

A Comparative Study Between Neutrophil- Lymphocyte Ratio And Procalcitonin To Predict The Severity Of Acute Pancreatitis Among Patients Attending Tertiary Care Hospital

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ABSTRACT:

INTRODUCTION:

Acute pancreatitis (AP) is the result of abnormal pancreatic enzyme activation inside acinar cells. ⁽¹⁾ As the severity of acute pancreatitis at the initial stage of manifestation is critical to improve the patients prognosis, there is a need for simple indicator that can easily predict the patient's prognosis within 24 hours of the manifestation of the disease to halt the disease progression and reduce morbidity and mortality. The nature and purpose of this study is to evaluate the ability of serum procalcitonin (PCT) and neutrophil- lymphocyte ration (NLR) as important biochemical markers in predicting the severity of acute pancreatitis for early intervention so as to reduce morbidity and mortality.

OBJECTIVES:

To compare NLR and serum procalcitonin with Modified CT severity index (CTSI) to predict early morbidity and mortality in acute pancreatitis

METHODS:

Neutrophil leukocyte ratio and serum procalcitonin were sent along with other routine investigations on the day of admission in patients diagnosed with acute pancreatitis. Patients are kept nil by mouth and treated conservatively with aggressive IV fluids, IV antibiotics and analgesics. Severity of the disease is graded based on the Modified Atlanta criteria for acute pancreatitis on the day of admission. Patients will undergo a contrast enhanced CT 48 hours after the onset of symptoms and CT severity index is thus obtained.

RESULTS:

The F-value for NLR is 0.47, with a p-value of 0.627, suggesting that NLR ratios do not differ significantly across the severity levels of acute pancreatitis.

The F-value for procalcitonin is 65.28, with a p-value of <0.001, indicating a statistically significant difference in procalcitonin levels across the severity categories. These findings indicate that while procalcitonin is a significant predictor of severity, NLR does not show significant variability with the severity of acute pancreatitis.

CONCLUSION:

This study posits that serum procalcitonin may be more reliable as an early prognostic indicator of severity in cases of acute pancreatitis than NLR. The results demonstrated a noteworthy correlation between procalcitonin and severity levels as categorized by the Modified Atlanta Criteria, suggesting its potential usefulness in clinical decision-making.

KEY WORDS : PROCALCITONIN, NLR RATIO, RANSON'S SCORE, MODIFIED ATLANTA CRITERIA, MODIFIED CT SEVERITY INDEX, ACUTE PANCREATITIS

INTRODUCTION:

Acute pancreatitis (AP) is the final result of abnormal pancreatic enzyme activation inside acinar cells and the exact mechanism whereby predisposing factors such as ethanol and gallstones produce pancreatitis is not completely known.⁽¹⁾

The incidence of acute pancreatitis (AP) has increased during the past 20 years. AP is responsible for more than 300,000 hospital admissions annually in the United States. Most patients develop a mild and self-limited course, however 10% to 20% of the patients have a rapidly progressive inflammatory response associated with prolonged length of hospital stay and significant morbidity and mortality. Patients with mild pancreatitis have a mortality rate of less than 1%, but in severe pancreatitis, this increases up to 10% to 50% and it is therefore important to recognize those patients who are at risk to progress to severe acute pancreatitis at the earliest.⁽¹⁾

As the severity of acute pancreatitis at the initial stage of manifestation is critical to improve the patient's prognosis, there is a need for a simple indicator that can easily predict the patient's prognosis within 24 hours of the manifestation of the disease to halt the disease progression and reduce morbidity and mortality.

