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

Dissertation Submitted To

THE TAMILNADU

DR. M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations required for the award of

M.S. (GENERAL SURGERY) BRANCH – I

DEPARTMENT OF GENERAL SURGERY

CHENGALPET MEDICAL COLLEGE

CHENGALPATTU - 603001

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DECLARATION

I, **DR. S. SIDDARTH** solemnly declare that this dissertation titled **"A COMPARATIVE STUDY BETWEEN BISAP AND APACHE II SCORE IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS IN CHENGALPET MEDICAL COLLEGE"** is a bonafide work done by me in the Department of General Surgery, Government Chengalpattu Medical College and Hospital under the guidance and supervision of my unit chief and **HOD Prof. J. SELVARAJ, 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 May 2020.

Place: Chengalpattu **DR. S. SIDDARTH**

Date: **Reg No: 221711263**

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 IN CHENGALPET MEDICAL COLLEGE"** is the bonafide work done by **Dr. S. SIDDARTH**, Post Graduate student (2017 – 2020) in the Department of General Surgery, Government Chengalpattu Medical College and Hospital 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 May 2020.

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CERTIFICATE FROM THE GUIDE

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY BETWEEN BISAP AND APACHE II SCORE IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS IN CHENGALPET MEDICAL COLLEGE"** submitted by the candidate **DR. S. SIDDARTH** in partial fulfilment for the award of the degree of Doctor of Surgery in General Surgery by the Tamilnadu Dr. M. G. R. Medical University, Chennai – 32 is a record of original and bonafide work done by him under my guidance and supervision in the department of General Surgery, Chengalpattu Medical College, Chengalpattu during the tenure of this course in M. S. General Surgery from December 2018 to December 2019 submitted in partial fulfilment of the requirements for the award of M. S. Degree in General Surgery by the Tamilnadu Dr. M. G. R. Medical University, Chennai – 32.

Signature of the Guide **DR. S. SIDDARTH**

ETHICAL COMMITTEE CERTIFICATE

INSTITUTIONAL ETHICAL COMMITTEE

CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU

Title of Work	:	A Comparitive study between bisap and apache II scoring in assessing the severity of Acute Pancreatitis in Chengalpattu Medical College.
Principal Investigator	:	Dr.S.Siddarth
Designation	:	1st yr PG
Co-Investigators	:	Dr.J.Selvaraj,M.S., Professor and HOD, Department of General Surgery
Department	:	General Surgery

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It is my earnest duty to thank my parents without whom accomplishing this task would have been impossible.

I am extremely thankful to my patients who consented and participated to make this study possible.

CONTENTS

INTRODUCTION

Acute pancreatitis is a common disorder with substantial burden on the healthcare system. 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.

In 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.

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.

AIMS & 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.

Source of data:

Study is a prospective type which will include all patients who will be admitted in CHENGALPATTU MEDICAL COLLEGE with ACUTE PANCREATITIS. The study will be conducted during the period of December 2018 to December 2019.

METHODS OF COLLECTION OF DATA:

Study type: Prospective study

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 will be evaluated clinically and subjected to laboratory and radiological investigations as per the designed proforma. 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 will be 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.

REVIEW OF LITERATURE

ETYMOLOGY

PANCREAS was first described in writings of Eristratos (around 300 B.C.). However an anatomist RUFUS coined the term “PANCREAS” four hundred years later.

PANCREAS originates from Greek “pan: all, kreas: flesh”Johann Georg Wirsüng, a German emigrant in 1600 discovered the pancreatic duct but his colleague named it as “The Duct of Wirsüng” . Vater in 1720 discovered the papilla. In 1734, the accessory duct was discovered by Santorini.

Paul Langerhans, a student of Professor Rudolph Virchow, described the islets of the pancreas and it was named after him. Jean de Meyer coined the term 'insulin’.

HISTORY

The first histologic description of pancreas was given by Claudius Galenus who was a Physician of the Roman Emperor. He taught that the pancreas acts as a cushion and prevents damage to large blood vessels covered by it.

In 1893, it was discovered that islet cells produced a hormone which was termed “insulin “. Eugene Lindsay Opie in 1901 showed a correlation between diabetes and damage or reduction of islet cells and proposed common channel hypothesis.

Serum amylase was found to be a strong predictor of pancreatic pathology and since 1908 , Wohlgemuth Julius discovered a method of measuring concentration of s. amylase. Surgical management for carcinoma pancreas was started from 1898, Allen Whipple took various steps for resection of tumpurs of pancreatic duct , ampulla and head and he was recognized as the " father of pancreatic surgery "

He was the first successful surgeon to resect pancreatic head tumour in a single stage surgery. Acute Pancreatitis was classified in First Marseilles symposium and revised in 1984.However it was only in 1992 at the Atlanta Symposium, that a classification system which was clinically oriented was established for acute pancreatitis.

Although acute pancreatitis has been known for a long time its severity and mortality and morbidity was not well established till mid-1800s . In the upcoming years, we may expect further refinements in classification systems with the availability of MRI and other newer innovative technologies.

SURGICAL ANATOMY

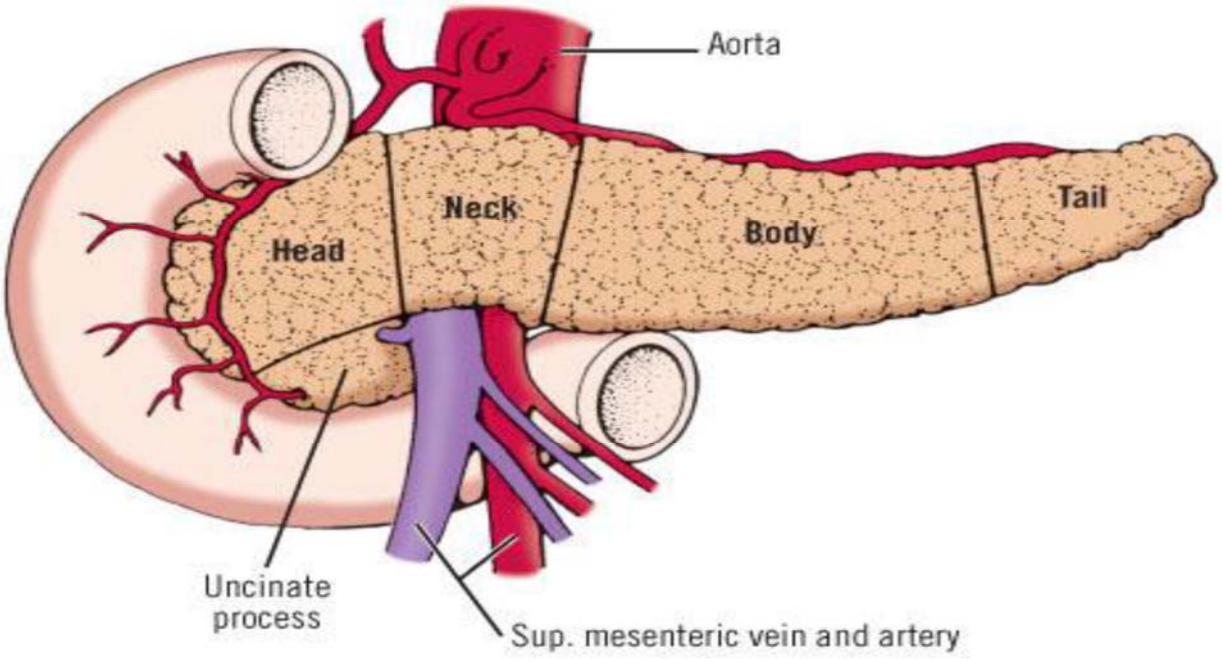
It is imperative for a surgeon to understand the exact anatomy of pancreas, its ductal systems, its blood supply, nervous supply and adjacent vessels and neurovascular bundle and relation to other organs, this achieves great importance during operating and also helps to understand the pathophysiology of pancreas. Pancreas is one of the most treacherous organs

to operate on owing to the complications occurring during pancreatic surgery which may be fatal.

The pancreas lies posterior to the stomach, roughly in the Trans pyloric plane. The gland weighs approximately 80 g, varying from 70 – 120g and measures about 15 to 22 cm length in adults.

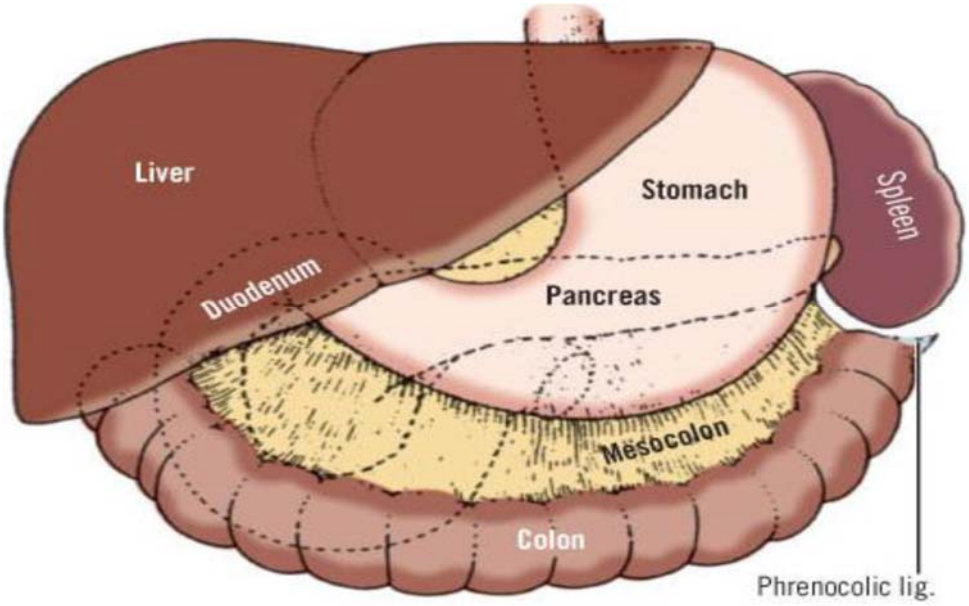
It is a retroperitoneal organ occupying the epigastric region. It is situated posterior to the stomach and overlying omental bursa. Pancreas extend from the medial edge of the second part of duodenum upto the hilum of the spleen. Portal vein formation occurs posterior to the neck of pancreas. The Abdominal aorta and inferior vena cava, two major abdominal vessels are situated behind the pancreas.

PARTS OF PANCREAS:

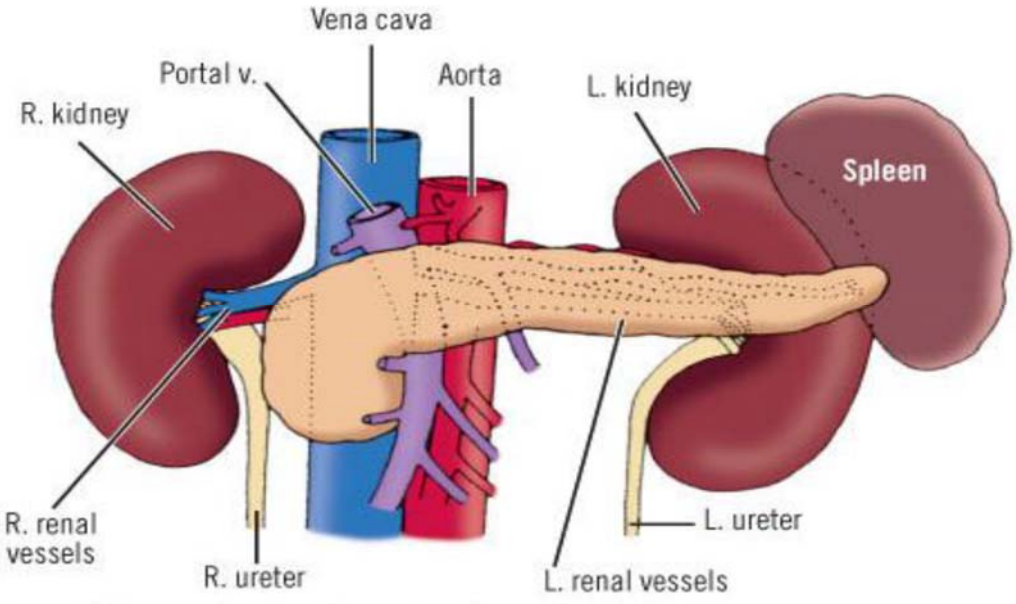


Five parts of pancreas. Line dividing body and tail is entirely arbitrary.

ANTERIOR RELATIONS OF PANCREAS



POSTERIOR RELATIONS OF PANCREAS



Ductal System of the Pancreas

The ductal system consists of collection of acinar cells, pancreatic lobules, intercalated ducts, branching ducts , minor and major ducts. About 25 to 200 acinar cells are found within each pancreatic lobule and each lobule drain into small intercalated ducts , multiple small intercalated ducts merge to form intralobular ducts, multiple intralobular ducts merge together to form branching ducts or secondary pancreatic ducts that ultimately drain into main pancreatic duct which is also known as Duct of Wirsung.

