

OBSERVATIONAL STUDY ON LFT AND PT-INR CHANGES IN ACUTE PANCREATITIS AT A TERTIARY CARE HOSPITAL

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Abstract

Background: Acute pancreatitis (AP) is a prevalent gastrointestinal condition marked by sudden inflammation of the pancreas, often requiring urgent hospital care. It can range from mild, self-limiting episodes to severe forms involving multi-organ dysfunction. The primary causes include gallstones and chronic alcohol consumption, leading to enzyme activation and pancreatic tissue damage. Accurate assessment of disease severity is critical for effective management and prognosis. Liver function tests (LFT) and prothrombin time-international normalised ratio (PT-INR) are essential biochemical markers that may provide valuable insights into early detection and severity of AP, aiding in prompt clinical decision-making and improved patient outcomes. **Materials and Methods:** Conducted at the Rajendra Institute of Medical Sciences, Ranchi, this prospective observational study included 110 patients diagnosed with acute pancreatitis. The correlation between liver function test (LFT) changes, prothrombin time-international normalised ratio (PT-INR), and disease severity was studied. **Result:** The average age of patients was 40.5 years, with the majority 56 (50.9%) between 18-39 years. Males constituted 75 (68.2%) of the study population. The study observed significant alterations in liver enzymes, particularly AST and LDH, which were notably higher in severe pancreatitis cases. The mean AST value was 155.24 ± 129.60 mg/dl. Serum bilirubin levels were elevated but they were not associated with severe disease. There was a progressive increase in the mean PT-INR values from day 0 to day 7 among severe pancreatitis cases. On day 7, the mean PT-INR was 1.50 ± 0.20 , significantly higher in severe cases. Serum amylase and lipase levels were substantially elevated in severe cases, with mean values of 1530.65 ± 1298.06 and 1764 ± 1650.23 , respectively. C-reactive protein (CRP) and white blood cell counts were significantly higher in severe cases, indicating a strong inflammatory response. According to the Glasgow-Imrie scoring system, 60 (54.5%) of the patients had severe pancreatitis. Severe cases showed significant biochemical and coagulation abnormalities, with elevated levels of amylase, lipase, total count, CRP, urea, and creatinine, and a lower mean PaO₂. **Conclusion:** The study underscores the relevance of LFT, PT-INR, and other biochemical markers in evaluating the severity of acute pancreatitis and emphasises the importance of early diagnostic assessment for better management and prognosis.

INTRODUCTION

Acute pancreatitis (AP) has been one of the most common causes of acute hospital admissions among gastrointestinal diseases, with an incidence of about

10–100 per 100,000 populations.^[1] Acute pancreatitis was defined in the Atlanta symposium as an acute inflammatory process involving the pancreas that further involves peri-pancreatic tissues and organs remote from the pancreas.^[2] The theory behind the pathogenesis of acute pancreatitis was proposed as