Neutrophils and lymphocytes reflect the immune response better than the total WBC count. The Neutrophil-lymphocyte Ratio (NLR) has been recognized as a critical sign in assessing systemic inflammation associated with various medical disorders. Several prognostic scoring systems have been developed to predict severe acute pancreatitis. However, they are complex and some laboratory data are not obtained immediately. The NLR ratio can be obtained easily and is usually included in routine orders.⁽²⁾

The NLR is computed by calculating the ratio of absolute neutrophil and lymphocyte counts and the analysis is conducted using NLR values on the day of hospitalization. Continuous NLR monitoring on each admission day offers a dynamic representation of the varied course of acute pancreatitis.⁽³⁾

Procalcitonin (PCT) is a 116-amino acid propeptide of calcitonin with a molecular weight of 13 kDa that acts as an early indicator of systemic bacterial infection, sepsis, and multiorgan failure. Procalcitonin is synthesized in the thyroid gland's C-cells as the intracellular prohormone of calcitonin and is detected at picogram levels in the plasma (0.05 ng/ml). Secretion begins four hours after stimulation and reaches a maximum level eight hours later.^{(4),(5)}

In patients who suffer from acute pancreatitis, PCT has been shown to predict the development of infected pancreatic necrosis. In addition, PCT has been found to be an early predictor of severity and organ failure in patients with acute pancreatitis.⁽⁶⁾

PCT proved to be an excellent variable to assess overall prognosis throughout the course of severe acute pancreatitis. The diagnostic accuracy of PCT is not limited to a specific time interval after onset of symptoms.⁽⁷⁾

The nature and purpose of this study is to evaluate the ability of serum PCT and NLR as important biochemical markers in predicting the severity of acute pancreatitis for early intervention so as to reduce morbidity and mortality.

OBJECTIVES:

To compare NLR and serum procalcitonin with Modified CT severity index (CTSI) to predict early morbidity and mortality in acute pancreatitis

METHODS:

This is a prospective comparative study design with purposive sampling. The study was carried out for a duration of 18 months in JSS Hospital Mysuru with a sample size of 25 patients which was based on the incidence of pancreatitis.

After receiving approval by the Institute Ethics Committee of our hospital and written informed consent from the patients diagnosed with acute pancreatitis, the neutrophil leukocyte ratio and serum procalcitonin will be sent along with other routine investigations on the day of admission. Patients are kept nil by mouth and treated conservatively with aggressive IV fluids, IV antibiotics and analgesics.

Severity of the disease is graded based on the Modified Atlanta criteria for acute pancreatitis on the day of admission. Patients will undergo a contrast enhanced CT 48 hours after the onset of symptoms and CT severity index is thus obtained.

Inclusion Criteria for the study sample include patients aged 18-60 years, belonging to either sex, diagnosed with Acute pancreatitis of any etiology with onset of symptoms less than 48 hours of duration before admission. Patients with Acute on chronic pancreatitis were also included in the study. Patients with Chronic pancreatitis and acute pancreatitis with symptoms onset more than 48 hrs of duration were excluded from the study.

Data for this study were entered into Microsoft Excel 2019 and subsequently analyzed using SPSS version 26, licensed to the institution. The statistical analysis involved descriptive and inferential methods to address the research objectives.

Descriptive statistics were computed to summarize the demographic and clinical characteristics of the study participants. This included calculating frequencies and percentages for categorical variables such as age, gender, and complications.

Inferential statistical tests were utilized to explore the relationships between the variables and the severity of acute pancreatitis.

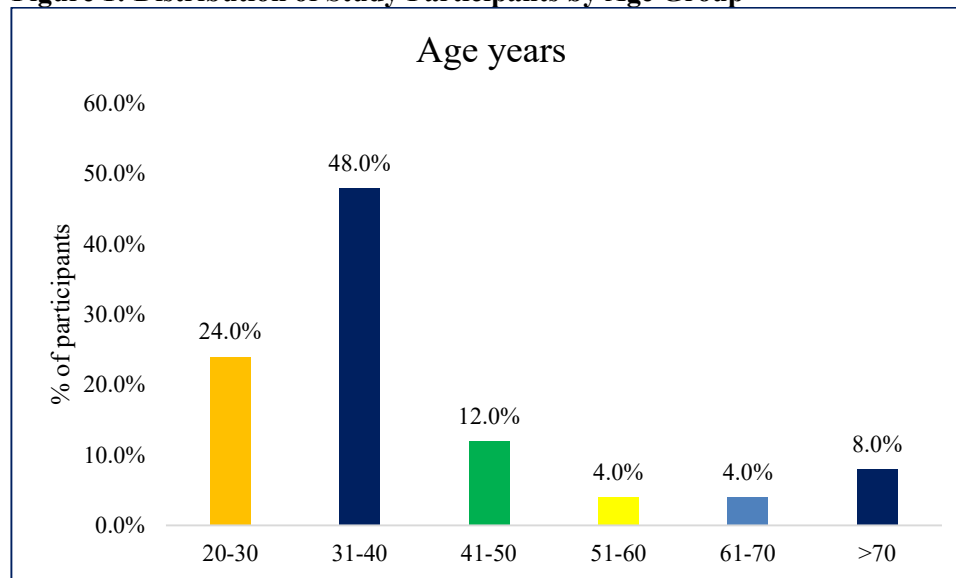
ANOVA (Analysis of Variance): ANOVA was performed to compare mean values of serum procalcitonin and NLR ratios across different severity levels of acute pancreatitis as defined by the Modified Atlanta Criteria.

