbuminemia is indicative of a poor prognosis, methemalbumin levels are usually not measured. Circulating levels of several inflammatory mediators and acute phase reactants (e.g., IL-1, 6, TNF-alpha, and CRP) also increase during pancreatitis, and the magnitude of those increases can be used to predict the severity of an attack. C reactive protein is readily available in all centers and vales > 120mg/L, after 72 hours are closely related to necrotising pancreatitis.

Imaging:

In general, the plain chest and abdominal radiographs can be useful in the management by identifying other causes for the patient's symptoms (e.g., pneumonia, perforated hollow viscous, mechanical bowel obstruction). Plain abdominal X-ray findings are either generalized or local ileus (known as sentinel loop), colon “cut-off” sign or “renal halo” sign. A chest radiograph may show left pleural effusion, elevated left hemi diaphragm or basal atelectasis[17].

Ultrasonography:

Abdominal ultrasound (US) examination is the gold standard for confirmation of gallstones pancreatitis. It also helpful to detect extra pancreatic ductal dilations & pancreatic edema, swelling, free peritoneal fluid and peripancreatic acute fluid collections (PFCs).It may not be sensitive in about 20% of cases, due to bowel gas interference with the imaging.

CT scan:

The contrast-enhanced computed tomography (CECT), has become gold standard for[17]

- Diagnosis
- Assessing the severity
- Detection of complications of acute pancreatitis.

The Balthazar scoring system and other similar grading systems have incorporated various CT findings such as inflammation and fluid collections in & around the pancreas to correlate radiographic appearance with morbidity and mortality[19].

Early CT scans often fail to detect evolving necrosis, which become well demarcated by 2 to 3 days after the onset of symptoms. The CT scans are not useful in diagnosing necrosis or predicting the severity within the 24 hours of onset of illness. The sensitivity for identifying pancreatic necrosis using contrast-enhanced CT scan approaches 100%, 4 days from diagnosis. CT scans also been useful in the early diagnosis of infected pancreatic necrosis and image guided aspiration of necrosis, when patient not improving clinically or who experience clinical decline. In the patient with moderate renal impairment or allergy to intravenous contrast material, magnetic resonance imagining (MRI) may be useful. MRI has been found to have sensitivity and specificity similar to contrast-enhanced CT for detecting severe acute pancreatitis.

ERCP should be done in patients with acute pancreatitis , whose clinical course fails to improve despite full intensive care support, and in whom ampullary or common bile duct stone impaction is suspected, based on ultrasonography, or clinical/biochemical signs of cholangitis. It may also be helpful in patients with

recurrent attacks of acute pancreatitis, without any obvious cause. It is useful in correcting potentially correctable lesions such as CBD stones with impaction, pancreas divisum, ampullary stenosis, pancreatic duct stenosis etc.

Mild acute pancreatitis (MAP) Vs. Severe acute pancreatitis (SAP):

Characteristic	MAP	SAP
Process	Mild, self-limiting	Fatal attack or failure to settle on supportive therapy
Course	Resolves rapidly	Emergence of local and systemic complications
Hallmarks	Edematous, interstitial inflammation of the pancreas	Extensive and prolonged, pancreatic and retroperitoneal inflammation with superimposed patchy or generalized areas of necrosis and hemorrhage in the pancreas and surrounding tissues
Fatality rate	Does not exceed 3%	Fatality rate between 10-20%
CECT	Normal in 15-30% of patients	May show pancreatic abscess, intra-abdominal fluid collection

Assessment of Severity:

An early interpretation between mild and severe necrotizing pancreatitis is the most important thing for providing optimal care to the patient[7]. There are so many predictors available for assessing the severity, which includes early prognostication signs, serum markers, and CT scan[15].

Scoring systems in acute pancreatitis: The various prognostic scoring systems for assessing the severity will be discussed in detail later.

UK guidelines for the management of AP[20]:

- The correct diagnosis has to be made within 48 hrs. of admission.
- The etiology has to be determined in 80% of cases at least and idiopathic cause should not exceed 20%.
- The serum lipase assay has been preferred over serum amylase assay for diagnosis the acute pancreatitis.
- The contrast enhanced computed tomography has to be preferred over USG for detection of the presence/absence of pancreatitis.

Treatment:

There are two phases in evolution of an acute attack of pancreatitis. Both phases are overlapping on each other[15, 17].

The initial phase, which lasts for 1 to 2 weeks, involves an acute inflammatory and autodigestive process that takes place within and around the pancreas. It may have systemic effects as well.

The second phase, that may last for weeks or months, is primarily characterized by the development of local complications that are, themselves, the results of necrosis, infection and pancreatic duct rupture.

The initial management of patients with pancreatitis focuses on early establishment the diagnosis, assessing the severity, treating the major symptoms, and haltering the disease progression. The treatment for acute pancreatitis is largely supportive. Since 15-30 % patients develop severe pancreatitis, so each and every patient should be treated aggressively. The main aim of the treatment is 'allowing rest to the gland' by oral feed and fluids restriction[21]. The goal of initial management consists of adequate fluid replacement, correction of electrolyte imbalance, nutritional support and prevention of local & systemic complications.

Management of Pain

Good analgesics should be given to these patients as the pain can be very severe in intensity. Most patients require narcotic analgesics. Meperidine is preferred as morphine induces spasm of the sphincter of Oddi, which can, at least theoretically, worsen biliary pancreatitis.

Fluid and Electrolyte Management

Aggressive fluid resuscitation is important to replenish extravascular, or "third space," fluid losses, which may be considerable. The fluid resuscitation is of

utmost importance to prevent systemic complications, mainly acute renal insufficiency, that may occur with hypovolemia. Transudation of the fluid from intravascular space into the areas of inflammation (i.e., peripancreatic, retroperitoneum and into the pulmonary parenchyma and soft tissues elsewhere in the body) is the principle cause of hypovolemia. Furthermore, studies have shown that inadequate resuscitation may add upon as a significant risk that leads to further pancreatic injury.

Banks and colleagues have showed that while aggressive fluid resuscitation might not prevent the progression to develop pancreatic necrosis. The degree and intensity of monitoring depends upon the disease severity[22].

During the first several days of a severe attack, circulating levels of many proinflammatory factors, including cytokines and chemokines, are elevated. This so-called ***"cytokine storm"***, in many cases, triggers the systemic immune response syndrome, and as a result, the hemodynamic parameters of these patients may resemble those of sepsis associated with other disease states[23]. Heart rate, cardiac output, and cardiac index usually rise, and total peripheral resistance falls. Hypoxemia can also occur as a result of the combined effects of increased intrapulmonary shunting and a pancreatitis-associated lung injury that closely resembles that seen in other forms of ARDS. Fluid management, though critical, may be difficult when hypovolemia is combined with respiratory failure of ARDS.

Measurement of central filling pressures, using a Swan-Ganz or central venous pressure catheter, can be helpful in guiding fluid management, particularly when hypovolemia is combined with lung injury.

Nasogastric Decompression

The nausea and vomiting of pancreatitis can result in significant fluid as well as electrolyte losses and retching can lead to gastro-esophageal mucosal tears and result in upper gastrointestinal bleeding (i.e., the Mallory-Weiss syndrome). For symptomatic relief and to increase patient comfort, nasogastric decompression may be needed, although the institution of nasogastric drainage does not shown to alter the eventual outcome of an attack[7, 8].

Prophylactic Antibiotics

Infection is a serious complication of acute pancreatitis and is the most common cause of death[17]. It is mostly caused by the enteric bacteria and was seen commonly in necrotizing pancreatitis. Local infection were common with larger amounts of pancreatic necrosis, and this increases in incidence as time progresses for at least the first 3 weeks in the course of the disease. Aerobic and anaerobic gastrointestinal floras are the primary organisms involved, and infections may be either mono or polymicrobial in nature. The predominant microbes seen were E. coli (35%), Kleb. pneumoniae (25%), Streptococcus (25%), Staphylococcus (15%), and Pseudomonas (10%).The association of high mortality with pancreatic

infection has been the rationale behind the use of prophylactic antibiotics widely in patients with pancreatic necrosis. In severe pancreatitis, beneficial effects have been observed with regimens that included imipenem alone, imipenem with cilastatin, metronidazole and third-generation cephalosporin (cefuroxime). Because *Candida* species are common inhabitants of the upper GI tract, *Candida* sepsis and secondary fungal infection of pancreatic necrosis is a risk in severe disease, and many surgeons advocate empirical therapy with fluconazole in severe acute pancreatitis.

The duration of treatment has not defined clearly. A treatment course of 1week to 4 weeks has been recommended commonly, but many of them limit the treatment to 2 weeks[17].

According to the current UK guidelines (Johnson 2005), the duration of antibiotic prophylaxis is 1 to 2 weeks[20].

Nutritional Support

Classically speaking, the enteral feeding should be limited, thereby pancreatic stimulation and further pancreatic injury by the release of proteolytic enzymes can be avoided. Recent data, suggests that such strict limitations of enteral nutrition may have been unnecessary. Most of the severe acute pancreatitis patients found to have prolonged course of illness with hyper catabolic state and ileus that have led to a generous use of parenteral nutrition in them.

The points favoring enteral nutrition are[7, 15]:

- It might feasible, safe, and desirable in severe pancreatitis.
- It has the advantage of avoiding the high cost of total parenteral nutrition (TPN) as well as its associated catheter-related complications.
- The use of enteral nutrition may support intestinal mucosal integrity by avoiding the alteration in intestinal permeability & barrier function as seen with use of TPN.

Treatments of Limited or Unproven Value

In patients who develop severe disease, other treatment modalities may be tried. The antiproteases like gabexate/aprotinin, antisecretory agents like octreotide and anti-inflammatory drugs or PAF antagonists like lexipafant were found to be less useful[15, 17].

Treatment of Early Systemic Complications of Pancreatitis

The pathogenesis and management of the cardiovascular collapse, respiratory failure, renal failure, metabolic encephalopathy, gastrointestinal bleeding, and disseminated intravascular coagulation that complicate severe pancreatitis appear to be identical to those involved when these processes are

superimposed on other disease states that are characterized by peritonitis and hypovolemia[8].

Cardiovascular collapse is largely caused by hypovolemia, and its management requires aggressive fluid and electrolyte repletion.

The pulmonary manifestations of pancreatitis include atelectasis and acute lung injury. The latter appears to be similar to the acute lung injury caused by other systemic processes, including septic shock, ischemia and reperfusion, and massive blood transfusion. Management includes good pulmonary toilet combined with close monitoring of pulmonary function. For many patients, intubation and respiratory support may be required.

Renal failure in pancreatitis is usually prerenal and is associated with a poor prognosis. In severe cases, dialysis, usually hemodialysis, may be required.

Stress-induced gastro duodenal erosions account for most of the gastrointestinal bleeding, prophylaxis with antacids, H_2-receptor antagonists, or proton pump inhibitors may be appropriate.

Rarely, massive bleeding can result from injury to peripancreatic vascular structures, leading to hemorrhage into the retroperitoneum. The peripancreatic inflammatory process can also cause thrombosis of major gastrointestinal vessels and result in ischemic lesions involving the stomach, small intestine, or colon that

can cause bleeding. Management of these complications of pancreatitis is similar to that involved when they occur in the absence of pancreatitis.

Some patients with severe pancreatitis develop disseminated intravascular coagulation, but it rarely causes bleeding, and prophylactic heparinization is usually not indicated.

Removal of precipitating factors, such as drugs or alcohol, is appropriate. Once the acute phase has been survived, usually by the end of the first week, and major organ failure is under control, then local complications become pre-eminent in the management of these patients.

An indication for operative intervention in acute pancreatitis is the drainage of an infected pancreatic necrosis. These patients require removal of as much as possible of the infected necrosis and drainage for the remaining viable exocrine tissue. Current opinion is against debridement in sterile necrosis unless it is accompanied by life threatening systemic complications[17].

A pancreatic abscess occurs 2 to 6 weeks after an initial attack of acute pancreatitis, in contrast to infected necrosis which occurs in the first few hours or days. Treatment consists of external drainage, either by surgical or percutaneous catheter based measures[17].

Treatment of Biliary Pancreatitis

The presence of gallstones leading to choledocholithiasis is recognized as a major etiological factor worldwide. Endoscopic retrograde cholangio pancreatography (ERCP) has both diagnostic and most therapeutic utility in patients with biliary obstruction or cholangitis. By randomizing patients with AP to early ERCP versus no ERCP, both Neoptolemos and colleagues, and Fan and colleagues have showed a significant decrease in morbidity but there was no significant improvement in mortality with routine use of ERCP. A metacentric randomized control study in the ERCP group by Folsch and colleagues recently, have demonstrated increased complication rate and mortality rate, after excluding the patients with biliary sepsis or obstruction. It therefore, found that early ERCP may be harmful even in the absence of ongoing biliary obstruction. Magnetic resonance cholangio pancreatography (MRCP) is an additional alternative to ERCP as a diagnostic tool that avoids the risk of post procedure pancreatitis.

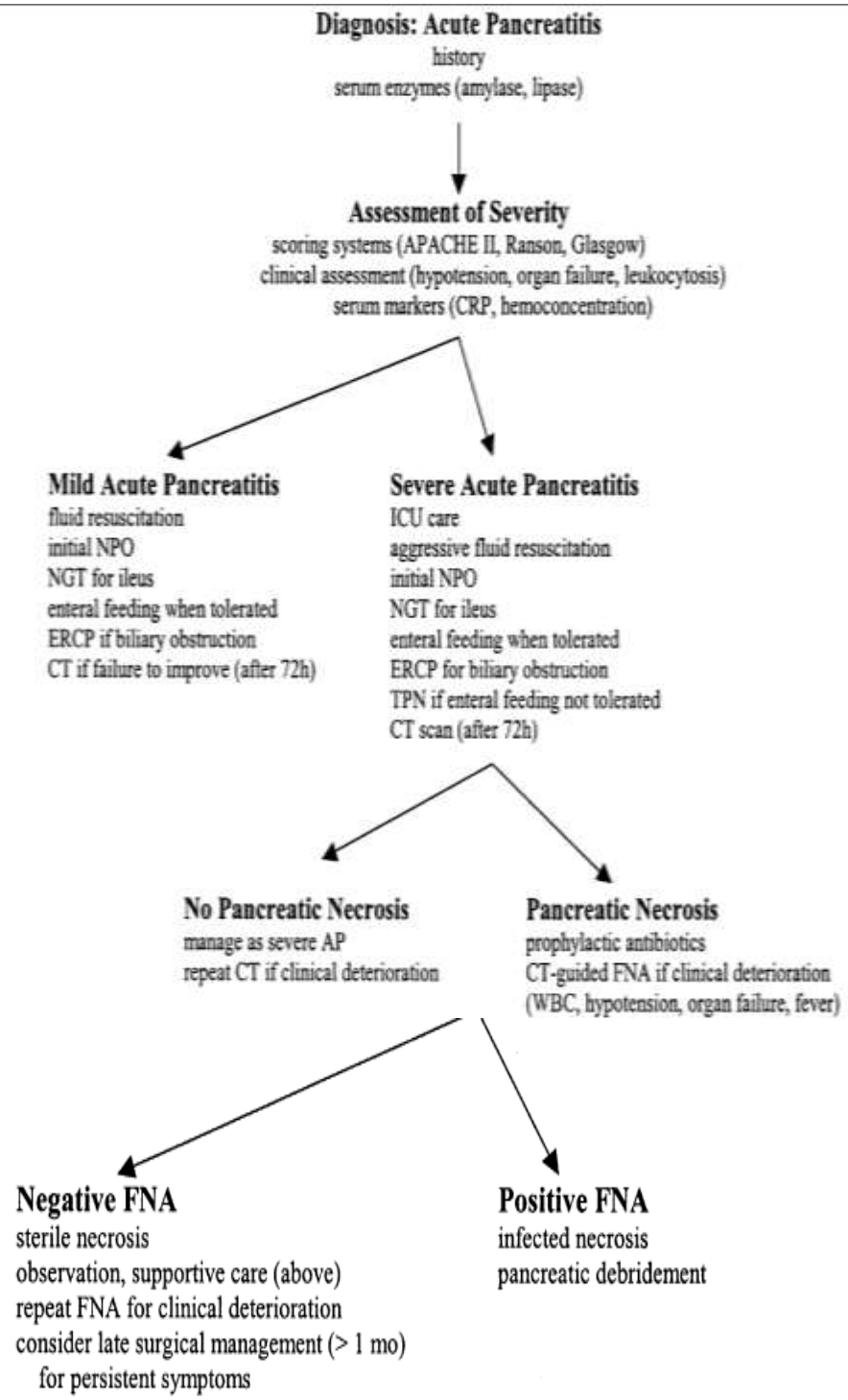
In general, either early intervention (cholecystectomy) within the first 48 to 72 hours of admission, or briefly delayed intervention (after 72 hours, but during the initial period of hospitalization) may be favored[8, 15]. Cholecystectomy with intra-operative CBD exploration is probably the best option for otherwise healthy patients with obstructive pancreatitis. However, patients who are at high risk for surgical intervention are best treated by endoscopic sphincterotomy, with clearance of stones by ERCP.