The Main Pancreatic Duct gradually increases in caliber as we move from tail to head from approximately 1 - 2 mm in tail, 2 - 3 mm in body and 3 to 4 mm in the head. Uncinate process of pancreas usually has its own pancreatic duct which drains directly into the duct of wirsung just prior to major duodenal papilla as the duct becomes more horizontal.

The Duct of Santorini which is also known as accessory pancreatic duct is the proximal portion of the duct which drains the dorsal pancreas. As embryologically the dorsal and ventral pancreas fuse, the role of accessory duct is restricted to a secondary role as it tends to drain only the anterosuperior portion of the pancreatic head. However, in case of anomalies where the ducts do not fuse (this occurs in ≈ 10% of individuals), such a scenario is called pancreas divisum, the major draining duct of entire dorsal pancreas and uncinate is carried out by accessory duct of santorini .

There are two duodenal papillae, major and minor duodenal papilla. The major duodenal papilla is usually found on the posteromedial wall of D2 (duodenum), in the second part, approx. 7 to 10 cm distal to the pylorus. The minor papilla is located anteroproximal to major duodenal papilla approx. 1 to 2cm proximally.

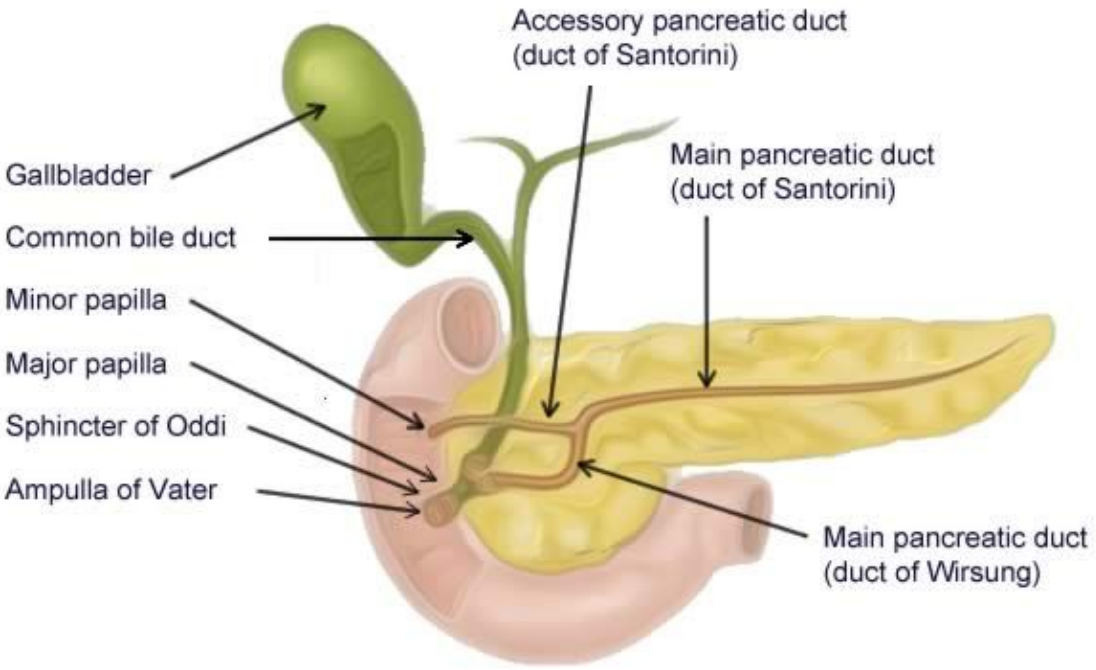
The sphincter complex of pancreas is also important during endoscopic procedure and is discussed here. The anatomy of the sphincter complex at the major duodenal papilla, (Boyden and Oddi,) is also variable. The length of the sphincter complex may vary from 5 to 30 mm.

The sphincteric fibers have a separate choledochal part. Only 30 % of individuals have a pancreatic sphincter. The end of pancreatic duct has a zone of high pressure which is relaxed by secretin hormone , which enhances the pancreatic secretions to flow into ampulla.In 75 % individuals, the biliary and pancreatic ducts unite and form the common duct before they enter into the duodenum. The sphincters have a regulatory action on rate of flow into duodenum and prevents back flow of duodenal contents into duct.

The duct passes obliquely into the duodenal wall and the mucosal valves prevent the reflux. Sphincter of Oddi is controlled by the neural pathways. During feeding it reduces the sphincter pressure.

Cholecystokinin causes relaxation of the sphincter after food intake. The sphincter complex has four elements:

1. superior biliary sphincter
2. inferior biliary sphincter which is submucosal
3. common ampullary sphincter
4. pancreatic sphincter

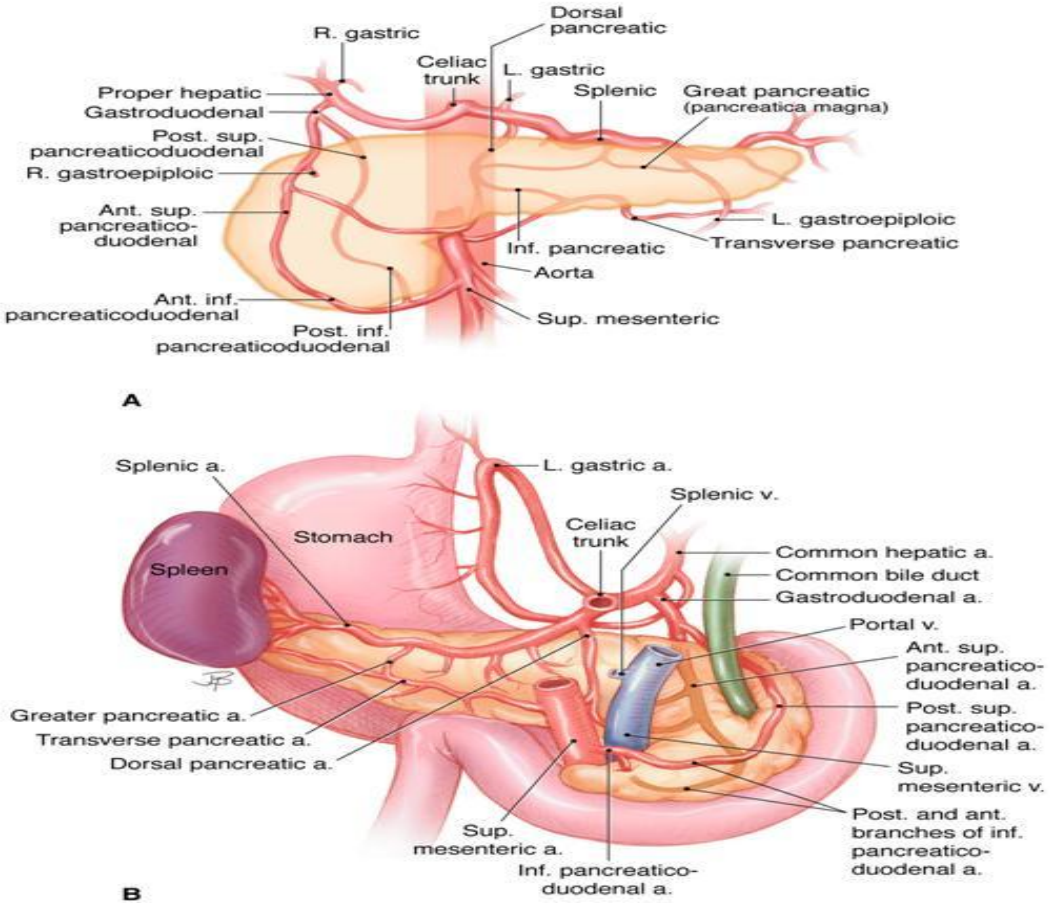


VASCULAR SUPPLY

Arterial supply is from superior pancreatico duodenal artery and inferior pancreaticoduodenal artery. The superior pancreaticoduodenal artery arises as a branch of gastro duodenal artery which arises from celiac artery while the inferior pancreatico duodenal artery is a branch of superior mesenteric artery.

Branches from the splenic artery also supply the body and tail of pancreas.

Veins from the pancreas drain into splenic and superior mesenteric, portal veins.



LYMPHATIC DRAINAGE

Lymphatic drainage of different parts of the pancreas is by different lymphatic groups.

Pancreatic head and uncinate process are mainly drained by lymph nodes of the infra pyloric group and drained to a minor extent by the periportal, mesenteric, mesocolic, pre and paraaortic lymph nodes.

Body of pancreas drains into coeliac group of lymph nodes and are also drained by the mesenteric and aortic group of lymph nodes.

Tail of pancreas drains into celiac groups and splenic hilar nodes

Nerve Supply of the Pancreas

Efferent Innervation of the pancreas occurs by the

1. Splanchnic nerves (sympathetic) and
2. The vagus nerve (parasympathetic).

The nervous supply to pancreas contain efferent vasomotor which control the exocrine and endocrine functions to the pancreatic acini, ducts, and blood vessels and ducts.

Sympathetic nerve supply - Preganglionic sympathetic nerves arise from the greater splanchnic (T5-T10), the lesser splanchnic (T9-T11), and seldom the least splanchnic nerves. The preganglionic parasympathetic nerves which arise from the celiac division of the posterior vagal trunk synapse with ganglia

which are present within the pancreas. Postganglionic nerve fibers reach pancreas via accompanying branches of arteries such as periarterial plexi. The postganglionic fibers terminate at the pancreatic islet cells.

Parasympathetic nerve supply – Origin is the vagus nerve . The islets cells are almost exclusively innervated from the parasympathetic side, and these fibers frequently synapse with acinar cells before reaching the islet cells. This suggests a neural coordination between both exocrine and endocrine components.

Afferent nervous supply bring pain sensation which is a feature of both benign and malignant pancreatic diseases.

Pain occurs due to carcinomatous perineural infiltration, damage to perineurium, release of inflammatory mediators such as cytokines, interleukins, ductal hypertension, and compartment syndrome. Pancreatic pain is often poorly localized mostly referred to the epigastrium and radiating to back. One of the end points of management is interruption of pain, which is considered an important therapeutic goal.

This includes various modalities and approaches such as surgical, thoracoscopic, radiologic, and endoscopic chemical approaches. The mainstay of analgesia remains pharmacology.

Afferent pain fibres arise in the pancreas and cranially through the celiac plexus to their cell bodies in the dorsal root ganglia within the splanchnic nerves, these fibres cross to the spinal nerves along the white communicating rami and at a spinal level comparable to the preganglionic sympathetic fibers.

Histology

Pancreas consists of both exocrine and the endocrine glands. The exocrine component of pancreas consists of acinar glands while the endocrine aspect consists of islets of Langerhans.

The pancreas constitute 85% exocrine gland, 10% extracellular matrix, and 4% neurovascular bundles & the major ducts, and just 2% of pancreatic tissue is endocrine in nature. Though the endocrine and exocrine pancreas are thought to function separately, they are coordinated well for regulating the feedback system of digestive enzyme and hormone secretion.

ENDOCRINE PART

Endocrine component of pancreas constitutes only 2% of the pancreatic tissue. Endocrine portion of the pancreas has islets of Langerhans cells. Around 10 lakhs Langerhans islets present in matured normal pancreas.

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

There are five major types of cells present in the endocrine portion.

1) Alpha cells
2) Beta cells
3) Delta cells
4) Epsilon cells
5) Pancreatic polypeptide cells

Alpha cells function is to secrete glucagon hormone, which is involved in glucose metabolism.

Beta cells function is to secrete hormone insulin. Insulin is released into the blood stream in response to high levels of glucose in blood. It functions to reduce blood glucose level by converting glucose into glycogen and storing it in liver and muscles.

Delta cells secrete the hormone somatostatin. It is involved in reducing gastrointestinal secretions. It can also inhibit secretion and functions of other gastro intestinal hormones.

Epsilon cells secrete the hormone Ghrelin. It acts to reduce the level of insulin release and blocks the actions of insulin.

Pancreatic polypeptide is secreted by PP cells. It blocks exocrine secretions of pancreas.

EXOCRINE PART

Exocrine pancreas constitutes more than 75% of pancreas. Exocrine pancreas comprises two types of cells which are acinar cells and ductal cells.

The acinar cells, named after the cluster of grapes on the stem of a vine that they resemble, are organized into lobules. The main duct ramifies as intralobular and interlobular ducts, ductules which finally end up in acini, that secretes into a centrally located space called acinar space which communicates with the main pancreatic duct.

Microscopically, acinar cells have a high content of endoplasmic reticulum with an abundance of eosinophilic zymogen granules which are apically located. The cells lining the main pancreatic duct are made up of tall columnar cells, and they contain mucin granules. As progression occurs from large ducts to the smaller intralobular and interlobular ducts, the lining cells become flatter, assuming a cuboidal configuration, and mucin granules are no longer visible. Centriacinar cells, situated at the junction between ducts and acini, resemble acinar cells in size and shape but differ in not having zymogen granules.

It can cause pain from localized inflammatory process or bleeding manifestations. Rarely tumours of Langerhans cells arise from this ectopic pancreas.

