Original article

Correlation between the Neutrophil-to-Lymphocyte Ratio and the Severity of Acute Pancreatitis

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Abstract

Background: Acute pancreatitis (AP) is a potentially lethal condition triggered by various factors, with a poor prognosis if it escalates to severe acute pancreatitis. Traditional methods for evaluating the severity of AP such as the Ranson criteria, the Acute Physiology and Chronic Health Evaluation (APACHE) II score, and the Bedside Index of Severity in Acute Pancreatitis (BISAP) scores, are cumbersome and resource-intensive, requiring costly investigations. To overcome this limitation, this study investigated the relationship between the neutrophil-to-lymphocyte ratio (NLR) and AP severity, exploring the potential of NLR as a simple and more affordable predictive indicator of AP severity.
Methods: This cross-sectional study was conducted at Benazir Bhutto Hospital (BBH) in Rawalpindi, Pakistan, from January 2022 to January 2024, among 210 diagnosed patients of AP. Consecutive sampling and a set of inclusion and exclusion criteria were used to recruit patients. Informed consent was acquired prior to data collection. A self-created form was used to gather data. The severity of AP was assessed using the Ranson criterion score. Based on the severity of their AP (Ranson score), the patients were split into two groups. Descriptive and inferential statistics were used in the Statistical Package for the Social Sciences (SPSS) to analyse the data. P-values below 0.05 were regarded as significant.
Results: From 210 patients, n=136 (64.76%) had non-severe AP while n=74 (35.24%) had severe AP. Significant variations were found in the age, gender, WBC count, serum AST level, blood glucose level, serum LDH level, serum amylase level, serum lipase level, Ranson score, lymphocyte count, neutrophil count, and neutrophil-to-lymphocyte ratio with $p < 0.05$. Pearson's correlation showed that NLR was positively and significantly correlated with the Ranson scores ($r = 0.82$ $p < 0.002$). Linear regression analysis also indicated NLR as a significant predictor of AP severity ($\beta = 3.20$, 95% CI: 1.80-4.70, $p < 0.002$).
Conclusion: In the present study, NLR was found as an efficient indicator of AP severity in patients as a positive and significant association was noted between the NLR and the severity of AP. Higher NLR was correlated with higher Ranson scores, suggesting the increase in severity of AP. This current study findings endorse the use of NLR as a supplementary, cost-effective tool for prompt identification of high-risk AP patients, facilitating timely interventions and improved outcomes, particularly in resource-constrained setting.

Keywords: Heart failure, ECG, Ejection Fraction, Arrhythmia.

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1. Introduction

Acute pancreatitis (AP) is a sudden and severe pancreatic inflammation, characterized by abdominal pain, nausea, vomiting, and potentially life-threatening complications[1]. Symptoms can vary from mild to severe, including abdominal pain, nausea, vomiting, fever, and jaundice[2]. AP is a significant global health issue, with an estimated annual incidence of 34 cases per 100,000 people worldwide. In the United States, AP accounts for approximately 210,000 hospitalizations annually[3]. In Pakistan, between 13 and 45 incidences of AP are thought to occur annually per 100,000 persons[4].

The pancreas plays a crucial role in digestion and glucose regulation, and any impairment can have devastating consequences. Acute pancreatitis (AP) can be categorized into mild, moderate, and severe forms. Its severity dictating its treatment and prognosis[5]. If untreated, AP can lead to life-threatening complications, including pancreatic necrosis, pseudocysts, fistulas, ascites, splenic vein thrombosis, and progression to chronic pancreatitis[6]. Moreover, AP is linked to a high mortality rate, which can range from 4% to 255%[1, 7].

Acute pancreatitis (AP) has different underlying causes, with gallstones and excessive alcohol consumption being the leading culprits. Additional factors that can trigger AP include elevated triglyceride levels, certain medications, infections, physical trauma, smoking, and genetic predispositions[4, 8].

The diagnosis of acute pancreatitis (AP) relies on a multidisciplinary approach, incorporating clinical symptoms, laboratory results, and imaging findings. Key laboratory tests include measurements of serum

amylase and lipase, complete blood counts, and liver function tests[9, 10]. Additionally, imaging modalities such as CT scans and ultrasound can also help confirm the diagnosis and evaluate the severity of AP[2, 6].

The treatment approach for acute pancreatitis (AP) is tailored to the severity of the condition. Mild AP cases can often be effectively managed with conservative measures, including aggressive fluid replacement, pain control, and nutritional support[11]. On the other hand, more drastic measures like surgery, artificial ventilation, and intensive care unit (ICU) admission might be required for severe AP patients[12].