acinar cell injury, which leads to pancreatic enzyme leakage into pancreatic tissue. These enzymes get activated and initiate the process of auto-digestion. The activated proteases, i.e., elastase, trypsin and lipase, break down cell membranes and tissues which in turn causes vascular damage, oedema, haemorrhage and necrosis.^[3] The two major causes of acute pancreatitis are biliary calculi, which occur in 50-70% of patients, and alcohol abuse, which accounts for 25% of cases.^[4] Patients presenting with clinical symptoms and features consistent with acute pancreatitis include epigastric abdominal pain, nausea, vomiting, and abdominal pain radiating to the back (seen in 40%-70% of patients).^[4] To make a diagnosis, at least two out of the following three features must be observed.^[4] 1) Abdominal pain characteristic of acute pancreatitis. 2) Serum amylase and /or lipase which is 3 times the upper limit of normal and 3) characteristics findings in Imaging (USG/CT scan). The severity of acute pancreatitis does not correlate with the rise in level of serum lipase and amylase. According to the revised Atlanta classification acute pancreatitis is divided into three broad categories.^[5] There are prognostic system criteria for assessing severity including Atlanta severity criteria, Ranson's criteria, Glasgow score, APACHE-II score, SIRS score, recent severity scores like BISAP score, PANC 3 score, Japanese severity score and Harmless acute pancreatitis score. Apart from these, there are other biochemical scores like C-reactive protein (CRP), procalcitonin, serum amyloid A, trypsinogen activation peptide, polymorphonuclear granulocyte elastase, interleukins IL-6 & MCP-1, hematocrit and BUN.^[6] Despite all these clinical and biological markers, there is yet no single marker that could serve as an optimal predictor of disease severity in acute pancreatitis.^[7] Hence, imaging methods like ultrasonogram, computed tomography, echo-enhanced ultrasound, and magnetic resonance imaging have been used to assess the severity of acute pancreatitis. Of the imaging methods contrast-enhanced CT scan abdomen is currently the best imaging method recognised for assessment of severity in acute pancreatitis. Balthazar and his co-workers formulated a new index called as CT severity index (CTSI) which showed a good correlation with the clinical parameters in patients with acute pancreatitis. This index scores the degree of pancreatic inflammation and necrosis on a scale of 10 points. Patients with a severity index of 0-1 exhibited no morbidity or mortality, whereas a 4% morbidity rate and no mortality rate were seen with a CT severity index of 2. In contrast, patients with a CT severity index of 7-10 yielded 92% morbidity and 17% mortality rate.^[8] The BISAP scoring system in particular is very useful with an initial assessment of AP patients with a score of greater than or equal to three being an appropriate score to identify a patient with a high risk of mortality and hence should undergo evaluation for ICU admission.^[9] The cornerstones in the management of AP include aggressive early intravenous hydration,

appropriate nutrition, necessary interventions, and pain management.^[4] Haematological and coagulation changes have been reported in acute pancreatitis as evidenced by Benjamin et al and Inner field et al in 1952, who did their study on coagulation changes in acute pancreatitis.^[10] Acute Pancreatitis produces a severe inflammatory response mainly responsible for acinar cell damage, leading to the release of inflammatory mediators like cytokines, TNF and PAF, thereby resulting in a systemic inflammatory response.^[11] These inflammatory mediators alter the normal hemostatic mechanism by acting in paracrine or autocrine loops to activate the monocytes, and neutrophils at the site of injury and these activated cells in turn express the tissue factor in the injured pancreatic cell and alter the coagulation pathway.^[10] More than 80% of acute pancreatitis cases are caused by alcohol ingestion and gallstones.^[11,12] Pathophysiology of gallstone pancreatitis includes small stones travelling down the bile duct and getting lodged at the end, distal to the area where the pancreatic duct attaches a condition known as choledocholithiasis. The result is obstruction of the flow of pancreatic enzymes, allowing them to accumulate in the organ. Elevated liver enzymes observed in the setting of acute pancreatitis point toward choledocholithiasis as the underlying cause, with an alanine aminotransferase greater than three times the upper limit of normal having a positive predictive value of 95% for gallstone pancreatitis in the non-alcoholic patient.^[12,13] In this context, the present study was conducted to assess the LFT and PT-INR changes in acute pancreatitis and these indices are correlated with the early diagnosis and severity of disease. The primary objective of the study is to assess the LFT and PT-INR changes in patients. Secondary objectives are to study the socio-demographic and clinical profile of patients and the risk factors associated with acute pancreatitis among the study subjects.

MATERIALS AND METHODS

After approval from the Institutional Ethics Committee, RIMS, Ranchi, a prospective observational study was conducted over 1 year from June 2023 to May 2024 in Rajendra Institute of Medical Science, Ranchi. The study population included all the patients diagnosed with acute pancreatitis admitted to the Department of General Surgery, as per the inclusion and exclusion criteria.