PHYSIOLOGY

PANCREATIC SECRETION

Pancreas consists of exocrine and endocrine glands and hence has two types of secretions. One is exocrine gland which secretes enzymes which are needed digestion. The endocrine gland synthesizes hormones needed for carbohydrate metabolism and gastro intestinal hormonal regulation.

EXOCRINE PANCREAS

Pancreatic tissue in adults secretes approximately between 2000 to 2500 milliliters of pancreatic secretion. This secretion is characteristically clear, odorless and has a pH > 8. It has high amount of bicarbonate. It is also rich in protein. Pancreatic secretion is released from exocrine cells i.e. both acinar and ductal cells of pancreas. It is the second most protein rich fluid after mammary glands.

Pancreatic acinar cells are responsible for secretion of amylase, lipase, protease enzymes. Amylase is responsible for the metabolism and digestion of carbohydrates. Lipase is an enzyme involved in digestion of fat. Protein digestion is mediated by proteases.

Amylase

Amylase the enzyme for carbohydrate digestion is the only digestive enzyme synthesized in the active form in the intra pancreatic part. It metabolises saccharides, after salivary amylase from saliva in mouth which is involved in initiation of carbohydrate metabolism.

The salivary amylase which inititiates carbohydrate metabolism breaks polysaccharides into disaccharides inside the oral cavity itself. The similar enzyme pancreatic amylase enzyme breaks remaining polysaccharides (ex glycogen and Starch) into disaccharides (ex maltose, sucrose, glucose). The glucose is absorbed by intestinal mucosal cells by transport mechanism.

ENZYME SYNTHESIS:

The exocrine enzymes which are digestive account for approx. 80 to 85 percent of protein synthesis in pancreas. To avoid autodigestion of pancreas greater parts of the enzymes are synthesized in inactive form called proenzymes or zymogens secreted from acinar cells and are activated later. Some enzymes are synthesized in an active form as they don't need activation for its target action examples of such enzymes are amylase, lipase and ribonuclease.

Acinar cells also have additional function of synthesizing some other kind of proteins only for the purpose of using within the cell itself. These are structural proteins and hydrolytic enzymes.

PROCESS OF SECRETION:

Synthesized enzymes are collected and stored in the endoplasmic reticular organelles. After the enzymes are transported into the Golgi apparatus which are the transport medium of the cells. These enzymes are then packed in vacuoles inside the cells and formed into granules which are called as zymogen granules. Finally, these zymogen granules are then migrated into the acinar cell

membranes. The zymogen granules are released into the lumen of acinar cells thereby releasing enzymes into acini and hence ducts by the mechanism of fusion and fission.

Synthesis of enzymes in acinar cells occurs in an orderly fashion. During resting there is a low level or basal secretion of enzymes. After neuronal and hormonal stimulation due to external signals as per metabolic need the rate of secretion is increased into a marked amount. Pancreatic acini has some receptors for neurotransmitters from cholinergic nervous system which uses acetylcholine as neurotransmitter and chemical messenger, and receptors for other gastro intestinal hormones like kinins, secretin, vasoactive peptides. This stimulation for secretory process is initiated by neurotransmitters or kinin which acts by causing activation of intracellular transmitters like phospholipase C, creation of phosphorylated inositol (ITP) and diacyl glycerol, which then leads to increased ionized calcium inside the cells which act as secondary messengers. The rate of release of enzymes from acinar cells will be by an unexplained regulatory process

ELECTROLYTE SECRETION

Pancreatic secretion has high ph and is a highly alkaline solution because of its high content of bicarbonate ions. Acinar cells also secrete minimal level of serous fluid. But a major part of the fluid and bicarbonate rich secretion is by ductal epithelial cell. Initially blood CO_2 gas diffuses into ductal epithelium , then CO_2 is converted into carbonic acid (HCO_3) by the enzyme carbonic

anhydrase. Carbonic acid is further broken down into hydrogen ions (H^+) and bicarbonate ions. These hydrogen ions then efflux out of the cells and enter into blood stream. But the ions of bicarbonate alone are sequestered inside the cells.

The enzyme secretin stimulates the secretion of fluids and electrolytes. It acts through secondary mediators such as cyclic AMP and inturn results in secretion of chloride ions in the surface of acinar cells. This is regulated by cystic fibrosis (CFTR) membrane conductance regulator which acts in channels for chloride. The secreted chloride ions then get reabsorbed into ductal cells and inturn are involved in the exchange of bicarbonate ions via the mechanism of chloride bicarbonate exchanging system.

Final event in this process is the secretion of fluid which is rich in bicarbonate into the lumen of ductal system. Pancreatic juice will contain only plasma like clear fluid if the secretin stimulation is absent because there is little or no activation of ductal epithelium which is needed for bicarbonate exchange.

ACTIVATION OF PANCREATIC ENZYMES:

The digestive enzymes from pancreas are released as pro enzymes , this protects against pancreatic autodigestion. These need to be activated by some enzymes, to act on target sites. Trypsinogen is secreted in its inactive form and the active form is trypsin. Trypsinogen is activated by the enzyme called enterokinase which is secreted from lumen of intestine. Trypsin in turn activates other inactive digestive enzymes of pancreas.

Trypsinogen is normally in the inactivated form inside the pancreas, because there are some inhibitors of trypsinogen synthesized inside the acinar cells.

Failure to express these inhibitors of trypsinogen will lead to familial type of pancreatitis in which there is intraparenchymal activation of trypsinogen leading to autodigestion of pancreas. The trypsinogen is activated in the lumen of (D2) duodenum where it is secreted into intestine and comes in contact with enterokinase enzyme in intestinal lumen. Activation of trypsinogen in pancreas is called premature activation which causes pancreatitis, this occurs in one condition in which there is a mutation in cationic trypsinogen. This condition constitutes about sixty percent of familial pancreatitis. The gene is PRSS1 in long arm of chromosome [7].

Chymotrypsinogen which is the inactive form is activated into the active form called chymotrypsin by trypsin.

Trypsin also activates the enzymes like elastase, phospholipase, carboxy peptidases type A and B.

PROTEIN DIGESTION:

The above digestive enzymes in their active form act on particular amino acids of peptide chains and cleave proteins and polypeptides in between the amino acids. Carboxy peptidases help in breaking the amino acids at their peptide chain ends. The amino acids and di peptides are absorbed into intestinal epithelial cells by luminal transport system.

FAT DIGESTION:

Triglycerides are metabolized and broken down into fatty acids and glycerol which are end products by the action of lipase. Trypsin is also needed to activate phospholipase A2 (PLA2) which is also secreted as a pro enzyme. This enzyme hydrolyzes and metabolizes the phospholipids.

Lipases will act on lipids only after the action of bile salts on lipids which is needed to reduce its surface tension and thus activates it.

Cholesterol esters, fat soluble vitamins like vitamin A,D,E,K and triglycerides are metabolized and hydrolyzed by enzymes like (CE hydrolases) carboxylic ester hydrolases and cholesterol esterase. The micelles then formed are transported into epithelium of intestinal mucosa by luminal absorption. Chylomicrons which are transported via the lymph ducts finally enter into the blood circulation.

PHASES OF PANCREATIC SECRETION

Pancreatic secretion occurs in phases as is the norm with any secretion, amount of pancreatic secretion is very minimal during resting phase of digestive tract as when compared with activated stage.

Pancreatic secretion occurs in three phases or stages.

CEPHALIC STAGE:

This is the first phase and constitutes only twelve to sixteen percent of food induced secretion of pancreatic enzymes and juice. It is the phase which occurs in response to visual, olfactory or gustatory stimulus such as smelling or chewing the food leading to secretion of pancreatic juice. This phase is said to be due to the peripheral stimulation of cholinergic nerve fibers of parasympathetic system via Vagus which induces secretion of hydro chloric acid in stomach and electrolyte rich pancreatic secretion. This will inturn lead to secretin release by the acidic stimulus to duodenum.

GASTRIC PHASE:

This phase is due to gastric stimulus, this stage also constitutes only minimal portion of food stimulated pancreatic secretion. This phase occurs due to distension of stomach by food particles entering into stomach. The entry of food particles and gastric distension stimulates gastrin release and vagal nerve stimulation which inturn stimulate pancreatic secretion.

INTESTINAL PHASE :

When food particles along with acidic gastric juice enters the duodenum the acidic nature of gastric secretion stimulates pancreas to secrete pancreatic juice which is rich in bicarbonate and alkaline in nature to counteract the gastric acidity.

The lipids and proteins and their partially broken-down digested products triglycerides and polypeptides stimulate cholecystokinin release from mucosa of duodenum. This enzyme CCK results in release of enzyme rich secretion from pancreas. This stage constitutes the maximum amount of pancreatic secretion about three fourth of total pancreatic secretion.

FEEDBACK MECHANISM:

As there is positive stimulus for pancreatic secretion there also negative feedback mechanisms.

The duodenal mucosa secretes a releasing factor which monitors the release of cholecystokinin, pancreas secretes a peptide for monitoring of pancreatic enzymes. Trypsin proteolysis these two factors.

When there is a high presence of protein in the diet inside the duodenum, releasing factor from duodenal mucosa stimulates cholecystokinin which again lead onto stimulation of pancreatic secretion as the positive loop of feedback mechanism.

When there is a lack of food inside the duodenum, trypsin causes the lysis of the releasing factor which will in turn control cholecystokinin secretion leading to a decrease in pancreatic secretion.

Applied physiology here is that in cases of pancreatitis, there is insufficient pancreatic secretion due to pancreatic damage which causes insufficient duodenal proteolysis. So the level of cholecystokinin release is not regulated by trypsin or releasing factor and thereby increased. Most probably this is the reason for pain in chronic pancreatitis. It can be controlled or reduced by the administration of exogenous pancreatic enzymes which can help to reduce pancreatic stimulation and also replace pancreatic enzymes.

ACUTE PANCREATITIS

Acute pancreatitis is “an inflammatory disease which is associated with little or no fibrosis of the pancreas”. Acute pancreatitis has several initiating factors, which include stones in biliary system, gallstones, alcohol, trauma, and infections, and, seldom hereditary.

ETIOLOGY OF ACUTE PANCREATITIS:

Acute pancreatitis have been implicated to be cause by so many different factors. On comparing worldwide data on pancreatitis, the most common cause is Gallstones which make up for about 45 percent of cases, followed by Alcohol which is the second common cause, in about 35 percent of cases. In a study done in, India, New Delhi, gall stones and alcohol were found to be the cause in 49% and 25% cases, respectively.

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

CAUSES OF ACUTE PANCREATITIS

1. Alcohol
2. Biliary tract disease
3. Obstructive causes:
    a) Choledocholithiasis
    b) Ampullary carcinoma or pancreatic malignancy

c) Papillary obstruction by worms/foreign bodies

d) Pancreas divisum with minor duct obstruction

e) Choledochocele

f) Duodenal diverticula at periampullary region

g) Spasm sphincter of Oddi

4. Toxins or drugs:

Toxins:- ethanol/methanol, scorpion sting, organo phosphorous compounds

Drugs:- The following drugs can definiteively cause pancreatitis

5-Aminosalicylate (ASA)

6-Mercaptopurine (6-MP)

Azathioprine

Cytosine arabinoside (cytarabine)

Didanosine

Diuretic agents

Estrogens, etc.

Drugs which may probably cause pancreatitis

Acetaminophen

α-Methyl-DOPA

L-Asparaginase

Isoniazid (INH)

Phenformin, etc.

5. Trauma:

   Blunt injury abdomen

   Surgical trauma

   Iatrogenic injury- postoperative trauma, post ERCP, post endoscopic Sphincterotomy and manometry

6. Metabolic abnormalities:

   Hypercalcemia

   Hypertriglyceridemia

7. Inherited conditions

8. 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 pneumophila, leptospiral infection

9. Vascular causes: ischemic diseases (e.g., after major cardiac vascular surgery)

   Athero-embolism, Vasculitis-SLE, PAN, malignant hypertension

10. Miscellaneous causes: Peptic ulcer penetration, Cystic fibrosis, Crohn's disease, Reye's syndrome, Hypothermia

GALL STONES

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

In 1900, Opie, at the Johns Hopkins Hospital in Baltimore, recorded impaction of gallstone in the ampulla of Vater when they performed autopsy of a patient operated on by Halsted, who had died due to gallstone induced pancreatitis and thereby tried first to describe the pathogenic mechanism of gallstone induced pancreatitis. He proposed that the stone might have caused outflow obstruction from a common ‘biliopancreatic channel’. This led him to propose the previously accepted "common-channel hypothesis" in which a blockage below the junction of the biliary and pancreatic ducts would cause bile to flow into the pancreas, which could then damage the pancreas by the detergent action of bile salts.

Although this reflux theory was originally favored, now most observers believe that it is stone-induced pancreatic duct obstruction causing increased intraductal pressure ductal hypertension, rather than bile reflux perse that triggers acute pancreatitis.

Opie’s hypothesis regarding the pathogenesis of pancreatitis was widely accepted during much of the twentieth century, but it’s regarded as a myth today. By experiments in animal models of opossum with easily accessible long common channel, Lerch et al. had demonstrated that pancreatic duct

obstruction alone causes necrotizing pancreatitis which is distinguishable from pancreatitis that occurred when CBD was also occluded simultaneously.