To evaluate the severity of acute pancreatitis (AP), several scoring systems have been established, including the Ranson criteria, APACHE II score, and BISAP score. While these systems aid clinicians in predicting AP severity and informing treatment decisions, they can be cumbersome to use due to the need for multiple investigations and calculations, which can add complexity to the assessment process[8, 13, 14].

Recently, various biomarkers have become crucial in predicting acute pancreatitis (AP) severity and guiding treatment decisions. Notably, the Neutrophil-to-Lymphocyte Ratio (NLR) has emerged as a promising marker due to its ease of calculation, rapid availability of results, cost-effectiveness, and potential to indicate AP severity. By quantifying the immune response, NLR has shown promise in studies exploring its relationship with AP severity. However, most studies have been limited by small sample sizes or focused on specific patient populations, emphasizing the need for larger, more diverse studies to confirm these findings[15-19].

Despite growing recognition of the Neutrophil-to-Lymphocyte Ratio (NLR) in acute pancreatitis (AP) management around the globe, research in Pakistan on NLR's utility in assessing AP severity is scarce. This study aims to bridge this knowledge gap by exploring NLR's predictive value for AP severity. By doing so, it seeks to contribute to the development of simple, affordable biomarkers for early AP identification and management, particularly in resource-limited settings. The ultimate goal is to facilitate timely treatment, prevent life-threatening complications, and improve outcomes for AP patients in Pakistan.

2. Materials & Methods

Study design and study population: This is cross-sectional study which was conducted at the Department of Emergency at Rawalpindi's Benazir Bhutto Hospital in Pakistan, over a two-year period, starting from January 2022 to January 2024. 210 patients of acute pancreatitis were enrolled through consecutive sampling. The sample size was calculated based on a 15% prevalence of acute pancreatitis from the reference study, with a margin of 5% margin of error and with a confidence interval of 95%[1]. To ensure the study's validity, rigorous inclusion and exclusion criteria were applied.

Inclusion and exclusion criteria: The study included patients of any gender, aged 18 years or older, with complete medical records and a confirmed diagnosis of acute pancreatitis. In contrast, patients under 18 year of age, or those with a history of previous acute biliary pancreatitis, recent antibiotic or steroid use, chemotherapy, radiation therapy, alcohol consumption, or underlying medical conditions such as dyslipidemia, blood disorders, malnutrition, or chronic inflammatory diseases were excluded from the study. Additionally, patients who declined to provide informed consent for participation were also excluded.

Primary Outcome and Secondary Outcomes: This study's primary objective was to explore the relationship between Neutrophil-to-Lymphocyte Ratio (NLR) and acute pancreatitis (AP) severity, using the Ranson criteria. Three secondary objectives were also investigated: identifying AP causes, comparing NLR levels in severe and non-severe acute biliary pancreatitis (ABP) patients, and assessing NLR's prognostic value in predicting ABP severity progression.

Acute Pancreatitis and its Severity Measurement: A diagnosis of acute pancreatitis was made based on the presence of at least two of the following: acute abdominal pain and significantly elevated serum lipase or amylase levels (at least three times the normal upper limit)[1]. The Ranson criteria were then applied to evaluate the severity of acute pancreatitis (AP), with a total score of 2 or less indicating mild AP and a score of 3 or more indicating severe AP[2].

Neutrophil-to-Lymphocyte Ratio: From the peripheral blood sample, the Neutrophil-to-Lymphocyte Ratio (NLR) was measured by dividing the neutrophil count

by the lymphocyte count. Its normal value varies between 0.78 and 3.53 for an adult with good health[22].

Data collection: Data collection for this study was conducted using a specially designed questionnaire, divided into three sections. Section one gathered demographic details (age and gender), medical history, and physical examination results. Section two focused on laboratory test reports. Section three utilized data from the first two sections to calculate the Ranson criteria score and Neutrophil-to-Lymphocyte Ratio (NLR).

Statistical analysis was performed using IBM SPSS Statistics Version 25. Qualitative data were described using frequencies and percentages, while quantitative data were summarized as mean ± standard deviation. The two study groups' numerical and nominal variables were compared using independent t-tests and their nominal variables were compared using chi-squared testing. Analysis of Pearson's correlation was employed to examine the relationship between Ranson scores and Neutrophil-to-Lymphocyte Ratio (NLR). Linear regression model was used to assess the predictive value of NLR for Ranson scores. Statistical significance was set at a p-value of <0.05.

3. Results

From 210 patients, non-severe acute pancreatitis was identified in n=136 (64.76%) patients while severe acute pancreatitis was found in n=74 (35.24%) patients. The main causes of AP in this population were gall stones (n=86, 40.95%), followed by idiopathic etiology (n=75, 35.71%), smoking (n=40, 19.04%), and Post-ERCP (Endoscopic Retrograde Cholangiopancreatography) (n=9, 4.30%).