ROC (Receiver Operating Characteristic) Analysis: ROC analysis was conducted to assess the diagnostic performance of procalcitonin and NLR in predicting moderate acute pancreatitis. All statistical tests were performed with a significance level set at $p < 0.05$.

RESULTS:

Among the total participants, 48% were between 31 and 40, making it the most represented age group. This was followed by the 20-30 age group, which constituted 24% of the participants. The 41-50 age group accounted for 12% of the participants. The age groups 51-60 years and 61-70 years each represented 4% of the study population, and those aged above 70 years comprised 8%.

Figure 1: Distribution of Study Participants by Age Group



Most participants were male, comprising 72% of the study population, while females accounted for 28%.

Table 1: Distribution of Study Participants by Gender

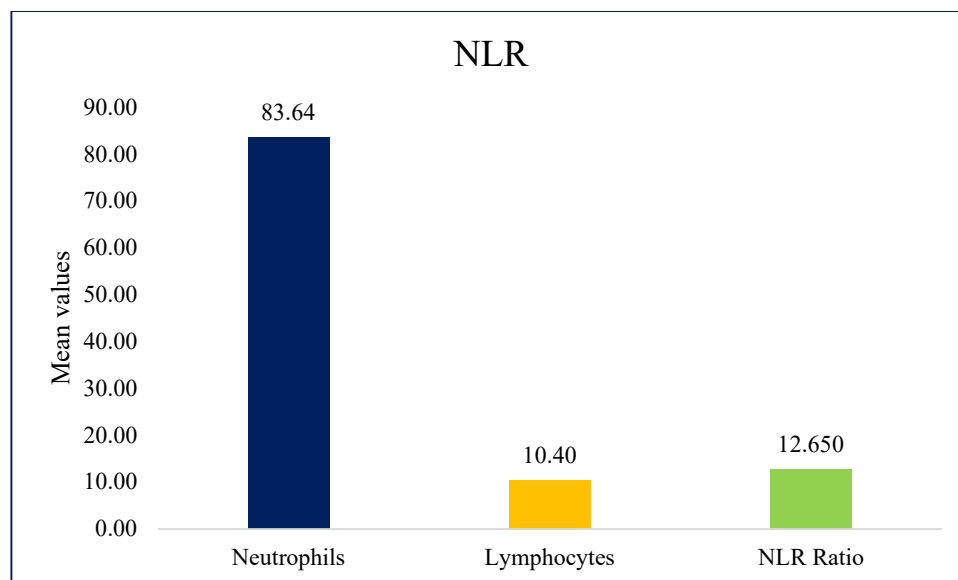
Gender	N	%
Male	18	72.0%
Female	7	28.0%
Values are expressed as frequency and percentage.		

The TLC among the participants ranged from a minimum of 5760 to a maximum of 33100. The mean TLC was 14135.04 with a standard deviation of 5735.08, indicating variability in the leukocyte counts within the study population.

Table 2: Descriptive Statistics of Total Leukocyte Count (TLC) Among Study Participants

	Minimum	Maximum	Mean	Std. Deviation
TLC	5760	33100	14135.04	5735.08

Neutrophil percentages ranged from 48 to 95, with an average of 83.64 and a standard deviation of 10.01, reflecting moderate variability in neutrophil levels among the participants. Lymphocyte percentages varied between 2 and 24, with a mean of 10.40 and a standard deviation 5.85, indicating greater variability. The NLR ratio, a vital focus of this study, ranged from 2.0 to 47.5, with a mean value of 12.650 and a standard deviation of 10.68, suggesting significant variability in the inflammatory response among the study population.

**Figure 2: Descriptive Statistics of Neutrophil-Lymphocyte Ratio (NLR) and Its Components Among Study Participants**

The levels of procalcitonin ranged from a minimum of 0.1 ng/mL to a maximum of 12.0 ng/mL, with a mean value of 1.71 ng/mL and a standard deviation of 3.2.

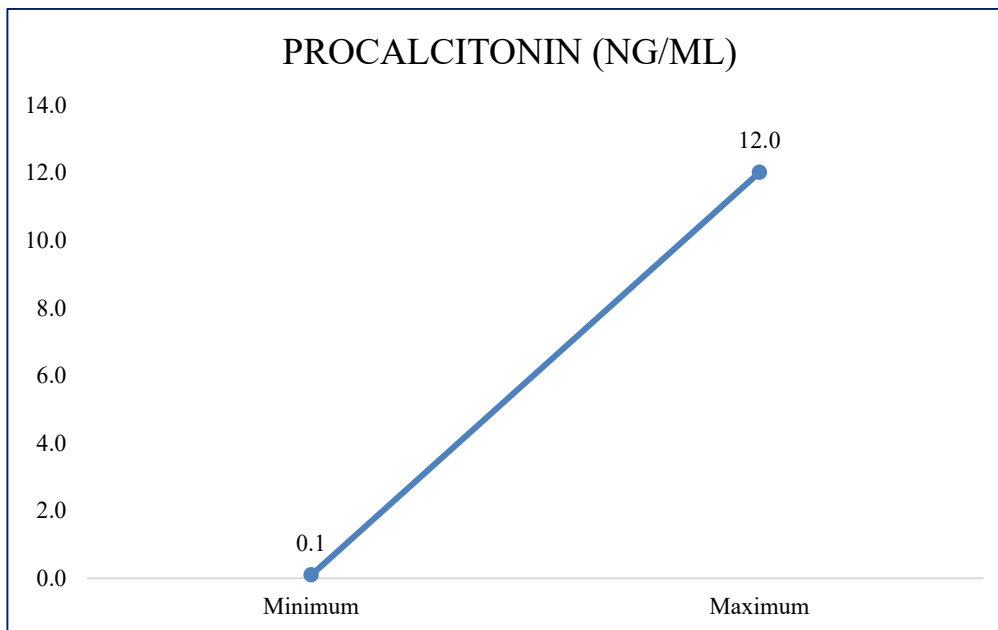


Figure 3: Descriptive Statistics of Serum Procalcitonin Levels Among Study Participants

Of the study population, 52% required ICU admission, while 48% did not. These results highlight the substantial proportion of patients with acute pancreatitis who needed intensive care during their hospital stay.

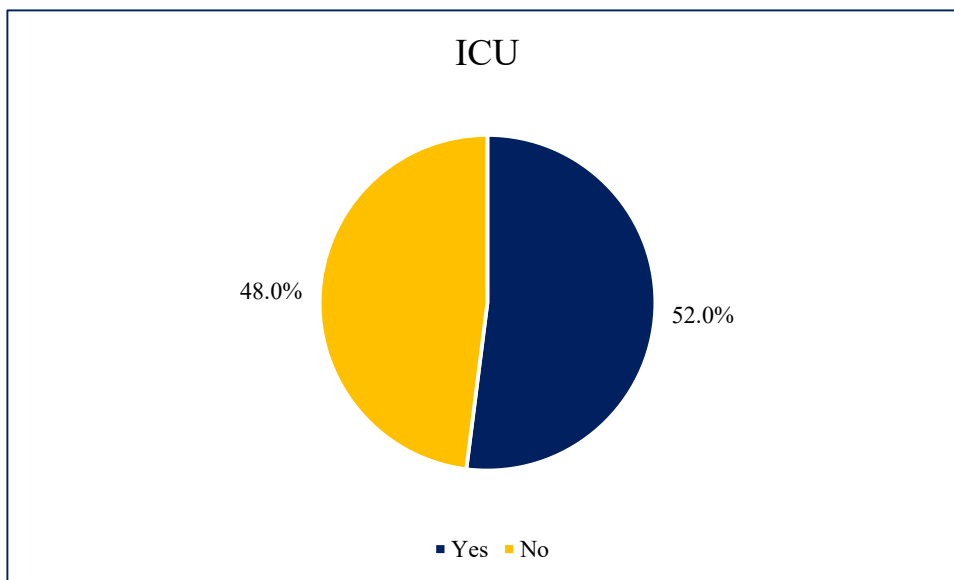


Figure 4: Distribution of Study Participants by ICU Admission

According to the Atlanta classification, 52% of participants had mild acute pancreatitis, 44% had moderate acute pancreatitis, and 4% had severe acute pancreatitis.

Table 3: Distribution of Study Participants by Atlanta Classification

Atlanta Classification	N	%
Mild	13	52.0%
Moderate	11	44.0%
Severe	1	4.0%
Values are expressed as frequency and percentage.		

Table 4 presents the descriptive statistics for the Modified CT Severity Index (MCTSI) used to assess the severity of acute pancreatitis. The MCTSI scores ranged from a minimum of 2 to a maximum of 10, with a mean score of 5.36 and a standard deviation of 2.29.

Table 4: Descriptive Statistics of Modified CT Severity Index (MCTSI) Among Study Participants

	Minimum	Maximum	Mean	Std. Deviation
MCTSI	2	10	5.36	2.29

Of the participants, 12% experienced ascites, 28% had pleural effusion, 4% had both pleural effusion and ascites, and 4% had pseudocyst or superior vena cava thrombosis. The remaining 52% of participants did not experience any of these complications.

Table 5: Distribution of Study Participants by Complications

Complications	N	%
Ascites	3	12.0%
Pleural Effusion	7	28.0%
PE & ascites	1	4.0%
pseudocyst, sv thrombosis	1	4.0%
Nil	13	52.0%
Values are expressed as frequency and percentage.		

In the current study, All participants (100%) survived, with no recorded deaths.

Figure 5 summarizes the Receiver Operating Characteristic (ROC) analysis of serum procalcitonin for

predicting moderate acute pancreatitis based on the Atlanta Classification. The Area Under the Curve (AUC) is 0.727, with a standard error of 0.103 and a p-value of 0.05, indicating statistical significance. The 95% confidence interval for the AUC ranges from 0.525 to 0.929. The optimal cutoff value for procalcitonin was determined to be 0.45, with a sensitivity of 81.8% and a specificity of 64.3% for predicting moderate pancreatitis.

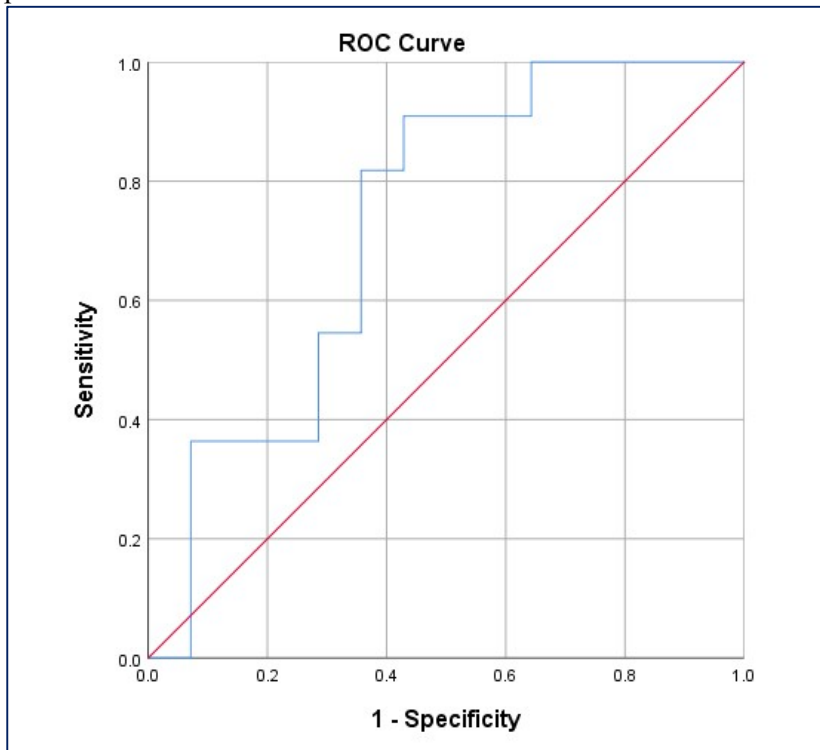


Figure 5 : ROC Analysis of Procalcitonin in Predicting Moderate Acute Pancreatitis

Table 6: ROC Analysis of Neutrophil-Lymphocyte Ratio (NLR) for Predicting Moderate Acute Pancreatitis

AUC	Std. Error	p-value	95% Confidence Interval	
			Lower Bound	Upper Bound
0.659	0.115	0.180	0.434	0.884

Table 6 presents the Receiver Operating Characteristic (ROC) analysis of the Neutrophil-Lymphocyte Ratio (NLR) for predicting moderate acute pancreatitis according to the Atlanta Classification. The Area Under the Curve (AUC) is 0.659, with a standard error of 0.115 and a p-value of 0.180, which suggests the result is not statistically significant. This indicates that while NLR shows some predictive value, its effectiveness in predicting moderate pancreatitis is less robust than other markers.

Table 7: ANOVA of Serum Parameters by Atlanta Classification

Serum Parameters	ATLANTA CLASSIFICATION						F Value	Mean Square	p-value
	Mild		Moderate		Severe				
	Mean	SD	Mean	SD	Mean	S D			
PROCALCITONIN (NG/ML)	0.45	0.39	2.28	3.36	12.02		12.52	65.28	<0.001
NLR Ratio	10.60	11.61	14.84	10.04	15.17		0.47	56.98	0.627

Values are expressed as Mean and SD. The p-value is calculated using ANOVA, and a p-value of less than 0.05 is considered statistically significant.

Table 7 shows the ANOVA results comparing serum procalcitonin and Neutrophil-Lymphocyte Ratio (NLR) across different severity levels of acute pancreatitis as classified by the Atlanta Classification.

Procalcitonin (NG/ML): The mean procalcitonin levels significantly differ among the classifications. For mild cases, the mean is 0.45 ng/mL (SD = 0.39); for moderate cases, it is 2.28 ng/mL (SD = 3.36); and for severe cases, it is 12.02 ng/mL (SD = 12.52). The F-value for procalcitonin is 65.28, with a p-value of <0.001, indicating a statistically significant difference in procalcitonin levels across the severity categories. This significant difference underscores the utility of procalcitonin as a marker in predicting the severity of acute pancreatitis.

NLR Ratio: The mean NLR ratios are 10.60 (SD = 11.61) for mild cases, 14.84 (SD = 10.04) for moderate cases, and 15.17 (SD = 0.47) for severe cases. The F-value for NLR is 0.47, with a p-value of 0.627, suggesting that NLR ratios do not differ significantly across the severity levels of acute pancreatitis.

These findings indicate that while procalcitonin is a significant predictor of severity, NLR does not show significant variability with the severity of acute pancreatitis.