Inclusion Criteria

- Age more than 18 years and less than 75 years.
- Serum amylase/lipase level elevated more than three times the upper range of normal limit.
- Radiologically diagnosed case of Acute Pancreatitis

Exclusion Criteria

- Patients with Pancreatic carcinoma
- Patients with Chronic Pancreatitis
- Patients with known Coagulation Disorder

- Patients with known Congenital and Chronic Liver Disease
- Hemodynamically unstable patients.

Sample size and sampling procedure: The sample size was calculated assuming the prevalence of event of interest i.e. prevalence of abnormal LFT in acute pancreatitis as 14.5% [74]. Considering the baseline prevalence with a 95% confidence interval (1.96) and absolute allowable error of 7.5% (d) the sample size was calculated using the formula $n = (Z_{1-\alpha/2})^2 p(1-p)/d^2$. Where, n= sample size, $Z_{1-\alpha/2}=1.96$, $p=0.14$, $(1-p)=0.86$. The calculated final minimum required sample size came out to be 82. All the eligible study population during the data collection period was approached, and after applying the inclusion and exclusion criteria, 110 subjects were included applying a drop-out rate of 20% and selected using the total enumeration technique.

The purpose of the study was explained to the patient and the relatives of the patient. Informed written consent was taken from each study participant. Serum amylase/ lipase, liver function tests, PT-INR, and CRP were done at admission and repeated on day 3 and day 7 of admission.

Data analysis: Data were entered into MS Excel and analysed using the SPSS version 20. Descriptive analysis was done in the form of proportion for categorical variables, and mean or median for continuous variables. Data were checked for normal distribution and parametric or non-parametric tests were done accordingly for continuous variables. A chi-square test and Student-t Test were done to measure the statistical association between categorical variables; a p-value of less than 0.05 was taken as statistically significant.

RESULTS

The present study was conducted among 110 patients having acute pancreatitis in the Department of General Surgery, Rajendra Institute of Medical Sciences (RIMS) to correlate the severity of acute pancreatitis with LFT and PT-INR changes. The findings of the study are being described as follows:

Demographic profile: The majority of the patients 56 (50.9%) were in the age group of 18-39 years, 44

(40%) were patients in the 40-59 years group and 10 (9.1%) were 60 years and older. The mean (SD) age of the study population was 40.50 ± 12.17 years. In the study 75 (68.2%) were males and 35 (31.8%) were females.

Alteration in biochemical parameters: The mean bilirubin level was 1.47 ± 0.83 mg/dl and the mean AST value was 155.24 ± 129.60 mg/dl. The mean albumin and LDH levels were 5.79 ± 1.96 and 717.34 ± 510.25 respectively. The mean serum amylase and lipase were 1530.65 ± 1298.06 and 1764 ± 1650.23 . The mean total count and CRP were as high as $16,500.80 \pm 8036.04$ and 185.20 ± 138.92 . The mean PaO₂ was low (73.15 ± 11.94) shown in [Table 1].

3. Disease severity of patients according to Glasgow-Imrie score: [Figure 1] shows 60 (54.5%) patients had severe disease among the study population.

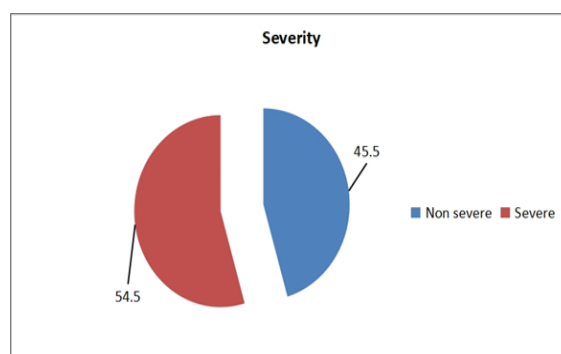


Figure 1: Distribution of study subjects according to severity by Glasgow-Imrie score (n=110)

Correlation of changes in biochemical parameters and disease severity: [Table 2] shows that biochemical parameters like AST, LDH, CRP, renal function tests, serum amylase, and lipase levels were significantly elevated in patients with severe disease (p-value < 0.05).