Table 1: Characteristics of the Study demograph along with Independent t-test and Chi-squared test analysis

Variables Patients with Acute Pancreatitis N=210		Expression of Variables	Severity of Acute Pancreatitis		Chi-Square test/Independent t-test Test Statistics	
			Non-Severe AP Group n=136 (64.76%)	Severe AP Group n=74 (35.24%)	χ^2-value for Chi-Square test/ t-value for Independent-test	p-values
Gender	Male (n) (%)	148 (70.48%)	101 (74.26%)	47 (63.51%)	3.55	0.04
	Female (n) (%)	62 (29.52%)	35 (25.74%)	27 (36.49%)		
Age (Years) Means ± SD		60.94±18.12	56.09±12.62	63.22±11.32	2.43	0.03
White Blood Cell count (cells/mm^3)		15.54±6.65	14.21±4.30	18.64±5.93	3.21	0.02
AST (IU/L)		240.34±130.48	252.32±40.10	289.24±150.07	2.91	0.01
Blood Glucose Level (mg/dL)		230.70±60.46	160.34±.35.99	240.56±50.76	3.51	0.003
LDH (IU/L)		510.56±110.22	380.17±60.99	559.87±140.09	3.42	0.002
Serum Amylase Level (U/L)		430.14±132.48	255.45±130.10	519.33±170.32	5.45	0.003
Serum Lipase Level (U/L)		460.32±160.15	321.72±139.08	560.05±167.41	5.10	0.004
Ranson Score		3.04±1.24	1.39±0.50	3.79±1.10	4.21	0.001
Lymphocytes count (cells/mm^3)		1.30±0.48	1.49±0.40	1.29±0.32	2.81	0.001
Neutrophils count (cells/mm^3)		12.32±5.15	10.72±4.08	15.06±7.41	3.19	0.001
Neutrophil-to-lymphocyte Ratio		9.47±5.24	7.19±4.02	11.67±5.40	3.42	0.002

Table 1 indicates that the study population's demographic and clinical features. It has also demonstrated significant differences between the two study groups (Non-severe AP group and severe AP group) in several primary parameters including age, gender, WBC count, AST level, blood glucose level, serum LDH, serum amylase level, serum lipase level, Ranson score, lymphocyte count, neutrophil count, and neutrophil-to-lymphocyte ratio ($p < 0.05$).

Table 2 shows a statistically significant positive correlation between Neutrophil-to-Lymphocyte Ratio (NLR) values and acute pancreatitis (AP) severity, as determined by Pearson's correlation analysis. This correlation indicates that higher NLR values are associated with increased Ranson scores, suggesting a direct and positive relationship between NLR and AP severity.

Table 3 presents that the simple linear regression model demonstrated an excellent fit ($R^2 = 0.80$, $p < 0.0001$), revealing a statistically significant positive association between Neutrophil-to-Lymphocyte Ratio (NLR) values and Ranson scores. The positive beta coefficient indicates that as NLR values increase, Ranson scores also rise, suggesting a strong correlation between higher NLR values and greater acute pancreatitis (AP) severity.

Table 2: Association between NLR and the severity of AP in the study demograph

Variables N=210	Severity of Acute Pancreatitis		Independent t test		Pearson's Correlation	
			Test Statistics		Test Statistics	
	Non-Severe AP Group	Severe AP Group	t-value	p-value	Correlation Coefficient (r)	p-value
Ranson Score Means ± SD	1.39±0.50	3.79±1.10	4.21	0.001	0.82	0.002
Neutrophil-to-Lymphocyte Ratio Means ± SD	7.19±4.02	11.67±5.40	3.42	0.002		

Table 3: Assessment of predictive value of NLR for severity of AP via simple linear regression model

Variable	Test Statistics for Simple Linear Regression Model				
	Unstandardised Regression Coefficient (β)	95% CI	p-value	R^2 value	p-value of F test
Neutrophil-to-Lymphocyte Ratio	3.20	1.80 to 4.70	0.002	0.80 (80.00%)	0.0001

4. Discussion

Acute pancreatitis is a fatal condition that poses a substantial global healthcare burden, necessitating early identification and prompt management to improve survival rates and prevent complications[1, 2]. This study provides valuable insights into the correlation between Neutrophil-to-Lymphocyte Ratio (NLR) and AP severity, shedding light on a critical aspect of AP management. Furthermore, the study undertakes a comprehensive comparison of key parameters, including age, serum biomarkers, and NLR, between patients with non-severe and severe AP, offering a nuanced understanding of the differences between these two patient groups.