Surgical Management: Indications and Timing

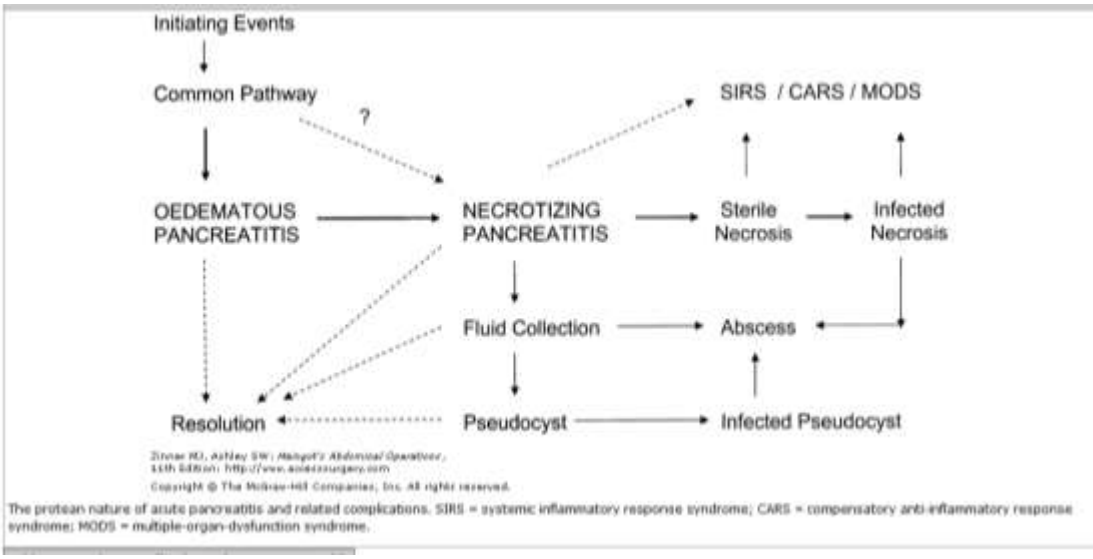
There are very limited indications for surgical intervention; specifically, intervention may be needed to address the etiology of pancreatitis or its complications. Interventions, either surgical or endoscopic, to prevent recurrent gallstone pancreatitis are recommended in any patient with suspected choledocholithiasis. Delayed surgery is also, rarely needed for the treatment of local complications like pseudocysts[17].

Table 36–3. Indications for Surgical Intervention in Necrotizing Pancreatitis
Diagnostic uncertainty
Intra-abdominal catastrophe unrelated to necrotizing pancreatitis such as perforated viscus
Infected necrosis documented by FNA or extraluminal gas on CT
Severe sterile necrosis
Symptomatic organized pancreatic necrosis

Early surgical intervention can lead to significant hemorrhage from the pancreatic bed, which may difficult to control, due to the fact that endarteritis obliterans was incomplete and the delineation between viable & non-viable tissue might not be clearly made out.


Diagnosis: Acute Pancreatitis
history
serum enzymes (amylase, lipase)
Assessment of Severity
scoring systems (APACHE II, Ranson, Glasgow)
clinical assessment (hypotension, organ failure, leukocytosis)
serum markers (CRP, hemoconcentration)
Mild Acute Pancreatitis
fluid resuscitation
initial NPO
NGT for ileus
enteral feeding when tolerated
ERCP if biliary obstruction
CT if failure to improve (after 72h)
Severe Acute Pancreatitis
ICU care
aggressive fluid resuscitation
initial NPO
NGT for ileus
enteral feeding when tolerated
ERCP for biliary obstruction
TPN if enteral feeding not tolerated
CT scan (after 72h)
No Pancreatic Necrosis
manage as severe AP
repeat CT if clinical deterioration
Pancreatic Necrosis
prophylactic antibiotics
CT-guided FNA if clinical deterioration
(WBC, hypotension, organ failure, fever)
Negative FNA
sterile necrosis
observation, supportive care (above)
repeat FNA for clinical deterioration
consider late surgical management (> 1 mo)
for persistent symptoms
Positive FNA
infected necrosis
pancreatic debridement

Complications[17]:



The protean nature of acute pancreatitis and related complications. SIRS = systemic inflammatory response syndrome; CARS = compensatory anti-inflammatory response syndrome; MODS = multiple-organ-dysfunction syndrome.

Complications may be classified as[15, 17]:

I. LOCAL:

Fluid collections
Pancreatic ascites/pleural effusion
Pancreatic pseudocyst
Pancreatic necrosis
Infected pancreatic abscess
Hemorrhage/pseudo aneurysm

II. REGIONAL:

Venous thrombosis
Paralytic ileus
Intestinal obstruction
Intestinal ischemia/necrosis

Cholestasis

III. SYSTEMIC:

A. Pulmonary
1. Pneumonitis, basal atelectasis
2. ARDS
3. Pleural effusion (L)
B. Cardiovascular
1. Hypotension
2. Hypovolemia
3. Sudden arrest &death
4. Nonspecific ECG(ST-T wave) changes
5. Pericardial effusion
C. Hematologic
1. Hemoconcentration
2. Disseminated intravascular coagulopathy
D. GI hemorrhage
1. Acid peptic disease
2. Gastric erosion
3. Portal/splenic vein thrombosis with variceal bleed
E. Renal
1. Oliguria
2. Azotemia
3. Renal vessel thrombosis
F. Metabolic
1. Hyperglycemic state
2. Hypocalcemic state
3. Hyperlipidemia (triglyceridemia)
4. Metabolic encephalopathy
5. Sudden loss of vision (Purtscher's retinopathy)
G. Central nervous system
1. Acute psychosis

2. Fat embolism occlusion
3. Alcohol withdrawal syndrome (AWS)
H. Fat necrosis
1. Intra-abdominal saponification
2. Subcutaneous tissue necrosis

SCORING SYSTEMS IN ACUTE PANCREATITIS

Pancreatitis is a serious disease with high morbidity and mortality rates. Some 80% were mild attack which recovers rapidly with conservative management. The rest of 20% were severe, with protracted course that needs intensive care and specialized management. Several predictors of severity are commonly used for this purpose[24].

Scoring systems can be used to predict mortality, severity of disease and intensity of its complications. Prognostic factor analysis found to helpful in comparing the results, in-between the series of patients under study.

Several scoring scales exist that predict both mortality and morbidity in patients with acute pancreatitis.

These systems include[25]:

- Ranson's criteria
- Balthazar computed tomography (CT) grading
- Imrie Glasgow coma score (GCS)
- Bank's clinical Criteria

- Simplified acute physiology score(SAPS)
- Marshall Multiple organ failure (MOF) score and
- Acute physiology and chronic health evaluation (APACHE) I, II, III & O.

The GCS and Ranson's multiple scoring systems require 48 hours of data collection; however, APACHE can be calculated at any time and shows prognostic correlation with acute pancreatitis, as increasing scores are associated with poor prognosis.

Once the acute pancreatitis has been diagnosed, assessment of severity is extremely important for execution of appropriate measures, preferably in an ICU setup with close monitoring.

1) RANSON'S CRITERIA[27]:

In 1974, Ranson and Pasternak identified 11 parameters with prognostic significance. Mortality was related to the number of parameters present: 0-0.9% in patients with less than three positive prognostic signs, 10-20% in those with three to five positive signs, mortality increases to > 50% in those with > 7 positive signs[26].

Criteria for Pancreatitis not due to gall stones:

At admission or diagnosis:

Age more than55 years

WBC count > 16,000/mm^3

Blood sugar> 200 mg/dL

Serum LDH> 350 IU/L

AST > 250 U/dL

During initial 48 hours:

Fall in hematocrit> 10 percentage points

BUN elevation > 5 mg/dL

Serum calcium level < 8 mg/dL

Arterial Po_2 less than 60 mm Hg

Base deficit more than 4 meq/L

Estimated fluid sequestration > 6 L

Gall stone induced pancreatitis:

Recently, the cutoff values of these signs were modified in biliary pancreatitis. This limits the use of early prognostic signs; it now requires memorization of 18 separate parameters and etiology is not always known. Therefore the revisions for biliary pancreatitis have not had wide acceptance, and the original system is the one that is widely utilized[31].

On admission or diagnosis:

Age > 70 yrs

WBC count > 18,000/mm^3

Blood sugar> 220 mg/dL

Serum LDH> 400 IU/L

AST > 250 U/dL

During initial 48 hours:

Fall in hematocrit greater than 10 percentage points
BUN elevation > 2 mg/dl
Serum ca^{2+} level < 8 mg/dl
Base deficit more than 5 meq/L
Estimated fluid sequestration > 4 L

2) IMRIE'S PROGNOSTIC CRITERIA:

During initial 48 hours
WBC count > 15000/mm^3
Blood sugar > 10 mmol/L
Serum urea > 16 mmol/L (no response to IV fluids)
Po_2 level < 60 mm Hg
Serum ca^{2+} level < 2 mmol/L
Lactic dehydrogenase> 600 IU/L
AST / ALT>200µm/l
Serum albumin level < 32 g/L

Ranson's and Imrie's scores indicate the severity at the time of admission and are not intended for monitoring the clinical course[27].

3) BANK'S CLINICAL CRITERIA:

Cardiac	Shock, tachycardia, arrhythmia, ECG changes
Pulmonary	Dyspnoea, basal rales, PO_2< 60 mm Hg, ARDS
Renal	Urine output < 50 ml/h, rising BUN& creatinine
Metabolic	Low Ca^{2+}&pH; ↓ albumin
Haematological	↓ HCT, DIC
Neurological	cerebral Irritation & confused state
GIT	paralytic ileus, free fluid, hgic peritoneal tap

- If the score was ≥ 1, the disease was severe in intensity.

4) BALTHAZAR COMPUTED TOMOGRAPHY SEVERITY INDEX (CTSI):

Emil J. Balthazar et al, developed CTSI, a grading system used to determine the acute pancreatitis severity[19, 33].

Prognostic Indicator	Points	Grade
Pancreatic inflammation		
Normal pancreas	0	A
Focal or diffuse enlargement of the pancreas	1	B
Intrinsic pancreatic abnormalities with inflammatory changes in peripancreatic fat	2	C
Single, ill-defined fluid collection or phlegmon	3	D
Two or more poorly defined collections or presence of gas in or adjacent to the pancreas	4	E
Pancreatic necrosis		
None	0	
≤ 30%	2	
> 30–50%	4	
> 50%	6	

Modified CT Severity Index[28]

Prognostic Indicator	Points
Pancreatic inflammation	
Normal pancreas	0
Intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat	2

Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis	4
Pancreatic necrosis	
None	0
≤ 30%	2
> 30%	4
Extrapancreatic complications	
(one or more of pleural effusion, ascites, vascular complications, parenchymal complications, or gastrointestinal tract involvement)	2

5) MODIFIED GLASGOW CRITERIA:

This one was useful in both alcoholic and biliary pancreatitis[27].

The score ≥ 3 means severe disease requires ICU care.

- P - PaO2 <8kPa or < 60 mmhg
- A - Age more than 55 years old
- N - Neutrophilia with WBC count>15x10^9/L
- C - Ca^{2+}<2mmol/L or < 8 mg/dl
- R - Renal function, Urea >16mmol/L or > 45 mg/dl
- E – Enzymes:- serum LDH >600 IU/L; AST>200 IU/L
- A - Albumin <3.2g/dL
- S - Sugar: >10mmol/L or >180 mg/dl

6) CRITERIA FOR ORGAN FAILURE BASED ON MARSHALL SCORINGSYSTEM:

Table 2. Criteria for organ failure based on Marshall scoring system

Organ system	Score				
	0	1	2	3	4
Respiratory (P_aO_2/F_IO_2)	>400	301–400	201–300	101–200	<101
Renal (serum creatinine, mg/dl)	≤1.5	>1.5 to ≤1.9	>1.9 to ≤3.5	>3.5 to ≤5.0	>5.0
Cardiovascular (systolic blood pressure, mm Hg)	>90	<90, fluid responsive	<90, fluid unresponsive	<90, pH <7.3	<90, pH <7.2

According to this scoring system score of ≥ 2 indicates presence of organ failure. These scores were calculated within 72 hours of admission into the hospital. The organ failure was classified as[27]:

- Transient (less than 48 hrs.)
- Persistent (more than 48 hrs.)

7) THE APACHE (ACUTE PHYSIOLOGICAL AGE AND CHRONIC HEALTH EVALUATION) SYSTEM

Knaus et al (1981) proposed a scoring system APS for classifying the patients according to the disease severity[29]. This was based on recording the abnormal physiological parameters. In consultation with a large number of intensive care specialists, they devised a scale. That included an acute physiological assessment, which examined abnormality among 34 possible measurements obtained during the 1st day of admission to the intensive care units.

A number from zero to four was assigned to each measurement according to how far from normal the measurements vary.

When multiple values for the same measurement were available, the worst was chosen. The final score, which ranged from zero to 124, indicates how far from normal homeostasis a patient had strayed because of acute illness.

The true APACHE score was more difficult to calculate because of practical problems like collection of large number of variables. Also under the rules of APACHE system any unmeasured variable was assumed to be normal and weighted as zero. This gave rise to questions about the model's general applicability. Another major criticism of original APACHE system was that the variables were chosen by a group of physicians and there was a potential of bias. These inaccuracies in the original APACHE system prevented its widespread use. However, it did serve as the prototype for the development of two subsequent systems.

APACHE II

In 1985, Knaus et al developed this scoring system based on 12 physiological variables[30]. To calculate the score, 0 - 4 values were assigned to all the 12 physiological and laboratory values with 0 being normal and 4 being the

Beginning : Date ---------- Time ---------- APACHI II patients study number Patients initial									
Acute Physiology and Chronic health evaluation									
A: Acute physiology score (12 variables)	**High abnormal rage**					**Low abnormal range**			
Physiological Variables	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature – rectal (°C)	≥41	39-40.9		38.5–38.9	36–38.4	34–35.9	32–33.9	30–31.9	≤29.0
Mean arterial pressure (mm Hg)	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate-ventricular response	≥180	140–179	110–139		70–109		55–69	40–54	≤39
Respiratory rate non ventilated or ventilated	≥50	35–49		25–34	12–24	10–11	6–9		≤5
Oxygen: A – a DO or PaO_2 (mm Hg) FiO^2 ≥ 0.5 record A – aDO2 FiO_2 < 0.5 record only PaO_2	≥500	350-499	200–349		<200 PO_2>70	$PO_2$61–70		$PO_2$55–60	PO_2<55
Arterial pH	≥7.7	7.6–7.69		7.5-7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
Serum HCO_3 – only if no ABGs	≥52	41.5–1.9		32–40.9	23–31.9		18–21.9	15–17.9	<15
Serum sodium (mmol/l)	180	160–179	155–159	50–154	130–149		120–129	111–119	≤110
Serum potassium (mmol/l)	≥7	6–6.9		5.5–5.9	3.5–5.4	3–3.4	2.5–2.9		<2.5
Serum creatinine (umol/l)	≥350	200–340	150–190		60–140		<60		
Haematocrit (%)	≥60		50–50.9	46–49.9	30–45.9		20–29.9		<20
White Blood cell court (x1000 /mm^3)	≥40		20–39.9	15–19.9	30–14.9		1–2.9		<1
Glasgow Coma Score (GCS)	Score = 15 minus actual GCS								

[Table/Fig-1]: The APACHE II chart for scoring

B. Age points					
Age years	Points	History	Points for elective surgery	Points for emergency surgery and non-operative patients	Apache II score: sum of A + B + C
≥ 44	0	Liver: Biopsy proven cirrhosis and documented portal hypertension or prior episodes of hepatic failure	2	5	A: APS score
45–54	2	Cardiovascular NYHA class IV	2	5	B: Age Points score
55–64	3	Respiratory eg. Severe COPD, hypercapnia, home O2 pulmonary hypertension	2	5	C: Chronic health points score
65–74	5	Renal chronic dialysis	2	5	
≥ 75	6	Immunocompromised	2	5	Total apache II

[Table/Fig-2]: The APACHE II chart for scoring

most abnormal. APACHE II did not strictly depend on ICU setting only but it was found to be as reliable as APS outside the ICU settings. The age and chronic health problems were included in this score as they reflect the physiological reserve status.

APACHE II Score as published by Knaus et al is composed of three parts:

1) Acute Physiological Score (0 to 60 points)
2) Age points (0 to 6 points)
3) Chronic health points (0 to 5 points).

Range of potential score is 0 to 71 but scores above 40 are uncommon. Score above 30 are associated with mortality rate of at least 70%. Roumen et al, in their study on acute hemorrhagic necrotising pancreatitis, concluded that of Ranson, Imrie, Multiple organ failure (MOF) and Sepsis sensitivity score (SSS), APACHE II is the best for grading the severity of disease on admission[32]. It is well suited for stratification of patients and comparisons of treatment methods.

The advantages are:

1) Objective determination of AP within few hours of admission, which might helpful in detection of cases for ICU care or for clinical trial.
2) Use of routine laboratory tests available 24 h a day.

3) Ability to be recalculated daily. Sequential monitoring of APACHE II enables determination of improvement or deterioration in the physiologic status of the patient. Over the initial 48 h, the score increase significantly in those with severe disease (median increase three points) but decrease (median decrease one point) in patients with mild pancreatitis. Thus this might be useful for follow up of the disease course and helps to assess the therapeutic response.
4) This score was used universally for all serious illnesses, thereby avoiding the need for a separate grading for acute pancreatitis.

The major drawbacks of APACHE II are:

1) Complexity and poor feasibility
2) The ideal 'cut-off' score for APACHE II in acute pancreatitis remains to be determined
3) As shown by Wilson et al, the cut-off scores having the greatest prognostic values on admission are different from the peak scores during the hospital course. The use of a single cut-off score APACHE II ≥ 9, as suggested by Larvin and McMohan needs to be validated in more studies.
4) Influenced by delay during presentation or the type of resuscitation treatment.