Correlation of PT-INR changes during hospital stay with disease severity: [Table 3] shows that there was a significant increase in PT-INR levels from day 0 to day 7 of admission in severe disease patients in comparison to non-severe patients. (p-value < 0.05)

Table 1: Distribution of study subjects according to biochemical parameters (n=110); AST- aspartate transaminase, LDH- lactate dehydrogenase, CRP- C- reactive protein, RBS- random blood sugar, PaO₂- partial pressure of oxygen.

Biochemical parameters	Mean	SD
Total bilirubin	1.47	0.83
Direct bilirubin	0.74	0.48
Indirect bilirubin	0.72	0.43
Alkaline phosphatase	121.66	45.84
AST	155.24	129.60
Albumin	5.79	1.96
LDH	717.34	510.25
Serum Amylase	1530.65	1298.06
Serum Lipase	1764	1650.23
Total count	16,500.80	8036.04
CRP	185.20	138.92
RBS	134.54	31.89
Urea	50.50	24.90
Creatinine	1.16	0.53

PaO2	73.15	11.94
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Table 2: Distribution and association of disease severity and liver function test (n=110); AST- aspartate transaminase, LDH- lactate dehydrogenase, CRP- C- reactive protein, RBS- random blood sugar, PaO2- partial pressure of oxygen.

Biochemical parameters	Disease severity, mean (SD)		p value
	Non-severe	Severe	
Total bilirubin	1.41 (0.56)	1.52 (1.01)	0.490
Direct bilirubin	0.74 (0.42)	0.75 (0.53)	0.737
Indirect bilirubin	0.66 (0.24)	0.77 (0.55)	0.333
Alkaline phosphatase	117.61 (41.67)	126.86 (50.64)	0.308
AST	75.26 (41.93)	223.28 (140.89)	0.001*
Albumin	4.72 (3.85)	3.57 (1.45)	0.545
LDH	353.40 (156.43)	1026.73 (506.96)	0.001*
Serum Amylase	601.62 (243.60)	2318.49 (1319.46)	0.001*
Serum Lipase	648.08 (253.13)	2709.69 (1741.32)	0.001*
Total count	12242.10 (3768.33)	20067.51 (8982.31)	0.001*
CRP	63.02 (42.59)	289.06 (104.34)	0.001*
RBS	126.44 (20.07)	141.95 (37.95)	0.058
Urea	38.62 (18.35)	60.55 (25.62)	0.001*
Creatinine	0.89 (0.38)	1.47 (0.52)	0.001*
PaO2	76.32 (8.22)	70.59 (13.95)	0.006*

Table 3: Distribution and association of disease severity and PT/INR ratio (n=110); PT-INR- prothrombin time-international normalised ratio.

PT/INR ratio	Disease severity, mean(SD)		p value
	Non-severe	Severe	
Day 0	1.26 (0.23)	1.31 (0.26)	0.489
Day 3	1.39 (0.34)	1.45 (0.26)	0.018*
Day 7	1.48 (0.19)	1.52 (0.20)	0.424

