STUDY OF ROLE OF C- REACTIVE PROTEIN AND LACTATE DEHYDROGENASE AS PROGNOSTIC FACTORS OF SEVERITY IN ACUTE PANCREATITIS

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI-600 032

in partial fulfillment of the regulations for the award of the degree of

M.S. GENERAL SURGERY - BRANCH I

COIMBATORE MEDICAL COLLEGE

Coimbatore - 641 014

MAY 2020

UNIVERSITY REGN NO: 221711306

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This is to certify that the dissertation entitled **"STUDY OF ROLE OF C- REACTIVE PROTEIN AND LACTATE DEHYDROGENASE AS PROGNOSTIC FACTORS OF SEVERITY IN ACUTE PANCREATITIS"** is a bonafide dissertation done by **DR.GAYATHRI. B** in Department of General Surgery, Coimbatore Medical College and Hospital and is submitted in partial fulfillment of the requirement for the Degree of **M.S. GENERAL SURGERY, BRANCH I** of the Tamilnadu Dr. M.G.R. Medical University, Chennai.

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I solemnly declare that the dissertation titled "**STUDY OF ROLE OF C- REACTIVE PROTEIN AND LACTATE DEHYDROGENASE AS PROGNOSTIC FACTORS OF SEVERITY IN ACUTE PANCREATITIS**" was done by me from January 2018 to January 2019 under the guidance and supervision of **DR. T. SRINIVASAN M.S.,** Professor, Department of General Surgery, Coimbatore Medical College and Hospital. This dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University towards the partial fulfillment of the requirement for the award of M.S Degree in General Surgery (Branch I).

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Dear **Dr.Gayathri B**

The Institutional Ethics Committee of Coimbatore Medical College, reviewed and discussed your application for approval of the proposal entitled **"Study of Role of C- Reactive Protein and Lactate Dehydrogenase as prognostic factors of Severity in Acute Pancreatities."**No.0111/2017.

The following members of Ethics Committee were present in the meeting held on 30.11.2017.conducted at MM - II Seminar Hall, Coimbatore Medical College Hospital Coimbatore-18

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We approve the Proposal to be conducted in its presented form.

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The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

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ACKNOWLEDGEMENT

Firstly I owe my reverential gratitude to the almighty for his blessings and my parents for being on my side and helping me complete this dissertation.

I am obliged to record my immense gratitude to **DR. B. ASOKAN M.S. M.Ch (Plastic Surgery)** Dean, Coimbatore Medical College Hospital for providing me with all the facilities required to complete this study.

I am extremely thankful indebted to my respected teacher and guide **DR. T. SRINIVASAN M.S,** Professor, Department of General Surgery for his valuable guidance and constant help throughout this study.

I would like to express my sincere thanks to Professor and HOD **Dr..A. Nirmala M.S. DGO**, Professor **Dr. V. LekshmiNarayani M.S**., Associate Professor **Dr. V.S. Venkatesan M.S. and** Associate Professor **Dr. R. Narayanamoorthy M.S.**

I am also thankful to Assistant Professors **DR. V.Umamaheshwari M.S** and **DR. R.Vijayshankar M.S** for their help and support.

I express my gratitude to all my Professors, Assistant Professors, Staff members of Department of General Surgery and all my Postgraduates colleagues and friends for their help and co-operation during this study and preparation of this dissertation.

Lastly I express my sincere thanks to all my patients without whom this study would not have been possible.

DR. GAYATHRI. B

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LIST OF ABBREVIATIONS

AP	:	Acute Pancreatitis
CRP	:	C-Reactive Protein
LDH	:	Lactate Dehydrogenase
USG	:	Ultrasonogram
CECT	:	Contrast Enhanced Computerised Tomography
CT	:	Computerised Tomography
ERCP	:	Endoscopic Retrograde Cholangiopancreaticography
MRCP	:	Magnetic Resonance Cholangiopancreaticogram
ARDS	:	Acute Respiratory Distress Syndrome
INH	:	Isoniazid
PT	:	Prothrombin Time
DIC	:	Disseminated Intravascular Coagulation

INTRODUCTION

Acute pancreatitis is most common, life-threatening condition in day-to-day life requiring hospitalisation. About 25% of the patients develop severe acute pancreatitis and eventually will develop complications such as necrosis, pseudocyst and organ failure. The mortality of severe acute pancreatitis ranges from 15 to 35% whereas its mild form has mortality of only about 1%.

Most of the patients of acute pancreatitis are treated conservatively. In about 25-30% of the patients, secondary infection of necrosis can occur, mortality of whom reaches 100% if left untreated. It is therefore necessary to assess the severity of the disease and start treatment in patients admitted with acute pancreatitis in order to prevent development of complications.

Various scores have been used for assessing the severity of acute pancreatitis such as RANSON score, APACHE score and GLASCOW score. (5)Various serum markers have recently emerged in diagnosing the severity of acute pancreatitis. This study emphasizes the importance of C-reactive protein and lactate dehydrogenase as markers in diagnosing severe acute pancreatitis.

AIMS AND OBJECTIVES

1. To study the level of CRP and LDH in patients admitted with acute pancreatitis.

2. Assessment of severity of acute pancreatitis using serum amylase and CT findings.

3. To assess the correlation of CRP and LDH with CT findings for assessing severity.

REVIEW OF LITERATURE

Acute pancreatitis is defined as acute inflammatory process of the pancreas with little or no fibrosis and ranges from mild self-limiting disease to critical disease characterised by infected pancreatic necrosis to multiple organ failure.(2) Alcohol intake and gallstones are most important and common causes of acute pancreatitis.

Other causes of pancreatitis include ERCP, hyperlipidemia, hypertriglyceridemia, biliary tract operations, pancreatic neoplasms, parasitic infection of the biliary tree, sphincter of oddi dysfunction and pancreas divisum. Age at presentation and gender distribution depends upon the etiology of acute pancreatitis.

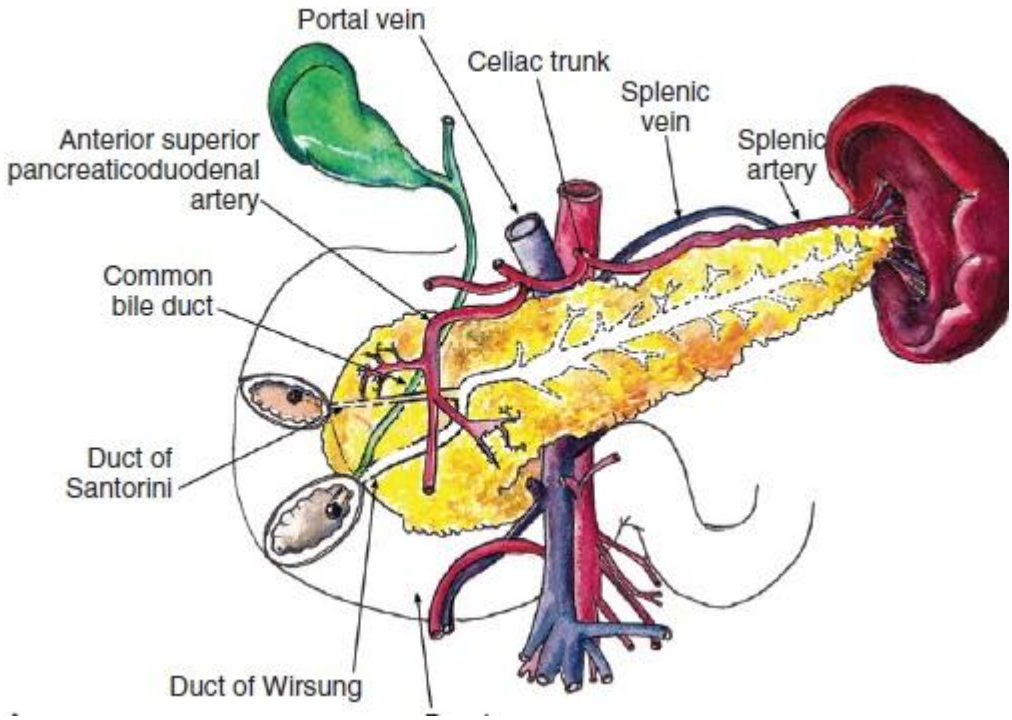
Embryology:

Pancreas is an endodermally derived organ, having two distinct parts viz exocrine and endocrine pancreas. These two tissues present together inside the pancreas despite its morphological functions. Endocrine pancreas is called as Islets of Langerhans consisting of 5 subtypes of cells secreting glucagon, insulin, somatostatin, ghrelin and pancreatic polypeptide hormones and it constitutes only 2% of the total pancreas. The remaining 98% is formed by exocrine pancreas and it is composed of acinar and ductal epithelial cells.

Anatomy:

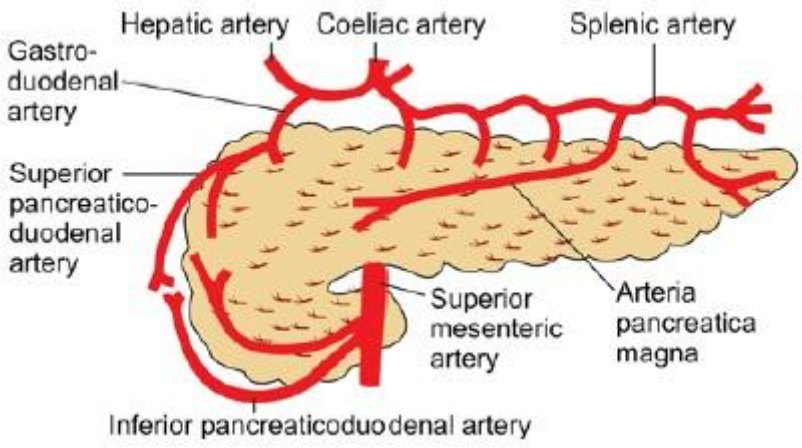
The pancreas is a glandular organ having four main parts namely head, neck, body and tail. It also has an accessory lobe or uncinate process . It is situated retroperitoneally, lying obliquely with the head and the uncinate process lies in the curvature of second part of duodenum and the tail at the region of hilum of the spleen. It is 12 to 15cms in length. Accumulation of acinal cells forms the acini which secretes bicarbonates and digestive enzymes into centrally placed acinar space which are connected to tiny ductal networks. These ducts join to form main pancreatic ducts namely duct of wirsung and duct of santorini. These ducts drain into the duodenum through major and duodenal papilla at the ampulla of vater.

The islet of langerhans are scattered through the pancreas and produces endocrine hormones.



Blood supply:

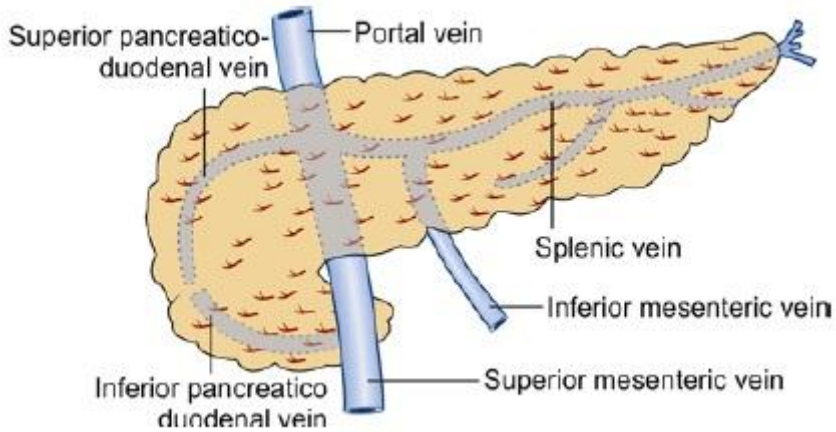
The arterial supply of pancreas comes primarily from celiac trunk and superior mesenteric arteries by forming arterial arcades within the pancreas. From the celiac trunk, splenic and common hepatic arteries arises. Splenic artery gives rise to dorsal and greater pancreatic arteries and the common hepatic artery gives rise to gastroduodenal artery. Gastroduodenal artery is divided into anterior and posterior superiorpancreaticoduodenal arteries around the head of the pancreas and these two anastamoses with anterior and posterior inferiorpancreaticoduodenal arteries which are the branches of superior mesenteric artery.



Venous drainage:

The head and neck of the pancreas drains into superior and inferior pancreaticoduodenal veins.

Body and tail of the pancreas drains into splenic vein.



Venous drainage mainly drains into the portal system.

Lymphatic drainage:

Body and tail drains into pancreaticosplenic nodes.

Head and neck of the pancreas drains into lymph nodes present along the superior mesenteric artery, hepatic and pancreaticoduodenal arteries.

Nerve supply:

Pancreas derives its nerve supply from autonomic nervous system- both by sympathetic and parasympathetic fibres.

Vagus is parasympathomimetic and sympathetic supply is from splanchnic nerves.

Thus, for treatment of chronic pain arising from pancreatic tumours, celiac plexus block or ablation can be useful.

Physiology:

Normal pancreatic juice is bicarbonate rich fluid containing 15grams of protein. Normal pancreas secretes around 2.5 litres ofpancreatic juice /day. It helps in alkalinising the duodenal content and thereby in digestion.pancreas secretes inactive proenzymes in to the duodenum and it is activated by trypsin in the duodenum. Amylase and lipase are also secreted into the duodenum in active forms. Basal secretin of these enzymes are low in resting phase and increases during neural and hormonal stimulation. (3)Its secretion is controlled

by secretin and cholecystokinin. Protein part of the pancreatic juice is secreted by acinar cells whereas fluid and electrolytes are secreted by duct cells.

Pancreatic juice secretion is very low at resting phase. During eating, 10% of pancreatic juice stimulation is done in the cephalic phase mediated through acetylcholine whereas gastric phase mediates15% of secretion through gastrin release and vagal stimulation. During intestinal phase, 75% stimulation occurs through secretin due to duodenal acidification and by the release of bile and cholecystokinin following the entry of fat and proteins into the duodenum.

Serum amylase:

Normal level is 200-250units. Its level increases in acute pancreatitis. Half life of serum amylase is 24hours. (3)

It is not very sensitive. It also increases in other conditions as follows:

- diseases of salivary gland
- Mesenteric ischaemia
- Ruptured aortic aneurysm
- Intestinal obstruction
- Ectopic gestation
- Salpingitis
- Perforated duodenal ulcer

Two types of amylase is there. Amylase-P is specically increased in pancreatitis. Amylase-S is increased in other conditions also other than pancreatitis. Amylase level is also measured in ascitic fluid. If ascitic fluid amylase is higher than serum amylase , it is highly significant for pancreatitis. Amylase level in pseudocyst of pancreas is very high. It is not used to predict the severity of pancreatitis. (3)

Persistent elevation suggests pseudocyst, abscess and ascitis. 10% of cases of necrotising pancreatitis will have normal level of serum amylase. Increase in amylase due to pancreatic causes is higher than due to nonpancreatic causes.

Amylase enters the lymphatics and circulation from the basal part of acinar cells and also, weakened intercellular adhesions in pancreatitis allow amylase to seep into the space to enter circulation.

Amylase inhibitors are present in the circulation sometimes which masks the serum amylase level.

Occasionally amylase binds with albumin which cannot be cleared from the circulation normally leading to false rise in serum amylase level, which causes false positives in the absence of pancreatitis. It occurs in 0.2% of the population.

Pancreatitis:

Pancreatitis is defined as inflammation of the pancreas which may be acute, chronic or relapsing which may lead to various complications.

Classification:

Two types of classification are there.

1) Marseilles classification: based on clinical classification

2) Trapnell's classification: based on etiology

Marseilles classification:

- Acute pancreatitis
- Acute relapsing pancreatitis
- Chronic relapsing pancreatitis
- Chronic pancreatitis

In acute pancreatitis, changes are reversible whereas in chronic pancreatitis, changes are irreversible.

Trapnelle's classification:

- Biliary tract disease due to stones
- Alcohol
- Trauma
- After biliary, gastric, splenic surgeries, ERCP
- Hyperparathyroidism
- Hypercalcemia, hyperlipidemia
- Diabetes
- Porphyria
- Autoimmune conditions
- Vascular diseases
- Drugs like steroids, INH, diuretics, tetracycline, estrogens, septran, azathioprine, valproic acid, 5-aminosalicylic acid, etc.,
- Biliary ascariasis, clonorchis sinensis
- Viral infections
- Infectious mononucleosis

- Mycoplasma
- Pancreas divisum
- Idiopathic

Acute pancreatitis:

Acute pancreatitis is defined as acute inflammation of normally existing pancreas. It may be first attack or relapsing one with normally existing gland in between. The most common causes are alcoholism and biliary tract disease.

Alcohol causes direct injury to the pancreas, hypersecretion of pancreatic juices or injury by free radicals. Biliary tract disease causes pancreatitis due to pancreatic duct obstruction.

All these factors cause spasm of sphincter of oddi or increased secretion of pancreatic enzymes which causes activation of trypsinogen into trypsin which in turn causes activation of other enzymes such as proelastase to elastase and prolipase to lipase. elastase causes capillary rupture and lipase causes metabolisation of triglycerides to glycerol and fatty acids. These fatty acids combines with calcium and forms saponified fat. Sequestrated fluid, saponified fat, toxins and blood all combine to form chicken broth fluid.

Lecithinase, amylase and other factors like lysolecithinase, prostaglandins, bradykinins, cytokines, free radicals, platelet activating factor

and tumour necrosis factor are also released which causes local and systemic effects. Infection results in bacteremia and septicaemia.

Sequestration of large amount of toxic fluid leads to hypovolemiaand in turnleads to hypovolemic shock.

Pathogenesis of development of complications:

These toxins causes acute tubular necrosis of renal tubules which in turn leads to acute renal failure.

Pancreatitis can also lead to development of left sided pleural effusion.

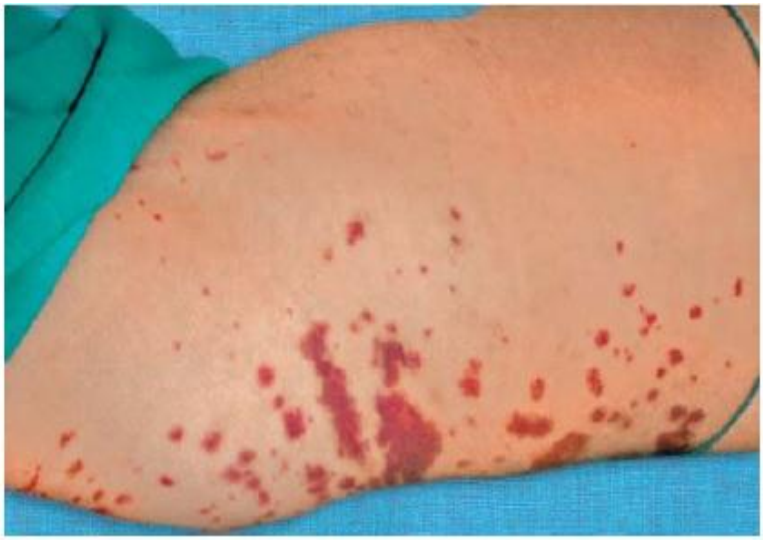
Lecithinase causes decrease in the surfactant in the alveoli of lung which in addition to infection causes pulmonary insufficiency, ARDS and eventually respiratory failure.

Hypocalcemia can occur due to usage of calcium in the process of saponification of fats.

Diffuse oozing occurs in the pancreatic bed in pancreatitis for which platelets are used which leads to disseminated intravascular coagulation.

In severe cases, acute hemorrhagic necrotising pancreatitis can occur due to extensive necrosis with hemorrhage. It is called as fulminant pancreatitis, which has got higher mortality.

It can also cause hemorrhagic pots and ecchymosis in the retroperitoneal regions- in the flanks called as grey turner's sign, around the umbilicus called as cullen's sign, below the inguinal ligament called as fox's eye.



GREY TURNER SIGN

Hereditary pancreatitis:

Genetic mutation causes defective trypsin inhibitors which leads to high concentration of intrapancreatic trypsin which in turn causes activation of other enzymes and subsequently pancreatitis.

Autoimmune pancreatitis:

It is associated with primary sclerosing cholangtis,biliary cirrhosis, sjogrens syndrome. Lymphoplasmacytic autoimmune pancreatitis is another entity in which there is high level of IgG4, pancreatitis, pancreatic head mass,

pancreatic and biliary strictures(double duct sign), mimicking pancreatic carcinoma.

Idiopathic pancreatitis:

Though it is due to some unidentified cause, it is probably due to GB sludge or microcrystals or due to malfunction of sphincter of oddi which can be successfully managed by cholecystectomy and sphicterotomy.

Atlanta classification

1. Acute oedematous pancreatitis (80%): Milder form, mortality is <1%
2. Acute necrotising pancreatitis (20%): Characterised by pancreatic and peripancreatic necrosis. Mortality is ≈ 15% - 30%

ATLANTA CLASSIFICATION

Interstitial acute pancreatitis with mortality less than 1%.
Necrotizing pancreatitis.

- Sterile necrosis with mortality 10%.
- Infected necrosis with mortality 30-40%. It is confirmed by CT guided aspiration and Gram's stain. When confirmed, needs pancreatic necrosectomy.

PRESENT CLASSIFICATION

Organisms causing pancreatitis:

Infection is polymicrobial.

Mostly infection spreads from gallbladder, colon or small bowel by means of transmural migrationorhematogenous route. Most common organism causing pancreatitis are E.Coli followed by klebsiella, enterococcus. Others include staphylococci, pseudomonas, proteus, anaerobes, candida, enterobacter.

Clinical features:

- Sudden onset of abdominal pain mostly in the epigastric region which is referred to back.

  Pain is severe and relieved or reduced by leaning forward.

- Vomiting, fever, tachypnoea

- Tenderness, rebound tenderness, guarding, rigidity and abdominal distension

- Jaundice (due to cholangitis). Jaundice may also be due to bile duct disease / obstruction or cholestasis.

- Features of shock and dehydration such as Oliguria, hypoxia and acidosis.

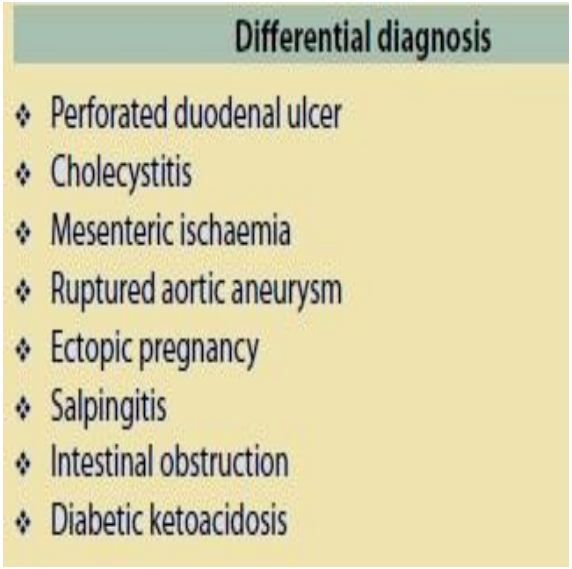
- Grey-Turner’s sign, Cullen’s sign, Fox sign.
- Hematemesis and malena due to duodenal necrosis, gastric erosions, decreased coagulability or disseminated intravascular coagulation.
- Hiccough is occasionally present and it is mostly refractory.
- Ascites
- Paralytic ileus is common.(3)
- Pleural effusion (20%), pulmonary oedema, consolidation, features of ARDS can occur.
- Neurological abnormalities occurs due to toxaemia, fat embolism, hypoxia, respiratory distress. It may ranges from mild psychosis to coma.

Metabolic and biochemical changes:

- Hypovolemia due to capillary leak and vomiting. It causes raise in haematocrit, blood urea, serum creatinine levels.
- Hypoalbuminaemia which becomes more relevant after fluid correction.
- Hypocalcaemia is either due to decreased level of albumin or loss of ionized calcium. Hypocalcaemia occurring due to reduced ionised

calcium carries poor prognosis. Response of calcium reserve in bone to PTH is also reduced.

- Total count is raised with significant neutrophilia.
- Thrombocytopenia, raised FDP, decreased fibrinogen, prolonged partial thromboplastin time and PT—are common. Later it can lead to the development of DIC.
- Hypochloraemic metabolic alkalosis is common due to repeated vomiting.
- Reduced insulin secretion, increased glucagon and catecholamine secretion lead to the development of hyperglycaemia. It is more pronounced in diabetics.
- Hyperbilirubinaemia due to biliary stone/ obstruction or cholangitis or non-obstructive cholestasis.
- Hypertriglyceridaemia is more common especially in patients with hyperlipidemia.
- Methemalbuminemia occurs rarely and when it occurs in acute pancreatitis , it indicates poor prognosis.



DIFFERENTIAL DIAGNOSIS OF PANCREATITIS

Management of acute pancreatitis:

The management of acute pancreatitis covers a wide range of spectrum of disease. It ranges from mild , moderate to severe acute pancreatitis. The duration of hospital stay and mortality varies between these categories. The mortality of mild pancreatitis is less than 1% and for moderate pancreatitis , the mortality is around 10%. The mortality of severe acute pancreatitis ranges from 20 to even greater than 50%. Early identification of these categories is thus important.

Various scoring systems such as RANSON'S score, and various serum markers are used in assessing the severity of acute pancreatitis.

The diagnosis of acute pancreatitis is made when the patient presents with severe epigastric pain radiating to the back and rise in serum amylase and lipase level more than three times the normal. Imaging is only required when these criteria are not met.

Investigations:

- Serum amylase is very high (>1000 Somogyi units) or shows rising titre. Amylase level rises immediately after the onset of disease and peaks 3to 5 days after the onset. There is no significant correlation of serum amylase level with the severity of the disease.

- Amylase creatinine clearance ratio is increased. It is – urine amylase/serum amylase X serum creatinine/ urinary creatinine X 100. Normal value is 1-4%. In acute pancreatitis, its value increases upto 6%.

- Serum lipase- it is more specific than amylase. It persists for longer period than amylase. Pancreas is the only source for lipase unlike amylase, hence more specific than amylase.

- Serum lactescence which is a metabolite of triglycerides. Most specific in hereditary hyperlipidaemia or in pancreatitis due to alcohol.

- Serum trypsin is most accurate for pancreatitis, but it is not commonly used.

- Trypsinogen activation polypeptide (TAP) assay in serum and urine. It is useful in assessing the severity of the acute pancreatitis.

- CRP (>150 mg/L) is also useful(7). Phospholipase A2, LDH levels

  are also often assessed. These are useful in assessing the severity of acute pancreatitis.

Local complications of acute pancreatitis

CONTENT	ACUTE (<4 WEEKS, NO DEFINED WALL)		CHRONIC (>4 WEEKS, DEFINED WALL)	
	NO INFECTION	INFECTION	NO INFECTION	INFECTION
Fluid	Acute pancreatic fluid collection (APFC)	Infected APFC	Pseudocyst	Infected pseudocyst
Solid ± fluid	Acute necrotic collection (ANC)	Infected ANC	Walled off necrosis (WON)	Infected WON

LOCAL COMPLICATIONS OF ACUTE PANCREATITIS

Imaging in acute pancreatitis:

The most important imaging modality is ultrasound which is used to identify stones or sludge in the gallbladder or common bile duct. When these are present, it indicates biliary pancreatitis.

In the absence of stones or gallbladder sludge, measurement of diameter of common bile duct should be done. If there is dilatation of common bile duct >8mm in patients of 75 years or younger or >10mm in patients of older age group, elevation of ALT >100U/L and ALT level greater than AST strongly

suggests that the disease is of biliary origin. Endoscopic USG is also used to detect the presence of gallstones or sludge.

CECT is used to diagnose peripancreatic collections and pancreatic parenchymal or peripancreatic fat necrosis. Magnetic resonance imaging

(MRI) or ultrasonography are the only modalities capable of demonstrating the presence or absence of necrosis in such collections. The absence of necrosis is a prerequisite for the collection to be called a pseudocyst. A true pseudocyst in the initial 4 weeks of acute pancreatitis is very rare.

Sequential organ failure assessment (SOFA) score in acute pancreatitis

	0	1	2	3	4
Respiration (PaO_2FIO_2) (mm Hg)	>400	≤400	≤300	≤200 with respiratory support	≤100 with respiratory support
Coagulation Platelets ($x10^1$ per µL)	>150	≤150	≤100	≤50	≤20
Liver Bilirubin (µmol/L)	<20	20–32	33–101	102–204	>204
Cardiovascular Hypotension	No hypotension	MAP <70mm Hg	Dopamine ≤5 or dobutamine (any dose)*	Dopamine >5 or epi ≤0.1* or norepi ≤0.1*	Dopamine >15 or epi >0.1* or norepi >0.1*
Central nervous system Glasgow coma score	15	13–14	10–12	6–9	<6
Kidney Creatinine (µmol/L) or urine output	<110	110–170	171–299	300–440 or <500 ml/day	>440 or <200 ml/day

Prediction of severity:

Most of the classifications are used to predict the past or present severity of the disease, it is important to predict the future outcome of the patient. This prediction is important in making decisions about fluid therapy, and the need for ERCP. The most widely used method is Ranson's or modified Glascow's score. Both use clinical and biochemical parameters for predicting severity. These parameters are scored over 48 hours of admission. If there are 3 or more positives, it is considered as severe disease. Another score used is APACHE II which is scored at 24 hours of admission. If there are 8 or more positives, it is considered severe. C- reactive protein is also used to predict the severity. CRP level > 150mg/dl has similar accuracy of predicting severity as Ranson's score.(4)

The more recently proposed score is BISAP (Bedside Index for Severity of Acute Pancreatitis)is calculated from blood urea nitrogen (>25mg/dl), altered mental status (GCS<15), age >60years, presence of severe inflammatory response syndrome (SIRS) and pleural effusion.

Classification of severity of acute pancreatitis:

A four- category classification of acute pancreatitis is developed. The key variables of severity are local complications and systemic compications.

Four categories of acute pancreatitis severity based on organ failure and local complications			
DETERMINANTS	NO LOCAL COMPLICATIONS	STERILE LOCAL COMPLICATIONS	INFECTED LOCAL COMPLICATIONS
NO ORGAN FAILURE	MILD	MODERATE	SEVERE
TRANSIENT ORGAN FAILURE	MODERATE	MODERATE	SEVERE
PERSISTENT ORGAN FAILURE	SEVERE	SEVERE	CRITICAL

Ranson's prognostic signs of pancreatitis	
Criteria for acute pancreatitis not due to gallstones	
At admission	During the initial 48 h
Age >55 y	Hematocrit fall >10 points
WBC >16,000/mm^3	BUN elevation >5 mg/dL
Blood glucose >200 mg/dL	Serum calcium <8 mg/dL
Serum LDH >350 IU/L	Arterial PO_2 <60 mm Hg
Serum AST >250 U/dL	Base deficit >4 mEq/L
	Estimated fluid sequestration >6 L
Criteria for acute gallstone pancreatitis	
At admission	During the initial 48 h
Age >70 y	Hematocrit fall >10 points
WBC >18,000/mm^3	BUN elevation >2 mg/dL
Blood glucose >220 mg/dL	Serum calcium <8 mg/dL
Serum LDH >400 IU/L	Base deficit >5 mEq/L
Serum AST >250 U/dL	Estimated fluid sequestration >4 L

Necrotising pancreatitis is defined as the presence of parenchymal necrosis and/or necrosis of peripancreatic fat.

Commonly Used Predictive Laboratory Scoring Systems in Acute Pancreatitis and Their Cutoff for Predicted Severe Pancreatitis

Predictive Score	Cutoff
APACHE II	≥8 in first 24 hours
BISAP	≥3 in first 24 hours
Modified Glasgow (or Imrie)	≥3 in first 48 hours
Ranson	≥3 in first 48 hours
Urea at admission	>60 mmol/L
C-reactive protein	>150 U/L in first 72 hours

Early and late organ failure:

Acute pancreatitis runs a biphasic course. The first phase is severe inflammatory response syndrome and lasts for about 2 weeks. The second phase is counteractive anti-inflammatory response syndrome (CARS) which is characterised by stage of immunosupression. (1)

Organ failure in SIRS phase is related to severe systemic inflammation and not to local infection whereas organ failure in CARS phase is related to secondary infections such as infected necrosis of the pancreas. Infection can also occur in SIRS phase but mostly of bacteremia and pneumonia.

Organ failure occurs in all organs but most commonly involves pulmonary and cardiovascular system. The gastrointestinal system is also affected by acute pancreatitis and it is reflected by urine output. Organ failure

due to SIRS occurs at 2 days of admission. Half of the patients who die from acute pancreatitis are due to organ failure and not due to infected necrosis.

The clinical course of necrotizing pancreatitis is highly variable, and there may be a continuum between the SIRS and CARS phases. Discrimination into three scenarios is potentially helpful to understand the underlying pathophysiologic processes:

- Early onset organ failure – occurs in week 1. Intensive care management and supportive measures are needed. If clinical deterioration occurs through week 3 to 5, it indicates infective necrosis.

- Without organ failure, if clinical condition is suddenly complicated by deterioration, there are high chances of infected necrosis.

- Even after 2 to 3 weeks of intensive care treatment, if there is no improvement in condition of the patient, a fine- needle aspiration of the collection should be done to differentiate between persistent SIRS and infected necrosis. However, if there are presence of gas bubbles on CT scan, no further diagnostic procedures is required.

TREATMENT:

Conservative management:

SIRS phase:

Adequate fluid resuscitation with pain management is the mainstay of treatment. Pain is the main complaint of pancreatitis and its management is a clinical priority. Intravenous analgesia is mandatory before starting oral intake. Those patients with a mild pain are managed with NSAIDs such as methimazole 2g/8h IV and those with severe pain are managed with opioids such as buprenorphine 0.3mg/ 4h IV.

Other analgesics used in the management of acute pancreatitis are pentazocine, procaine hydrochloride, meperidine. Morphine should be avoided because it causes spasm of sphincter of oddi. (2)

A diuresis-guided fluid regimen (1 mL/kg/hr urine production) is required in the initial phase. Close monitoring and intravenous fluid supplementation in the initial 24 hours are most important. Crystalloid resuscitation volumes as high as 20 L may be required. In this phase, there is no need for radiological interventions as resuscitation is most important in this phase.

CARS phase:

If the patient does not improve or deteriorates, peripancreatic fluid collections or infected necrosis has to be ruled out. Presence of gas bubbles on CECT is pathognomic of infected necrosis. Some authors suggest FNAC of the collection for diagnosing peripancreatic collections or infected necrosis.

Prevention of infection:

Enteral bacteria is most common organism causing pancreatitis. Bacteremia or ventilator associated pneumonia occurs by 8 days of onset of the disease whereas infectd necrosis occurs by 25 days of onset of the disease. Bacteremia increases the risk of infection of necrosis from 38 to 65%. Persistent organ failure and bacteremia are strongest predictors of mortality. Intravenous antibiotics, enteral nutrition, selective bowel decontamination, probiotics all have been tried to lower the rate of infection.

Enteral nutrition:

Enteral nutrition is hypothesized to reduce bacterial overgrowth and also to improve intestinal mucosal barrier function and thereby reducing infections. In patients of mild disease, oral feeding can be started as early as possible. In patients of severe pancreatitis, enteral feeding through nasojejunal route can be started by 3 days if the patient is not expected to resume oral diet. It reduces both infections and mortality compared to total parenteral nutrition.

Systemic intravenous antibiotics:

Many studies suggests the use of prophylactic systemic antibiotics in lowering the rate of infected necrosis. A recent metaanalysis showed that there is no beneficial effect in prophylactic use of antibiotics.

Selective bowel decontamination (SBD):

Since the small bowel is the main source of infection, selective bowel decontamination is needed in acute pancreatitis. There was one randomised control study in which compared the effect of norfloxacin, amphotericin, colistin in paients with acute pancreatitis which showed significant reduction in mortality by reducing the chances of infection with gram negative organisms.

Interventional treatment:

SIRS phase: (first and second weeks)

Interventions in this phase are only to treat the acute life threatening complications or prevention of further deterioration. Currently the only means to prevent deterioration is by ERCP with sphicterotomy, but its therapeutic significance is yet to be established. Surgical necrosectomy in this phase is associated with higher mortality and hence it is contraindicated within 72hours, since the main clinical picture in this phase is systemic inflammation rather than presence or absence of infected necrosis.(1)

The only acute complications which warrants intervention are abdominal compartment syndrome, bowel ischemia,perforation and severe bleeding unresponsive to angiographic coiling.

According to 2007 international consensus meeting,abdominal compartment syndrome is defined as intraabdominal pressure higher than 20mmhg with signs of new organ failure. Percutaneous drainage can be used as initial management if drainage fluid is present.

If percutaneous drainage does not lower the abdominal pressure immediately or if thereis more free fluid, laparatomy and decompression is advised. It is not advisable to explore the pancreas because it is too early to remove the necrosis safely and there is risk of introduction of infection into the necrosis.

It is not advisable to do percutaneous drainage of sterile collections since there is risk of introducing iatrogenic infection by drains.

The current concept of acute biliary pancreatitis is gallstone, released from the gallbladder into the common bile duct causing temporary obstruction at the level of ampulla of vater which in turn causes obstruction of pancreatic duct with obstruction of pancreatic flow and secondary damage to exocrine cells of pancreas due to autodigestion of exocrine pancreas.

Theoretically, ERCP with sphicterotomy causes early relief by stopping the process of acute pancreatitis at an early stage and thus reducing the complications.

But recent study showed that there is no benefit of routine ERCP in patients of severe biliary pancreatitis in absence of cholangitis.

A recent study demonstrated that ERCP with endoscopic sphincterotomy reduces the complication rate in patients with predicted severe biliary pancreatitis and cholestasis (bilirubin >2.3 mg/dL [>40 μmol/L] and/or dilated common bile duct). (1)

Intervention in CARS phase:

During this second phase the patient has another episode of systemic infection or sepsis caused by secondary infection of necrosis. Evidence of pancreatic or peripancreatic necrosis with signs of sepsis is the most acceptable indication of intervention.

In this phase, less frequent indications for intervention include gastric outlet obstruction, abdominal compartment syndrome, bleeding, bowel perforation and common bile duct obstruction. Intervention may be done by open laparatomy with necrosectomy or by minimally invasive surgery, endoscopic or radiographic percutaneous methods.

Intervention in case of infected necrosis: (third week and later)

It is beneficial to postpone intervention until intra or extrapancreatic collections have been encapsulated. This process ofencapsulation takes about 4 weeks and these encapsulated collections are called as ‘walled off necrosis’.

Administration of antibiotics may be needed to allow for encapsulation under the close monitoring of patient’s clinical condition and CECT scan performed at regular intervals is a valid option to postpone surgical intervention.

Necrosectomy was performed 27days after onset of the disease with a mortality rate of 25%. When performed within first 2 weeks , the mortality rate was higher of about 75%.

Based on current concept, postponing surgical intervention until 4weeks of onset of disease is widely accepted as the management of choice. This interval time is mainly determined by the completeness of encapsulation and the clinical condition of the patient.

This policy is only applicable to patients who survive the initial phase of SIRS and develop infection of necrosis with signs of sepsis in the CARS phase.

Treatment of Acute Pancreatitis in Various Clinical Scenarios

Clinical Situation	Advice	Exception
	WEEKS 1-2	
Predicted severe pancreatitis	Fluid supplementation based on urine production, enteral nutrition, adequate pain control. Not useful: routine antibiotic prophylaxis antioxidants, and oral probiotics.	
Abdominal compartment syndrome	Decompression laparotomy without accessing the retroperitoneum	Large amounts of intraabdominal fluid. In these cases percutaneous catheter drainage may be used but should lead to immediate clinical improvement.
Sterile necrosis (collections) and multiple organ failure	Treat organ failure. No evidence that necrosectomy and/or drainage of collections will improve outcome. There is evidence that drainage will increase the risk of infection.	Abdominal compartment syndrome, bowel ischemia, bleeding
	WEEK 3 AND THEREAFTER	
Infected necrosis (collections) without or with only partial encapsulation	If possible, postpone intervention using antibiotics	Rapid deterioration without treatable cause
Infected walled-off necrosis (collections)	Intervention according to the "step-up" approach, starting with (retroperitoneal) catheter drainage. If needed, followed by (minimally invasive) necrosectomy.	Lack of experience; if so, transfer the patient to a more experienced center

Types of intervention:

Catheter drainage:

It is the least invasive method for treating infected necrosis. The drain can be placed percutaneously through the left retroperitoneum or transabdominally or can be placed through the wall of stomach or duodenum transluminally. In around 55% of the patients with necrotising pancreatitis, percutaneous drainage is the only intervention needed for cure. The technical success rate for this method was 99% and the mortality rate was 17%a RCT study showed that the feasibility of this percutaneous drainage was 99%.

If the patient donot improve after adequate drainage, necrosectomy should be done as the next step. The percutaneous drain can be used as a guidance for minimally invasive necrosectomy.

This two stage approach – drainage followed by minimally invasive necrosectomy is called as stepup approach and now considered as standard of care in patients with infected necrosis.

Minimally invasive necrosis:

The most commonly used minimally invasive procedure is video assisted retroperitoneal debridement (VARD). The first step consists of placement of left sided percutaneous retroperitoneal drain through the left flank. The patient is then placed in supine position with the left side elevated. A

5-7cm incision is made and the necrotic collection is opened by the guidance of the drain. Initially the pus andthe necrotic material are removed blindly. Then a 0-degree laparascope is introduced to remove all the necrotic material under direct vision. The loosely adherent necrotic pieces are only removed in order to minimize bleeding. In contrast to percutaneous drainage, VARD allows removal of large pieces of necrotic material. The more degree of encapsulation, the more easier the necrosectomy.

Following this near total necrosectomy, two suction drains are kept. Postoperatively, continuos lavage with increasing amounts of 0.9% saline (2, 4. 6L) per day in the first 3 days. In a dutch study , the results of minimally invasive step-up approach and open necrosectomy was compared which showed significant difference with respect to development of complications and costs was observed all in favour of VARD and there was no significant difference in mortality.

A purely percutaneous minimally invasive retroperitoneal necrosectomy using operating nephroscope developed by Carter at al suggested a decrease in mortality by using this technique.

Endoscopic transluminal necrosectomy:

If VARD technique is not feasible, due to difficulty in reaching the necrotic site, endoscopic transluminal or transgastric necrosectomy can be done. The success rates ranges from 80% to 93% with mortality of 0% to 6%.

The advantages of this technique are that no abdominal incision(s) are required, and chances of external pancreatic fistula may not occur, because an internal fistula to the stomach is iatrogenically created. The chances of occurrence of incisional hernia, often difficult to treat after open necrosectomy, is also less. The major disadvantage of this technique is that the need for repeated, multiple procedures to remove sufficient amounts of necrosis.

Open necrosectomy:

Till the results of the PANTER study were published, primary open necrosectomy was considered as the standard treatment in patients with infected necrotizing pancreatitis. The most commonly used technique of open necrosectomy is laparotomy with a retroperitoneal lavage system placement after complete necrosectomy has been performed.(1)

In this technique, drains are placed in the lesser sac after necrosectomy. Continuous lavage with increasing amounts (2, 4, then 6 L) of 0.9% saline are given per day for about 3 days. Lavage is useful for many purposes such as

mechanical debridement, prevention of tube obstruction, and dilution of pancreatic juice.The mortality of this technique is approximately 25%.

Another open technique is open necrosectomy with closed packing. A group from Boston used transmesenteric approach of open necrosectomy with 11% mortality rate. The necrosed part is approached through transverse mesocolon and debridement was done bluntly, with the aim of removing all necrotic tissue and debris. The cavity is packed with gauze-stuffed Penrose drains which are removed one by one after a week.

Someof the surgeons continue to use an open abdomen strategy with regular, relaparotomies as a routine, done every 3 to 5 days. The mortality of this procedure is around 70%, hence it is advised to use this technique only as a part of rescue strategy, when it is difficult to close the abdomen.

Techniques for Treating Infected Necrotizing Pancreatitis

	Minimally Invasive	No Open Necrosectomy Needed	Mortality
Percutaneous drainage	++++	25%-55%	17%
Endoscopic transgastric necrosectomy	+++	80%-93%	0%-6%
Percutaneous retroperitoneal necrosectomy	++	86%	19%
Video-assisted retroperitoneal debridement	+	93%	19%
Open necrosectomy (reference standard)	–	–	11%-39%

Prevention of recurrent pancreatitis:

If the cause of pancreatitis are gallstones, cholecystectomy with bile duct clearance is needed to prevent recurrent attacks. Early cholecystectomy in patients with severe pancreatitis such as necrotizing pancreatitis may be harmful, as these collections may become infected secondary to cholecystectomy.

Complications of acute pancreatitis:

Complications of acute pancreatitis include pseudocyst formation, acute fluid collections, pancreatic abscess and infected necrosis, pancreatic ascites, pancreatic-pleural effusion, pancreaticoenteric and pancreatic-cutaneous fistulas.

Pancreatic pseudocyst:

A pseudocyst is defined as a localized collection of pancreatic secretions surrounded by a wall of granulation tissue or sometimes by fibrous tissue which arises as a result of acute or chronic inflammation of the pancreas, pancreatic trauma, or obstruction of the duct of the pancreas by a neoplasm. (1)The incidence of pseudocysts ranges between 50% and 75% of cystic lesions of the pancreas. They are differentiated from other peripancreatic fluid collections such as cystic neoplasms, parasitic cysts and congenital cysts by their lack of an epithelial lining and a high concentration of pancreatic enzymes within the pseudocyst, and formation of pseudocyst at least 4 weeks after an episode of acute pancreatitis or pancreatic trauma.

Pseudocysts are caused by the inflammatory response that occurs after extravasated pancreatic collections. The capsule of the pseudocyst may be thin fibrous tissue which eventually becomes thickened when the pseudocyst matures.

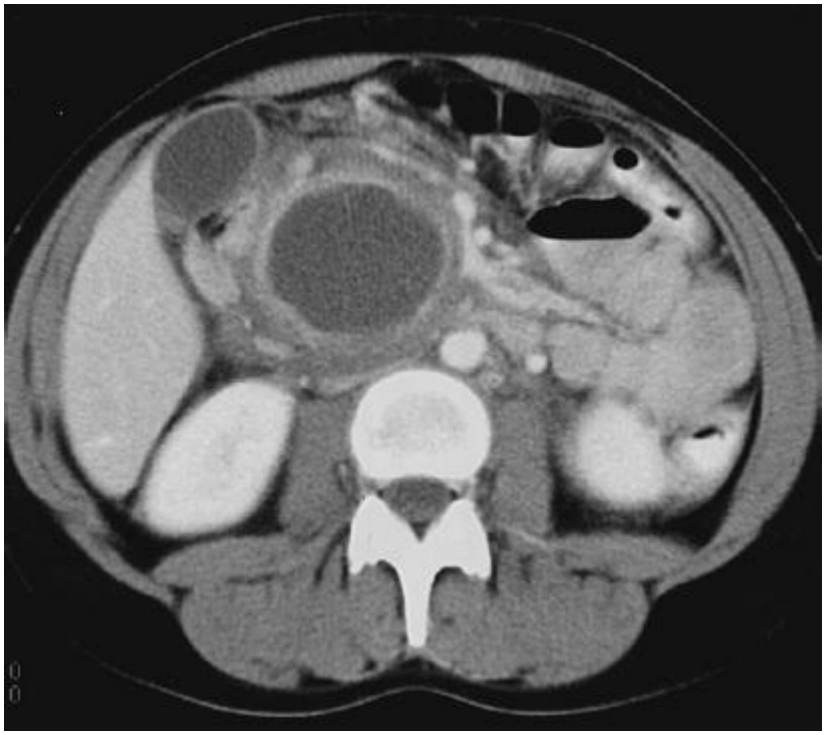
Subsequently, the contents of the pseudocyst which are liquid in nature are gradually reabsorbed by the body followed which the pseudocyst resolves. It indicates that the communication between the pseudocyst and the pancreatic duct is closed. Persistence of a pseudocyst indicates persistent communication of the pseudocyst with the pancreatic duct.

Acute fluid collections lack a discrete wall of fibrous or granulation tissue and form early in the course of acute pancreatitis. They are common in patients with severe pancreatitis. Acute fluid collections occur in about 30% to 50% of cases of acute pancreatitis. Majority of these lesions regress spontaneously without specific treatment like drainage.

Most acute fluid collections do not have a communication with the pancreatic duct. They are just a serous or exudative reaction to inflammation and trauma. Since they lack communication with the pancreatic duct,they are also called as pseudopseudocysts.

A pancreatic abscess is defined as a circumscribed collection of purulent fluid which contains little necrotic material and it is formed as a complication of acute pancreatitis or pancreatic trauma. A pancreatic abscess occurs late in the course of severe acute pancreatitis (i.e) 4 weeks after the onset of symptoms.

Presence of a purulent exudate, a positive culture and absence of necrotic pancreatic material is used to differentiate from infected pancreatic necrosis. This differentiation is necessary for the management since the treatment for both the conditions differs. A pancreatic abscess may be treated by percutaneous drainage whereas infected pancreatic necrosis requires operative debridement.



PSEUDOCYST

Incidence of pseudocyst is more in males than females, since it is mostly associated with alcoholic pancreatitis. Most of the pseudocysts occur in the head of the pancreas, but it can also occur in the neck, body and tail of the pancreas.

Abdominal pain is the most common symptom in pseudocyst in about 90% of patients. A pseudocyst may also known to cause increased or refractory pain in a patient of chronic pancreatitis. Other symptoms include early satiety, nausea and vomiting, jaundice, fever and loss of weight.

Clinical examination reveals upper abdominal tenderness and often a palpable abdominal mass. The symptoms of early satiety, nausea and vomiting

are all due to gastroduodenal obstruction because of the mass effect of pseudocyst.

Patients with pseudocysts may not come to hospital until complication occurs.

The complications of pancreatic pseudocyst are sepsis secondary to infection, hypovolemic shock due to hemorrhage, jaundice due to CBD obstruction, and severe abdominal pain due to intraperitoneal rupture of a pseudocyst.

Trauma to the pancreas is uncommon. It may occur after blunt or penetrating injury. Pancreatic ductal disruption may occur as a direct result of penetrating trauma or blunt trauma which may contribute to pseudocyst formation. These injuries may be

missed during initial radiologic evaluation or laparotomy. In this case the diagnosis of pseudocyst is made many weeks after the injury.

Diagnosis of pseudocyst:

Persistently elevated amylase after resolution of acute pancreatitis should suggests formation of pseudocyst. Some have mild leukocytosis, elevated liver enzymes indicating compression of the biliary tree. CT scan is used for diagnosis of a pancreatic pseudocyst. Ultrasound examination is also

used to identify pseudocysts. It is least invasive and it is used in follow up of the size of the cysts.(1)

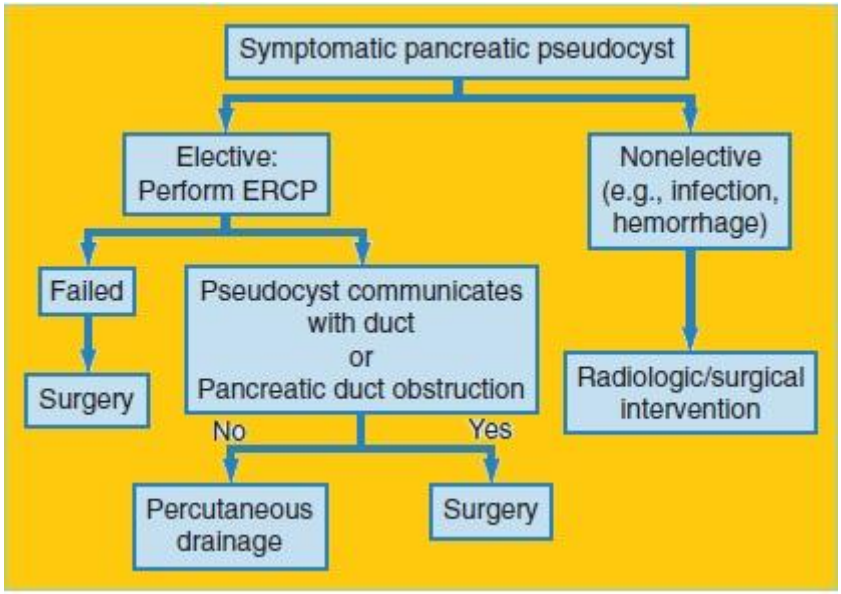
MRI is used to predict whether solid debris within a pseudocyst will prevent drainage. Conventional MRI coupled with magnetic resonance cholangiopancreatography (MRCP) is used to define pancreatic ductal anatomy. MRCP is also used in the evaluation of duct strictures and filling defects.

Some authors use endoscopic retrograde cholangiopancreatography (ERCP) for the diagnosis and treatment of patients with pseudocyst formation. Another use of ERCP is the ability to define pancreatic ductal anatomy.

Cyst Fluid Parameters Useful in Diagnosis

Diagnosis	Amylase	Cytology	Viscosity	CEA/CA-125	CA 19-9
Pseudocyst	High	Negative	Low	Low/low	Variable
Serous cystic neoplasm	Variable	Negative	Low	Low/variable	Variable
Mucinous cystic neoplasm	Variable	Usually positive	Usually high	High/variable	High

Ahearne et al assumed that pseudocysts associated with disruption of main pancreatic duct or communication with the main pancreatic duct are managed by surgical drainage, whereas absence of these findings in ERCP can be drained percutaneously.



ERCPALGORITHM

This study thus shows the advantage of an ERCP-based algorithm in lowering the adverse outcomes in patients with pancreatic pseudocysts.

Management Options for Pancreatic Pseudocysts

Observation
Percutaneous aspiration/drainage
Endoscopic aspiration/drainage
Transpapillary endoscopic drainage or stenting
Operative approaches (open or laparoscopic)
- Internal drainage
- External drainage
- Resection

MANAGEMENT:

The intervention in the management of pseudocyst is required in patients who do not meet the criteria for conservative non-operatory management. concomitant intervention is necessary for ductal disruption, biliary obstruction, and chronic pancreatitis. Percutaneous drainage, endoscopic drainage, operative internal or external drainage, and resection are current management methods for a pseudocyst patient. There should be a significant distinction between percutaneous aspiration and percutaneous drainage.

The aim of percutaneous aspiration is to aspire all pseudocyst fluid in one operation, without leaving a indwelling drainage catheter. Less than 50% of patients who are subject to this technique shall have full pseudocyst resolution. The remaining patients will require repeat aspiration technique. According to the review of patients, the most successful applicants of percutaneous aspiration were provided with pseudocysts in the tail of the pancreas of less than 100 ml in the whole volume with low intracystic amylase.

Percutaneous catheter drainage:

It involves placement of a catheter into a pseudocyst by the Seldinger technique usually done under USG or CT guidance. The pseudocyst

is entered through the flank or by transgastric approach, and the tract is dilated to accept a catheter of size 7 to 14 French. Saline irrigation should be given through the catheter two to three times a day to ensure patency.

Contraindications to percutaneous drainage are the presence of necrosis or solid debris in the pseudocyst, hemorrhage within the pseudocyst, lack of a safe access route and complete obstruction of the main pancreatic duct.

Complications of percutaneous drainage include infection of the drain tract, persistent of pseudocyst or recurrent pseudocyst, and pancreatic-cutaneous fistula.

Endoscopic procedures:

Endoscopic methods in the treatment of pseudocysts have recently evolved. Currently the technique involve the use of flexible scope in localizing and draining the pseudocysts by creating a tract between the pseudocyst and the stomach or duodenum. This fistulous tract communication is created with electrocautery and an endoprosthesis is placed to keep the fistula open.

Endoscopic drainage technique requires the pseudocyst to be located in the head or body of the pancreas and the pseudocyst should be bulging into the wall of stomach or duodenum.

Endoscopic ultrasound (EUS) is used to identify the pseudocyst and to identify a suitable site for drainage. Complications of this procedure include hemorrhage and perforation. Endoscopic and percutaneous techniques are usually combined to identify and drain pseudocysts which are adjacent to the wall of the stomach or duodenum but that do not bulge into the lumen.(1)

Transmural endoscopic drainage:

Approximately 50% of pseudocysts can be drained by transmural approach based on location of the pseudocyst and its relation to the stomach or duodenum. Successful drainage was achieved in 86% of patients of pseudocyst, whereas 11% of the patients had a recurrence following this approach.

Transampullary pancreatic stents:

These stents are used in the treatment of chronic pancreatitis, pancreatic ductal disruption, pancreatic fistulas, and pseudocysts. Drainage of a pseudocyst through this approach has been attempted in patients with pseudocysts having communication with the main pancreatic duct. The stents are placed through the ampulla, along the pancreatic duct, and placed into the lumen of the pseudocyst.

When it is difficult to place the stent into the lumen of the pseudocyst, the tip of the stent is placed as close as possible to the site of communication between the pseudocyst and pancreatic duct. Complications associated with this

method includes mild postprocedure pancreatitis, bleeding, and abscess formation. The abscess formation is secondary to stent obstruction.

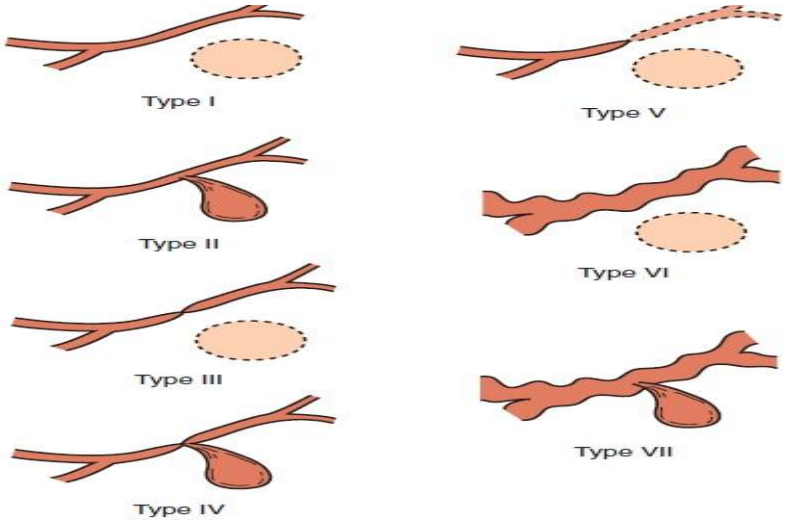
Endoscopic transpapillary nasopancreatic drain is recently used for management of pseudocysts in atypical locations such as mediastinal, intrahepatic, intrasplenic, pelvic regions. Transampullary drainage and pancreatic stenting may play a role in drainage of the pseudocyst in selected patients. Complications of endoscopic and percutaneous drainage include sepsisfollowed by hemorrhage, shock, renal failure and ventilator-dependent respiratory failure.

Some patients require operative management even after endoscopic and percutaneous drainage. These failures of percutaneous/endoscopic drainage were easily identified by ERCP which detects stricture of the main pancreatic duct and other pancreatic ductal anomalies.

Anomalies of the pancreatic duct type I and II can be managed by percutaneous drainage. Types V to VII are managed by surgical or endoscopic internal drainage or surgical resection since these types of duct are associated with complicated duct strictures and stones.Types III and IV may be managed by either of these methods. But percutaneous drainage alone in this situation may be associated with increased rates of recurrence because of the presence of underlying duct strictures.

Some salvage procedures are followed after failed percutaneous and endoscopic drainage. These procedures include cyst debridement and external drainage, internal pseudocyst drainage, and pancreatic resection. Morbidity following these salvage procedures was about 56% with complications include hemorrhage, wound infection, and pulmonary complications.

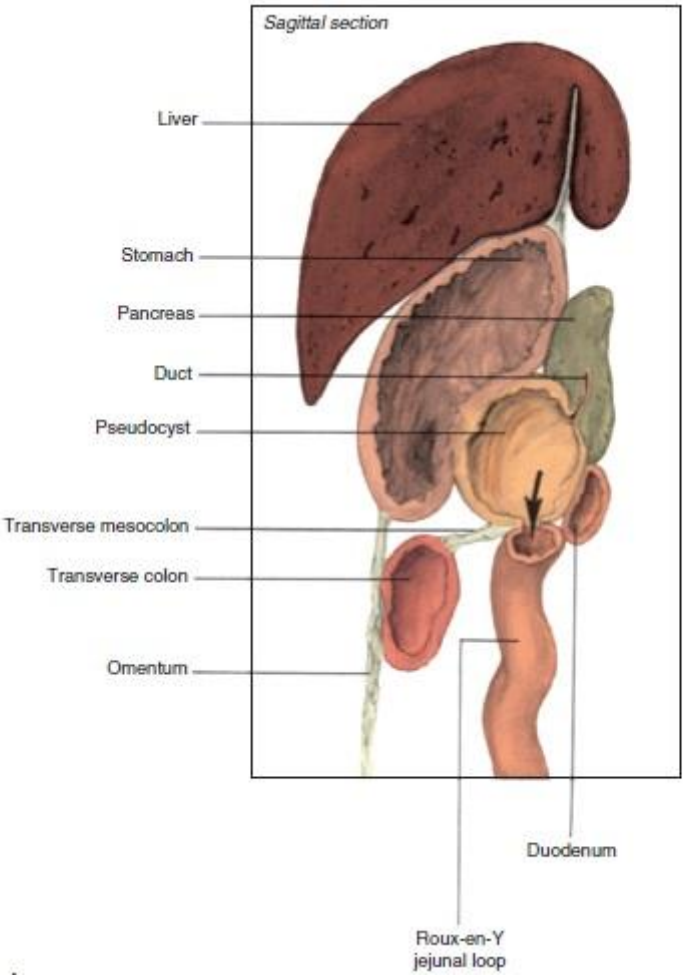
CATEGORIES OF DUCTAL ABNORMALITIES IN PSEUDOCYST:

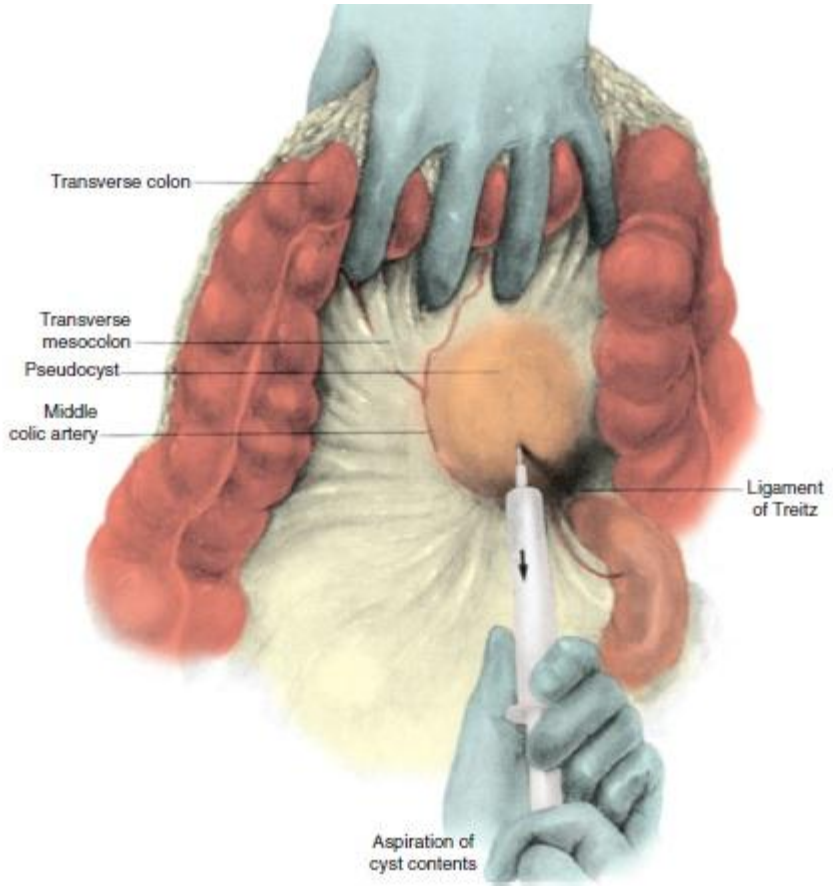


The preferred approach for uncomplicated pseudocysts requiring surgical intervention is internal drainage. Internal drainage can be done by three methods viz

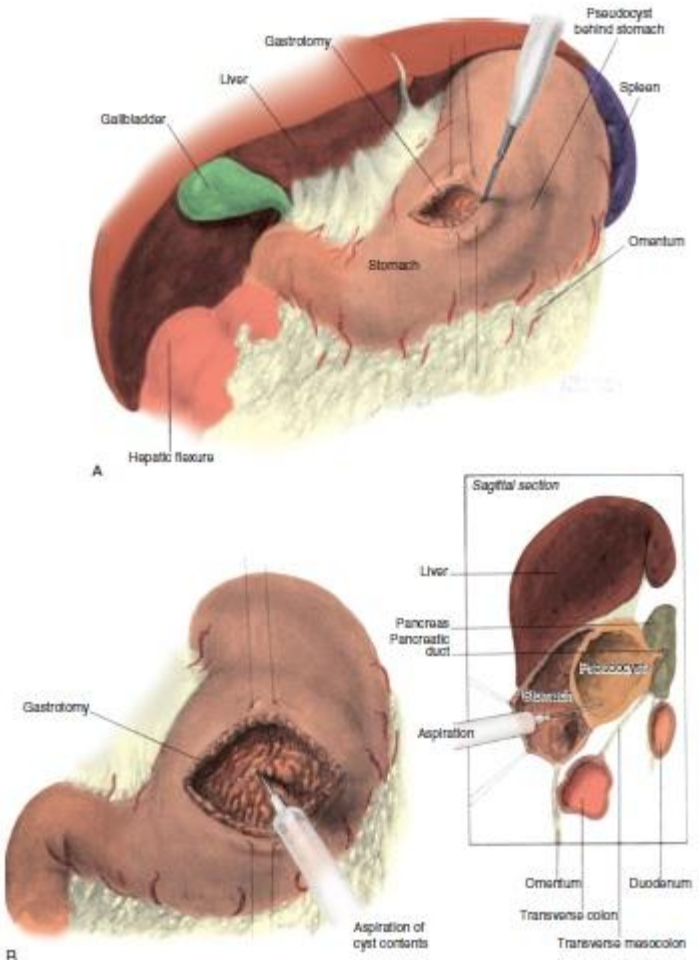
cystojejunostomy to a Roux-en-Y jejunal limb, cystogastrostomy and cystoduodenostomy. Cystojejunostomy is the most commonly used method and

is mostly done when the pseudocyst is located at the base of the transverse mesocolon and is not adherent to the gastric or duodenal wall.





Cystogastrostomy is relatively a faster procedure which is used when the pseudocyst is adherent to the gastric or duodenal wall. Cystoduodenostomy is the least used procedure, which is mostly used for pseudocysts in the head or uncinate process which lies within 1 cm of the lumen of the duodenum. Cystoduodenostomy is performed similar to that of cystogastrostomy. Both these procedures are performed by opening the lateral wall of the duodenum and a communication is created between the pseudocyst and the duodenum. This communication is brought out by medial duodenotomy. Cystoduodenostomy has many risks such as duodenal leak and fistula thus it is rarely used nowdays.



Laparascopic drainage procedures:

Laparascopic approaches are beneficial in cases of large retrogastric pseudocysts. It includes transgastric and extragastric approaches. It also allows biopsy of the cyst wall and cyst debridement.

Natural orifice transluminal endoscopic surgery (NOTES) cystogastrostomy:

It has similar results as compared to that of open and laparascopic methods. It uses EUS-guided pseudocyst drainage along with transoral cystogastrostomy anastomosis by use of a stapler delivered via a flexible endoscopic shaft. This technique is also used in the debridement of infected pancreatic necrosis.

Some pseudocysts are best treated by *pancreatic resection*. This operation involves distal pancreatectomy in case of pseudocyst located in the body or tail of the pancreas. Presence of peripancreatic and peripseudocyst inflammation makes distal pancreatectomy a challenging procedure. After distal pancreatectomy, a Roux-en-Y pancreaticojejunostomy is done. This is done to decompress an obstructed or abnormal pancreatic duct.

In patients with symptomatic pseudocysts in the head of the pancreas, pancreaticoduodenectomy is required. In this case, pylorus-preserving pancreaticoduodenectomy is the choice of procedure. Less commonly done procedures, such as duodenum-preserving resection of the head of the pancreas, may be performed in some patients.

External drainage:

External drainage of a pancreatic pseudocyst is indicated when gross infection is present at the time of surgery or presence of immature, thin-walled pseudocyst that will not allow for internal drainage.

COMPLICATIONS

Infections, hemorrhage, obstruction or compression of adjacent structures and rupture are the most frequently reported complications.

Infection:

Some pseudocysts contain small amounts of bacteria, but the pseudocyst fluid is not purulent and patients do not have clinical evidence of infection. Nevertheless, true infections were shown by fever, leukocytosis and increased pain in patients with pseudocysts.

Purulent fluid aspiration from the pseudocyst confirms an infection.These patients are described as having pancreatic abscess by the Atlanta International Symposium and the use of the word infected pseudocyst should be avoided. Pancreatic abscess bacteriology is highly variable, but up to 60% include aerobic and anaerobic gram-negative species. A pancreatic abscess is a medical condition and it is treated by means of percutaneous drainage. In addition, with percutaneous drainage, the mortality rate is less and a major open operative procedure is avoided. Nevertheless, some patients may

need operative external drainage. Percutaneous catheters often do not provide for quick drainage or cannot fully address multi-loculated collections. Interventional radiologists strategies include upsizing drainage catheters, biweekly imaging, and aggressive manipulation to break up loculations. These are not always effective strategies.Open operating drainage facilitates the complete evacuation of all infected material and outside drains can be placed under direct vision. Percutaneous endoscopic techniques have most recently allowed necrotic tissue debridement in direct endoscopic vision.

Through previous percutaneous drainage tracts, ureteroscopes are progressed into the retroperitoneum and devitalized tissues are eliminated and the cavity is constantly irrigated. It shows positive results and a minimal pressure to the patients. Recent reports shows that transampullary drainage is not only an effective means to achieve complete abscess resolution. Multivariable analysis showed improvement in patients who underwent pancreatic duct stenting. In patients who has no improvement, operative drainage should be performed.

Hemorrhage:

Arterial hemorrhage occur in a few patients with pancreatic pseudocysts. The splenic artery is the most common source of pseudocyst-associated bleeding. The gastroduodenal and pancreaticoduodenal arteries also cause significant hemorrhagic events. Bleeding also occurs from the portal, superior

mesenteric, or splenic veins but that bleeding is less common. The pathogenesis of arterial hemorrhage follows erosion of the vessel wall leading to pseudoaneurysm formation and rupture. Massive hemorrhage is followed by a sentinel hemorrhage. Thus bleeding associated with a pseudocyst should be investigated quickly. Angiography is essential for diagnosis and provides a mode of treatment.

Initial embolization of the pseudoaneurysm is done which is a technique performed by skilled radiologists. (1)Most haemorrhages can be controlled by current embolic techniques. When embolic therapy fails or if patient becomes hemodynamically unstable, they require emergency surgical exploration. After the blood vessel is ligated, the pseudocyst should be drained with large-bore catheters. Then distal pancreatectomy, splenectomy, and splenic artery ligation are the most common procedures if resection is required. Emergency pancreaticoduodenectomy may rarely be needed.

Obstruction:

Because of their mass effect on other structures, pancreatic pseudocysts may become symptomatic. While duodenal obstruction is secondary to pseudocyst formation as the most common type of mechanical obstruction, stomach obstruction, oesophagus, jejunum and colon may be identified.

Obstruction of the mesenteric vasculature and the portal venous system may cause hypertension, splenomegaly and gastric varices. Pseudocysts are also identified as obstacles to other retroperitoneal structures such as inferior vena cava and ureters. In addition, pseudocysts with mediastinal and pleural extension impeding cardiac output have been identified.

Pseudocyst also cause biliary obstruction leading to complications such as jaundice, biliary cirrhosis and cholangitis. The diagnosis of biliary obstruction in a patient with a pancreatic pseudocyst is done by cholangiography.

RUPTURE

Spontaneous rupture, the least common complication of the development of pseudocysts, occurs in less than 3% of patients, but it may lead to dramatic clinical manifestations. Spontaneous rupture of a pseudocyst into the peritoneal cavity can result chemical peritonitis which causes severe acute abdominal pain. These patients are treated as a surgical emergency, especially those without a known pseudocyst. In these cases,history of pseudocyst, acute abdominal pain should raise the intraperitoneal rupture or rupture into an associated hollow viscus, most commonly a segment of the gastrointestinal tract.

Rupture may be due to progressive growth, but it also signify an infected or hemorrhagic pseudocyst. Silent rupture of a pseudocyst also occur. Some pseudocysts are presumed to resolve by rupture or fistulization into an associated portion of the stomach. Pseudocysts that rupture silently anteriorly into the peritoneal cavity or posteriorly into the pleural cavity may lead to the development of pancreatic ascites or pancreatic pleural effusion.

Endoscopic and minimally invasive therapy for complications of acute pancreatitis:

ENDOSCOPIC NECROSECTOMY

Endoscopic necrosectomy has emerged as a therapeutic alternative to surgery for the patients having organized pancreatic necrosis located to the gastric or duodenal wall in close proximity. This technique involves initial access to the necroma either through direct puncture or by endoscopic ultrasound-guided needle puncture and subsequent wire guide access. Once accessed, the tract is dilated using either a graduated dilating catheter, needle knife sphincterotome, or cystotome. To allow passage of an upper endoscope into the necroma, subsequent dilation to 15 to 20 mm is performed using a balloon dilator. A combination of endoscopic accessories is then used to perform debridement. Tract maintenance is accomplished by inserting two or more pigtail stents or a self-expanding metal stent through the gastric or

duodenal wall into the cavity.It allows repeated access and debridement after initial necrosectomy.(1)

In some cases, it may be necessary to place a nasocystic drain for continuous lavage.Although the technique is effective in preventing surgery and pancreaticocutaneous fistulas, the technique has several disadvantages like high morbidity rate and high mortality rate. In some cases, where the necroma is not adherent to the gastric wall, air introduced can dissect freely into the lesser sac during endoscopic insufflation which will lead to air emboli. Furthermore, large-diameter balloon dilatation may increase the risk of bleeding, especially in left-sided portal hypertension and gastric varices. The resource-intensive nature of endoscopic necrosis is another drawback as it involves several procedures that may not be feasible on consecutive days with the same patient.

PERCUTANEOUS DRAINAGE AND COMBINED MODALITY THERAPY

The large-caliber percutaneous drainage in necroma is another method for drainage of IPN. Drains were gradually increased to a maximum of 30 French (F) for the liquefied necrotic tissue debridement. The high rate of chronic pancreaticocutaneous fistula formation is the major drawback of this technique. This is mostly seen in patients with the disconnected duct syndrome where drains were placed into the disconnected segment of pancreas which

results in the formation of a chronic pancreaticocutaneous fistula. Before percutaneous drainage, when disconnected duct syndrome is suspected based on central necrosis with normal perfused distal pancreatic tissue, endoscopic or magnetic resonance pancreatography should be performed.

A combined-modality approach involves placement of large-caliber percutaneous drains into the necroma followed by endoscopic placement of double pigtail stents into the necrotic cavity. The pigtail stents are placed to create an internal fistula. Then the transenteric stents were allowed for redirection of pancreatic juice into the GI tract. In disconnected duct syndrome patients, it prevents the formation of chronic pancreaticocutaneous fistula. A recent comparison among standard percutaneous drainage and combined-modality therapy has shown that the latter technique lowers hospital stay, external drainage duration and radiographic resource utilization. In the combined drainage group there was no procedural mortality. Combined-modality drainage is only used in patients whose necrosum is confined to the lesser sac where the cavity is within close proximity to the gastric or duodenal wall.

PANCREATIC PSEUDOCYST

The pancreas duct disruption may contribute to the leaking of amylase-rich fluid into peripancreatic tissues and retroperitoneum. Collections with a distinctive round encapsulation on cross sectional images that last for more than six weeks are referred to as Pseudocysts due to a lack of a true epithelium lining the cyst wall.Those that occur after AP are considered acute pseudocysts, whereas those that follow CP are called chronic pseudocysts. Although they are often asymptomatic, the pseudocysts can become infected and dissect to nearby vascular structure and obstruct the gastric outlet and these are the indications for drainage. Larger pseudocysts are most symptomatic due to their large spatial existence and the subsequent compression or erosion into contiguous structures. A sufficient time is needed before the drainage to allow robust development of the pseudocyst wall. Endoscopic drainage with or without endoscopic ultrasound (EUS) can be approached via a transenteric or transpapillar approach are used in the management of pseudocyst. EUS-facilitated procedures have similar effectiveness and complications as compared to open pseudocystogastrostomy, and endoscopically treated patients have reduced utilization of resources and costs than open-surgery treated patients. The laparoscopic method have a greater rate of success and a lower risk of complications and recurrence.

Endosonographic guidance is required where a bulge is not visible within the gastric or duodenal lumen. In the presence of luminal bulge, the pseudocyst can be punctured using a sclerotherapy needle through which contrast is injected under fluoroscopic control for entry into the lesion. A cystotome can be used to access the pseudocyst and allow for guidewire placement. The cystogastrostomy or cystoduodenostomy is done by placement of two transenteric double-pigtail stents. When EUS is required, the cyst is accessed using 19-gauge needle through which a guidewire is placed. Dilation and stent placement are then proceeded in the same manner using echoendoscope or duodenoscope. In situations where the pseudocyst interacts directly with the central PD, transpapillary drainage may be performed.A guidewire and subsequent stent are placed directly into the pseudocyst cavity across the major or minor papilla. Small PD-related pseudocysts can resolve to bridge the leak after transpapillary stent placement and reduce transpapillary pressures. In cases where transenteric drainage is done, pancreatography — whether endoscopic or magnetic resonance — should be performed to identify ductal anatomy and determine the existence of leaks the treatment of which may enable pseudocysts to be resolved more quickly. Pancreatic pseudocysts helps to define the duration of transenteric stent placement. If there is no communication between the pseudocyst and main PD, transenteric stents can be removed 6 to 8 weeks after the pseudocyst has been completely drained. The major complications in endoscopic pseudocyst drainage are infection, bleeding,

stent migration, and perforation. Infection typically results from incomplete cyst cavity evacuation, particularly when stents are blocked, or from inadvertent drainage of organized pancreatic necrosis. The former can usually be avoided by putting at least two large-caliber double-pigtail stents in the cyst cavity, while radiologist inadequate-quality imaging studies can result in the misidentification of the pseudocyst necroma. Collections which are filled with debris, irregular in shape and having thick septations are more likely to be organized pancreatic necrosis or cystic neoplasms.

Bleeding associated with pseudocyst drainage is mostly due to puncture of blood vessels during the drainage procedure. Patients at high risk are those with concomitant gastric varices, in them the use of EUS with color Doppler may reduce the risk of puncture of blood vessels. The use of electrocautery for creating internal fistula may also increase the risk of bleeding. If the bleeding is mild, it can be treated by endoscopic techniques such as infiltration with epinephrine, heater probe application or hemoclip placement. In the presence of severe bleeding, electrocautery applied through a cystotome can be done, or it can be managed by angiography or surgery.

Abdominal perforation and stent migration are rare with endoscopic procedure. Some may treat the perforation by surgery while others are in favour of bowel rest, antibiotics and percutaneous drainage if needed.

Laparoscopic drainage of pseudocyst can be achieved through pseudocystogastrostomy, Roux-en-Y cystojejunostomy, or cystoduodenostomy, based on the anatomic location of the cyst. It allows for debridement of pancreatic necrosis within the pseudocyst, assessment and control of hemorrhage from the pseudocyst wall.

The simplest technique for a lesser sac pseudocyst is cystgastrostomy. Laparoscopic ultrasound is used to localize the pseudocyst. The opening into the pseudocyst is widened by use of ultrasonic energy source to accommodate the stapling device, and to take biopsy from the wall of the cyst.The staple height is based on the thickness of the stomach and pseudocyst to achieve hemostasis without excessive tissue necrosis.

If the thickness of the tissue exceeds capacity for stapling, absorbable monofilament suture is used to approximate the edges of the opening. The pseudocyst cavity is explored, and tissues are gently debrided. The anterior gastrotomy is closed, and the patient can be started on oral diet. Cystgastrostomy can also be done through a lesser sac approach which has better drainage compared to the anterior approach. Laparoscopic Roux-en-Y cystojejunostomy is useful in cases of large pseudocyst extending inferiorly to the stomach. A small window is made in the mesocolon connecting the wall of the pseudocyst avoiding injury to middle colic vessels and inferior mesenteric vein. After transection of the proximal jejunum, the Roux limb is approximated

to the pseudocyst wall by interrupted suture. Cystojejunostomy is then performed.The jejunojejunostomy is performed 50 to 60 cm distally to decrease the reflux of enteric contents into the cavity.

Laparoscopic cystoduodenostomy is done for symptomatic pseudocysts located in the head of the pancreas when drainage of the cyst is inadequate by endoscopic means.

MATERIALS AND METHODS

STUDY DESIGN

Prospective type of study

PLACE OF STUDY

Department of general surgery, Coimbatore medical college hospital, Coimbatore.

DURATION OF STUDY

Period of 1 year from jan 2018 to jan 2019

SAMPLE SIZE

N=100

STUDY POPULATION

INCLUSION CRITERIA

1)Patients diagnosed as acute pancreatitis by combination of clinical signs, serum amylase and imaging studies(ultrasound or CT)

2)Patients of acute pancreatitis with complications such as necrosis, abscess or pseudocyst by imaging studies

EXCLUSION CRITERIA

1) Patients of chronic pancreatitis
2) Patients of acute on chronic pancreatitis

SAMPLE COLLECTION

After getting consent from the patient, clinical examination is done. Laboratory investigations such as serum amylase, CRP and LDH and imaging studies such as ultrasound or CECT was done. Analysis of these parameters were done systematically.

DATA MANAGEMENT AND ANALYSIS

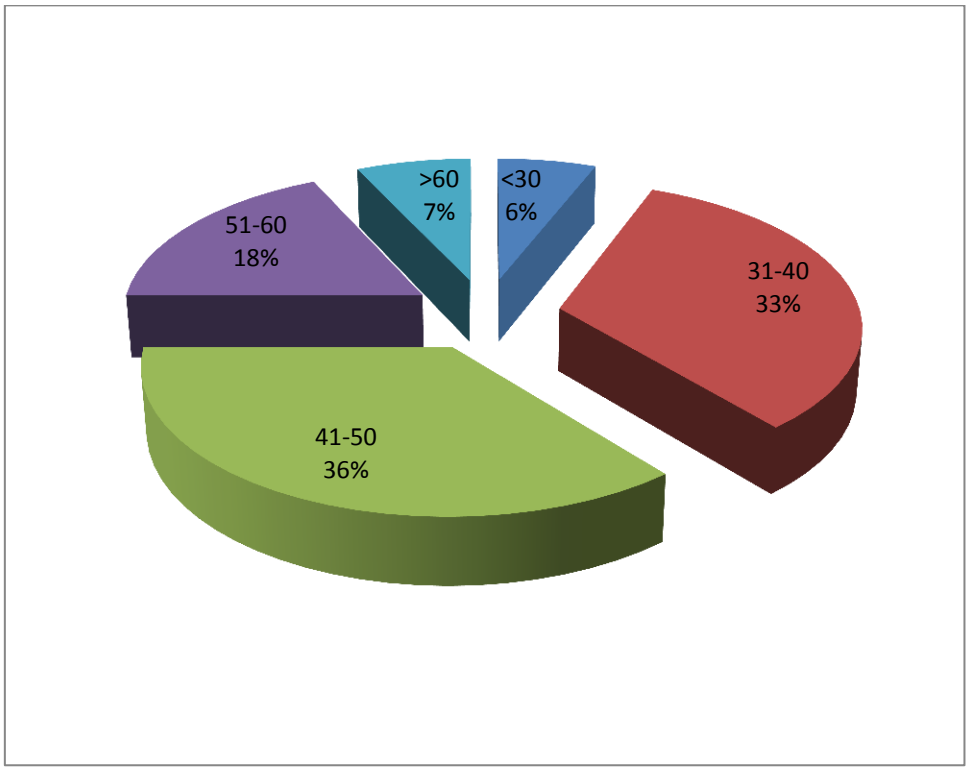
Data was entered in Microsoft excel. Statistical analysis was done.

OBSERVATIONS AND RESULTS

Distribution of study population according to age group

Age group	**Frequency**	**Percentage**
<30	6	6
31-40	33	33
41-50	36	36
51-60	18	18
>60	7	7
Total	**100**	**100**

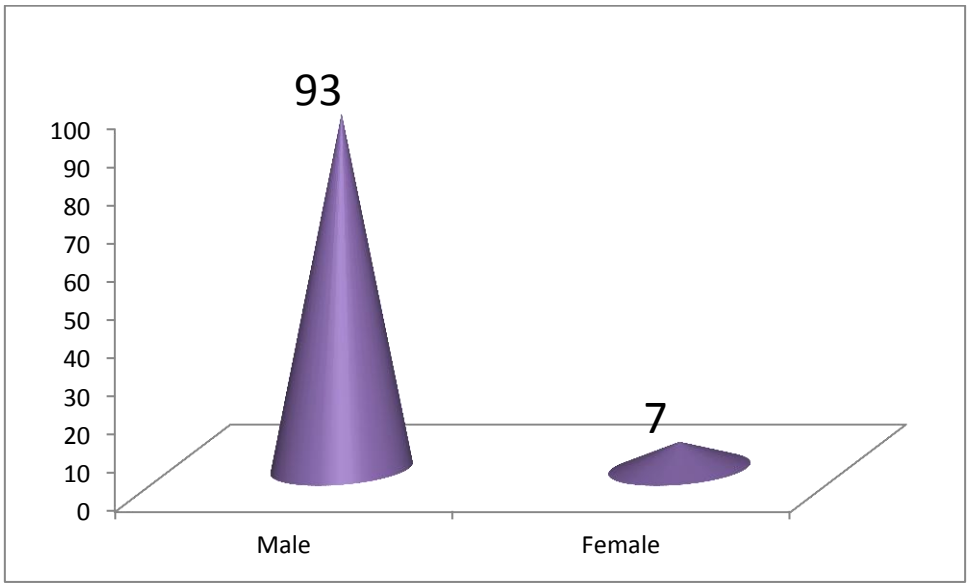
Majority of the patients are in the age group of 31-50 years(74%)



Distribution of study population according to gender

gender	Frequency	Percentage
Male	93	93
Female	7	7
Total	**100**	**100**

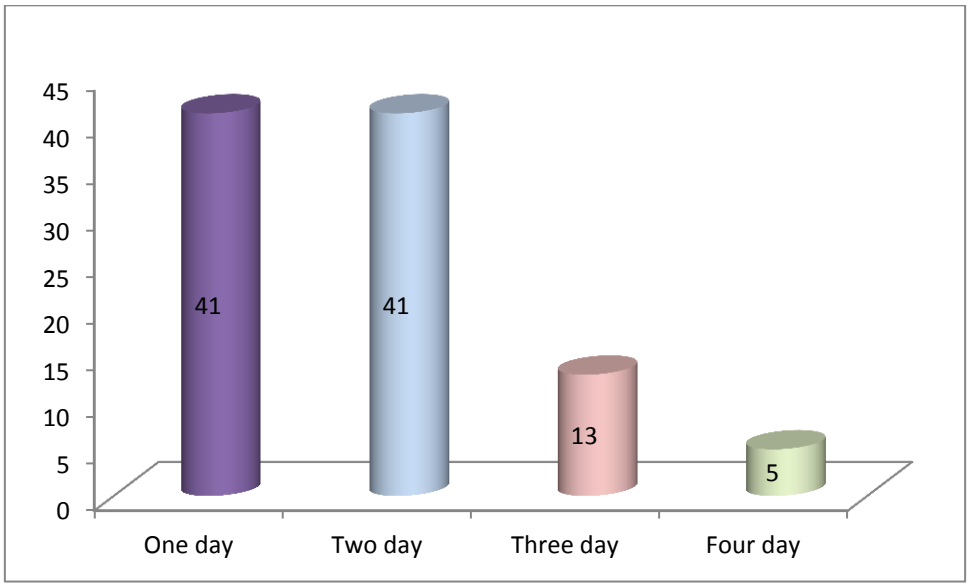
Around 93 % of study population were Males



Distribution of study population according to duration of symptoms

Duration of symptoms	**Frequency**	**Percentage**
One day	41	41
Two day	41	41
Three day	13	13
Four day	5	5
Total	**100**	**100**

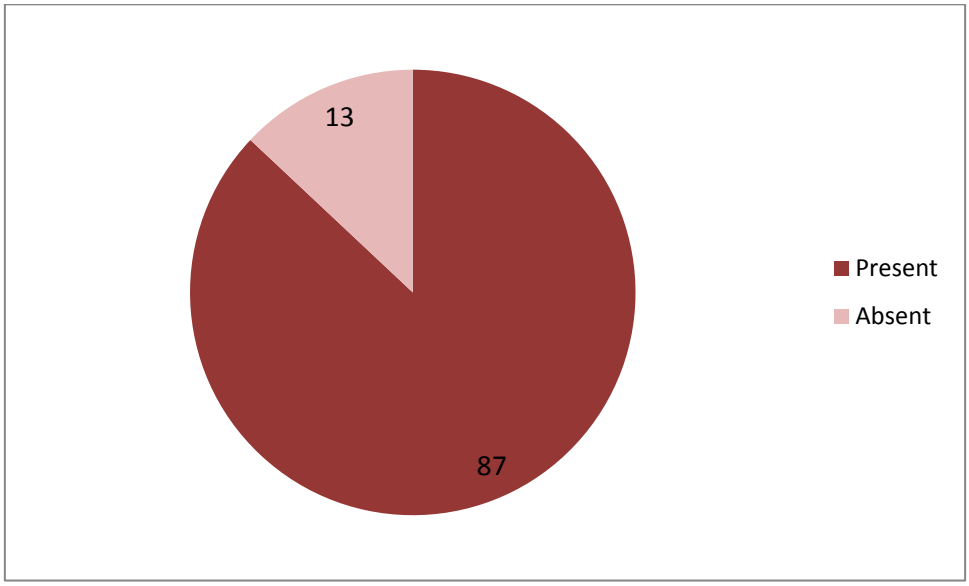
Around 82 % of study population had symptoms within two days.



Distribution of study population according to regular alcohol consumption

Regular alcohol	**Frequency**	**Percentage**
Present	87	87
Absent	13	13
Total	**100**	**100**

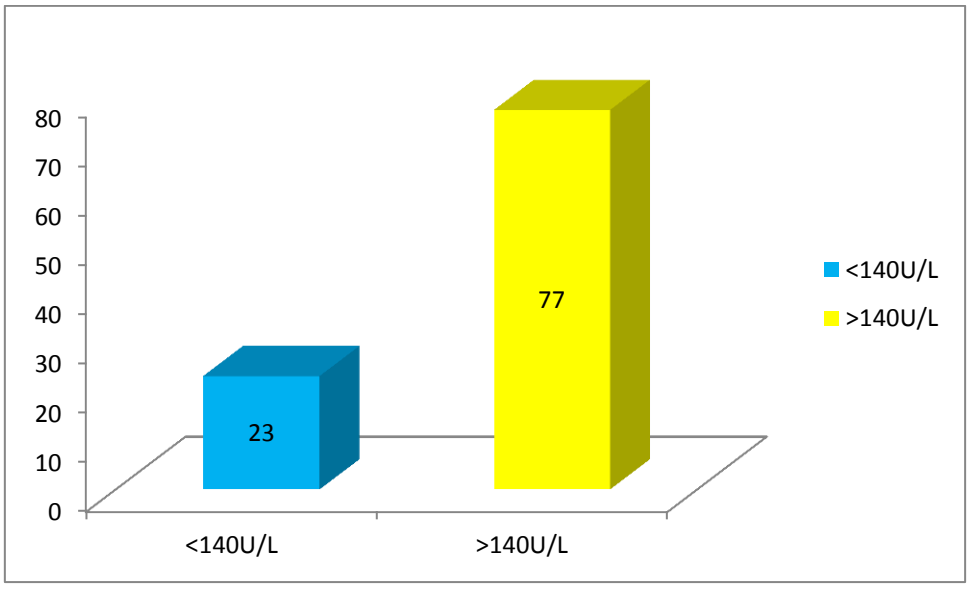
Around 87 % of those who had acute pancreatitis consumed alcohol daily



Distribution of study population according to serum amylase levels

Type	Frequency	Percentage
<140U/L	23	23
>140U/L	77	77
Total	**100**	**100**

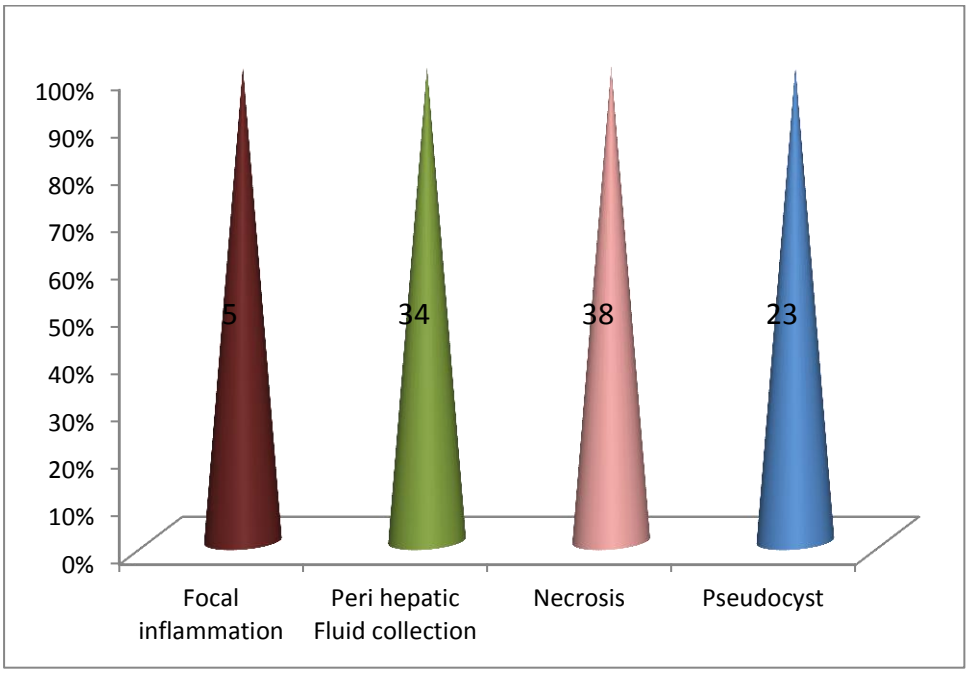
77% of the study population had elevated serum amylase levels.



Distribution of study population according to CT findings

CT findings	Frequency	Percentage
Focal inflammation	5	5
Peri hepatic Fluid collection	34	34
Necrosis	38	38
Pseudocyst	23	23
Total	**100**	**100**

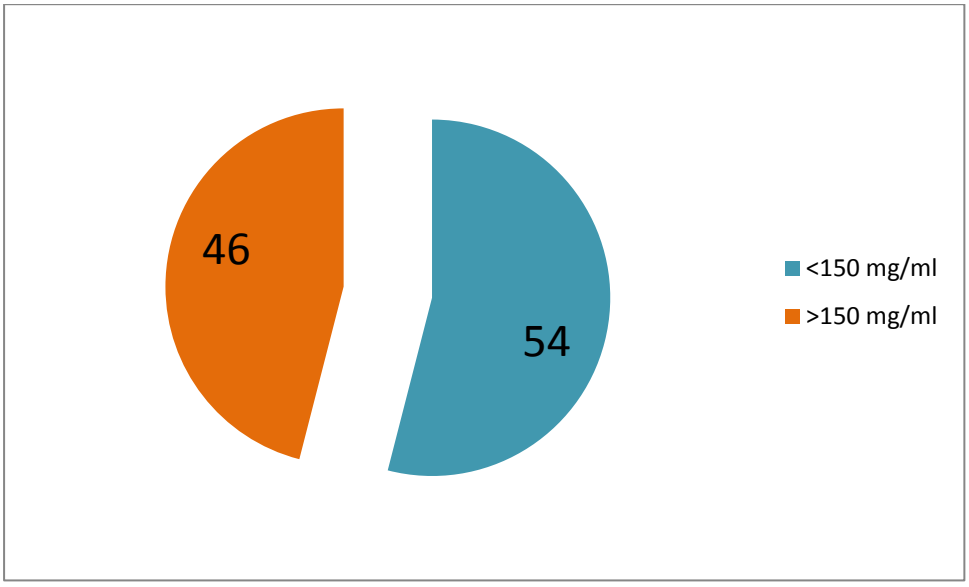
34 % of the study population had peri hepatic fluid collection, while 38 % had necrosis while 23% had pseudocyst. Only 5% had focal inflammation



Distribution of study population according to CRP levels

CRP Levels	Frequency	Percentage
<150 mg/ml	54	54
>150 mg/ml	46	46
Total	**100**	**100**

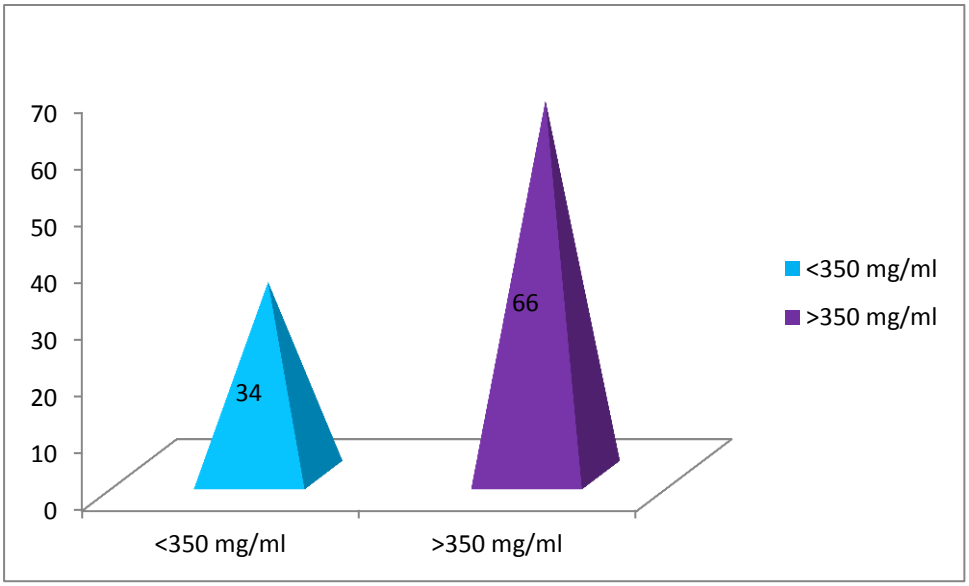
Around 46% of study population had CRP levels above 150mg/ml



Distribution of study population according to LDH levels

LDH Levels	Frequency	Percentage
<350 mg/ml	34	34
>350 mg/ml	66	66
Total	**100**	**100**

Around 66 % of study population have LDH levels more than 350 mg/ml.



Comparison of Mean CRP levels in each CT grading levels using ANOVA

CT findings		Frequency	CRP Levels		ANOVA sum of squares	Significance
Grade	**Findings**	**No**	**Mean**	**SD**		
Grade I	Focal inflammation	5	96	8.60	14326.817	0.000
Grade II	Peri hepatic Fluid collection	34	122.91	9.12		
Grade III	Necrosis	38	163.13	13.86		
Grade IV	Pseudocyst	23	157.48	13.77		

POST HOC test to compare significance of means between each grade

	Grade I	Grade II	Grade III	Grade IV
Grade I	_	0.226	0.000	0.000
Grade II	0.226	-	0.000	0.000
Grade III	0.000	0.000	_	1
Grade IV	0.000	0.000	1	-

As the CT grade increases, the mean CRP level increases and the results are statistically significant .on further analysis using post hoc to compare between each group, there is a significant difference in mean between each grade except between two categories grade I with Grade II and Grade III vs grade IV.

Comparison of Mean LDH levels in each CT grading levels using ANOVA

CT findings		Frequency	LDH Levels		ANOVA sum of squares	Significance
Grade	Findings`	No	Mean	SD		
Grade I	Focal inflammation	5	200	67.82	315327.641	0.000
Grade II	Peri hepatic Fluid collection	34	300.29`	52.07		
Grade III	Necrosis	38	644.47	238.20		
Grade IV	Pseudocyst	23	656.08	235.50		

POST HOC test to compare significance of means between each grade

	Grade I	Grade II	Grade III	Grade IV
Grade I	_	0.009	0.000	0.000
Grade II	0.009	-	0.000	0.000
Grade III	0.000	0.000	-	1
Grade IV	0.000	0.000	1	-

As the CT grade increases, the mean CRP level increases and the results are statistically significant .on further analysis using post hoc to compare between each group, there is a significant difference in mean between each grade except between Grade III and grade IV.

DISCUSSION

Our study was conducted in 100 confirmed patients of acute pancreatitis. Out of these 6 cases were in the age group of less than 30 years and 33 cases, 36 cases , 18 cases were in the age group of 31-40 years, 41-50 years and 51-60 years respectively whereas 7 cases were in the age group of more than 60 years. 74% of the patients were in the age group of 31- 50 years.

Male patients were 93 and females were 7.

41 patients present to the hospital in the first day of onset of symptoms. Another 41 patients present within 2 days of onset of symptoms. 18 patients present to the hospital after 2 days of onset of symptoms. That is , around 82% of the patients had symptoms within 2 days of onset of the disease.

Most of the admitted to our hospital were having history of alcohol consumption. Almost all patients admitted to our hospital were presented with abdominal pain. Some had fever, vomiting, jaundice and even symptoms pertaining to ileus. On examination, these patients were found to have tenderness in the epigastric region and some had guarding and rigidity.

Serum amylase had been evaluated in all the patients. Around 77 patients had increased serum amylase levels, whereas only 23 patients had low or normal serum amylase levels.

All these patients were subjected to CECT examination. Among those, around 5% of the patients had focal inflammation of the pancreas, 34%had peripancreatic fluid collection, 38% had necrotising pancreatitis and 23% of the patients had pseudocyst of pancreas. These CT findings were assigned as grade 1,2,3 and 4 respectively.

CRP is an acute phase protein increased after any inflammation process and subsequently this was used as a prognostic factor of severe pancreatitis. Values greater than 150mg/ml can detect between 67 and 100 of the presence of infected necrosis. However, a 24 to 36 hours latency is necessary before detecting a CRP increase in plasma.

LDH is one of the Ranson's score has also been studied independently in acute pancreatitis. Among the subtypes of LDH, LDH-4 and LDH-5 were the isoforms increased during the disease and LDH-4 was the only isoform used to differentiate between severe and mild attacks.

Zrnic IK et al showed that the diagnostic accuracy for Ranson's score and CRP on the 3rd day after admission was around 50% and CRP and LDH are simple, available biochemical parameters in the predicting the complications of acute pancreatitis in the early phase of the disease.

Jean –Louis Frossard, Antoine Hadengue et al showed that the CRP remains the most effective method in prediction of severity between day 2 and 3.

Jun Zeng et al showed that the sensitivity, specificity and accuracy of combined CRP and LDH were 85.7%, 87.5% and 86.6% respectively.

Similar results were obtained in our study that is CRP and LDH were higher in patients presented with complications such as necrotising pancreatitis and pseudocyst.

That is , around 46% of the patients had CRP levels more than 150mg/ml and 66% of the study population had LDH levels more than 350mg/ml.

Our study showed mean values of CRP levels of 96, 122.91, 163.13 and 157.48 in patients with grade 1,2,3 and 4 CT findings respectively and the mean CRP levels increases with increase in grading of CT findings.

Similarly, our study showed mean value of LDH levels of 200, 300.29, 644.47 and 656.08 in patients with grade 1,2,3 and 4 CT findings respectively. This shows that the mean LDH levels increases with increase in grading of CT findings.

CONCLUSION

Acute pancreatitis is an inflammatory process which is mainly diagnosed by acute abdominal pain with a concomitant increase in serum amylase levels. Alcohol consumption is the main etiology followed by gallstone disease. The CECT findings were focal inflammation, peripancreatic fluid collection, necrosis and pseudocyst formation. There were significant rise in CRP and LDH levels among patients with severe grades of disease. Thus this study showed that CRP and LDH were useful parameters in assessing the severity of acute pancreatitis.

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PROFORMA

NAME: IP NO:

AGE: SEX:

ADDRESS:

OCCUPATION:

DATE:

PRESENT HISTORY:

- H/o abdominal pain
- h/o fever
- h/o vomiting
- h/o jaundice
- h/o abdominal distention
- h/o constipation
- h/o not passed flatus
- h/o respiratory distress
- h/o black tarry stools

PAST HISTORY:

- h/o diabetes/ hypertension/ copd/ tuberculosis/ epilepsy
- h/o previous surgeries
- h/o drug intake
- h/o previous similar illness

PERSONAL HISTORY:

- smoker
- alcoholic
- food habits

ON EXAMINATION:

GENERAL EXAMINATION:

- conscious
- oriented
- pallor
- icterus
- cyanosis
- clubbing
- pedal edema
- body temperature

VITALS:

- pulse rate
- blood pressure
- respiratory rate
- oxygen saturation

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

PER ABDOMEN

CENTRAL NERVOUS SYSTEM

PER RECTAL EXAMINATION

INVESTIGATIONS:

- serum amylase
- ultrasound
- contrast enhanced computerised tomography
- blood ures
- serum creatinine
- C-reactive protein
- Lactate dehydrogenase

CONSENT FORM

I Mr/Mrs_____hereby volunteer to participate in the study **"“STUDY OF ROLE OF C- REACTIVE PROTEIN AND LACTATE DEHYDROGENASE AS PROGNOSTIC FACTORS OF SEVERITY IN ACUTE PANCREATITIS”**. I was explained about the nature of the study by the doctor, knowing which I fully give my consent to participate in this study. I also give consent to take clinical photographs for the purpose of the study.

Date :

Place :

Signature of the Patient

ஒப்புதல் படிவம்

பெயர் :

வயது / பாலினம் :

முகவரி :

அரசு கோவை மருத்துவக் கல்லூரி மருத்துவமனையில் பொது அறுவை சிகிச்சை பிரிவில் பட்ட மேற்படிப்பு பயிலும் மாணவி **மரு. பா. காயத்ரி** அவர்கள் மேற்கொள்ளும் **"STUDY OF ROLE OF C-REACTIVE PROTEIN AND LACTATE DEHYDROGENASE AS PROGNOSTIC FACTORS OF SEVERITY IN ACUTE PANCREATITIS"**குறித்த ஆய்வில் செய்முறை மற்றும் அனைத்து விபரங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்திக் கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

எனது இந்த ஆய்வில் கலந்து கொள்ள முழு சம்மமத்துடனும், சுய சிந்தனையுடனும் சம்மதிக்கிறேன்.

இந்த ஆய்வில் என்னுடைய விபரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் இந்த ஆய்விலிருந்து நான் விலிகிக் கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம் : கையொப்பம்

நாள் :

KEY TO MASTER CHART

ALCOHOL- YES= 1; NO=0

S.AMYLASE <140U/L =1; >140U/L= 2

CT FINDINGS:

1= FOCAL INFLAMMATION

2= PERIPANCREATIC FLUID COLLECTION

3= NECROSIS

4= PSEUDOCYST

CRP = 150MG/ML

LDH = 350IU/L

MASTER CHART

S.No	Name	Age (in yrs)	Sex	Duration of Abdominal Pain (in days)	Alcohol	S.Amylase	CT Findings	CRP(mg/ml)	LDH(IU/l)
1	VELLINGIRI	48	M	2	1	2	3	160	540
2	PALANISAMY	46	M	1	1	2	2	110	260
3	GOVIND	32	M	2	1	2	3	148	460
4	NATARAJ	50	M	2	1	2	3	172	750
5	GOVINDARAJ	50	M	1	1	2	3	158	620
6	RAMASAMY	35	M	3	1	1	1	90	120
7	CHINNASAMY	58	M	1	1	2	4	150	810
8	DURAI	47	M	2	1	2	3	162	380
9	RAMU	36	M	2	1	2	3	152	490
10	RABIYA BEEVI	40	F	4	0	1	2	125	410
11	MANOHAR	32	M	2	1	2	3	176	590
12	DHILIP	28	M	2	1	1	1	96	240
13	GURUMOORTHY	41	M	1	1	2	3	180	690
14	GANESHAN	54	M	3	1	1	1	100	220
15	GOPINATH	33	M	2	0	2	3	124	1220
16	RAGHURAMAN	46	M	3	1	2	4	126	760
17	CHINDHAMANI	38	F	1	0	2	1	108	280
18	SAMPATHKUMAR	36	M	1	1	2	4	148	680
19	DURAISAMY	40	M	2	1	1	2	112	300
20	ROSY	30	F	3	0	2	2	140	260

21	RAMARAJAN	32	M	1	1	1	2	120	320
22	DEIVANAI	48	F	2	0	2	2	124	200
23	KARUNAKARAN	66	M	2	1	2	3	158	980
24	JEIGANESH	29	M	3	1	1	2	132	240
25	ARUNACHALAM	46	M	1	1	2	3	176	690
26	MOHIT	26	M	2	1	2	2	118	240
27	PALANISAMY	40	M	1	1	2	3	165	1110
28	PANDIAN	52	M	1	1	2	2	124	330
29	PRAVEEN	34	M	2	1	2	4	190	410
30	RAMASAMY	39	M	1	1	2	4	168	390
31	ELANGO	60	M	2	1	2	3	170	540
32	VISWANATHAN	55	M	1	1	2	3	152	490
33	SUBRAMANI	37	M	2	0	2	3	158	900
34	VIJAYAKUMAR	40	M	2	1	1	2	124	350
35	HARIRAJ	35	M	1	1	2	4	164	700
36	DHAYASHANKAR	48	M	3	1	2	3	160	510
37	DHARMARAJ	56	M	1	1	1	2	120	230
38	SATHISHKUMAR	41	M	1	1	1	2	128	300
39	SENTHILUMAR	49	M	3	1	2	3	150	370
40	ASHOK	42	M	2	1	2	4	156	820
41	MUNUSAMY	61	M	4	1	2	2	118	260
42	PARASURAMAN	50	M	2	0	2	3	172	470
43	JAYARAJ	48	M	1	1	2	2	124	330
44	PARAMESHWARAN	46	M	1	1	2	3	148	400

45	ELANGOVAN	38	M	2	1	1	2	106	240
46	GANAPATHY	66	M	2	1	2	3	160	630
47	SUDHAN	58	M	1	1	2	3	186	1020
48	DINESH	33	M	1	0	2	4	150	520
49	ARAVIND	42	M	1	1	2	2	132	300
50	PASUPATHY	58	M	3	1	2	2	118	360
51	KANAGARAJ	36	M	2	1	1	1	86	140
52	RAMU	30	M	2	1	1	2	110	200
53	RANGASAMY	69	M	1	0	1	2	124	290
54	MANIAPPAN	55	M	1	1	2	4	162	380
55	LURTHUSAMY	60	M	4	1	2	3	158	980
56	BALAJI	45	M	2	1	2	4	154	660
57	GUNASEKARAN	48	M	1	1	2	3	144	1070
58	DHARMARAJ	50	M	1	1	1	2	116	300
59	MANOHAR	52	M	1	1	2	3	172	390
60	PUVIARASAN	43	M	2	1	2	4	146	540
61	SHANKAR	30	M	3	1	2	4	160	620
62	SETHURAMAN	47	M	1	1	1	2	126	290
63	SHAKTHIKUMAR	42	M	2	1	2	3	156	350
64	KUPPUSAMY	59	M	1	1	2	2	128	300
65	VIDHYA	38	F	2	0	2	2	130	320
66	DURAISAMY	66	M	1	1	2	4	152	930
67	PRASAD	49	M	1	1	2	2	122	360
68	NANDAKUMAR	37	M	2	1	2	3	158	650

69	RAJA	33	M	2	1	2	3	186	420
70	VASUDEVAN	55	M	1	1	2	4	154	500
71	MOORTHY	41	M	3	1	2	3	174	710
72	PUSHPALATHA	40	F	1	0	1	2	118	400
73	BALUSAMY	56	M	2	1	2	3	180	630
74	MOHAMMED FAIZ	40	M	1	1	2	2	136	310
75	SURESH	62	M	2	1	2	4	146	480
76	SIVAKUMAR	44	M	4	1	2	3	174	630
77	CHOKKALINGAM	51	M	1	1	2	4	166	630
78	THANGAMANI	66	M	3	1	2	3	158	490
79	APPUSAMY	45	M	2	1	2	3	160	1020
80	MARAGATHARAJA	50	M	2	1	1	2	118	290
81	KESAVAN	45	M	1	0	2	2	128	300
82	ANANDKUMAR	42	M	1	1	2	3	192	410
83	ANTON PREM	38	M	1	1	2	3	166	830
84	SOMASUNDARAM	41	M	2	1	2	2	108	310
85	KARTHIKEYAN	49	M	1	1	2	3	150	490
86	KANAGARAJ	56	M	2	1	1	2	138	260
87	KUMARASAMY	59	M	3	1	2	2	140	340
88	SARAVANAN	52	M	2	1	2	4	182	410
89	KUPPURAJ	39	M	1	1	1	2	108	360
90	RANGASAMY	46	M	2	1	2	4	146	440
91	DHARMALINGAM	45	M	1	1	2	4	166	910
92	MARIAPPAN	49	M	2	1	1	3	158	530

93	ABBAS	40	M	2	1	2	3	146	390
94	GURUSAMY	39	M	3	1	2	4	170	1080
95	MOORTHY	40	M	1	1	2	2	132	380
96	ALAGARSAMY	31	M	2	1	1	3	180	650
97	VISWANATHAN	37	M	4	1	2	4	166	690
98	RANGASAMY	44	M	1	1	2	4	160	1280
99	CHINNAMAL	40	F	2	0	1	2	122	270
100	NAGARAJ	36	M	2	1	2	4	140	450