The correlation between Neutrophil-to-Lymphocyte Ratio (NLR) and acute pancreatitis (AP) with sepsis is rooted in the complex interplay between neutrophil and lymphocyte reactions. When the pancreas becomes inflamed, neutrophils are activated, leading to an elevated NLR, which reflects the severity of the inflammatory response. Neutrophils contribute to tissue damage and organ dysfunction, while lymphocytes play a crucial role in resolving inflammation and promoting immune homeostasis. An increased NLR indicates an imbalance between these immune responses, predicting poor outcomes due to unchecked inflammation, tissue damage, and organ dysfunction[18-21].

In this study, 64.76% (n=136) of patients had non-severe acute pancreatitis (AP), while 35.24% (n=74) had severe AP. These findings are similar to a Turkish study[2], but differ from a South Korean study[16], which conveyed a lesser frequency of severe AP and a greater frequency of non-severe AP. The variation in AP severity across studies may be attributed to differences in etiology, patient presentation, environmental factors, and comorbidities between populations.

The main causes of AP in the current study population were gall stones, followed by idiopathic etiology, smoking, and Post-ERCP. In literature, several studies have been highlighted alike etiologies of AP[1, 15].

The demographic characteristics of patients played a significant role in determining the severity of acute pancreatitis (AP). Notably, male patients and older individuals were more likely to experience severe AP. These findings are consistent with previous studies, which have also highlighted the influence of

demographics on AP severity, thereby validating the results of the present study[4, 7].

A statistically significant difference was found between patients with non-severe and severe acute pancreatitis (AP) in various study variables, including serum AST level and serum LDH level, serum blood glucose level, WBC count, serum amylase level, serum lipase level, Ranson score, neutrophil and lymphocyte counts, and Neutrophil-to-Lymphocyte Ratio (NLR). These findings are consistent with previous studies that have used Ranson score and NLR to assess AP severity, highlighting the importance of these factors in determining the severity of AP[19, 20].

In the current study, NLR was positively and significantly associated with the AP severity as patients with raised severity of AP had raised NLR. This primary finding of this study was consistent with many past studies that were carried out in different parts of the world. A study from India has also indicated the function of NLR as a significant and cost-efficient predictor of AP severity[15]. Another study has also reported that NLR raise with the increase in the severity of the AP and high NLR predicts poor prognosis among patients with AP[16]. Similarly, a Turkish study has similar results about the significant correlation between NLR and severity of AP as this present study[17]. A meta-analysis has also shown similar findings regarding NLR and AP severity. It has presented that with the rise in NLR, the severity of AP increases[18]. Another study has also found that patients with higher NLR had more severe AP in contrast to the patients with lower NLR[19]. Another study from Ireland has also observed that the variation in NLR values in the various categories of patients with different severity of AP[21]. The results of this study back the employ of NLR as inaccurate and effective supplementary biomarker for determining the severity of AP and they are in similar with the previous studies.

The results of our study have significant clinical implications. The Neutrophil-to-Lymphocyte Ratio (NLR) can be used as a simple, inexpensive, and readily available biomarker to identify patients at high risk of severe acute pancreatitis and its life-threatening complications. Early detection of these patients enables healthcare providers to initiate timely interventions, leading to improved patient outcomes. Additionally, NLR can be used to monitor disease progression and treatment response, allowing clinicians to adjust their treatment strategies accordingly. Our study's findings also suggest that NLR can become a useful tool for stratifying patients in clinical trials, thereby enhancing the accuracy and reliability of research on acute pancreatitis.

While this study provides very important insights into the predictive value of Neutrophil-to-Lymphocyte Ratio (NLR) in acute pancreatitis (AP), it has some limitations as well. The relatively small sample size, single-centered population, and cross-sectional design may limit the applicability of our findings to broader populations. To build upon our research and confirm the prognostic value of NLR in AP, future studies with larger, more diverse samples and varied study designs are essential to validate and expand our results.

5. Conclusion

This study reveals a strong link between NLR and the severity of AP. The results show that higher NLR values consistently correlate with more severe AP cases. A statistical analysis confirms this direct relationship, suggesting that NLR is a reliable, efficient, and cost-effective predictor of AP severity. Regular monitoring of NLR can help clinicians intervene promptly and improve patient outcomes. The study recommends that clinicians consider NLR alongside other diagnostic tools to assess AP severity comprehensively. By incorporating NLR into clinical practice, healthcare providers may be able to improve treatment outcomes and reduce mortality rates among AP patients, further solidifying NLR's role in managing AP.

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