DISCUSSION

Acute pancreatitis (AP) is characterized as a sudden onset of pancreatic parenchymal inflammation with the involvement of nearby tissues or distant organ systems. The histology may return to normal between bouts, or it may manifest as a solitary attack or reoccur in discrete episodes.^[15] It has a wide range of signs and symptoms, from those associated with mild, self-limiting illnesses to those associated with fulminant conditions that cause multi-organ failure and trivial mortality.^[16] Acute pancreatitis (AP) has an overall mortality rate ranging from 2% to 10%. This relates to 10%-30% of patients with severe illness that is characterized by pancreatic and peripancreatic necrosis. Together, alcoholism and gallstones cause 80% of the cases. Most of these individuals had mild to moderately severe pancreatitis and recovered with conservative management. Only 15% of individuals developed severe disease.^[17] The disease can be identified using computed tomography (CT) scans and ultrasounds. In acute pancreatitis, serum biochemical markers of liver function frequently exhibit changes. These alterations in liver function can be correlated with the severity of the condition and its overall prognosis.^[18] The level of serum bilirubin indicates how well hepatocytes can take up, bind, and excrete bilirubin through the liver's reticuloendothelial system. When hepatocytes are damaged, the liver's ability to clear bilirubin is impaired, leading to an increase in blood bilirubin levels.^[19] When bilirubin levels in the serum are elevated, the patient develops jaundice. An increase in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) typically indicates

the severity of liver disease, often before any abnormal clinical symptoms appear. However, as liver injury worsens, many hepatocytes become necrotic and die, leading to a depletion of these enzymes. Therefore, a decrease in aminotransferase levels can occur in the advanced stages of liver disease. As a result, elevated aminotransferase levels do not accurately reflect the severity of liver disease or effectively assess prognosis.^[20] The serum levels of ALT and AST are positively correlated with the severity of pancreatitis, returning to normal after the condition resolves.^[21]

Acute Pancreatitis produces a severe inflammatory response producing inflammatory mediators that alter the normal hemostatic mechanism by acting in paracrine or autocrine loops to activate the monocytes and neutrophils to the site of injury and these activated cells in turn express the tissue factor in the injured pancreatic cell and alter the coagulation pathway.^[22] The Hypothesis states that these coagulation changes may be due to early consumption of coagulation factors which are secondary to enzymes of the pancreas, especially trypsin, or it may be secondary to vascular injury.^[23] In the present study, we observed that the mean (SD) age of the study population was 40.50 ± 12.17 years with the majority of the subjects in the age group of 18-39 years and most of the patients were males (68.2%), labourer (22.7%) and farmers (20.9%). Saxena R et al,^[24] in their study found that the most common age group was 30-44 years, followed by 45-59 years, and the mean and median ages were 44.54 and 47 years, respectively. They also observed that the majority of cases 62% were males. Reddy et al,^[25] showed that out of 60 AP cases, most of the patients

28 (46.6%) were in the age group of 15-30 years, 26 (43.3%) were in the age group of 30-45 years, 3 (5%) were in the age group of 45-60 years, and 3 (5%) were in the age group of 60-75 years. However, Nandu et al,^[26] found that the highest incidence was noted in patients in the age group of 20-40 years, accounting for 52.11% of patients, and the mean age of presentation was 38.94 years. Also, Jha et al,^[27] found that the mean age of the study group (n = 104) was 40.9 ± 1.3 years, and 104 patients were grouped in ages of less than 25, 25-35, 36-45, 46-55, and greater than 55 years.

The present study observed that 50% of the patients had nausea at presentation, 51.8% of the patients had a history of vomiting and only 1.8% of the patients had jaundice. Saxena, R et al,^[24] in their study stated that most patients had abdominal pain 95.90% followed by vomiting 88.37% and 14.28% of patients presented with yellowish discolouration of skin or eyes.

We observed that 30% of the patients had an oedematous pancreas with fat stranding on USG, followed by necrotic pancreas in 22.7% and gallstone disease in 20.9%.

In the present study, it is seen that the mean bilirubin was 1.47 ± 0.83 mg/dl. The mean AST value was 155.24 ± 129.60 mg/dl. The mean albumin and LDH were 5.79 ± 1.96 and 717.34 ± 510.25 respectively. There was a marked derangement in various biochemical parameters among the subjects. The mean serum amylase and lipase were 1530.65 ± 1298.06 and 1764 ± 1650.23 IU/L. The mean total count and CRP were as high as $16,500.80 \pm 8036.04$ and 185.20 ± 138.92 respectively. The mean PaO₂ was low (73.15 ± 11.94).