5) APACHE II generally underestimates mortality in many series of critically ill surgical patients as pre-ICU resuscitation not taken into account and young patients score few points despite severe pancreatitis.
6) APACHE II mortality predictions were based on treatment that lasts for 20 years ago.

APACHE III

In 1991, Knaus et al presented a revised and improved form of APACHE-II and termed it as the APACHE-III prognostic system[34].

The following variables were included in this score; blood urea, urine output, Sr. albumin, Sr. bilirubin, blood glucose, pCO2 in comparison to APACHE-II.

APACHE III is regarded as a good prognostic scoring system by using it serially and sequentially in acute pancreatitis. APACHE III score shows significant differences in mild and severe AP and correlates well with severity[35]. APACHE evaluation proves very suitable for serial monitoring of patients and gives an objective indication of progress in the individual patient. Williams et al found that an APACHE III score >30 indicated a much higher morbidity and mortality rate[36].

Overall, the APACHE III score appeared to be inferior to its predecessor[37].It is expensive to calculate APACHE III scores daily so it is not feasible for

financially constrained ICUs. As compared to APACHE II, the data collection was very much complex, and it was not accurate for predicting the risk in post-op cases.

8) BISAP (**The bedside index for severity in AP):**

This new scoring system has been developed recently for early detection of patients with risk of in hospital mortality[1].

The BISAP score has been developed and validated retrospectively on a large population based study, done by Cardinal Health Clinical Outcomes Research Database, Marlborough, USA[38].

This score was published recently for clinical and research purpose, for its accuracy and reliability in patient stratification.

The BISAP includes[38]:

1) Blood urea nitrogen (BUN) >25 mg / dl.
2) Impaired mental status (GCS < 15).
3) SIRS.
4) Age >60 years.
5) Pleural effusion.

SIRS was defined by presence of two or more of the following criteria:

1) Pulse rate > 90/min.

2) Respiratory rate > 20/min or PaCO 2 < 32 mm Hg.
3) Temperature >100.4 F or < 96.8 F / < 36 or > 38 ° C.
4) WBC count >12,000 or < 4,000 cells/$mm^{3,}$ or presence of more than 10% immature blasts.

(SIRS - Systemic Inflammatory Response Syndrome)

One point will be given for each variable present for a total of 5, score ranges from 0 to 5.

The presence of a pleural effusion was determined by a CT scan, chest radiograph or abdominal ultrasound obtained within 24 h of presentation. Imaging obtained within 24 h of presentation at the hospital of origin for transferred patients was also collected and reviewed.

A BISAP score of three or more has been found to have high mortality and have predicted the necrosis and organ failure very well[39].

ADVANTAGES:

1. Simple and easy to calculate, usually done at the time of admission or within 24 hrs. Of hospitalization[40].
2. The scores prediction ability was tested across 390 hospitals among large number (36,248) of populations, in contrast to other studies which were based on small number patients.
3. This predicts in-hospital mortality.

DISADVANTAGES:

1. The Glasgow Coma Scale used for evaluating mental status was subject to interobserver variation.
2. It could not discriminate transient from persistent organ failure within 24 hrs. Of hospitalization.
3. This could not predict the preventable complications of acute pancreatitis like any other scoring system.

AIMS AND OBJECTIVES OF THE STUDY

- To evaluate the role of BISAP score in place of traditional APACHE II scoring system in analyzing severity and early treatment intervention.
- Stratification of the patients with acute pancreatitis according to their scores observed at the time of hospitalization.
- To correlate the outcome of the study with the scores observed, in terms of disease severity and mortality.

MATERIALS AND METHODS

Study design: Comparative Analytical study.

Setting: Department of General Surgery, Govt. Stanley Medical College and Hospital, Chennai. The study was conducted after obtaining the Institutional Ethical Committee approval (**annexure 2**).

Inclusion criteria:

- Age >20 years including both sexes.
- Serum amylase/ Serum lipase equal to or more than 3 times the upper limit of normal.
- Radiological evidence of presence of acute pancreatitis.

Exclusion criteria:

- Patients were excluded from the study if they were younger than 20 years.
- Proven cases of chronic pancreatitis.
- Hereditary pancreatitis.
- Patients with comorbidities like COPD, renal impairment, immunosuppressive state, etc.
- Traumatic pancreatitis associated other visceral injuries.

Methods:

- First 100 patients attending the surgical emergency ward with clinical features of Acute Pancreatitis are evaluated clinically and subjected to laboratory and radiological investigations as per the designed proforma (**annexure 1**). Data pertinent to the scoring systems will be recorded within 24 h of admission to the hospital.
- Once diagnosis is established the patient disease severity will be assessed by following two scoring systems
    - BISAP
    - APACHE II

Statistical Analysis: Appropriate statistical tools.

For each of 100 patients included in the study, APACHE II and BISAP scores were calculated by using the APACHE II prognostic system in the manner described by Knaus et al and the Cardinal Health Database system for BISAP scoring.

Patients were classified to have mild or severe acute pancreatitis according to the definitions set by the Atlanta Classification guidelines (1992)[42]:

Severe attack--Criteria for severity included:

1) presence of one or more local complications:
    - Pancreatic necrosis
    - Pancreatic abscess
    - Pancreatic pseudo cyst.
2) Presence of one or more organ failures:

- Shock (systolic BP< 90 mm Hg).
- Pulmonary insufficiency (PaO_2< 60 mm Hg on room air).
- Renal failure (Sr. creatinine > 2mg/dl after fluid replacement).
- Gastrointestinal bleeding (> 500 ml estimated loss of blood within 24 hrs.).
- DIC (thrombocytopenia and hypofibrinogenemia and fibrin split products).
- Severe hypocalcemia (<8 mg/dl).

Survivors were defined as patients discharged alive from the hospital and non-survivors were those who died from pancreatitis or its complications during hospitalization.

Biliary Pancreatitis was presence of gall stones/biliary sludge in the gall bladder or bile duct, which was documented by any radiological methods. Alcoholic Pancreatitis was considered, when the patient found to have regular high intake of alcohol daily, or if there was binge of alcohol consumption prior to the onset of illness and has no signs of other etiologies present. Idiopathic pancreatitis was the one with no identifiable etiological factor based on the history, or after initial investigations.

Patients were observed prospectively until discharge or death.

APACHE II score of ≥ 9 and BISAP score of ≥ 3 were expected to predict severe Acute Pancreatitis.

OBSERVATION &RESULTS

This study was conducted in the department of general surgery, Govt. Stanley Medical College & Hospital, Chennai for a period of one year. The 100 persons with features of acute pancreatitis who fulfilled the inclusion criteria were enrolled in this study after obtaining an informed consent.

Table: 1 Age distribution

Age Range (years)	No. of patients	Percentage (%)
21yrs - 30yrs	22	**22**
31yrs - 40yrs	25	**25**
41yrs - 50yrs	37	**37**
51yrs - 60yrs	14	**14**
>60yrs	2	**2**
Total	**100**	**100 %**

The age group of patients enrolled in this study ranges from 20 to 80 yrs. The peak incidence of the disease was noted in the 4^{th} decade of life.

FIGURE -1

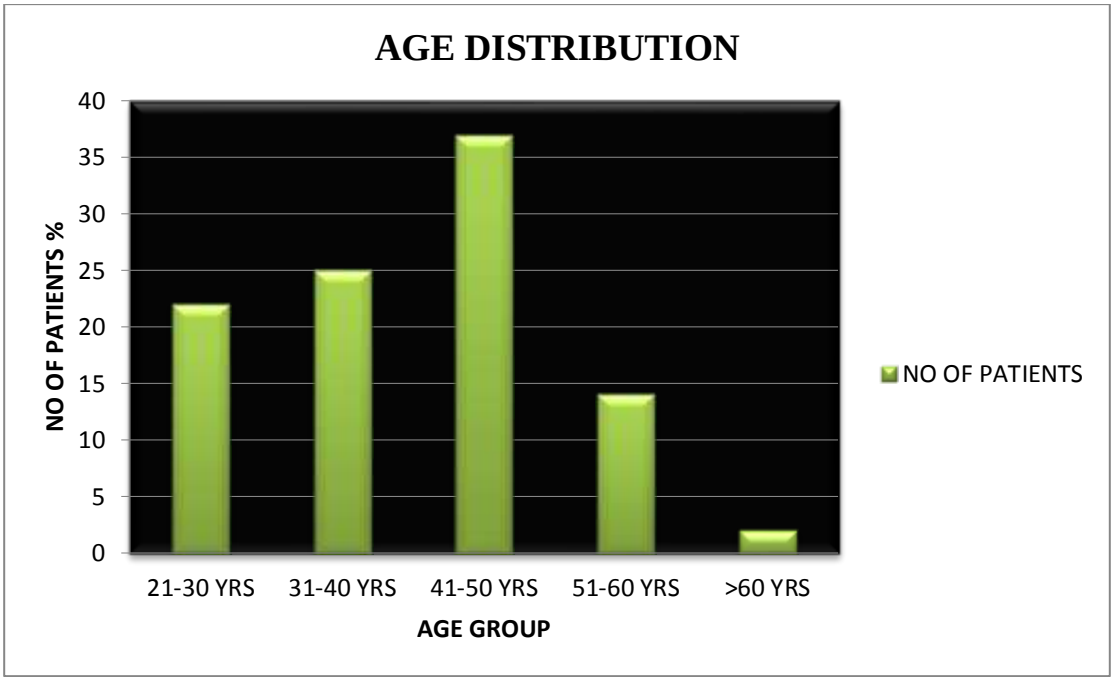

AGE DISTRIBUTION
40
35
30
25
20
15
10
5
0
NO OF PATIENTS %
21-30 YRS
31-40 YRS
41-50 YRS
51-60 YRS
>60 YRS
AGE GROUP
NO OF PATIENTS

Table: 2 Gender distributions:

Sex	No. of patients	Percentage (%)
Male	91	**91**
Female	9	**9**
Total	**100**	**100**

Out of 100 patients enrolled in this study there were 91 male and 9 female patients.

Male: Female ratio-10.1:1

Table: 3 Age wise Sex Distribution:

Age group (years)	Sex					
	Male		Female		Total	
	N	%	N	%	N	%
21 - 30	19	20.9	3	33.3	22	22.0
31 - 40	24	26.4	1	11.1	25	25.0
41 - 50	34	37.4	3	33.3	37	37.0
51 - 60	12	13.2	2	22.2	14	14.0
>60	2	2.2	0	.0	2	2.0
Total	91	100.0	9	100.0	100	100.0

Mean age group of males: 41.23 years.

Mean age group of females: 40.67 years.

FIGURE -2

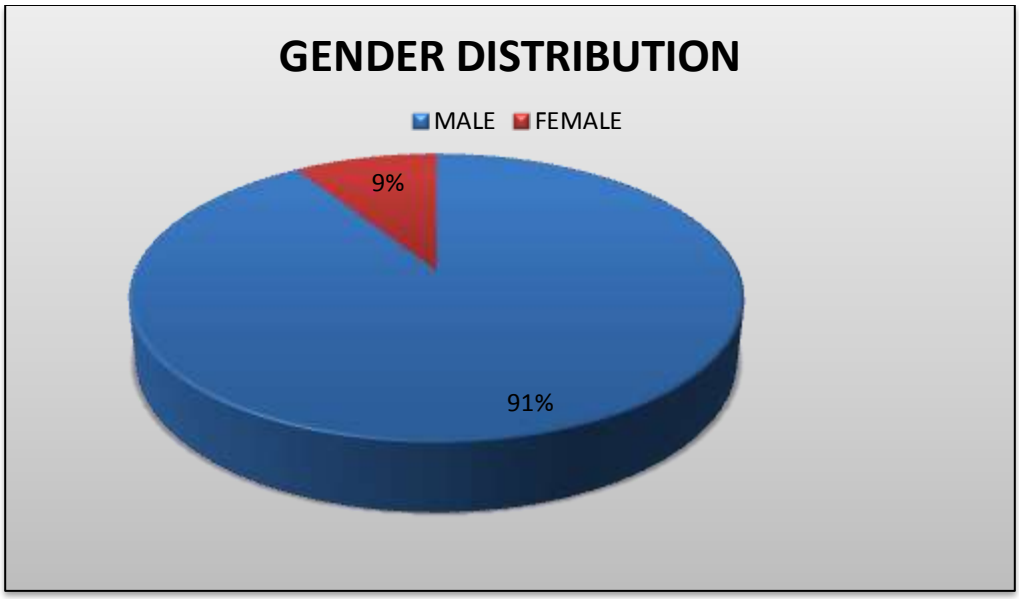

GENDER DISTRIBUTION
MALE
FEMALE
9%
91%

FIGURE -3

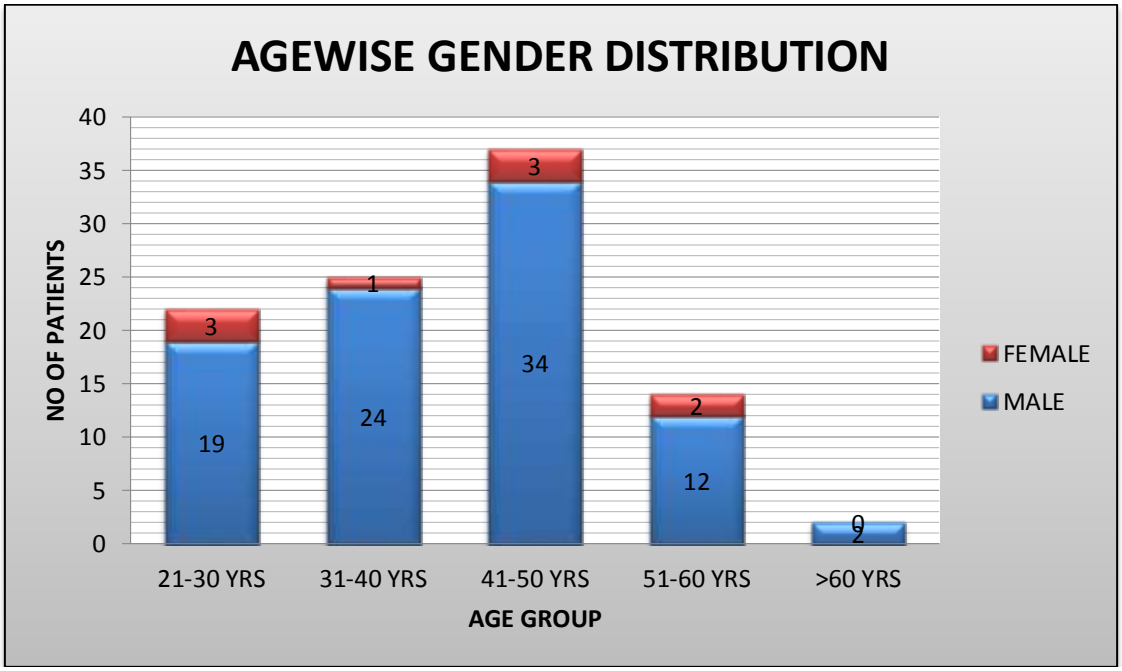

AGEWISE GENDER DISTRIBUTION
NO OF PATIENTS
40
35
30
25
20
15
10
5
0
3
19
1
24
3
34
2
12
0
2
21-30 YRS
31-40 YRS
41-50 YRS
51-60 YRS
>60 YRS
AGE GROUP
FEMALE
MALE

Table: 4 Hospital Stay:

Days in hospital	No. of patients	Percentage (%)
1day - 7days	33	**33**
8days - 14 days	37	**37**
15days - 21days	20	**20**
22days - 28days	8	**8**
>28 days	2	**2**
Total	**100**	**100**

The length of hospital stay ranges from 1 day to 32 days.

The mean length of hospital stay was 12.03 ± 6.8 days.