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 & endosonography 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. Various theories have been put forward,

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 microcirculation8. 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, 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.

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.

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

(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 trypsinogen7. 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 colocalizes 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.

SCORING SYSTEMS IN ACUTE PANCREATITIS

Acute Pancreatitis is a serious disease with high morbidity and mortality rates. 80% of the cases were usually mild which recovers rapidly with conservative management. The remaining 20% cases were severe, with protracted course that needs intensive care and specialized management. Several predictors of severity are commonly used for this purpose.

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

Scoring systems to predict both mortality and morbidity in patients with acute pancreatitis include:

- Ranson's criteria
- Imrie Glasgow Coma Score (GCS)
- Balthazar Computed Tomography (CT) grading
- Bank's clinical Criteria
- Simplified Acute Physiology Score (SAPS)
- Modified Glascow Criteria
- Marshall Multiple Organ Failure (MOF) score and
- Acute Physiology and Chronic Health Evaluation (APACHE) I, II, III
- BISAP (Bedside Index for Severity in Acute Pancreatitis)

The Ranson's multiple scoring system and GCS require 48 hours of data collection whereas APACHE score can be calculated at any time and it shows significant correlation with acute pancreatitis, as increasing scores are associated with poor prognosis.

Once the acute pancreatitis has been diagnosed, assessment of severity of disease has to be made for accomplishment of appropriate measures, preferably in an intensive care setup with close monitoring.

RANSON'S CRITERIA:

Ranson and Pasternak identified 11 parameters with prognostic significance in the year 1974. Disease Mortality was related to the number of parameters present in the scoring system: 0-0.9% in patients with < 3 positive prognostic signs, 10-20% in those with three to five positive prognostic signs, mortality increases to more than 50% in those with > seven positive signs.

Ranson's scoring system analyzes the severity from the clinical and the biochemical parameters at the time of admission and 48 hours after admission. A total of 11 points were included. Five points from the time of admission and the remaining six points were included from the next assessment after 48 hours from the abnormal values. Since the positive predictive values and accuracy are low in case of biliary disease induced pancreatitis, this scoring system has undergone some modifications for biliary pancreatitis.

GALL STONE INDUCED PANCREATITIS:

In recent years, the cut off values of these signs were modified in biliary pancreatitis which limits the use of early prognostic signs and requires memorization of 18 separate parameters. The etiology is always unknown.

The revisions for biliary pancreatitis have not gained worldwide acceptance, and the original system is the one that is widely utilized.

At the time of admission or diagnosis:

Age > 70 yrs

WBC count > 18,000/mm3

Blood sugar more than 220 mg/dL

Lactate Dehydrogenase > 400 IU/L

SGOT > 250 U/dL

During initial 48 hours:

Fall in hematocrit greater than 10 percentage points

BUN elevation > 2 mg/dl

Serum calcium level less than 8 mg/dl

Base deficit > 5 meq/L

Estimated fluid sequestration more than 4 L

Criteria for Pancreatitis not due to gall stones:

At admission or diagnosis:

Age more than 55 years

WBC count more than 16,000/mm^3

Blood sugar> 200 mg/dL

Serum LDH> 350 IU/L

SGOT > 250 U/dL

During initial 48 hours:

Fall in haematocrit more than 10 percentage points

BUN elevation > 5 mg/dL

Serum Ca^{2+} level < 8 mg/dL

Arterial Po2 < 60 mm Hg

Base deficit more than 4 meq/L

Estimated fluid sequestration more than 6 L

IMRIE'S PROGNOSTIC CRITERIA:

This system is based on an interventional study in acute pancreatitis. It includes age of the patient at the time of admission and physiological and biochemical parameters obtained during the first two days of admission.

During initial 48 hours

- WBC count > 15000/mm3
- Blood sugar > 10 mmol/L
- Serum urea > 16 mmol/L (no response to IV fluids)
- Po2 level < 60 mm Hg
- Serum Ca2+ 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 indicates the severity of disease at the time of admission and are not suitable for monitoring the clinical course.

BALTHAZAR COMPUTED TOMOGRAPHY SEVERITY INDEX (CTSI):

Emil J. Balthazar et al, proposed CTSI, a grading system to determine severity of the acute pancreatitis.

Prognostic Indicator	Points	Grade
Pancreatic inflammation:		
• Normal pancreas (15%-29%)	1	A
• Focal or diffuse enlargement of the pancreas and heterogenous attenuation in parenchyma	2	B
• Intrinsic pancreatic abnormalities with inflammatory changes (streaky densities) in peripancreatic fat	3	C
• Single, ill-defined fluid collection or phlegmon in the peri pancreatic region	4	D
• Two or more poorly defined collections or presence of gas in or adjacent to the pancreas multiple fluid collection in the peripancreatic fat along with retroperitoneal air	5	E
Pancreatic necrosis		
• None	0	
• ≤ 30%	2	
• >30–50%	4	
• > 50%	6	

CORRELATION OF MODIFIED CTSI WITH OTHER PARAMETERS:

With increasing severity of the disease, there is associated increase

1) Length of hospitalization

2) Number of patients undergoing surgical procedure

3) Occurrence of infection

4) Organ dysfunction

Modified CT Severity Index

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**

BANK'S CLINICAL CRITERIA:

Cardiac	Tachycardia,shock,arrhythmia, ECG changes
Renal	Urine output < 50 ml/hr, rising BUN & creatinine
Pulmonary	Dyspnoea, basal rales, PO_2 less than60 mm Hg, ARDS
GIT	paralytic ileus, free fluid, hgic peritoneal tap
Neurological	Cerebral Irritation, confusion
Haematological	↓Hematocrit,DIC
Metabolic	Low Calcium & pH; ↓albumin

- SCORE ≥ 1 INDICATES THE DISEASE WAS SEVERE IN INTENSITY.

MODIFIED GLASGOW CRITERIA:

This criterion was useful in both alcoholic and biliary pancreatitis. Score more than 3 indicates severe disease

P - PaO_2 <8kPa or < 60 mmHg

A - Age more than 55 years

N - Neutrophilia with WBC count>$15x10^9$/L

C – Calcium< 8 mg/dl or <2mmol/L

R - Renal function- Urea >16mmol/L or less than 45 mg/dl

E – Enzyme - serum LDH >600 IU/L; AST>200 IU/L

A - Albumin - less than 3.2g/dL

S – Sugar - >180 mg/dl or >10mmol/L

CRITERIA FOR ORGAN FAILURE BASED ON MARSHALL SCORING SYSTEM:

Marshall scoring system is a modified scoring system because it excludes the liver function and other major systems are monitored. The scores were calculated within 72 hours of admission. The organ failure was classified as Transient (less than 48 hours) and Persistent (more than 48 hours.).

According to this scoring system score of ≥ 2 indicates presence of organ failure. The parameters closely coincides with Atlanta classification Marshall

scoring system shows comparable results with APACHE II scoring system in predicting mortality of acute pancreatitis

ORGAN SYSTEM	**SCORE**				
	0	1	2	3	4
RESPIRATORY($Pa0_2/FiO_2$)	>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,mmHg)	>90	>90, fluid responsive	<90, fluid unresponsive	<90, pH<7.3	<90, pH<7.3

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

In 1985, Knaus et al developed a scoring system APS for classifying the patients according to the disease severity based on physiological variables. To calculate the score, 0 - 4 values were assigned to all the physiological and laboratory values with 0 being normal and 4 being the most abnormal. The age and chronic health problems were also included in this score as they reflect the physiological status.

Collection from large number of variables made the true APACHE score more difficult. Any unmeasured variable was assumed to be normal and weighted as zero as per the rules of APACHE system. The variables were chosen by a group of physicians and this created a potential of bias.

These inaccuracies in the original APACHE system prevented its widespread use. Despite several inaccuracies this system serve as the prototype for the development of two subsequent systems.

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

- Acute Physiological Score (0 to 60 points)
- Age (0 to 6 points)
- Chronic health (0 to 5 points).

The system evaluates the patient at 24 hours and in 48 hours. The performance of APACHE scoring system remains the same during hospitalization and also at 24 hours. Range of potential score is 0 to 71 but scores more than 40 are uncommon. Scores above 30 are associated with 70% mortality rate.

This scoring system is well suited for stratification of patients and comparisons of treatment methods. Depending upon the etiology of the disease and intensive care set up, the results may vary. APACHE II score of 8 or more indicates severe attack as proposed by the Atlanta classification

ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION									
Acute physiology score	High abnormal range					Low abnormal range			
Physiological variables	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature(*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(mmHg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart rate	>180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory rate	>50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation	≥ 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 bicarbonate-only if no ABGs	≥52	41.5-41.9		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		
Hematocrit (%)	≥60		50-50.9	46-49.9	30-45.9		20-29.9		<20
White blood cell count(X1000/mm3)	≥40		20-39.9	15-19.9	30-14.9		1-2.9		<1
Glasgow coma scale	Score = 15 minus actual GCS								

AGE IN YEARS	POINTS
≥44	0
45-54	2
55-64	3
65-74	5
≥75	6

Chronic health points score	POINTS FOR ELECTIVE SURGERY	POINTS FOR EMERGENCY AND NON OPERATIVE PATIENTS
LIVER: Biopsy proven cirrhosis and documented portal hypertension or prior episodes of hepatic failure	2	5
Cardiovascular: NHYA class IV	2	5
Respiratory eg: severe COPD, hypercapnia, pulmonary hypertension	2	5
Renal: Chronic dialysis	2	5
Immunocompromised	2	5

APACHE II SCORE: SUM OF A+B+C

Advantages:

- Quick and Easy to calculate
- Recalculation is possible at any time throughout the disease for monitoring
- APACHE II score allows objective determination of acute pancreatitis within few hours of admission which aids in detection of cases for intensive care management.
- The score can be used universally for all critical illnesses, thereby it avoids the need for a separate grading system for acute pancreatitis.
- Utilizes routine laboratory tests available 24 hours a day. Ability to be recalculated daily. Continuous Sequential monitoring of APACHE II score helps to determine the improvement or deterioration in the physiologic status of patient.
- The score increases significantly in those with severe disease (median increase three points) but decrease in patients with mild pancreatitis (median decrease one point) over the initial 48hours.Thus this might be helpful for follow up of the disease course and also in assessing the therapeutic response.

Drawbacks:

- Complexity and poor feasibility
- The ideal ‘cut-off’ score remains to be determined
- The cut-off scores with greatest prognostic values on admission were different from the peak scores during the hospital stay as shown by Wilson et al.Hence the use of a single cut-off score APACHE II ≥ 9 needs to be validated in more studies.
- Delay in disease presentation or the type of resuscitation treatment may influence the score
- Underestimates mortality in many critically ill surgical patients because the pre-ICU resuscitation measures were not taken into account and young patients score may have few points despite severe pancreatitis.
- Mortality predictions of APACHE II were based on treatment that lasts 20 years before.

APACHE III:

A revised form of APACHE-II known as the APACHE-III prognostic system was presented by Knaus et al, in 1991.The variables in APACHE III score includes blood urea, urine output, serum albumin, serum bilirubin, blood glucose, pCO_2.

When used serially and sequentially in acute pancreatitis. APACHE III can be regarded as a good prognostic scoring system. APACHE III score shows differences in mild and severe AP and the scores correlates significantly with severity.

APACHE provides an objective indication of progress in the individual patient and also proves to be an effective tool for serial monitoring of patients. APACHE III score more than 30 indicates higher morbidity and mortality rate according to Williams et al.

Drawbacks:

- Expensive
- Not feasible for financially constrained ICUs
- Data collection was complex when compared to APACHE II
- Inaccurate in predicting the risk in post-op cases

BISAP (The bedside index for severity in AP):

Newer scoring system which has been developed recently for early detection of patients with higher risk of in hospital mortality. The BISAP score was developed and validated retrospectively on a large population based study. This work was done by Cardinal Health Clinical Outcomes Research Database, Marlborough, United states and recently published for clinical and research purpose because of its accuracy and high reliability in patient stratification.

The BISAP includes

Blood urea nitrogen (BUN)	>25 mg / dl
Impaired mental status	GCS < 15
SIRS (Systemic Inflammatory Response Syndrome)	presence of 2 or more of the following criteria: Pulse rate: more than 90/min. Respiratory rate : > 20/min or $PaCO_2$ < 32 mm Hg. Temperature : < 36 or > 38 ° C/ >100.4 F or < 96.8 F.

	WBC count : >12,000 or < 4,000 cells/mm3, or presence of more than 10% immature blasts.
Age	>60 years
Pleural effusion	Can be determined by chest Radiograph, CT scan or abdominal ultrasound obtained within 24 hours of presentation

For each variable present one point will be given and the total score ranges from 0 to 5.

A BISAP score of $\geq$3 is associated with high mortality and have predicted the necrosis and organ failure also.

