EVALUATION OF D-DIMER LEVEL IN PREDICTING THE SEVERITY OF ACUTE PANCREATITIS AND EARLY ASSESSMENT OF ORGAN FAILURE

Submitted by

Dr. RADHA R BANAHATTI

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MASTER OF SURGERY

In

GENERAL SURGERY

UNDER THE GUIDANCE OF

Dr. RAMAKANTH BALOORKAR MS

ASSOCIATE PROFESSOR

DEPARTMENT OF GENERAL SURGERY

B.L.D.E. (D. U) SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA- 586103 KARNATAKA.

2020

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I hereby declare that this dissertation, "EVALUATION OF D-DIMER LEVEL IN PREDICTING THE SEVERITY OF ACUTE PANCREATITIS AND EARLY ASSESSMENT OF ORGAN FAILURE" is a bonafide and genuine research work carried out by me under the guidance of **Dr RAMAKANTH BALOORKAR** $_{MS}$ **,Associate Professor ,** Department of General Surgery at BLDE (Deemed to be university), Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapura.

Date:30/09/2020 **Dr. RADHA R BANAHATTI**

Place: Vijayapura

B. L. D. E. (Deemed to be university)

SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL &

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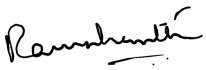

DR RAMAKANTH BALOORKAR MS

Associate Professor

Department of General Surgery

B. L. D. E. (Deemed to be university)

Shri. B. M. Patil Medical College

Hospital &Research Centre, Vijayapura.

Date: 30/9/2020

Place: Vijayapura

B. L. D. E. (Deemed to be university)

SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL &

RESEARCH CENTRE, VIJAYAPURA.

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Dr RAMAKANTH BALOORKAR.$_{M.S,}$ **Associate** Professor, Department of GENERAL SURGERY at BLDE (Deemed to be university) Shri. B. M. Patil Medical College Hospital and Research Centre, Vijayapura.

Dr. M. B. PATIL M.S, FIAGES.
Professor and HOD
Department of General Surgery
B. L. D. E. (Deemed to be university)
Shri. B. M. Patil Medical College
Hospital & Research centre
VIJAYAPURA.
Date: 30/9/2020
Place: Vijayapura

Dr. ARAVIND V PATIL M.S.
Principal
B. L. D. E. (Deemed to be university)
Shri B.M. Patil Medical College
Hospital & Research Centre,
VIJAYAPURA.
Date: 30/9/2020
Place: Vijayapura

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Place: Vijayapura

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DR RADHA R BANAHATTI

LIST OF ABBREVIATIONS:

MMC	Migrating motor complexes
CCK	Cholecystokinin
APACHE	Acute Physiology and Chronic Health Evaluation
SIRS	Systemic inflammatory response syndrome
CARS	Counter-active anti-inflammatory response syndrome
ARDS	Acute respiratory distress syndrome
MODS	Multi organ dysfunction syndrome
TAP	Trypsinogen activated peptide
EUS	Endoscopic ultrasound
CECT	Contrast enhanced computer tomogram
ERCP	Endoscopic retrograde cholangio pancreaticogram
USG	Ultra sonogram
IPMN	Intraductal papillary mucinous neoplasm
TPN	Total parenteral nutrition
CBD	Common bile duct

ABSTRACT

AIMS & OBJECTIVES:

To evaluate D-dimer levels in predicting the severity of acute pancreatitis .To evaluate the ability of the D-dimer to assess early development of organ failure.

MATERIALS AND METHODS:

This is a prospective observational study of 115 patients presented with Acute Pancreatitis in B.L.D.E (DU)'S Shri B.M.Patil Medical College and the D-dimer values for these patients were measured on day 1, 3, 5.

RESULTS:

Out of 115 patients of acute pancreatitis 31-40 years age group was predominant (20.6 %). Majority were the male patients (91.3%) in the study. Gall stones is the major etiological factor observed in the patients (62%).

Age of the total patient was compared with raised d-dimer values using spearman's and was considered significant. Common modes of presentation in this study were pain abdomen (85%), vomiting (27%). D-dimer values measured on admission day and subsequently on day 3 and 5 showed increased association with acute pancreatitis, as well as predicted early the occurrence of organ failure.

Diagnostic accuracy and ROC analysis of D-dimer score was compared with the remaining three scoring systems that is APACHE 2, SOFA, Ranson's score were (p less than 0.001).

It has a sensitivity of 94% and specificity of 86.2%. This is much higher than the sensitivity and specificity compared with other three studies.

CONCLUSION:

D-dimer value is a useful tool for Diagnosis of acute pancreatitis as well as predicting the occurrence of organ failure early.

LIST OF FIGURES:

LIST OF TABLES:

CONTENTS:

1) INTRODUCTION:

Acute pancreatitis is a hazardous illness. Characterized as "Incendiary cycle of pancreas with conceivable peri-pancreatic tissue contribution and multi-organ dysfunction with expanding mortality rate"[1]

Incidence is inaccurately estimated most of the times as mild cases are unreported and severe cases lead to death before diagnoses.

Around 20% of the cases of severe acute pancreatitis are associated with complications such as pancreatic necrosis, pseudocyst, distant organ failure and hemorrhage. In such cases the mortality is 15-30% where as it is only 0-1% in Mild cases. [2, 3]

The patho-physiology in occurrence of acute pancreatitis isn't completely reasonable however relegated to anomalous enactment of pancreatic catalysts inside acinar cells. Co-restriction of zymogen granules, lysosomes happen leading to enzyme activation, eventually auto-digestion of pancreas. The acinar cells release pro-inflammatory cytokines, like tumor necrosis factor and anti-inflammatory mediators like interleukin receptor antagonist in retaliation to primary insult.

These mediators are responsible for various responses both systemically and locally. The local response increases permeability and alters microcirculation which further advances the illness.

Acute pancreatitis can be divided into mild and severe form. Mild acute pancreatitis can be distinguished by self limiting interstitial edema of the gland. But the severe form is characterized by necrosis of pancreas , SIRS and failure

of multiple organs eventually leading to death. Hence judiciously identifying risk stratification tools, aid management of the disease in a finer way.

Ranson and colleagues in 1974 made the initial risk stratification[4]. This predicts disease severity, considering 11 parameters obtained at admission and after 48 hours. It has a positive predictive value of only 50% and a negative predictive value of around 90%. Therefore its usage is primarily in predicting a severe attack5.

The APACHE II, most widely practiced scoring , was originally developed as a risk stratification tool in intensive care setting. It considers a lot of parameters, some are not be related to the severity.

D-dimer:

Mostly used as an effective diagnostic tool in pulmonary embolism (PE) has been reported to have great predictive power in early phase of acute pancreatitis[6, 7].

The mechanism of increase in D-dimer levels was formation of multiple intravascular thrombi and consequently process of fibrinolysis.

Most patients with Acute Pancreatitis recover, but 20-25% progress to necrotizing pancreatitis and even multiorgan dysfunction syndrome with 30-35% mortality[8].

D-dimer concentrations measured during first few hours of admission and after 48hrs and 72hrs later were an accurate method for identification of patients who would develop organ failure in the further course of acute Pancreatitis[9, 10.]

It has a molecular weight of 180kDa. It is a final product of fibrin degradation, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis.

It consists of the remnants of all three chains that are alpha, beta and gamma of fibrinogen, cross linked by disulphide bonds. So named because it contains 2 D fragments of the fibrin protein joined by a cross link. A normal D-dimer result less than or equal to 500ng/ml[6] Feu (fibrinogen equivalent units).

2) **AIMS AND OBJECTIVES OF THE STUDY**:

- To evaluate D-dimer levels in predicting the severity of acute pancreatitis.

- To evaluate the ability of the D-dimer to assess early development of organ failure.

3) RESEARCH HYPOTHESIS:

D-dimer is a simple, easy and effective parameter for diagnosing Acute Pancreatitis as well as early prediction of organ failure.

4) REVIEW OF LITERATURE:

HISTORY:

Pancreas was generally ignored in the distant past, both in terms of its existence as well as in disease. It was first discovered by a Greek anatomist and surgeon Herophilus, who was born during the 336 BC in Bosporus, Chalcedon[11]. Pancreas as a word was first mentioned in literature given by Eristratos (310-250B.C.). Rufus (1st Century AD), an anatomist in addition to a surgeon from Ephesus, gave the name “pancreas” 400 years after the initial discovery.

Written in Greek language, it signified "pan": all, kreas: flesh “Galen (Claudius Galenus 138-201 AD), "Doctor to the Fighters" of Rome, this Emperor, encouraged that pancreas fills as a pad to secure the huge veins lying posterior to it[12].In March 2, 1642, a German émigré, Johann Georg Wirsung, found channel at San Francisco Monastery in Padua, Italy.

It was named by his partner as "The Duct of Wirsüng"[13]. While papilla, the broadening of that pipe at its intersection with the basic bile conduit (CBD) which ventures into the second some portion of duodenum, were first portrayed by Vater in 1720. Santorini depicted the extra channel that bears his name in 1734.

In 1869, Paul Langerhans (“Junior”), belonging to the prestigious Berlin Institute of Pathology, the eminent Professor Rudolph Virchow, explained the islets of the pancreas that was later known as the “islets of Langerhans” an endocrine system within 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.

GROSS ANATOMY:

The intriguing embryological improvement of this organ has stunned the scientists. An endodermally determined organ, with two morphologically various parts, the exocrine and endocrine tissue[14]. Likewise called "two organs in one”, on the basis of its ability to carry out various functions.

It is a posterior lying retroperitoneal organ, at the rear of stomach. It stretches out from the C-circle of the duodenum to splenic hilum at L1 spinal level. The verity that the pancreas is fixed in the retroperitoneum, can't be confined effectively, subsequently its pathology presents this way. It tends to be divided into head, body, neck, tail including one projection or "uncinate process".

The pancreas is 15-20cm long, weighing around 91.8g. The head of pancreas present on right of midline within the duodenal C loop.

The body , tail of pancreas extends across the midline, anterior to splenic artery and vein, just above the Gerota’s fascia and slightly, ending at the splenic hilum. The capsule of the pancreas is fixed to its surface and contiguous with the anterior layer of mesocolon.

BLOOD SUPPLY OF THE PANCREAS:

ARTERIAL SUPPLY: Most of the blood supply of pancreas is from the celiac trunk and superior mesenteric vessels. The common hepatic artery and splenic artery originates from the celiac trunk.

The more prominent pancreatic supply routes branch from the splenic corridor, while the gastro duodenal conduit branches from the basic hepatic vein. It at this point isolates around the top of the pancreas as two branches.

The two branches in particular anterior and posterior pancreatic-duodenal branches, anastomosing with the respective branches of the inferior pancreatic duodenal artery.

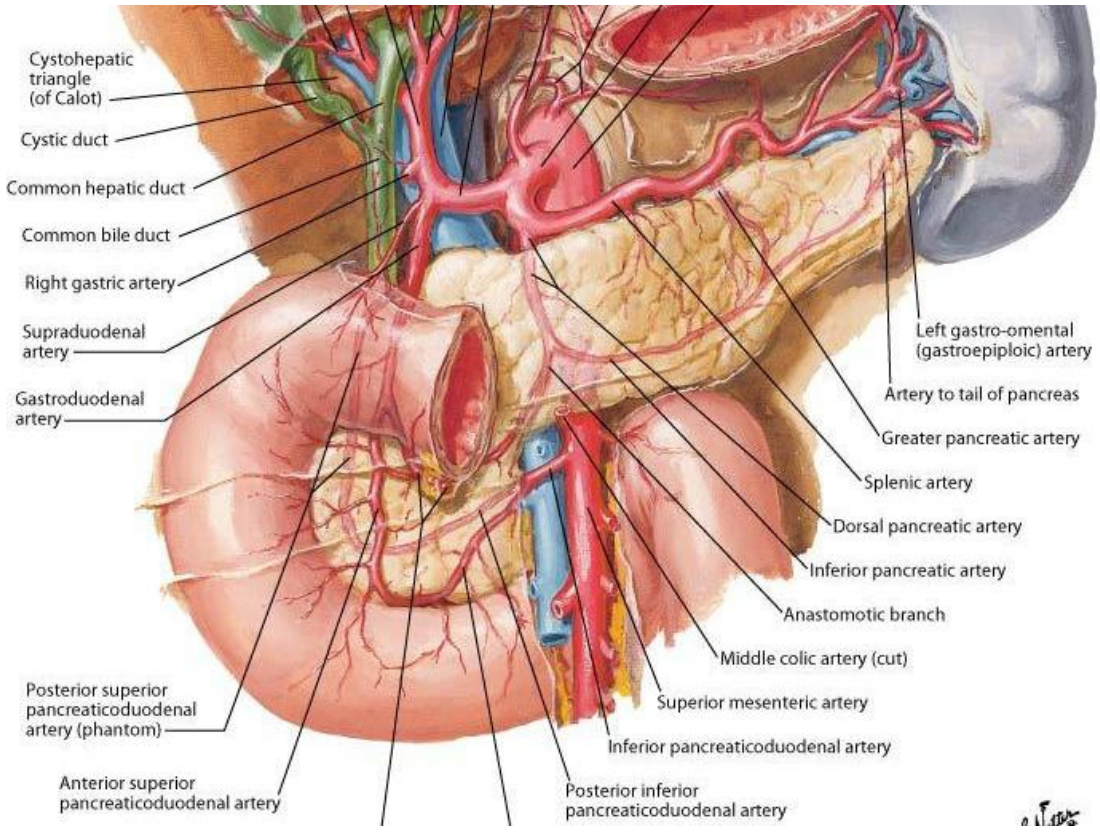


FIGURE 1: ARTERIAL SUPPLY

The pancreatic head and uncinate process are supplied by the pancreatic-duodenal arteries. Rest receives its blood supply from the splenic artery.

The splenic artery gives a dorsal pancreatic branch , which runs behind the pancreatic body to form the inferior pancreatic artery, to terminate at the tail.

The head and neck of pancreas drain through the superior and inferior pancreatic-duodenal veins, and body and tail drain into the splenic vein.

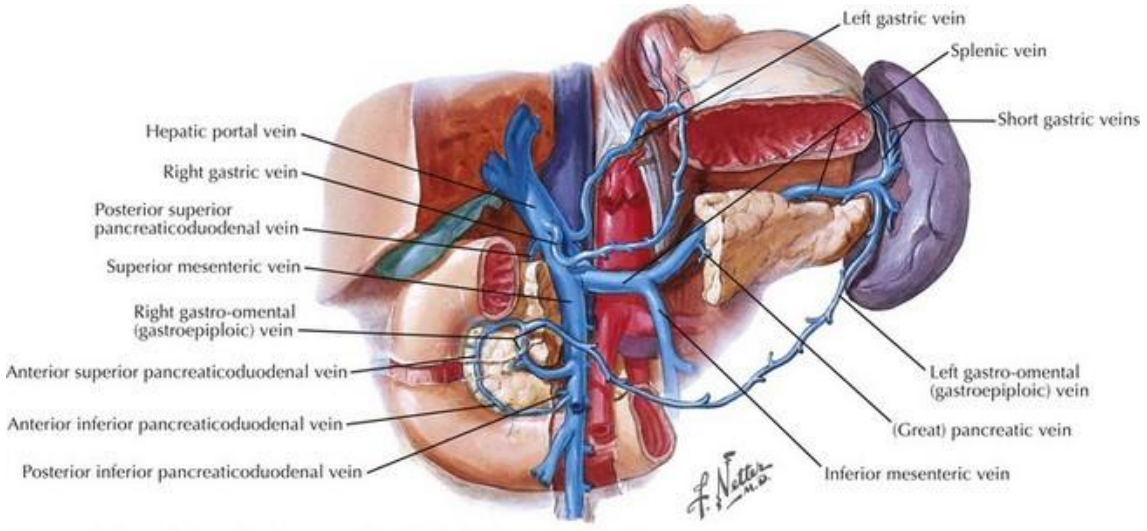


FIGURE 2: VENOUS DRAINAGE

The venous seepage copies the blood vessel gracefully. The head channels into the anterior and posterior pancreatic-duodenal veins. The posterior superior pancreatic-duodenal vein enters the unrivaled mesenteric vein, horizontally at the prevalent fringe of neck of the pancreas.

LYMPHATIC DRAINAGE:

The lymphatic drainage from the pancreas is widespread. They drain the surface network of lymph toward regional lymph nodes and are formed near the larger blood vessels[15]

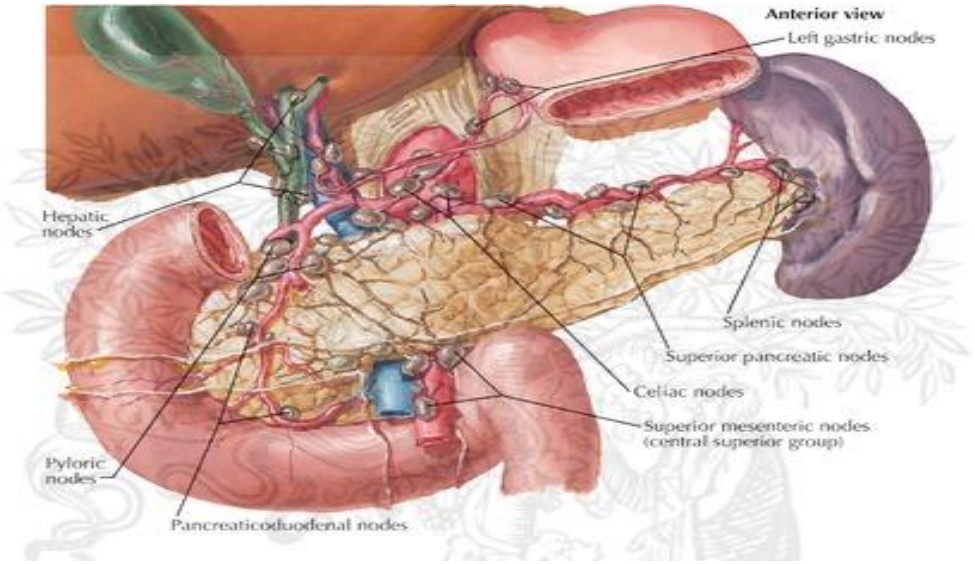


FIGURE 3: LYPHATIC DRAINAGE

The superior lymphatics run close to the splenic blood vessels. The lymphatic's on the left side of the body and tail of pancreas, empty into lymph nodes of splenic hilum. Lymphatics on right of the body and the neck of pancreas, empty into lymph nodes near the superior border of the head.