Table: 5 Clinical features:

Symptoms	No. of patients	Percentage (%)
Pain abdomen	95	**95**
Fever	31	**31**
Vomiting	25	**25**
Jaundice	14	**14**
Abdominal distension	**13**	**13**

FIGURE -4

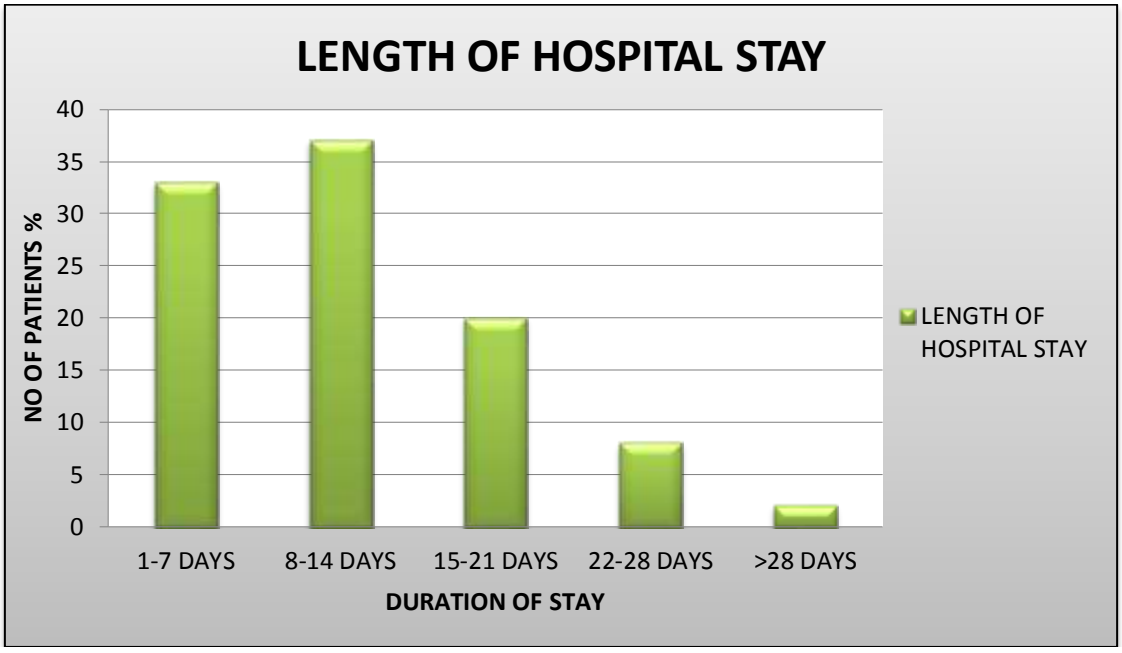
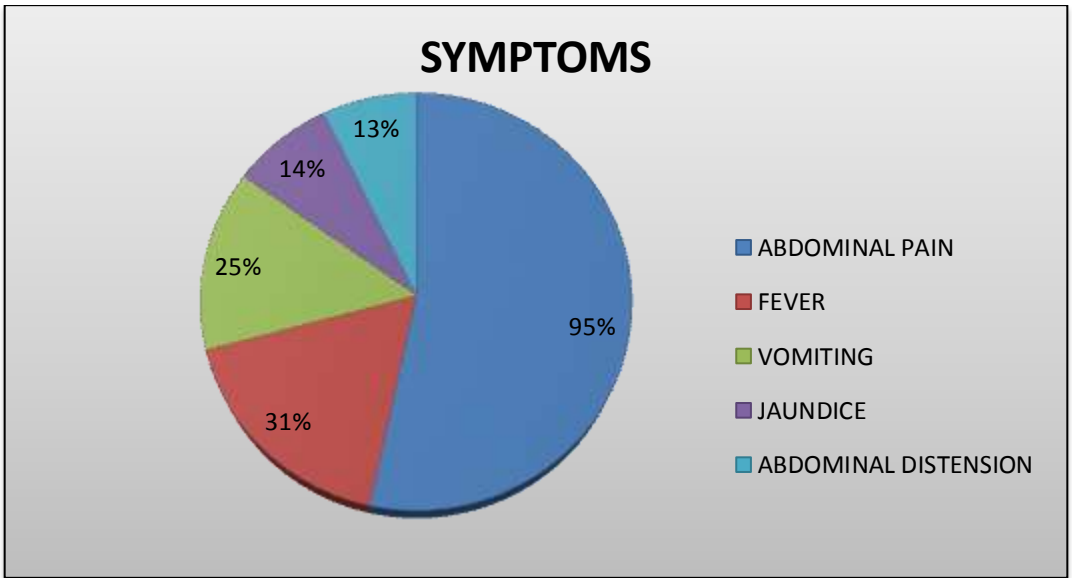


FIGURE -5



On clinical presentation, 95% of patients were presented with abdominal pain as chief complain. Rest of 5% who didn't have abdominal pain had vomiting and fever as presenting symptoms.

Table: 6 Etiologies:

Etiology	No. of patients	Percentage (%)
Alcohol	49	**49**
Gall stone disease	23	**23**
Drug induced	2	**2**
Hypertriglyceridemia	3	**3**
Trauma	2	**2**
Idiopathic	**21**	**21**

History of consumption of alcohol and the possibility of it being the etiological factor were found in 49 patients. Gall stone disease was attributed in 23 patients. Hyperlipidemia and drugs as causative factor presented in 3 & 2 patients, respectively. There was clear cut history of blunt trauma with CT scan showed isolated pancreatic laceration presented in 2 cases. No cause could be attributed in rest of the 21 patients.

FIGURE -6

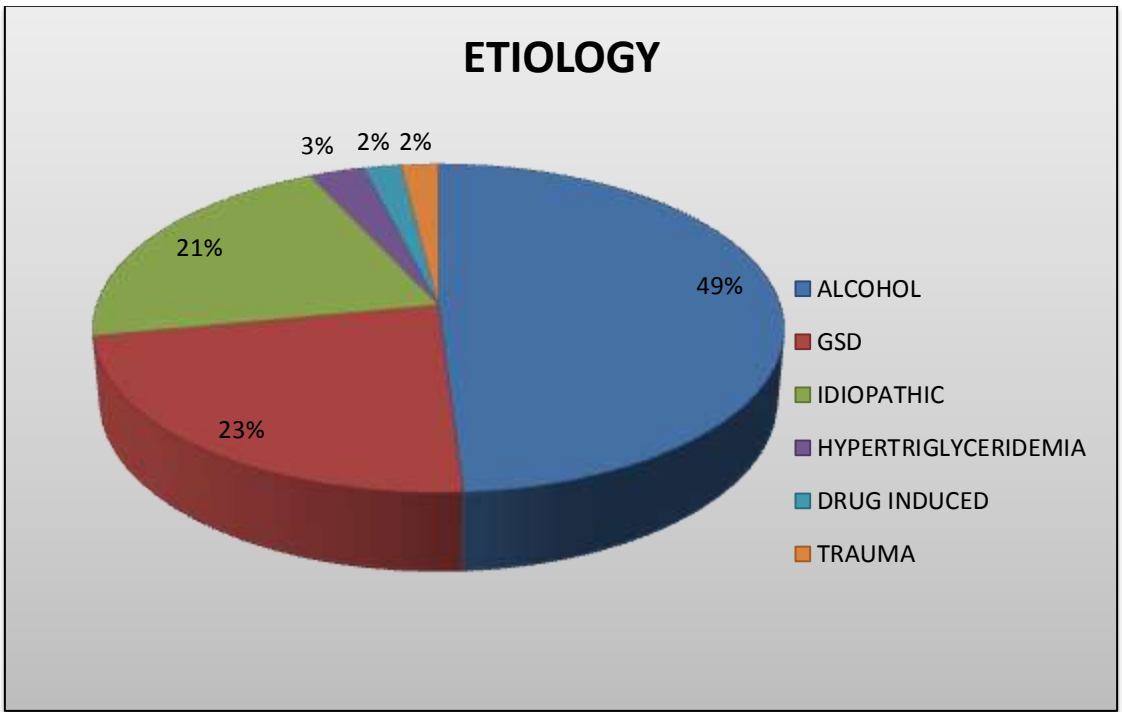

ETIOLOGY
3%
2%
2%
21%
49%
23%
ALCOHOL
GSD
IDIOPATHIC
HYPERTRIGLYCERIDEMIA
DRUG INDUCED
TRAUMA

Table: 7 Outcomes:

	Number of patients	Organ failure	Pancreatic Necrosis	Mortality
BISAP				
< 2	86	3	2	0
≥ 3	14	10	9	4
APACHE II				
< 9	58	1	1	2
≥ 9	42	13	10	2

Out of 100 patients, 86 patients presented with mild acute pancreatitis and 14 patients presented with severe acute pancreatitis. Out of 14 with severe attack, 4 patients expired.

In mild group the BISAP score ranges from 0 to 2, APACHE II score ranges from 0 to 8.

In severe attack group the BISAP score ranges from 3 to 5, APACHE II score ranges from 9 to 31.

The severity of acute pancreatitis was assessed by correlating the scoring systems with outcome in terms of organ failure, pancreatic necrosis and mortality, based on revised Atlanta classification system of acute severe pancreatitis.

Table: 8 Correlation of BISAP & APACHE II with severity

	BISAP < 2	APACHE < 9	x^2	P VALUE
ORGAN FAILURE	4	1	0.2275	0.6334
NECROSIS	2	1	0.1204	0.7286
MORTALITY	0	2	0.9629	0.3265

Out of 86 patients presented with BISAP score <2, organ failure, pancreatic necrosis were presented in 4 & 2 patients respectively. There was no mortality in this group.

Of 58 patients presented with APACHE II score <9, 1 patient developed organ failure and 1 patient developed pancreatic necrosis. There were 2 mortalities in this group.

Thus, using Chi^2test, there was no significant difference between these two scores [BISAP <2, APACHE II <9] in predicting the organ failure (p=0.633), necrosis(p=0.728) and mortality (p=0.326), respectively in mild AP.

FIGURE -7

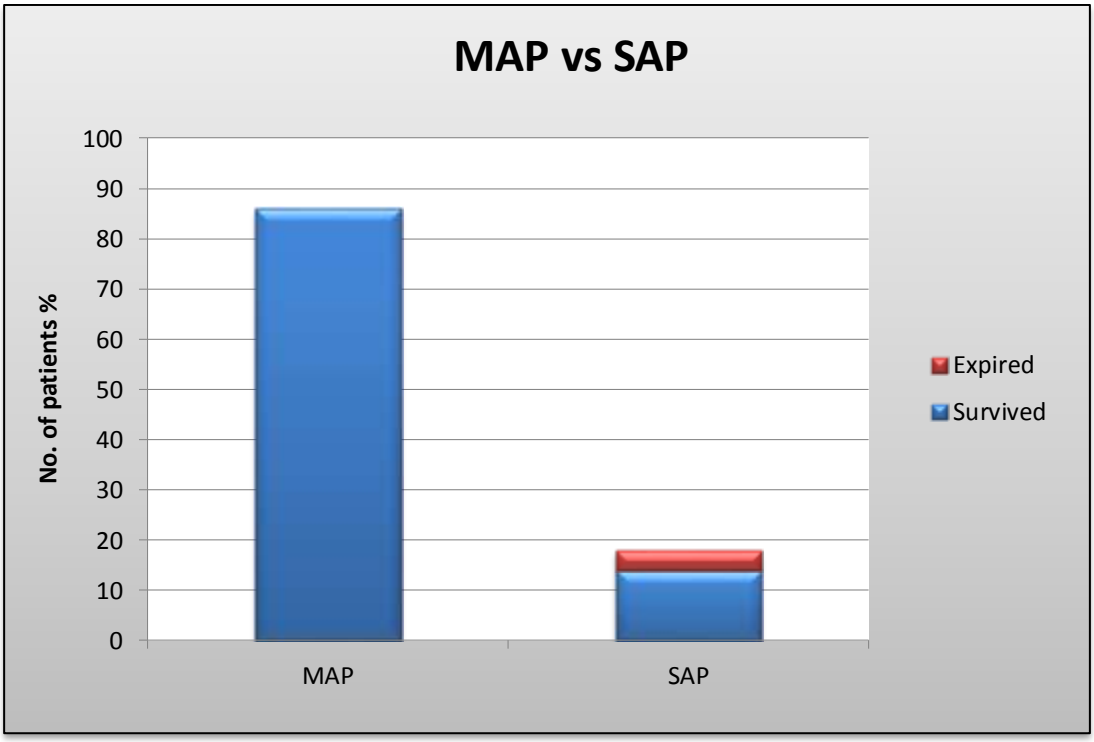
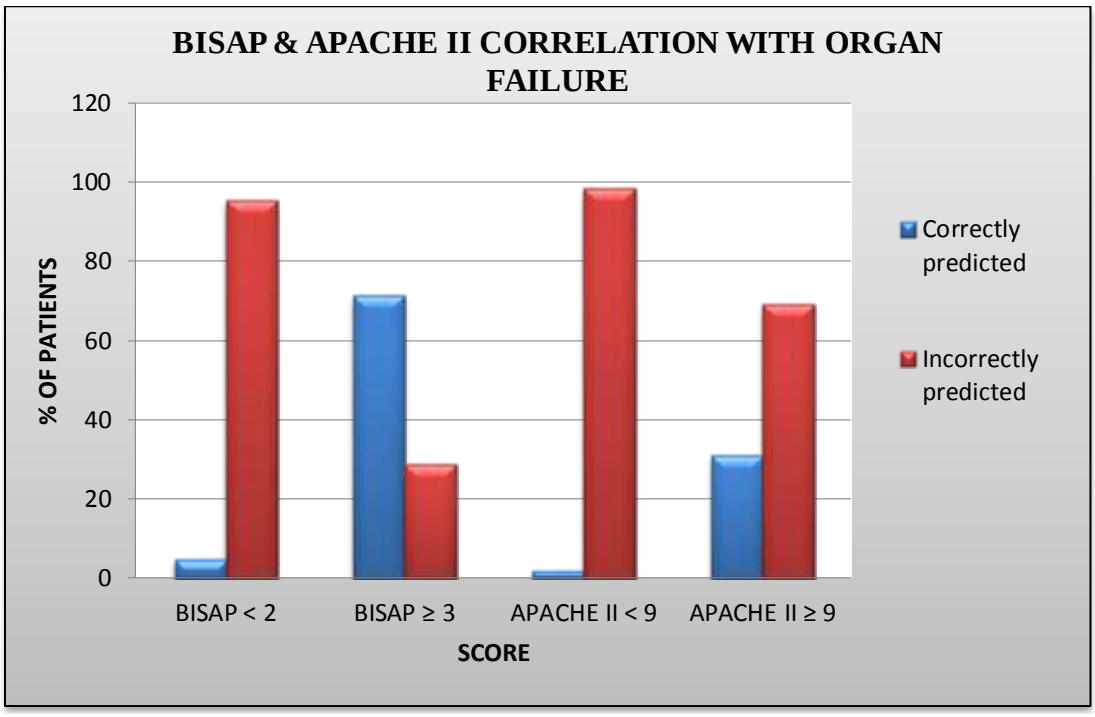
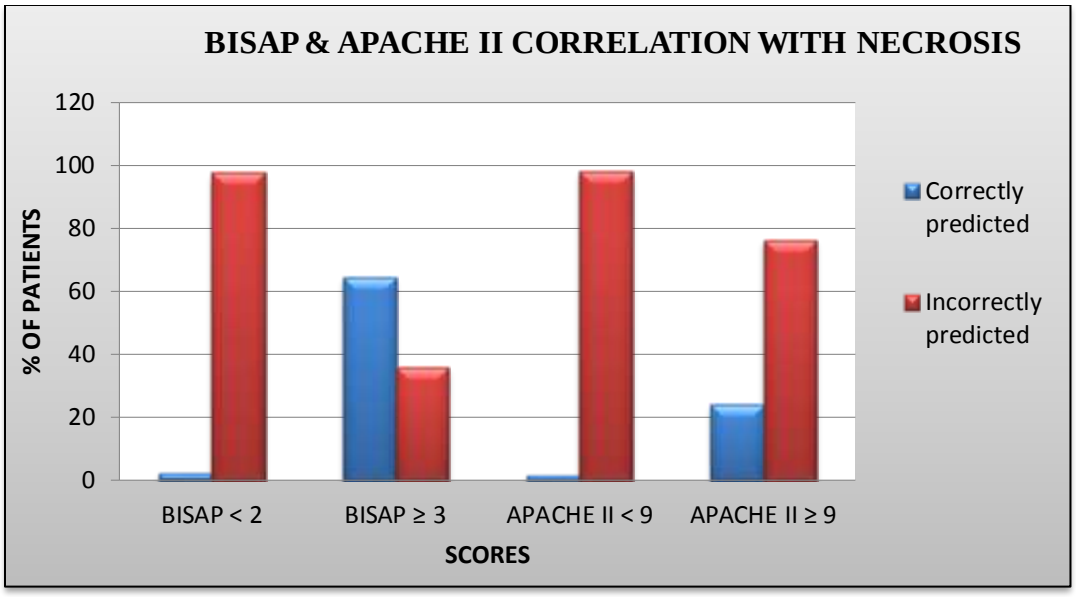

MAP vs SAP
No. of patients %
100
90
80
70
60
50
40
30
20
10
0
MAP
SAP
Expired
Survived

Table: 9 Correlation of BISAP & APACHE II with severity

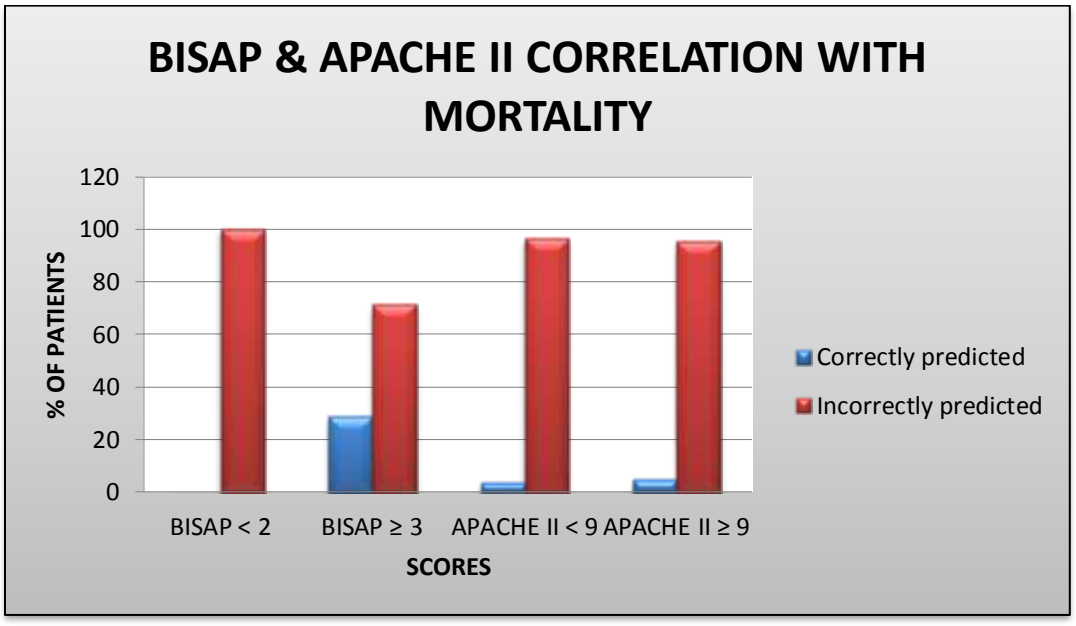
	BISAP ≥ 3	APACHE ≥ 9	x^2	P VALUE
ORGAN FAILURE	10	13	5.5336	0.0187
NECROSIS	9	10	5.9744	0.0145
MORTALITY	4	2	3.9822	0.046



Here, 10 out of 14 patients with BISAP >3 and 13 out of 42 patients with APACHE II >9, developed organ failure. Thus using Chi^2 test, the occurrence of organ failure correlates well with outcome with a p value <0.0187.