ADVANTAGES:

1. Simple and much easier to calculate
2. It is done at the time of admission or within 24 hours of hospitalisation
3. Prediction ability of the scores was tested among large number of populations across 390 hospitals in contrast to other scoring systems which were based on small number of population
4. Helps in predicting in-hospital mortality.

DISADVANTAGES:

1. For evaluating mental status, Glasgow Coma Scale was used which may be subjected to interobserver variation.

2. Not able to discriminate transient from persistent organ failure within 24 hours of hospitalisation.

3. Not able to predict the preventable complications of acute pancreatitis like other scoring system

ASSESSMENT OF SEVERITY:

Acute pancreatitis has a challenging clinical course in the early prediction of severity and prognosis. 15-25% of acute pancreatitis cases are found to be severe. Severity of the disease can be assessed in the following ways

APPROACH:

Severity can be assessed from patient's history, symptoms and signs, laboratory findings, characteristic radiological imaging findings. Serum amylase was the only investigation used for severity analysis during the early periods. An attempt to use the objective criterias for assessing the severity of acute pancreatitis was provided by John Ranson in 1970.

During the early phase of 1980, intra operative severity assessment was done only after seeing the amount of necrosis and the presence of infective

signs in necrotic tissues. Introduction of Computerized Tomography(CT) has made the severity assessment of acute pancreatitis to an uncomplicated one.

FACTORS DETERMINING THE SEVERITY OF PANCREATITIS:

The severity of acute pancreatitis varies significantly for patients. Some patients may have mild form of the disease that is self-limiting, while some patients exhibit more severe form of disease. The factors which are helpful in determining the severity of acute pancreatitis are multifactorial, but their identification is of utmost therapeutic importance, because their manipulation can decrease the morbidity and mortality associated with the acute pancreatitis. The pancreatic acinar cells are also acts as a source of inflammatory mediators during episodes of pancreatitis.

The factors associated with acute pancreatitis and associated lung injury include:

- Platelet activating factor
- Tumor necrosis factor alpha(TNF-α)
- Monocyte chemotactic protein-1(MCP-1)
- Interleukin-1β (IL1β),
- Substance P
- Interleukin-6, 8, 10

- Adhesion molecules [intercellular adhesion molecule-1 (ICAM-1) and selectins]
- CCR1 receptor and its ligands
- Macrophage migration inhibitory factor
- Granulocyte-macrophage colony-stimulating factor(GMCSF),
- Prostaglandin E1
- COX-2
- Nitric oxide (NO)
- Reactive oxygen species

Heat shock proteins(HSP) are found to be protective in pancreatitis. The balance between the pro-inflammatory and anti-inflammatory factors determines the severity of pancreatitis associated with lung injury.

Recent studies shows that Toll-like receptor 4 (TLR4) is a major significant factor in determining the severity of acute pancreatitis. Upon interaction with lipopolysaccharides, the TLR4 initiates a complex signaling pathway which results in a proinflammatory response.

Mice with genetically deleted TLR4 gene have significantly reduced pancreatitis. This suggests that TLR4 is a promoter of proinflammation and TLR4 antagonists would likely be employed as a good therapy against pancreatitis.

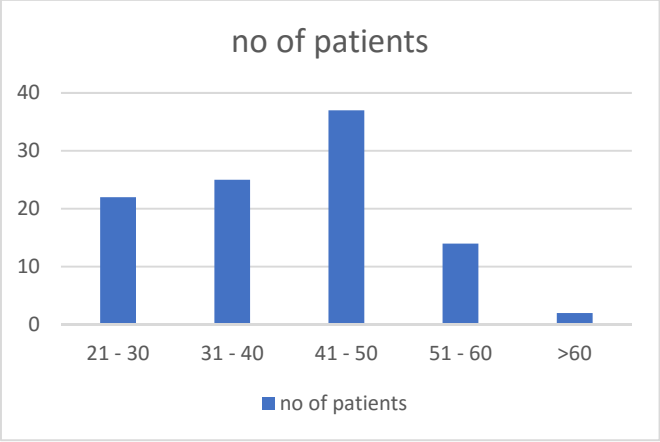
The two major events which occurs early in pancreatitis includes intrapancreatic trypsinogen and NF-κB activation. Approaches to inhibit these events may result in reducing the severity of pancreatitis.

OBSERVATION & RESULTS

This study was conducted in the department of general surgery, Govt. Chengalpattu Medical College & Hospital, Chengalpattu 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.

Age wise distribution

Age range (yrs)	**No. of patients**	**Percentage**
21 – 30	22	22
31 – 40	25	25
41 – 50	37	37
51 – 60	14	14
>60	2	2

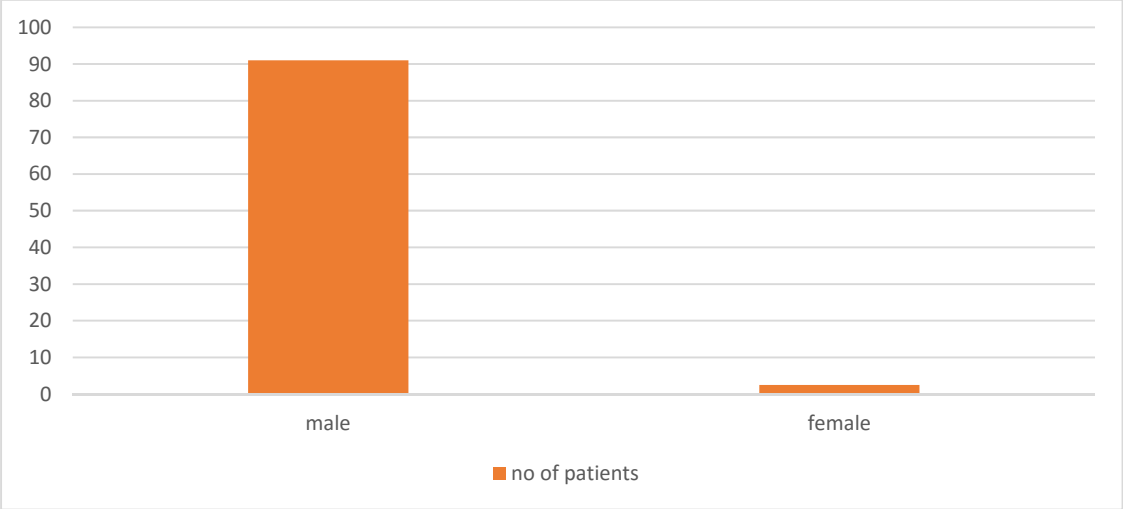


The age group of patients enrolled in this study ranges from 20 to 80 yrs.

The peak incidence of the disease was noted in the 4th decade of life.

Gender distribution

Sex	No. of patients	Percentage
Male	91	91
Female	9	9



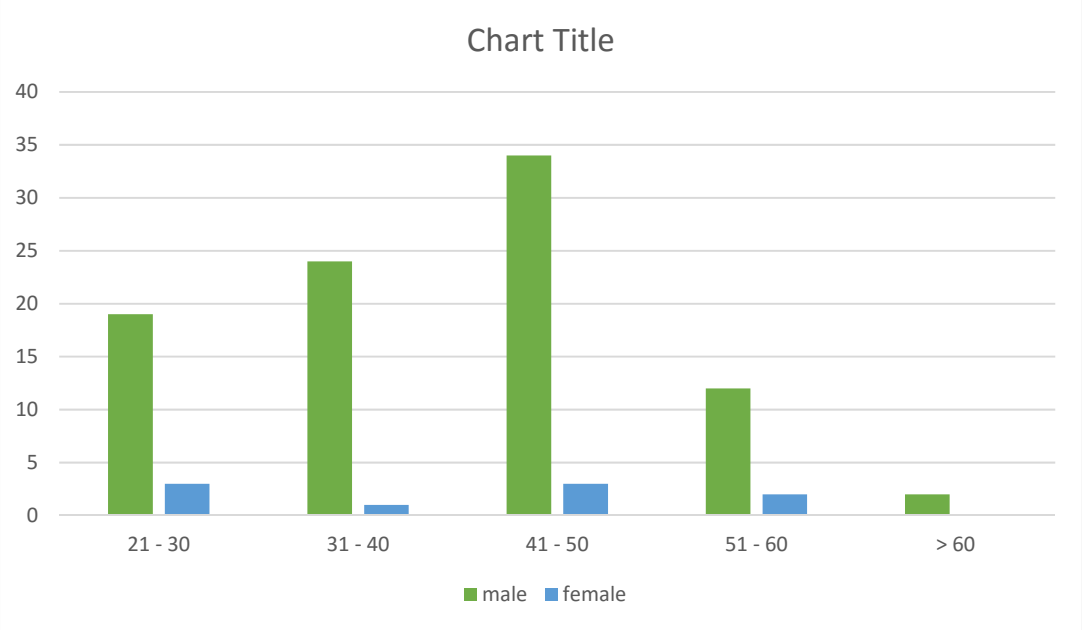
Out of 100 patients enrolled in this study there were 91 males and 9 female

patients.

Male: Female ratio-10.1:1

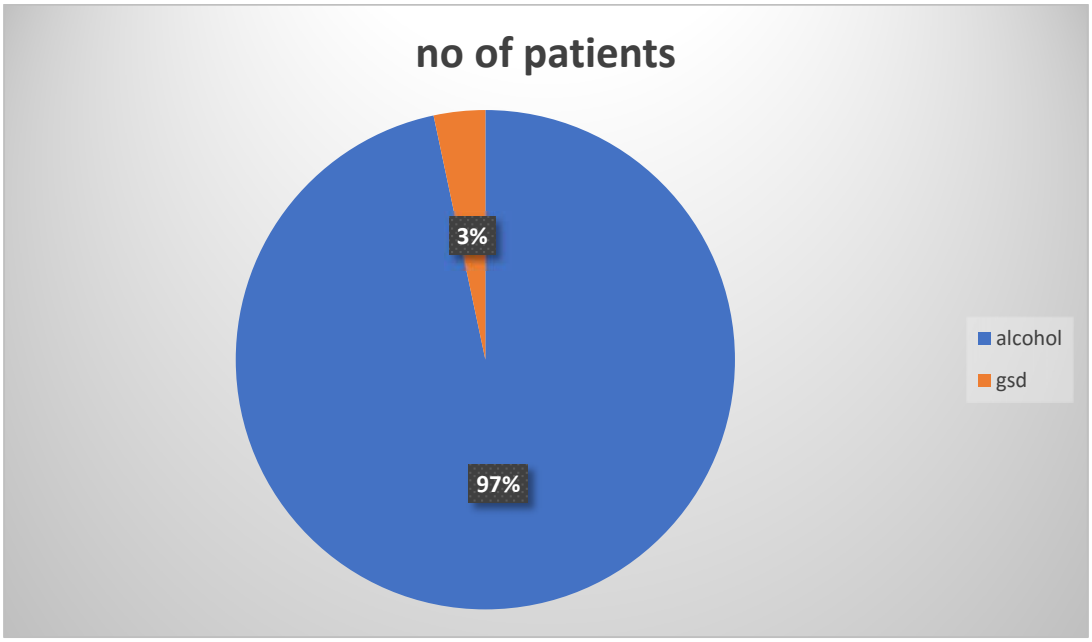
AGE GENDER WISE DISTRIBUTION

Age (yrs)	Male		Female		Total	
	N	%	N	%	N	%
21 -30	19	20.9	3	33.3	22	22
31 – 40	24	26.4	1	11.1	25	25
41 – 50	34	37.4	3	33.3	37	37
51 – 60	12	13.2	2	22.2	14	14
>60	2	2.2	0	0	2	2
Total	91	100	9	100	100	100



AETIOLOGY

Aetiology	No of patients
Alcohol	97
Gall stone disease	3



Of the 100 patients studied 97 % were found to have alcohol as an aetiology and 3 % had gall stone disease as aetiology.

SEVERITY OF PANCREATITIS

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

SAP – severe acute pancreatitis, Patients with BISAP ≥ 3 , APACHE > 9 were considered in severe acute pancreatits .

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.

Scoring system	No. of patients	Organ failure	Pancreatic necrosis	Mortality
BISAP < 2	86	3	2	0
>2	14	10	9	4
APACHE II < 9	58	1	1	2
> 9	42	13	10	2

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.

Grading of patients with MAP with organ failure, necrosis and mortality.

	BISAP ≥ 3	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.