The possible reason as to why the pancreatic cancer presents with positive lymph nodes is mainly because of its diffuse lymphatic drainage. Because of this very same reason they also have high incidence of local recurrence after resection.

DUCTAL ANATOMY OF PANCREAS:

The duct of Wirsung, begins at the distal tail of pancreas as a confluence of small anastomosing ductules draining the lobules of the gland. It usually passes downward and backward in close juxtaposition to the common bile duct.

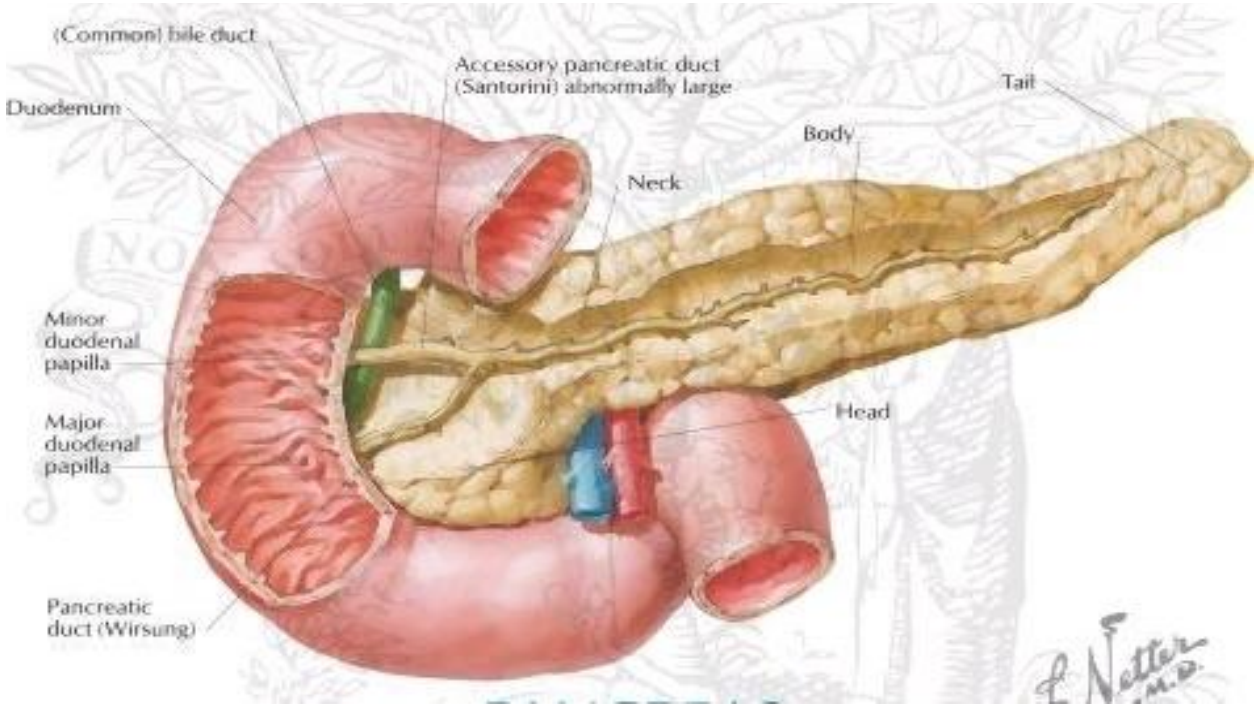


FIGURE 4: DUCTS IN PANCREAS

In the head of the pancreas, the duct turns inferiorly at its genu to joins the common bile duct, and drains into duodenum at the ampulla of Vater, 7 to 10 cm distal to the pylorus. The main pancreatic duct is widest at the head of the pancreas (5mm), and tapers at the body (4mm) and tail (3mm).

The duct of Wirsung has around 20 secondary branches throughout the pancreas, which drain the acinar units. At the level of the major papilla, it turns horizontally to join bile duct. This short common segment is the ampulla of the bile duct, which terminates at the duodenal papilla.

The papilla of Vater at the termination of the common bile duct is a small, nipple like structure that protrudes into the duodenal lumen and is marked by a longitudinal fold of duodenal mucosa.
A patent accessory duct of Santorini, also known as the "minor duct" in seen in a large number of individuals.

The accessory pancreatic duct lies anterior to the bile duct. It drains the uncinate process and inferior portion of the pancreatic head into the duodenum, proximal to the ampulla of Vater, at the confluence of minor papilla of duodenal mucosa.

NERVE SUPPLY:

The visceral efferent innervations of the pancreas are through the vagi and the splanchnic nerves by plexuses. The efferent fibers of the vagi, pass through these plexuses without synapsing, and they terminate in parasympathetic ganglia within the interlobular septa of the gland.
The postganglionic fibers innervate the ducts, acini and islets. The bodies of the preganglionic symphathetic neurons originate in the lateral gray matter of the thoracic and the lumbar spinal cord.
The bodies of the postganglionic sympathetic neurons are located in the great plexuses of the abdomen. They innervate only blood vessels. The autonomic fibers are located near the blood vessels of the pancreas.

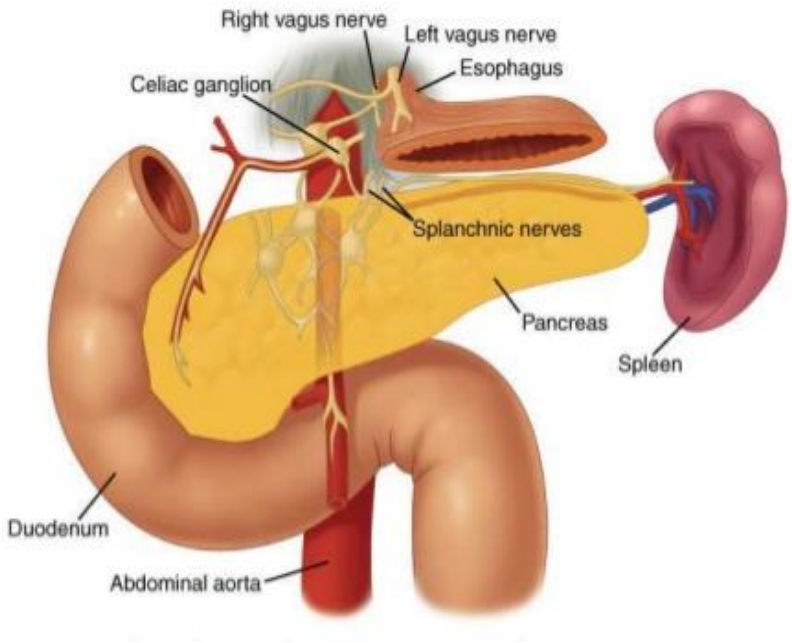


FIGURE 5: NERVE SUPPLY

The parasympathetic pathway stimulates, where as the sympathetic pathway inhibits it.

The pancreas in addition secretes amines and peptides, like somatostatin, vasoactive intestinal peptide, calcitonin gene-related peptide and galanin. The afferent sensory fibers are responsible for the intense pain in pancreatic cancer, as well as acute and chronic pancreatitis[16].

EMBRYOLOGY:

The pancreas grows in three different stages[17]. The first is the undifferentiated stage, wherein the endoderm evaginates to begin the basic morphogenesis. The next one includes epithelial stretching with arrangement of crude channels.

The final stage begins with formation of acinar cells with development of zymogen granules which contain enzymes. The posterior foregut endoderm gives rise to this

organ. The two dorsal and one ventral bud migrate towards one another, and fuse to form a single unit.

Around 1st month of gestation, the foregut evaginates into a condensation of the overlying mesenchyme and forms the first morphologic dorsal bud.

Approximately one week later, one ventral bud forms. These two buds undergo elongation of a stalk and branching. At 37-42 days of gestation, ventral pancreas rotates around the duodenum to fuse with dorsal pancreas.

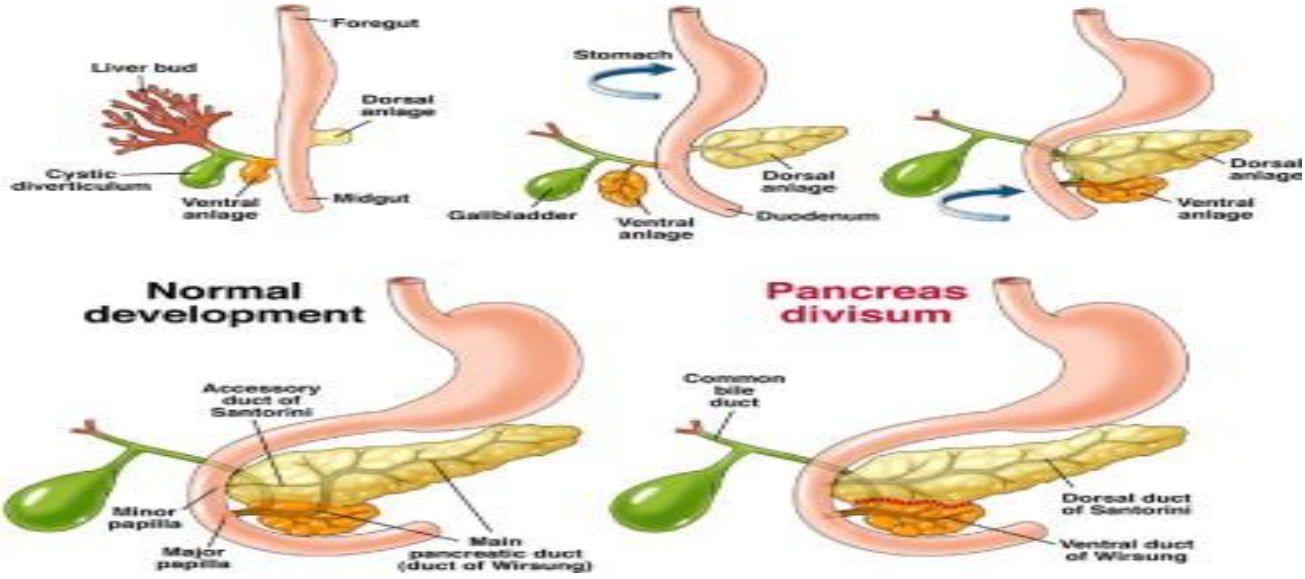


FIGURE 6: EMBRYOLOGY

The dorsal pancreas forms body, tail, superior part of the pancreatic head, including the distal part of main pancreatic duct (of Wirsung), along with the entire minor accessory pancreatic duct (of Santorini).

The ventral pancreas forms the uncinate process, inferior part of the head of the pancreas including proximal part of the main pancreatic duct.

Omission of the ventral pancreas to fully rotate around the duodenum leads to a condition called annular pancreas, which leads to circumferential pancreatic tissue surrounding the second part of the duodenum.

HISTOLOGY OF PANCREAS:

The pancreas is a finely nodular organ. The lobules are noticeable and associated by connective tissue septa which contain the channels, veins, lymphatic's, and the nerves.

The essential subunit of the exocrine part is the acinus, which is at its base a circular mass of secretory cells called acinar cells.

Its ducts are lined by columnar epithelium. The endocrine part comprises of the islets of Langerhans cell. Various eosinophilic zymogen granules fill the apical aspect of the cell.

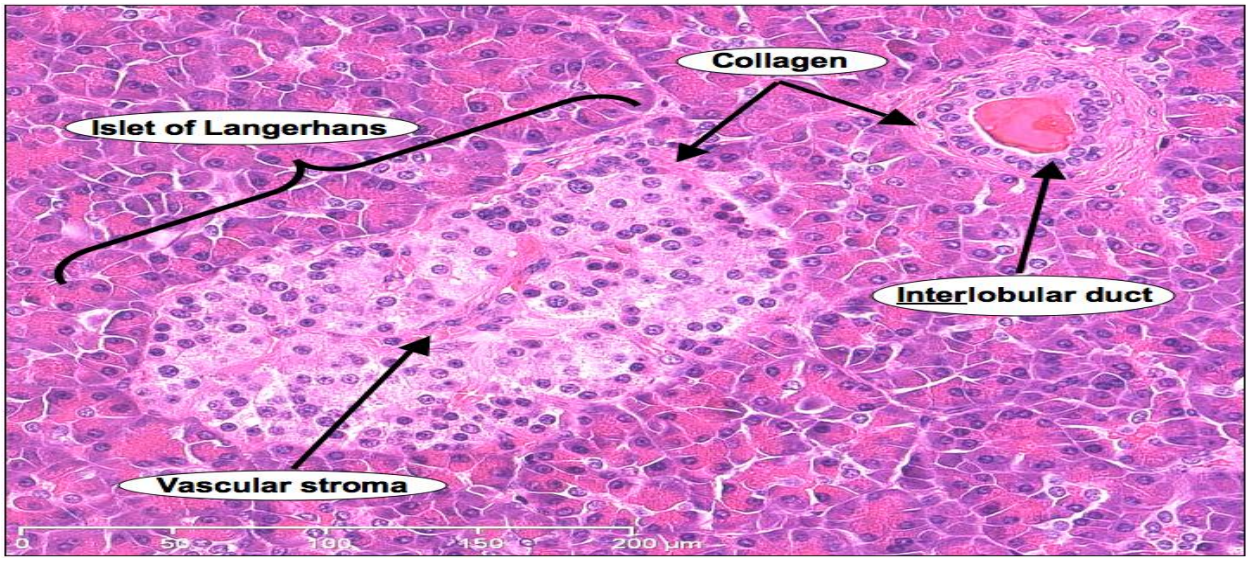


FIGURE 7: HISTOPATHOLOGY

PANCREATIC SECRETIONS:

EXOCRINE SECRETIONS:

The functional unit of exocrine pancreas has an acinus and its draining ductile. The basolateral aspect of acinar cell membrane has receptors for enzymes for receptors and transmitters.

COMPOSITION OF EXOCRINE SECRETIONS:

The pancreas secretes colorless, odorless, alkaline, isosmotic pancreatic juice. Acini and ducts are parts of the exocrine system. Its secretions are 500ml per day.

The acinar cells produce amylase, proteases, and lipases, which aid in digestion of carbohydrates, proteins, and fat. Its inorganic components include water, sodium, potassium, chloride, and bicarbonate.

Whenever secretins are stimulated, they release pancreatic juice .This pancreatic juice has an average flow rate of 0.2 or 0.3mL/min during relaxation phase and 4.0mL/min during postprandial stimulation. Approximately 2.5 L is secreted every 24hours.

ORGANIC CONSTITUENTS:

Pancreas has a large capacity to synthesize proteins. Amylases digest the starch and glycogen by hydrolyzing 1,4-glycoside linkages at every alternate junction between carbon 1 and oxygen. It produces maltose, maltotriose, α-dextrins.

The pancreas secretes three lipases namely: Lipase, Phospholipase A2 and Carboxylesterase. Lipase hydrolyzes a TG molecule to form 2 fatty acid molecules released from carbons 1 and 3 .

PROTEASES:

Trypsin changes over the supportive of catalysts discharged by pancreas to a functioning structure, in duodenum. Trypsinogen is changed over to trypsin, by enterokinase, which discharged by duodenal mucosal cells.

In the event that trypsinogen inhibitor, pancreatic secretory trypsin inhibitor (PSTI) or SPINK1, isn't communicated then it causes familial pancreatitis.

PHYSIOLOGY:

Exocrine secretions begin with intake of food and also in fasting state. The "migrating myoelectric complex" or MMC play a role in this.

The exocrine pancreas secretes digestive enzymes, fluid and bicarbonate in response to food ingestion. This is a digestive process regulated by neural reflexes, gastro intestinal hormones and nutrients.

Secretion is regulated by stimulatory and inhibitory influences that coordinate the delivery of digestive enzymes with food emptying into the intestine to assure adequate digestion of a meal.

Exocrine pancreatic emission with ingestion of food consists of 3 stages: 1.Cephalic, 2.Gastric, 3.Intestinal

CEPHALIC PHASE OF DIGESTION:

Sensory inputs during this phase are by vagus stimulation. Approximately one fourth of total pancreatic secretions are released in this phase.

GASTRIC PHASE OF DIGESTION:

This stage is because food in the stomach. A significant upgrade is the distension of stomach that prompts dominating protein emission with immaterial discharge of water and bicarbonates.

INTESTINAL PHASE OF DIGESTION:

It is interceded by hormones and vagovagal reflexes. Ductal emission starts by hydrogen particles in intestinal lumen. Secretin is delivered from entero-endocrine S cells in the duodenal mucosa when the pH is acidic.

The further chemicals released are neural and humoral. Cholecystokinin is the main humoral arbiter of catalyst emission during the intestinal stage. Its level normally expands following a meal.

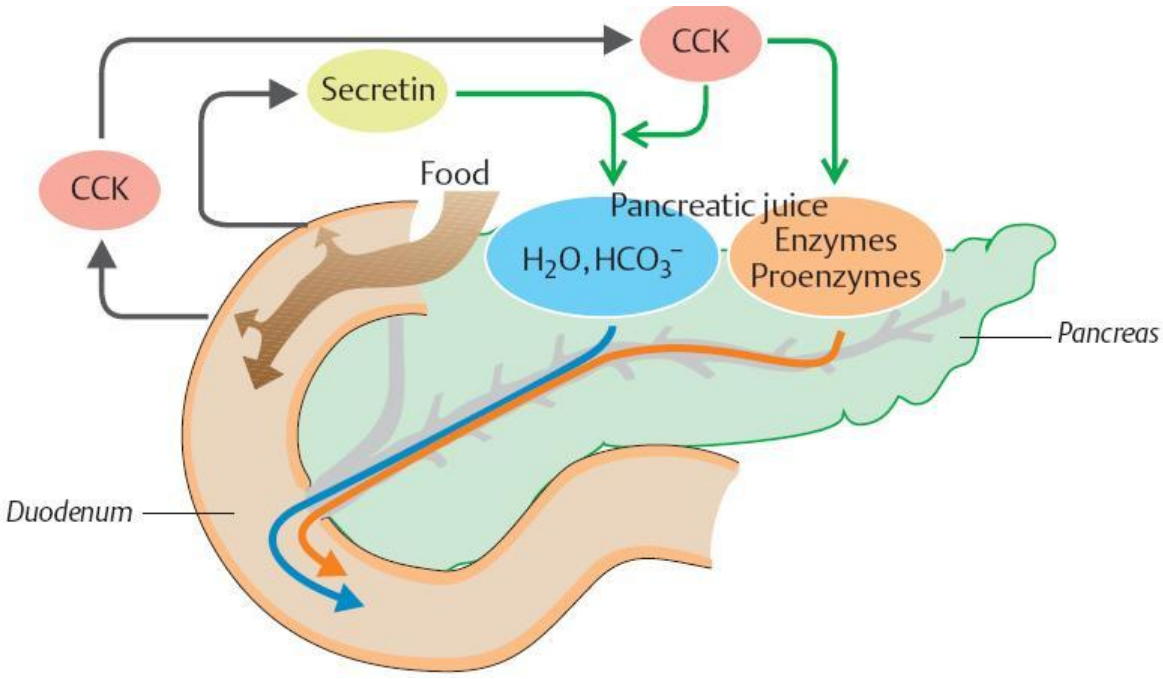


FIGURE 8: REGULATION OF SECRETION

ENDOCRINE SECRETIONS OF PANCREAS:

The endocrine secretions of pancreas is by islet of langerhans .There are different cells which secrete a variety of hormones. These cells are distributed based on their size, mostly larger once situated near arterioles and smaller ones are fixed deeper in the gland.