Here, 9 out of 14 patients with BISAP >3 and 10 out of 42 patients with APACHE II >9, developed pancreatic necrosis. Thus, using Chi^2 test, development of necrosis correlates well with outcome with p value <0.0145.

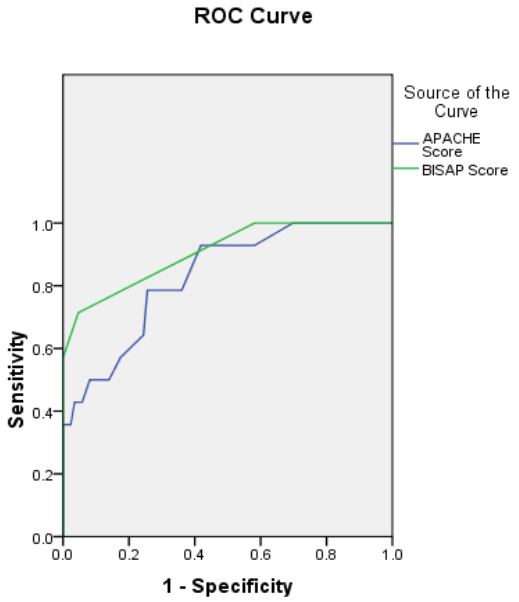


There were 4 deaths in severe acute pancreatitis group. Of them, 2 had BISAP score of 4 & APACHE II score of 8 and the other 2 had BISAP score of 5

& APACHE II score of >20 respectively. Thus, using Chi^2 test, the disease severity correlates well with mortality with p value <0.046.

Organ failure:

ROC Curve Analysis to find the best cut-off point for BISAP score and APACHE II score to Organ failure:



Area under the Curve by BISAP score = 0.907

Area under the Curve by APACHE score = 0.830

The ROC curve analysis predicted that the BISAP score of 3 or more will predict the organ failure.

Sensitivity and Specificity analysis: BISAP score.

		Organ Failure		Total
		Yes	No	
BISAP Score	≥ 3	10	4	14
	< 3	4	82	86
Total		14	86	100

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	71.43%	45.35, 88.28
Specificity	95.35%	88.64, 98.18
Positive Predictive Value	71.43%	45.35, 88.28
Negative Predictive Value	95.35%	88.64, 98.18
Diagnostic Accuracy	92.00%	85.00, 95.89

The ROC curve analysis predicted that the APACHE II score of 10 or more will predict the organ failure.

Sensitivity and Specificity analysis: APACHE II score.

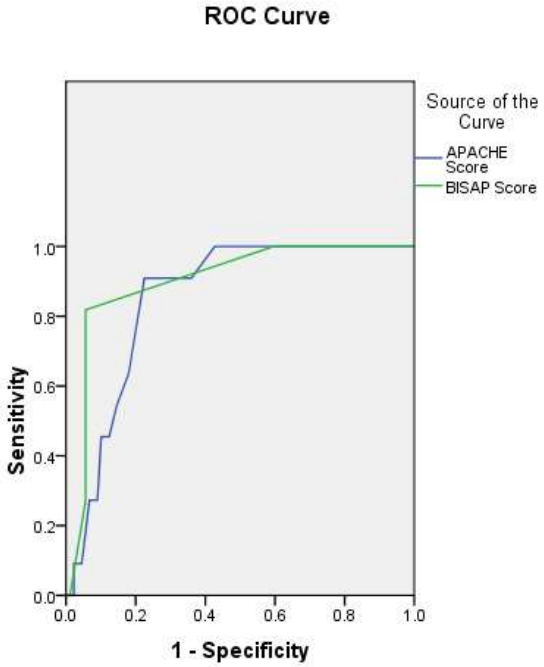
		Organ Failure		Total
		Yes	No	
APACHE Score	≥ 10	11	22	33
	< 10	3	64	67
Total		14	86	100

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	78.57%	52.41, 92.43
Specificity	74.42%	64.29, 82.46
Positive Predictive Value	33.33%	19.75, 50.39
Negative Predictive Value	95.52%	87.64, 98.47
Diagnostic Accuracy	75.00%	65.70, 82.45

The ROC analysis for prediction of organ failure shows BISAP score has diagnostic accuracy of 92% compared to 75% with APACHE II score.

Necrosis:

ROC Curve Analysis to predict the best cu-off point for BISAP score and APACHE II score to NECROSIS:



Area under the Curve by BISAP score = 0.901

Area under the Curve by APACHE score = 0.852

The ROC curve analysis predicted that the BISAP score of 3 or more will predict the NECROSIS.

Sensitivity and Specificity analysis: BISAP score:

		NECROSIS		Total
		Yes	No	
BISAP Score	≥ 3	9	5	14
	< 3	2	84	86
Total		11	89	100

Parameter	**Estimate**	**Lower - Upper 95% CIs**
Sensitivity	81.82%	52.30, 94.86
Specificity	94.38%	87.51, 97.58
Positive Predictive Value	64.29%	38.76, 83.66
Negative Predictive Value	97.67%	91.91, 99.36
Diagnostic Accuracy	93.00%	86.25, 96.57

The ROC curve analysis predicted that the APACHE score of 11 or more will predict the NECROSIS.

Sensitivity and Specificity analysis: APACHE II score.

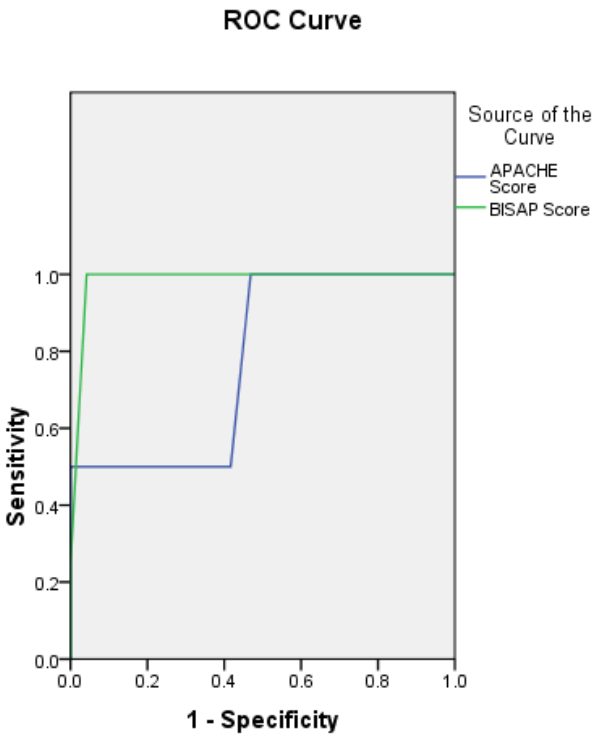
		NECROSIS		Total
		Yes	No	
APACHE Score	≥ 11	10	20	30
	< 11	1	69	70
Total		11	89	100

Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	90.91%	62.26, 98.38
Specificity	77.53%	67.82, 84.96
Positive Predictive Value	33.33%	19.23, 51.22
Negative Predictive Value	98.57%	92.34, 99.75
Diagnostic Accuracy	79.00%	70.02, 85.83

The ROC analysis for prediction of necrosis shows BISAP score has diagnostic accuracy of 93% compared to 79% with APACHE II score.

Mortality:

ROC Curve Analysis to find the best cu-off point for BISAP score and APACHE II score to predict mortality:



Area under the Curve by BISAP score = 0.984

Area under the Curve by APACHE II score = 0.779

The ROC curve analysis predicted that the BISAP score of 4 or more will predict the non-survival status.

Sensitivity and Specificity analysis: BISAP score:

		MORTALITY		Total
		Yes	No	
BISAP Score	≥ 4	4	4	8
	< 4	0	92	92
Total		4	96	100

Parameter	**Estimate**	**Lower - Upper 95% CIs**
Sensitivity	100.00%	51.01, 100.00
Specificity	95.83%	89.77, 98.37
Positive Predictive Value	50.00%	21.52, 78.48
Negative Predictive Value	100.00%	95.99, 100.00
Diagnostic Accuracy	96.00%	90.16, 98.43

The ROC curve analysis predicted that the APACHE score of 8 or more will predict the non-survival status.

Sensitivity and Specificity analysis: APACHE II score:

		MORTALITY		Total
		Yes	No	
APACHE Score	≥ 8	4	45	49
	< 8	0	51	51
Total		4	96	100

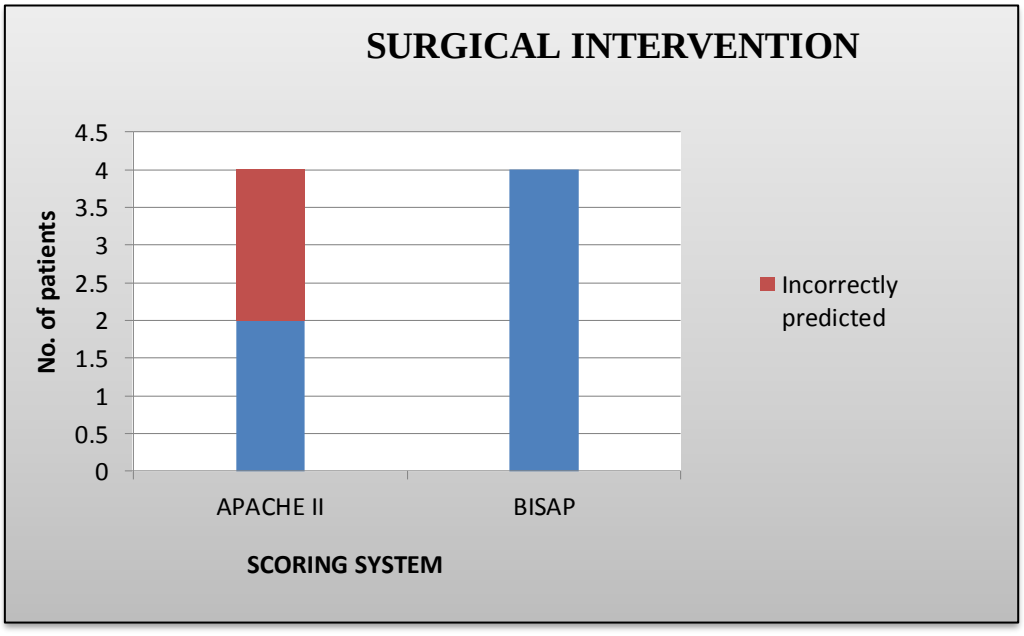
Parameter	Estimate	Lower - Upper 95% CIs
Sensitivity	100.00%	51.01, 100.00
Specificity	53.13%	43.22, 62.79
Positive Predictive Value	8.163%	3.22, 19.19
Negative Predictive Value	100.00%	93.00, 100.00
Diagnostic Accuracy	55.00%	45.24, 64.39
Likelihood ratio of a Positive Test	2.133	2.042 - 2.228

The ROC analysis prediction for mortality shows BISAP score has diagnostic accuracy of 96%, whereas APACHE II score has 55%.

Management:

All except four patients managed conservatively.

Three patients underwent emergency laparotomy. Two patient had traumatic injury to pancreas which was initially managed conservatively later they developed severe pancreatitis with intra-abdominal abscess, that required laparotomy and drainage procedure.



One patient with severe disease have developed pseudocyst, underwent laparotomy and internal drainage.

Another patient who had severe pancreatitis underwent necrosectomy initially& has developed pancreatic fistula later, which was managed by pancreatic duct stenting.

The BISAP score has predicted all the four patients correctly as severe pancreatitis, whereas APACHE II score predicted only two of the cases as severe pancreatitis.

Table: 10 Complications:

Complication	No. of patients	Percentage (%)
Acute renal failure	5	35.7
Respiratory failure	1	7.14
Pancreatic necrosis	11	78.5
Intra-abdominal abscess	1	7.14
Upper gastrointestinal bleeding	1	7.14
Multi-organ dysfunction syndrome	3	21.4
Septicemia	2	14.2
Encephalopathy	1	7.14
Portal vein thrombosis	1	7.14
Disseminated intravascular coagulation	1	7.14
Pancreatic Fistula	1	7.14
Pseudo cyst	1	7.14
Hypocalcemia	1	7.14

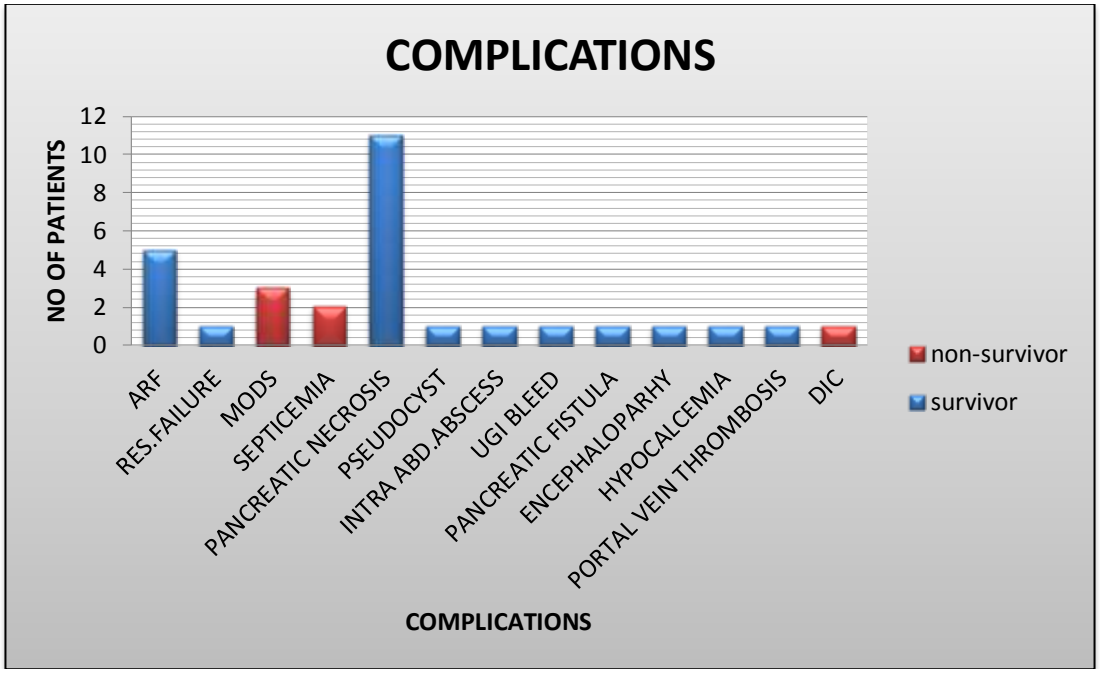
All the 14 patients with BISAP score > 3, developed major organ failure.

Local complications like pancreatic necrosis developed in 78.5% and 7.1% developed abscess, pseudo cyst and fistula formation.

35.7% developed acute renal failure, 21.4% developed MODS, 14.2% developed septicemia and 7.1% developed rest of the complications.

Of 4 deaths, 3 patients died of multi organ failure and 1 died of DIC with septicemia.

FIGURE- 8


COMPLICATIONS
NO OF PATIENTS
12
10
8
6
4
2
0
ARF
RES.FAILURE
MODS
SEPTICEMIA
PANCREATIC NECROSIS
PSEUDOCYST
INTRA ABD.ABSCESS
UGI BLEED
PANCREATIC FISTULA
ENCEPHALOPARHY
HYPOCALCEMIA
PORTAL VEIN THROMBOSIS
DIC
COMPLICATIONS
non-survivor
survivor

Fatal outcome:

Out of 100 patients, there were 96 survivors and 4 non-survivors.

The mean age of non-survivors was 60 yrs.