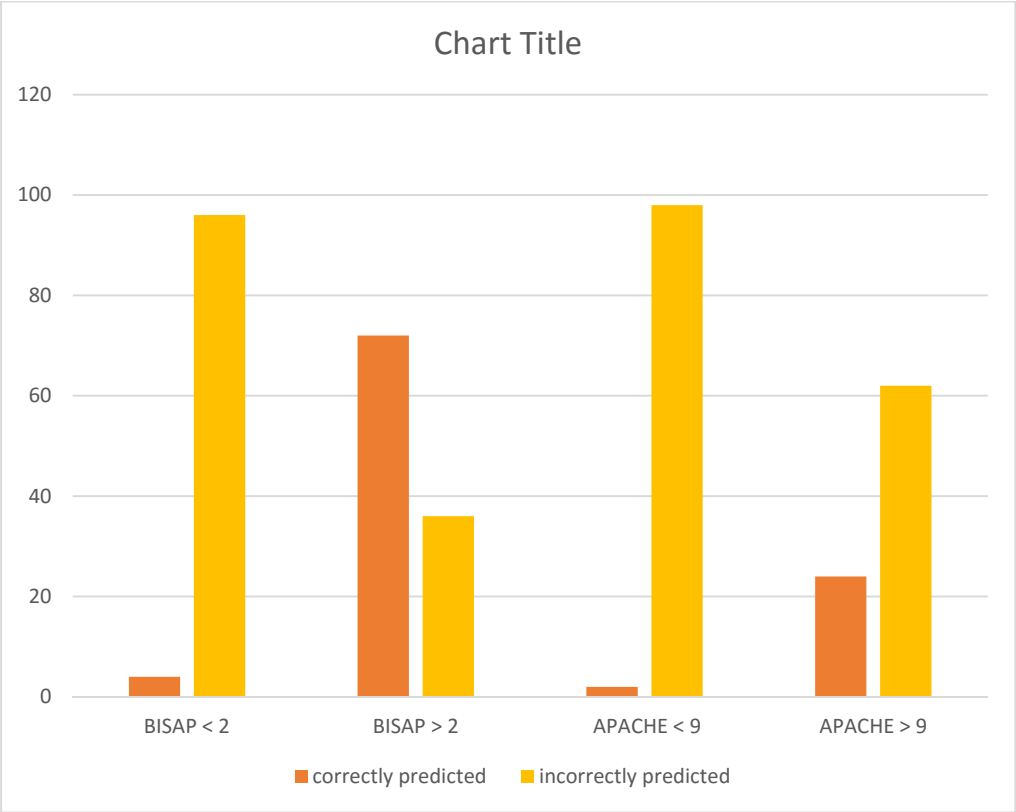
Of 58 patients presented with APACHE II score <9, 1 patient developed organ failure and 1 patient developed pancreatic necrosis. There were 2 mortalities in this group.

Thus, using Chi^2 test, 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.

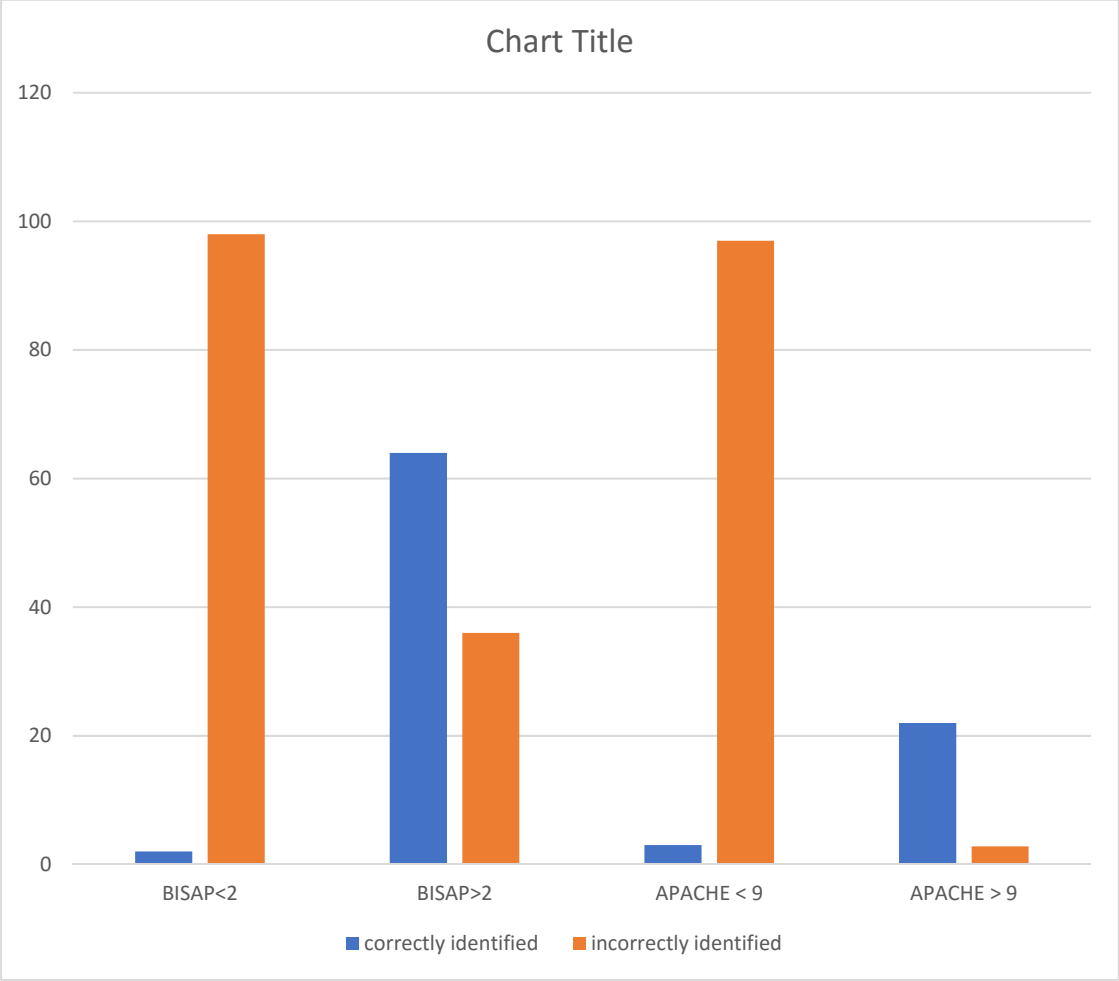
Grading of patients with SAP with organ failure, necrosis and mortality.

	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

Comparing BISAP and APACHE II in predicting organ failure.

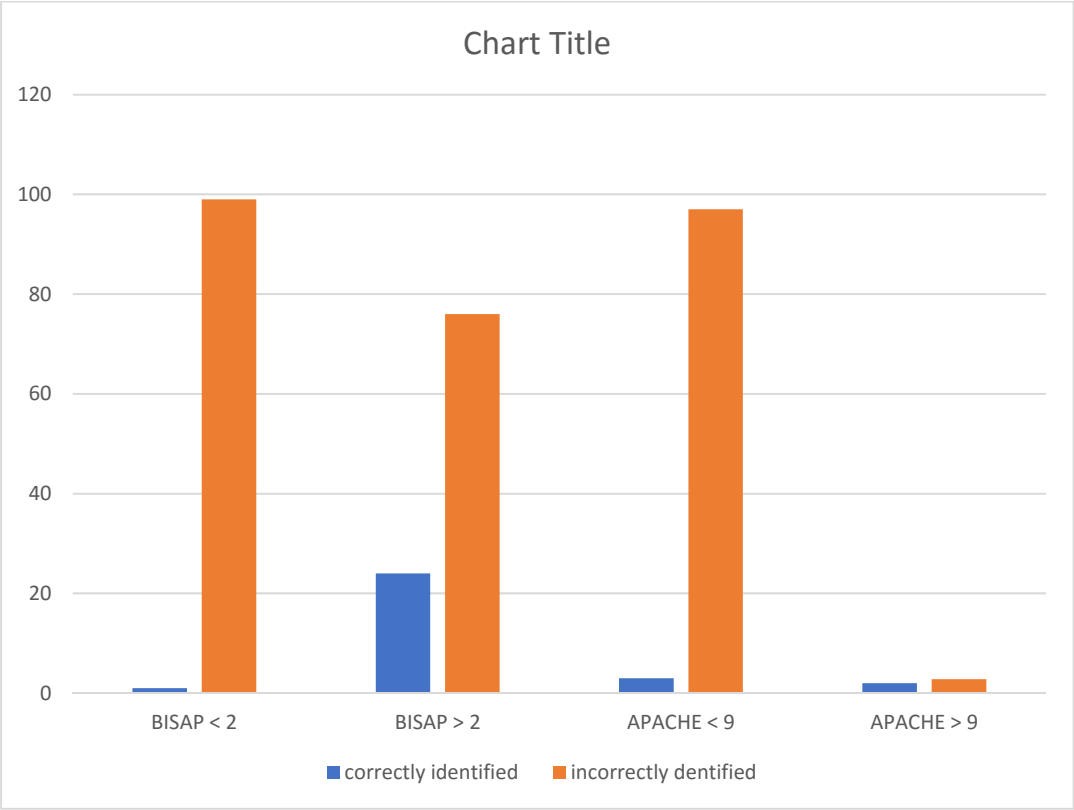


Here, 10 out of 14 patients with BISAP >3 and 13 out of 42 patients with APACHE II >9, developed organ failure. Thus using Chi2 test, the occurrence of organ failure correlates well with outcome with a p value <0.018. Comparing BISAP and APACHE II in predicting pancreatic necrosis.



Here, 9 out of 14 patients with BISAP ≥ 3 and 10 out of 42 patients with APACHE II >9, developed pancreatic necrosis. Thus, using Chi2 test, development of necrosis correlates well with outcome with p value <0.0145.

Comparing BISAP and APACHE II in predicting mortality.



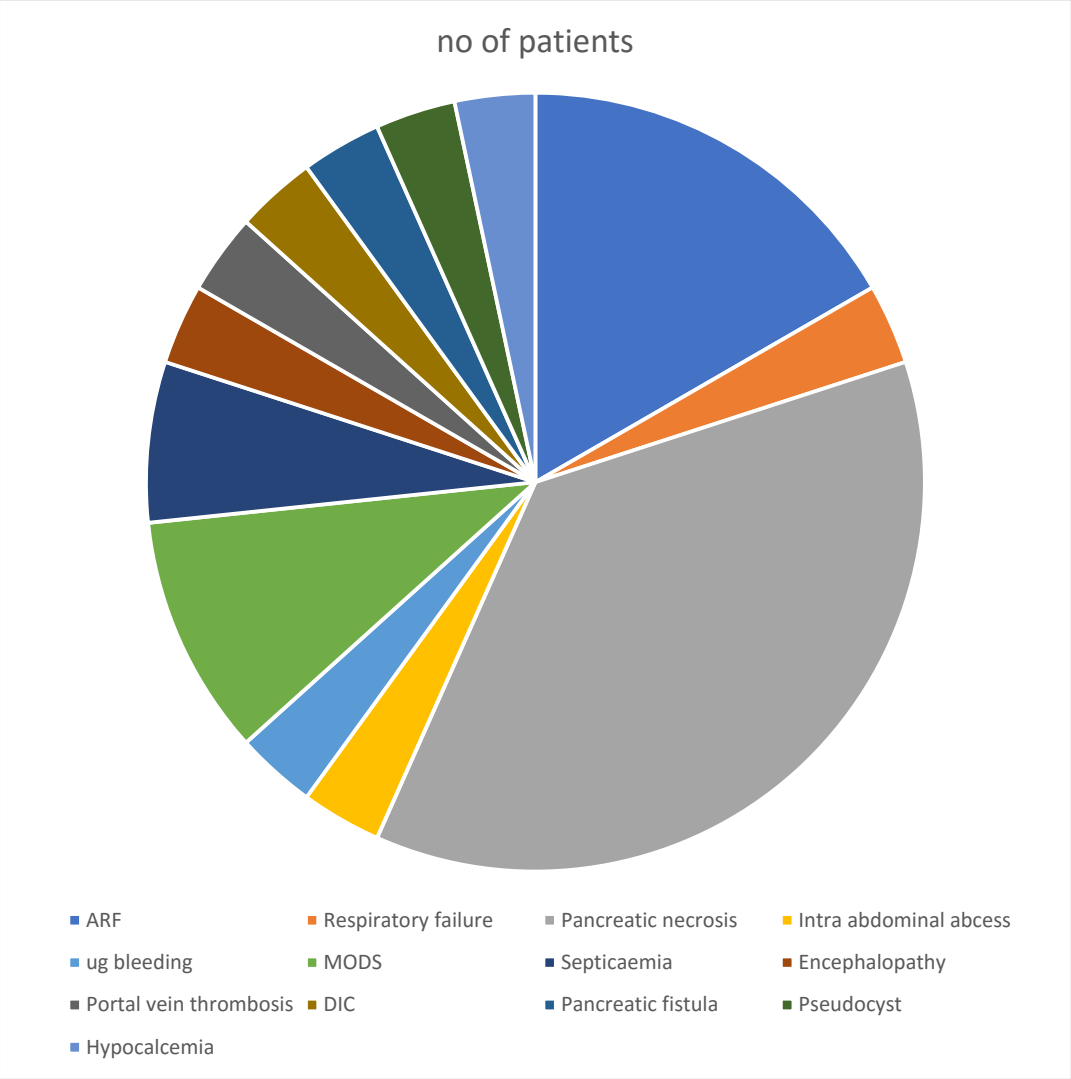
There were 4 deaths in severe acute pancreatitis group. Of them, 2 had BISAP score of 4 & APACHE II score of 8 and the other 2 had BISAP score of 5 & APACHE II score of >20 respectively. Thus, using Chi2 test, the disease severity correlates well with mortality with p value <0.046.

Comparing incidence of complications in acute pancreatitis.