The five main types of cells are:

Alpha Cells: Secrete glucagon, responsible for hepatic glycogenolysis and gluconeogenesis.

Beta Cells: Secrete insulin, Diminished gluconeogenesis, glycogenolysis, unsaturated fat breakdown, ketogenesis, increased glycogenesis, protein union.

Delta Cell: Release Somatostatin, Inhibits activity of GI endocrine peptides.

Epsilon Cells: Release ghrelin, Decreases insulin release and its action.

PP Cells: Release Pancreatic peptides, prevents pancreatic exocrine secretion and insulin, helps hepatic activity of insulin.

ACUTE PANCREATITIS:

DEFINITION OF ACUTE PANCREATITIS:

Pancreatitis is an "inflammation of glandular parenchyma lead to injury or destruction of acinar components associated with little or no fibrosis of the pancreas".

ETIOLOGY OF ACUTE PANCREATITIS:

Most commonly gallstones, that includes 50% of the patients, followed by alcohol includes 20%[18].

GALLSTONES:

Lifetime occurrence of acute pancreatitis in these patients is 3-9%. Female preponderance is noted[19].

An acute episode is generally caused by distally obstructed stones less than 5mm in diameter. Theses stones traverse down the cystic duct easily to obstruct the ampulla as compared to larger stones.

Uninterrupted or fragmented blockage of the ampullary orifice due to a gallstone or edema induced by stone passage leads to pancreatitis.

Aggregates of cholesterol crystals or calcium bilirubinate particles less than 5 mm in diameter, are detected as "sludge" within the gallbladder" on ultrasonography.

ALCOHOL:

The second commonest cause of acute pancreatitis all over the world. It is mostly seen in young men (30 to 45 years of age) than in women[20]. Although, only a few percent of patients who drink alcohol develop acute pancreatitis.

Heavy alcohol abuse with a daily consumption of more than 100 g for a minimum of 5yrs, cigarette or beedi and genetic defects, causes acute pancreatitis.

The risk of alcohol-induced pancreatitis in smokers is way significantly more than compared to non smokers[21]. The type of alcohol consumed is less significant than the quantity of ethanol.

The "secretion with blockage" theory suggests that ethanol consumption leads to increased contraction of sphincter of Oddi.

Alcohol also a metabolic toxin to pancreas, disrupts enzyme synthesis and secretion.

TUMOURS:

Malignancies with rapid growth compressing on the duct or encasing it could lead to pancreatitis. Adult in their 30-40 yrs age are most commonly affected.

The commonest malignancy which presents this way is Intraductal papillary mucinous neoplasm (IPMN) [22].

Occasionally a papillary adenoma causes subsequent acute attack of pancreatitis secondary to blockage.

METABOLIC DISORDERS CAUSING ACUTE PANCREATITIS:

HYPERTRIGLYCERIDEMIA:

Third most common cause of pancreatitis. Level of triglyceride more than 2000 mg/do were seen in these cases, with very high concentrations of chylomicrons23.

The free fatty acids released induce free radical damage. This directly injures cell membranes and acinar cells.

HYPERCALCEMIA:

Hypercalcemia leading to acute pancreatitis is very rare. The excess deposition of calcium salts and activation of trypsinogen within the pancreatic parenchyma causes pancreatitis[24].

INFECTIONS:

- Viruses like mumps, herpes viruses, EBV.
- Bacterial disease like Legionella Salmonella and brucellosis;
- Fungi and Parasites like Toxoplasma, Cryptosporidia, Ascaris lumbricoides.

VASCULAR DISORDERS:

Ishacemic pancreatitis is very rare. Mostly mild episodes are seen. Severe necrotizing pancreatitis may be seen rarely secondary to embolisations , atheromas , hypovolemic shock , vascultis.

TRAUMATIC CAUSES:

Following penetrating or blunt trauma. Mechanism here is pancreatic injury by compression of pancreas against the spine leading to its ischemia and gland inflammation.

IATROGENIC:

Mainly due to ERCP, causing significant morbidity. Abnormal enzyme elevations seen in 35% to 70% of ERCPs[25].

POSTOPERATIVE PANCREATITIS:

Post alimentary tract or thoracic cavity operations. Its incidence is 1-7 % of heart surgeries. 30% of these patients develops deranged pancreatic enzymes and few develop necrotizing pancreatitis.

DYSFUNCTION OF THE SPHINCTER OF ODDI:

The main reason in favor of this entity leading to acute pancreatitis is that many studies reported that endoscopic pancreatic sphincterotomy and sphincteroplasty has shown the reduced re-occurrence of pancreatitis.

PANCREATIC DIVISUM:

One of the rare causes of acute pancreatitis. Obstruction of minor papilla being the triggering factor.

RARE CAUSES:

Crohn's disease, Celiac disease associated rarely. The disruption of small bowel mucosal barrier causing pancreatitis is also secondary to hyper amylesia.

PATHOPHYSIOLOGY OF DISEASE:

Acute pancreatitis has varying degrees of severity, with multifactorial causation. It is generally believed that, the indirect activation and injury of acinar cells is the basic path physiology in disease causation.

CO- LOCALISATION HYPOTHESIS THEORY:

The activation of trypsinogen inside acinar cells is the key factor for pathogenesis. Once activated the trypsin activates proenzymes, like elastase, phospholipase A2 including the complement and kinin systems.

These activated enzymes auto-digest the pancreas, leading to a vicious cycle releasing more active enzymes. The lysosomal hydrolase cathepsin B, which activatates trypsinogen are also present here.

The normal trypsin produced physiologically is destructed by its inhibitors. The auto digestion is avoided by intracellular collecting the latent forerunners of proenzymes or zymogens.

Their actuation happens in the duodenum by the brush-fringe catalyst enteropeptidase which enacts the trypsinogen.

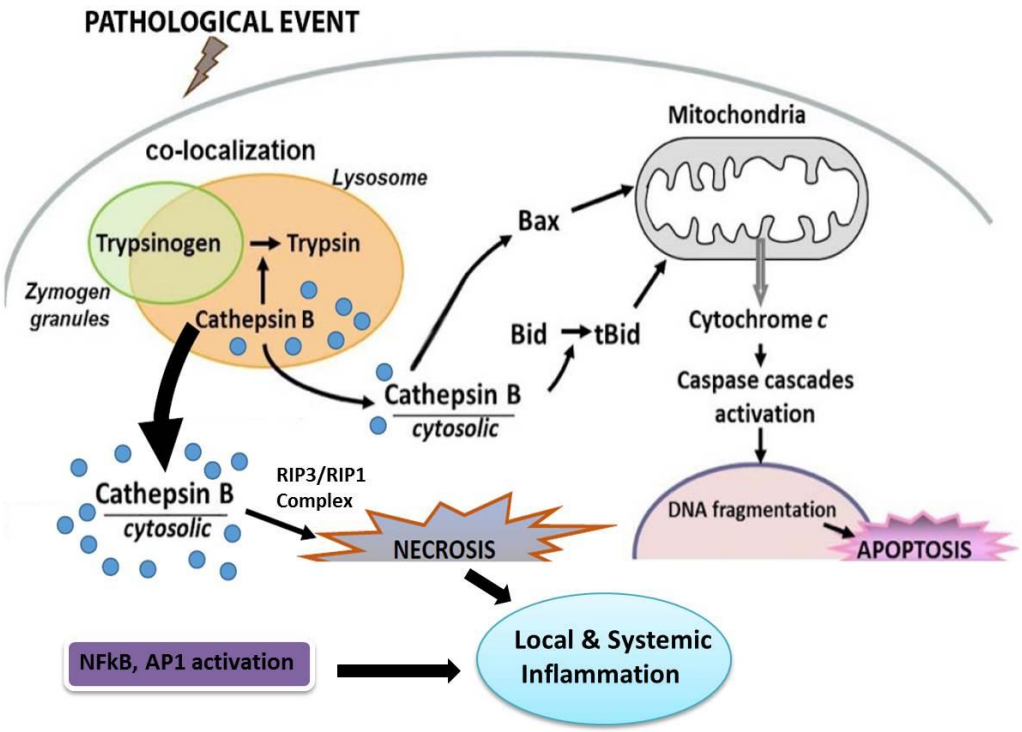


FIGURE 9: ACTIVATION OF ENZYMES

When dynamic, trypsin at that point enacts different zymogens in a course. To shield the pancreas from these unsafe proteins, they are isolated from their cytoplasmic space by being encased inside film bound organelles, called zymogen granules.

They repress modest quantities of rashly actuated trypsinogen inside pancreatic acinar cells. They are stored with zymogens. Injury to acinar cells results in expression of adhesion molecules such as VCAM, which worsens the inflammatory response.

The end pathway leads to enhanced vascular permeability and gland edema causing "interstitial pancreatitis" [26].The complement pathway is activated and releases C5a. This further releases inflammatory mediators like macrophages and leukocytes. They further activate pro inflammatory cytokines and platelet aggregates.

The leakage of cytokines from liver and Kupffer cells into the systemic circulation occurs. This causes acute phase protein synthesis leading to development of SIRS and damage major organ. Eventually MODS and death occur.

ARDS can be caused by active phospholipas e-A, that cleaves lecithin, a constituent of pulmonary surfactant. Acute renal failure occurs secondary to hypotension. Myocardial depression and shock are caused by release of vasoactive peptides and amyocardial-depressant factor.

Metabolic complications are hyperlipidemia, hyperglycemia with or without ketosis , hypoglycemia and low calcium levels. Hypocalcemia occurs secondary to hypoalbuminemia, decreased magnesium, calcium-soap formation, imbalances in hormones.

CLINICAL FEATURES:

The Diagnosis of acute pancreatitis by history and examination is difficult , because the signs and symptoms are very similar to other acute abdomen presentations .

Following presentations may be noted:

- Abdominal pain of varying intensity
- Elevated levels of serum enzymes namely amylase and lipase to almost its double
- CT abdomen
- Other conditions mimicking acute pancreatitis like gangrenous bowel, acute cholecystitis should be ruled out.

ABDOMINAL PAIN:

Most common site of pain in acute pancreatitis being upper abdomen. The tracking of leakage of pancreatic secretion to the left of parabolic gutter may rarely present as lower abdominal pain.

Typically characterized as "knifing" or “boring through” to back. Sometimes this pain is relieved in bending forward position.

The pain is sudden onset and reaches its peak in 10-20 minutes. Occasionally pain can be gradually progressive also. The pain radiates to back in a belt like radiation in 50% of patients. It is absent in around 5% -10% of attacks.

A painless presentation also is sometimes suggestive of a serious fatal disease[27]. Nausea, vomiting, with retching often persists even on an empty stomach.

90% of individuals affected show association of nausea, vomiting and retching. Intractable pain or the inflammation of the wall of stomach causes vomiting.

PHYSICAL EXAMINATION:

The intensity of the attack directly corresponds to the physical examination findings. Mild disease patients are often asymptomatic. The examination findings are tachycardia, tachypnea, hypotension, and hyperthermia.

The temperature in uncomplicated pancreatitis is usually normal. Pulse rate ranges from 100 to 150 /minute. Blood pressure may be high or low depending on whether there is third space fluid loss with decreased circulatory volume.

Painful shallow breathing with respiratory distress is secondary to contaminants at the diaphragm. Breathlessness is due to effusion, atelectasis, ARDS. Minimal tenderness and associated guarding of abdomen is sometimes observed. In severe pancreatitis, patient is toxic. Abdomen shows distension mostly in the epigastria, because of paralytic ileus.

Rigidity occurs rarely, and if so other causes of diffuse peritonitis should be ruled out. Bowel sounds could be sluggish or absent. Ecchymosis is observed over the flanks and is termed “Grey Turner’s sign”. In Umbilical area ecchymosis is called “Cullen’s sign”. Extravasation of hemorrhagic secretions causes ecchymosis.

Pleural effusion occurring after pancreatitis presents as a dull note on percussion. The breath sounds on auscultation are precariously heard in right hemi thorax suggest pleural effusion.

Patients may be drowsy, agitated, comatose, may hallucinate, with fall in BP, electrolyte imbalances, hypoxia, fever or toxic manifestations of abnormal enzymes on the central nervous system.

Other rare presentations could be with panniculitis, subcutaneous nodular fat necrosis and polyarthritis. This fat necroses is 0.5- to 2-cm tender red nodules seen over distal extremities, scalp, trunk and buttocks. These nodules appear during an episode of acute pancreatitis and disappear with improvement.

Hepatomegaly, spider angioma and Dupuyten's contracture indicate ethanol induced pancreatitis. Whereas Tendon xanthoma and lipemia-retinalis suggest pancreatitis due to hyperlipidemia .

DIAGNOSES OF ACUTE PANCREATITIS :

PANCREATIC ENZYMES :

In acute pancreatitis, a three to four times increase in levels of serum amylase or lipase in the blood is diagnostic [27].

SERUM AMYLASE:

Pancreatic diseases causes raised isozymes of amylase, and measuring these specifically is accurate for diagnosis. It's routinely measured, as it is cheap and easy. It increases 6 to 12 hours after an acute episode and cleared gradually with a half life of 10 hrs with a clearance of less than 25 %.

From first day of disease onset the enzyme levels are raised and persist for 3-5 days. Serum amylase has a sensitivity of around 85%. Sometimes its levels are normal even after pancreatitis due to small amount of acinar tissue after multiple

episodes. Hypertriglyceridemia causing pancreatitis could have normal level of amylase.

SERUM LIPASE :

Serum lipase has a higher sensitivity as compared to serum amylase and is 67%[28]. Nonetheless it has a very high specificity also . Another advantage of serum lipase being that, it is raised on first day of the disease and is detectable for a longer period as compared to serum amylase .

ROUTINE HEMATOLOGICAL INVESTIGATIONS:

The polymorphonucleocyte count is strikingly raised in severe disease, unrelated to presence of infection.

The blood glucose is even higher than levels of glucagon. Liver enzymes and bilirubin are raised in pancreatitis secondary to stones.

The reduced Serum calcium in these patients is mainly due to decreased serum albumin. Alcohol causes higher MCV, secondary to its toxic effects on erythrocytosis in the bone marrow.

TRYPSINOGEN AND CHYMOTRYPSIN:

The content of trypsinogen activated peptide, in urine shows increased correlation with the severity of disease at admission.

TAP is the commonest activation peptide in acute pancreatitis evaluated so far. Unfortunately, the TAP testing kit is not commercially available, hence it cannot be a part of routine clinical measurement.

IMAGING:

PLAIN X-RAY:

A Focal ileus of segment of small bowel that is the "colon cut-off " sign is seen.

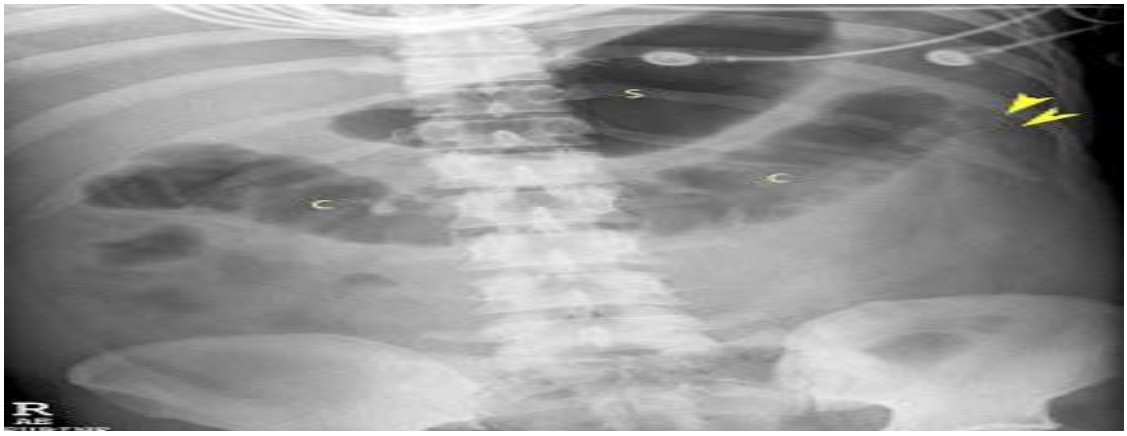


FIGURE 10: COLON CUTOFF SIGN

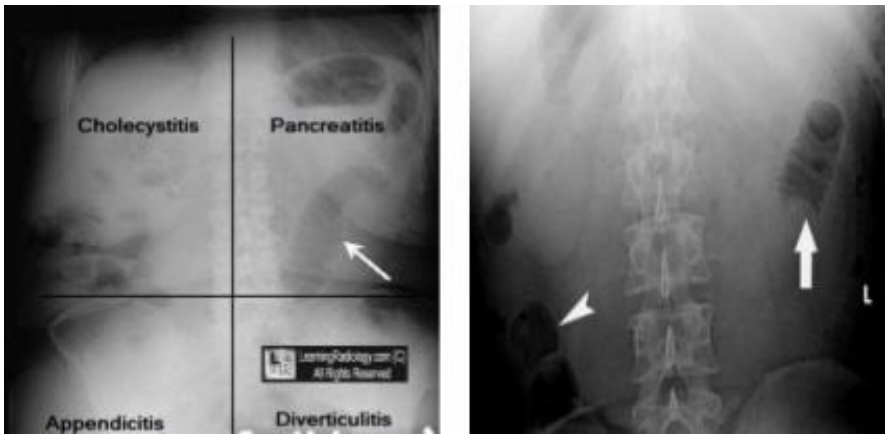


FIGURE 11: SENTINEL LOOP SIGN

X-ray abdomen erect excludes other acute abdominal conditions of immediate intervention. Exudates in the lesser sac, causes forward displacement of the stomach.

Small bowel pathology mainly occurs due to irritation and inflammation . They present as paralytic ileus that is described as sentinel loop sign on radiology . The

colon cut-off sign on radiology is nothing but the dilated colon proximal to the spasm produced by spread of the thick infected fluid to specific areas of colon leading to spasm of those areas .

USG ABDOMEN :

It is more significant in the first 24 hours of admission, to visualize gallstones, CBD dilatation as a result of choledocholithiasis, and ascites. Fluid with high protein content extravasates from the intravascular compartment to peritoneal cavity in moderate to severe pancreatitis is nothing but ascitis . Pancreas enlarges uniformly and appears hypoechoic. Sometimes obscured by bowel gas.

CECT ABDOMEN :

This is a very significant investigation as it is associated with both accurate diagnoses of disease and also for diagnosing its complications .

CECT also helps to stage the disease based on its severity. The most common imaging modality is helical CT. It is taken after oral and intravenous contrast. It identifies necrosis of pancreas, perfusion of the organ, interstitial pancreatitis. It is done when patients do not improve after the first week of symptoms.

If air bubbles are visualized on CT , it denotes infected necrosis or pancreatic abscess. Early CT is not very sensitive to an evolving necrosis, which becomes well marked by 48-72 hours of disease onset .

The sensitivity to detect pancreatic necrosis approaches 100%, 96 hours after diagnosis of disease. CT also detects infected pancreatic necrosis. CT guided aspiration of necrosis is done , if patient condition worsens or doesn’t improve for prolong periods .

CT grade	
(A) Normal pancreas	0
(B) Oedematous pancreatitis	1
(C) B plus mild extrapancreatic changes	2
(D) Severe extrapancreatic changes including one fluid collection	3
(E) Multiple or extensive extrapancreatic collections	4
Necrosis	
None	0
<One third	2
>One third, <one half	4
>Half	6
CT severity index = CT grade+necrosis score	
	Complications
0–3	8%
4–6	35%
7–10	92%
	Deaths
0–3	3%
4–6	6%
7–10	17%

Modified from the World Association guidelines[3] and based on Balthazar and colleagues.[26]

TABLE 1: BALTHAZAR GRADING OF CT SEVERITY OF ACUTE PANCREATITIS

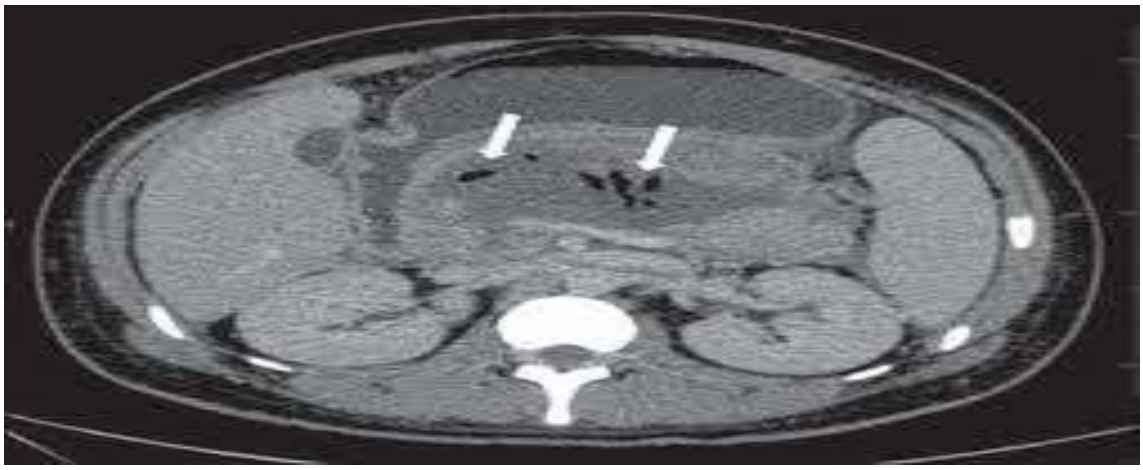


FIGURE 12: NECROSIS ON CT

MRI:

It is similar to CT in assessing disease severity, necrosis and collections. MRI is superior to CT, and as good as EUS and ERCP in detecting choledocholithiasis. The use of IV Secretin, prior to MRCP helps in finer delineation of the pancreatic duct [29].

ENDOSCOPIC ULTRASOUND :

It has lower significance in early acute pancreatitis. In an ongoing attack of acute pancreatitis and few weeks after, EUS cannot differentiate AP from chronic pancreatitis and cancer.

After around 30-45days specifically in patients suffering from idiopathic interstitial pancreatitis, it can be used to detect the presence of tumors, anomalies like pancreas divisum, and stones. EUS is as sensitive as MRCP and ERCP .

EUS is extremely sensitive as related to both abdominal ultrasound and CT in detecting duct stones[29].

ERCP usage is mostly justified in the setting of biliary pancreatitis, with high serum bilirubin levels leading to sepsis.

CLASSIFICATION OF PANCREATITIS :

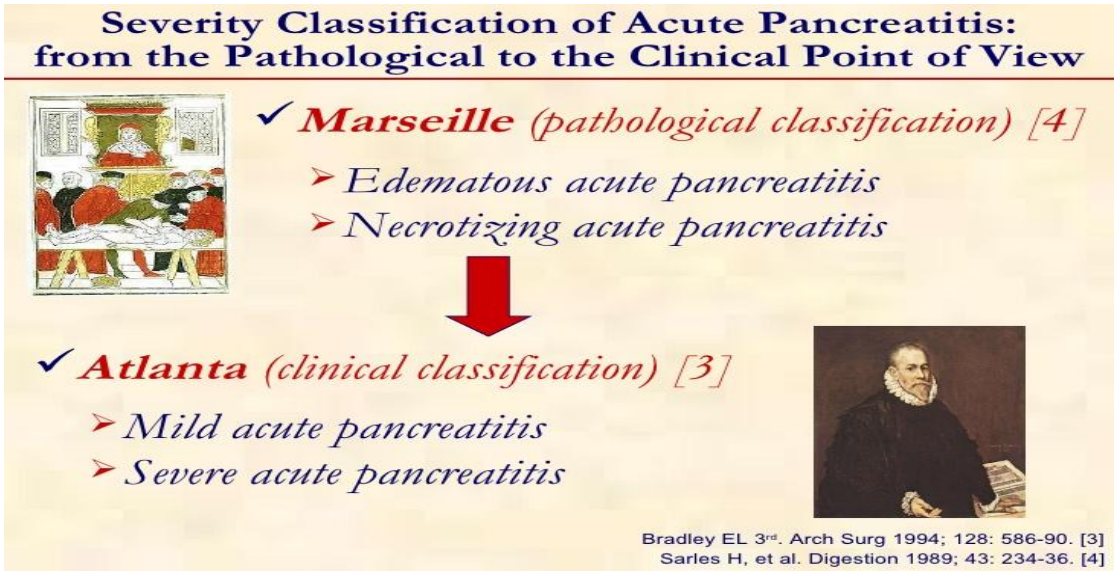


TABLE 2: CLASSIFICATION OF PANCREATITIS

Universally accepted classification for severity in acute pancreatitis, the Atlanta classification, reported in 1992. This divides acute pancreatitis into two groups: mild and severe.

Severe disease is identified by presence of organ failure, local pancreatic complications on imaging (acute fluid collection, pancreatic necrosis, pseudocyst and pancreatic abscess), poor prognostic scores **.**

Atlanta in 1992 offered a widely applicable classification system, that successfully served clinical studies and helped in equating of data obtained over 20 years.

Due to limitations of the 1992 Atlanta classification and better understanding of the pathogenesis of acute pancreatitis, it was updated. The revised of the Atlanta classification of 2012 divides acute pancreatitis based on its severity into three groups that are mild, moderate, and severe[30].

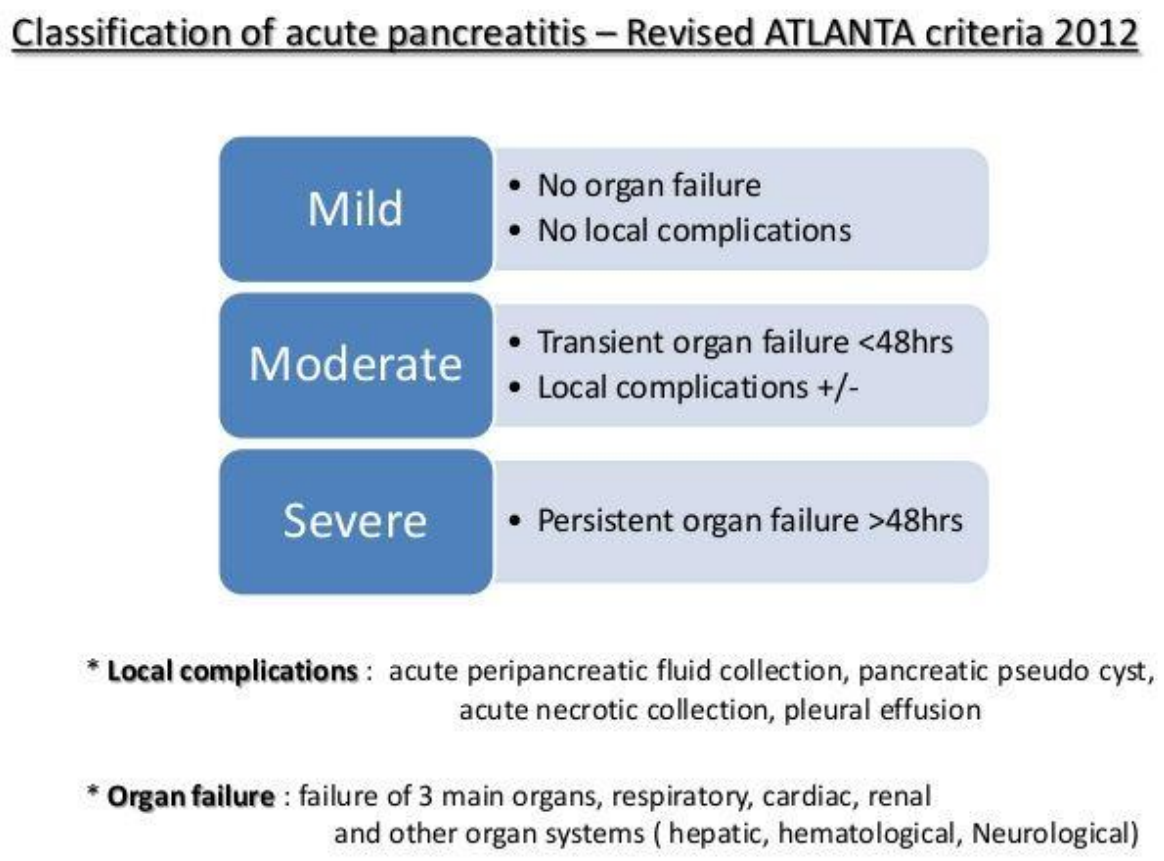


TABLE 3: REVISED ATLANTA CRITERIA

Based on clinical parameters in the initial phases whereas later on this subdivision is based on a combination of various morphologic complications. They might require an active intervention or supportive treatment in the form of vasopressors , ventilator support or renal dialysis .

Necrotizing pancreatitis is defined as “The presence of parenchymal necrosis with or without necrosis of peri-pancreatic fat.”

The improvised Atlanta classification, includes patients with only peri-pancreatic necrosis only. Edematous interstitial pancreatitis is usually mild, but rarely a fulminant attack may occur and cause patient death within 48-96hrs

these patients though suffer severe disease, but fail to the meet criteria of necrotizing pancreatitis.

EARLY AND LATE ORGAN FAILURE :

Acute pancreatitis has a dual course. Firstly characterized by a systemic inflammatory response syndrome (SIRS) which lasts for about 2 weeks. The second phase consists of counter-active anti-inflammatory response syndrome (CARS), as a result of immune suppression. Organ failure in the SIRS phase occurs due to severe systemic inflammation and not because of infection initially .

In CARS phase, the organ failure is related to secondary infections, like infected pancreatic necrosis. The SIRS phase sometimes cause bacteremia and pneumonia. The pulmonary and cardiovascular systems are predominantly affected.

Organ failure in the SIRS phase, is diagnosed 2 days after admission most commonly. More than 50% of deaths from acute pancreatitis involve organ failure but not from infected pancreatic necrosis.

Organ failure can present as any of the following:

1)Early-onset organ failure : With ICU admission and supportive care these patients get well in 2-3 weeks. Later on their condition suddenly deteriorates after 5-6weeks. This cycle is strongly suggestive of infected necrosis.

2)without early organ failure : initially stable later on suddenly deteriorate due to infected necrosis.

3)Early-onset organ failure :their condition remains critical even after 2-3weeks of ICU and supportive care .In such a clinical setting FNAC helps to differentiate between persistent SIRS and infected necrosis. Gas bubbles on CECT scan confirms infected necrosis and also the need for intervention.

VARIOUS SCORING SYSTEMS :

1)RANSONS SCORING :

This was the most initial scoring system in used , designed by Ranson and colleagues in 1974. It is easier to predict the mortality in this scoring as it is directly proportional to the positive data obtained .

The original criteria were used for patients with alcoholic pancreatitis. This was later modified after 8 years later for patients with gallstone pancreatitis. Higher the score , more is the severity .

Ranson (alcoholic or other)	Ranson (biliary)
At admission	**At admission**
Age >55 y	Age >70 y
GB > 16 000/mm^3	GB > 18 000/mm^3
LDH > 350 U/l	LDH > 250 U/l
AST > 250 U/l	AST > 250 U/l
Glycemia >200 mg/dl	Glycemia >220 mg/dl
In 48 h	**In 48 h**
Drop in hematocrit > 10%	Drop in hematocrit > 10%
BUN increase >5 mg/dl	BUN increase >2 mg/dl
Calcium <8 mg/dl	Calcium <8 mg/dl
PO^2 <60 mmHg	PO^2 <60 mmHg
Bases deficit >4 mEq/l	Bases deficit >5 mEq/l
Fluid loss >6L	Fluid loss >4L
Each item worth 1 point (0 a 11 points)	

TABLE 4: RANSONS CRITERIA

The complications of acute pancreatitis resonate with Ranson's score. Its drawbacks are :

1.The criteria is complicated

2.There are two different lists based on the etiology

3.It takes 48 hours to fully calculate the criteria

4.Validation beyond 48 hours has not been studied

5.Some of the parameters in the criteria are not widely used routinely

Its sensitivity is only 40% to 88%, and specificity is 43% to 90%. With a positive predictive value of 50%, and negative predictive value of 90%.

2) IMRIE'S PROGNOSTIC CRITERIA :

During initial 48 hours:

WBC count of more than 15000/mm3

Blood sugar more than 10 mmol/L

Serum urea more than 16 mmol/L

Po2 level less than 60 mm Hg

Serum ca2+ level less than 2 mmol/L

Lactic dehydrogenase more than 600 IU/L

AST / ALT more than 200μm/l

Serum albumin level less than 32 g/L

Both the above scores suggest the disease severity at admission only . They are not used for the clinical course monitoring .

3) MODIFIED GLASGOW CRITERIA :

Both alcoholic and biliary pancreatitis patients are assessed with this score[31].

The score of more than 3 means severe disease and requires ICU care.

P - PaO2 less than 8kPa or less than 60 mmhg

A - Age more than 55 years old

N - Neutrophilia with WBC count more than 15x109/L

C - Ca2+ less than 2mmol/L or less than 8 mg/dl

R - Renal function : Urea more than16mmol/L or more than 45 mg/dl

E – Enzymes:- serum LDH more than 600 IU/L;

AST more than 200 IU/L

A - Albumin less than 3.2g/dL

S - Sugar: more than 10mmol/L or more than 180 mg/dl

4) AGA GUIDELINES :

The American Gastroenterological Association has issued guidelines to assess acute pancreatitis severity .

A. Prediction of severe disease can be done using the APACHE II system

B. Those with actual or severe disease associated with severe comorbid conditions are considered for triage in an ICU

C. Those patients with predicted severe disease and documented organ failure in the initial 72 hours, rapid- bolus CT is done after 72 hours to assess severity of pancreatic necrosis.

5) APACHE II SCORING :

Acute Physiology and Chronic Health Evaluation , is the most widely studied scoring system. Due to high negative predictive value and positive predictive value it can be performed daily.

If values decrease in the first 48 hours it indicates mild attack, whereas progressive rise of values suggest a severe attack.

The major advantage of this scoring as compared to any other scoring system that it is used in monitoring patient's response to therapy.

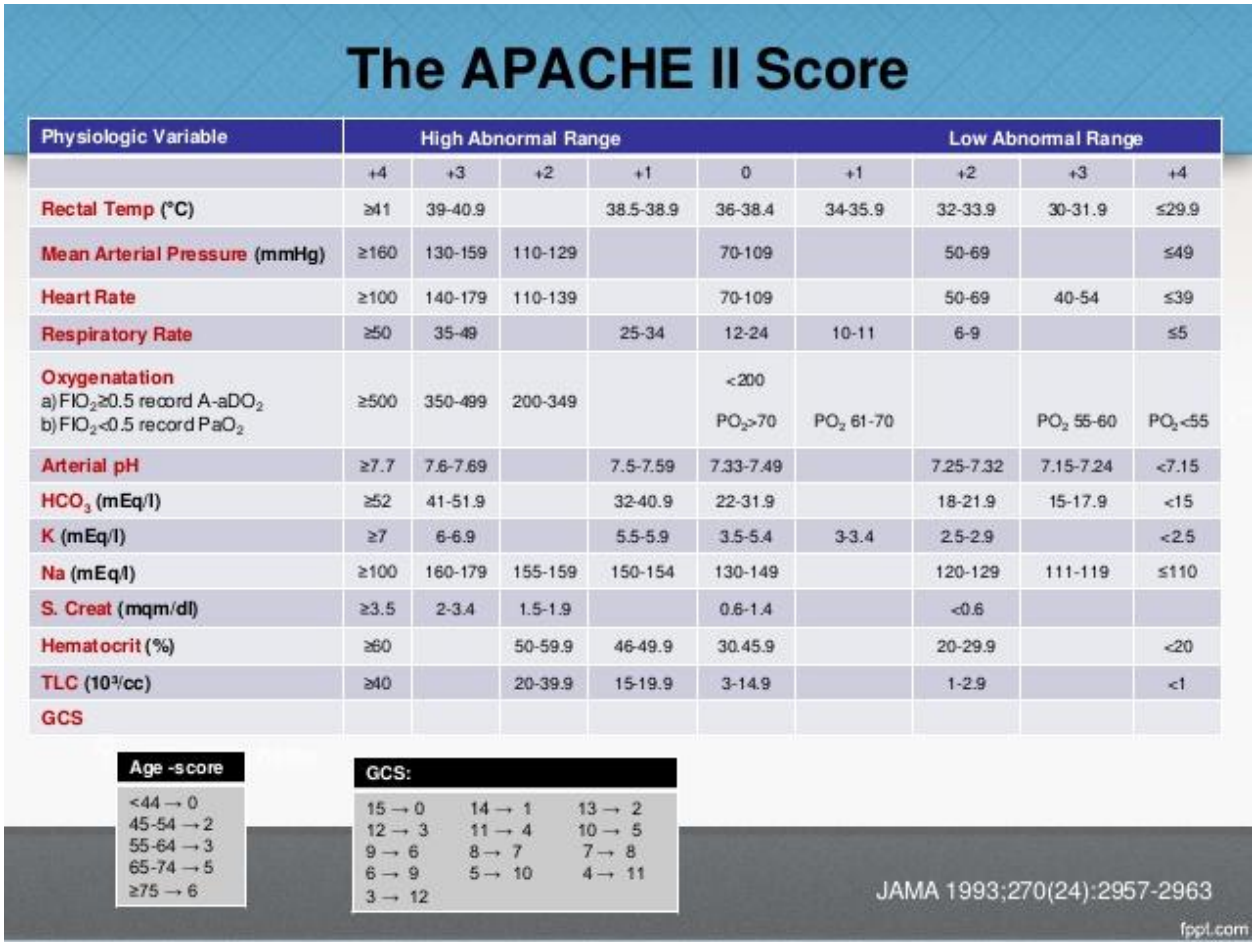
The laboratory tests in APACHE 2 are simple, routine and readily available. The scores on admission and 48 hours later distinguishes mild from severe disease.

Its sensitivity is 34% - 70%, and specificity is 76% - 98%. At 48 hours, sensitivity reduces to 50%, but specificity is close to 90% .

The organ failure was classified as[32]:

Transient less than 48hrs

Persistent more than 48hr



The APACHE II Score

Physiologic Variable	High Abnormal Range						Low Abnormal Range		
	+4	+3	+2	+1	0	+1	+2	+3	+4
Rectal Temp (°C)	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure (mmHg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart Rate	≥100	140-179	110-139		70-109		50-69	40-54	≤39
Respiratory Rate	≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation a) FIO_2≥0.5 record A-aDO_2 b) FIO_2<0.5 record 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
HCO_3 (mEq/l)	≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
K (mEq/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Na (mEq/l)	≥100	160-179	155-159	150-154	130-149		120-129	111-119	≤110
S. Creat (mqm/dl)	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	≥60		50-59.9	46-49.9	30.45.9		20-29.9		<20
TLC (10^3/cc)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
GCS									

Age -score

<44 → 0
45-54 → 2
55-64 → 3
65-74 → 5
≥75 → 6

GCS:

15 → 0
12 → 3
9 → 6
6 → 9
3 → 12
14 → 1
11 → 4
8 → 7
5 → 10
13 → 2
10 → 5
7 → 8
4 → 11

JAMA 1993;270(24):2957-2963

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TABLE 5: APACHE 2 CRITERIA

6) D – DIMER :

- The pathology leading to a rise in D-dimer levels was formation of multiple intravascular thrombi , consequently fibrinolysis.
- Most of these patients recover, sometimes 20-25% progress to necrotizing pancreatitis and even multiorgan dysfunction syndrome with 30-35% mortality[33].
- D-dimer concentrations were measured during first hour of admission or 24hrs later, was an accurate method for identification of patients who would develop organ failure in the further course of acute pancreatitis[34] .

- In all patients, the plasma D-dimer level was determined on admission DAY 1 and DAY 3 and DAY 5.
- The upper limit of the reference interval for D-dimer was 500micro gm/ L.
- It is a simple, easy, cheap and effective method to diagnose acute pancreatitis as well as to predict the early occurrence of organ failure.

MANAGEMENT OF ACUTE PANCREATITIS:

GENERAL CONSIDERATIONS:

Acute pancreatitis once diagnosed requires early and aggressive fluid management for achieving hemodynamic stability and perfuse the kidneys and pancreas. These patients need proper pain management.

Patient is not allowed any oral intake till nausea and vomiting subsides. Opiate analgesics are used for management of abdominal pain.

Morphine increases the tone of sphincter of Oddi, and serum amylase. It does not affect pain outcome in acute pancreatitis adversely[35].

Early signs of organ failure like hypotension, pulmonary failure, or renal failure require close monitoring Tachypnea should not be assumed to be due to abdominal pain.

FLUID RESUSITATION:

The inflammatory process progresses in early acute pancreatitis, causes extravasations of protein rich intravascular fluid, into peritoneal cavity and retroperitoneum. This causes hemoconcentration with decreased renal perfusion and uremia .

The reduced perfusion pressure in pancreas causes microcirculatory changes leading to pancreatic necrosis.

If the hematocrit on admission is 44% and a fails to decrease after 24 hours, it indicates necrotizing pancreatitis. Ringer lactate is the preferred solution for initial fluid resuscitation. Since the bicarbonate content and pH of ringer lactate prevents metabolic acidosis.

RESPIRATORY CARE:

Hypoxemia requires supplementation, preferably by nasal prongs or face mask . If this doesn't treat hypoxia then early intubation ventilation are required. Swan-Ganz catheter helps to identify hypoxemia secondary to congestive heart failure or due to primary pulmonary damage.

Acute respiratory distress syndrome is the most severe respiratory complication of acute pancreatitis. It clinically is characterized by severe dyspnea, hypoxia, and increases mortality. Increased pulmonary alveolar capillary permeability causes interstitial edema. Preferably intubation to be done for such patients .

ANTIBIOTICS :

Not indicated in mild acute pancreatitis. Antibiotic usage is only appropriate in pancreatic sepsis like infected necrosis and abscess and in non pancreatic sepsis secondary to line sepsis or pneumonia . A recent metaanalysis demonstrated that there is no beneficial effect in the regular use of systemic antibiotic prophylaxis[36].

NUTRITION:

Artificial nutritional support may be required in 4-6weeks old cases of severely acute pancreatitis. Earlier , TPN was routinely used in such patients . Enteral nutrition is preferred since it is cheap and safe. It is thought to decrease the decrease small bowel bacterial overgrowth and improve intestinal mucosal barrier function.

ENDOSCOPY :

It helps in diagnosis as well as early management of impacted gallstones and thus prevents pancreatitis secondary to gallstones.

SURGICAL THERAPY :

In a patient of mild or severe gallstone pancreatitis, Cholecystectomy should be performed immediately after the acute inflammatory process subsides [37.]

Surgery also helps to debride pancreatic necrosis and drain a pancreatic abscess. Sterile necrosis is treated non-operatively because the mortality of such patients managed conservatively is only 5%[37].

However, mortality in patients of infected pancreatic necrosis undergoing surgery is 15% to 73%.

The various necrosectomy types includes :

- Those with closed continuous irrigation by indwelling catheters
- Necrosectomy with closed drainage without irrigation
- Necrosectomy and open packing.

BILIARY PANCREATITIS :

General consensus regarding intervention in a case of biliary pancreatitis is either urgent intervention within first few hours of admission or delayed intervention after 72 hours, but during the same admission.

Cholecystectomy and duct clearance is possibly the best option in patients without obstruction[37]. If surgery is contraindicated then the next best options for such patients is endoscopic sphincterotomy with clearance of stones by ERCP. If obstruction persists after 24hours of observation in acute cases then an emergency endoscopic sphincterotomy and stone extraction is performed.

COMPLICATIONS :

LOCAL :

Pancreatic ascites/ pleural effusion , Pseudocyst of pancreas, Necrosis of pancreas, Infected abscess and Aneurysm.

SYSTEMIC :

1. RESPIRATORY COMPLICATIONS: Pneumonitis, basal atelectasis , acute respiratory distress syndrome and Pleural effusion .

2. CARDIOVASCULAR COMPLICATIONS: Hypotension , Hypovolemia , non specific ecg changes , Sudden arrest leading to death and Pericardial effusion.

3. VASCULAR SYSTEM: Abnormal Hemoconcentration and DIC

4. GI hemorrhage secondary to Acid peptic disease , Gastric erosion or Portal/splenic vein thrombosis with variceal bleed

5. RENAL COMPLICATIONS: These include Oliguria , Azotemia and rarely renal vein thrombosis

6. METABOLIC DERANGEMENTS: Hyperglycemia hypocalcemic tetany , metabolic encephalopathy and retinopathy

7. NEURAL COMPLICATIONS : Acute psychosis , Fat embolism leading to occlusion , Alcohol withdrawal syndrome in chronic alcoholics .

5) **MATERIAL AND METHODS:**

SOURCE OF DATA:

All patients presenting to B.L.D.E.(D.U.)'s Shri B. M .Patil Medical College Hospital and Research Centre Vijayapura and admitted patients in whom the diagnosis of ACUTE PANCREATITIS are considered from OCTOBER 2018 to JUNE 2020.

METHOD OF COLLECTION OF DATA:

- This is a prospective observational study in which patients presenting with Acute Pancreatitis in B.L.D.E.(D.U)'s Shri B.M.Patil Medical College Hospital and research centre Vijayapura were taken up.
- Baseline data including age, sex, etiology, the RANSONS SCORE and the APACHE II SCORE were recorded on admission.
- The definitions of organ dysfunction were based on a score of 2 or more sequential organ failure assessment (SOFA) scoring system.
- Both SOFA and APACHE II Score were assessed on days 1, 3 , 5 .
- In all patients, the plasma D-dimer level was determined on admission DAY 1 and DAY 3^{rd} AND DAY 5^{th}.
- The upper limit of the reference interval for D-dimer was 500micro gm/ L.
- Other routine laboratory parameters such as serum concentrations of creatinine, bilirubin, Blood urea and C-reactive protein (CRP), serum amylase and serum lipase were determined at the same time as the plasma D-dimer level was measured, and at other time points.

- MULTIPLE ORGAN DYSFUNCTION SYNDROME (MODS) was defined as Combined dysfunction of 2 major organ systems.
- Data will be checked on master chart for analysis.
- The data will be analyzed by using student t-test .

1. **INCLUSION CRITERIA**:

a. All patients presenting with acute pancreatitis.

2. **EXCLUSION CRITERIA**

a. Patients who had received surgical intervention before admission

b. Patients with a known history of coagulative disorders or a recent history of MI or cerebral infarction, DVT, pulmonary thromboembolism.

SAMPLING:

Study period from OCTOBER 2018 to JUNE 2020. All the patients admitted during this period, who fulfill the inclusion criteria, will be included in this study.

ESTIMATION OF SAMPLE SIZE :

With 95% confidence level and margin error of +/-6% , a **Sample size of 115** subjects will allow the study to determine the evaluation of D-dimer levels in predicting the severity of Acute pancreatitis and early assessment of organ failure with finite population correction.(N=200)[11].

FORMULA:

$n = z^2 p(1-p)/ d^2$

Where d= margin of error

z= z statistic at 5% level of significance

P= anticipated prevalence rate (50%)

Statistical Analysis:

All characteristics will be summarized descriptively.

For continuous variables, the summary statistics of N, mean and standard Deviation will be used.

For categorical data the number and percentage will be used in data summaries and data will be analyzed by Chi square test for association, comparison of mean using t-test, ANOVA and diagrammatic representation.

Data will be represented using Mean ±SD, percentages and diagrams.

Data will be analyzed using:

-ROC CURVE

-Sensitivity, Specificity , PPV and NPV

-Scores will be compared using independent t test

6) RESULTS:

This study was conducted in the department of general surgery, BLDE SHRI B M PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE VIJAYAPURAA . The 115 persons with features of acute pancreatitis who fulfilled the inclusion criteria were enrolled in this study after obtaining an informed consent.

Table 6: Age distribution

Age(yrs)	**N**	**%**
≤30	25	21.7
31-40	32	27.8
41-50	22	19.1
51-60	16	13.9
>60	20	17.4
Total	115	100

Descriptive Statistics	**Min**	**Max**	**Mean**	**SD**
Age(yrs)	17	85	43.8	14.7

Peak incidence in this study was noted in 4^{th} decade

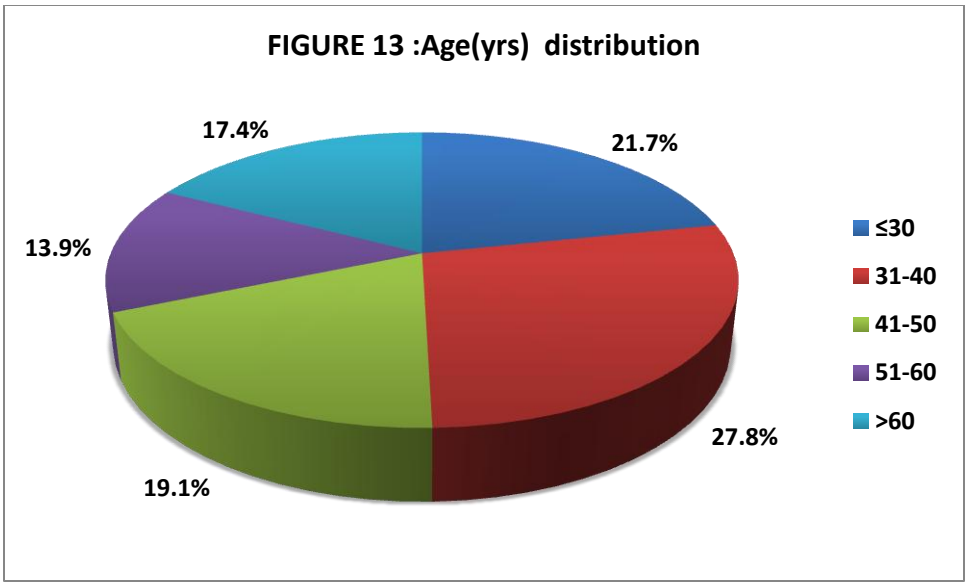


Table 7 : Gender distribution:

Sex	N	%
Male	105	91.3
Female	10	8.7
Total	115	100

Out of 115 patients enrolled in this study there were 105 males and 10 females .

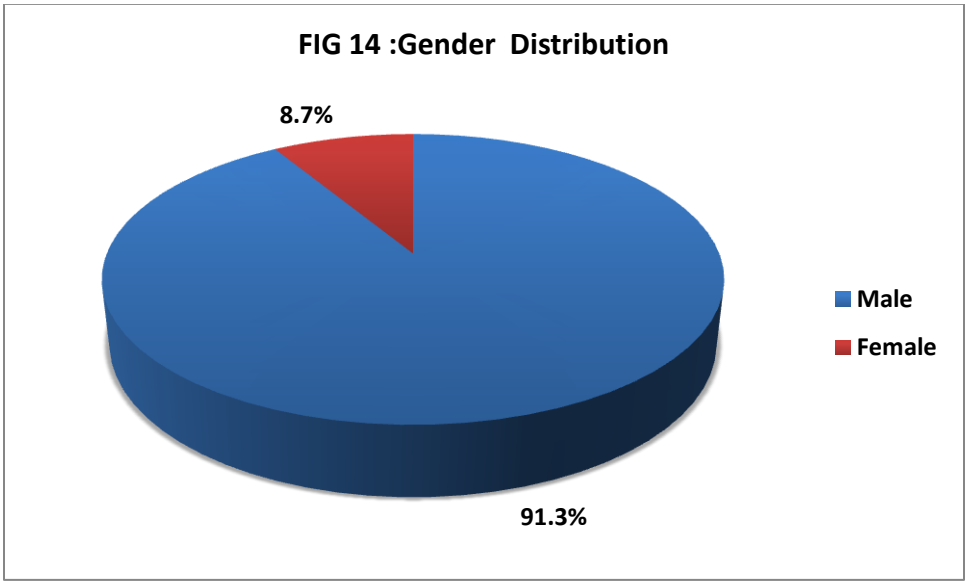
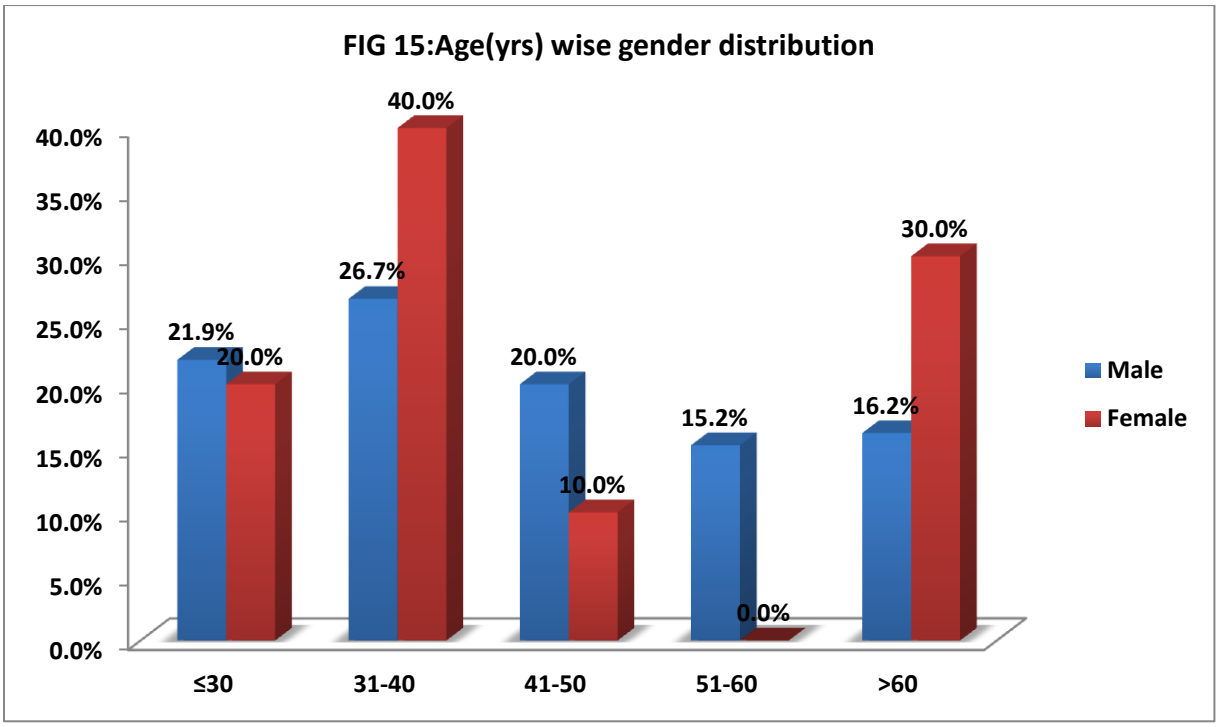


FIGURE 3: Age wise sex distribution :



Mean age group of males : 41yrs

Mean age group of females: 39yrs

Table 8: Clinical Features:

SYMPTOMS	NO. OF PATIENTS	PERCENTAGE (%)
PAIN ABDOMEN	98	85
FEVER	25	21
VOMITING	32	27
JAUNDICE	08	6.9

On clinical presentation, 85% of patients were presented with abdominal pain as chief complain. Rest of 15% who didn't have abdominal pain had vomiting and fever as presenting symptoms.

ETIOLOGICAL FACTORS:

Consumption of alcohol and it being the etiological factor were found in 23 patients. Gall stone disease was attributed in 72 patients. Hyperlipidemia and drugs as causative factor presented in 04 and 01 patients, respectively.

There was clear cut history of blunt trauma with CT scan showed isolated pancreatic laceration presented in 06 cases. No cause could be attributed in rest of the 09 patients.

FIG 16 :ETIOLOGY

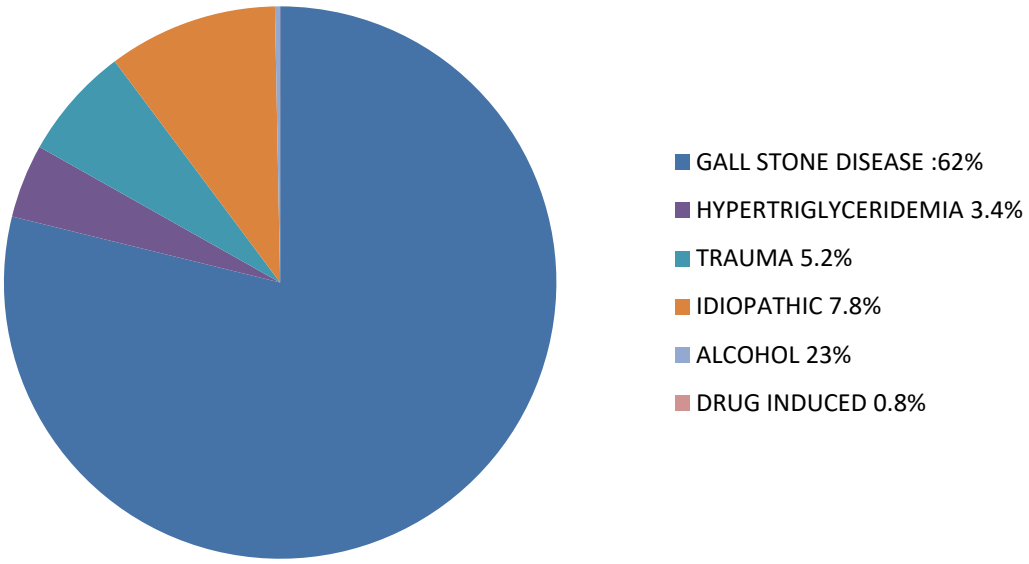


TABLE 9: D-DIMER ASSOCIATION WITH ACUTE PANCREATITIS :

Acute Pancreatitis	N	%
Definite	97	84.3
Moderate	18	15.7
Total	115	100

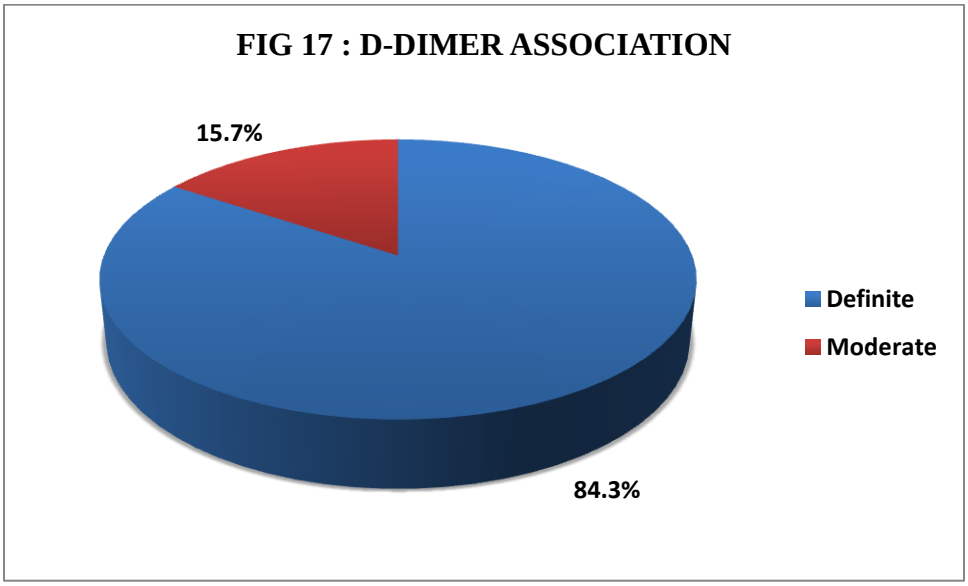


Table 10: Distribution of D DIMER according to Acute Pancreatitis:

D DIMER	Acute Pancreatitis				p value
	Definite		Moderate		
	Mean	SD	N	%	
DAY 1	4701.6	2880.7	503.9	164.0	<0.001*
DAY 3	5204.9	3029.4	560.6	167.5	<0.001*
DAY 5	5861.5	3402.9	662.2	186.6	<0.001*

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

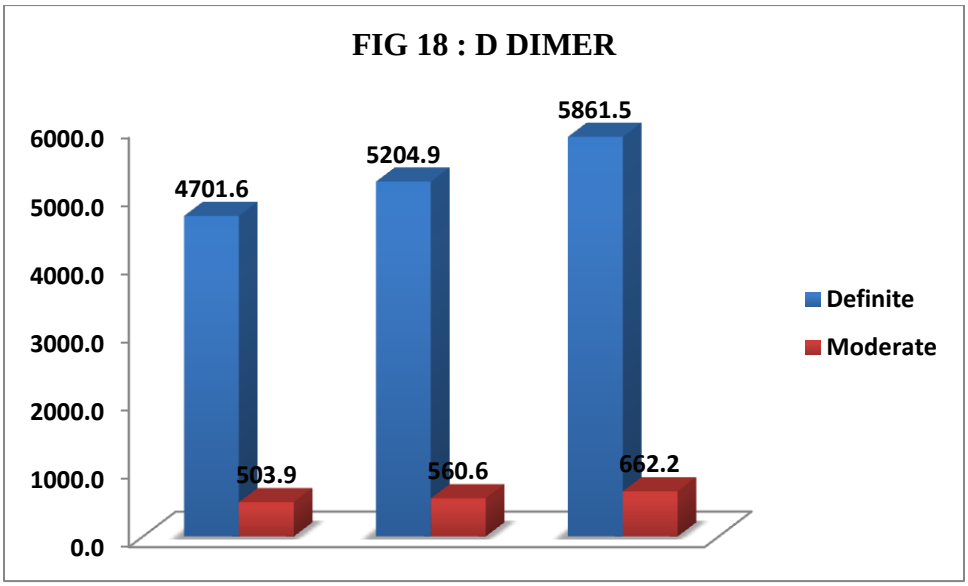


Table 11: Pearson Correlation of D Dimer at Day 1 with Day 3 & Day 5:

Pearson Correlation of D Dimer at Day 1 with	**DAY 3**		**DAY 5**	
	r value	**p value**	**r value**	**p value**
	0.941	<0.001 *	0.853	<0.001 *

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

Figure 19a: Pearson Correlation of D Dimer at Day 1 with Day 3

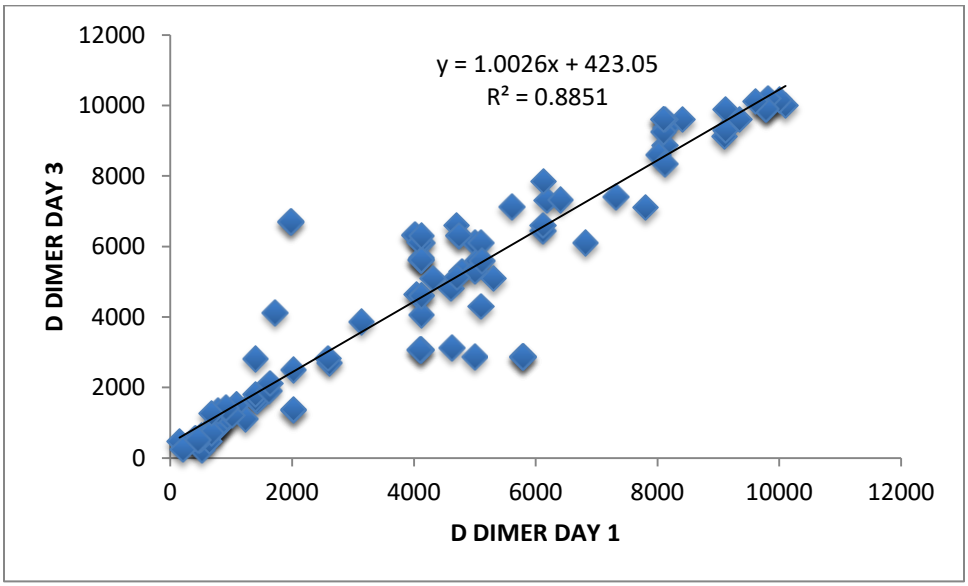


Figure 19b: Pearson Correlation of D Dimer at Day 1 with Day 5:

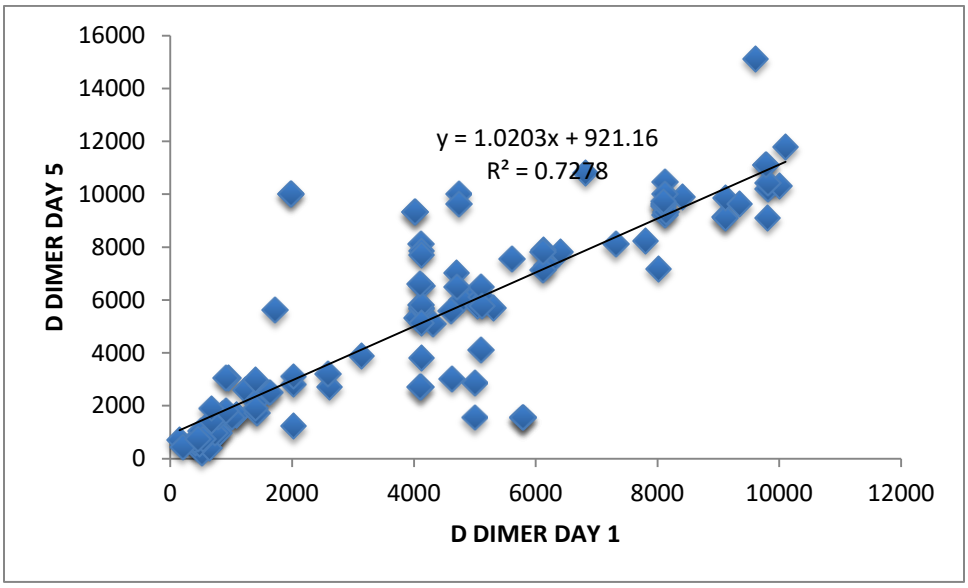


Table 12: Distribution of Cases according to Ransons score :

Ransons score (%Mortality)	**N**	**%**
0-2(3%)	92	80
3-4(15%)	21	18.3
5-6(40%)	2	1.7
Total	115	100

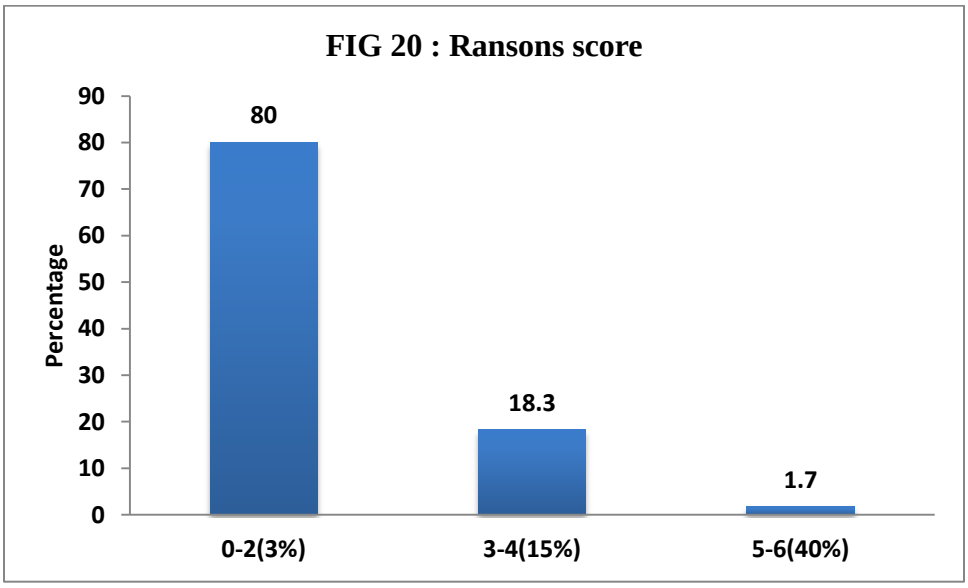


Table 13: Distribution of Cases according to SOFA score :

SOFA score (%Mortality)	N	%
0-6(<10%)	78	67.8
7-9(15-20%)	29	25.2
10-12(40-50%)	4	3.5
13-14(50-60%)	2	1.7
15(>80%)	2	1.7
Total	115	100

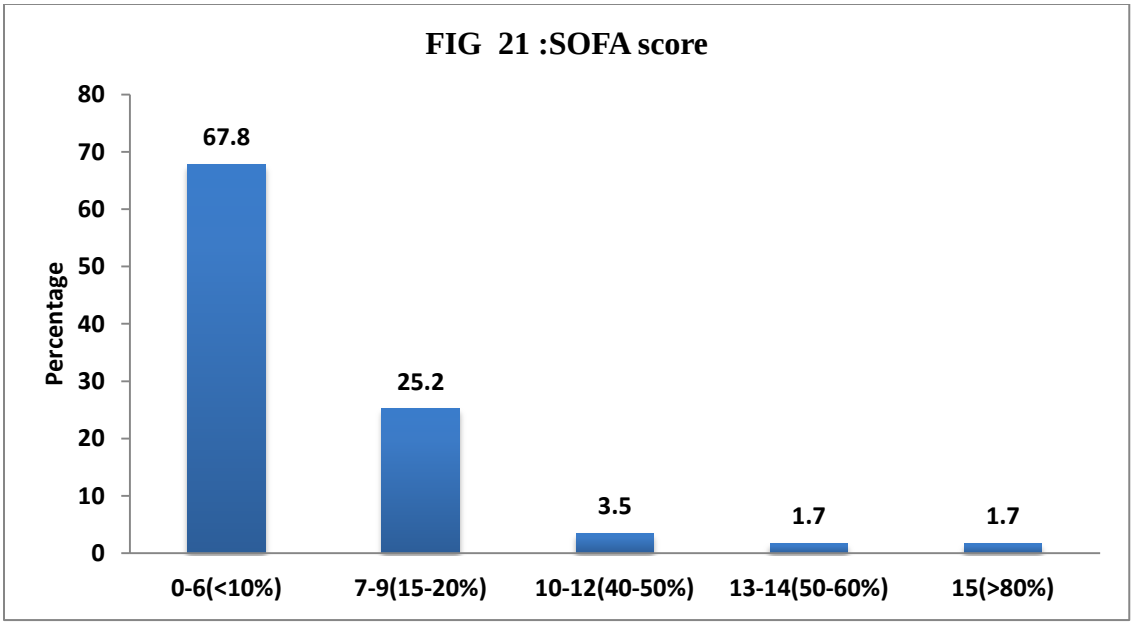


Table 14: Distribution of Cases according to APACHE 2 score:

APACHE 2 score (%Mortality)	N	%
0-4(4%)	93	80.9
5-9(6%)	0	0
10-14(12%)	17	14.8
15-19(22%)	5	4.3
Total	115	100

FIG 22:APACHE 2 score

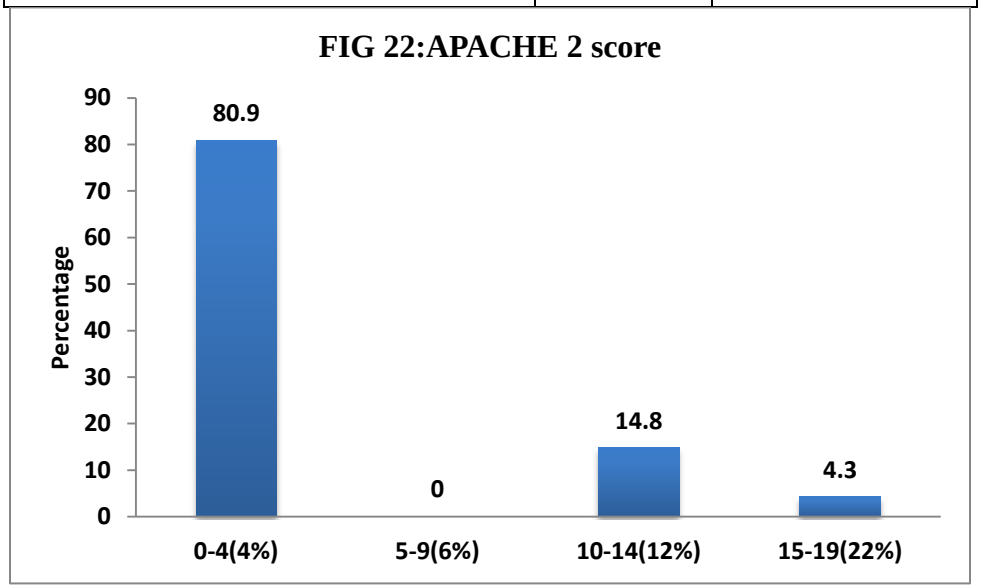


Table 15: ROC Analysis of Scores in Predicting Acute Pancreatitis:

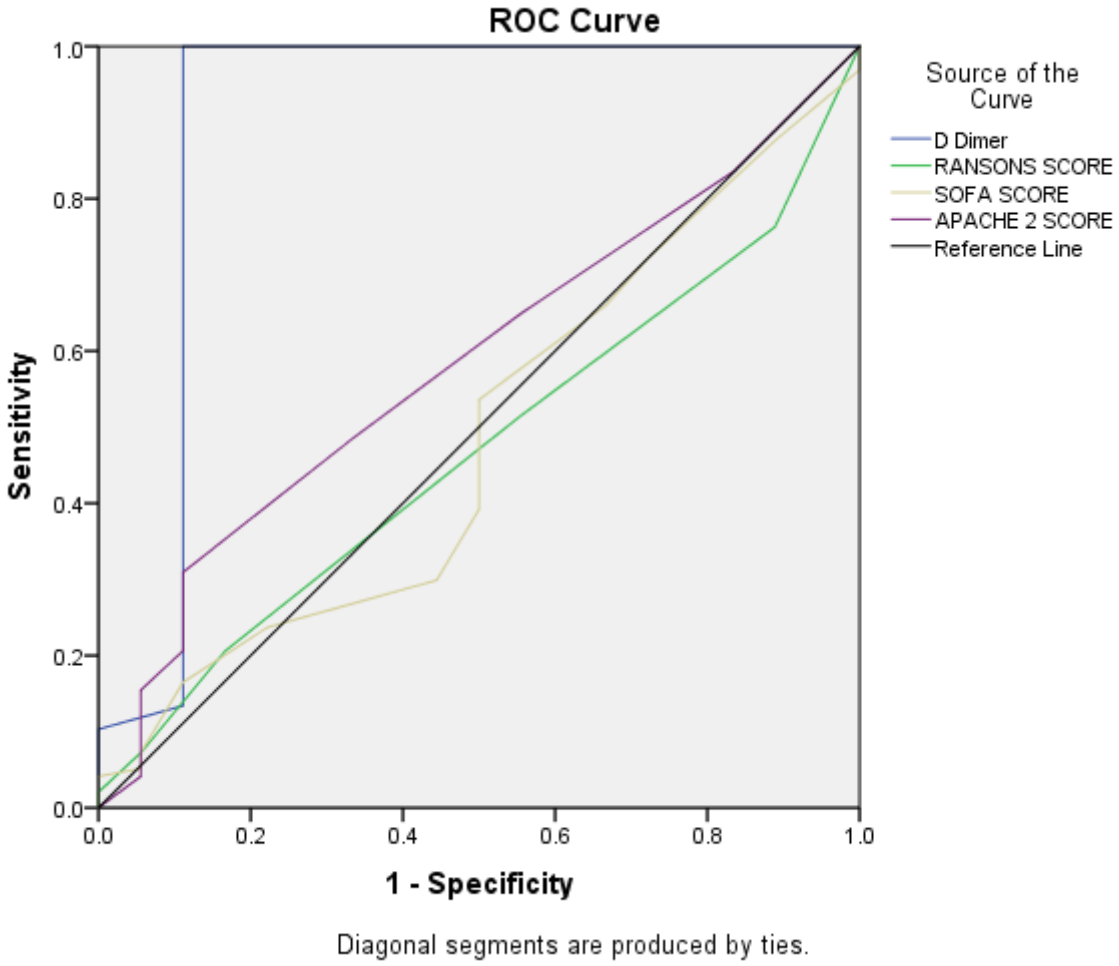
Parameters	Area Under the Curve	p value	95% Confidence Interval	
			Lower Bound	Upper Bound
D Dimer	96.0%	<0.001 *	0.74	1.00
Ransons Score	46.9%	0.680	0.34	0.60
SOFA Score	48.4%	0.829	0.34	0.63
APACHE 2 Score	58.4%	0.256	0.45	0.72

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

TABLE 16 :SENSITIVITY AND SPECIFICITY PARAMETERS :

Parameters	cutoff value	Sensitivity	Specificity
D Dimer	965.5	94.0%	86.2%
Ransons Score	1.5	51.5%	44.4%
SOFA Score	4.5	53.6%	50.0%
APACHE 2 Score	1.5	64.9%	44.4%

Figure 23: ROC Curve of Scores in Predicting Acute Pancreatitis:



Out of 115 patients, 96 patients presented with mild acute pancreatitis and 19 patients presented with severe acute pancreatitis.

In mild group the D-dimer values ranges from 500-1500. In severe attack group, the D-dimer value ranges from 1500-4100.

The severity of acute pancreatitis was assessed by correlating the scoring systems with outcome in terms of organ failure and mortality, based on SOFA score.

Out of 96 patients of mild acute pancreatitis, organ failure was present in only 1 patient with no mortalities in this group. Out of the 19 patients who presented with severe attack,5 developed organ failure and 2 deaths .

TABLE 17: CORRELATION WITH ORGAN FAILURE:

	ORGAN FAILURE		TOTAL
D-DIMER	YES	NO	
500-1500 (mild AP)	01	95	96
1500-4100 (severe AP)	05	14	19
TOTAL	06	109	115

Sensitivity	83.33%
Specificity	90.90%
Positive Predictive Value	55.56%
Negative Predictive Value	97.56%
Diagnostic Accuracy	90.00%

TABLE 18: CORRELATION WITH MORTALITY:

	MORTALITY		TOTAL
D-DIMER	YES	NO	
500-1500 (mild AP)	00	96	96
1500-4100 (severe AP)	02	17	19
TOTAL	02	113	115

Sensitivity	100%
Specificity	95%
Positive Predictive Value	50%
Negative Predictive Value	100%
Diagnostic Accuracy	96%

TABLE 19: COMPLICATIONS :

COMPLICATIONS	NO. OF PATIENTS	PERCENTAGE
ARF	28	24.3%
MODS	12	10.34%
SEPSIS	04	3.4%
ARDS, UGI BLEED , OTHERS	03	2.6%

7) **DISCUSSION:**

This study was conducted in the department of general surgery, BLDE SHRI B M PATIL MEDICAL COLLEGE , HOSPITAL VIJAYAPURAA . The 115 persons with features of acute pancreatitis who fulfilled the inclusion criteria were enrolled in this study after obtaining an informed consent.

Acute pancreatitis is a relatively common disorder which presents with a wide range of symptoms clinically. It is also associated with very high morbidity and mortality. Hence early diagnoses and prompt treatment would help in prevent unnecessary deaths .

A relatively simple parameter D-dimer was used to predict the severity of acute pancreatitis. It was also used to predict the early occurrence of organ failure. An important difference between this study and the previous ones is that, to increase accuracy, the plasma level of D-dimer levels were monitored for 3 days and the maximum and mean values of all results were used as predictors, instead of using the level on admission.

A genuine attempt was also made to compare this study with previous similar studies done before and well as simultaneous comparison with other routine scoring systems that is Ranson's scoring , APACHE 2 scoring and SOFA score .

This examination has shown that both the greatest and the mean values of D-dimer in the 1, 3,5 days after confirmation had all the earmarks of being exact markers of the seriousness of AP and were amazingly significant in forecast of numerous organ involvement and failure .

Disturbance of the coagulative system has long been thought to be implicated in the pathogenesis of the systemic and local complications of pancreatitis[43.] As for

D-dimer, which is a fibrin degradation product, there have been very few studies so far about its value in the prediction of severity during AP.

Majority of the patients in present study were in the age group of 31-40years (27.6%) with a mean age of 43.8 ± 14.7 years. The earlier study also reported the mean age of 42yrs done by Anil Kumar M S ET al[39] which was comparable to the present study. Another past similar study by Dejan Radenkovic et al (50yrs)[10] reported that patients mean age was 50yrs and study by Lu Ke et al[40] done previously showed comparable results(47yrs).

The mean age of non-survivors in this study was found to be 54 years as compared to survivors being 41.23 years. Taking 54yrs of age as cut-off value, increasing age was found to be correlated well with increasing incidence of mortality. Thus age also helps in predicting the outcome of severe acute pancreatitis.

Acute pancreatitis was found to be 9.1 times more common in males than females in this study and is similar to the previous study done by Anil Kumar M.S et al (8.8:1)[39]. It is also comparable to another similar study done by Lu Ke , Hai-bin Ni et al(6.6:1)[40] .

The most common etiological factor in this study was gall stone disease (62%), and matches with the study done by Lu Ke , Hai-bin Ni et al[40] (60%) and Dejan Radenkovic et al[10] (67%) but did not correlate with the study done by Anil Kumar M. S., Ranjith Kothagattu et al [39](23%) in which alcohol consumption was the most common cause (80%).

The most common presentation was predominantly abdominal pain (85%), followed by vomiting (27%), fever (21%) & other manifestations.

The set cut off of D-dimer of more than 500micro g/l was used to assess disease severity , based on previous studies in this regard[39] . That is in the study done by Anil Kumar M. S., Ranjith Kothagattu were AUC (0.650 , 0.65) significant correlation with prediction of organ failure . According to this set cut off, in our study, 84.3% showed definite association with acute pancreatitis and 15.7% showed moderate association with disease .

The values of d-dimer shows an increasing trend from day 1 to day 5 , that is suggestive of increased association with severity of acute pancreatitis and is similar to the study done by Anil Kumar M. S., Ranjith Kothagattu et al[39] .

Irrespective of whether D-dimer concentrations were measured during the first hours of admission or 24 hours later, excellent diagnostic accuracy was obtained.

This is an important finding as it is one of the very few parameters that reveal an extremely high diagnostic accuracy within the first hours after symptom onset.

Both the maximum and mean levels of D-dimer on day 1, 3 and 5 after admission were comparable with the maximum and mean APACHE II scores (i.e., common prognostic factor and scoring system for the severity of acute pancreatitis). ROC curve analysis was also applied for these parameters (Fig. 12), and their predictive powers are shown in Table 12.

According to the AUCs of each parameter, D-dimer seemed to have predictive power similar to that of the APACHE II score and Ranson's score. These results were comparable to a study done previously by Zhang, Guang-Quan et al[41].

The patients developing MODS in this study was determined by observing the progressive increase in d-dimer values from day 1 to day 5 and compared to the

SOFA scoring systems .It was observed that those showing MODS according to the SOFA score were having a exponentially higher d-dimer values[39].

Our results showed that both maximum and mean values of D-dimer correlated well with the maximum and mean values of the Ransons and APACHE II score, especially with the APACHE II score[39-41], which was thought to be more reliable.

Additionally, the results of ROC curve analysis also support the idea that Ddimer could be a better predictor as evidenced by significantly greater AUCs for the prediction of both MODS and pancreatic infection. This is comparable to the study done by Lu Ke , Hai-bin N et al[40] .

Sensitivity and specificity of predicting organ failure, in this study with a D-dimer value of more than 500micro g/l was found to be 83.33% and 90.90% respectively, with a positive and negative predictive value of 55.56% and 97.56% respectively. Diagnostic accuracy of this study was found to be 90%. This is very similar to previous study[39] .

In this study, the patients with D-dimer values suggestive of mild AP showed no mortality but patients with severe AP had 2 mortalities which is comparable to previous study done by Anil Kumar M. S., Ranjith Kothagattu et al (3 deaths)[39].

In this study, 24.3% developed acute renal failure, 10.34% developed MODS, 3.4% developed septicemia and 2.6% developed other complications like ARDS, UGI bleed, etc. This correlates to the previous studies done by Anil Kumar M. S., Ranjith Kothagattu et al[39] and is comparable to the study done Dejan Radenkovic et al [10].

These complications were more likely seen in patients with a d-dimer value of more than 1500, hence concluded that these are the patients in high risk group, who requires intensive monitoring and probably early intervention if necessary.

The sensitivity(94%) and specificity(86.2%) in the present study is higher than a previous similar study done by Maeda et al[42], with a sensitivy of 85% and specificity of 67%. The differences in the present study could be explained by the fact that we have evaluated d-dimer not only on day1 but also on day 3 and 5 to increase the strength of association of d-dimer in predicting outcome .

8) SUMMARY:

This was a observational study of 115 patients of acute pancreatitis admitted and treated in our hospital during the period from November 2018 to june 2020.

In the present study, 31-40 years age group was predominant (20.6 %). Majority were the male patients (91.3%) in the study. Two factors, i.e. gall stones and alcohol consumption were considered to be most common etiological factors in our study in the study. Out of which, gall stones is the major etiological factor observed in the patients (62%).

Age of the total patient was compared with raised d-dimer values using spearman's and was considered significant .Youngest patient was 18yr old and oldest was 78yrs old. Common modes of presentation in this study was pain abdomen (85%), vomiting(27%) and fever(25%) .

D-dimer values measured on admission day and subsequently on day 3 and 5 showed increased association with acute pancreatitis , as well as predicted early the occurrence of organ failure .

The population of patients under this study that developed organ failure were significant. Around 24% developed Acute renal failure , another 10% developed MODS, and 3% developed sepsis.

Diagnostic accuracy and ROC analysis of D-dimer score was compared with the remaining three scoring systems that is APACHE 2 , SOFA , and Ranson's score were (p less than 0.001). The D-dimer score showed significant diagnostic accuracy in predicting Acute pancreatitis with AUC OF 96%. It has a sensitivity of 94% and specificity of 86.2% . This is much higher than the sensitivity and specificity compared with other three studies .

9) CONCLUSION:

Acute Pancreatitis is an inflammatory condition which can be self limiting or progress to severe systemic disease with multi organ involvement. Coagulative derangements and disturbance of the microcirculation are known to occur in the acute phase of AP and are related to its severity. D-dimer has a good predictive power in early phase of AP.

The present study demonstrates that measurement of plasma levels of D-dimer on the admission to the hospital promises to be an accurate method for identifying the patients who will develop OF in the further course of AP.

As it is well established in every routine laboratory, the widespread availability is another advantage for the use in daily clinical practice and under emergency conditions. Based on the results of the present study, further investigation, preferably in a multicenter setting, seems to be very promising.

D-dimer shows more sensitivity, specificity, positive and negative value, and diagnostic accuracy in predicting the severity of acute pancreatitis. Hence, D-dimer was found to predict more number of patients, likelihood of progressing to severe disease. D-dimer is considered a simple, good and cost effective diagnostic marker in predicting severity in acute pancreatitis.

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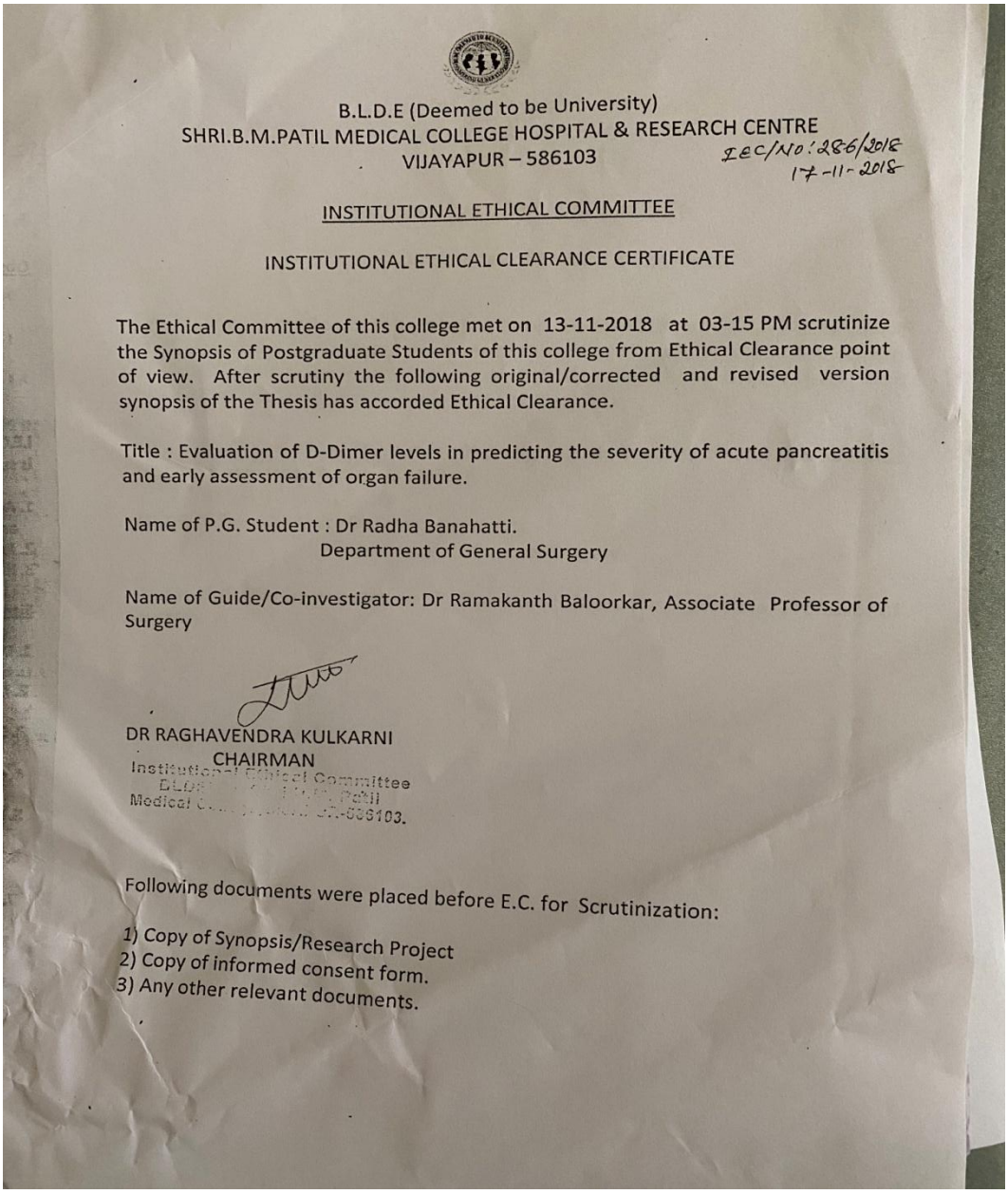
11)ANNEXURE I:

ETHICAL CLEARANCE CERTIFICATE



B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/No:286/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Evaluation of D-Dimer levels in predicting the severity of acute pancreatitis and early assessment of organ failure.

Name of P.G. Student : Dr Radha Banahatti.
Department of General Surgery

Name of Guide/Co-investigator: Dr Ramakanth Baloorkar, Associate Professor of Surgery

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDE (Deemed to be University) Shri B.M. Patil
Medical College Hospital & Research Centre, Vijayapur-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

12)**ANNEXURE II**

SAMPLE INFORMED CONSENT FORM

EVALUATION OF D-DIMER LEVEL IN PREDICTING THE SEVERITY OF ACUTE PANCREATITIS AND EARLY ASSESSMENT OF ORGAN FAILURE

B.L.D.E(D.U)'s SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA – 586103, KARNATAKA.

TITLE OF THE PROJECT:

PRINCIPAL INVESTEGATOR: **DR .RADHA R BANAHATTI**

Department of General Surgery

Email:- radhabanahatti@.com

PG GUIDE: **DR. RAMAKANTH BALOORKAR** **MS**

Associate Professor of Surgery

B.L.D.E. Deemed to be University's

Shri B.M. Patil Medical College & Research Centre,

Sholapur Road, Vijayapura 586103

PURPOSE OF RESEARCH:

I have been informed that this study will evaluate the efficacacy of d-dimer in predicting the severity of acute pancreatitis and assess organ failure.

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

PROCEDURE:

I understand that relevant history will be taken. I will undergo detailed clinical examination after which necessary investigations will be done whenever required, which would help the investigator for

appropriate management.

RISKS AND DISCOMFORTS:

I understand that I/my ward may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that I/my wards participation in this will help to evaluate the efficacacy of d-dimer in predicting the severity of acute pancreatitis and assess organ failure early.

CONFIDENTIALITY:

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

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

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. DR.RADHA R BANAHATTI is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

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

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

INJURY STATEMENT:

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

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

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

Dr. RAMAKANTH B	Dr .RADHA R BANAHATTI
(Guide)	(Investigator)

STUDY SUBJECT CONSENT STATEMENT:

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

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

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

13) ANNEXURE III :

PROFORMA:

CASE NO:

- Name: IP no.:
- Age/sex: DOA:
- Occupation: DOD:
- Address:

CHIEF COMPLAINTS:

PAIN ABDOMEN:

- DURATION
- SITE
- MODE OF ONSET
- RADIATION
- AGGREVATING FACTORS
- RELIEVING FACTORS
- OTHER COMPLAINTS
- PAST HISTORY OF SIMILAR COMPLAINTS
- PERSONAL HISTORY

PAST HISTORY:

- SIMILAR COMPLAINTS
- DIABETES
- HYPERTENSION

PERSONAL HISTORY:

- DIET
- APPETITE
- SLEEP
- BOWEL/BLADDER
- HABITS

GENERAL PHYSICAL EAMINATION:

- PALLOR
- ICTERUS
- PULSE
- BP

SYSTEMIC EAMINATION:

PER ADOMEN:

INSPECTION

PALPATION

PERCUSSION

AUSCULATION

DIAGNOSIS:

INVESTIGATIONS:

D-DIMER LEVELS:

1. DAY 1
2. DAY 3
3. DAY 5

- **RANSONS SCORE**:
- **At admission:**
  - Age in years:
  - WBC count :
  - Blood glucose :
  - Serum AST :
  - Serum LDH :

  - **Within 48 hours:**
  - Serum calcium :
  - Hematocrit fall :
  - Oxygen:
  - BUN increased by 1.8 or more mmol/L (5 or more mg/dL) after IV fluid hydration
  - Base deficit (negative base excess) > 4 mEq/L

- Sequestration of fluids:

- **APACHE II SCORE**:
- PaO2 (depending on FiO2)
  - Temperature
  - Mean arterial pressure
  - pH arterial
  - Heart rate
  - Respiratory rate
  - Sodium (serum)
  - Potassium (serum)
  - Creatinine
  - Hematocrit
  - White blood cell count
  - Glasgow Coma Scale

SOFA SCORE:

1. RESPIRATION(PaO):
2. COAGULATION(PLATELET COUNT):
3. LIVER(BILIRUBIN):
4. CVS(HYPERTENSION):
5. CNS(GLASGOW COMA SCALE):
6. KIDNEY(S.CREATININE):

MANAGEMENT :

INFERENCE

KEY TO MASTERCHART :

SL NO : SERIAL NUMBER

IP NO : IN PATIENT NUMBER

M:MALE, F: FEMALE

I: INFERENCE , S:SCORE

14)MASTERCHART :

SL NO.	NAME	AGE/SEX	I P NO.	D DIMER DAY 1	DAY 2	DAY 3	INFERENCE	ransons S AND I	SOFA S AND I	APACHE 2 S,I
1	Madivalappa b m	45y/M	35374	5794	2876	1553	D	2 AND 3%	0 AND1%	0 and4%
2	Shrikanth l n	45y/M	37477	4740	6300	10000	D	1 AND 3%	0 AND1%	1 and4%
3	Bhalbhimayya	35y/M	41025	5000	2870	1550	D	0 AND 3%	0 AND1%	2 and4%
4	Mahadevi	75y/F	42851	410	475	610	M	1 AND 3%	2 AND 1%	3 and4%
5	Tukaram	30y/M	822	4700	6600	7010	D	1 AND 3%	2 AND 1%	4 annd4%
6	Chandrashekhar	38y/M	4415	576	613	818	M	3 AND 15%	9 AND15%	10 AND15%
7	Gous B M	30y/M	7229	4118	3064	2693	D	1 AND 3%	2 AND 1%	0 and4%
8	Parshuram J	37y/M	7321	1983	6700	10000	D	1 AND 3%	2 AND 1%	1 and4%
9	Gangadhar M A	52y/M	8846	763	1012	1500	D	4 AND 15%	9 AND15%	10 AND15%
10	Vasudev M	55y/m	10420	4020	6310	9330	D	0 AND 3%	4 AND 1%	0 and4%
11	Prakash	60y/M	14902	5000	6100	6140	D	0 AND 3%	4 AND 1%	1 and4%
12	Sadashiv	32y/M	15023	9781	9900	11100	D	2 AND 3%	4 AND 1%	2 and4%
13	Mallanna	62y/M	12006	4790	5300	6010	D	2 AND 3%	5 AND9%	0 and4%
14	Anil	42y/M	12008	1092	1500	1640	D	1 AND 3%	5 AND9%	1 and4%
15	Parasappa	65y/M	17368	5794	2876	1550	D	2 AND 3%	5 AND9%	2 and4%
16	Anand	23y/M	17473	790	876	1050	D	0 AND3%	6 AND10%	3 and4%
17	Kumar	36y/M	16984	5102	5600	6121	D	0 AND3%	6 AND10%	3 and4%
18	Naseem	44y/M	21512	960	1266	3031	D	0 AND3%	6 AND10%	3 and4%
19	Mallimath	67y/M	26428	2021	1360	2800	D	1 AND3%	5 AND9%	4 annd4%
20	Basappa	45y/M	23428	5050	5600	5779	D	1 AND3%	1 AND4%	0 and4%
21	Kumar	36y/M	23412	1234	1100	2600	D	2 AND3%	1 AND4%	0 and4%
22	Gurubasappa	46y/M	27231	2023	2500	3108	D	2 AND 3%	2 AND 1%	0 and4%
23	Maruti	30y/M	28628	4043	4643	5321	D	1 AND3%	2 AND 1%	1 and4%
24	Devaraj	21y/M	28609	2617	2700	2711	D	0 AND3%	4 AND 1%	1 and4%
25	Niayz	37y/M	27466	860	1020	1678	D	3 AND15%	8 AND15%	12 AND15%
26	Chanappa	40y/M	38201	4118	3064	8123	D	1 AND3%	5 AND9%	1 and4%
27	Rahul	40y/M	38188	9810	9960	9100	D	0 AND3%	4 AND 1%	2 and4%
28	Gurubasappa	65y/M	37514	8413	9610	9881	D	2 AND3%	3 AND4%	2 and4%
29	Parvati	40y/F	38190	9813	10001	10201	D	2 AND3%	2 AND 1%	2 and4%
30	Ramesh	64y/M	38189	10102	10000	11800	D	0 AND3%	1 AND4%	3 and4%
31	Manappa	35y/M	37513	4610	4810	5600	D	0 AND3%	9 AND15%	3 and4%
32	Yuraj	29y/M	32545	6183	7313	7300	D	2 AND3%	9 AND15%	4 annd4%
33	Sangeeta	46y/F	37867	8123	8860	9200	D	2 AND3%	8 AND15%	3 and4%
34	Sanju	32y/M	37710	6820	6100	10800	D	0 AND3%	7 AND15%	3 and4%
35	Annappa	60y/M	36450	5310	5100	5700	D	1 AND3%	6 AND10%	1 and4%
36	Shreemant	72y/M	36453	9101	9120	9130	D	2 AND3%	5 AND9%	1 and4%
37	Mahesh	62y/M	36859	8101	9600	9548	D	3 AND15%	8 AND15%	13 AND15%
38	shrikant	33y/M	37011	7800	7100	8232	D	1 AND3%	5 AND9%	2 and4%

39	Ramappa	46y/M	37110	9123	9300	9101	D	0 AND3%	4 AND 1%	2 and4%
40	Sharanappa	66y/M	39446	8020	8600	7180	D	1 AND3%	4 AND 1%	2 and4%
41	Shivanand	44y/M	37772	10010	10158	10302	D	3 AND15%	9 AND15%	10 AND15%
42	Bhimavva	62y/M	37982	6412	7320	7814	D	3 AND15%	9 AND15%	11 AND15%
43	Rajesh	45y/M	39517	9120	9888	9860	D	0 AND3%	3 AND4%	3 and4%
44	Laxman	58y/M	38338	8143	9362	9310	D	1 AND3%	3 AND4%	3 and4%
45	Mahesh	39y/M	38469	4123	5680	5660	D	2 AND3%	2 AND 1%	3 and4%
46	Devendra	36y/M	38671	9820	10200	10410	D	0 AND3%	2 AND 1%	4 annd4%
47	Yamanappa	53y/M	38964	4320	5100	5100	D	2 AND3%	1 AND4%	4 annd4%
48	Ramesh	45y/M	39153	8130	8340	10450	D	0 AND3%	1 AND4%	0 and4%
49	Gangappa	50y/M	39157	9348	9610	9611	D	0 AND3%	8 AND15%	1 and4%
50	Gurubasappa	29y/M	39158	4121	4060	3801	D	2 AND3%	7 AND15%	2 and4%
51	Hulgappa	48y/M	39892	2596	2830	3210	D	2 AND3%	6 AND10%	0 and4%
52	Pradeep	30y/M	38168	4744	6310	9612	D	3 AND15%	8 AND15%	13 AND15%
53	Sangamma	65y/F	41026	5000	5300	2870	D	1 AND3%	5 AND9%	0 and4%
54	sidappa h a	43y/M	17239	450	500	610	M	2 AND3%	4 AND 1%	0 and4%
55	Ramya s teli	29y/F	41149	4141	6100	6516	D	2 AND3%	3 AND4%	1 and4%
56	Manjunath T	52y/M	41270	576	613	820	M	2 AND3%	2 AND 1%	1 and4%
57	Prakash H	44y/M	41740	4100	3060	2696	D	0 AND3%	1 AND4%	2 and4%
58	Prakash N	61y/M	41723	1980	6700	10001	D	3 AND15%	8 AND15%	13 AND15%
59	Arasina K	41y/M	41682	760	1001	1410	D	0 AND3%	7 AND15%	2 and4%
60	Chetan P	24y/M	42031	4022	6333	9310	D	1 AND3%	6 AND10%	3 and4%
61	Malappa K	45y/M	42083	5100	6100	6500	D	0 AND3%	5 AND9%	3 and4%
62	Parvati M	43y/M	42034	9781	9900	11100	D	0 AND3%	4 AND 1%	3 and4%
63	Prapoadhandji P	85y/M	42134	4710	5123	6481	D	3 AND15%	9 AND15%	13 AND15%
64	Haseena N	63y/F	42133	1090	1500	1640	D	2 AND3%	3 AND4%	4 annd4%
65	Chandrashekhar	54y/M	42008	5790	2876	1550	D	2 AND3%	2 AND 1%	4 annd4%
66	Ramakanth A	53y/M	2102	790	870	1055	D	1 AND3%	1 AND4%	0 and4%
67	Govind D	35Y/M	2099	4112	5612	5800	D	3 AND15%	11 AND46%	13 AND15%
68	Shankar T	18y/M	954	920	1260	3031	D	1 AND3%	5 AND9%	0 and4%
69	Tulasi J	36y/F	2802	2021	1380	1212	D	2 AND3%	4 AND 1%	1 and4%
70	Moreppa K	66Y/M	3122	5123	5600	5778	D	2 AND3%	3 AND4%	1 and4%
71	Prakash W	58y/M	3576	1423	1610	1712	D	2 AND3%	2 AND 1%	2 and4%
72	Hanumant M	45y/M	3924	680	712	720	M	0 AND3%	1 AND4%	2 and4%
73	Sundar B	34Y/M	3977	516	234	210	M	3 AND15%	12 AND 57%	16 and24%
74	Prakash M	64Y/M	4303	6120	6440	7123	D	2 AND3%	9 AND15%	3 and4%
75	Soujanya	34y/F	4323	812	940	971	M	1 AND3%	8 AND15%	0 and4%
76	Veeresh M	24y/M	4464	412	560	584	M	2 AND3%	7 AND15%	1 and4%
77	Revappa	68y/M	5745	1720	4120	5612	D	2 AND3%	6 AND10%	2 and4%
78	Nagraj K	51y/M	5836	8100	9243	9610	D	5 AND40%	15 AND80%	16 and24%
79	Sidappa K	26Y/M	6275	1403	1680	2121	D	1 AND3%	5 AND9%	0 and4%

80	Bupesh c	33y/M	7283	512	640	673	M	2 AND3%	4 AND 1%	0 and4%
81	Nandini	35y/F	7942	490	584	634	M	4 AND15%	3 AND4%	1 and4%
82	Hanumantray	39y/M	5368	6132	7843	7900	D	2 AND3%	2 AND 1%	1 and4%
83	Umakanth P	45Y/M	9349	646	480	400	N	1 AND3%	1 AND4%	2 and4%
84	Ningappa M	58Y/M	9469	740	812	960	M	1 AND3%	8 AND15%	2 and4%
85	Shrishail W	25y/M	10693	780	1340	1561	D	3 AND15%	8 AND15%	13 AND15%
86	Vijayakumar	41y/M	15631	480	516	550	M	2 AND3%	7 AND15%	1 and4%
87	Basavraj L	40Y/M	16257	4123	5610	5700	D	6 AND40%	15 AND80%	16 and24%
88	Irayya W	30Y/M	9059	4123	4610	5800	D	4 AND15%	4 AND80%	11 AND15%
89	Shashikumar M	34Y/M	8482	4100	6123	6600	D	1 AND3%	7 AND15%	4 annd4%
90	Nagaraj l	36y/M	7613	1400	1811	1890	D	4 AND15%	10 AND58%	10 AND15%
91	Veeresh M	26Y/M	4465	1620	1910	2501	D	3 AND15%	12 AND 57%	16 and24%
92	Tarun Hugar	26y/M	4400	4123	5610	7862	D	2 AND3%	7 AND15%	4 annd4%
93	Hanumant M	46y/M	3920	410	560	713	M	1 AND3%	7 AND15%	3 and4%
94	Manjunath C	35Y/M	3888	8123	9611	10000	D	3 AND15%	14 AND66%	13 AND15%
95	Basu ankalagi	78y/M	9476	1016	1200	1560	D	3 AND15%	14 AND66%	16 and24%
96	Raman racheri	30y/M	10586	150	480	710	M	0 AND3%	7 AND15%	3 and4%
97	Kallappa N	58y/M	35134	3140	3860	3880	D	4 AND15%	9 AND15%	11 AND15%
98	Anand P	32Y/M	13546	510	545	1040	**D**	3 AND15%	9 AND15%	10 AND15%
99	Prakash K	58Y/M	3576	910	1423	1810	D	2 AND3%	6 AND10%	1 and4%
100	Rachappa B	53Y/M	35651	540	612	746	M	2 AND3%	6 AND10%	2 and4%
101	Revappa P	76Y/M	13681	5100	4300	4123	D	1 AND3%	6 AND10%	1 and4%
102	Shobha k	28y/F	17453	8100	9611	9730	D	2 AND3%	5 AND9%	2 and4%
103	Devappa H	40Y/M	5105	1640	2122	2500	D	1 AND3%	5 AND9%	3 and4%
104	Ravikanth Y	38Y/M	1528	1400	2812	2961	D	0 AND3%	5 AND9%	3 and4%
105	Siddalingappa	60y/M	1412	680	710	1410	D	2 AND3%	2 AND 1%	1 and4%
106	Ayappa L	38Y/M	819	210	250	460	M	2 AND3%	2 AND 1%	1 and4%
107	Balachandra	35y/M	43774	7320	7400	8100	D	2 AND3%	2 AND 1%	0 and4%
108	Mareppa K	66Y/M	3122	4123	4600	5120	D	1 AND3%	4 AND 1%	4 annd4%
109	Manjunath	22y/M	16865	460	510	730	M	1 AND3%	4 AND 1%	3 and4%
110	Jagadish B	30Y/M	13681	4123	6300	7700	D	1 AND3%	4 AND 1%	3 and4%
111	Sachin D	32/M	18342	4630	3123	3010	D	4 AND15%	7 AND15%	10 AND15%
112	Pramod R	27Y/M	1832	9610	10120	15110	D	0 AND3%	2 AND 1%	2 and4%
113	Alisab K	25Y/M	18138	6123	6600	7800	D	2 AND3%	2 AND 1%	1 and4%
114	Vilas G	17Y/M	18124	5610	7133	7560	D	0 AND3%	1 AND4%	0 and4%
115	Pirahmed G	30Y/M	39043	680	1270	1900	D	1 AND3%	1 AND4%	0 and4%