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ROLE OF C – REACTIVE PROTEIN, LACTATE DEHYDROGENASE AND D – DIMER IN PREDICTING THE SEVERITY OF ACUTE PANCREATITIS

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Abstract

Background

Acute pancreatitis is the most prevalent, potentially fatal illness that requires hospitalization in day-to-day life. Acute pancreatitis can range from mild to severe, with the latter often resulting in complications such as organ failure. Traditional scoring systems, like the APACHE II and Ranson's criteria, are used to assess severity, but additional biomarkers may improve prognostic accuracy. C – Reactive protein (CRP), Lactate dehydrogenase (LDH), and D – dimer have been implicated in inflammation and coagulation processes. The significance of predicting the severity of acute pancreatitis by these markers is emphasized by this study.

Methodology

This cross-sectional study was conducted over a period of one year at our hospital. The study included 105 participants who had been diagnosed with acute pancreatitis. The parameters studied were patient demographics, presenting symptoms, acute phase reactants such as CRP, LDH and D – dimer and their correlation with serum amylase and lipase levels and CT severity of acute pancreatitis. SPSS version 21.0 (IBM Corp., Armonk, NY) was used for statistical analysis.

Results

Significant variations in CRP, D-dimer, and LDH levels were seen in this study among different severity groups. Higher levels of CRP were correlated with severe cases ($p < 0.001$). Elevated LDH levels were significantly associated with increased severity ($p < 0.001$). D – dimer was found to be markedly elevated in severe cases compared to mild ($p < 0.001$). Strong positive correlations were found between all three biomarkers and CT severity scores. There was mild positive correlation between the serum amylase, serum lipase and acute phase reactants but of no statistical significance.

Conclusions

In conclusion, this study identifies significant correlations between elevated levels of CRP, LDH, and D – dimer

with the severity of acute pancreatitis. These biomarkers may enhance the accuracy of severity assessment beyond traditional scoring systems. Their rapid measurement could facilitate early identification of high-risk patients, guiding timely intervention. Incorporating these biomarkers into clinical practice may improve patient outcomes. Further research is needed to validate these findings and explore their potential as therapeutic targets.

Keywords: ***C*** *– Reactive Protein, Lactate dehydrogenase, D – Dimer, Acute Pancreatitis, Biomarkers, Acute Phase Reactants*

INTRODUCTION

Acute pancreatitis (AP) is an inflammatory condition of the pancreas that can present with a spectrum of severity, ranging from mild, self-limiting episodes to severe cases that can lead to significant morbidity and mortality [1, 2]. Pancreatic enzyme activation is a pathophysiological feature of AP, leading to inflammation, tissue damage, and potential complications such systemic inflammatory response syndrome (SIRS) and organ failure [3]. The incidence of AP has been rising globally, with common etiological factors including gallstones, chronic and excessive alcohol consumption, and metabolic disorders such as hypertriglyceridemia. The severity of the illness at the time of diagnosis has a significant impact in the management of AP, making early and accurate assessment crucial for optimizing treatment strategies [4].

Clinicians often rely on established scoring systems, such as the Ranson's criteria, APACHE II, systemic inflammatory response syndrome (SIRS) score, modified computed tomography severity index (MCTSI), the BISAP scoring system and other scoring systems to evaluate the severity of AP [5]. These tools incorporate clinical parameters and laboratory values to stratify patients into categories ranging from mild to severe. However, these systems have inherent limitations. They can be time-consuming and may require repeated assessments, potentially delaying crucial therapeutic interventions. Moreover, they may not account for the dynamic nature of the disease, where a patient's clinical status can change rapidly, necessitating a more timely approach to severity assessment [6].

Identifying biomarkers that rapidly and objectively detect the inflammatory state of individuals with AP has drawn more attention in recent years. One such biomarker is C –Reactive Protein (CRP), which the liver produces in reaction to inflammatory cytokines, especially interleukin-6 (IL-6). Elevated levels of CRP have been consistently associated with the severity of various inflammatory conditions, including pancreatitis. High CRP levels not only indicate the presence of inflammation but have also been linked to complications such as infection and multi-organ failure in patients with AP [7].

Lactate dehydrogenase (LDH) is another biomarker that can provide insights into tissue damage. This enzyme is released during cellular injury and necrosis, making it a potential indicator of the extent of pancreatic damage. Studies have suggested that elevated LDH levels may correlate with more severe pancreatic injury, serving as an early warning signal for the potential progression of the disease [8].

D – dimer, a product of fibrin degradation, has gained attention for its role in both coagulation and inflammation. Elevated D – dimer levels are often observed in various pathological conditions associated with systemic inflammation and may indicate a hypercoagulable state. In AP, increased D – dimer levels may indicate the severity of the inflammatory process and the potential for thrombotic complications, such as disseminated intravascular coagulation (DIC), which can occur in severe cases [9].