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
Septicaemia	2	14.2
Encephalopathy	1	7.14
Portal vein thrombosis	1	7.14
DIC	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.



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 al38 (6:1), Papachristou et al1 (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.

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 (93%)

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.

Thus by using Chi2 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 al38 and B U Wu et al.In this study, 9/14 with BISAP > 3 and 10/42 with APACHE II > 9 developed pancreatic necrosis. Thus by using Chi2 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. 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. Thus by using Chi2 test, BISAP ≥ 3 was found to be significantly associated ($p < 0.04$) with high mortality than APACHE II score.

This again matches well with previous study by Vikesh k. Singh et al38 and Papachristou et al. 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, UGI bleed, etc.

These complications were more likely seen in patients with BISAP ≥ 3 and APACHE ≥ 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. However, in our study other aetiologies of pancreatitis have not been considered and intervention have not been study, still large scale studies are pending to arrive at a final outcome of which scoring system is better.

CONCLUSION AND SUMMARY

- From this study, Alcohol (97%) 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 4th 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 can arrive a presumptive conclusion that the BISAP score could be a simple and accurate clinical scoring system for the evaluation of disease severity in acute pancreatitis. However further large scale studies are needed to confirm this.

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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

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 _____

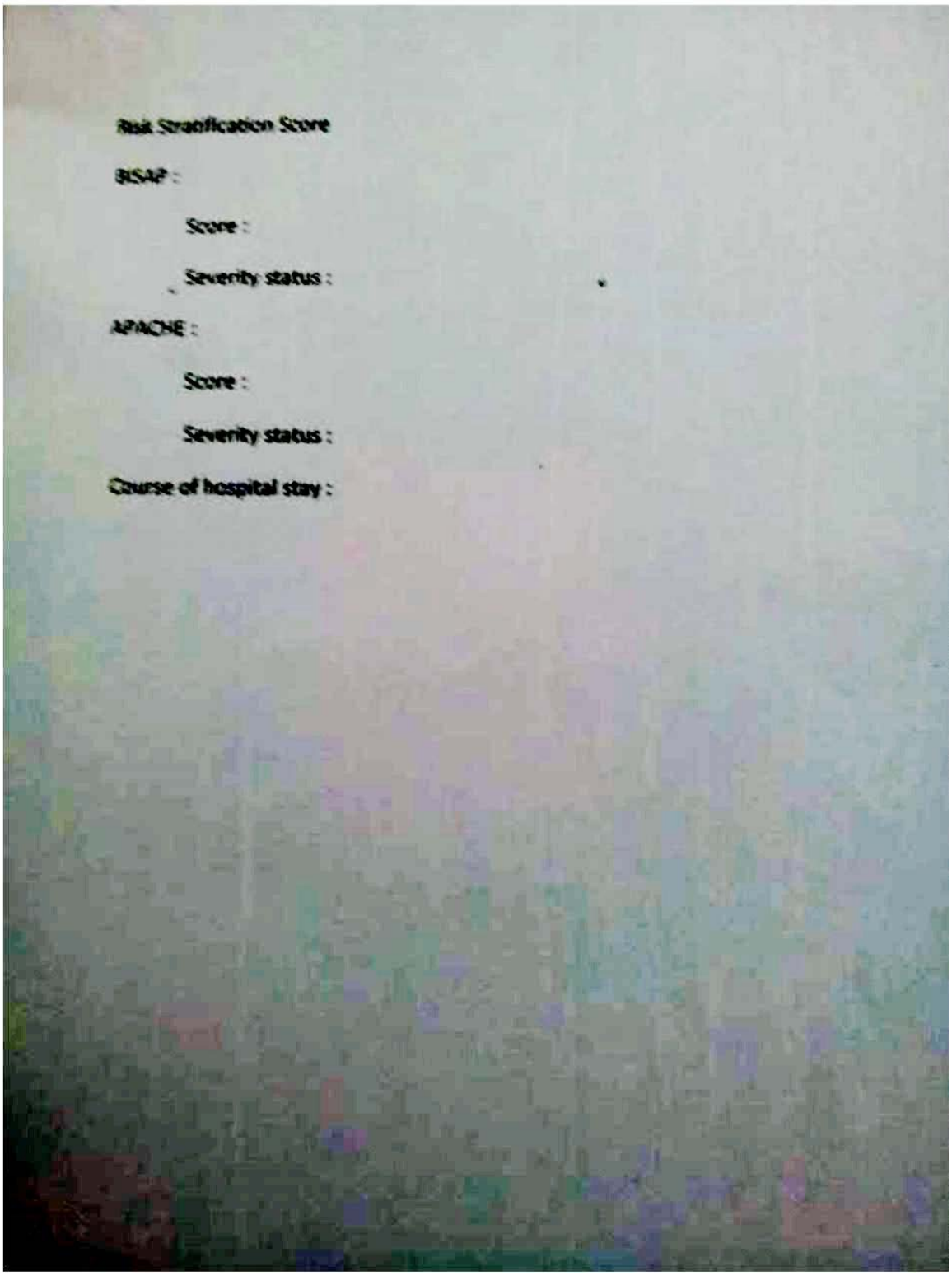
   (3) Pulse > 90 beats/min _____

   (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
RSAP :
Score :
Severity status :
APACHE :
Score :
Severity status :
Course of hospital stay :

S.NO	NAME	IP. NO	AGE	SEX	AGE	TEMP	HR	RR	OXY	MAP	NA+	K+	HCO3-	S.Cr	PCV	WBC	GCS	Chronic	APACHE	BUN	GCS	SIRS	AGE	PE	BISAP	OUTCOME	ETIOLOGY	LOS
1	SURESH	53231	45	M	2	1	0	0	1	0	2	0	2	2	2	0	3	0	15	0	1	1	0	0	2	ALIVE	ALCOHOL	18
2	KRISHNAN	56038	41	M	0	0	0	0	0	0	0	0	0	1	0	0	3	0	4	0	1	1	0	0	2	ALIVE	ALCOHOL	12
3	KUMAR	55878	55	M	3	0	0	1	0	0	1	0	2	3	1	0	2	0	13	0	1	1	0	0	2	ALIVE	ALCOHOL	17
4	RAJENDRAN	59052	40	M	0	0	2	3	1	2	2	0	4	3	3	0	2	0	22	0	1	1	0	1	4	ALIVE	ALCOHOL	28
5	SIVAKUMAR	64597	28	M	0	0	0	0	0	0	2	2	2	0	0	0	2	0	8	1	0	1	0	0	2	ALIVE	ALCOHOL	13
6	VADIVEL	67410	32	M	0	0	0	0	0	0	3	0	0	0	0	0	2	0	5	0	1	1	0	0	2	DEATH	ALCOHOL	19
7	KUMARAN	67386	47	M	0	2	2	3	1	3	2	2	3	3	1	0	4	5	31	1	1	1	0	1	4	ALIVE	ALCOHOL	3
8	RAVI	68556	50	M	2	0	0	0	0	3	2	1	0	0	0	0	2	0	10	0	1	1	0	0	2	ALIVE	ALCOHOL	22
9	BALAKRISHNAN	67304	26	M	0	0	3	1	0	0	0	1	2	1	0	0	3	0	11	0	1	1	0	0	2	ALIVE	ALCOHOL	16
10	RAMESH	4063	48	M	2	1	0	1	0	2	0	1	0	0	0	0	1	0	8	1	1	1	0	0	3	ALIVE	ALCOHOL	13
11	ANBALAGAN	12387	26	M	0	0	0	1	0	0	0	2	2	2	0	0	2	0	9	0	1	1	0	0	2	ALIVE	ALCOHOL	17
12	LOGANATHAN	13514	33	M	0	0	0	0	1	0	1	2	2	1	4	0	2	0	13	0	1	1	0	0	2	ALIVE	ALCOHOL	12
13	VENKATESAN	23347	32	M	0	0	0	0	0	0	2	0	2	0	0	0	2	0	6	0	0	1	0	0	1	ALIVE	ALCOHOL	7
14	KALIYAPPAN	24790	33	M	0	3	0	0	0	2	3	1	2	0	0	0	0	0	11	0	1	1	0	0	2	ALIVE	ALCOHOL	8
15	KUMARESAN	32319	32	M	0	0	0	0	0	0	2	0	0	0	0	0	0	0	2	0	0	1	0	0	1	ALIVE	ALCOHOL	6
16	VIMAL RAJ	32225	21	M	0	0	0	1	0	0	0	1	0	0	0	0	0	0	2	0	0	1	0	0	1	ALIVE	ALCOHOL	7
17	SURESH	34310	46	M	2	0	0	0	0	0	0	1	0	0	0	0	1	0	4	0	1	1	0	0	2	ALIVE	ALCOHOL	7
18	MARI	35358	33	M	0	0	2	0	0	0	0	2	2	0	0	0	2	0	10	1	0	1	0	0	2	ALIVE	ALCOHOL	16
19	PANEERSELVAM	34455	48	M	2	0	0	0	0	0	2	0	1	0	0	0	0	0	5	0	1	0	0	0	1	ALIVE	ALCOHOL	6
20	KUMAR	29450	35	M	0	1	0	0	0	0	0	0	2	1	0	0	0	0	4	0	0	1	0	1	2	ALIVE	ALCOHOL	9
21	MUTHU	37386	55	M	3	0	0	1	0	3	0	0	0	2	1	0	0	0	10	0	0	1	0	0	1	ALIVE	ALCOHOL	9
22	KRISHNAN	39214	35	M	0	0	0	0	0	0	3	1	0	0	0	0	0	0	4	1	0	1	0	0	2	ALIVE	ALCOHOL	9
23	RAJAN	39206	57	M	3	0	0	0	0	2	2	0	0	0	0	0	0	0	7	0	1	1	0	0	2	ALIVE	ALCOHOL	8
24	ANBUVALLI	39216	45	F	0	0	0	0	0	0	0	2	2	0	0	0	1	0	5	0	1	0	0	0	1	ALIVE	ALCOHOL	6
25	SELVAM	42570	23	M	0	0	0	1	0	2	0	2	2	0	0	0	2	0	9	0	1	1	0	0	2	ALIVE	ALCOHOL	7
26	MAGESH	37469	50	M	2	0	0	0	0	0	1	1	2	0	0	0	0	0	6	0	1	1	0	0	2	ALIVE	ALCOHOL	5
27	ARUMUGAM	37419	58	M	3	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	1	0	0	1	ALIVE	ALCOHOL	4
28	RAMASAMY	49947	43	M	0	1	0	1	2	2	0	1	2	0	0	2	2	0	13	0	1	1	0	1	3	ALIVE	ALCOHOL	18
29	RAMESH	50684	25	M	0	1	0	1	2	2	2	1	2	0	0	0	0	0	11	0	1	1	0	0	2	ALIVE	ALCOHOL	8
30	DAS	38345	60	M	3	0	0	0	0	0	0	0	0	0	0	0	2	5	10	0	1	1	0	0	2	ALIVE	ALCOHOL	10
31	RAJESWARI	42262	24	F	0	1	0	1	0	0	0	0	0	0	0	0	1	0	3	0	0	1	0	0	1	ALIVE	ALCOHOL	6
32	CLINTON	40667	39	M	0	0	0	1	0	0	1	1	0	2	0	0	1	0	6	0	1	1	0	0	2	ALIVE	ALCOHOL	7
33	SEENU	42845	30	M	0	0	0	0	0	0	1	1	0	0	0	0	1	0	3	0	1	0	0	0	1	ALIVE	ALCOHOL	6
34	SURESH	42942	37	M	0	0	0	0	2	0	1	0	0	0	0	0	1	0	4	0	1	0	0	0	1	ALIVE	ALCOHOL	6
35	SYED	42947	33	M	0	0	0	1	0	0	0	0	0	0	2	0	1	0	4	0	1	1	0	0	2	ALIVE	ALCOHOL	8
36	IBRAHIM	42954	48	M	0	0	0	0	0	0	0	0	2	2	0	0	1	0	5	0	1	1	0	0	2	ALIVE	ALCOHOL	5
37	MUTHURANI	34781	49	F	2	0	2	1	2	2	0	1	0	2	2	2	2	5	23	1	1	1	0	1	4	ALIVE	ALCOHOL	19
38	KATHIR	34520	43	M	2	0	0	0	0	0	2	0	2	0	0	0	0	0	6	0	1	1	0	0	2	ALIVE	ALCOHOL	9
39	ELUMALAI	33291	40	M	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	1	2	ALIVE	ALCOHOL	9
40	RAJI	33413	40	M	0	0	2	1	0	0	0	0	2	0	0	0	1	0	6	0	1	1	0	0	2	ALIVE	ALCOHOL	9
41	GEETHA	30611	42	F	0	0	0	1	0	0	0	0	2	0	0	1	2	0	6	0	1	1	0	0	2	ALIVE	IDIOPATHI	19
42	RAMAN	33444	27	M	0	1	2	3	2	2	2	1	2	2	2	0	2	5	26	1	1	1	0	1	4	ALIVE	ALCOHOL	22
43	JAYARAJ	32075	56	M	3	1	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	1	1	ALIVE	ALCOHOL	6
44	PAZHANI	32520	33	M	0	0	2	1	0	0	0	0	2	2	1	0	1	0	9	0	1	1	0	0	2	ALIVE	ALCOHOL	11
45	BASKARAN	28928	47	M	2	0	2	1	0	0	0	0	2	0	0	0	1	0	8	0	0	1	0	0	1	ALIVE	ALCOHOL	7
46	DINAKARAN	30619	21	M	0	0	2	1	2	2	0	0	1	0	0	0	0	0	8	1	0	0	0	0	1	ALIVE	ALCOHOL	8
47	BOOSHAN	28937	26	M	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	1	0	0	0	2	ALIVE	ALCOHOL	12
48	IYAPPAN	29188	33	M	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	ALIVE	ALCOHOL	10
49	VASAN	29136	28	M	0	1	2	1	0	0	0	0	2	0	2	0	0	0	8	0	0	1	0	1	2	ALIVE	ALCOHOL	10
50	PREM	26628	26	M	0	0	2	1	0	0	0	0	2	0	0	0	0	0	5	1	0	1	0	0	2	ALIVE	ALCOHOL	14