Jagatheesan S et al,^[28] in their study observed that mean haemoglobin levels were 12.36 ± 1.45 , platelets were 256.30 ± 43.34 and leucocytic count was 9.87 ± 3.67 . LFT finding among the participants showed, mean bilirubin as 2.79 ± 1.01 , direct bilirubin as 0.98 ± 0.23 , aspartate transaminase AST (U/l) as 26.92 ± 10.78 , alanine transaminase ALT (U/l) as 33.97 ± 4.46 , alkaline phosphatase (U/l) as 155.49 ± 39.38 and albumin (g/dl) as 4.23 ± 1.94 . Renal function test showed mean urea (mg/dl) as 20.89 ± 12.78 and creatinine (mg/dl) as 1.98 ± 0.09 . The mean serum amylase (U/l) was 789.98 ± 333.01 and the mean serum lipase (U/l) was 687.01 ± 230.54 . Farhan MN et al showed a significant decrease in serum levels of BUN and a significant increase in serum levels of AST, ALT, ALP, total protein, total bilirubin, and direct bilirubin.^[29] In the present study, 60 (54.5%) of the patients had severe pancreatitis according to the Glasgow score and among the biochemical parameters of the liver function test, AST and LDH were significantly higher among the severe cases of pancreatitis, which corresponds to various studies showing the serum levels of ALT and AST are positively correlated with the severity of pancreatitis.^[19,21]

The mean PT/INR ratio at days 0, 3 and 7 was 1.28 ± 0.24 , 1.42 ± 0.31 and 1.50 ± 0.20 , which was

gradually increasing from day 0 to day 7. The mean PT/INR ratio was significantly increased from day 0 to day 7 among the cases with severe cases of pancreatitis than the non-severe ones. Shafique A. et al,^[30] in their study found that 14 (28%) patients showed an increase in PT-INR values in their study. Out of their patients, 64.3% were in the severe group and 35.7% in the mild group. 24% of study subjects have high APTT value and the value was more in the severe pancreatitis group (83.3%) than in the mild group (16.7%).

Coagulation parameters like prothrombin time (PT) and the activated partial thromboplastin time (APTT) measure the extrinsic and intrinsic coagulation pathways, respectively. Clinical studies have shown an elevated prothrombin time in patients with AP,^[31] which corresponds to our study findings.

The present study being a single institution-based descriptive observational study somehow limits the generalization of the result from the study, therefore, a larger multi-centric study with a better study design and larger sample size would be recommended in this direction.

CONCLUSION

The mean (SD) age of the study population was 40.50 ± 12.17 years and the majority of the subjects were in the age group of 18-39 years, suggesting that acute pancreatitis primarily affects the population in 18-39 years and is more prevalent in males than female. There was a marked derangement in various biochemical parameters among the subjects. Among the biochemical parameters, mean amylase, lipase, total count, CRP, urea and creatinine were significantly higher among the cases with severe cases of pancreatitis than the non-severe ones. 54.5% of the patients had severe pancreatitis according to the Glasgow score.

The mean PT/INR ratio was significantly increased from day 0 to day 7 among the cases with severe cases of pancreatitis than the non-severe ones. Haematological and coagulation abnormalities were more common in severe acute pancreatitis. The clinical manifestations of severe acute pancreatitis are usually the presence of abnormal serum biochemical indexes and abnormal liver perfusion. Acute pancreatitis (AP) can lead to a range of complications, including secondary liver injury, due to multiple contributing factors. These elements interact in a way that triggers a cascade of reactions, ultimately resulting in liver damage. Timely treatment of liver injury can help reduce the severity of acute pancreatitis and its associated complications. **Acknowledgement:** All the authors would like to thank Prof Dr Shital Malua for allowing us to conduct this study.

REFERENCES

1. Dumnicka P, Maduzia D, Ceranowicz P, Olszanecki R, Drożdż R, Kuśnierz-Cabala B. The Interplay between

- Inflammation, Coagulation and Endothelial Injury in the Early Phase of Acute Pancreatitis: Clinical Implications. *Int J Mol Sci.* 2017;18(2):354. doi: 10.3390/ijms18020354.
2. Bollen TL, Besselink MG, van Santvoort HC, Gooszen HG, van Leeuwen MS. Toward an update of the Atlanta classification on acute pancreatitis: Review of new and abandoned terms. *Pancreas* 2007; 2:107-113. [PMID : 17632315 DOI : 10.1097/mpa.0b013e31804fa189]
 3. Bhatia, M., Wong, F. L., Cao, Y., Lau, H. Y., Huang, J., Puneet, P., & Chevali, L. Pathophysiology of acute pancreatitis. *Pancreatolgy* 2005; 5:132. Doi: 10.1159/000085265. Epub 2005 Apr 21.
 4. Bailey, H. and Love, R. (1948) *A short practice of surgery.* 28th Edition, Lewis, London, 72,1269-1270.5.
 5. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013; 62:102-111. doi: 10.1136/gutjnl-2012-302779. Epub 2012 Oct 25.
 6. Agarwal N, Pitchumoni CS, Sivaprasad AV. Evaluating tests for acute pancreatitis. *An J Gastroenterol* 1990; 85:356-66. PMID: 2183590
 7. Eland IA, Sturkenboom MJ, Wilson JH, Stricker BH. Incidence and mortality of acute pancreatitis between 1985 and 1995. *Scand. J. Gastroenterol.* 2000; 10:1110-116.
 8. Blamey SL, Imrie CW, O'Neill J, Gilmour WH, Carter DC. Prognostic factors in acute pancreatitis. *Gut* 1984; 12:1340-1346. PMID: 6510766 PMID: PMC1420197]
 9. Gao W, Yang HX, Ma CE. The Value of BISAP Score for Predicting Mortality and Severity in Acute Pancreatitis: A Systematic Review and Meta-Analysis. *PLoS One* 2015; 10: e0130412. Gao W, Yang HX, Ma CE. The Value of BISAP Score for Predicting Mortality and Severity in Acute Pancreatitis: A Systematic Review and Meta-Analysis. *PLoS One* 2015; 10: e0130412.
 10. Shinowara, G.Y., Stutman, L.J., Walters, M.I., Ruth, Hypercoagulability in acute pancreatitis, *American Journal of Surgery*, 105,714. doi: 10.1016/0002-9610(63)90483-5.
 11. Hiravama, A., Uehara, S., Itagaki, Y., Izumiyama, S. Kudo, M. & SATO, T. Coagulation study in pancreatitis. *Japanese Journal of Clinical Haematology*, 1974;15,171.
 12. Amerine E. Get optimum outcomes for acute pancreatitis patients. *Nurse Pract.* 2007; 32:44-48. doi: 10.1097/01.NPR.0000275355.10064.aa.
 13. Whitcomb DC. Clinical practice. Acute pancreatitis. *N Engl J Med.* 2006; 354:2142-2150. doi: 10.1056/NEJMc054958.
 14. Dholakia K, Pitchumoni CS, Agarwal N. How often are liver function tests normal in acute biliary pancreatitis? *J Clin Gastroenterol.* 2004;38(1):81-83. doi: 10.1097/00004836-200401000-00017. PMID: 14679333.
 15. Dooley JS, Lok AS, Garcia-Tsao G, Pinzani M, et al.: *Sherlock's Diseases of the Liver and Biliary System.* Wiley, New York; 2018. *Clin Med (Lond).* 2011 Oct;11(5):506. doi: 10.7861/clinmedicine.11-5-506
 16. Beger HG, Matsuno S, Cameron JL, Rau BM, Sunamura M, Shulick RD: *Diseases of the Pancreas: Current Surgical Therapy.* Springer, Berlin, Germany; 2018. doi: 10.1007/978-3-540-28656-1