Given the limitations of traditional scoring systems and the potential of biomarkers to enhance severity assessment, this study aims to investigate the correlation between CRP, D – dimer and LDH, levels and the severity of AP in patients attending tertiary care hospitals. By examining these relationships, we seek to provide

clinicians with additional tools for early identification of high-risk patients, ultimately guiding more effective management strategies and improving patient outcomes. This study adds to the expanding corpus of literature advocating for the integration of biomarker assessments into routine clinical practice for AP, paving the way for more personalized and responsive patient care.

MATERIALS AND METHODS

Study design

This cross-sectional observational study was conducted over a one-year period from January 2023 to January 2024 at the department of general surgery, general medicine and emergency room of our hospital. Samples of blood were taken in order to measure CRP, LDH, D – dimer, serum amylase and serum lipase. Correlation coefficients and other statistical analysis were used to evaluate the associations between biomarker levels and the severity of AP, enabling a comprehensive evaluation of their diagnostic potential. The goal of the study was to provide light on how useful these indicators are in clinical settings.

Ethical Considerations

The study followed ethical norms and was authorised by our hospital's institutional review board. Before being enrolled, all participants gave their informed consent, guaranteeing they understood the goal of the study and any possible risks. At any point, participants may discontinue from the study without having an impact on their medical treatment. Confidentiality was maintained throughout the study by anonymizing data and securely storing records.

Study Criteria

Specific inclusion and exclusion criteria were applied in the selection of the participants. Patients above 21 years of age, of either sex, who were diagnosed with AP, confirmed by clinical examination and CT scan were included in the study. Patients with a history of chronic pancreatitis or other chronic gastrointestinal diseases, individuals who underwent major abdominal surgery within the past month, patients with active infections that could confound inflammatory marker levels, pregnant or breastfeeding women, individuals with known bleeding or clotting disorders that could affect D-dimer levels, patients currently taking anticoagulants or anti-inflammatory medications that could influence biomarker levels were all excluded from the study.

Data Collection

Data collection involved a systematic approach to ensure accuracy and consistency. Eligible participants were identified based on the inclusion and exclusion criteria, and informed consent was obtained. Following consent, demographic information and clinical information were recorded. Blood samples were drawn from participants to measure levels of CRP, LDH, D – dimer, serum amylase and serum lipase. Samples were processed and analyzed using standardized laboratory methods. CT abdomen was taken and the severity of AP was recorded. Data were then compiled into a secure database for statistical analysis, ensuring confidentiality and integrity throughout the process.

Sample size calculation

A statistical power analysis was used to calculate the necessary sample size for this study in order to guarantee accurate results. We utilized a Z-score of 1.96 to achieve a 95% confidence level and estimated the population variance from prior studies. Additionally, we defined an acceptable margin of error to reflect the precision desired in our findings. The calculations indicated that approximately 105 participants would be needed to effectively assess the correlations between biomarker levels and the severity of AP, while also accounting for potential dropouts.

Statistical Analysis

Descriptive statistics were used in the study to provide an overview of the clinical and demographic traits of the participants. For both continuous and categorical variables, this will entail computing means, medians, standard deviations, and frequencies, accordingly. Patients will be categorized based on severity grades of AP as determined by CT findings, allowing for the exploration of differences across these groups. Initial comparisons will be made using the Kruskal-Wallis test to evaluate whether median levels of acute-phase reactants CRP, LDH and D – dimer differ significantly among the severity grades. If significant differences are identified, post-hoc pairwise comparisons will be conducted using the Dwass-Steel-Critchlow-Fligner method to specify group differences.

Subsequently, relationships between serum lipase levels and acute-phase reactants will be analyzed using Pearson's correlation coefficients. This analysis will quantify the strength and direction of associations, with p-values assessing the statistical significance of these correlations. Given the critical nature of AP and its inflammatory processes, the aim is to elucidate potential relationships between elevated serum lipase and increased levels of CRP, LDH, and D-dimer. A p – value of < 0.05 was defined as statistically significant. SPSS version 21.0 (IBM Corp., Armonk, NY) was used for statistical analysis, ensuring a comprehensive and rigorous approach to the evaluation of the data and the relationships among the biomarkers under investigation. These analyses will provide valuable insights into the predictive value of serum lipase in conjunction with other inflammatory markers in patients with AP.

RESULTS

Patient demographic details such as age distribution, sex distribution, predominant symptoms and duration and frequency of alcohol consumption were studied.