51	RINCENT	26849	60	M	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	ALIVE	ALCOHOL	4
52	RANJINI	26682	60	F	3	0	1	1	0	0	0	0	0	0	0	0	1	5	14	0	0	1	0	1	2	ALIVE	IDIOPATHI	28
53	KUMAR	25379	45	M	2	0	0	1	0	0	0	0	0	0	0	0	0	0	4	0	0	1	0	0	1	ALIVE	ALCOHOL	6
54	BABURAJ	25328	30	M	0	1	0	1	0	0	0	0	2	2	2	1	1	0	7	0	1	0	0	0	1	ALIVE	ALCOHOL	8
55	VIJAYAKUMAR	24611	33	M	0	0	2	1	0	0	0	0	2	2	0	0	1	0	9	0	1	1	0	0	2	ALIVE	ALCOHOL	12
56	MOORTHY	24700	48	M	2	1	2	1	0	0	0	0	2	2	0	0	1	0	11	1	1	1	0	0	3	ALIVE	ALCOHOL	19
57	SELVAN	22840	30	M	0	1	2	1	0	1	0	0	0	1	0	0	2	0	8	0	1	1	0	0	2	DEATH	ALCOHOL	15
58	SUKUMAR	22619	56	M	0	0	2	1	0	0	0	0	2	0	0	1	1	0	8	1	1	1	0	1	4	ALIVE	ALCOHOL	1
59	LAKSHMI	40173	27	F	0	0	2	1	0	0	0	0	0	2	0	0	0	0	3	0	0	1	0	0	1	ALIVE	ALCOHOL	6
60	RAJU	22757	50	M	2	0	1	0	0	0	0	0	2	0	0	0	2	5	16	0	1	1	0	0	2	ALIVE	ALCOHOL	21
61	ANAND	21681	37	M	0	0	2	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0	0	0	0	ALIVE	ALCOHOL	5
62	LINGAM	21240	45	M	2	0	0	0	0	0	0	1	0	2	0	0	0	0	3	0	0	0	0	1	1	DEATH	ALCOHOL	7
63	JAGAN	49951	80	M	6	0	0	1	0	2	2	1	2	0	1	1	4	5	28	1	1	1	1	1	5	ALIVE	ALCOHOL	1
64	VASU	7827	47	M	2	0	2	1	0	0	0	0	2	0	0	0	0	0	7	0	0	1	0	0	1	ALIVE	ALCOHOL	8
65	MUNUSAMY	34601	60	M	3	0	0	1	0	0	2	1	0	3	0	0	0	5	15	0	1	0	1	0	2	ALIVE	ALCOHOL	19
66	SHANMUGAM	35947	46	M	2	0	2	1	0	0	2	2	2	0	0	0	2	5	18	0	1	1	0	0	2	ALIVE	ALCOHOL	24
67	UDHAY	34982	33	M	0	1	2	1	0	0	0	0	0	0	0	1	0	5	6	0	0	0	0	1	1	ALIVE	ALCOHOL	10
68	KUNDHAVI	17445	37	F	0	0	1	1	0	0	0	0	2	2	0	1	2	0	9	1	1	1	0	0	3	ALIVE	GSD	23
69	KUMAR	17447	23	M	0	1	2	1	0	2	0	0	2	1	0	1	2	0	12	1	1	0	0	0	2	DEATH	ALCOHOL	11
70	SUNDARAM	28542	57	M	2	1	2	1	0	0	0	1	0	0	0	0	1	0	8	1	1	1	0	1	4	ALIVE	ALCOHOL	2
71	NANDAN	45342	55	M	3	1	2	1	0	2	0	0	2	0	0	1	3	0	15	0	1	1	0	1	3	ALIVE	ALCOHOL	32
72	VASANTHAN	45186	22	M	0	1	2	1	0	2	0	1	2	0	0	0	0	0	9	0	0	1	0	0	1	ALIVE	ALCOHOL	7
73	VEERAN	38112	43	M	0	1	0	0	0	0	0	0	2	0	2	0	0	0	5	0	0	0	0	0	0	ALIVE	ALCOHOL	6
73	VALLI	43336	50	F	2	0	1	1	0	0	0	1	2	2	0	0	0	0	9	0	0	1	0	1	2	ALIVE	GSD	8
75	LOGANATHAN	45411	52	M	2	1	2	1	0	2	0	1	2	0	0	1	1	0	13	0	1	1	0	0	2	ALIVE	ALCOHOL	21
76	RAGAVAN	2461	37	M	0	1	1	1	0	0	0	0	0	0	0	1	5	0	9	0	1	0	0	1	1	ALIVE	ALCOHOL	9
77	SENGUTUVAN	3382	45	M	2	0	1	1	0	0	0	0	2	2	0	0	0	0	8	0	1	0	0	1	2	ALIVE	ALCOHOL	29
78	KRISHNAN	33501	45	M	2	0	2	1	0	0	0	1	2	2	2	0	2	5	19	0	1	1	0	0	2	ALIVE	ALCOHOL	26
79	ANANDAN	51474	47	M	2	0	0	0	0	0	0	0	0	2	0	0	0	0	4	1	0	0	0	0	1	ALIVE	ALCOHOL	6
80	PILLAAYSAMY	26918	49	M	2	0	2	1	0	0	0	1	2	0	0	1	2	0	11	0	1	1	0	0	2	ALIVE	ALCOHOL	20
81	ARIVU	24123	46	M	2	0	2	1	0	0	0	0	0	0	0	0	0	0	5	0	0	1	0	0	1	ALIVE	ALCOHOL	6
82	SURESH	64734	24	M	0	1	2	1	0	0	0	1	2	0	0	2	0	0	9	0	0	1	0	0	1	ALIVE	ALCOHOL	9
83	NAGESH	241232	25	M	0	0	0	0	0	0	0	0	0	2	2	1	0	0	5	1	0	1	0	0	2	ALIVE	ALCOHOL	11
84	ARUNKUMAR	31829	45	M	2	0	2	1	0	0	0	0	2	0	0	0	1	0	8	0	1	1	0	0	2	ALIVE	ALCOHOL	12
85	BAKKIYAM	28043	27	M	0	0	0	1	0	0	0	0	2	0	0	0	0	0	3	0	0	1	0	0	1	ALIVE	ALCOHOL	7
86	HAMEED	28086	72	M	5	1	0	0	0	0	0	0	2	0	0	0	0	5	13	1	1	0	0	0	2	ALIVE	ALCOHOL	18
87	ABDUL	29630	45	M	2	0	0	1	1	0	0	0	2	0	0	0	0	0	6	0	0	0	0	0	0	ALIVE	ALCOHOL	6
88	SIVARAM	30475	50	M	2	0	2	1	0	0	0	1	0	0	0	0	0	0	6	1	0	1	0	0	2	ALIVE	ALCOHOL	9
89	NASER	29624	45	M	2	0	0	0	0	0	0	0	2	0	0	0	0	0	4	0	0	0	0	0	0	ALIVE	ALCOHOL	7
90	GNANI	34711	45	M	2	0	2	1	0	0	0	0	0	0	0	0	0	0	5	0	0	1	0	0	1	ALIVE	ALCOHOL	6
91	RANGAN	35579	40	M	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	ALIVE	ALCOHOL	8
92	MURUGAMAL	36497	30	F	0	1	0	1	0	0	0	0	2	0	0	0	1	5	12	0	1	1	0	0	2	ALIVE	GSD	19
93	PALANI	36509	37	M	0	0	1	1	0	0	0	0	0	2	2	1	0	0	7	0	0	1	0	0	1	ALIVE	ALCOHOL	9
94	DILLIBABU	35639	60	M	3	1	2	1	0	0	0	1	2	0	0	1	2	5	18	1	1	1	0	1	4	ALIVE	ALCOHOL	26
95	BASHA	35685	45	M	2	1	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	1	0	0	1	ALIVE	ALCOHOL	9
96	EGAMBARAM	38623	32	M	2	0	2	0	0	0	0	0	0	2	0	0	0	0	6	1	1	0	0	0	2	ALIVE	ALCOHOL	11
97	KAMALESH	51612	55	M	0	0	2	3	0	0	0	0	2	2	0	0	1	0	10	1	1	0	0	0	2	ALIVE	ALCOHOL	21
98	RAJESH	51658	45	M	3	0	2	1	0	0	0	0	2	2	0	1	2	5	18	0	1	1	0	1	3	ALIVE	ALCOHOL	19
99	GIRI	33762	41	M	2	0	2	1	0	0	0	0	2	0	1	1	1	0	10	0	1	1	0	0	2	ALIVE	ALCOHOL	20
100	JEEVA	34448	40	M	0	0	2	1	0	0	0	0	2	0	0	0	0	0	5	0	0	1	0	0	1	ALIVE	ALCOHOL	10

PATIENT CONSENT FORM

STUDY DETAIL:

A COMPARITIVE STUDY BETWEEN BISAP AND APACHE II SCORING IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS IN CHENGALPATTU MEDICAL COLLEGE

STUDY CENTER:

CHENGALPATTU MEDICAL COLLEGE & HOSPITAL, CHENGALPATTU

PATIENT NAME: PATIENT AGE:
IDENTIFICATION NUMBER:

I confirm that I have understood the purpose of procedure for the above study.
I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.
I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reasons, without my legal rights being affected.
I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if withdraw from the study, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.
I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperative with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms.
I hereby give consent to participate in this study.
I hereby give permission to undergo complete clinical examination and diagnostic test.

Signature/Thumb impression: Place: Date:
Patient name and address:

Signature of the investigator: Place: Date:
Study investigator's name:

INFORMED CONSENT FORM

Title of the Study : **:** A COMPARITIVE STUDY BETWEEN BISAP AND APACHE II SCORING IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS IN CHENGALPATTU MEDICAL COLLEGE

Name of the Participant :

_____.

Name of the Principal (Co-Investigator) :

_____.

Name of the Institution : Government Chengalpattu medical college and Hospital

Name and address of the sponsor / agency(ies) (If any) :

_____

_____

_____

Documentation of the informed consent :

I _____have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in A COMPARITIVE STUDY BETWEEN BISAP AND APACHE II SCORING IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS IN CHENGALPATTU MEDICAL COLLEGE

(title of the study).

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____ months including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.*
7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.*
8. I have not participated in any research study within the past _____month(s).*
9. I have not donated blood within the past _____months----add if the study involves extensive blood sampling.*
10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.*
11. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.
12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.
13. I have understand that my identity will be kept confidential if my data are publicly presented .
14. I have had my questions answered to my satisfaction.
15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

சுயஒப்புதல்படிவம்

ஆய்வுசெய்யப்படும் தலைப்பு : A COMPARITIVE STUDY BETWEEN BISAP AND APACHE II SCORING IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS IN CHENGALPATTU MEDICAL COLLEGE

ஆய்வுசெய்யப்படும் இடம்:

பங்குபெறுபவரின் பெயர்:

பங்குபெறுபவரின் வயது: பங்குபெறுபவரின் எண் :

மேலேகுறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கபட்டுள்ளது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கின்றேன். எந்தகாரணத்தினாலோ, எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக்கொள்ளலாம் என்றும் அறிந்துகொண்டேன்.

இந்த ஆய்வுசம்பந்தமாகவோ, இதைசார்ந்து மேலும் ஆய்வுமேற்கொள்ளும்போதும் இந்த ஆய்வில்பங்கு பெறும் மருத்துவர், என்னுடைய மருத்துவஅறிக்கைகளைபார்ப்பதற்கு என் அனுமதிதேவைஇல்லை என அறிந்துகொள்கிறேன். இந்த ஆய்வின் மூலம்கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்க மாட்டேன். இந்த ஆய்வில் பங்குகொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன்.

பங்கேற்பவரின்கையொப்பம்: சாட்சியாளரின்கையொப்பம்:
இடம்: இடம்:
தேதி: தேதி :

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்:

ஆய்வாளரின் கையொப்பம்:
இடம்: தேதி: