“NEUTROPHIL-LYMPHOCYTE RATIO (NLR) AS PROGNOSTIC MARKER IN ASSESSING ACUTE PANCREATITIS OUTCOME”

A DISSERTATION SUBMITTED TO THE TAMILNADU

DR MGR MEDICAL UNIVERSITY

CHENNAI

In partial fulfillment of the requirement for the degree of

M.S. (GENERAL SURGERY)

BRANCH – I

Register No: 221711367

DEPARTMENT OF GENERAL SURGERY

TIRUNELVELI MEDICAL COLLEGE

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PROF Dr. S.M. KANNAN M.S, M.Ch (Uro)

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I solemnly declare that the dissertation titled **"NEUTROPHIL-LYMPHOCYTE RATIO (NLR) AS PROGNOSTIC MARKER IN ASSESSING ACUTE PANCREATITIS OUTCOME"** is done by me at Tirunelveli Medical College hospital, Tirunelveli. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, or diploma to any other University, Board, either in or abroad. The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.S. Degree (Branch I) in General Surgery.

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PROTOCOL TITLE: NEUTROPHIL-LYMPHOCYTE RATIO (NLR) AS PROGNOSTIC MARKER IN ASSESSING ACUTE PANCREATITIS OUTCOME

PRINCIPAL INVESTIGATOR: Dr.S.SANKAR, MBBS.,
DESIGNATION OF PRINCIPAL INVESTIGATOR: PG STUDENT
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear Dr.S.SANKAR, MBBS, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting held on 27.10.2017.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of The Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor The study
6. At The time of PI's retirement/leaving the institute, The study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in The original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and The revised budget form should be submitted.
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This is certify that this dissertation work title **"NEUTROPHIL-LYMPHOCYTE RATIO (NLR) AS PROGNOSTIC MARKER IN ASSESSING ACUTE PANCREATITIS OUTCOME"** of the candidate **Dr.SANKAR.S** with registration Number **221711367** for the award of M.S. Degree in the branch of **GENEARL SURGERY (I).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows **17 percentage** of plagiarism in the dissertation.

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LIST OF ABBREVIATION

ALC	-	Absolute Lymphocyte Count
ANC	-	Absolute Neutrophil count
ANC	-	Acute necrotic collection
ANOVA	-	Analysis Of Variance
AP	-	Acute Pancreatitis
APACHE	-	Acute Physiology ,Age,Chronic Health Evaluation
APFC	-	Acute pancreatic fluid collection
ARDS	-	Adult respiratory distress syndrome
CECT	-	Contrast Enhanced Computed Tomography
CRP	-	C-Reactive Protein
CTSI	-	Computed tomography severity index
ERCP	-	Endoscopic Retrograde CholangioPancreatography
ICU	-	Intensive Care Unit
IL-6	-	Interleukin-6
LFT	-	Liver Function Test
MCTSI	-	Modified computed tomography severity index
MODS	-	Multi Organ Dysfunction Syndrome .
MRCP	-	Magnetic Resonance CholangioPancreatography
MRI	-	Magnetic Resonance Imaging
NLR	-	Neutrophil Lymphocyte Ratio
PLR	-	Platelet Lymphocyte Ratio
RBS	-	Random Blood Sugar
RDW	-	Red cell distribution width
RFT	-	Renal Function Test
SIRS	-	Systemic Inflammatory Response Syndrome
SOFA	-	Sequential Organ Failure Assessment
TNF-alpha	-	Tumor Necrosis Factor alpha
TPN	-	Total Parenteral Nutrition
USG	-	Ultrasonogram
WBC	-	White Blood Count
WON	-	Walled-off necrosis

CONTENTS

INTRODUCTION

Acute pancreatitis is one of the most common cause of emergency hospital admissions in india. The overall mortality due to acute pancreatitis has remained 10-15% in the past 20 years. Accurate predictors of the severity of acute pancreatitis are important because they influence clinical decision making. The neutrophil–lymphocyte ratio (NLR), calculated from the white cell differential count, provides a rapid indication of the extent of an inflammatory process. India being a developing country has a low Doctor: Patient ratio and limited facilities are available at the peripherally located hospitals, differential WBC count would be a cheaper and an easier blood test that can be performed. NLR is calculated on day 0 (admission),day 1, and day 2 and correlated with severity. Severity is defined using modified computed tomography severity index classification for acute pancreatitis.

AIMS AND OBJECTIVES

- To determine an optimal ratio of NLR for severity prediction.
- To study the age, sex distribution.
- To study the etiology of acute pancreatitis.

REVIEW OF LITERATURE

PANCREAS ANATOMY

The pancreas is an essential organ of body which is situated in retroperitoneum, weighs about 75 to 100g and it is about 15 to 20 cm long. It lies in oblique position. It has both exocrine and endocrine functions. The pancreas is divided into different parts like head,neck, body, tail, and uncinate process ,with the head of pancreas enclosed by the C loop of duodenum and the tail which abuts the spleen. superior mesenteric vein joins with splenic vein and continues towards porta hepatis as portal vein at inferior border of neck of pancreas . Three distinct types of cells are seen, namely the acinar cells, endocrine cells and the ductal cells. The acinar cells group to form acini which in turn form distinct lobules and secrete the digestive enzymes. The ductal cells form the pancreatic duct which joins with the common bile duct and opens into the second part of duodenum. The endocrine cells namely the Islets of Langerhans secrete hormones which help in regulation of glucose uptake, release and maintenance of serum glucose levels[7,8,9].

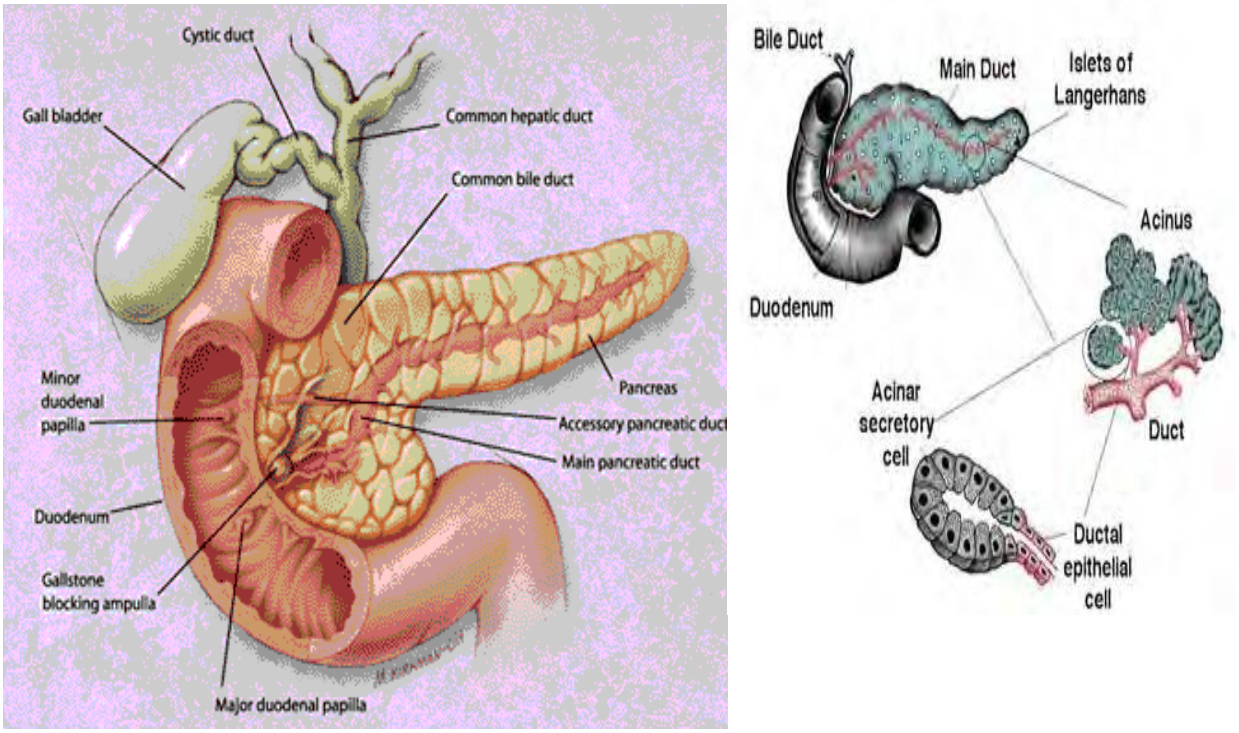

Fig 1: Anatomy of Pancreatic cells and the Ductal system

The blood supply of pancreas are from the Superior and Inferior Pancreaticoduodenal arteries and branches from the Splenic artery. Venous drainage is by Splenic vein, Superior mesenteric vein and the Portal vein. Lymphatics of pancreas drain into the Splenic, Celiac and Superior mesenteric lymph nodes[8].

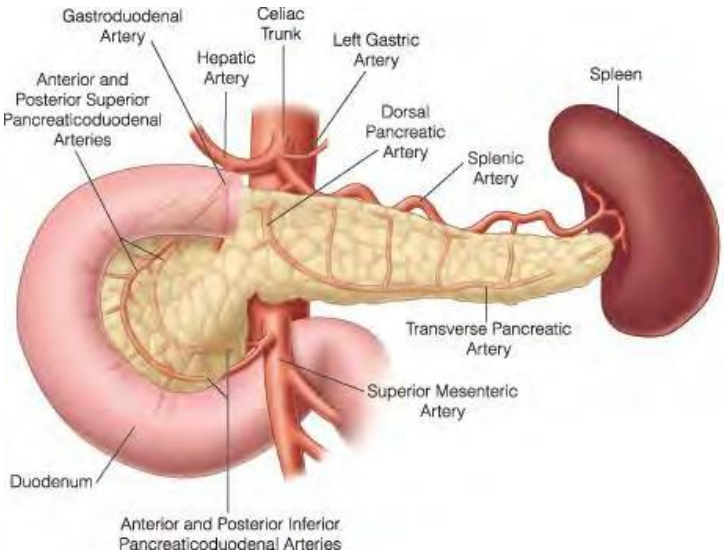

Fig 2: Blood Supply of Pancreas

Pancreas is essential for digestion and absorption of food from the gut and in regulating glucose homeostasis. Humoral control is by two hormones namely secretin and pancreozymin secreted by duodenum and proximal jejunum. Secretin induces alkaline secretion and pancreozymin produces juice rich in amylase, lipase, and trypsinogen[(9)].

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ACUTE PANCREATITIS:

Acute pancreatitis is one of the common clinical condition encountered in our day to day surgical practice. Acute pancreatitis poses a great challenge to the treating surgeon.

In 1925, Lord Moynihan stated that, in connection with the abdominal viscera, the dreaded calamity is the Acute Pancreatitis. He substantiated his statement with the following features of acute pancreatitis "Its sudden onset,

unbearable agony and the mortality rate depending on its severity are the aspects of acute pancreatitis, which make it the most formidable to overcome"[10].

Acute pancreatitis is an inflammation of the pancreatic tissue secondary to acinar cell necrosis. Pathology is auto digestion by pancreatic enzymes.

Epidemiology:

Most patients develop a mild and a self-limited course, however 10% -20% of patients have a rapidly progressive course with prolonged length of hospital stay and significant morbidity and mortality. Mild pancreatitis is associated with a mortality rate of less than 1% but, it increases up to 10%- 30% in severe pancreatitis[11].

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CLASSIFICATION:

In 1992, the International Symposium in Atlanta was conducted on acute pancreatitis. According to it, acute pancreatitis was classified into mild and severe pancreatitis. Severe pancreatitis is diagnosed if there is any evidence of organ failure or local pancreatic complications[5,6].

Table 1: Atlanta classification of Acute Pancreatitis

Classification	Clinical features	Morphologic findings
Mild ("edematous pancreatitis")	Minimal organ dysfunction and uneventful recovery	Interstitial edema and disseminated, usually microscopic, fatty tissue necrosis
Severe ("necrotizing pancreatitis")	Organ failure and/or local complications such as necrosis, abscess, or pseudo cyst	Extensive fatty tissue necrosis and/or hemorrhagic necrosis involving both the pancreatic parenchyma and the extra pancreatic fatty tissue: development of pseudo cysts and abscesses

Definition of organ failure by Atlanta
Shock–systolic pressure <90 mmHg
PaO2 ≤60 mmHg
Creatinine >2.0 mg/L after rehydration
Gastrointestinal bleeding >500 cc/24 h

REVISED ATLANTA CLASSIFICATION[05,06]:

The revised Atlanta classification 2012 requires atleast two of the following three criteria for the diagnosis of acute pancreatitis.

- Abdominal pain consistent with the disease,
- Threefold increase in serum amaylase or lipase level,
- Imaging findings (CT or USG Abdomen) consistent with acute pancreatitis

SEVERITY CLASSIFICATION:

Disease severity is stratified by organ failure ,local complications and systemic complications

MILD PANCREATITIS:

No organ failure

No local complications

MODERATE PANCREATITIS:

Transient organ failure < 48 hours

With or without local complications

SEVERE PANCREATITIS:

Persistent organ failure for> 48 hours

Local complications includes:

Acute pancreatic fluid collection

Pancreatic pseudocyst

Acute necrotic collection

Pleural effusion

Organ failure:

Failure of three main organs respiratory, cardiac,renal and other organ systems(hepatic,hematological and neurological)

OTHER DEFINITIONS:

- **Pancreatic necrosis:**

It is the non viable pancreatic tissue which can be focal or diffuse and is usually associated with peripancreatic fat necrosis. It can be infected or sterile.

- **Acute fluid collection:**

It is the fluid found inside or around the pancreas which does not have a definitive wall. It usually occurs in the earlier stages of acute pancreatitis in around 30% - 50% patients and resolves spontaneously.

- **Pancreatic pseudocyst:**

It is the fluid collection that remains for 4 - 6 weeks and is walled off by fibrous or granulation tissue.

- **Walled-off necrosis (WON)**
- Usually occurs >4 weeks after onset of necrotizing pancreatitis
- Heterogeneous with liquid and nonliquid density with varying degrees of loculation
- Well-defined wall; that is completely encapsulated
- intrapancreatic and/or extra pancreatic

- **Hemorrhagic pancreatitis:**

It is pancreatitis associated with hemoperitoneum which occurs due to erosion of pseudoaneurysm of the peripancreatic blood vessels. It can sometimes erode the retroperitoneal vessels resulting in acute hemorrhage which is an acute emergency. Management for this hemorrhage requires immediate angiographic embolisation or surgery.

Balthazar CTSI Scoring (1990)

Prognostic Indicator	Points
Normal pancreas	0
Focal or diffuse enlargement of pancreas	1
Intrinsic pancreatic abnormalties with inflammatory changes in peripancreatic fat	2
Single, ill defined fluid collection or phlegmon	3
Two or more poorly defined collections or presence of gas in or adjacent to the pancreas	4
Extent of pancreatic inflammation was assigned points from 0-4. The presence and extent of necrosis was classified into four categories and awarded points from 0-6.	

Necrosis	Points
None	0
≤30%	2
30-50%	4
≥50%	6
The Balthazar CTSI was calculated by adding the above points in each case and the total score was then categorized as: Mild Pancreatitis CTSI Score 0-3 Moderate Pancreatitis CTSI Score 4-6 Severe Pancreatitis CTSI Score 7-10	

Modified computed tomography severity index by Mortele et al(2004)

Pancreatic inflammation

- 0: normal pancreas
- 2: intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat
- 4: pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis

Pancreatic necrosis

- 0: none
- 2: 30% or less
- 4: more than 30%

Extrapancreatic complications

- 2: one or more of pleural effusion, ascites, vascular complications, parenchymal complications and/or gastrointestinal involvement

Total score

- 0-2: mild pancreatitis
- 4-6: moderate pancreatitis
- 8-10: severe pancreatitis

PATHOPHYSIOLOGY:

Acute pancreatitis is a final result of abnormal pancreatic enzyme activation inside acinar cells.Normally Enterokinase converts trypsinogen into trypsin. Trypsin which is derived from trypsinogen is the principal activator of all enzymes. Even normally a small proportion of trypsinogen gets activated spontaneously inside the acinar cells. But the various protective mechanisms present within pancreas wash out the activated trypsin so that there wont be any damage to the gland.

These include:

- Serine Protease Inhibitor Kazal type 1 (SPINK1)
- Mesotrypsin
- Enzyme Y
- α1-antitrypsin
- α2-macroglobulin

In acute pancreatitis, Colocalisation is the first step as per Immunolocalisation studies. After a pancreatic injury, the above defensive mechanisms are overcome, zymogen granules and lysosome granules containing enzymes like cathepsin B colocalise inside the acinar cells resulting in intra acinar pancreatic enzyme activation[(11)]..

This induces auto digestion of the pancreatic parenchyma. In response, the acinar cells release pro-inflammatory cytokines such asTNF-alpha (Tumour Necrosis Factor-α), IL-2, IL-1 and IL-6 .These mediators propagate the response both locally and systemically.

Neutrophils and macrophages are recruited into the pancreatic parenchyma which cause the release of more TNF-α, IL-1, IL-6, reactive oxygen species, prostaglandins, platelet activating factor and leukotrienes. This further increases the permeability and damages the microcirculation of the pancreas[(11)]..

The inflammatory cascade is self-limited in approximately 80% - 90% of patients. In small number of patients, there is massive release of inflammatory mediators into systemic circulation. Active neutrophils mediate acute lung injury and induce adult respiratory distress syndrome (ARDS). Similarly it affects the kidneys and gut and progresses to Multi- Organ Dysfunction Syndrome (MODS).

Also Trypsin activates other pathways, such as complement, coagulation or fibrinolysis, extending the process outside the gland which is responsible for systemic manifestation of the disease.

Genetic factors have also been implicated in pathogenesis of acute pancreatitis which is:

- Cationic Trypsinogen gene (PRSS1)
- Cystic Fibrosis Transmembrane Conductance Regulator Gene (CFTR)
- Polymorphisms in SPINK1

ETIOLOGY:

Gall stones and Alcohol are the most common (70% to 80%) causes of pancreatitis[11].Other etiological factors are as follows:

Table 2: Etiological factors of Pancreatitis

Other causes
Shock
Toxins Scorpion venom, Methyl alcohol, Organophosphorous insecticides Drugs Alpha- methyldopa 5-Aminosalicylate (mesalamine) Azathioprine Furosemide Isoniazid 6- Mercaptopurine Metronidazole Dexamethasone Trimethoprim/sulfamethoxazole

Antiretroviral drugs
Metabolic- hypertriglyceridemia, Hypercalcemia
Ductal obstruction- Tumors, Parasites, Duodenal diverticula, Annular pancreas, Choledochocele
Surgical procedure- ERCP
Trauma
Infection Viral- Mumps, Coxsackie A, HIV, CMV Bacterial- M.tuberculosis Mycoplasma Hereditary/ familial/ genetic

Biliary Pancreatitis:

It is one of the commonest etiologies of acute pancreatitis. Studies have shown that, episodes of acute pancreatitis are frequently preceded by passage of stone into the duodenum. In about 90% of patients with stone induced pancreatitis, stones can be retrieved from their stools.

Various mechanisms have been proposed for biliary pancreatitis.

- The theory proposed by Opie, termed as "Common channel theory". The lodging of biliary stone in the common channel between the biliary tract and the pancreatic duct causes pancreatitis as a result of reflux of bile into the pancreatic duct.
- Numerous studies have shown that the above theory may be not being as appropriate as the bile reflux is not sufficient to cause acute pancreatitis. This paves the way for the proposal of "Duct obstruction theory", which states that the edema induced by the stones leads to the obstruction of the duct which in turn results in duct hypertension, triggering pancreatitis.

Alcohol Induced Pancreatitis*(11)*.:

Although alcohol is the most frequent cause for chronic pancreatitis, it can also cause acute episodes. Various mechanisms have been proposed for pancreatitis induced by alcohol.

- Ductal hypertension caused by alcohol induced spasm of sphincter of oddi.
- Free fatty acids produced by alcohol induced hypertriglyceridemia have a toxic effect on the pancreatic acinar cells.
- Alcohol stimulates the production of free radicals within the pancreas which in turn injure the acinar cells.
- Pancreatic ischaemia caused by alcohol induced microcirculation failure.
- Alcohol stimulates the pancreatic acinar cells to produce protein-rich pancreatic juice, which has the following effects,

1) Formation of protein plug by the protein rich fluid, which causes duct obstruction.
2) The protective enzymes are overwhelmed resulting in auto-digestion of pancreas.

Acute pancreatitis occurs in 5-10% of patients following endoscopic retrograde cholangiopancreatography (ERCP). Use of a prophylactic pancreatic duct stent and rectal nonsteroidal anti-inflammatory drugs (NSAIDs) has been shown to reduce pancreatitis after ERCP.

Risk factors for post-ERCP pancreatitis

- minor papilla sphincterotomy,
- sphincter of Oddi dysfunction,
- prior history of post-ERCP pancreatitis,
- age <60 years,
- >2 contrast injections into the pancreatic duct,
- endoscopic trainee involvement

Hypertriglyceridemia is the cause of acute pancreatitis in l.3-3.8% of cases; serum triglyceride levels are usually > 1l.3 mmol/L (> 1000 mg/dL). Most patients with hypertriglyceridemia when subsequently examined show evidence of an underlying derangement in lipid metabolism probably unrelated to pancreatitis. Such patients are prone to recurrent episodes of pancreatitis. Any factor (e.g., drugs or alcohol) that causes an abrupt increase in serum triglycerides can precipitate a bout of acute pancreatitis. Patients with a deficiency of apolipoprotein CII have an increased incidence of pancreatitis; apolipoprotein CII activates lipoprotein lipase which is important in clearing chylomicrons from the bloodstream. Patients with diabetes mellitus who have developed ketoacidosis and patients who are on certain medications such as oral contraceptives may also develop high triglyceride levels.

Idiopathic Pancreatitis:

In spite of extensive studies, in about 20% of patients presenting with acute pancreatitis, no cause can be identified.

The mechanisms proposed in such instances are:

- Sludge or microcrystals in the gall bladder
- Dysfunction of the sphincter leading to ductal hypertension
- Subclinical mutations in cystic fibrosis transmembrane regulator gene (CFTR gene)

CLINICAL FEATURES[(11)]:

Symptoms:

- Abdominal pain is the most common symptom. the pain is usually epigastric radiating to the back
  - Constant severe pain
  - Typically relieved by leaning forward
- Nausea and vomiting
- Dyspnoea if there is associated pleural effusion

Signs:

- General examination reveals dehydration, tachycardia, tachypnoea, hypotension
- Abdominal examination usually reveals severe epigastric tenderness associated with guarding and rigidity

- Bowel sounds may be absent due to paralytic ileus
- Retroperitoneal hemorrhage leading to bluish discoloration in
- Umbilical area- Cullen's sign
- Loin- Grey Turner's sign
- Groin- Fox's sign

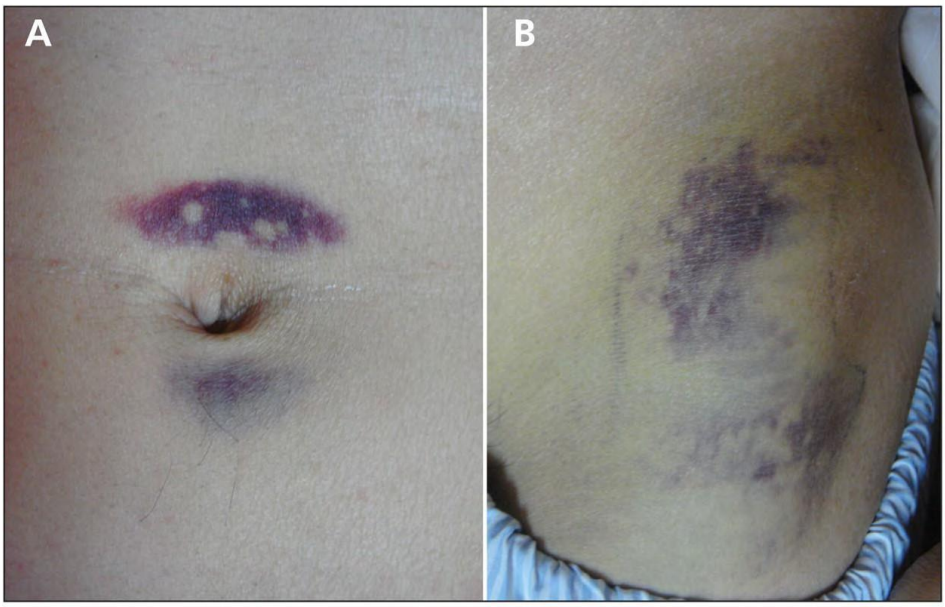


Fig 3: A) Cullen's sign B) Grey Turner's sign

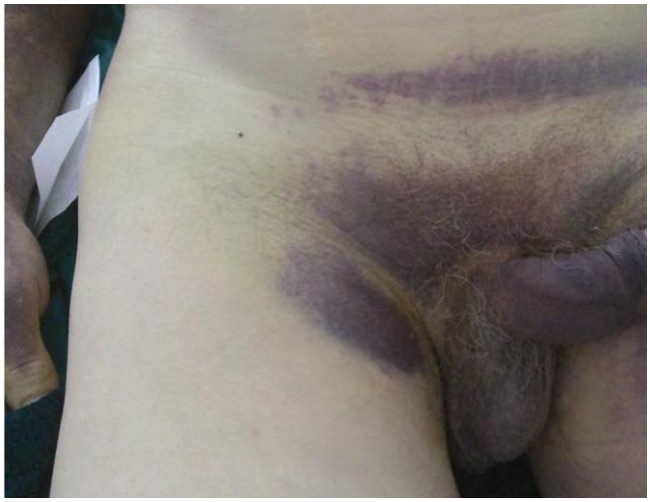


Fig 4: Fox's sign

- Pain or resistance in the zone where the head of pancreas is located (in the epigastrium, 6–7 cm above the umbilicus) - Korte's sign
- Pain with pressure under the xiphoid process - Kamenchik's sign
- Tenderness on pressure at the Mayo-Robson's point - a point at the junction of the inner 2/3 and the outer 1/3 of the line that represents the bisection of the left upper abdominal quadrant. At this point the tail of pancreas is projected on the abdominal wall.
- Thrombophlebitis in the legs

INVESTIGATIONS:

A. **Blood investigations:**

- Serum Amylase: Most common serum marker used in diagnosis. It elevates within 2-12 hours of onset of symptoms and remains elevated for 3-6 days. In acute pancreatitis there is loss of cell to cell adhesions and so amylase gets access to vessels and is increased in serum. It has no prognostic value.
- Extrapancreatic sources of amylase need to be considered which are the salivary gland, lung, ovary, prostate. Other causes of hyperamylasemia also need to be considered like acute cholecystitis, intestinal ischaemia, hollow viscus perforation, intestinal obstruction and macroamylasemia.

- Serum Lipase: More specific for pancreas. Its limitation is that it remains elevated for 1 week, so it is not sensitive enough to detect complications.
- Other investigations:
    i. Increased hemoglobin, hematocrit, Blood Urea Nitrogen (BUN) and creatinine due to hypovolemia.
    ii. Hypoalbuminemia secondary to fluid replacement with crystalloids
    iii. Hyperbilirubinemia which may be a cause or effect of acute pancreatitis
    iv. Hypochloraemic metabolic alkalosis secondary to excessive vomiting
    v. Hypocalcemia due to sequestration in pancreatic fat necrosis or associated hypoalbuminemia
    vi. Hyperglycemia due to associated diabetes mellitus, increased glucagon release, increased catecholamine release.

i. **Hypoxemia**

- arterial PO2 < 60 mmHg
- indicates the onset of ARDS

ii. **ECG**

- ST-segment & T-wave abnormalities

B. **Imaging Studies:**

- X-Ray abdomen: Not specific for pancreatitis, but may show signs due to ileus

1. Sentinel loop sign
2. Colon cut-off sign
3. Renal halo sign

Ultrasonography abdomen: limited value in visualizing pancreas since it is usually obscured by bowel gas shadows. However, when detected following findings may be noted

1. Bulky edematous pancreas
2. Any associated biliary stone
3. Dilated pancreatic duct
4. Any fluid collections

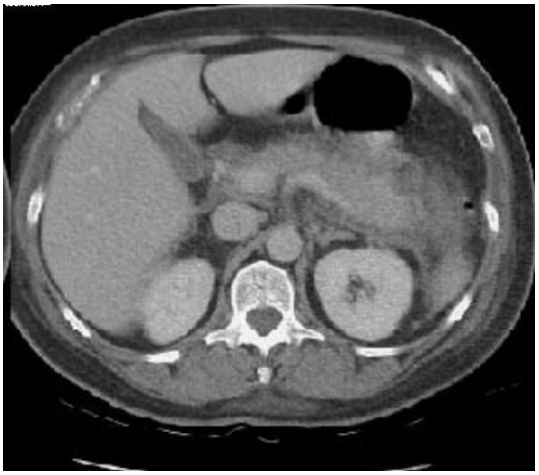


Fig 5: CT showing features of Acute pancreatitis

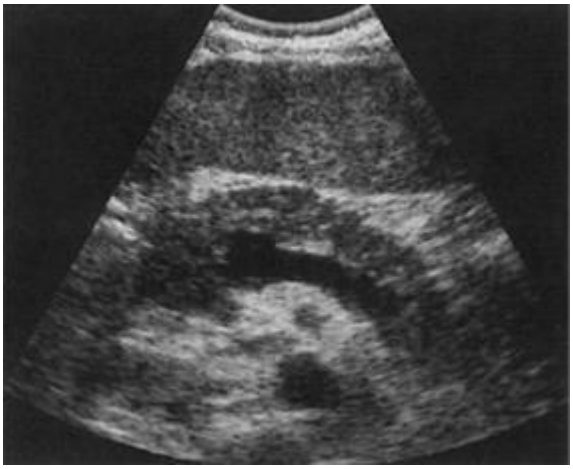


Fig 6: USG abdomen showing bulky hypo echoic pancreas

- CECT Abdomen: it is the investigation of choice to diagnose acute pancreatitis and its complications. Following features may be noted

  1. Enlarged pancreas
  2. Loss of peripancreatic fat plane
  3. Areas of decreased density
  4. Localized fluid collection
  5. Detects pancreatic necrosis which is of great importance which is identified by non enhancement of > 30% or > 3cm of parenchyma of pancreas.

  CT is usually performed around 48hours after diagnosis as earlier done CT misses necrosis. The sensitivity of CECT to detect necrosis at 4 days is 100%[(12)].

- MRI Abdomen: Can also be used in diagnosis and staging severity. Usually taken when CECT is contraindicated like in case of renal dysfunction or contrast allergy. Following table compares various imaging modalities used in acute pancreatitis[(12)]:

Table 3: Comparison of various imaging modalities in acute pancreatitis

Imaging Technique	Effectiveness
CECT abdomen	78% sensitivity and 86% specificity For severe acute Pancreatitis
Endoscopic USG	100% sensitivity and 91% specificity for gallstones
MRCP	81% to 100% sensitivity for detecting CBD stones
	98 % negative predictive value and 94% positive predictive value for bile duct stones
	As accurate as CECT in predicting severity of pancreatitis and identifying pancreatic necrosis.
MRI	83% sensitivity and 91% specificity for severe acute pancreatitis
USG abdomen	87 to 98% sensitivity for the detection of gallstones.

DIAGNOSIS:

Diagnosing acute pancreatitis requires clinical, serological and imaging correlation. Various serum markers are used in the diagnosis and prognosis of acute pancreatitis. Some of them have been summarized in the following table[(13)].

Table 4: Various Serum markers in Acute Pancreatitis

Laboratory Test	Time of onset (Hours)	Purpose	Clinical observation / limitations
Alanine transaminase	12 to 24 hours	Diagnosis and etiology	Associated with gallstone pancreatitis; threefold elevation or greater in the presence of acute pancreatitis has a positive predictive value of 95 percent in diagnosing acute gallstone pancreatitis
Amylase	2 to 12hours	Diagnosis	Most accurate when at least twice the upper limit of normal; amylase levels and sensitivity decrease with time from onset of Symptom
C-reactive protein	24 to 48hours	Predictive of severity	Late marker; high levels associated with pancreatic necrosis
Lipase	4 to 8 hours	Diagnosis	Increased sensitivity in alcohol- induced pancreatitis; more specific and sensitive than amylase for detecting acute pancreatitis
Phospholipase A2	24 hours	Predictive of severity	Associated with development of pancreatic necrosis and pulmonary failure
Procalcitonin	24 to 36 Hours	Predictive of severity	Early detection of severity; high concentrations in infected Necrosis
Trypsinogen activation peptide	Within few hours	Diagnosis and predictive of severity	Early marker for acute pancreatitis and close correlation to severity
IL-6	18 to 48 hours	predictive of severity	Early detection of severity, high concentration in infected necrosis
IL-8	12 to 24 hours	predictive of severity	Early marker for acute pancreatitis and close correlation to severity

COMPLICATIONS OF PANCREATITIS[11]:

Local complications:

1. Fluid collections
2. Pancreatic Ascites/ Pleural effusion
3. Pseudocyst
4. Pancreatic necrosis
5. Pancreatic abscess
6. Pseudoaneurysm/hemorrhage
7. Splenic vein rupture
8. Portal vein rupture
9. Gastrointestinal bleeding
10. Postnecrosectomy bleeding
11. Splenic infarction
12. Enteric fistula
13. Smoldering pancreatitis:

In this entity, despite adequate supportive therapy, the pain persists for 2-3 weeks or more with persistent hyperamylasemia. The cause may be varied and includes any of the causes of acute pancreatitis. Imaging shows significant pancreatic injury suggesting a functional obstruction to the pancreatic duct secondary to edema or spasm. Transpapillary stenting relieves the symptoms.

Regional complications:

1. Venous thrombosis
2. Paralytic ileus
3. Intestinal obstruction
4. Intestinal ischaemia.

Systemic complications :

1. SIRS-Systemic Inflammatory Response Syndrome
2. MODS-Multi organ Dysfunction Syndrome
3. ARDS-Acute Respiratory Distress Syndrome
4. Renal failure
5. Cardiovascular complications
6. Hypocalcemia
7. Hyperglycemia
8. Disseminated Intravascular Coagulation
9. Protein malnutrition
10. Encephalopathy
11. Fat necrosis (subcutaneous nodules)
12. Retinopathy
13. Death

SEVERITY SCORING SYSTEMS:

Acute severe pancreatitis is associated with the high morbidity and mortality hence, many scoring systems have been formulated to stratify the risk of developing severe pancreatitis. All the scoring systems have been devised keeping the Atlanta's classification[5,6] as a standard. The Clinical scoring system and certain laboratory tests are the most common methods of assessing the prognosis in acute pancreatitis[14].The most commonly used systems are the Ranson's criteria, The Modified Glasgow system (Imrie Scoring), APACHE II scoring system.

Ranson's criteria were devised in 1974 which consists of 11 parameters which are derived from patients at the time of admission and at 48 hours. Severe pancreatitis is defined if 3 or more of its parameters are fulfilled. The disadvantage of this criteria is that it can predict severity only at the end of 48 hours. Also it has a low positive predictive value (50%) but a high negative predictive value (90%). So, it is mainly used to rule out a severe disease. The same is true for the Modified Glasgow system[11].

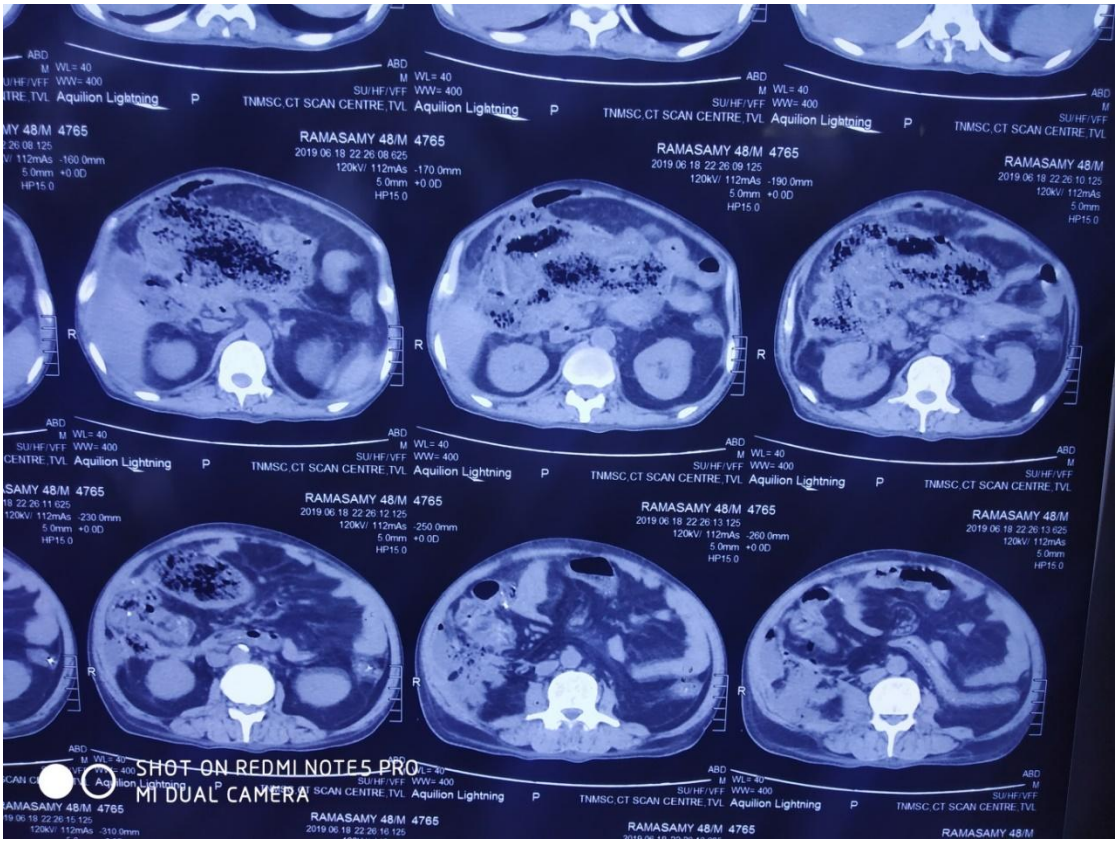


Fig 7:Acute Necrotising Pancreatitis

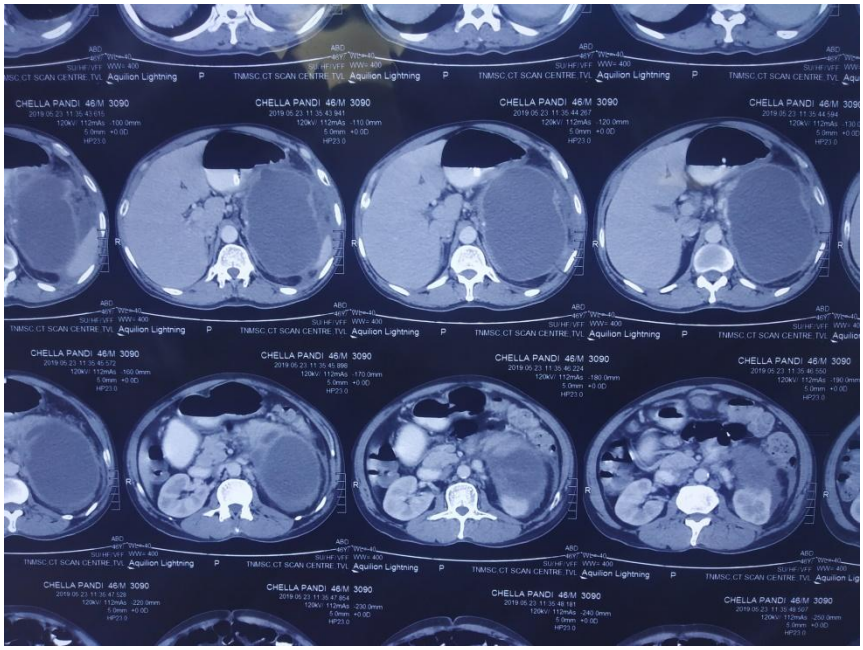


Fig 8:Acute pancreatitis with pseudocyst

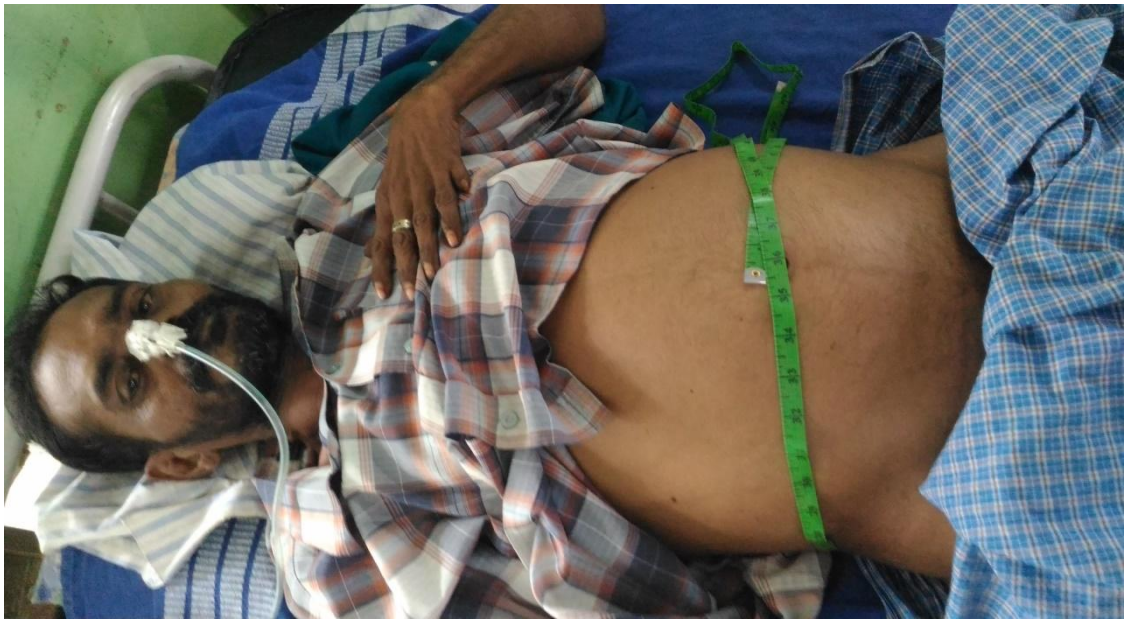


Fig 9:Acute Pancreatitis With Ascites

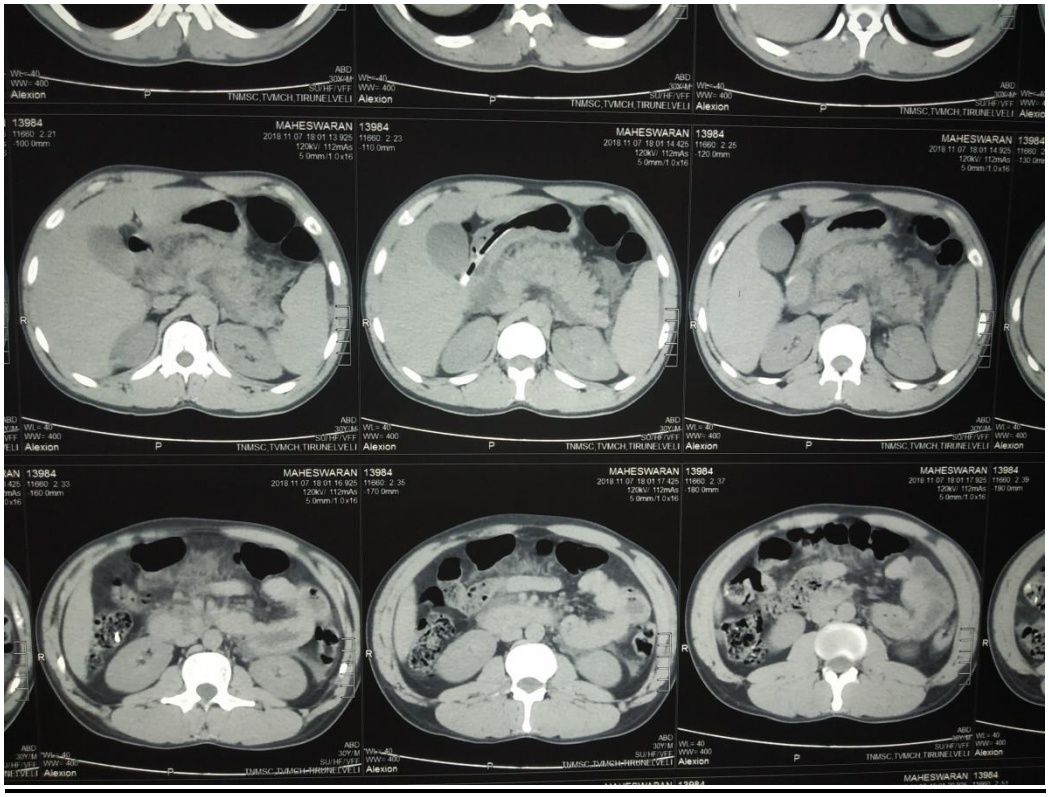


Fig 10:Acute Pancreatitis With Ascites

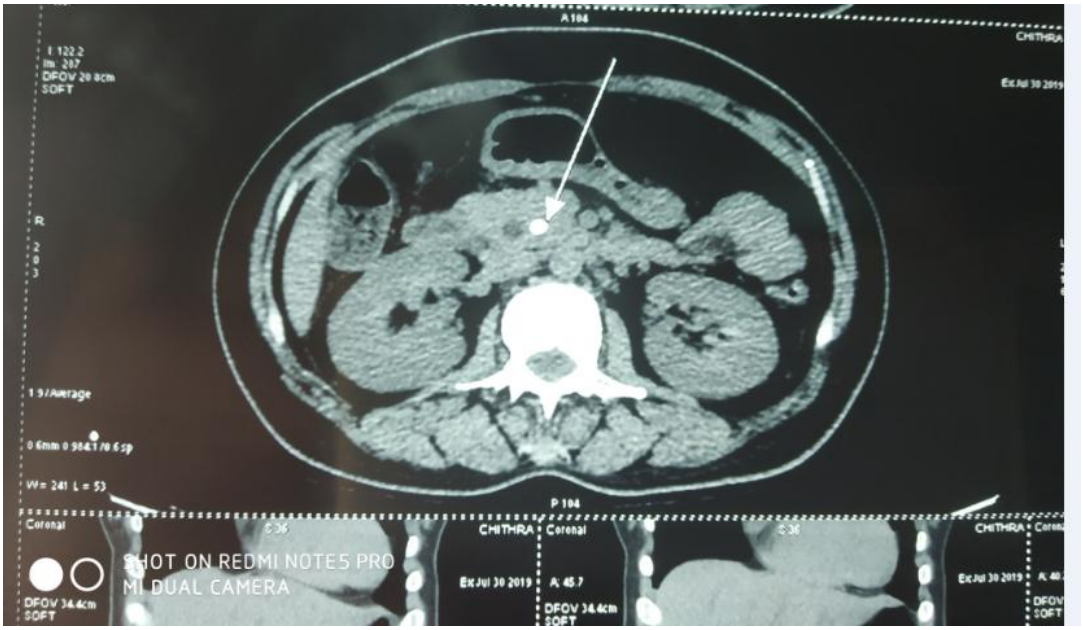


Fig 11:Pancreatic ductal calculi

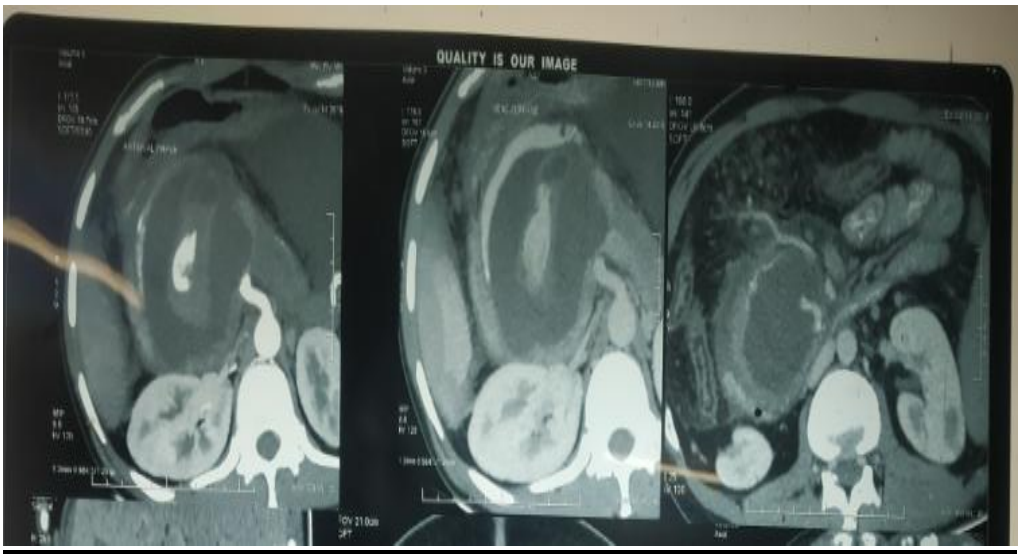


Fig 12:Pseudoaneurysm with extravasation of contrast from right colic branch of SMA

Because of the severity of acute pancreatitis and high mortality and morbidity, various extensive studies were conducted regarding the evaluation of severity of acute pancreatitis and designed various scoring systems. They also even compared these scoring systems with one another to find out a single best possible way to predict the severity of acute pancreatitis

DIFFERENTIAL DIAGNOSIS

(1) Perforated viscus, especially peptic ulcer

(2) Acute cholecystitis and biliary colic

(3) Acute intestinal obstruction

(4) Mesenteric vascular occlusion

(5) Dissecting aortic aneurysm

(6) Connective tissue disorders with vasculitis

TREATMENT[(11)]:

Treatment of acute pancreatitis mainly depends on the severity of pancreatitis. Most cases of acute pancreatitis are managed conservatively except in cases of acute severe necrotizing pancreatitis and complications in which surgical intervention is necessary.

1. Aggressive fluid resuscitation
2. Control of pain
3. Strict monitoring of hemodynamic status
4. Nutritional support and
5. Surveillance for complications are important in management of patients

with acute pancreatitis.

The cornerstone of the treatment of pancreatitis is aggressive volume replacement using crystalloid solution. The rate of fluid administration should be individualized and based on age, associated co morbidities, vital signs, mental status,haemotocrit,BUN, skin turgor and urine output. Maintain urine output >0.5 ml/kg per hour. RL is better crystalloid. Increase in hematocrit or BUN during monitoring should be treated with a repeat volume challenge with bolus.

Patients require monitoring of oxygen saturation because one of the most common systemic complication is hypoxemia caused by acute lung injury. They should receive supplementary oxygen to maintain arterial saturation above 95%.

It is also essential to provide adequate analgesia. Opioids cause sphincter of oddi spasm.

Nutritional support in the form of TPN or enteral nutrition is vital in the treatment of acute pancreatitis. It has been shown that enteral nutrition has many benefits over total parenteral nutrition in severe acute pancreatitis. However, a meta-analysis showed that total enteral nutrition has no better advantage over total parenteral nutrition with respect to outcome in those patients[(24)].

Role of antibiotics in pancreatitis is controversial. Recent meta- analyses have proven that prophylactic antibiotics do not decrease the frequency of

surgical interventions, infected necrosis, or mortality in patients with severe pancreatitis. Further, some meta- analyses conclude that the use of antibiotics prophylactically can reduce the infection rate, surgical intervention, sepsis and in turn mortality in acute pancreatitis patient. Thus, the use of prophylactic antibiotics for necrotizing pancreatitis must be weighed carefully with the benefits and risks[24].

The role of Somatostatins and octreotide in acute pancreatitis is that, they inhibit both the basal and stimulated pancreatic secretion. They also stimulate reticuloendothelial system activity, modulate the cytokine cascade and are cytoprotective with respect to the pancreas.

These effects of somatostatin and octreotide suggest that both drugs may be useful either in the treatment of acute pancreatitis.

Special Considerations Based on Etiology :

Increased risk of recurrence seen in GALLSTONE PANCREATITIS. Within 24-48 h of admission , if patients have evidence of ascending cholangitis, ERCP and stone removal or performing a cholecystectomy or endoscopic biliary sphincterotomy during the same admission or within 4-6 weeks of discharge is advisable.

If acute pancreatitis caused by HYPERTRIGLYCERIDEMIA (Serum triglycerides > 1 000 mg/ dL) initial therapy may include anti hyperlipidaemia agents, weight loss , insulin, heparin, or plasmapheresis .

Other causes that may be treated accordingly are

- Hypercalcemia (diagnose and treat hyperparathyroidism)

- Autoimmune pancreatitis (treated with glucocorticoid administration)

- Post-ERCP pancreatitis (ICU care)

- Drug-induced pancreatitis (Drugs should be discontinued)

The indications for surgical intervention in necrotizing pancreatitis are:

1.Diagnostic uncertainity

2.Complications of pancreatitis like aneurysmal rupture

3.Infected necrosis

Options for infected necrosis are: STEP UP APPROACH

1.Minimally invasive management – Pig tail catheter drainage+antibiotics

2. Conventional management - necrosectomy along with simple drainage

- Closed lavage of the debrided cavity,
- Closed management - necrosectomy with continuous closed postoperative lavage
- Open management - necrosectomy with staged reoperations at appropriate intervals with repeated lavage.

In patients with Gall stone induced pancreatitis, in mild cases early laparoscopic cholecystectomy is indicated , during the initial admission itself.. In severe pancreatitis cases however,interval cholecystectomy is planned only after 6 weeks.

ERCP with sphincterotomy in pancreatitis is only indicated in:

1.Severe acute biliary pancreatitis.

2.Patients with cholangitis.

3. In older patients unfit for surgery

4. Patients with persistent bile duct obstruction

The disadvantages with ERCP procedure are:

(1) ERCP can precipitate pancreatitis and it may introduce infection to sterile pancreatitis

(2) Risk of bleeding is present

Role of Pancreatic resection in acute pancreatitis:

Ductal necrosis can result in the entity called disconnected duct syndrome, most commonly involving the mid pancreatic body along with the ductal epithelium. Disconnected pancreatic duct is an anatomic situation where there is a lack of ductal continuity between viable secreting pancreatic tissue and the gastrointestinal tract .The isolated viable pancreatic segment continues to have an exocrine output that is not drained into the bowel. The resultant fistula and inflammatory collections are persistent and are unlikely to resolve with conservative drainage measures, mandating surgical treatment.

The criteria for diagnosing disconnected duct syndrome include:

i) ERCP evidence of main pancreatic duct cut-off or discontinuity with inability to access or cannulate the upstream pancreatic duct;

ii) CT evidence of viable pancreatic tissue upstream from the pancreatic duct cut-off or discontinuity and

iii) A non healing pancreatic fistula, pseudocyst or fluid collection despite a course of conservative medical management.

iv) Pancreatic duct leaks and fistulas occur at times in acute necrotizing pancreatitis. The damage to the pancreatic ductal system allows pancreatic juice to leak from the gland. Sudden development of hypocalcemia or a rapid increase in retroperitoneal fluid on CT scan is suggestive of this condition.

Ductal disruption following acute pancreatitis can result in pancreatic fluid collection or pseudocyst, pleural effusion, pancreatic ascites, pancreaticocutaneous fistulas and severe pancreatic necrosis. Main pancreatic ductal disruption causes continuous enzymatic insult to the pancreas and a disconnected gland syndrome.

Ductal disruption can be associated with a pancreatico-cutaneous fistula, especially after surgical necrosectomy or percutaneous drainage. If surgical necrosectomy is mandated in severe cases with infected necrosis, the percutaneous drainage of fluid collections should be avoided because it transforms a collection easily accessible to endoscopic drainage into a permanent fistula with a high rate of relapse, when the percutaneous drain is removed.

PSEUDOCYST

Incidence is low & collections resolves in most acute cases.

After 6 weeks, less than 10% of patients have persistent fluid collections. Only symptomatic collections should be drained with surgery or endoscopy or by percutaneous route.

PERIVASCULAR COMPLICATIONS

Splenic vein thrombosis with gastric varices Pseudo aneurysms.

Gastric varices bleed less than 5%. Life-threatening bleeding can occur, it must be diagnosed and treated with "mesenteric angiography and embolization"

EXTRAPANCREATIC INFECTIONS

- Incidence of Hospital acquired infections are up to 2 to 20%.
- Mostly as pneumonia, urinary tract infection .
- Routine urine culture, monitoring of chest x-rays & routine changing of intravenous lines are important during hospitalization.

Follow-Up Care

For assessment of

- Development of diabetes
- Exocrine insufficiency
- Recurrent cholangitis
- Development of infected fluid collections.

PROGNOSIS

- Mortality rates for acute pancreatitis have declined from at least 10% to around 5% since the 1980s, but the mortality rate for severe acute pancreatitis remains at least 20%, with rates of 10% and 25% in those with sterile and infected necrosis, respectively.
- Severe acute pancreatitis is predicted by features of the systemic inflammatory response on admission.
- Half of the deaths occur within the first 2 weeks, usually from multiorgan failure.
- Multiorgan failure is associated with a mortality rate of at least 30%, and if it persists beyond the first 48 hours, the mortality rate is over 50%.
- Later deaths occur because of complications of infected necrosis.
- The risk of death doubles when both organ failure and infected necrosis are present.

- Moreover, hospital acquired infections increase the mortality of acute pancreatitis, independent of severity.
- Readmission to the hospital for acute pancreatitis within 30 days may be predicted by a scoring system based on five factors during the index admission:
    - Eating less than a solid diet at discharge
    - Nausea, vomiting, or diarrhea at discharge;
    - Pancreatic necrosis;
    - Use of antibiotics at discharge;
    - Pain at discharge.

- Recurrences are common in alcoholic pancreatitis but can be reduced by repeated, regularly scheduled interventions to eliminate alcohol consumption after discharge from the hospital.
- The risk of chronic pancreatitis following an episode of acute alcoholic pancreatitis is 13% in 10 years and 16% in 20 years.

MATERIALS AND METHODS

Study design: This is a cross sectional study

Sample size: 100

Source of study:

General surgery department in tirunelveli medical college hospital,tirunelveli-tertiary care hospital.

Study period:

During the period from Dec 2017 to June 2019.

Inclusion criteria:

- All cases of acute pancreatitis with age>12 years.

Exclusion criteria:

- Age less than 12 years
- Chronic pancreatitis
- A history of cancer or hemoproliferative disorder

Technique:

Atleast two of the following three criteria for the diagnosis of acute pancreatitis.

- Abdominal pain consistent with the disease,
- Threefold increase in serum amaylase or lipase level,
- Imaging findings (CT or USG Abdomen) consistent with acute pancreatitis

Those patients who fit in the criteria are taken for study after informed written consent.

Information on age,sex,other complaints, medical history, smoking habit, alcohol consumption, with thorough general and clinical examination of all patients will be done.

Blood samples are collected within 2hours(day 0) after hospitalization,day1 and day2 . Relevant biochemical investigation will be done.

Radiological investigations including plain chest radiograph, erect abdominal radiograph, abdominal ultrasonography and CT/CECT(contrast enhanced) scan of the abdomen in study patients will be done and radiologist reports were obtained.

The NLR(Neutrophil-Lymphocyte ratio) is defined as the ratio of the absolute neutrophil Count to the absolute lymphocyte count measured.

Calculation

ANC = [(%neutrophils + %bands)*wbc]/100

ALC = [(%lymphocytes)*wbc]/100

NLR=ANC/ALC

Normal values

Absolute neutrophil count -1500 - 8000 cells per microlitre

Absolute lymphocyte count-1300 - 3500 cells per microlitre.

MODIFIED COMPUTED TOMOGRAPHY SEVERITY INDEX

Pancreatic inflammation

- 0: normal pancreas
- 2: intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat
- 4: pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis

Pancreatic necrosis

- 0: none
- 2: 30% or less
- 4: more than 30%

Extrapancreatic complications:

- 2: one or more of pleural effusion, ascites, vascular complications, parenchymal complications and/or gastrointestinal involvement

Total score

- 0-2: mild pancreatitis.
- 4-6: moderate pancreatitis.
- 8-10: severe pancreatitis.

RESULTS

STATISTICAL ANALYSIS AND INTERPRETATIONS:

The study subjects were described their demographic profiles such as age and other continuous variables in terms of average and interpreted by ANOVA (Analysis Of Variance) since there were more than two groups. The categorical variables were described and interpreted by χ^2 (Chi square) test. The above statistical procedures were performed with the help of the statistical package namely IBM SPSS statistcs-20: The P-values less than or equal to 0.05 ($P \leq 0.05$) were considered as statistically significant.

Results:

Table : 5- Comparison of three groups namely CT Severity according to their age.

Group No	CT Severity	Mean	SD	"F"	Df	Significance
1	Mild	41.8	9.9	0.128	2, 97	P=0.880
2	Moderate	41.2	10.9			
3	Severe	43.1	11.6			

The above table compares the age of the study subjects namely mild moderate and severe. The mean age of mild, moderate and severe were 41.8±9.9 years, 41.2 ± 10.9 years and 43.1± 11.6 years respectively. The differences between the three groups were not statistically significant (P>0.05).

Chart-1: Comparison of mean ages between the CT Severity

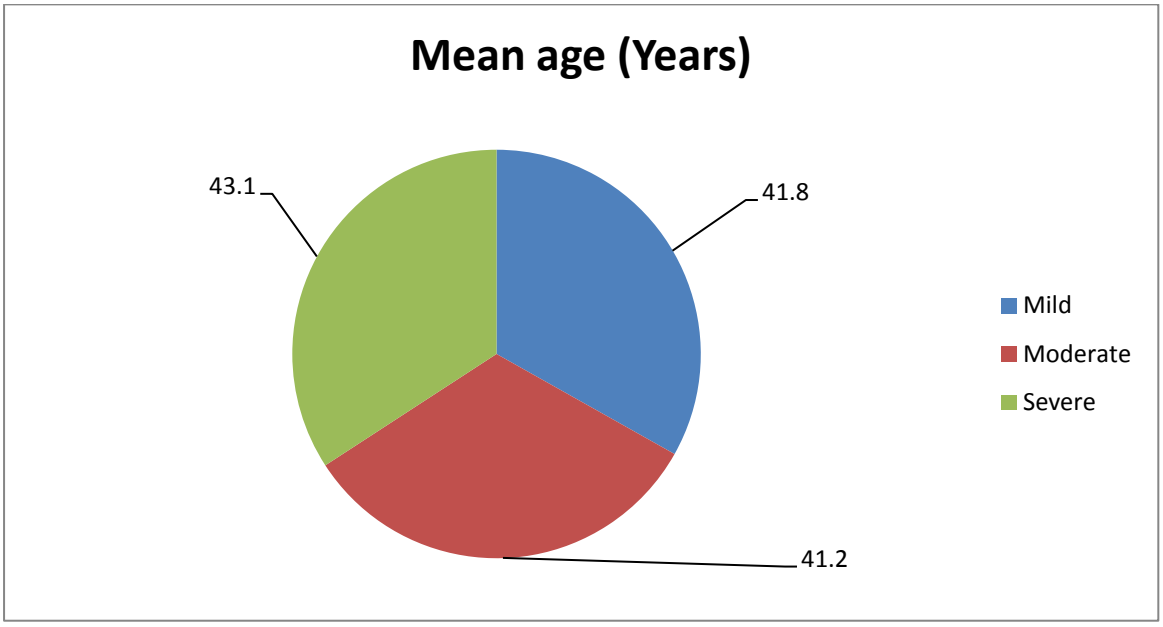


Table-6: Comparison of genders between the three groups:

Group	CT Severity	Males		Females		Total		Significance
		No	%	No	%	No	%	
1	Mild	53	53.0	2	2.0	55	55.0	χ^2 =1.681 df=2 P=0.431
2	Moderate	32	32.0	3	3.0	35	35.0	
3	Severe	10	10.0	0	0.0	10	10.0	
Total		95	95.0	5	5.0	100	100.0	

The table-2: compares the severity between the genders. The severity between the gender was not statistically significant (P>0.05).

Chart -2: Comparison of gender between three groups of Severity (%)

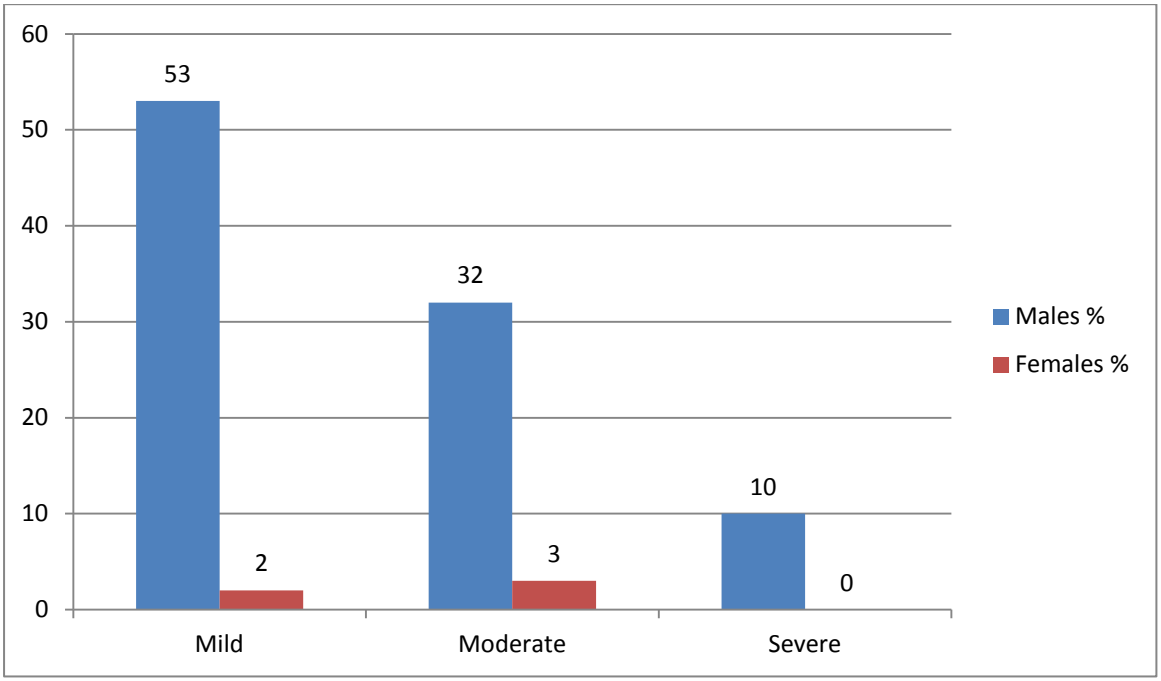


Table-7: **Comparison of alcoholism between the CT severity:**

Group	CT Severity	Alcoholism		Non-Alcoholism		Total		Significance
		No	%	No	%	No	%	
1	Mild	53	53.0	2	2.0	55	55.0	χ^2 =3.356 df=2 P=0.187
2	Moderate	30	30.0	5	5.0	35	35.0	
3	Severe	9	9	1	1.0	10	10.0	
Total		92	92.0	8	8.0	100	100.0	

The table-3 states the comparison between CT severity with alcoholism. There was no statistically significant association between the alcoholism and non -alcoholism (P>0.05).

Chart -3: Comparison of alcoholism between CT severity:

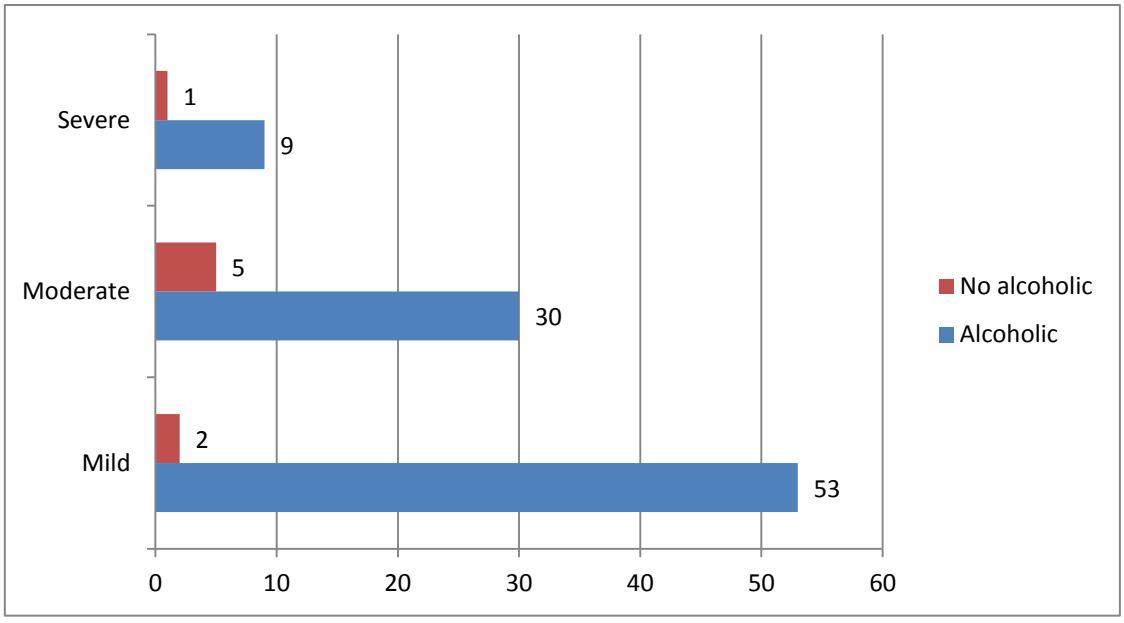


Table-8: Comparison of Gallstone between the CT severity:

Group	CT Severity	Gall stone Yes		Gallstone No		Total		Significance
		No	%	No	%	No	%	
1	Mild	0	0.0	55	0.0	55	55.0	χ^2 =8.055 df=2 P=0.018
2	Moderate	5	5.0	30	5.0	35	35.0	
3	Severe	1	1.0	9	1.0	10	10.0	
Total		6	6.0	94	6.0	100	100.0	

The above table-4 states the comparison between CT severity with Gall stone. The results revealed that the Gall stone was significantly correlated with moderate CT severity (P<0.05).

Chart -4: Comparison of Gallstone between the CT severity:

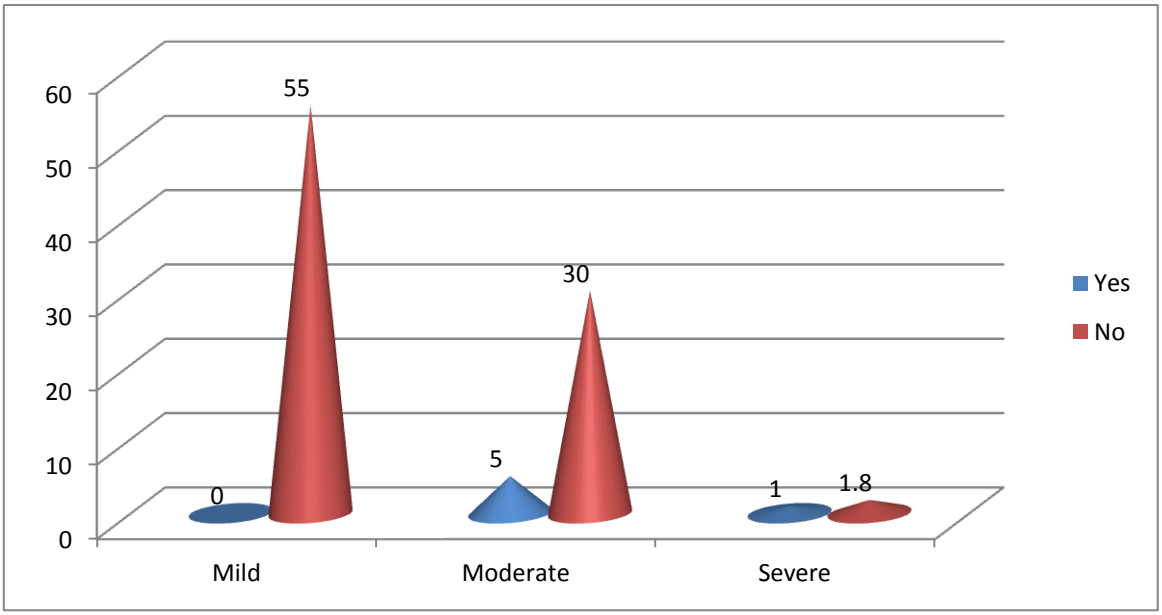


Table-9: Comparison of choledochol cyst between the CT severity:

Group	CT Severity	choledochol cyst						Significance
		No		Yes		Total		
		No	%	No	%	No	%	
1	Mild	53	53.0	2	2.0	55	55.0	χ^2 =1.670 df=2 P=0.434
2	Moderate	35	35.0	0	0.0	35	35.0	
3	Severe	10	10.0	0	0.0	10	10.0	
Total		98	98.0	2	2.0	100		

The table-5 states the comparison of choledochol cyst between CT severity. There was no statistically significant difference between the choledochol cyst and ct severity. (P>0.05).

Chart -5: choledochol cyst comparison between the CT severity:

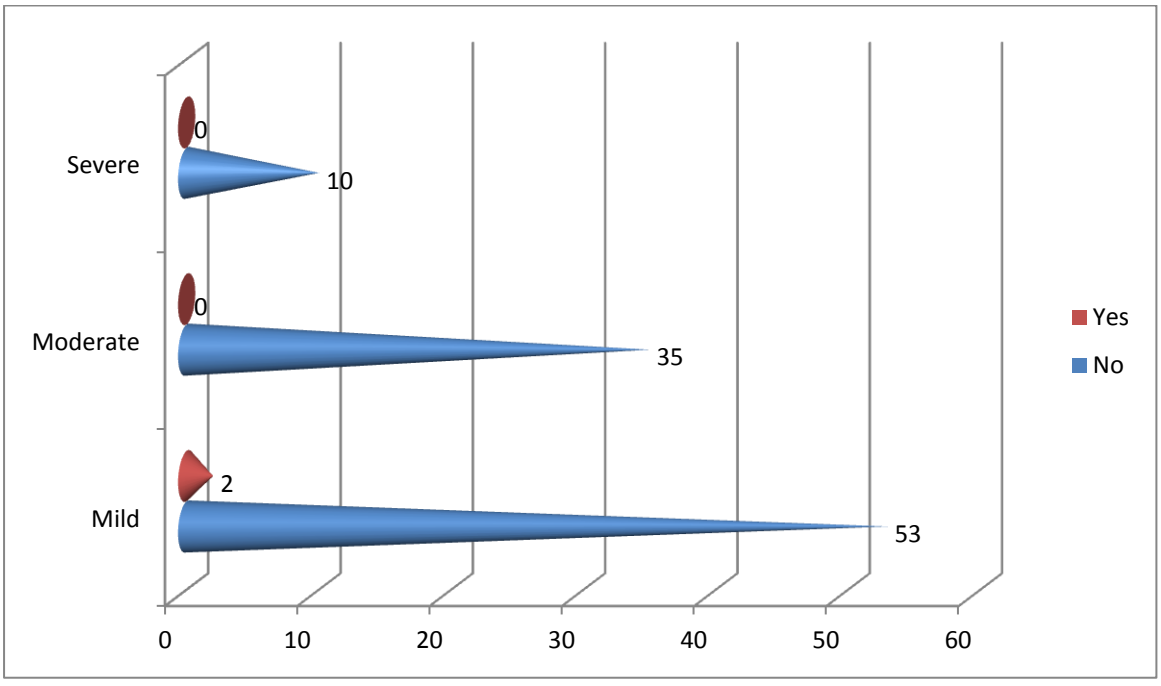


Table-10: Comparison of serum Amylase between the CT severity:

Group No	CT Severity	Serum Amylase		"F"	Df	Significance
		Mean	SD			
1	Mild	633.1	242.6	6.277	2, 97	P=0.003
2	Moderate	754.8	341.8			
3	Severe	1011.4	576.8			

The table-6 states the comparison between serum Amylase between the three groups. The mean of the three groups were Mild as 633.14 ± 242.6, moderate as 754.8± 341.8 and severe were 1011.4±576.8. The differences between the three groups were statistically highly significant (P<0.01) .

Chart -6:Comparison of Serum Amylase between the CT severity:

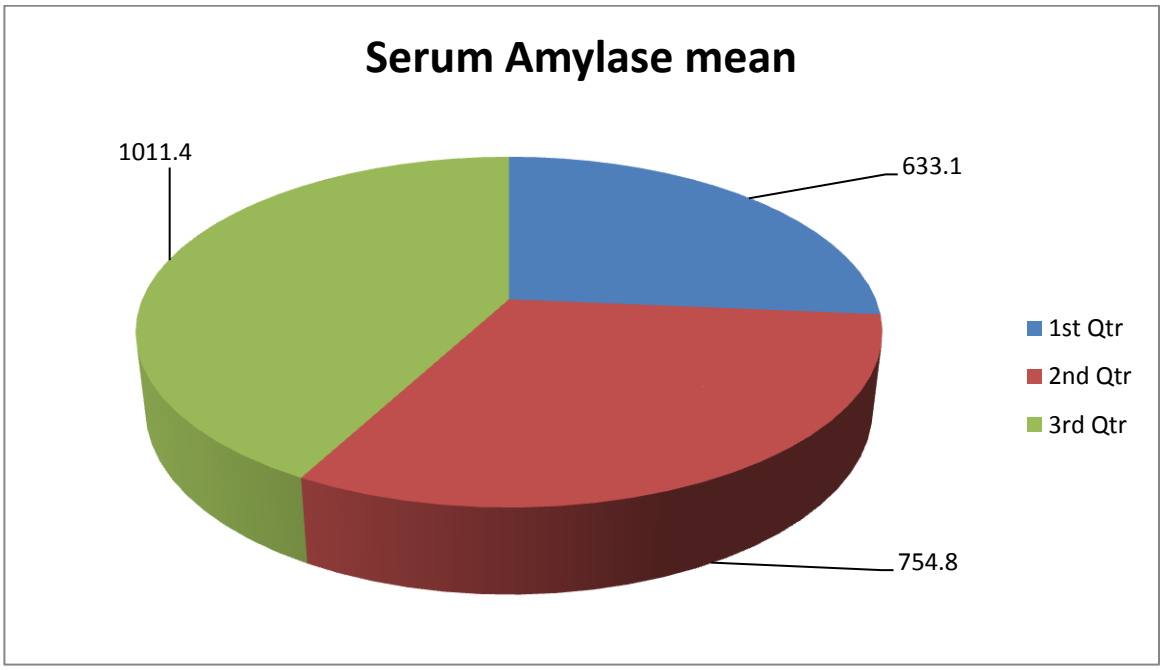


Table-11: Comparison of serum Lipase between the CT severity:

Group No	CT Severity	Serum Lipase		"F"	df	Significance
		Mean	SD			
1	Mild	298.1	102.2	100.967	2, 97	P<0.001
2	Moderate	491.9	197.9			
3	Severe	1238.1	437.6			

The table-7 states the comparison between serum lipase between the three groups. The mean of the three groups were Mild as 298.1 ± 102.2, moderate as 491.9± 197.9 and severe were 1238.1±437.6. The difference between the three groups were statistically very highly significant (P<0.001) .

Chart -7: Comparison of Serum Lipase between the CT severity:

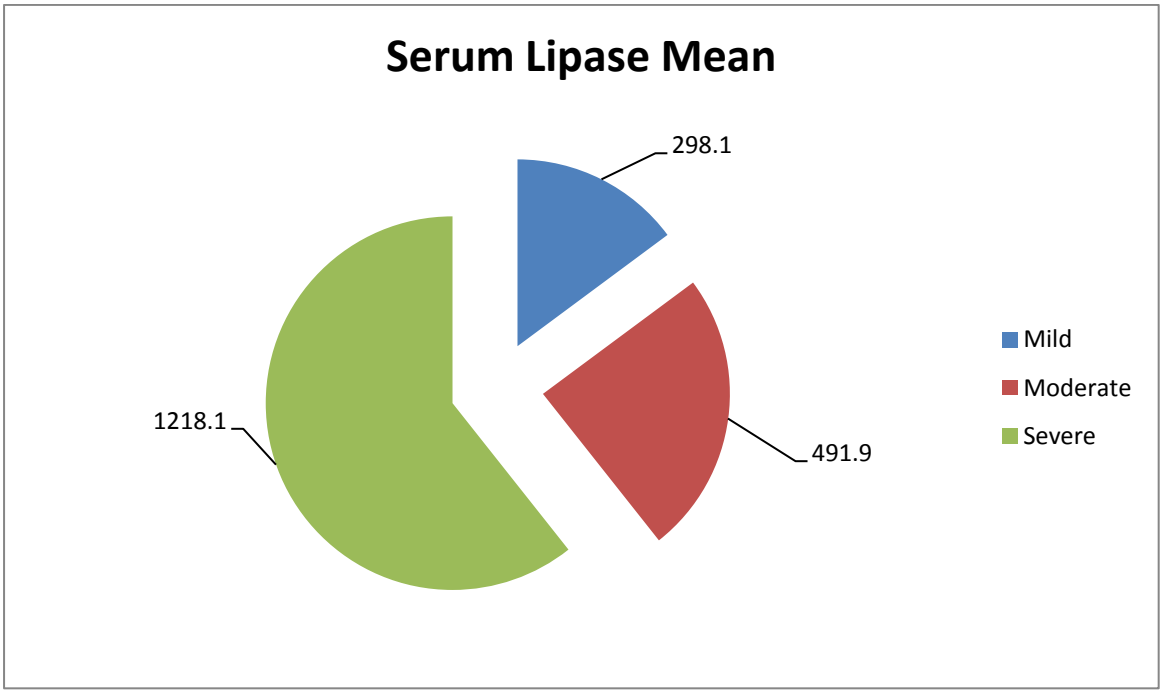


Table-12: Comparison of ICU stay between the three groups:

Group	CT Severity	ICU stay						Significance
		Yes		No		Total		
		No	%	No	%	No	%	
1	Mild	0	0.0	55	55.0	55	55.0	χ^2 =70.574 df=2 P<0.001
2	Moderate	4	4.0	31	31.0	35	35.0	
3	Severe	10	10.0	0	0.0	10	10.0	
Total		14	14.0	86	86.0	100	100.0	

The table-8 compares the ICU stay between the three groups. The ICU stay of mild group was nil. The same of the moderate group was 4.0% and the severe was 10%. The ICU stay of moderate and severe groups were statistically very highly significantly differed with mild group (P<0.001).

Chart -8: Comparison of ICU stay between the three groups:

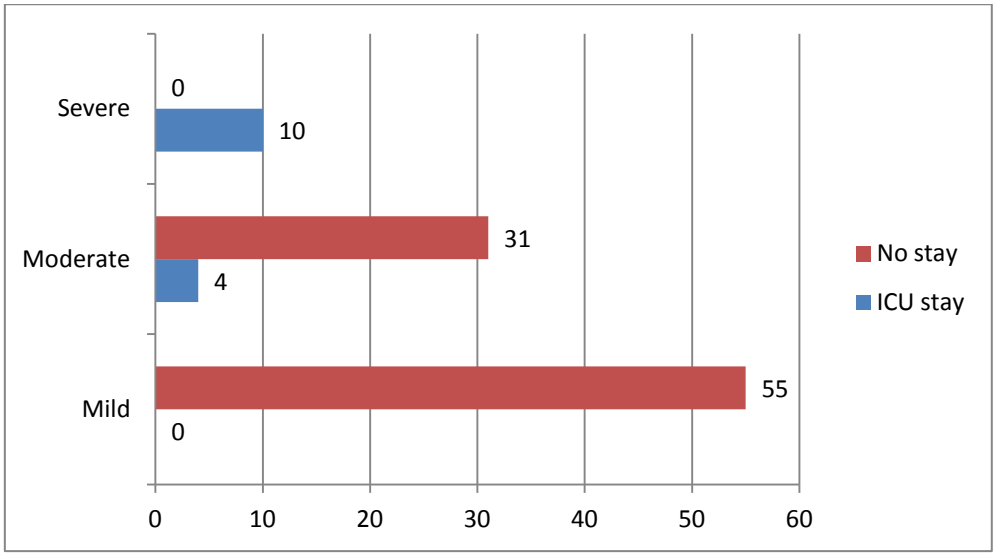


Table-13: Comparison of mortality between the three groups:

Group	CT Severity	Mortality						Significance
		Yes		No		Total		
		No	%	No	%	No	%	
1	Mild	0	0.0	55	55.0	55	55.0	χ^2 =37.500 df=2 P<0.001
2	Moderate	0	0.0	35	35.0	35	35.0	
3	Severe	4	4.0	6	6.0	10	10.0	
Total		4	4.0	96	96.0	100	100.0	

The table-9 compares the mortality between the three groups. The mortality of mild group was nil. And moderate group mortality was also nil. But, the mortality of severe group was 4%. The difference between the three groups was statistically very highly significant (P<0.001).

Chart -9: Comparison of mortality between the three groups:

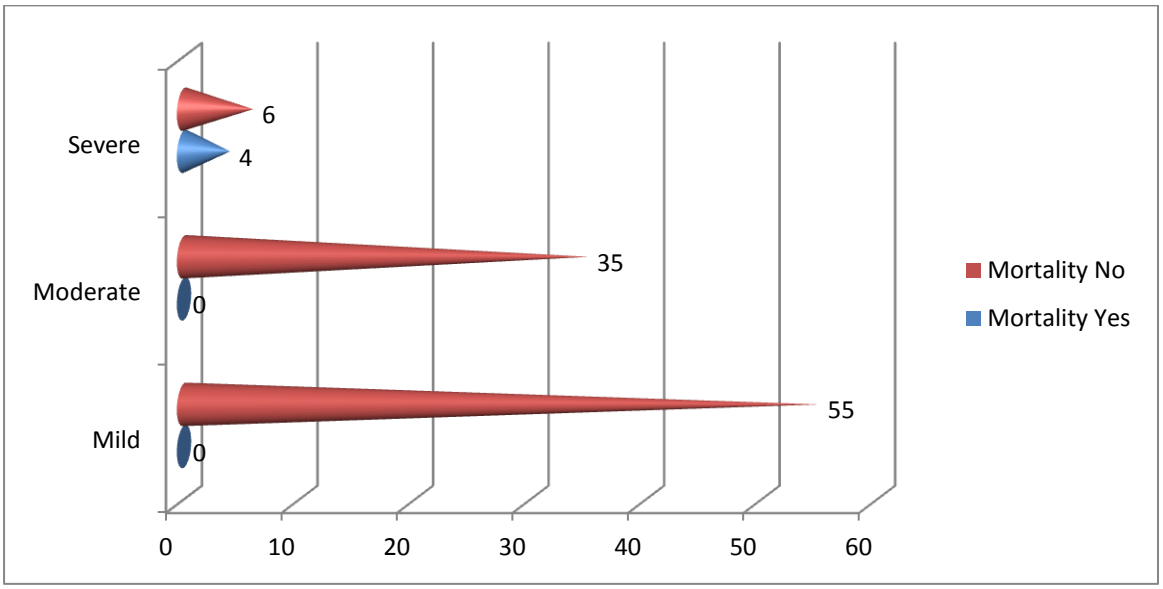


Table-14: **Comparison of Neutrophils at day 0 between the three groups**:

. Group No	CT Severity	Neutrophils		"F"	df	Significance
		Mean	SD			
1	Mild	81.8	3.9	32.941	2, 97	P<0.001
2	Moderate	86.3	4.4			
3	Severe	91.6	1.3			

The above table-10 compares the Neutrophils at 0 hour between the three groups. The mean of mild group was 81.8 ±3.9. The same of the other two groups were 86.3±4.4 and 91.6± 1.3. The differences between the three groups were statistically very highly significant(P<0.001).

Chart -10:**Comparison of Neutrophils at day 0:**

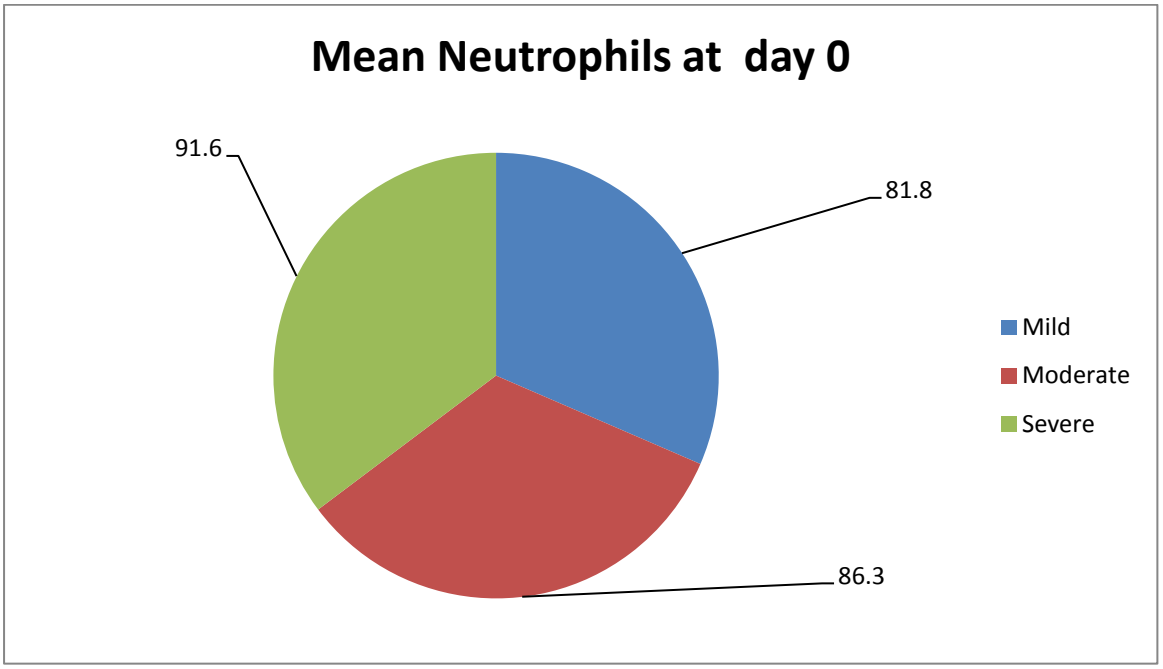


Table-15: Comparison of Lymphocytes at day 0 between the three groups:

. Group No	CT Severity	Lymphocytes		"F"	df	Significance
		Mean	SD			
1	Mild	13.7	2.2	79..051	2, 97	P<0.001
2	Moderate	9.7	1.4			
3	Severe	6.9	1.1			

The above table-11compares the Lymphocytes at day 0 between the three groups. The mean of mild group was 13.7 ±2.2. The same of the other two groups were 9.7±1.4 and 6.9± 1.1. The differences between the three groups were statistically very highly significant (P<0.001).

Chart -11: Comparison of Lymphocytes at day 0

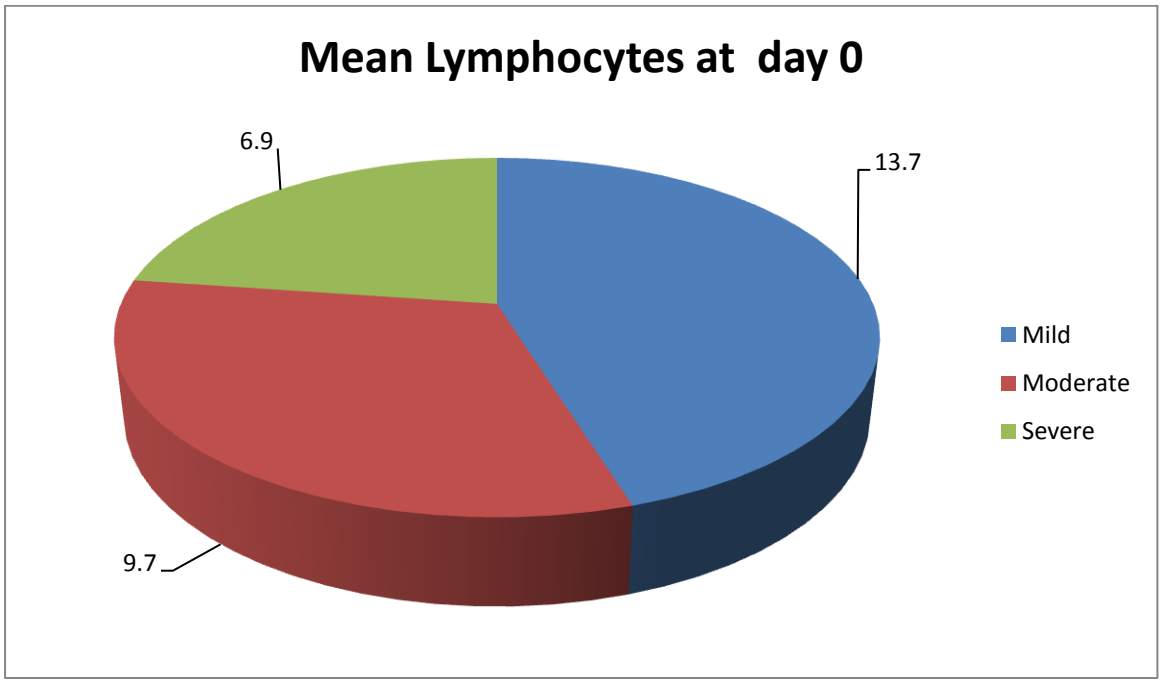


Table-16: **Comparison of NLR at day 0 between the three group:**

Group No	CT Severity	NLR		"F"	df	Significance
		Mean	SD			
1	Mild	6.2	1.2	118..700	2, 97	P<0.001
2	Moderate	9.1	1.6			
3	Severe	13.6	2.5			

The above table-12 compares the NLR at 0 hours. The mean NLR of Mild group was 6.2±1.2 and the moderate group was 9.1± 1.6. The mean NLR of severe group was 13.6±2.5. The differences between the severity was statistically significant (P <0.001)

Chart -12: Comparison of NLR at day 0:

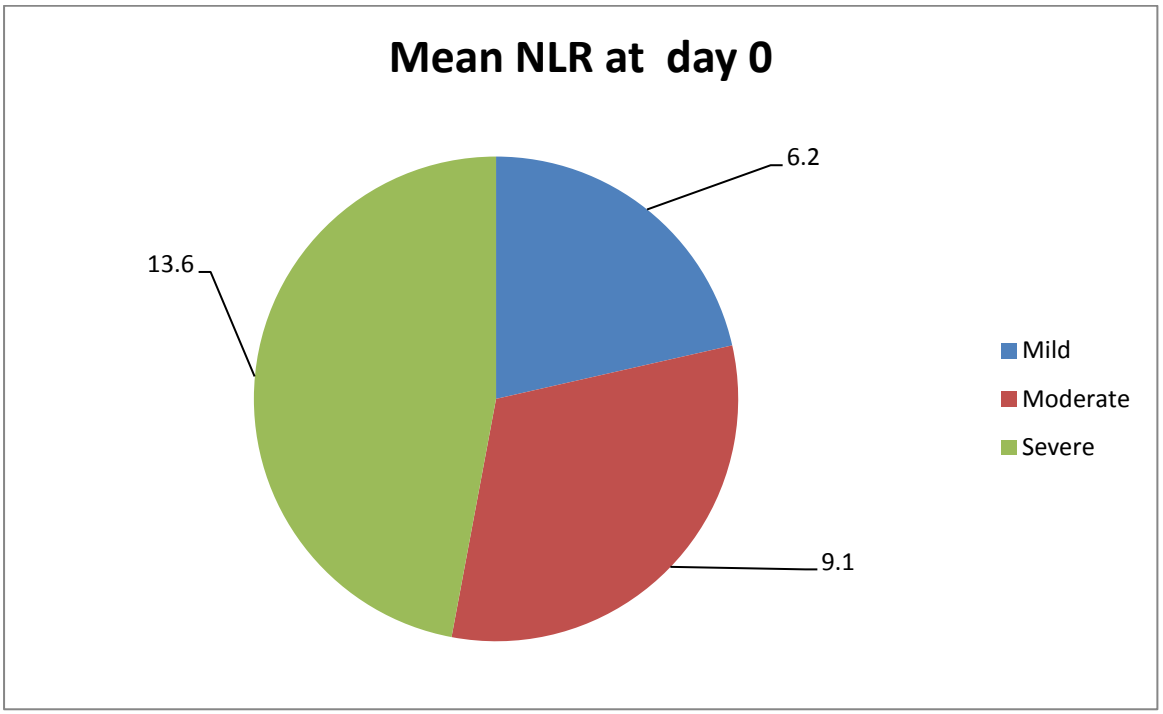


Table-17: Comparison of Neutrophils at day1 between the three groups:

Group No	CT Severity	Neutrophils		"F"	Df	Significance
		Mean	SD			
1	Mild	80.1	3.6	39.476	2, 97	P<0.001
2	Moderate	85.2	5.4			
3	Severe	91.6	1.1			

The above table-13compares the Neutrophils at day 1 between the three groups. The mean of mild group was 80.1 ±3.6. The same of the other two groups were 85.2±5.4 and 91.6± 1.1. The differences between the three groups were statistically very highly significant(P<0.001).

Chart -13: Comparison of Neutrophils at day1 :

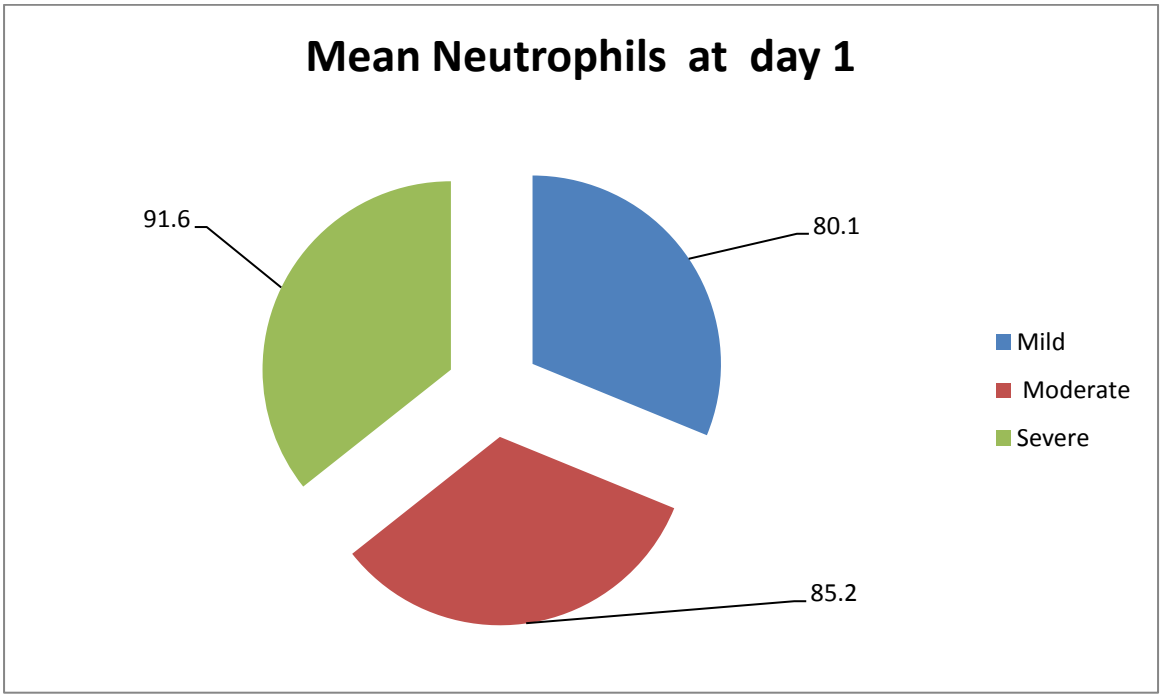


Table-18: Comparison of Lymphocytes at day1 between the three groups:

Group No	CT Severity	Lymphocytes		"F"	Df	Significance
		Mean	SD			
1	Mild	15.1	2.4	115..688	2, 97	P<0.001
2	Moderate	9.9	1.4			
3	Severe	6.7	0.8			

The above table-14 compares the Lymphocytes at day1 between the three groups. The mean of mild group was 15.1 ±2.4. The same of the other two groups were 9.9±1.4 and 6.7± 0.8. The differences between the three groups were statistically very highly significant (P<0.001).

Chart -14: Comparison of Lymphocytes at day1

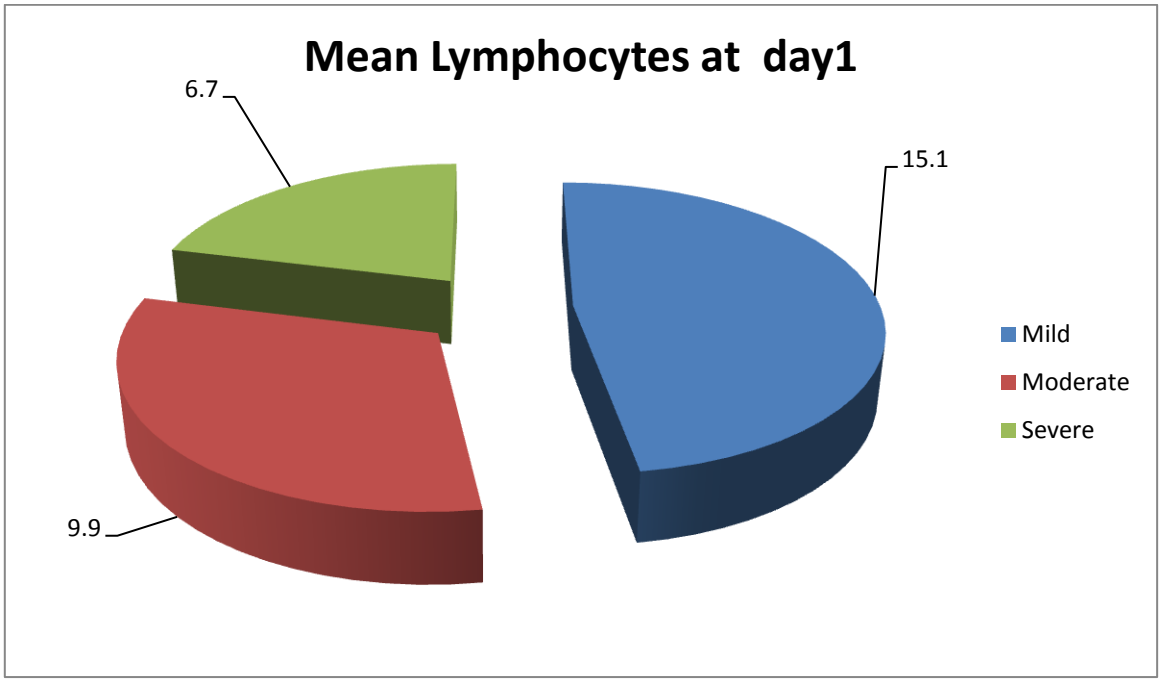


Table-19: Comparison of NLR at day1 between the three group:

Group No	CT Severity	NLR		"F"	df	Significance
		Mean	SD			
1	Mild	5.4	0.9	203..322	2, 97	P<0.001
2	Moderate	8.8	1.7			
3	Severe	13.8	1.6			

The above table-15 compares the NLR at day1. The mean NLR of Mild group was 5.4±0.9 and the moderate group was 8.8± 1.7 and the mean NLR of severe group was 13.8±1.6. The differences between the severity was statistically significant (P <0.001)

Chart -15: Comparison of Mean NLR at day1

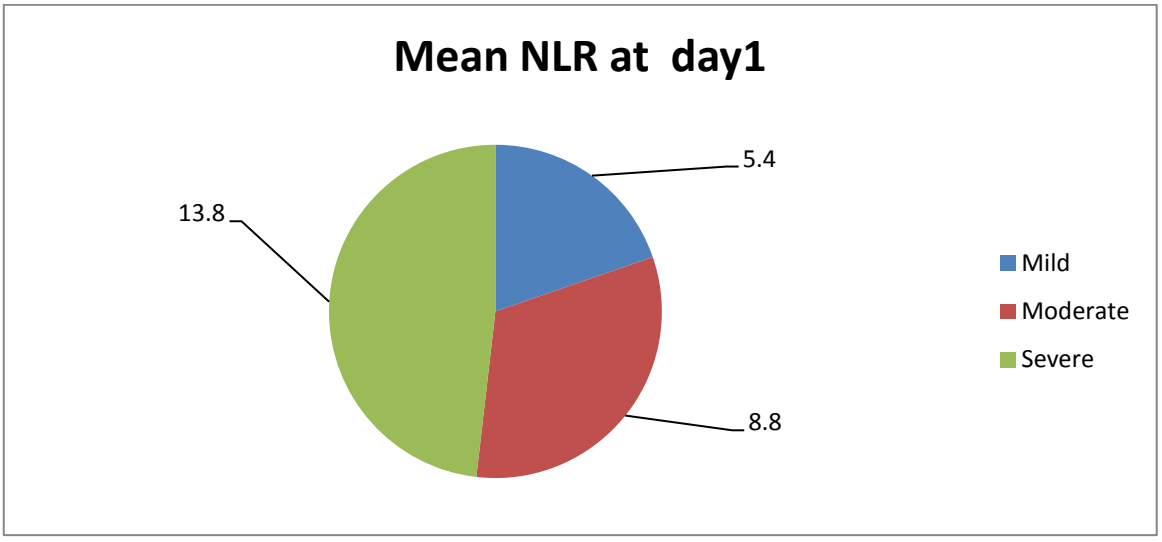


Table-20: Comparison of Neutrophils at day2 between the three groups:

Group No	CT Severity	Neutrophils		"F"	df	Significance
		Mean	SD			
1	Mild	78.8	3.3	39.476	2, 97	P<0.001
2	Moderate	84.1	5.0			
3	Severe	89.6	4.2			

The above table-16 compares the Neutrophils at day2 between the three groups. The mean of mild group was 78.8 ±3.3. The same of the other two groups were 84.1±5.0 and 89.6± 4.2. The differences between the three groups were statistically very highly significant(P<0.001).

Chart -16: Comparison of Neutrophils at day2:

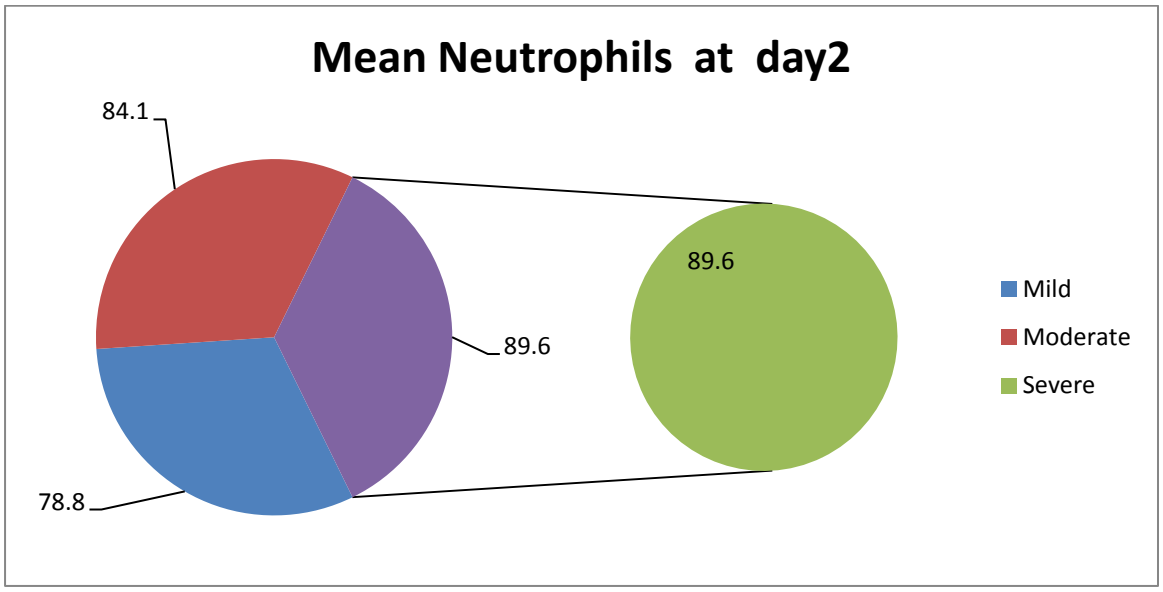


Table-21: **Comparison of Lymphocytes at day2 between the three groups:**

Group No	CT Severity	Lymphocytes		"F"	df	Significance
		Mean	SD			
1	Mild	17.0	2.3	237..521	2, 97	P<0.001
2	Moderate	10.3	1.4			
3	Severe	6.1	0.6			

The above table-17compares the Lymphocytes at day2 between the three groups. The mean of mild group was 17.01 ±2.3. The same of the other two groups were 10.3±1.4 and 6.1± 0.6. The differences between the three groups were statistically very highly significant (P<0.001).

Chart -17: Comparison of Lymphocytes at day2

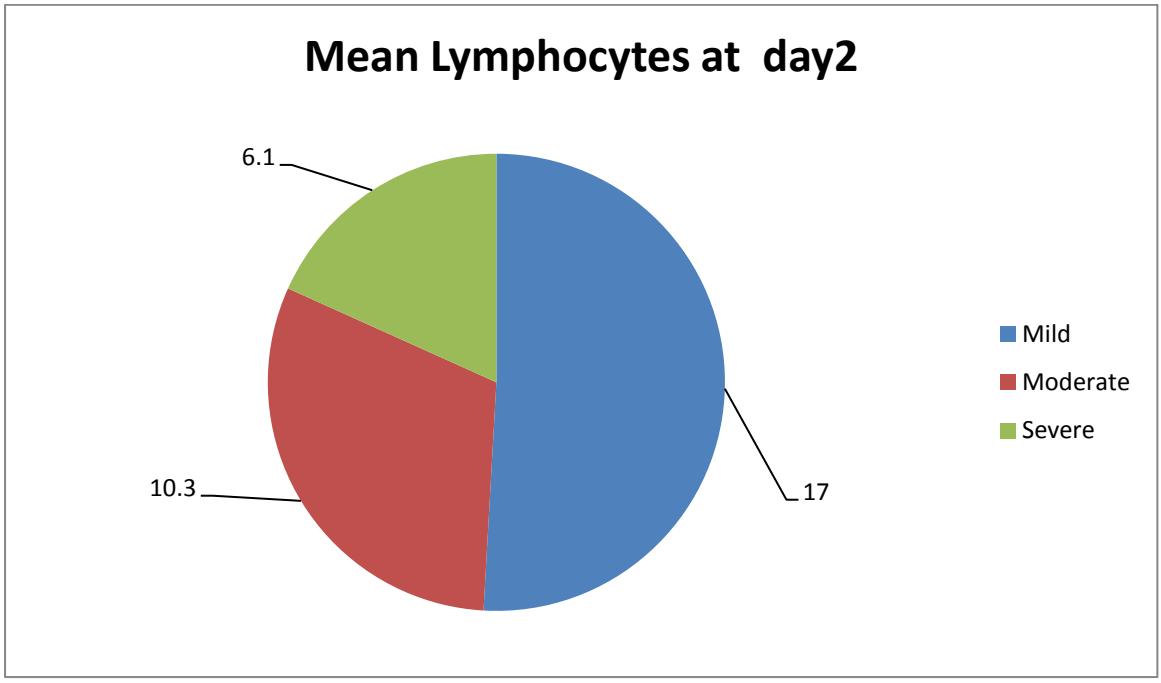


Table-22: Comparison of NLR at day2 between the three groups:

Group No	CT Severity	NLR		"F"	df	Significance
		Mean	SD			
1	Mild	4.7	0.7	476..945	2, 97	P<0.001
2	Moderate	8.3	1.2			
3	Severe	14.8	1.6			

The above table-18 compares the NLR at day2. The mean NLR of Mild was 4.7± 0.7, The moderate group was 8.3± 1.2 and the mean NLR of severe group was 14.8±1.6. The differences between the severity was statistically very highly significant (P <0.001).

Chart -18: Comparison of NLR at day2

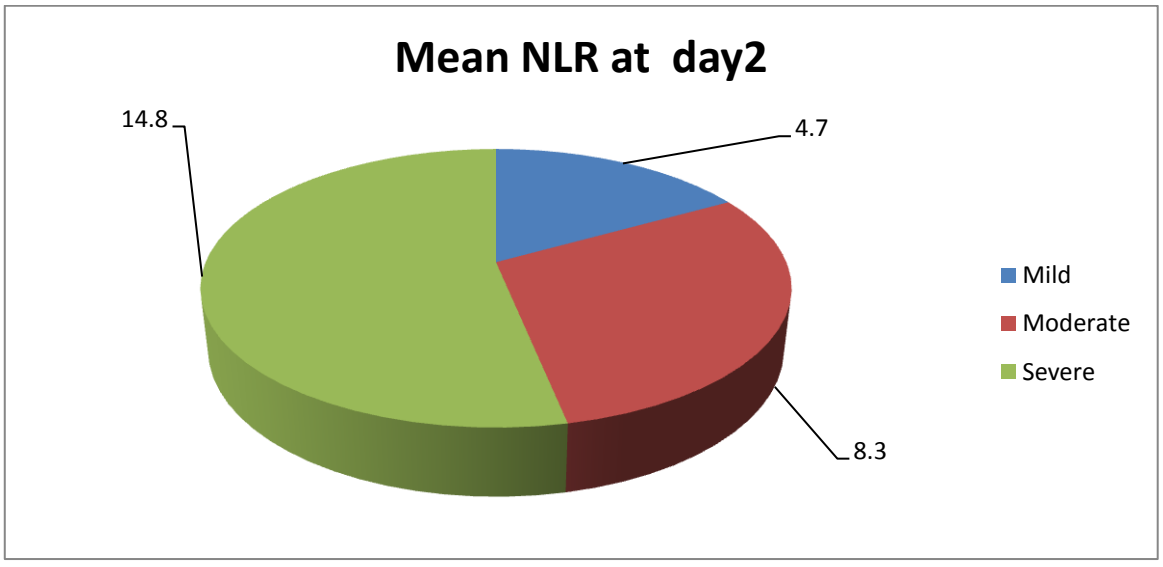


Chart 19 :TRENDS IN NEUTROPHILS ON Day0,Day1,Day2

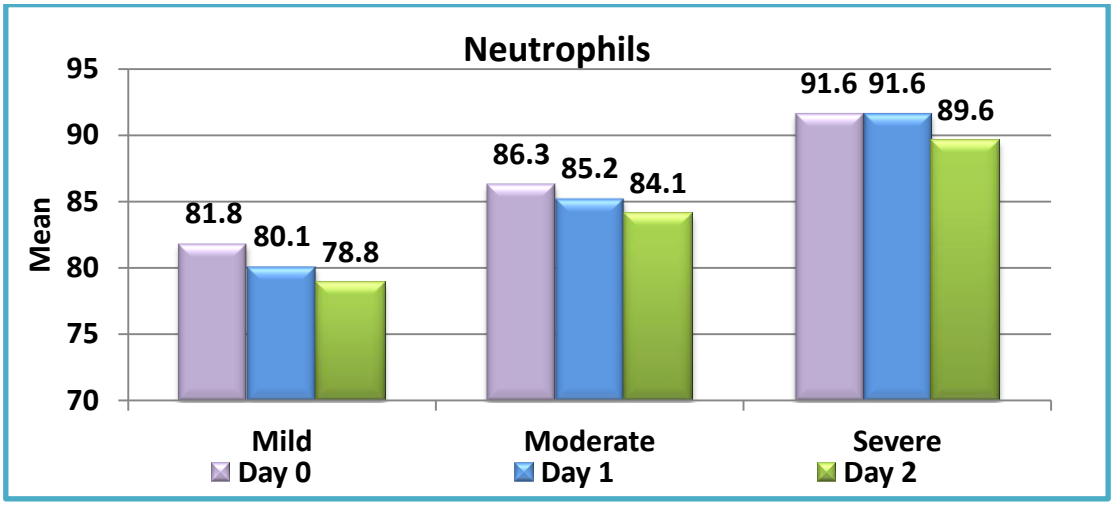


Chart 20 :Trends in lymphocytes on Day0,Day1,Day2

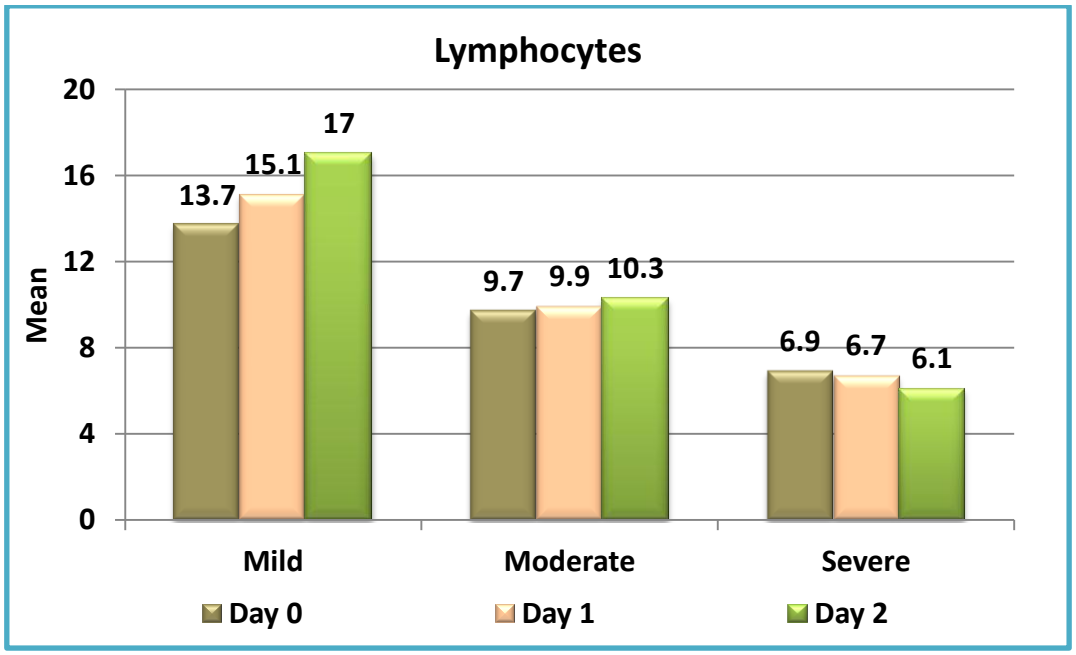
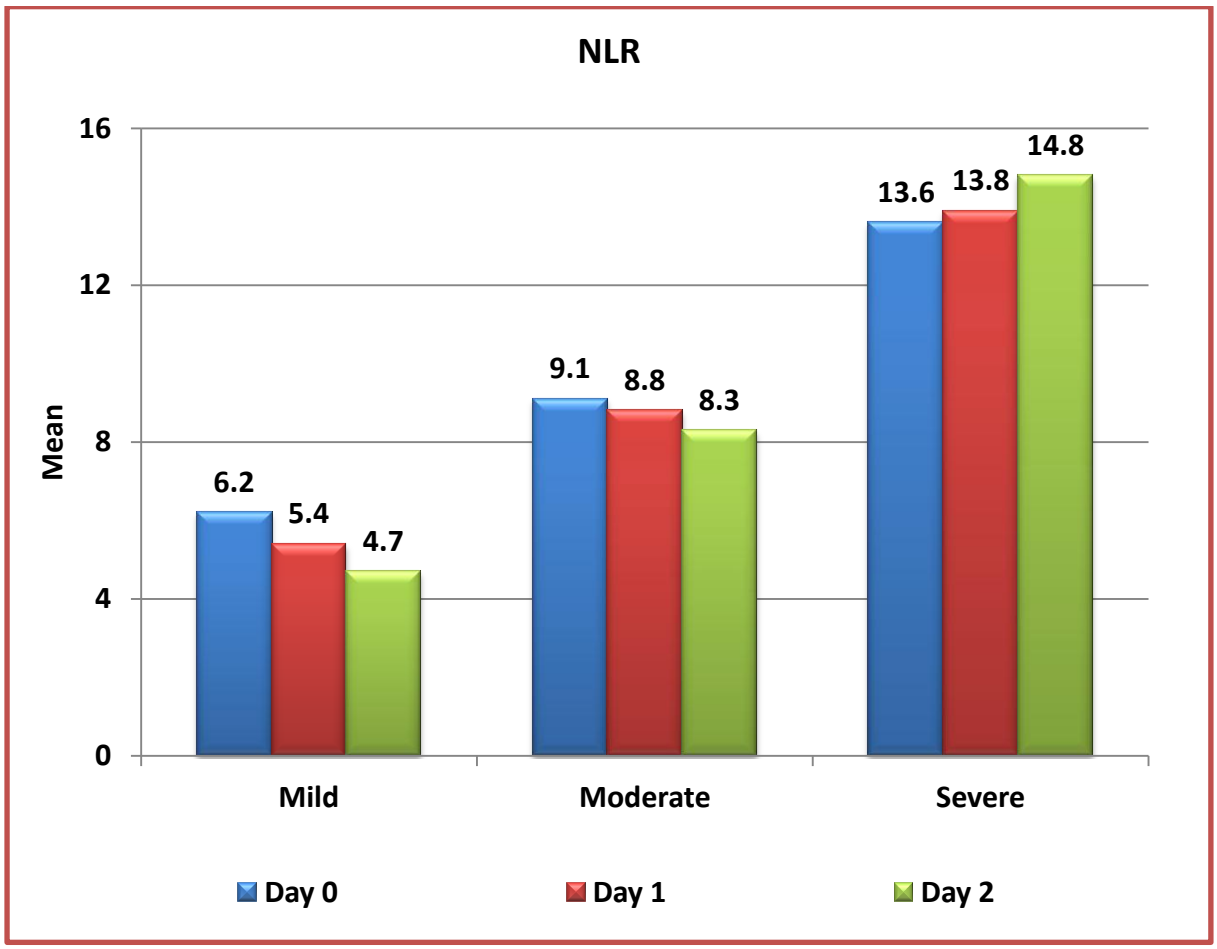


Chart 21 :Mean Neutrophil-Lymphocyte Ratio on Day0,Day1,Day2



DISCUSSION

In our study on 100 patients, acute pancreatitis was more predominant among males (95%) than females (5%). This was similar to a study done by Rithin et al. in which pancreatitis was common among males. Out of the 100 patients, 55(55%) had mild pancreatitis, 35(35%) moderate pancreatitis and 10(10%) patients had severe acute pancreatitis as compared to study by Savio G Barreto et al, 67 % had mild pancreatitis.

In our study, most of the patients who presented with acute pancreatitis belonged to 30-50 years of age group.Comparing the age group the mean age group for mild, moderate and severe pancreatitis were 41.8±9.9 years, 41.2 ± 10.9 years and 43.1± 11.6 years respectively. Compared to the study by Rithin et al in which the mean age was 40.9%. Similarly; mean age was 40yrs in a study by Savio G Barreto et al.

In our study, alcoholic etiology was 92%, gall stone 6%, choledochal cyst 2%. In our study alcoholic etiology was more .Among the alcoholic etiology 53 patients had mild pancreatitis,30 had moderate pancreatitis and 9 patients had severe pancreatitis.While comparing Alcohol with MCTSI, alcohol consumption is associated with all three types of pancreatitis. No statistical difference is seen (p- 0.187)

In the gall stone etiology group nil patient had mild pancreatitis , 5 patients had moderate pancreatitis and 1 patient had severe pancreatitis. Comparison between CT severity with Gall stone. Our study results revealed that the Gall stone was significantly correlated with moderate CT severity ($P<0.05$).

In our study, comparing rise in serum Amylase between the three groups shows the mean of the three groups were Mild as 633.14 ± 242.6, moderate as 754.8± 341.8 and severe were 1011.4±576.8. The differences between the three groups were statistically highly significant ($P<0.01$) .In our study there is statistically significant asscociation difference between the amylase value in three groups . But Lankisch P G et al in his study suggested that we should not depend on elevated enzyme levels of >3n for diagnosis. They concluded in their study that the severity of acute pancreatits is independent of the serum amylase enzyme level elevation at the time of the admission.

In our study comparing rise in serum lipase between the three groups shows the mean of the three groups were Mild as 298.1 ± 102.2, moderate as 491.9± 197.9 and severe were 1238.1±437.6. The difference between the three groups were statistically very highly significant ($P<0.001$).

The ICU stay of mild group was nil. The same of the moderate group was 4.0% and the severe was 10%. The ICU stay of moderate and severe groups were statistically very highly significantly differed with mild group (P<0.001). The mortality of mild group was nil. And moderate group mortality was also nil. But, the mortality of severe group was 4%. The difference between the three groups was statistically very highly significant (P<0.001).

The mean NLR Day0 of Mild group was 6.2±1.2 and the moderate group was 9.1± 1.6. The mean NLR of severe group was 13.6±2.5. The differences between the severity was statistically significant (P <0.001)

The mean NLR Day1 of Mild group was 5.4±0.9 and the moderate group was 8.8± 1.7 and the mean NLR of severe group was 13.8±1.6. The differences between the severity was statistically significant (P <0.001).

The mean NLR Day2 of Mild was 4.7± 0.7, The moderate group was 8.3± 1.2 and the mean NLR of severe group was 14.8±1.6. The differences between the severity was statistically very highly significant (P <0.001).

The primary finding in my study is that the Neutrophil Lymphocyte Ratio (NLR) was elevated in patients presenting with acute pancreatitis. The NLR was increased when compared to the normal (2.63).

The WBC count is a marker of infection and inflammation. It is a part of many scoring systems used to prognosticate acute pancreatitis. The two important components of WBC are the neutrophils and lymphocytes. In acute pancreatitis inflammatory cytokines like TNF-α are responsible for recruitment

of neutrophils and macrophages into the pancreatic tissue. The neutrophils in turn propagate inflammation and tissue destruction through proteolytic enzymes (myeloperoxidase, elastase, collagenase and β- glucoronidase), cytokines (IL6, IL8, TNF-α) and oxygen free radicles.

A rise in neutrophil count corresponds with the development of SIRS and MODS,which are the hall mark of acute pancreatitis.Lymphocyte number increases following the initial stress and mediate the subsequent inflammatory response.

In our study the neutrophil count tend to remain high in severe pancreatitis group compared to mild group .In our study the NLR in mild group is high at the time of admission and tends to decrease towards normalcy on the subsequent days.The NLR in severe group is very high compared to mild group and tends to remain at a higher level compared to mild pancreatitis group.

NLR has been shown to reflect SOFA (Sequential Organ Failure Assessment) and APACHE II scores in patients in intensive care setting. It is these scores which are also used in predicting severity in acute pancreatitis. So, NLR has been evaluated in predicting the severity in acute pancreatitis.

This variation in NLR was analyzed by Suppiah A et al and they reported that NLR was raised significantly in poor prognosis group than the favourable group. In their study the NLR was comparable at baseline that is at the time of admission. The NLR then gradually returned towards normal in favourable

group while was persistently high in the poor prognosis group which is similar to our study.

Similar study was conducted by Azab et al and they reported NLR to be superior to the total WBC count or individual neutrophil and lymphocyte counts in predicting ICU admission and death in acute pancreatitis patients. They further proceeded and recommended a cut-off value of ≥ 4.7 to identify poor outcome in acute pancreatitis but this value has high specificity and low sensitivity.

The benefit of our study is that NLR can be calculated by just doing a total WBC and a differential count. In comparison to other severity scoring systems, where there are multiple parameters required to calculate the prognosis, NLR analysis just needs a single blood test needs to be done serially.

In our study, NLR can be done at the time of admission and can be serially monitored which can act as a guide to detect those patients progressing to severe pancreatitis. Those patients progressing to severe pancreatitis can be identified earlier and can be managed intensively and hence reduce the mortality and morbidity.

NLR is a cost effective, simple tool which can be calculated in any level care of hospital be it a secondary care or a tertiary care hospital. NLR thus calculated can be used as a guide to refer poor prognosis patients to a higher center for intensive care and management.

REVIEW OF ARTICLES

In 2012 April, Thomas L Bollen[15] et al compared the radiological and clinical scoring systems in acute pancreatitis in his study and came to a conclusion that routine CT abdomen, on admission is not recommended in a case of acute pancreatitis for assessing its severity.

In 2012 June, Rawad Mounzer et al[16], compared all clinical scoring systems which are currently used to predict organ failure.He finally concluded that all scoring systems have reasonable accuracy in predicting persistent organ failure, but the Glascow score was found to be the best compared to other scoring systems.

In 2012 September, Fabre et al[17] compared several scoring systems in paediatric age group presenting with acute pancreatitis. He studied the sensitivity and specificity of each score and compared with one another and he found that CT severity score is the best parameter to assess the severity of acute pancreatitis in paediatric population.

In 2011 September, Zhang WW et al[18], compared the clinical scoring and CT severity scoring, he found that CT has superior role than clinical scoring and also found that CT severity index has good correlation with APACHE II and Ranson's scores.

In 2011 July, Su Mi Woo et al [19] conducted an extensive study about serum Procalcitonin in predicting the severity of acute pancreatitis and he compared the same with other severity indices. He concluded in his study that,

serum Procalcitonin was a simple promising biomarker as its accuracy in predicting the severity of acute pancreatitis, is similar to other scoring systems such as APACHE II score.

In 2011 January, Chavarri Herbozo et al[20] conducted a study about hemoconcentration as an early predictor of severity in acute pancreatitis and compared it with other scores such as APACHE II and Ranson's scores. He found that hemoconcentration as a single parameter, is not much useful in predicting the severity in patients with acute pancreatitis.

In 2007, Ekrem et al[21] conducted a study and found out definite relation between the elevation of the following parameters and mortality and morbidity in patients presenting with acute pancreatitis. The parameters include CRP, BUN, LDH, CT severity index and APACHE score.

In 2006, Yuk Pang et al[22], in his study compared Ranson's score with APACHE II scores in 101 patients of acute pancreatitis and concluded that APACHE II score is more accurate than that of Ranson's score in predicting the severity of acute pancreatitis.

In 2005, Ting-Kai Leung et al[23] conducted a study in which he compared Ranson's and APACHE II scores with that of helical CT in predicting the severity of acute pancreatitis and he found that CT severity index is superior to Ranson's score in predicting severity.

Tao Joo Jeon,Ji Young park, et al[28] conducted a study to find out the prognostic value of neutrophil lymphocyte ratio and to determine the optimal neutrophil lymphocyte ratio for severity prediction of acute pancreatits.They retrospectively analysed 490 patients with acute pancreatitis between march 2007 and December 2012 at the time of admission,24,48 and at 72 hours.They grouped the patients based on the severity ,which was defined by using revised Atlanta classification[16,17].In their study the neutrophil lymphocyte ratio in severe acute pancreatitis was significantly higher than the mild acute pancreatitis on all 4 days($p<0.05$).The neutrophil lymphocyte ratio is higher in patients with organ failure compared to patients without organ failure($p<0.05$).They determined optimal neutrophil lymphocyte cut-off value for severity prediction was 4.76 and 4.88 for organ failure.

The study concludes that elevated neutrophil lymphocyte ratio correlates with the severity and organ failure.

Azab B,Jaglal N, et al[29] conducted a study to evaluate the value of neutrophil lymphocyte ratio to predict the severity of acute pancreatitis.The study was conducted between 2004 and 2007 which included 283 patients with acute pancreatitis.They arranged the patients into their respective tertiles based on the neutrophil lymphocyte ratio and white blood cell count.In their study patients in the 3rd tertile (Neutrophil lymphocyte ratio >7.6) had more Intensive care admission and prolonged hospital stay compared to the patients in 1sttertile.

They concluded that neutrophil lymphocyte ratio superior to white blood cell count in predicting severity and cut-off value of >4.7 as a simple indicator for severity of acute pancreatitis.

Suppiah A,Malde D, et al[30] conducted a study to find out the prognostic value of neutrophil lymphocyte ratio and determine optimal cut-off value for severity prediction in acute pancreatitis.Their study included 146 patients with acute pancreatitis , neutrophil lymphocyte ratio was calculated for each patients on day 0,day1 and day 2 and correlated with severity,which was defined using revised Atlanta classification[16,17].The neutrophil lymphocyte ratio in severe acute pancreatitis was significantly increased compared to other groups on all 3 days and the optimal cut-off value of neutrophil lymphocyte ratio>4.7 had highest sensitivity but least accurate due to low specificity.

Their study concluded that there is a significant association between the elevated neutrophil lymphocyte ratio during first 48 hours and severity of acute pancreatitis and also an independent negative prognostic indicator.

Binit Katvwal, et al[31] conducted a study to determine the correlation between neutrophil lymphocyte ratio and severity of acute pancreatitis.Their study was conducted between January 2014 and January 2105 that included 79 patients.Total leukocyte count,neutrophil count ,lymphocyte count and neutrophil lymphocyte ratio was evaluated for each patient at the time of admission and 48 hrs.Severity was defined by using revised Atlanta classification[16.17].They found that there was statistically significant weak

positive correlation of neutrophil lymphocyte ratio to the severity of acute pancreatitis and the mean neutrophil lymphocyte ratio was high in higher grades of acute pancreatitis($p< 0.05$).

They concluded that neutrophil lymphocyte ratio as an easy and reliable prognostic marker for the severity prediction of acute pancreatitis.

Vijayakumar K,Arun Damodharan, et al[32] conducted a prospective study to evaluate the prognostic value of neutrophil lymphocyte ratio in acute pancreatitis.Their study included 100 patients with diagnosis of pancreatits based on atlanta criteria[16,17] and data collected for severity, amylase,lipase,contrast enhanced computed tomography,serum creatinine and neutrophil lymphocyte ratio at the time of admission,24 hours,48 hours and analysed using independent t test.Their study revealed there was a significant progressive increase in neutrophil lymphocyte ratio in severe group compared to mild group(p-0.004).

They concluded neutrophil lymphocyte ratio is a simple and reliable indicator of prognosis of the acute pancreatits.

Orak M,Mehmet Ustundag, et al[33] conducted a comparative study of apache ii score with neutrophil lymphocyte ratio and red cell distribution width for predicting the prognosis of acute pancreatitis. Healthy subjects were included as control group and according to the Atlanta classification ,patients with apache ii score less than 8 were classified into mild pancreatitis and score equal to 8 or greater than 8 were classified as severe pancreatitis.Neutrophil

lymphocyte ratio and red cell distribution width at the time of admission in both group were compared with each other.They found there is significant difference in neutrophil lymphocyte ratio and red cell distribution width in control and patient group and the severe pancreatitis group had significantly higher mean neutrophil lymphocyte ratio than the mild pancreatitis group.In their study neutrophil lymphocyte ratio difference between the dead and survived patients reached stastistical significance compared to the red cell distribution width.

Their study concluded there is elevation of both neutrophil lymphocyte ratio and red cell distribution in acute pancreatitis, but only neutrophil lymphocyte ratio should be considered as a useful marker for predicting severity and mortality of acute pancreatitis.

Li Y,Zhang Y, et al[34] conducted a retrospective comparative study of the prognostic value of inflammatory markers in patient with acute pancreatitis.The study population was 359 patients that includes 31 non survivors and the primary and secondary outcome were severity and mortality of acute pancreatitis respectively.Biochemistry and haematological results of the first test after admission were collected.Their study showed high red cell distribution width, high neutrophil lymphocyte ratio in non survivors group compared to the survivors of acute pancreatitis.C- reactive protein,red cell distribution width were independently associated with the occurrence of severe acute pancreatitis and for prediciting mortality neutrophil lymphocyte ratio had the largest area

under receiver operating characteristic curve(ROC) with an optimal cut-off value 16.64.

They concluded that neutrophil lymphocyte ratio was the most powerful marker of overall survival in acute pancreatitis.

Mustafs Kaplan MD, et al[35] conducted a study to find out the prognostic importance of neutrophil lymphocyte ratio and platelet lymphocyte ratio combination in acute pancreatitis and its relation with mortality.Their study included 142 patients with acute pancreatitis,Ranson,Atlanta[16,17] and BISAP score were calculated at 0 ,24 , 48 hours and the patients were divided into three groups as low,medium and high risk patients.They found the complications of acute pancreatitis and mortality rate were high in high risk patients compared to other patients.

The conclusion of their study was platelet lymphocyte ratio and neutrophil lymphocyte ratio combination had similar prognostic value with other scoring system used to determine the prognosis of acute pancreatitis.

Wang Y,Feuntes HE, et al[36] conducted a study to evaluate the prognostic value of neutrophil lymphocyte ratio in hypertriglyceridemia induced acute pancreatitis.They retrospectively analysed 110 patients and compared the neutrophil lymphocyte ratio,platelet lymphocyte ratio and red cell distribution width in different severity groups and performed receiver operating characteristic(ROC) to identify optimal cut off for severity prediction.Their study revealed neutrophil lymphocyte ratio was significantly increased in severe

acute pancreatitis($p<0.001$) and patients with organ failure($p=0.026$) compared to other groups.

They concluded that among the three inflammatory markers,neutrophil lymphocyte ratio has the highest discriminatory capacity for severe hypertriglyceridemia induced acute pancreatitis,with an optimal cut-off value of 10.

O'Connel RM, Boland MR ,et al[37] conducted a retrospective study to evaluate the red cell distribution width and neutrophil lymphocyte ratio as a predictor of outcome of acute pancreatitis.The study was conducted between August 2013 to August 2016,the study population included 185 patients with acute pancreatitis admitted in their institute.Data on survival ,intensive care unit stay,length of hospital stay and hematological parameters were collected.

Out of 185 patients 23 had a red cell distribution width above the upper limit of the normal which was associated with increase in intensive care unit stay.Patients with neutrophil lymphocyte ratio greater than 5 also associated with intensive care unit stay.Patients who had both elevated red cell distribution width and neutrophil lymphocyte ratio had an increased inpatient mortality

They concluded that red cell distribution width and neutrophil lymphocyte ratio can identify patients at increased risk of severe acute pancreatitis on presentation.

Abayl B, Gencdal G, et al[38] conduted a study to evalute the correlation between the neutrophil lymphocyte ratio and Ranson score in acute pancreatitis.Their study included a total of 435 patients and relevant data were collected.

Patients were classified based on etiology which revealed Gallstone 58.6%, hyperlipedemia 2.2%, viruses 0.7%, alcohol 2% and idiopathic 47.9%. Age,intensive care unit stay,serum aspartate transaminase, alalnine transaminase, serum total bilirubin, direct bilirubin, lactate dehydrogenase, gamma glutamyl transferase, total White blood cell count ,neutrophil count,lymphocyte count and neutrophil lymphocyte ratio were greater in the group with a RansoN score greater than or equal to 3.

They conclude their study that current scoring systems are complicated neutrophil to lymphocyte ratio is a simple ,practical and effective marker for acute pancreatitis.

Kamil Kokulu ,Ramzan Koylu, et al[39] conducted a prospective study to assess the relationship between neutrophil to lymphocyte ratio in acute pancreatitis and the severity and the systemic complications of the disease.Their study included 100 patients .Age ,sex, neutrophil to lymphocyte ratio ,Ransom score and the revised Atlanta classification of the patients were recorded.The patients were divided into two groups according to the ranson score as mild and severe acute pancreatitis.The patients were grouped into three mild,moderate and severe based on the revised Atlanta classification.

They found that the neutrophil to lymphocyte ratio was found to be statistically higher at the time of admission and 48 hrs in patients with severe acute pancreatitis compared to patients with mild pancretitis.Their study also showed that neutrophil to lymphocyte ratio cut off value of greater than7.13 had sensitivity of 87.5% and specificity of 69%.

They concluded their study that neutrophil to lymphocyte ratio is associated with severe acute pancreatitis and as a valuble parameter for predicting the development of systemic complications in patients with acute pancreatitis.

Chaoqun Han, Jun Zeng, et al[40] conducted study to assess the utility of neutrophil to lymphocyte ratio and fluid sequestration as an early predictor of acute pancreatitis.Their study included 1639 patients and all relevant data were collected.The sequential change in neutrophil to lymphocyte ratio and fluid sequestration were analysed and their utility for predicting severity was assessed by receptor operator characteristic curve(ROC).Correlation analysis was done by spearman's rank test

They found that the optimal neutrophil to lymphocyte ratio cut off value on day 0,1 and 2 were 9.6, 6.6 and 6.5 respectively.The optimqal cut off value for fluid sequestration were 1375 ml, 2345ml and 3424 ml respectively.In their study they also found that neutrophil to lymphocyte ratio and fluid sequestration together had higher sensitivity for severity prediction compared to Ranson score.

They concluded that increase in neutrophil to lymphocyte ratio and fluid sequestration were correlated with severity and can be used as a predictive factor in early stage of acute pancreatitis.

Zhang Y, Wu V,et al[41] conducted a study to evaluate the value of neutrophil to lymphocyte ratio in predicting persistent organ failure and in hospital mortality in Asian Chinese population of acute pancreatitis.Their study was conducted between 2009 and 2015 that included 974 patients .The outcome were measured in terms of persistent organ failure, intensive care unit stay more than 7 days and in hospital mortality rate.

In their study population 223 patients developed persistent organ failure, 202 patients required intensive care unit stay more than 7 days and 58 patients was dead. By using various statistical methods they found that the neutrophil to lymphocyte ratio had superior predictive performance in predicting the outcomes of acute pancreatitis.

They concluded that the neutrophil to lymphocyte ratio is an independent risk factor for persistent organ failure, intensive care unit stay more than 7 days and in hospital mortality rate.

Cho SK, Jung S et al[42] conducted a prospective study to evaluate the value of the neutrophil to lymphocyte ratio and platelet to lymphocyte ratio as a prognostic factor in acute pancreatitis.Their study was conducted from March 2014 to September 2016 that included 243 patients with an etiology of gall stone or alcohol. Neutrophil to lymphocyte ratio and platelet to lymphocyte

ratio were obtained at the time of the admission and were compared with the other known prognostic scoring systems.

They found that the neutrophil to lymphocyte ratio and platelet to lymphocyte ratio were significantly higher in gallstone acute pancreatitis than the alcoholic acute pancreatitis. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio is high in severe gallstone acute pancreatitis compared to mild group and also it cannot predict severity in alcoholic acute pancreatitis.

They concluded that Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio can predict the severity in acute pancreatitis ,but only in gallstone acute pancreatitis.

Gayathri B, Nisha B.Jain, et al[43] conducted a retrospective study to evaluate the neutrophil to lymphocyte ratio in acute pancreatitis as an early predictor of severity and outcome.The study was conducted between August 2017 and November 2017 that included 107 patients with acute pancreatitis based on Atlanta definition.The patients were grouped according to the severity and a comparative analysis was performed to compare the neutrophil to lymphocyte ratio in different groups. Neutrophil to lymphocyte ratio was compared with modified marshall score.

In their study they found that the neutrophil to lymphocyte ratio is significantly higher in severe group compared to mild and moderate group.There is also significant correlation between neutrophil to lymphocyte ratio , length of hospital stay,intensive care unit stay and organ failure. Their

study also showed that neutrophil to lymphocyte ratio greater than 8.5 at the time of admission is associated with adverse outcome in acute pancreatitis.

They concluded that neutrophil to lymphocyte ratio can be used as predictor of severity of acute pancreatitis and can be used as a tool to refer at risk patients to tertiary care needing intensive care unit admission.

Ilhan M, Ilhan G, et al[44] conducted a study to evaluate neutrophil to lymphocyte ratio, platelet to lymphocyte ratio and red cell distribution width-platelet ratio as an early predictor of acute pancreatitis in pregnancy.Their study group consists of 14 pregnant patients who developed acute pancreatitis and control group involved 30 healthy pregnant women. Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio and red cell distribution width-platelet ratio were calculated for each group.

Their study result showed that neutrophil to lymphocyte ratio was significantly elevated in acute pancreatitis group compared to the control group,but there was no statistically significant difference in platelet to lymphocyte ratio and red cell distribution width-platelet ratio between the two groups.

They concluded that neutrophil to lymphocyte ratio might be used as an early marker of acute pancreatitis and may have a role in predicting the severity of acute pancreatitis.

Edip Erdal, Zubeyir Bozdag, et al[45] conducted a study to evaluate the usefulness of neutrophil to lymphocyte ratio as a diagnostic tool for early

prediction of severity in acute pancreatitis and compared with that of c-reactive protein.Their study was conducted between 2006 and 2014 that included 464 patients.They found in their study that median neutrophil to lymphocyte ratio and c- reactive protein was higher in severe pancreatitis group.The sensitivity and specificity of cut off values of neutrophil to lymphocyte ratio and c-reactive protein were compared and found that c-reactive protein has better sensitivity and specificity.

They concluded their study that neutrophil to lymphocyte ratio can be used as a diagnostic tool but c- reactive protein is superior compared to neutrophil to lymphocyte ratio.

Sahu B et al conducted study in 2014 to 2016 and concluded that both CTSI and MCTSI showed significant correlation with clinical outcome parameters, as well as good concordance with grading of severity
as per the revised Atlanta classification. MCTSI showed a higher sensitivity whereas CTSI showed a higher specificity in differentiating between mild AP and moderate or severe disease.

Kaplan et al ,turkey conducted a retrospective study with 142 patients diagnosed with acute pancreatitis. Ranson, Atlanta and BISAP 0h, 24h and 48h scores of the patients were calculated by examining their patient files. The patients were divided into three groups as low-risk, medium-risk and high-risk patients according to their PLR and NLR levels. Those with both values greater than the determined thresholds were classified as high risk (PLR>342.31 and

NLR>13.6), those with either NLR or PLR value greater than the threshold classified as moderate risk and those with both values smaller than the threshold were classified as low risk . In conclusion, the PLR-NLR combination was found to have the highest AUC value in the ROC curve analysis in terms of survival and shown to have superior diagnostic discrimination compared to Ranson, Atlanta and BISAP scoring systems in terms of predicting mortality.

Mortele et al 2004 Boston assessed the correlation with patient outcome and interobserver variability of a modified CT severity index in the evaluation of patients with acute pancreatitis compared with the currently accepted CT severity index in 266 patients and found that The modified CT severity index correlates more closely with patient outcome measures than the currently accepted CT severity index, with similar interobserver variability.

Bollen et al compared the modified CT severity index (MCTSI) with the CT severity index (CTSI) regarding assessment of severity parameters in acute pancreatitis (AP). Both CT indexes were also compared with the Acute Physiology, Age, and Chronic Health Evaluation (APACHE II) index and concluded, no significant differences were noted between the CTSI and the MCTSI in evaluating the severity of AP. Compared with APACHE II, both CT indexes more accurately diagnose clinically severe disease and better correlate with the need for intervention and pancreatic infection.

Leung et al studied 121 patients between 1999 to 2003 to assess the accuracy of CTSI, Ranson score, and APACHE II score in course and outcome

prediction of AP. CTSI is a useful tool in assessing the severity and outcome of AP and the CTSI ≥5 is an index in our study. Although Ranson score and APACHE II score also are choices to be the predictors for complications, mortality and the length of stay of Acute Pancreatitis, the sensitivity of them are lower than CTSI.

LIMITATIONS OF THIS STUDY

1. Study population is small.
2. Follow up of cases is of short duration.

Further recommendations

1. A study with long follow up is needed in the future in larger population .
2. Combination of NLR along with other haematological parameters must be included in the prognostic criteria.
3. In further study more treatment particulars such as antibiotics , analgesics and other specific managements that alter neutrophil- lymphocyte ratio must be considered.

CONCLUSION

In our study, Neutrophil Lymphocyt Ratio has proved to be a single indicator in assessing the severity of acute pancreatitis .

NLR can be easily calculated and is a routine workup investigation that is done in all patients at the time of admission. Being a routine investigation, it bears no additional cost to the patient.NLR seems to correlate well with the severity and outcome of acute pancreatitis. Continuous monitoring on each day will provide a dynamic reflection of the immunity and inflammatory response of the body to pancreatitis and hence predict the prognosis earlier.

NLR assessment trespasses the limitation of Ranson's scoring system that, it can be used at the time of admission itself and monitoring is possible in the first 48 hours. It covers the limitation of APACHE II scoring system in a way that it avoids multiple parameters needed for assessment.

So, Future studies are needed which can accurately predict the optimal NLR and investigate if its incorporation would increase the accuracy of the current Acute pancreatitis prognostic scoring systems.

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PROFORMA

1. Case No :
2. Name :
3. Age /Sex :
4. Address :
5. I.P. No :
6. Unit / Ward :
7. Date of admission :
8. Date of discharge :
9. Education :
10. ICU stay :
11. Chief complaints

- Abdomen Pain-Onset, character, location, Duration, radiation, worsening & relieving factors.
- Nausea / vomiting
- Burning sensation in chest
- Haematemesis
- Malena
- Breathlessness
- Giddiness

11.Past history: comorbidities/previous surgery

12.Personal history:

Alcoholic Y/N.....years

Smoking Y/N..... years

13.Treatment history:

14.General physical examination

Pallor / Icterus/lymphadenopathy /pedal edema
BP -
PR -
SPO2-

15. Examination of abdomen
    a. Inspection
    b. Palpation
    c. Percussion
    d. Auscultation
    e. P/R
16. Clinical diagnosis
17. Biochemical investigation

    CBC

    NLR

    RBS

    RFT –urea, creatinine

    Serum electrolytes

    Serum AMYLASE/LIPASE

    LFT

    Lipid profile

    Serum CALCIUM

    URINE ROUTINE
18. Radiological investigation
    - Chest X-Ray
    - Abdominal X-Ray Erect
    - Abdominal ultrasonography
    - CECT Abdomen

	DAY0	DAY1	DAY2
ANC			
ALC			
NLR			

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
2.	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3.	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4.	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5.	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
ஆய்வாளரின் பெயர் .....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....