DISCUSSION

The primary objective of this prospective comparison study was to assess the efficacy of neutrophil-lymphocyte ratio (NLR) and serum procalcitonin as prognostic indicators for acute pancreatitis severity. This was achieved by comparing these markers with the Modified CT Severity Index (MCTSI) and Modified Atlanta Criteria. This study comprised a cohort of 25 individuals diagnosed with acute pancreatitis, aged 18 to 60. These patients were admitted to JSS Hospital in Mysore and experienced the onset of symptoms within 48 hours before admission. This study evaluated several important factors, namely NLR, serum procalcitonin levels, Total Leukocyte Count (TLC), serum amylase and lipase levels, Ranson score, MCTSI score, and severity categorization using the Modified Atlanta Criteria. Furthermore, the investigation analysed clinical outcomes, including the length of hospitalization, admission rates to the intensive care unit (ICU), and complications.

The observed study sample exhibited a significant age distribution; the largest proportion (48%) belonged to the 31-40 age bracket, while 24% fell within the 20-30 age frame. The observed age distribution indicates that acute pancreatitis primarily impacts individuals in the younger to middle-aged adult demographic within our study sample.

The analysis of gender distribution indicated a higher representation of males, with 72% of the participants identifying as male and 28% as female. The gender gap shown in this study is consistent with prior research conducted by *Iriana et al. (2021)*, which similarly documented a greater prevalence of acute pancreatitis among males.⁽³⁾

The neutrophil lymphocyte ratio (NLR), a primary focus of this investigation, exhibited variability. The proportion of neutrophils exhibited a range of 48% to 95% (mean 83.64%, standard deviation 10.01%), whereas

the percentage of lymphocytes displayed a variation between 2% and 24% (mean 10.40%, standard deviation 5.85%). The observed NLR values exhibited a range of 2.0 to 47.5, with a mean value of 12.650 and a standard deviation of 10.68. The observed variability in NLR readings aligns with the results reported in other research, such as the one conducted by *Kong et al. (2020)*, which examined the diagnostic use of NLR in cases of acute pancreatitis. ⁽⁸⁾

Serum procalcitonin levels, also considered a significant indicator in this investigation, ranged from 0.1 to 12.0 ng/mL, with an average value of 1.71 ng/mL and a standard deviation of 3.2 ng/mL. The range of values recorded in this study is comparable to that reported by *Woo et al. (2011)* in their comparative analysis of procalcitonin using several severity rating systems. ⁽⁹⁾

The length of hospitalization varied between 4 and 13 days, with an average of 7.40 days and a standard variation of 2.8 days, suggesting considerable heterogeneity in the progression of the pathology. A significant proportion of patients, precisely 52%, necessitated admission to the Intensive Care Unit (ICU), so underscoring the potential gravity of acute pancreatitis and the considerable allocation of healthcare resources it may demand. The present finding aligns with the research conducted by *O'Connell et al. (2018)*, which underscored the significance of early indicators for admission to the intensive care unit (ICU) in instances of acute pancreatitis. ⁽¹⁰⁾

A classification based on the Atlanta Classification revealed that 52% of cases were categorized as mild, 44% as moderate, and 4% as severe. The observed distribution exhibits similarities to the results published by *Gezer et al. (2020)* in their experimental investigation that compared radiological scoring methods with clinical scores. ⁽¹¹⁾

In the present study, the Modified CT Severity Index (MCTSI) scores ranged from 2 to 10, with a mean value of 5.36 and a standard deviation of 2.29. The extensive range illustrated herein indicates the severity continuum noticed in CT imaging. Although the statistical analysis in our study did not directly compare MCTSI with NLR and procalcitonin, existing literature indicates that MCTSI is a helpful clinical tool for evaluating the severity of acute pancreatitis, as reported by *Tahir et al. (2021)*. ⁽¹²⁾

Complicated outcomes were noted in 48% of the patient population. The most prevalent consequence observed in the study was pleural effusion, accounting for 28% of cases, followed by ascites at 12%. A subset of individuals encountered numerous problems, wherein 4% exhibited the coexistence of pleural effusion and ascites, while 4% developed pseudocyst or superior vena cava stroke. The incidence rate of complications in this study is comparable to the findings published by *Zhu et al. (2023)* in their investigation of early indicators of infected pancreatic necrosis. ⁽¹³⁾

Crucially, no deaths were documented within the sample population under investigation. The result constrains our capacity to evaluate the prognostic significance of the markers concerning death.