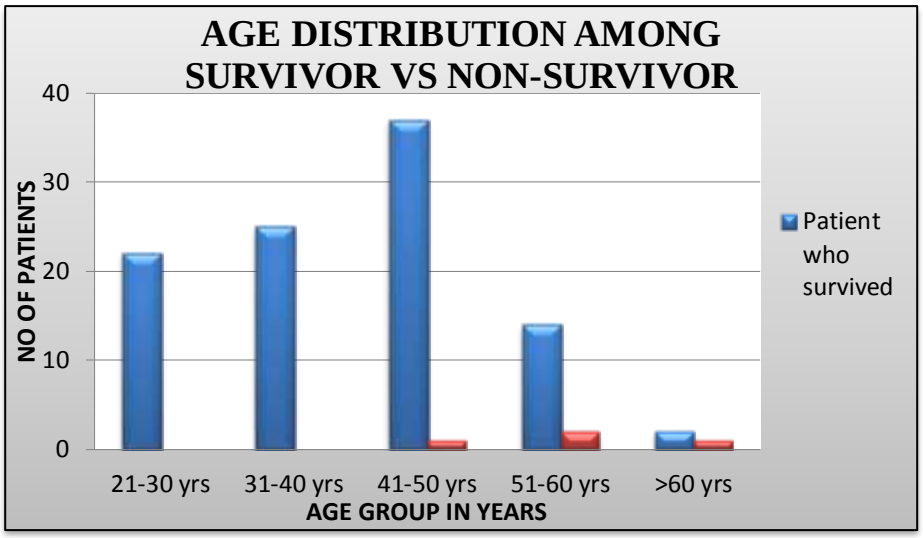


FIGURE -9

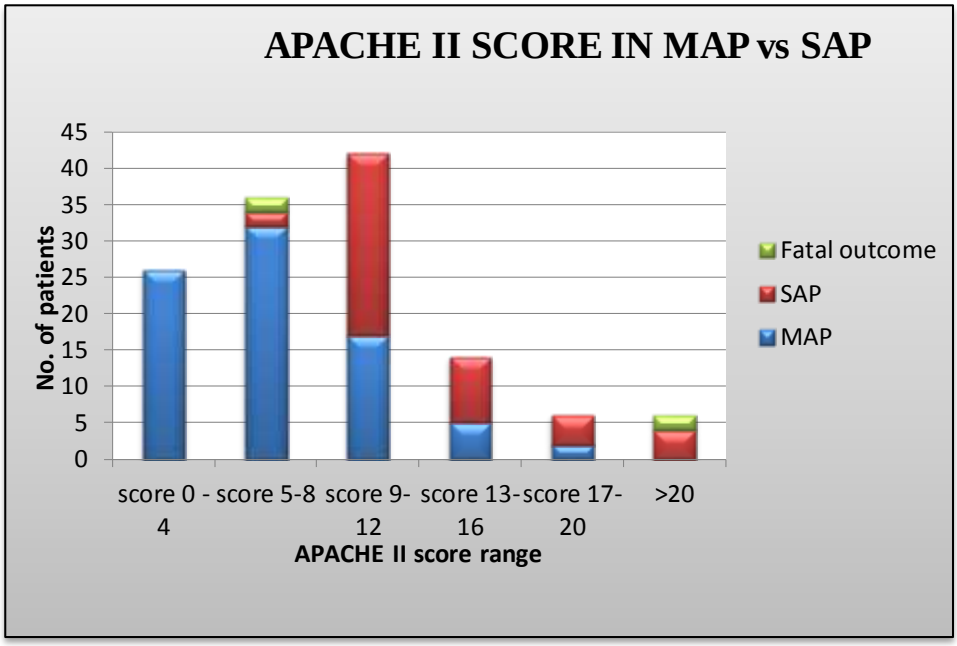
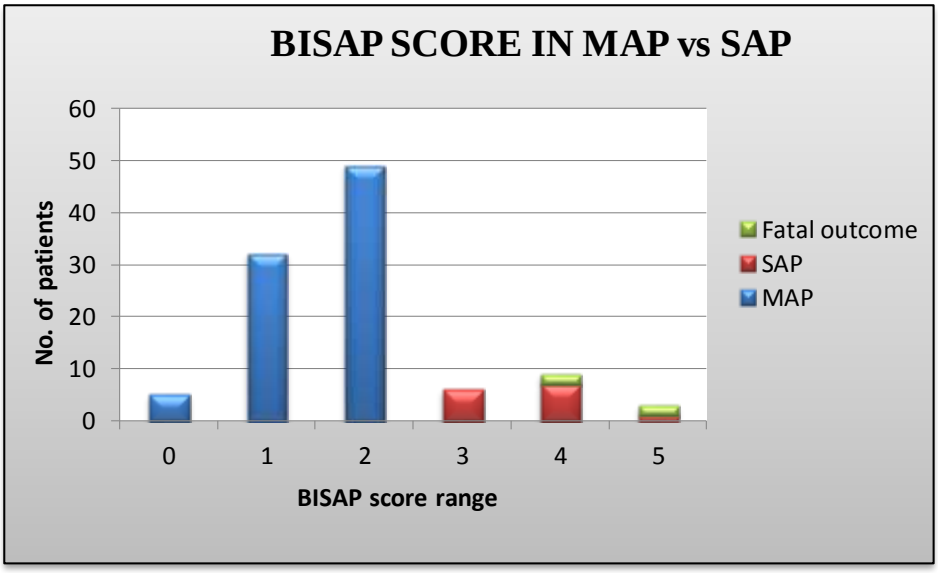


FIGURE -10



DISCUSSION

Acute pancreatitis is a common disorder with wide spectrum of illnesses. Severe acute pancreatitis having high morbidity and mortality rate, multiple interventions have been tried to prevent this. Early hospitalization may be beneficial to identify those who require aggressive interventions to prevent the severe attack of AP.

In this study, the two different scoring systems (BISAP and APACHE II) were compared and analyzed to assess the severity in patients with acute pancreatitis. An attempt also made to compare this study with previous similar studies done by others.

Acute pancreatitis found to be 10 times more common in males than females in this study. This result didn't match with previous study results, Vikesh K. Singh et al[38] (6:1), Papachristou et al[1] (5.1:1). This could be explained by the fact that, in this study alcohol has found to be most common etiological factor and it's more common in males.

Patients less than 20 years of age were excluded in this study, because the normal values of heart rate and respiratory rate are higher at younger age group. So, if these patients had been included in this study, they could have got higher

scores incorrectly and could have predicted incorrectly as at risk for developing severe pancreatitis, even with mild disease.

In this study, the mean age was 41.18 years which matches with the study of Sarath et al (40.8 yrs), nearly matches with Vikesh K. Singh et al[38] (49.6 yrs), Papachristou et al[1] (51.7 yrs).

The mean age of non-survivors in this study was found to be 60 years as compared to survivors being 41.23 years. Taking 60 yrs of age as cut-off value, increasing age was found to be correlated well with increasing incidence of mortality. Thus age is considered as a significant contributory factor in predicting the outcome of severe acute pancreatitis.

The most common etiological factor in this study was alcohol (49%) & matches with Bidarkundi et al[43](46.67%), but didn't correlate with results of Vikesh K. Singh et al[38] (21.4%), Papachristou et al[1] (14%) wherein gall stone disease found to be the most common cause, 27% & 36% respectively.

The mean length of hospital stay was 12.03 ± 6.8 days in this study. In this study, increasing BISAP & APACHE II scores was correlated well with the duration of hospital stay.

The most common presentation was predominantly abdominal pain (95%), followed by fever (31%), vomiting (25%) & other manifestations.

In this study, 86 patients were diagnosed to have mild acute pancreatitis and 14 patients found to have severe acute pancreatitis. All the 14 patients were correctly predicted by BISAP Score. The severity was assessed by correlating the scores with three factors: organ failure, necrosis and mortality.

The ROC analysis for organ failure showed BISAP score has AUC of 0.907, specificity of 95.35%, PPV of 71.4%, NPV 95.3% and diagnostic accuracy of 92%; whereas APACHE II score has AUC 0.830, sensitivity of 78.5%, specificity of 74.4%, PPV of 33.3%, NPV of 95.5% and diagnostic accuracy of 75%. This correlates well with the study by Papachristou et al[1] where AUC (0.81, 0.78), specificity (92.4%, 71.9%), PPV (57.7%, 40%) and NPV (84.3%, 90.1%), for BISAP and APACHE II scores, respectively. Thus by using Chi^2 test, BISAP ≥ 3 has

significant correlation with prediction of the occurrence of organ failure ($p < 0.01$), which matches well with study by Vikesh k. Singh et al[38] and B U Wu et al[41].

In this study, 9/14 with BISAP > 3 and 10/42 with APACHE II > 9 developed pancreatic necrosis. The ROC analysis for prediction of necrosis has AUC (0.901, 0.852), sensitivity (81.8%, 90.9%), and specificity (94.3%, 77.5%),

PPV (64.2%, 33.3%), NPV (97.6%, 98.5%) and diagnostic accuracy (93%, 79%) for BISAP and APACHE II scores, respectively. This correlates with the previous study by Papachristou et al[1], where AUC (0.78, 0.72), specificity (90.6%, 68.5%), PPV (46.2%, 29.2%), NPV (84.9%, 90.1%), for BISAP and APACHE II scores, respectively. Thus by using Chi^2 test, BISAP ≥ 3 has significant correlation with prediction of pancreatic necrosis ($p < 0.01$); this again matches with the study by Vikesh k. Singh et al[1].

In this study, 4% underwent surgical intervention which comparable with Sarath et al.

In this study, 4 patients with severe acute pancreatitis were expired. All four deaths were correctly predicted by BISAP score. Three patients were expired due to MODS and one patient expired due to DIC with septicemia. The ROC analysis for prediction of mortality has AUC (0.984, 0.779), sensitivity (100%, 100%), specificity (95.8%, 53.1%), PPV (50%, 8.1%), NPV (100%, 100%) and diagnostic accuracy (96%, 55%), for BISAP and APACHEII scores, respectively. This matches well with B U Wu et al[41], Papachristou et al[1], where specificity (87.6%, 65.7%), PPV (15.4%, 10.8%), NPV (98.1%, 100%), for BISAP and APACHE II scores, respectively. Thus by using Chi^2 test, BISAP ≥ 3 was found to be significantly associated ($p < 0.04$) with high mortality than APACHE II score by

ROC. It was found to have high specificity, PPV and NPV for mortality. This again matches well with previous study by Vikesh k. Singh et al[38] and Papachristou et al[1].

In this study, 35.7% developed acute renal failure, 21.4% developed MODS, 14.2% developed septicemia and 7.1% developed other complications like ARDS, UI bleed, etc. These complications were more likely seen in patients with BISAP $\geq$ 3 and APACHE $\geq$ 9 hence concluded that these are the patients in high risk group, who requires intensive monitoring and probably early intervention if necessary.

BISAP score was found to have more sensitivity, specificity, positive and negative value, and diagnostic accuracy than APACHE II score in predicting the severity of acute pancreatitis. Hence, BISAP score found to predict more number of patients, likelihood of progressing to severe disease. Larven et al stated in their study that, a prognostic scoring assay should preferably have high positive and negative predictive values or high negative predictive value to assess the severity of acute pancreatitis[44]. Hence, BISAP is considered as better score in assessing the severity than APACHE II score.

Limitations of this study are:

- Small number of patients in this study.
- The etiology in this study were found to be different from worldwide accepted one, hence might not be correct to compare with other studies.
- The GCS score used to assess the mental status of the patient got admitted were subject to interobserver variation.
- Various factors associated with the disease like cholangitis, alcohol withdrawal may interfere with the assessment of physiological scores, which may leads to difference in the results.
- Recently, it has been suggested that severe acute pancreatitis may have variable disease progression; therefore the lack of predictability might be associated with this disease variability.
- Variation in timing of presentation of patients to the hospital after onset of symptoms may interfere with assessment of the scoring systems.

CONCLUSION AND SUMMARY

- From this study, Alcohol (49%) was found to be the most common etiological factor for acute pancreatitis.
- Males were most commonly affected than female with a ratio of 10:1.
- The most common age groups of patients affected were in 4^{th} decade of life.
- The overall mortality in patients with severe acute pancreatitis was 4%.
- The BISAP score predicted the mortality significantly over the APACHE II score in patients with severe acute pancreatitis.
- The BISAP score predicted the disease severity significantly over the APACHE II score in patients with acute pancreatitis.

From this study, we conclude that the BISAP score could be a simple and accurate clinical scoring system for the evaluation of disease severity in acute pancreatitis.

BIBLIOGRAPHY

1. Comparison of BISAP, Ranson's, APACHE-II, and CTSI Scores in Predicting Organ Failure, Complications, and Mortality in Acute Pancreatitis Georgios I. Papachristou, MD, Venkata Muddana, MD, Dhiraj Yadav, MD, et al. *Am J Gastroenterology* 2010; 105: 435–441.

2. A brief history of pancreatitis. D A O'Reilly MRCS, A N Kingsnorth MS FRCS. Journal of the royal society of medicine. March 2001; volume 94; 130-132.

3. Opie EL. The etiology of acute hemorrhagic pancreatitis. Johns Hopks Hosp Bull 1901; 12; 182-8.

4. Steinberg W, Tenner S, Acute Pancreatitis. The New England Journal of Medicine 1994; 330(17): 1198-1210.

5. Bradley EL, A clinically based classification system for acute pancreatitis, Arch Surg; 128: 586-590.

6. Muhmet Ihan et al., The etio-pathogenesis of acute biliary pancreatitis, Dr. Sadikonuk training & research hospital, Istanbul, Turkey. DOI: 10.5772/26272.

7. Reber HA, Schwartz's Principles of Surgery (9th edition- 2010), McGraw Hill, 1467-1500.

8. Steer Michael L, Sabiston Textbook of Surgery, The biological basis of modern surgical practice (18th edition- 2007), Elsevier, 1643-60.

9. Skandalakis LJ, Rowe Jr JS, Gray SW, et al: Surgical embryology and anatomy of the pancreas. *Surg Clin North Am* 1993; 73:661-697.

10. Ellis Harold, Clinical anatomy, seventh edition-1983, Blackwell scientific publications, 121-23.

11. Standring S, Ellis H, Gray's Anatomy, Elsevier Churchill Livingstone 2005, 1231-1238.

12. Whitcomb DC, Gorry MC, Preston RA, et al. hereditary pancreatitis is caused by mutation in the cationic trypsinogen gene. Nat genet 1996; 14; 141-5.

13. Thomson SR, Hendry WS, McFarlane GA, Davidson AI, Epidemiology and outcome of acute pancreatitis, Br J Surg 1987; 74:398-401.

14. Russell R C G, Bailey and Love's Short Practice of Surgery (24th Edition-2004), Arnold Publishers, 1114-27.

15. Fisher WE, Andersen DK, Bell RH, Saluja AK, Brunicardi FC, Schwartz's Principles of Surgery(9th edition- 2010), McGraw Hill, 1222-40.

16. Wig JD, The Pancreas, (1st Edition-2000), Azad offset printers, 1-327.

17. Michael J. Zinner, Stanley W. Ashley et al., Maingot's abdominal operations, Management of acute pancreatitis. 11th edition. P 939-959.

18. Kazmierczak et al. Diagnostic accuracy of pancreatic enzymes evaluated by use of multivariate data analysis. *Clin Chem* 993; 39: 1960–1965.

19. Emil J. Balthazar, MD Acute Pancreatitis: Assessment of Severity with Clinical and CT Evaluation1 10.1148/radiol.2233010680 Radiology 2002; 223:603–613.

20. Glazer G, Mann DV, UK guidelines for the management of acute pancreatitis *Gut* 2005; 54; 1-9.

21. Yeo CJ, Cameron JL, Sabiston Text book of Surgery, The biological basis of modern surgical practice (18th edition-2008), W.B. Saunders company, 1112-43.

22. Toouli J, Smith MB, Bassi C, Carr-locke D, et al. Guidelines for the management of acute pancreatitis, Journal of Gastroenterology and hepatology 2002; 17 : S15-S39.

23. Balakrishnan V, Philip M. Cytokines as predictors of severity in acute pancreatitis. J Gastroenterology Hepatology 1998; 13: 1177-1179.

24. Bechien U. Wu MD MPH. Prognosis in acute pancreatitis. *CMAJ* 2011. DOI:10.1503/cmaj.101433.

25. Blamey S L, Imrie C W, O'Neill J, Prognostic factors in acute pancreatitis, GUT 1984; 25: 1340-46.

26. Williams M, Simms H, Prognostic usefulness of scoring systems in critically ill patients with severe acute pancreatitis. Crit Care Med 1999; 27: 901-7.

27. Taylor SL et al. a comparison of the Ranson, Glasgow & APACHE II scoring system to multi organ system score in predicting outcome in pancreatitis. Amj surg., 2005; 219-222.

28. Koenraad J. Mortele, Walter Wiesner, Lisa Intriere, et al. A Modified CT Severity Index for Evaluating Acute Pancreatitis: Improved Correlation with Patient Outcome. *AJR* 2004; 183: 1261–1265.

29. Knaus WA, Zimmerman JE, and Wagner DP: APACHE -Acute Physiological and Chronic Health Evaluation: A physiology based classification system. Crit Care Med 1981:9: 591-7.

30. Knaus WA, Draper EA, Wagner et al: APACHE II A severity of disease classification system. Crit Care Med-1985; 13(10): 818-29.

31. Ranson JHC, Acute Pancreatitis- Current problems in Surgery, 1979; 16: 1-84.

32. Roumen R.M.H., Schers T.J., de Boer H.H.M, Goris R.J.A, Scoring systems for predicting outcome in acute hemorrhagic necrotizing pancreatitis, Eur J Surg-1992; 158: 167-71.

33. Chatzicostas C, Roussomoustakaki M, Vardas E, et al, Balthazar computed tomography severity index is superior to Ranson criteria and APACHE II and APACHE III scoring systems in predicting acute pancreatitis outcome, J Clin Gastroenterol-2003; 36(3): 253-60.

34. Knaus WA, Wagner DP, Draper EA, et al. The APACIIE III prognostic system: risk prediction of hospital mortality for critically ill hospitalized patients. Chest 1991; 100; 1619-36.

35. Jack E Zimmerman, Douglous P Wagner, Elizabeth A. Draper: Evaluation of Acute Physiological and Chronic Health Evaluation III prediction in independent database. Crit Care Med 1998; 26: 1317-26.

36. Severity Scoring for Prognostication in Patients With Severe Acute Pancreatitis Comparative Analysis of the Ranson Score and the APACHE III Score Soumitra R. Eachempati, MD; Lynn J. Hydo, et al. *Arch Surg. 2002; 137:730-736.*

37. R. Mounzer et al. Comparison of existing clinical scoring systems to predict persistent organ failure in patients with acute pancreatitis. *Gastroenterology* June 2012; 142 (2), 1476-1482.

38. V. K. Singh et al. A Prospective Evaluation of the Bedside Index for Severity in Acute Pancreatitis Score in Assessing Mortality and Intermediate Markers of Severity in Acute Pancreatitis. *The American Journal of Gastroenterology* APR 2009; 104(4), 966-971.

39. J. Larino-Nola et al. assessing mortality in severe acute pancreatitis. Evaluation of the bedside index for severity in acute pancreatitis (BISAP). *Pancreatology* June 2010; 10(2-3), 344.

40. M. Bezmarevic et al. Procalcitonin and BISAP score versus C-reactive protein and APACHE II score in early assessment of severity and outcome of acute pancreatitis. Clinic for Abdominal and Endocrine Surgery, University of Belgrade, Belgrade, Serbia. Vojnosanit Pregl 2012; 69(5): 425–431.

41. B. Wu et al The early prediction of mortality in acute pancreatitis: a large population-based study. *Gut* JUN 2008; 57, 1698-1703.

42. De Beaux A C, Palmer K R, Carter D C, Factors influencing morbidity and mortality in acute pancreatitis; an analysis of 279 cases, GUT; 37: 121-126.

43. Bidarkundi GK et al. Clinical relevance of intracellular cytokines IL-6 and IL-12 in acute pancreatitis, and correlation with APACHE III score, Br J Biomedical Science 2002; 59(2): 85-89.

44. Larvin M et al. APACHE II scores for assessment and monitoring of acute pancreatitis. Lancet 1989; 2: 201-205.

PROFORMA

PROFORMA

A COMPARATIVE STUDY BETWEEN BISAP AND APACHE II SCORE IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS

Patient details :

Name : Patient ID No. :

Age :

Sex :

Hospital No.:

Date of Admission :

Date of Surgery (if any) :

Date of Discharge :

Address:

History :

Abdominal Pain:

- Duration
- Onset
- Progression
- Nature of pain
- Radiation
- Aggravation / Relieving factors

Vomiting :

- Duration
- Episodes
- Nature of Vomitus
- Hematemesis :

Fever

- Duration
- Grade
- Associated with chills / rigor

Trauma

Prolonged Drug Intake

Jaundice

Malena

Loss of appetite/ Loss of weight

Breathlessness

Past H/O:

Previous surgical illness

DM/ HT/ TB/ COPD/ IHD/ EPILEPSY/ BA

Personal H/O:

Occupation :

Socio-economic status :

Smoking :

Alcoholism :

Drug addiction :

Tobacco/Betel nut chewing:

Family H/O:

General Examination:

GCS : E V M

Vitals : PR

BP

RR

Temperature :

BMI :

Systemic examination :

Abdominal Examination :

Cardiovascular system Examination :

Respiratory system Examination :

Diagnosis :

Investigations :

Complete Hemogram

Hb : TC : DC:

ESR : PCV : Platelet :

Blood sugar:

Blood Urea : Sr. Creatinine :

Sr. Electrolytes : Na+ K+ Cl- HCO_3^-

Liver Function Test :

ABG analysis : pH $PaCO_2$

PaO_2

Sr. amylase / Sr.lipase :

Chest X-ray

Abdomen X-ray

ECG

USG abdomen & chest :

CT scan abdomen :

The APACHE II scoring system

(1) Body temperature : _____

(2) Mean arterial pressure (mmHg) : _____

(3) Heart rate (HR) : _____

(4) Respiratory rate (RR/min) : _____

(5) Oxygenation (mm Hg) : _____

(6) PH : _____

(7) Na (mmol/l) : _____

(8) K (mmol/l) : _____

(9) Creatinine (mg/100ml) : _____

(10) Haematocrit : _____

(11) Total leucocyte count : _____

(12) Glasgow coma score : _____

(13) HCO3 (if no ABG) : _____

(14) Age : _____

TOTAL SCORE: _____

BISAP scoring system

1. BUN (> 25 mg/dl) _____
2. Impaired mental status (Glasgow Coma Scale Score < 15) _____
3. SIRS

   SIRS is defined as two or more of the following:

   (1) Temperature of < 36 or > 38 °C _____

   (2) Resp. rate > 20 breaths/min or PaCO2 < 32 mm Hg _____

   (3) Pulse > 90 beats/min _____

   (4) WBC < 4,000 or >12,000 cells/mm 3 or >10% immature bands _____

4. Age > 60 years _____
5. Pleural effusion detected on imaging _____

TOTAL SCORE: _____

BISAP, bedside index for severity in acute pancreatitis;
SIRS, systemic inflammatory response syndrome.
One point is assigned for each variable within 24 h of presentation and added for a composite score of 0 – 5.

Risk Stratification Score

BISAP :

Score :

Severity status :

APACHE :

Score :

Severity status :

Course of hospital stay :

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work	: A Comparative study between BISAP and APACHE-II Score in assessing the severity of acute pancreatitis
Principal Investigator	: Dr.M. Sivakumar
Designation	: PG in M.S (Gen.Sur)
Department	: Department of Gen.Sur Government Stanley Medical College, Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 06.03.2012 at the Council Hall, Stanley Medical College, Chen

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nai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

30/10/12

MEMBER SECRETARY,
IEC, SMC, CHENNAI

A

COMPARATIVE STUDY BETWEEN

BISAP AND APACHE II SCORE

IN ASSESSING

THE SEVERITY OF ACUTE PANCREATITIS

A DISSERTATION SUBMITTED TO

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations for the award of the

Degree of M.S., (GENERAL SURGERY)

BRANCH – I

APRIL 2013

நோயாளி தகவல் தாள்

தீவிர கணைய அழற்சி நோயின் கடுமையை ஆராய பைசாப் (BISAP) மற்றும் அப்பாச்சி (APACHE-II) என்னும் மதீப்பீடு முறைகளை ஒப்பிடும் ஆய்வு

நோயாளிக்கான தகவல்கள் :

ஆராய்ச்சின் நோக்கமும், ஆதாரங்களும் :

தீவிர கணைய அழற்சி நோய் நமது நாட்டில் மிகவும் பரவலாக காணப்படும் ஒரு நோய் ஆகும். ஒட்டு மொத்தமாக ஓர் ஆண்டிற்கு 10-20% பேர் தீவிர கணைய அழற்சி நோயினால் இறக்க நேரிடுகிறது. அவர்களுள் 10-30% பேர் மிகவும் கடுமையான நோய் தன்மையால் பாதிக்கப்பட்டவர்கள்.

இந்த ஆய்வில் தீவிர கணைய அழற்சி நோயின் கடுமையை விரைவாக கண்டறிய பைசாப் (BISAP) என்ற மதீப்பீடு முறையும் அப்பாச்சி (APACHE-II) என்ற மதீப்பீடு முறையும் ஒப்பிடப்படுகிறது. இந்த ஆய்வில் பங்கேற்க தங்களை அழைக்கிறோம்.

இந்த ஆய்வில் இவ்விரு மதிப்பீடு முறைகளில் எந்த மதிப்பீடு நோயின் தீவிரத்தை மிகவும் துல்லியமாக கண்டறிய உதவுகிறது என்பது ஆராயப்படுகிறது.

இவ்வாறு நோயின் கடுமையை விரைவாக கண்டறிவதன் மூலம் நோயாளிகள் அவர்களின் நோயின் தன்மைக்கேற்ப வகைப்படுத்தப்பட்டு, அதற்கு ஏற்றார்போல் சிகிச்சை அளிப்பதற்கான முறைகளை ஆரம்ப நிலையிலேயே கண்டறிய முடியும்.

ஆய்வு முறை :

இந்த ஆய்வில் நீங்கள் மருத்துவமனையில் அனுமதிக்கப்பட்ட பின் உங்களுக்கு இரத்தப்பரிசோதனைகள், வயிறு மற்றும் நுரையீரல் எக்கோ போன்றவை எடுக்கப்படும்.

மேற்கூறிய ஆய்வு முறையில் செய்யப்படும் பரிசோதனைகளினால் தங்களுக்கு எந்தவித பக்கவிளைவுகளோ. உயிருக்கு ஏதேனும் ஆபத்தோ ஏற்படவாய்ப்பில்லை என்பதை தெளிவுபடுத்திக் கொள்கிறேன். மேலும் இந்த ஆய்வில் ஒப்பிடப்படும் மதிப்பீடுகளைக் கொண்டு தங்கள் நோயின் கடுமைத்தன்மையை அறிய இயலுமே தவிர இதனைக் கொண்டு தங்கள் நோயிற்கு புதிய சிகிச்சை முறைகள் எதுவும் தரப்படமாட்டாது என்பது தெளிவுப் படுத்தப்படுகிறது.

ஆய்வில் உங்கள் உரிமைகள் :

இந்த ஆய்வில் உங்கள் மருத்துவப் பதிவேடுகள் அனைத்தும் மிகவும் அந்தரங்கமாக வைத்துக் கொள்ளப்படும். இந்த ஆய்வின் முடிவுகள் அறிவியல் பத்திரிக்கைகளில் பிரசுரிக்கப்படலாம். ஆனால், பெயரை வெளியிடுவது மூலம் உங்களின் அடையாளம் வெளிக்காட்டப்படமாட்டது. இந்த ஆய்வில் உங்களின் பங்கேற்பு தன்னிச்சையானது, எந்தவித காரணங்கள் மற்றும் முன்னறிவிப்பின்றி நீங்கள் இந்த ஆய்விலிருந்து எந்த ஒரு நேரத்திலும் விலகிக் கொள்ளலாம்.

தாங்கள் இந்த ஆய்வில் பங்கேற்பதற்கு பின்வரும் ஒப்புதல் படிவத்தில் கையெழுத்து இடுமாறு கேட்டுக் கொள்ளப்படுகிறது.

நாள் :

நோயாளி/உறவினரின் கையொப்பம்
இடது பெருவிரல் ரேகை
(மருத்துவரால் படித்துகாட்டப்பட்டது)

சுய ஒப்புதல் படிவம்
ஆய்வு செய்யப்படும் தலைப்பு

தீவிர கணைய அழற்சி நோயின் கடுமையை ஆராய பைசாப் (BISAP) மற்றும் அப்பாச்சி (APACHE-II) என்னும் மதிப்பீடு முறைகளை ஒப்பிடும் ஆய்வு

ஆராய்ச்சி நிலையம் : அரசு ஸ்டான்லி மருத்துவமனை
சென்னை - 600 001.

பங்கு பெறும் நோயாளியின் பெயர் : வயது :

பங்கு பெறும் நோயாளியின் எண் : பாலினம் : ஆண் ☐ பெண் ☐

நோயாளியின் விலாசம் :

நோயாளி இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிடப்பட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும். அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் என்னை இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்க அனுமதிக்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் என்னை இவ்வாய்வில் இருந்து விலக்கி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். என்னை ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்குக் கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி, நடந்துக் கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ அதை உடனே மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதியளிக்கிறேன். ☐

இந்த ஆய்வில், எனக்கு இரத்தம், எக்ஸ்ரே, இ.சி.ஜி., ஸ்கேன், பரிசோதனை செய்துக்கொள்ள நான் முழுமனதுடன் சம்மதிக்கிறேன். ☐

நோயாளியின் கையொப்பம் ..... இடம் ..... தேதி

கட்டைவிரல் ரேகை (இந்த படிவம் படித்து காட்டப்பட்டு புரிந்து கைரேகை அளிக்கின்றேன்)

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி

ஆய்வாளரின் பெயர் .....

No.	NAME	IP No	AGE	SEX	Age	Temp	HR	RR	0xy.	MAP	Na+	K+	HCo3	Crea.	PCV	WBC	GCS	Chronic	APACHE	BUN	GCS	SIRS	AGE	PE	BISAP	OUTCOME	OF	pNEC.	MANAGEMENT	Comp.	LOH	ETIOLOGY	ABD. PAIN	VOMI.	FEV.	JAUN.	ABD. DIS.
1	JEGAN	38392	45	MALE	2	0	0	1	1	0	2	0	2	2	2	0	3	0	15	0	1	1	0	0	2	Alive			CONSERVATIVE		18	ALCOHOL	+	–	–	–	–
2	ANANDHAN	37332	42	MALE	0	0	0	0	0	0	0	0	0	2	0	0	2	0	4	0	1	1	0	0	2	Alive			CONSERVATIVE	pNEC	12	ALCOHOL	+	+	–	–	–
3	DHANAPAL	34612	55	MALE	3	0	0	1	0	0	2	0	2	3	0	0	3	0	14	0	1	1	0	0	2	Alive			CONSERVATIVE		17	ALCOHOL	+	+	+	–	–
4	MURUGAN	37377	40	MALE	0	1	2	3	1	2	2	0	4	3	3	0	2	0	23	1	1	1	0	1	4	ALIVE	+		CONSERVATIVE	ARF	28	ALCOHOL	+	+	+	+	–
5	PREMKUMAR	26628	29	MALE	0	1	0	0	0	0	3	2	2	0	0	0	0	0	8	1	0	1	0	0	2	Alive			CONSERVATIVE		13	GSD	+	–	–	-	–
6	CHELLAKANNU	26301	34	MALE	0	0	0	0	0	0	0	0	3	0	0	0	2	0	5	0	1	1	0	0	2	Alive			CONSERVATIVE		19	ALCOHOL	+	+	+	–	–
7	RAJENDRAN	46982	46	MALE	0	3	2	3	1	2	2	2	3	3	1	0	4	5	31	1	1	1	0	1	4	DEATH	+			MODS	3	ALCOHOL	+	+	+	–	+
8	RAFIQ	18441	50	MALE	2	0	0	1	0	3	0	1	0	0	2	0	2	0	11	0	1	1	0	0	2	Alive			CONSERVATIVE		22	ALCOHOL	+	–	–	–	–
9	PRAKASH	23987	29	MALE	0	0	3	1	0	0	0	1	2	2	0	0	3	0	12	0	1	1	0	0	2	Alive			CONSERVATIVE		16	GSD	+	+	+	–	–
10	ANANDHAN	6918	47	MALE	2	0	0	1	0	2	0	1	0	0	0	0	2	0	8	1	1	1	0	0	3	Alive		+	SURGERY	pNEC PF	13	ALCOHOL	+	–	–	–	–
11	GOPINATH	26635	25	MALE	0	1	0	1	0	0	0	1	2	2	0	0	2	0	9	0	1	1	0	0	2	Alive			CONSERVATIVE		17	ALCOHOL	+	–	–	–	–
12	ARUNPRASATH	39206	32	MALE	0	0	0	0	1	0	2	2	2	0	4	0	2	0	13	1	1	0	0	0	2	ALIVE			CONSERVATIVE		12	ALCOHOL	+	–	–	–	–
13	GOPINATH	22530	31	MALE	0	0	0	0	0	0	3	0	2	0	0	0	0	0	5	0	0	1	0	0	1	Alive			CONSERVATIVE		7	GSD	+	–	–	–	–
14	PRABU	22444	31	MALE	0	3	0	0	0	2	2	1	2	0	0	0	1	0	11	0	1	1	0	0	2	Alive			CONSERVATIVE		8	IDIOPATHIC	+	–	–	-	–
15	SENTHIL PANDI	6923	32	MALE	0	0	0	0	0	0	0	2	0	0	0	0	0	0	2	0	0	1	0	0	1	Alive			CONSERVATIVE		6	ALCOHOL	+	-	-	–	-
16	PRABU	17439	21	MALE	0	0	0	1	0	0	0	1	0	0	0	0	0	0	2	0	0	1	0	0	1	ALIVE			CONSERVATIVE		7	ALCOHOL	+	–	–	–	–
17	ARIVAZHAGAN	3E+05	46	MALE	2	0	0	0	0	0	0	1	0	0	0	0	1	0	4	0	1	1	0	0	2	ALIVE			CONSERVATIVE		7	IDIOPATHIC	+	–	–	–	–
18	KANNAN	26665	32	MALE	0	1	2	0	0	0	2	2	2	0	0	0	0	0	9	1	0	1	0	0	2	Alive			CONSERVATIVE		16	ALCOHOL	+	–	+	+	–
19	PILLAYARSAMY	37807	49	MALE	2	0	2	0	0	0	0	0	1	0	0	0	0	2	5	0	1	0	0	0	1	Alive			CONSERVATIVE		6	ALCOHOL	+	–	–	–	–
20	VIJAYAKUMAR	36395	35	MALE	0	0	0	0	0	0	0	0	2	2	0	0	0	0	4	0	0	1	0	1	2	Alive			CONSERVATIVE		9	ALCOHOL	+	+	–	-	–
21	KRISHNAN	37386	55	MALE	3	0	0	1	0	3	3	0	0	0	0	0	0	0	10	0	0	1	0	0	1	Alive			CONSERVATIVE		9	GSD	+	–	-	–	–
22	MURUGAN	39214	35	MALE	0	0	0	0	0	0	2	2	0	0	0	0	0	0	4	1	0	1	0	0	2	Alive			CONSERVATIVE		9	ALCOHOL	+	–	–	–	–
23	RAJAM	39206	56	MALE	3	0	0	0	0	2	0	1	0	0	0	0	1	0	7	0	1	1	0	0	2	ALIVE			CONSERVATIVE		8	ALCOHOL	+	–	–	–	–
24	PUSHPAVALLI	39216	45	FEMALE	0	0	0	0	0	0	0	2	2	0	0	0	1	0	5	0	1	0	0	0	1	Alive			CONSERVATIVE		6	GSD	-	+	–	–	–
24	MARISELVAM	42570	24	MALE	0	0	0	1	0	0	2	2	2	0	0	0	2	0	9	0	1	1	0	0	2	Alive			CONSERVATIVE		7	IDIOPATHIC	+	–	–	–	–
26	MOHAN	37469	50	MALE	2	0	0	0	0	0	0	1	2	0	0	0	1	0	6	0	1	1	0	0	2	ALIVE			CONSERVATIVE		5	ALCOHOL	+	–	–	–	–
27	ARUMUGAM	37419	58	MALE	3	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	1	0	0	1	Alive			CONSERVATIVE		4	ALCOHOL	+	–	+	–	–
28	MUNUSAMY	49947	42	MALE	0	0	0	1	0	2	2	1	2	2	0	0	2	0	12	0	1	1	0	1	3	Alive		+	CONSERVATIVE	NECROSIS	18	ALCOHOL	+	+	+	–	–
29	PRAKASH	50684	25	MALE	0	0	0	1	1	2	2	1	2	0	0	0	2	0	11	0	1	1	0	0	2	Alive			CONSERVATIVE		8	GSD	+	–	–	–	–
30	ARULDAS	38435	60	MALE	3	0	0	0	0	0	0	0	1	0	0	0	2	5	11	0	1	1	0	0	2	Alive			CONSERVATIVE		10	ALCOHOL	+	+	–	+	–
31	MALLESWARI	42262	24	FEMALE	0	0	1	1	0	0	1	0	0	0	0	0	0	0	3	0	0	1	0	0	1	Alive			CONSERVATIVE		6	GSD	+	–	+	–	–
32	WILSON	40677	39	MALE	0	0	1	1	0	0	2	1	0	0	0	0	1	0	6	0	1	1	0	0	2	Alive			CONSERVATIVE		7	ALCOHOL	+	–	–	–	–
33	SRINIVASAN	42845	30	MALE	0	0	0	0	0	0	2	0	0	0	0	0	1	0	3	0	1	0	0	0	1	Alive			CONSERVATIVE		6	IDIOPATHIC	+	–	–	–	–
34	RAMESH	42942	38	MALE	0	0	1	0	0	0	0	0	0	2	0	0	1	0	4	0	1	0	0	0	1	Alive			CONSERVATIVE		6	GSD	+	–	–	–	–
35	SYED IBRAHIM	42947	32	MALE	0	0	0	1	0	0	0	0	0	0	2	0	1	0	4	0	1	1	0	0	2	Alive			CONSERVATIVE		8	ALCOHOL	+	–	+	–	–
36	VIJAYAKUMAR	34459	40	MALE	0	0	1	1	0	0	0	0	2	0	0	0	1	0	5	0	1	1	0	0	2	ALIVE			CONSERVATIVE		5	ALCOHOL	+	–	–	–	–
37	ELUMALAI	34520	47	MALE	2	1	2	1	1	2	2	1	0	2	2	1	2	5	24	1	1	1	0	1	4	Alive	+		CONSERVATIVE	ARDS	19	ALCOHOL	+	+	+	–	+
38	MANIMEGALAI	34781	49	FEMALE	2	1	0	0	0	0	0	0	2	2	0	0	1	0	6	0	1	1	0	0	2	Alive			CONSERVATIVE		9	RUG INDUCE	+	–	–	–	–
39	KATHIRESAN	33291	42	MALE	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	1	2	Alive			CONSERVATIVE		9	IDIOPATHIC	+	–	–	–	–
40	RAJU	33413	40	MALE	0	0	2	1	0	0	0	0	2	0	0	0	1	0	6	0	1	1	0	0	2	Alive			CONSERVATIVE		9	IDIOPATHIC	+	–	–	–	–
41	GEETHA	30611	42	FEMALE	0	0	0	1	0	0	0	0	2	0	0	1	2	0	6	0	1	1	0	0	2	Alive			CONSERVATIVE		19	GSD	+	–	–	–	–
42	JAYARAMAN	33444	27	MALE	0	1	2	3	1	2	2	1	2	4	2	0	2	5	27	1	1	1	0	1	4	ALIVE	+	+	CONSERVATIVE	ARF	22	ALCOHOL	+	+	+	+	+
43	NAGARAJAN	32075	57	MALE	3	0	1	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	1	1	Alive			CONSERVATIVE		6	TRIGLYCER	+	–	–	–	–
44	PALANI	32520	32	MALE	0	1	2	1	0	0	0	0	2	2	0	0	1	0	9	0	1	1	0	0	2	Alive			CONSERVATIVE		11	ALCOHOL	+	–	–	–	–
45	BASKAR	28928	48	MALE	2	1	2	1	0	0	0	0	2	0	0	0	0	0	8	0	0	1	0	0	1	Alive			CONSERVATIVE		7	IDIOPATHIC	+	–	+	–	–
46	DHINAKARAN	30619	22	MALE	0	1	2	1	0	2	0	0	2	0	0	0	0	0	8	1	0	0	0	0	1	ALIVE			CONSERVATIVE		8	IDIOPATHIC	+	–	–	–	+
47	JAGABOOSANAI	28937	38	MALE	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	1	0	0	0	2	Alive			CONSERVATIVE		12	GSD	+	+	–	–	–
48	AYYAPPAN	29188	27	MALE	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	Alive			CONSERVATIVE		10	ALCOHOL	+	–	–	–	–
49	SRINIVASAN	29136	34	MALE	0	0	2	1	0	0	0	0	2	0	2	1	0	0	8	0	0	1	0	1	2	Alive			CONSERVATIVE		10	IDIOPATHIC	+	–	–	–	–
50	PREMKUMAR	26628	29	MALE	0	0	2	1	0	0	0	0	2	0	0	0	0	0	5	1	0	1	0	0	2	Alive			CONSERVATIVE		14	GSD	+	–	–	+	–
51	VINCENT	26849	28	MALE	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	Alive			CONSERVATIVE		4	IDIOPATHIC	+	–	–	–	–
52	SIVARANJANI	26682	60	FEMALE	3	0	1	1	1	0	0	0	0	2	0	0	1	5	14	0	0	1	0	1	2	Alive			CONSERVATIVE		28	TRIGLYCER	+	+	+	–	+
53	KUMAR	25379	46	MALE	2	1	0	1	0	0	0	0	0	0	0	0	0	0	4	0	0	1	0	0	1	Alive			CONSERVATIVE		6	IDIOPATHIC	+	–	–	–	–
54	BABU	25328	30	MALE	0	0	0	1	0	0	0	0	2	0	2	1	1	0	7	0	1	0	0	0	1	Alive			CONSERVATIVE		8	GSD	+	–	–	–	–
55	VIJAYAKUMAR	24611	32	MALE	0	1	2	1	0	0	0	0	2	2	0	0	1	0	9	0	1	1	0	0	2	Alive			CONSERVATIVE		12	ALCOHOL	+	–	–	+	–
56	RAMAMOORTHY	24700	48	MALE	2	1	2	1	0	0	0	0	2	2	0	0	1	0	11	1	1	1	0	0	3	Alive	+	+	CONSERVATIVE	p.NEC UGIB	19	GSD	+	+	–	–	+
57	SELVAKUMAR	22840	30	MALE	0	1	2	1	0	1	0	0	0	2	0	0	2	0	9	0	1	1	0	0	2	Alive			CONSERVATIVE		15	IDIOPATHIC	+	–	–	–	+
58	SUBRAMANI	22619	56	MALE	0	0	2	1	0	0	0	0	2	1	0	1	1	0	8	1	1	1	0	1	4	Death	+	+		SEPSIS	1	ALCOHOL	+	+	+	+	+
59	GOVINDHAMMAL	40173	27	FEMALE	0	1	1	1	0	0	0	0	0	0	0	0	0	0	3	0	0	1	0	0	1	Alive			CONSERVATIVE		6	RUG INDUCE	+	–	+	–	–

60	RAJENDRAN	22757	50	MALE	2	1	2	0	0	0	0	0	2	2	0	0	2	5	16	0	1	1	0	0	2	Alive			CONSERVATIVE		21	ALCOHOL	+	+	–	–	–
61	ANANDHAN	21681	38	MALE	0	0	0	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0	0	0	0	Alive			CONSERVATIVE		5	IDIOPATHIC	+	–	–	–	–
62	RAMALINGAM	21240	45	MALE	2	0	0	0	0	0	0	1	0	0	0	0	0	0	3	0	0	0	0	1	1	Alive			CONSERVATIVE		7	IDIOPATHIC	+	–	–	–	–
63	JAYAKUMAR	49951	80	MALE	6	1	1	1	0	2	2	1	2	2	1	1	4	5	29	1	1	1	1	1	5	DEATH	+			MODS/ SEPSIS	1	ALCOHOL	+	+	+	+	+
64	VASUDEVAN	7827	48	MALE	2	0	2	1	0	0	0	0	2	0	0	0	0	0	7	0	0	1	0	0	1	Alive			CONSERVATIVE		8	GSD	+	–	–	–	–
65	MUNUSAMY	34601	60	MALE	3	0	2	1	0	0	2	1	0	0	0	0	2	5	16	0	1	0	1	0	2	Alive			CONSERVATIVE		19	ALCOHOL	+	–	–	–	+
66	SHANMUGAM	35947	47	MALE	2	0	0	0	0	0	2	2	2	3	0	0	2	5	18	0	1	1	0	0	2	Alive			CONSERVATIVE		24	GSD	+	–	+	+	–
67	UDAYAKUMAR	34982	34	MALE	0	0	0	1	0	0	0	0	0	0	0	0	0	0	5	6	0	0	0	0	1	1	Alive			CONSERVATIVE		10	IDIOPATHIC	+	–	–	–	–
68	ESWARI	17445	37	FEMALE	0	1	2	1	0	0	0	0	2	0	0	1	2	0	9	1	1	1	0	0	3	ALIVE	+	+	SURGERY	ABSCESS	23	TRAUMA	+	+	+	–	+
69	KUMAR	17447	24	MALE	0	0	2	1	0	2	0	0	2	2	0	1	2	0	12	1	1	0	0	0	2	ALIVE			CONSERVATIVE		11	GSD	+	–	–	–	–
70	BALASUNDARAN	28542	58	MALE	2	0	2	1	0	0	0	1	0	1	0	0	1	0	8	1	1	1	0	1	4	DEATH	+			MODS/DIC	2	ALCOHOL	+	+	+	+	+
71	NANDHA	4E+05	55	MALE	3	1	2	1	0	2	0	0	2	0	0	1	3	0	15	0	1	1	0	1	3	Alive		+	SURGERY	ABSCESS	32	TRAUMA	+	–	+	+	–
72	VASANTH	45186	23	MALE	0	1	2	1	0	2	0	1	2	0	0	0	0	0	9	0	0	1	0	0	1	Alive			CONSERVATIVE		7	IDIOPATHIC	+	–	–	–	–
73	VEERAIAH	38112	42	MALE	0	0	0	0	0	0	0	0	2	0	2	1	0	0	5	0	0	0	0	0	0	Alive			CONSERVATIVE		6	IDIOPATHIC	+	–	–	–	–
74	LOGANATHAN	43336	50	MALE	2	1	2	1	0	0	0	1	2	0	0	0	0	0	9	0	0	1	0	1	2	ALIVE			CONSERVATIVE		8	TRIGLYCER	+	–	–	–	–
75	AMSA	2461	52	FEMALE	2	1	2	1	0	0	0	0	2	2	0	0	1	0	13	0	1	1	0	0	2	ALIVE		+	CONSERVATIVE	p.NEC	21	GSD	+	–	+	–	–
76	RAGAVARAJ	3382	36	MALE	0	0	2	1	0	0	0	0	0	0	0	1	5	0	9	0	0	1	0	0	1	Alive			CONSERVATIVE		9	ALCOHOL	+	–	–	–	–
77	SENGOOTUVAN	33501	45	MALE	2	1	2	1	0	0	0	0	2	0	0	0	0	0	8	0	1	0	0	1	2	Alive			CONSERVATIVE	ARF	29	GSD	+	+	+	+	+
78	KRISHNAMOORTH	51474	45	MALE	2	0	2	1	1	0	0	1	2	2	2	0	2	5	19	0	1	1	0	0	2	Alive			CONSERVATIVE		26	ALCOHOL	+	+	–	+	–
79	ANANDHAN	26918	47	MALE	2	0	0	0	0	0	0	0	0	2	0	0	0	0	4	1	0	0	0	0	1	Alive			CONSERVATIVE		6	ALCOHOL	+	+	+	–	-
80	PILLAIYARSAMY	37807	49	MALE	2	0	2	1	0	0	0	0	2	2	0	0	2	0	11	0	1	1	0	0	2	Alive		+	CONSERVATIVE	PVT	20	ALCOHOL	+	–	+	–	–
81	ARIVAZHAGAN	32076	46	MALE	2	0	2	1	0	0	0	0	0	0	0	0	0	0	5	0	0	1	0	0	1	Alive			CONSERVATIVE		6	GSD	+	–	–	-	–
82	SURESH	24123	24	MALE	0	1	2	1	0	0	0	1	2	0	0	2	0	0	9	0	0	1	0	0	1	Alive			CONSERVATIVE		9	IDIOPATHIC	+	–	+	–	–
83	NAGESWARA RA	64734	25	MALE	0	0	0	0	0	0	0	0	2	0	2	1	0	0	5	1	0	1	0	0	2	Alive	+		CONSERVATIVE		11	GSD	+	–	–	-	–
84	ARUN	31829	45	MALE	2	0	0	1	0	0	0	0	2	2	0	0	1	0	8	0	1	1	0	0	2	Alive			CONSERVATIVE		12	ALCOHOL	+	–	–	–	–
85	BAGIYANATHAN	28043	26	MALE	0	0	0	1	0	0	0	0	2	0	0	0	0	0	3	0	0	1	0	0	1	Alive			CONSERVATIVE		7	ALCOHOL	+	–	–	–	–
86	ABDULHAMEED	28086	72	MALE	5	0	0	0	1	0	0	0	2	0	0	0	10	5	13	1	1	0	0	0	2	Alive			CONSERVATIVE		18	ALCOHOL	+	–	+	–	–
87	GANI	29630	45	MALE	2	1	0	1	0	0	0	0	2	0	0	0	0	0	6	0	0	0	0	0	0	Alive			CONSERVATIVE		6	IDIOPATHIC	+	–	–	–	–
88	SIVARAMAN	30475	50	MALE	2	0	2	1	0	0	0	1	0	0	0	0	0	0	6	1	0	1	0	0	2	Alive			CONSERVATIVE		9	GSD	+	–	–	–	–
89	JASEER HUSSAI	29624	45	MALE	2	0	0	0	0	0	0	0	2	0	0	0	0	0	4	0	0	0	0	0	0	Alive			CONSERVATIVE		7	IDIOPATHIC	–	–	–	–	–
90	RAJENDRAN	34711	45	MALE	2	0	2	1	0	0	0	0	0	0	0	0	0	0	5	0	0	1	0	0	1	Alive			CONSERVATIVE		6	ALCOHOL	–	–	–	–	–
91	RANGARAJ	35579	40	MALE	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	Alive			CONSERVATIVE		8	ALCOHOL	+	–	–	–	–
92	MURUGAMMAL	36497	30	FEMALE	0	1	2	1	0	0	0	0	2	0	0	0	1	5	12	0	1	1	0	0	2	ALIVE	+		CONSERVATIVE	HYPOCAL	19	ALCOHOL	+	–	+	–	–
93	PALANI	36509	37	MALE	0	1	2	1	0	0	0	0	0	0	2	1	0	0	7	0	0	1	0	0	1	Alive			CONSERVATIVE		9	GSD	+	–	–	-	–
94	DILLY	35639	60	MALE	3	0	2	1	0	0	0	1	2	2	0	0	2	5	18	1	1	1	0	1	4	Alive	+	+	CONSERVATIVE	ARF/ MET.EN	26	ALCOHOL	+	+	+	–	–
95	MABU BASHA	35685	45	MALE	2	0	0	1	0	0	0	0	0	0	0	0	0	0	3	0	0	1	0	0	1	Alive			CONSERVATIVE		9	IDIOPATHIC	–	–	–	–	–
96	EKAMBARAM	38263	50	MALE	2	1	2	0	0	0	0	0	0	0	0	0	1	0	6	1	1	0	0	0	2	Alive			CONSERVATIVE		11	ALCOHOL	+	+	+	–	–
97	KAMALESWARAI	51612	32	MALE	0	1	2	3	0	0	0	0	2	2	0	0	1	0	10	1	1	0	0	0	2	ALIVE	+		CONSERVATIVE	ARF	21	GSD	+	–	–	+	–
98	RADHAKRISHNAI	51658	55	MALE	3	1	2	1	0	0	0	0	2	2	0	1	2	5	19	0	1	1	0	1	3	Alive		+	SURGERY	p.CYST /p.NEC	19	ALCOHOL	+	–	+	-	–
99	RAJESH	33762	45	MALE	2	0	2	1	0	0	0	0	2	0	1	1	1	0	10	0	1	1	0	0	2	Alive	+		CONSERVATIVE		20	ALCOHOL	+	–	–	–	–
100	JEEVA	34448	41	MALE	0	0	2	1	0	0	0	0	2	0	0	0	0	0	5	0	0	1	0	0	1	Alive			CONSERVATIVE		10	ALCOHOL	–	–	–	–	–