 17. Chauhan Y, Jindal N, Verma RK, Tyagi PK, Rana M, Singh S: A clinical profile and outcome of patients with acute pancreatitis: a prospective study in North India. *Arch Int Surg.* 2018;8:132. DOI:10.4103/ais.ais_3_19
 18. Xiao B, Zhang XM, Jiang ZQ, Tang W, Huang XH, Yang L, Feng ZS. Fatty liver in acute pancreatitis: characteristics in magnetic resonance imaging. *J Comput Assist Tomogr* 2012; 36: 400-405. doi: 10.1097/RCT.0b013e31825977c2.
 19. Xu X, Ai F, Huang M. Deceased serum bilirubin and albumin levels in the assessment of severity and mortality in patients with acute pancreatitis. *Int J Med Sci* 2020; 17: 2685-2695. doi: 10.7150/ijms.49606
 20. McCord KW, Webb CB. Hepatic dysfunction. *Vet Clin North Am Small Anim Pract* 2011; 41: 745-758. doi: 10.1016/j.cvsm.2011.04.002.
 21. Güngör B, Çağlayan K, Polat C, Seren D, Erzurumlu K, Malazgirt Z. The predictivity of serum biochemical markers in acute biliary pancreatitis. *ISRN Gastroenterol* 2011; 2011: 279607. Doi: 10.5402/2011/279607.
 22. Hirayama A, Uehara S, Izumiyama S, Kudo M, Sato T, Mitsuhashi H. The coagulation and fibrinolytic study in pancreatitis. *Blood and Vessel.* 1978; 9:24-27.
 23. Imrie CW, Whyte AS. A prospective study of acute pancreatitis. *Br J Surg* 1975; 62:490-4. doi:10.18203/2349-3933.ijam20174289
 24. Saxena, R., Kumar, S., Nafe, Z., Chatteraj, A., & Chauhan, S. (2023). Clinical, Biochemical, and Radiological Correlation in the Severity of Acute Pancreatitis: A Retrospective Study. *Cureus*, 15(2), e34996. Doi: 10.7759/cureus.34996
 25. Reddy MS, Ramana PV, Bhavani C, Lakshmi RNR, Khizar SM: A study on aetiology, severity, management and outcome of acute pancreatitis in tertiary care teaching hospital. *Int J Res Rev.* 2020, 7:534-44. E-ISSN: 2349-9788; P-ISSN: 2454-2237
 26. Nandu VV, Deshpande AV: Clinical study of pancreatitis and its management. *Int Surg J.* 2016, 3:1574-9. doi: http://dx.doi.org/10.18203/2349-2902.isj20162750
 27. Jha PK, Chandran R, Jaiswal P, Seema K: A clinical study of risk factors of acute pancreatitis in a tertiary care centre in North India. *Int Surg J.* 2017, 4:1878-83. DOI: http://dx.doi.org/10.18203/2349-2902.isj20172053
 28. Jagatheesan S, John N. A randomized controlled trial of acute pancreatitis in Thanjavur Medical College: an institutional experience. *Int Surg J* 2023; 10:1471-6.
 29. Farhan MN, Al-Fartusie FS, Hamed SL (2020): Evaluation of lipid profile and liver function in acute pancreatitis patients: a case-control study, *Ann Trop Med &Public Health*; 23(S18): SP231826. doi:10.36295/ASRO.2020.231826
 30. Shafique, T. Usha. A study on haematological and coagulation changes in acute pancreatitis – prospective study. *International Journal of Contemporary Medical Research* 2018;5(11): K1-K5.
 31. Radenkovic, D., Bajec, D., Ivancevic, N., Milic, N., Bumbasirevic, V., Jeremic, V. et al. (2009). D-dimer in acute pancreatitis: a new approach for an early assessment of organ failure. *Pancreas*, 38, 655-660. doi:10.1097/MPA.0b013e3181a66860