The analysis of variance (ANOVA) findings indicated no statistically significant difference in NLR levels across severity levels defined by the Atlanta Classification ($p=0.627$). The average NLR values were 10.60 (standard deviation 11.61) for mild instances, 14.84 (standard deviation 10.04) for intermediate cases, and 15.17 for severe cases. The absence of a substantial correlation in this study contrasts with the results reported by *Li et al. (2017)*, whereby NLR was identified as a significant prognostic factor for mortality and severity in cases of acute pancreatitis. ⁽¹⁴⁾

The receiver operating characteristic (ROC) analysis conducted to predict moderate acute pancreatitis using procalcitonin yielded an area under the curve (AUC) value of 0.727, accompanied by a standard error of 0.103 and a p-value of 0.05. The confidence interval for the 95% confidence level spanned from 0.525 to 0.929. A cutoff value of 0.45 ng/mL was identified as the best threshold, exhibiting a sensitivity of 81.8% and specificity of 64.3%.

The analysis of variance (ANOVA) findings indicated a statistically significant disparity in procalcitonin levels among severity categories as delineated by the Atlanta Classification ($p<0.001$). The average levels of procalcitonin were found to be 0.45 ng/mL (standard deviation = 0.39) in mild instances, 2.28 ng/mL (standard deviation = 3.36) in moderate cases, and 12.02 ng/mL in severe cases. The observed tendency is consistent with the results reported by *He et al. (2022)*, wherein procalcitonin, in conjunction with other biomarkers,

demonstrated favourable predictive efficacy in assessing the severity of acute pancreatitis. ⁽¹⁵⁾

The results of our study indicate that serum procalcitonin may be more reliable as an early indicator of severity in cases of acute pancreatitis than NLR. Establishing a correlation between procalcitonin and severity levels, as delineated by the Atlanta criteria, suggests its potential efficacy in therapeutic management. This observation is consistent with the findings reported by *Surana et al. (2022)*, wherein procalcitonin was identified as a dependable indicator for predicted severity. ⁽¹⁶⁾

Although the prognostic effect of NLR was not shown to be statistically significant in our investigation, its ease of calculation and widespread accessibility render it a potentially valuable tool in specific clinical scenarios. The observed disparity between our results and specific other investigations underscores the necessity for additional scholarly inquiry to understand NLR's significance in the prognosis of acute pancreatitis.

CONCLUSION

This study posits that serum procalcitonin may be more reliable as an early prognostic indicator of severity in cases of acute pancreatitis than NLR. The results demonstrated a noteworthy correlation between procalcitonin and severity levels as categorized by the Modified Atlanta Criteria, suggesting its potential usefulness in clinical decision-making. Although the prognostic usefulness of NLR was not shown to be statistically significant in this investigation, its ease of calculation and widespread accessibility may nevertheless render it a valuable tool in specific therapeutic scenarios.

The results emphasize the significance of employing a comprehensive strategy for evaluating the severity of acute pancreatitis, which involves integrating clinical, radiological, and biochemical indicators to achieve the most effective therapy for patients. However, the study's constraints, such as its limited sample size and reliance on a single institution, underscore the necessity for further extensive, multi-centre investigations to substantiate these results and delve deeper into the predictors of acute pancreatitis severity and outcomes. Future investigations in this field have the potential to make substantial contributions towards enhancing the early management and overall outcomes of individuals suffering from acute pancreatitis.

LIMITATIONS

It is a single-center design. The research conducted at a single hospital may not adequately consider the potential variances in patient demographics or treatment approaches across other healthcare settings. This has the potential to influence the broader generalizability of the results.

The restricted spectrum of severity observed within the study cohort, wherein merely 4% of cases were categorized as severe, may not comprehensively encompass the predictive efficacy of these indicators among the most critical patients. The tendency to focus on less severe instances may lead to underestimating these indicators' usefulness in critical acute pancreatitis cases.

Although the lack of fatality instances is beneficial for the patients under investigation, it restricts the study's capacity to evaluate the predictive efficacy of the markers for this crucial outcome. This gap in the severity spectrum can impact the thorough assessment of the markers' prediction capacities.

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