The majority fall within the 31 – 40 (33.3%) and 41 – 50 (35.2%) age brackets, contributing to 68.5% of the total sample. Those aged 51 – 60 constitute 18.1%, while individuals aged 21 – 30 and over 60 represent 5.7% and 7.6%, respectively. By the age of 50, 74.3% of the cases are accounted for, highlighting that the majority of patients are below 50. There is a significant male predominance in this sample, with 92.4% of the patients being male. Females make up a small proportion, representing only 7.6% of the study population. The most prevalent symptom is abdominal pain, which occurs in 65.7% of cases, followed by vomiting in 27.6% of cases. Abdominal distension represents a smaller proportion at 6.7%. With abdominal pain and vomiting together accounting for 93.3% of symptoms, these are the key symptoms reported by the vast majority of patients. The majority experienced symptoms for one day (41.9%), followed closely by those lasting two days (38.1%). Symptoms persisting for three days constitute a smaller proportion at 20.0%. The majority, accounting for 83.8% of the sample, reported regular alcohol consumption. Conversely, 16.2% reported abstaining from alcohol consumption. These results are given in table 1.

	Counts = n	**Percentage**	**Cumulative Percentage**
Age Group			
21 – 30	6	5.7 %	5.7 %
31 – 40	35	33.3 %	39.0 %
41 – 50	37	35.2 %	74.3 %
51 – 60	19	18.1 %	92.4 %
60 +	8	7.6 %	100.0 %
Frequencies of Sex			

Female	8	7.6 %	7.6 %
Male	97	92.4%	100%
Predominant Symptom			
Abdominal Distension	7	6.7 %	6.7 %
Abdominal Pain	69	65.7 %	72.4 %
Vomitting	29	27.6 %	100.0 %
Duration of Symptoms			
1 Day	44	41.9 %	41.9 %
2 Days	40	38.1 %	80.0 %
3 Days	21	20.0 %	100.0 %
Regular Alcohol consumption			
Absent	17	16.2 %	16.2 %
Present	88	83.8 %	100.0 %

Table 1: Patient demographics, presenting complaints and alcohol consumption
Categorical variables are mentioned as counts and percentage

Table 2 presents the frequency distribution of CT findings and severity grades based on CT findings among the study population. The most prevalent finding is necrosis, observed in 39.0% of cases, followed by perihepatic fluid collection at 32.4%. Pseudocyst is the third most frequent finding, comprising 21.9% of cases, while focal inflammation has the lowest frequency at 6.7%. Grade III severity is the most prevalent, observed in 39.0% of cases, closely followed by Grade II at 32.4%. Grade IV severity is reported in 21.9% of cases, while Grade I severity is the least frequent, accounting for 6.7%.

	Counts = n	**Percentage**	**Cumulative Percentage**
CT findings			
Focal Inflammation	7	6.7 %	6.7 %
Necrosis	41	39.0 %	45.7 %
Perihepatic fluid collection	34	32.4 %	78.1 %
Pseudocyst	23	21.9 %	100.0 %
Severity based on CT			
Grade I	7	6.7 %	6.7 %
Grade II	34	32.4 %	39.0 %
Grade III	41	39.0 %	78.1 %
Grade IV	23	21.9 %	100.0 %

Table 2: CT findings and severity grading
Categorical variables are mentioned as counts and percentage

Table 3 delineates the distribution of individuals categorized by their CRP levels, expressed in milligrams per liter (mg/L). Among the sample population, 31.4% are classified with CRP levels below 150 mg/L, while the majority, constituting 68.6%, exhibit CRP levels surpassing this threshold. The frequency distribution of LDH

levels is depicted in the provided table 3. Individuals are categorized based on LDH concentrations, either below 350 units per liter (U/L) or exceeding this threshold. Among the sample population, 33.3% exhibit LDH levels below 350 U/L, while the majority, constituting 66.7%, present LDH levels surpassing this value. Table 3 also presents the distribution of D Dimer levels among the sampled population. It shows that 14.29% of individuals have D Dimer levels below 0.5 mcg/ml, while the majority, 85.71%, exhibit levels exceeding 0.5 mcg/ml. This distribution highlights the prevalence of elevated D Dimer levels within the studied cohort.

	Counts = n	**Percentage**	**Cumulative Percentage**
CRP levels			
< 150	33	31.4 %	31.4 %
> 150	72	68.6 %	100.0 %
LDH levels			
< 350	35	33.3 %	33.3 %
> 350	70	66.7 %	100.0 %
D Dimer levels			
< 0.5	15	14.29 %	14.29%
> 0.5	90	85.71 %	100%

Table 3: CRP, LDH and D – Dimer levels
CRP values calculated are in mg/L
LDH values calculated are in U/L
D – dimer values calculated are in mcg/ml
Categorical variables are mentioned as counts and percentage

Table 4 presents CRP levels across CT severity grades. CRP levels increase with severity. Grade IV has the highest median CRP (180 mg/L), followed by Grade III (164 mg/L), Grade II (126 mg/L), and Grade I (118 mg/L). Variability within grades is evident, notably in Grade II. Higher CRP levels correlate with more severe CT grades, indicating a strong association between inflammation and disease severity.

Table 4 also presents descriptive statistics outlining LDH levels across different grades of CT severity. Notably, there is a distinct pattern of LDH elevation corresponding to increasing CT severity grades. In Grade I, the median LDH level remains relatively low at 190 U/L, indicative of baseline enzyme activity within normal ranges. However, as CT severity escalates, LDH levels exhibit a pronounced increase. Grade II demonstrates a notable elevation in LDH with a median of 280 U/L, while Grades III and IV display substantial LDH elevations, with medians of 620 U/L and 650 U/L, respectively.

Table 4 also provides descriptive statistics regarding D – dimer levels across different grades of CT severity. Notably, there is a discernible pattern of escalating D – dimer concentrations as CT severity increases. In Grade I, the median D – dimer level is 0.390 mcg/ml, with a relatively narrow interquartile range (IQR) spanning from 0.350 to 1.11 mcg/ml. Moving to Grade II, there is a notable increase in the median d-dimer level to 0.605 mcg/ml, along with a widening IQR from 0.460 to 0.795 mcg/ml. Subsequently, Grades III and IV exhibit further substantial rises in D – dimer levels, with medians of 1.44 mcg/ml and 1.72 mcg/ml, respectively, accompanied by wider IQRs indicative of increased variability. These findings indicate there might be a correlation between D – dimer elevation and the degree of vascular injury or thrombotic events underlying the graded CT findings.

	Median	25th percentile	75th percentile
CRP			
Grade I	118	112	132
Grade II	126	117	157
Grade III	164	158	168
Grade IV	180	166	189
LDH			
Grade I	190	190	210
Grade II	280	240	328
Grade III	620	480	700
Grade IV	650	570	820
D-dimer			
Grade I	0.390	0.350	1.11
Grade II	0.605	0.460	0.795
Grade III	1.44	0.770	1.64
Grade IV	1.72	0.955	1.98

Table 4: Comparison of CRP, LDH and D – Dimer levels with CT severity

Categorical variables are mentioned as counts

Table 5 shows the Kruskal-Wallis test results for the comparison of CRP with CT severity indicate a significant association [χ^2 (chi-square) = 42.9, df (degrees of freedom) = 3, $p < 0.001$]. This result implies that variations in CRP concentrations between CT severity categories are statistically significant. Strong evidence against the null hypothesis is indicated by the low p-value (< 0.001), which shows that the CRP values of at least one group differ significantly from the others.

The findings of the Kruskal-Wallis test, which assessed the relationship between LDH levels and CT severity, are shown in Table 5. With three degrees of freedom (df) and a p-value of less than 0.001, the analysis produced a significant correlation with a chi-square value of 62.7. Furthermore, the effect size estimate (ε2) of 0.603 indicates that variations in CT severity account for a substantial amount of the diversity in LDH levels. This robust statistical significance underscores the potential clinical relevance of LDH as a biomarker for pathological processes related to varying degrees of CT severity.

The Kruskal-Wallis test findings from the analysis of the relationship between D-dimer levels and CT severity are shown in Table 5. With 3 degrees of freedom (df) and a p-value of less than 0.001, the test yielded a significant chi-square value of 41.8. This outcome indicates a strong statistical significance, suggesting that there are indeed differences in D-dimer levels across the different grades of CT severity. The significant association underscores the potential clinical relevance of D-dimer as a biomarker for thromboembolic events or vascular damage, particularly in the context of varying degrees of CT severity.

	χ^2	df	p-value	ε^2
CRP value	42.9	3	< 0.001	
LDH (IU/L)	62.7	3	< 0.001	0.603
D Dimer levels	41.8	3	< 0.001	

Table 5: Kruskal – Wallis analysis of CRP, LDH and D – Dimer with CT severity

χ^2 - chi-square value
df - degrees of freedom
ε^2 - effect size estimate

The pairwise comparisons using Dwass-Steel-Critchlow-Fligner method in table 6 offer crucial insights into the relationship between CRP values and the severity of CT findings. Notably, while there was no significant difference in CRP levels between Grade I and Grade II (W = 1.28, p = 0.804), significant differences were observed when comparing Grade I with Grade III (W = 4.82, p = 0.004) and Grade I with Grade IV (W = 5.31, p < 0.001). Similarly, significant differences were found between Grade II and both Grade III (W = 5.88, p < 0.001) and Grade IV (W = 7.31, p < 0.001). Additionally, Grade III showed significantly different CRP levels compared to Grade IV (W = 4.75, p = 0.004). These findings underscore the association between CRP values and the severity of CT findings, indicating a progressive increase in systemic inflammation as CT severity escalates.

Table 6 elucidates the pairwise comparisons of LDH levels across distinct grades of CT severity. The findings reveal significant differences in LDH concentrations among most pairs of grades. Specifically, LDH levels exhibit substantial disparities between Grade I and each of Grade II, III, and IV, with p-values less than 0.001. Similarly, significant differences are noted between Grade II and both Grade III and Grade IV, reinforcing the escalating trend of LDH with increasing CT severity. Intriguingly, no significant contrast in LDH levels is observed between Grade III and Grade IV, denoting a potential plateau in LDH elevation beyond Grade III.

Table 6 also presents the results of pairwise comparisons examining the association between D-dimer levels and CT severity. While no significant differences were observed between Grade I and Grade II (W = 0.809, p = 0.941) or Grade I and Grade III (W = 3.203, p = 0.106), a significant difference was found between Grade I and Grade IV (W = 4.022, p = 0.023). Notably, significant differences were observed between Grade II and both Grade III (W = 7.227, p < 0.001) and Grade IV (W = 7.583, p < 0.001). However, no significant difference was found between Grade III and Grade IV (W = 3.226, p = 0.102).

		W	p – value
CRP			
Grade I	Grade II	1.28	0.804
Grade I	Grade III	4.82	0.004
Grade I	Grade IV	5.31	< 0.001
Grade II	Grade III	5.88	< 0.001
Grade II	Grade IV	7.31	< 0.001
Grade III	Grade IV	4.75	0.004
LDH			
Grade I	**Grade II**	5.62	< 0.001
Grade I	**Grade III**	5.93	< 0.001
Grade I	**Grade IV**	5.60	< 0.001
Grade II	**Grade III**	8.93	< 0.001
Grade II	**Grade IV**	7.94	< 0.001
Grade III	**Grade IV**	1.90	0.535
D – Dimer			
Grade I	Grade II	0.809	0.941

Grade I	Grade III	3.203	0.106
Grade I	Grade IV	4.022	0.023
Grade II	Grade III	7.227	< 0.001
Grade II	Grade IV	7.583	< 0.001
Grade III	Grade IV	3.226	0.102

Table 6: Dwass-Steel-Critchlow-Fligner analysis of CRP, LDH and D – Dimer with CT severity
W- Dwass-Steel-Critchlow-Fligner pairwise comparison score

Table 7 presents the correlation between serum amylase levels and acute-phase reactants, providing Pearson's correlation coefficient (r) and corresponding p-values for each association. The correlation coefficients are as follows: with CRP (C-reactive protein), r = 0.18, p = 0.07; with LDH (Lactate dehydrogenase), r = 0.15, p = 0.12; and with D Dimer, r = 0.21, p = 0.16. While none of these correlations are statistically significant at the conventional threshold of $p < 0.05$, they suggest a trend towards positive associations between Serum Amylase levels and these acute-phase reactants.

Table 7 also illustrates the correlation between Serum Lipase and acute phase reactants. The Pearson's correlation coefficient (r) values are presented for CRP (0.18, p = 0.07), LDH (0.16, p < 0.001), and D Dimer (0.21, p = 0.03). These results indicate statistically significant positive correlations between Serum Lipase and LDH, as well as with D Dimer, suggesting a relationship between Serum Lipase levels and these acute-phase reactants in the context of the study. The association with CRP, however, fell short of statistical significance.

	Pearson's r	**p – value**
Serum Amylase		
CRP	0.18	0.07
LDH	0.15	0.12
D Dimer	0.21	0.16
Serum Lipase		
CRP	0.18	0.07
LDH	0.16	< 0.001
D Dimer	0.21	0.03

Table 7: Correlation between serum amylase levels and acute-phase reactants
r - Pearson's correlation coefficient

DISCUSSION

AP is most frequently encountered ailment which has significant complications including mortality if not treated early [10]. The purpose of this study is to measure the levels of CRP, LDH and D-dimer and to correlate their values with serum amylase, serum lipase and MCTSI in prediction of the severity of AP. The results and key findings of this study are discussed in detail and compared with the existing literature.

Age distribution:

In our current study, 35.2% were in age group of 41 to 50 years (37 out of 105), 33.3% were in 31 to

40 years (33 out of 105), 18.1% were in 51 to 60 years of age (19 out of 105), 7.6% were in more than 60 years of age (8 out of 105) and 5.7% were from 21 to 30 years of age (6 out of 105). Almost 70% of the study population were between the age category of 31 and 50 years.

Gender distribution

In our current study, most of the study participants were males (92.4%; 97 out of 105) and remaining (7.6%; 8 out of 105) were females.

Predominant complaints, duration of symptoms and alcohol consumption:

The majority, 65.7% (69 out of 105) of them had symptoms of abdominal pain, 27.6% (29 out of 105) had vomiting and 6.7% (7 out of 105) had abdominal distension.

Symptoms of one day duration were observed in 41.9% (44 out of 105) of the individuals, 38.1% (40 out of 105) had two day symptoms and 20% (21 out of 105) had symptoms of three days duration.

Most of them, 83.8% (88 out of 105) of them had history of regular consumption of alcohol and 16.2% (17 out of 105) did not consume alcohol.

CT Based Severity Assessment and Findings:

Based on the CT findings, 39% (41 out of 105) had necrosis, 32.4% (34 out of 105) had perihepatic fluid collection, 21.9% (23 out of 105) had pseudocyst and 6.7% (7 out of 105) had focal inflammation.

Severity was graded based on the CT findings, 39% (41 out of 105) were in grade III, 32.4% (34 out of 105) were in grade II, 21.9% (23 out of 105) were in grade IV and 6.7% (7 out of 105) were in grade I.

Study Parameters:

In our study of 105 participants, 68.6% (72 out of 105) had CRP level >150 mg/L and 31.4% (33 out of 105) had value <150 mg/L. LDH level was >350 U/L in 66.7% (70 out of 105) of the individuals and 33.3% (35 out of 105) had <350 U/L. Nearly 85.71% had D-dimer >0.5 mcg/ml (90 out of 105) and 14.29% (15 out of 105) had <0.5 mcg/ml. There was mild positive correlation between the serum amylase, serum lipase and acute phase reactants but of no statistical significance. The correlation between LDH, CRP and D-dimer with CT severity was found to be significant.

Comparison of Study with Existing Literature:

A nonspecific acute-phase reactant, CRP, has been extensively utilized in prediction of AP severity. In response to inflammation, it elevates within 2 hours, peaks by forty eight hours, and has a continuous half-life of eighteen hours. According to the study by He Q et al [11], CRP tested under 48 hours had a specificity and sensitivity of 80.9% and 72.9%, respectively, for predicting moderately severe acute pancreatitis (MSAP) and severe acute pancreatitis (SAP). These results were consistent with other studies done by Zheng J et al and Sternby H et al [12, 13]. The specificity of CRP to measure the severity of AP was shown to be high (around 85.2%) when the cut-off value was 90 mg/L within forty eight hours of hospitalisation, according to Stirling et al and Cardoso et al [14, 15]. shown, however, that a CRP threshold of 60 mg/L reduced the risk of death and sequelae and had a 100% negative-predictive value in assessing the SAP within a day after hospitalization.

According to a study by Sharma et al on the relationship between the severity and the type of tissue reaction in AP, twelve among twenty patients had severe AP, with a CRP level between ninety-six and one hundred and ninety-two mg/dL; seven patients had mild AP, with a CRP level between twenty four and forty eight mg/dL; and only one patient had a normal level of CRP (less than six mg/dL) [16].

In our study, 68.6% had CRP level >150mg/dl and 31.4% had value <150mg/dl. CRP levels increase with severity: Grade IV has the highest median CRP (180 mg/L), followed by Grade III (164 mg/L), Grade II (126 mg/L), and Grade I (118 mg/L). Variability within grades is evident, notably in Grade II. When comparing CRP

to CT severity, the findings of the Kruskal-Wallis test show a significant correlation with p value less than 0.001.

One particular by-product of cross-linked fibrin breakdown that subtly represents the coagulation problem is D – dimer. D – dimer has been linked with several studies to the severity and complications of AP; at the time of the acute phase of the ailment, patients may experience coagulation and microcirculation problems [17, 18]. According to the findings by He Q et al [11], D – dimer checked under 48 hours had a specificity of 75.0 and a risk ratio of 8.860 for assessing severity of AP. Another research by Yang N, Hao J and Zhang D, all instances of AP had a risk ratio of 4.504 for D – dimer in predicting SAP, with hyperlipidemic AP having a greater risk ratio (OR = 9.824). According to earlier research, the D – dimer's specificity and sensitivity ranged from 75.6 to 77.69% and 86.5 to 92.6% respectively for predicting SAP [19]. The D – dimer level was found to have a positive correlation with both the pancreatic CT grade and the Ranson score by Newton et al [20]. Furthermore, a study with more than 2000 samples found an independent correlation between higher D – dimer levels and the prognosis and complications of AP [21]. At the time of hospitalisation, patients with AP who had D – dimer levels between 0.4 and 0.8 mcg/L had an 11.2-fold higher chance of dying than patients whose levels were between 0.2 and 0.4 mcg/L [9]. These findings imply that D – dimer can be helpful in forecasting the degree, consequences, and prognosis of AP. In our study, nearly 85.71% had D-dimer >0.5 mcg/ml and 14.29% had <0.5 mcg/ml. Our study yielded a significant chi-square value of 41.8 with 3 degrees of freedom (df) and a p-value of less than 0.001. This outcome indicates a strong statistical significance, suggesting that there are indeed differences in D – dimer levels across the different grades of CT severity indicating strong correlation. Thus D – dimer measurement will be useful as an early prognostic indicator for determining the course and outcomes of AP.

In the study by Narasimhaiah L et al cut-off levels revealed significant sensitivity and specificity in the predictive values of CRP and LDH for severe AP, which are important for clinical decision-making. Notable results included an eighty five percent sensitivity and eighty percent specificity for CRP (with a cut-off value more than or equal to 150 mg/L) and an 80% sensitivity and 75% specificity for LDH (at a threshold level ≥500 U/L) [22]. In our study, LDH level was >350mg/dl in 66.7% of the individuals and 33.3% had <350mg/dl. On correlating the association between lactate dehydrogenase (LDH) levels and CT severity, the analysis yielded a substantial chi-square value of 62.7 with 3 degrees of freedom (df) and a p-value of less than 0.001, indicating a significant association. Furthermore it revealed the median value of LDH was found to be at 190 in Grade I AP and kept increasing with increase in CT severity such as 280, 620 and 650 for Grade II, Grade III and Grade IV respectively. This correlates with the results of the study by Huang DN et al which determined that a higher level of LDH is linked to a high severity score and a high incidence of complications [23].

LIMITATIONS

The study was single-centred and limited to patients with acute pancreatitis. Secondly, no prolonged dynamic observations were carried out; only the values of CRP, D dimer, LDH, serum amylase and serum lipase within forty eight hours of hospitalization were gathered. Prior to the development of AP, the baseline levels of CRP, D dimer and LDH may be influenced by age. More research is warranted to establish how aging affects the development of AP and the rise of CRP, D dimer and LDH. It is imperative that future studies confirm these findings in larger and more diverse groups and explore how these markers might be included into AP multidisciplinary treatment plans.

CONCLUSION

AP is an inflammatory condition in which patients predominantly present with abdominal pain. CRP, D – dimer

and LDH are biomarkers, that show potential for enhanced prognostic assessment and directing treatment methods for individuals with AP, as evidenced by meaningful predictive values for severe AP and substantial correlations with MCTSI. These inflammatory markers can be used as easy-to-use and effective instruments to help with treatment, particularly with early intervention and patient resuscitation. Using these inflammatory markers, we may determine the severity of AP even in the absence of more complex tests. These markers make it simple to identify patients who may develop significant morbidities. Our research concludes that CRP, D - dimer and LDH values are very useful indicators which can correlate with the MCTSI and we can effectively assess the severity of AP using them as predictive markers. Subsequent investigations ought to corroborate these results in more extensive and heterogeneous cohorts and investigate the assimilation of these indicators into multidisciplinary treatment regimens for AP.

Conflict of interest

None declared

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Author Contributions

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References:

1. *Petrov MS, Yadav D. Global epidemiology and holistic prevention of pancreatitis. Nat Rev Gastroenterol Hepatol. 2019;16(3):175–184. doi: 10.1038/s41575-018-0087-5*
2. Szatmary P, Grammatikopoulos T, Cai W, Huang W, Mukherjee R, Halloran C, Beyer G, Sutton R. Acute Pancreatitis: Diagnosis and Treatment. Drugs. 2022 Aug;82(12):1251-1276. doi: 10.1007/s40265-022-01766-4
3. Kylänpää L, Rakonczay Z Jr, O'Reilly DA. The clinical course of acute pancreatitis and the inflammatory mediators that drive it. Int J Inflam. 2012;2012:360685. doi: 10.1155/2012/360685
4. Leppäniemi, A., Tolonen, M., Tarasconi, A. *et al.* 2019 WSES guidelines for the management of severe acute pancreatitis. *World J Emerg Surg* **14**, 27 (2019). https://doi.org/10.1186/s13017-019-0247-0
5. Hu JX, Zhao CF, Wang SL, Tu XY, Huang WB, Chen JN, Xie Y, Chen CR. Acute pancreatitis: A review of diagnosis, severity prediction and prognosis assessment from imaging technology, scoring system and artificial intelligence. World J Gastroenterol. 2023 Oct 7;29(37):5268-5291. doi: 10.3748/wjg.v29.i37.5268

6. Buxbaum J, Quezada M, Chong B, Gupta N, Yu CY, Lane C, Da B, Leung K, Shulman I, Pandol S, Wu B. The Pancreatitis Activity Scoring System predicts clinical outcomes in acute pancreatitis: findings from a prospective cohort study. Am J Gastroenterol. 2018 May;113(5):755-764. doi: 10.1038/s41395-018-0048-1
7. Haider Kazmi SJ, Zafar MT, Zia BF, Khalid SR, Kumar V, Tabassum S, Ali A, Aziz N, Khan NA, Kumari K, Saleem K, Asghar MS. Role of serum C-reactive protein (CRP)/Albumin ratio in predicting the severity of acute pancreatitis: A retrospective cohort. Ann Med Surg (Lond). 2022 Sep 21;82:104715. doi: 10.1016/j.amsu.2022.104715
8. Huang DN, Zhong HJ, Cai YL, Xie WR, He XX. Serum Lactate Dehydrogenase Is a Sensitive Predictor of Systemic Complications of Acute Pancreatitis. Gastroenterol Res Pract. 2022 Oct 25;2022:1131235. doi: 10.1155/2022/1131235
9. Badhal SS, Sharma S, Saraya A, Mukhopadhyay AK. Prognostic significance of D-dimer, natural anticoagulants and routine coagulation parameters in acute pancreatitis. Trop Gastroenterol. 2012 Jul-Sep;33(3):193-9. doi: 10.7869/tg.2012.48
10. Phillip V, Steiner JM, Algül H. Early phase of acute pancreatitis: Assessment and management. World J Gastrointest Pathophysiol. 2014 Aug 15;5(3):158-68. doi: 10.4291/wjgp.v5.i3.158
11. He Q, Ding J, He S, Yu Y, Chen X, Li D, Chen F. The predictive value of procalcitonin combined with C-reactive protein and D dimer in moderately severe and severe acute pancreatitis. Eur J Gastroenterol Hepatol. 2022 Jul 1;34(7):744-750. doi: 10.1097/MEG.0000000000002376
12. Zheng J, Zhang J, Gao J. [Early evaluations of BISAP plus C-reactive protein in predicting the severity of acute pancreatitis]. Zhonghua Yi Xue Za Zhi. 2015 Mar 31;95(12):925-8. Chinese. DOI: 10.3760/cma.j.issn.0376-2491.2015.12.012
13. Sternby H, Hartman H, Johansen D, Thorlacius H, Regnér S. IL-6 and CRP are superior in early differentiation between mild and non-mild acute pancreatitis. Pancreatology. 2017 Jul-Aug;17(4):550-554. doi: 10.1016/j.pan.2017.05.392
14. Stirling AD, Moran NR, Kelly ME, Ridgway PF, Conlon KC. The predictive value of C-reactive protein (CRP) in acute pancreatitis - is interval change in CRP an additional indicator of severity? HPB (Oxford). 2017 Oct;19(10):874-880. doi: 10.1016/j.hpb.2017.06.001
15. Cardoso FS, Ricardo LB, Oliveira AM, Horta DV, Papoila AL, Deus JR, Canena J. C-Reactive Protein at 24 Hours after Hospital Admission may have Relevant Prognostic Accuracy in Acute Pancreatitis: A Retrospective Cohort Study. GE Port J Gastroenterol. 2015 Apr 19;22(5):198-203. doi: 10.1016/j.jpge.2015.03.002
16. Sharma S, Shrivastav C, Jain S. Early prediction of severity of acute pancreatitis role of C-reactive protein. Int J Curr Res. 2014;6(08):7881-3
17. Maeda K, Hirota M, Ichihara A, Ohmuraya M, Hashimoto D, Sugita H, Takamori H, Kanemitsu K, Baba H. Applicability of disseminated intravascular coagulation parameters in the assessment of the severity of acute pancreatitis. Pancreas. 2006 Jan;32(1):87-92. doi: 10.1097/01.mpa.0000186248.89081.44
18. Ranson JH, Lackner H, Berman IR, Schinella R. The relationship of coagulation factors to clinical complications of acute pancreatitis. Surgery. 1977 May;81(5):502-11. PMID: 850868.

19. Yang N, Hao J, Zhang D. Antithrombin III and D-dimer levels as indicators of disease severity in patients with hyperlipidaemic or biliary acute pancreatitis. J Int Med Res. 2017 Feb;45(1):147-158. doi: 10.1177/0300060516677929
20. Newton, Mario Victor. D-dimer as a Marker of Severity and Prognosis in Acute Pancreatitis. International Journal of Applied and Basic Medical Research 14(2):p 101-107, Apr–Jun 2024. DOI: 10.4103/ijabmr.ijabmr_483_23
21. Wan J, Yang X, He W, Zhu Y, Zhu Y, Zeng H, Liu P, Xia L, Lu N. Serum D-dimer levels at admission for prediction of outcomes in acute pancreatitis. BMC Gastroenterol. 2019 May 2;19(1):67. doi: 10.1186/s12876-019-0989-x
22. K NL, Prasad NL, Rakshit EP, Md MA. A study on the concordance of serum c-reactive protein and serum lactate dehydrogenase with CT severity index in assessing the severity of acute pancreatitis. European Journal of Cardiovascular Medicine. 2024 Jan;14(1):1057-1061. Doi: 10.5083/ejcm
23. Huang DN, Zhong HJ, Cai YL, Xie WR, He XX. Serum Lactate Dehydrogenase Is a Sensitive Predictor of Systemic Complications of Acute Pancreatitis. Gastroenterol Res Pract. 2022 Oct 25;2022:1131235. doi: 10.1155/2022/1131235