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ORIGINAL ARTICLE

Comparison of the Inflammatory Markers with the Ranson Scoring System to Predict the Severity of Acute Pancreatitis

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ABSTRACT

OBJECTIVE: To assess the clinical usefulness of inflammation markers, including the Neutrophil-to-Lymphocyte Ratio, Lymphocyte-to-Monocyte Ratio, and Prognostic Nutritional Index (PNI), to determine the severity of AP dose in relation to the Ranson score.

METHODOLOGY: The cross-sectional study was conducted in the General Surgery Department of Dr Ruth K.M. Pfau Civil Hospital, Karachi, between January and June 2022. 288 adult patients with AP were recruited through a purposive sampling technique. Patients with chronic pancreatitis, severe comorbid illnesses, or incomplete records were excluded. Laboratory parameters and demographic information were noted on admission. Complete blood counts were used to calculate NLR, LMR, and PNI. Ranson score at admission and 48 hours was used to assess severity. The accuracy of the inflammatory measures in diagnosing (sensitivity, specificity, PPV, NPV, AUC) was compared with the Ranson score. SPSS v24.0 was used to analyze the data.

RESULTS: The average age of patients was 41.1± 11.1 years (55.2% were females). The percentage of severe cases of AP was 33%. The highest diagnostic accuracy was observed in NLR (90.97%), with a sensitivity of 81.1% and specificity of 95.9%, followed by PNI (85.42%) and LMR (80.03%). NLR had better performance among male patients and those aged 50 years or less.

CONCLUSION: NLR proves to be a sensitive early interpreter of the severity of acute pancreatitis with good diagnostic performance. It is easy to access; hence, it is an excellent resource for initiating treatment of an individual with AP in the early days, until conventional scoring systems are completed.

KEYWORDS: Acute Pancreatitis; Neutrophil-to-Lymphocyte Ratio; Lymphocyte-to-Monocyte Ratio; Prognostic Nutritional Index; Severity Prediction.

INTRODUCTION

Pancreatitis is referred to as inflammation of the parenchyma of the pancreatic gland. This disease has been found to range from mild to even fatal. Various kinds of gallstones and alcohol consumption lead to 30 to 50% of the cases[1,2]. Other common risk factors are smoking, endoscopic retrograde cholangiopancreatography (ERCP) (relative risk of approximately 3 to 5%), and hypertriglyceridemia (approximately 1 out of every 10 cases). The diagnosis is made based on clinical presentation, elevated serum lipase level (3 times the upper level of normal), and characteristic abnormal morphological patterns on imaging[2]. The overall mortality rate of acute pancreatitis is 5%, but when severe, it will rise to 17 to 30%, whereas mild cases have a rate of 1.5% [3]. Early oral nutrition, pain relief and fluid therapy are necessary in the management of acute pancreatitis[4,5].

Instead of the morbidity rate of severe acute pancreatitis and the death rate of patients with this disease being 1.77 and 1.6, respectively, the outcomes have been decreased because of the new developments within the field of management. The severity of the disease has been evaluated using several scoring systems, including the Glasgow score, the Modified CT Severity Index (MCTSI), the Revised Atlanta Classification (RAC), the Ranson criteria, the Acute Physiology and Chronic Health Evaluation (APACHE-II), and the Bedside Index of Severity in Acute Pancreatitis (BISAP)[6].

Ranson's scoring system is the first to predict acute pancreatitis, developed in 1974. The 48-hour calculation time of the full Ranson score is an inherent advantage, rather than a weakness, and there are no significant differences in the prognostic accuracy of the Ranson score compared to other scoring systems[7]. Nevertheless, the 48-hour rule is controversial and delays the accurate diagnosis and treatment of acute pancreatitis. To categorize patients with severe acute pancreatitis and administer appropriate treatment, a rapid evaluation variable is needed. Inflammatory markers in the blood of the patient (neutrophils, lymphocytes, and monocytes) can be easily evaluated with the help of the CP of blood, which means that the severity of the disease may be determined.

In 1992, the Atlanta classification of pancreatitis into mild and severe was proposed. In 2012, it was further divided and classified types of acute pancreatitis into mild, moderate and severe cases based on a Modified Marshall scoring system. In addition, the modified Atlanta classifications established acute pancreatitis in terms of local complications and the occurrence of organ failure[8].

A study done in the emergency department of a 1020-bed medical college hospital in Incheon City, South Korea, discovered that an increase in NLR was associated with severe acute pancreatitis. NLR is expected to be a useful prognostic marker for patients with acute pancreatitis visiting the emergency unit[9]. Akuzzu MZ et al.[10] concluded that the controlling nutritional status (CONUT) score and PNI have been proven effective as prognostic markers, with utility beyond accurately determining nutritional status, extending to the degree and consequences of AP[11]. A study conducted in the general surgery unit of a tertiary hospital in Karachi on 225 subjects revealed that, compared with CRP alone, the CRP/albumin ratio is more sensitive and has a higher negative predictive value of predicting severe pancreatitis.

The study is led by the idea not to use a system of criteria based on which the acute pancreatitis severity can be determined, the recommendation on which can be determined, e.g. Ranson criteria, which consists of eleven parameters and is traditionally performed 48 hours after admission, but is replaced by a more specific test ratio. The development of a test ratio system to predict the severity of acute pancreatitis would be of great help to patients.

METHODOLOGY

It was a cross-sectional study conducted between January and June 2022 at the Department of General Surgery, Dr Ruth K.M. Pfau Civil Hospital, Karachi. Written informed consent was obtained from all participants, and the study was approved by the College of Physicians and Surgeons, Pakistan, No. CPSP/REU/SGR-2018-183-9951. Only adult patients aged 18-65 years who were admitted with a diagnosis of acute pancreatitis and clinical, biochemical (elevated serum amylase/lipase), and/or radiologic characteristics were included through purposive sampling. A purposive sampling technique was employed to specifically include adult patients diagnosed with acute pancreatitis who met the study criteria. This approach was appropriate to ensure inclusion across the severity spectrum and to allow adequate subgroup analyses, given the specific clinical and laboratory data required for calculating NLR, LMR, and PNI.

Patients having recurrent or chronic pancreatitis, pancreatic malignancy, hematologic conditions, or those who refused to consent were not selected. Patients across the full spectrum of acute pancreatitis severity, mild, moderate, and severe, were included in the study. Severity was determined using the Ranson scoring system at admission and repeated at 48 hours. This ensured representation of all clinical severities, allowing assessment of the performance of inflammatory markers across the entire disease spectrum.

The principal investigator conducted a detailed clinical assessment, and a surgical consultant confirmed it on admission. Demographic data, comorbidities, and lab data, including complete blood count, serum calcium, blood sugar, serum albumin, liver function tests, arterial blood gases, amylase, lipase, and blood urea nitrogen, were noted. Blood samples for calculation of NLR, LMR, and PNI were collected on admission, before initiation of treatment, to ensure early assessment of inflammatory status. Admission blood work was used to calculate inflammatory markers, including neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and prognostic nutritional index (PNI). The formula was used to calculate PNI as *(10 × serum albumin [g/dL]) + (0.005 × total lymphocyte count [/mm³]).* According to the existing literature, the determinate values of the severe acute pancreatitis were NLR > 11.3, LMR < 1.43 and PNI < 41.1, based on thresholds reported in previous literature as indicative of severe acute pancreatitis[9-11]. These values were adopted to allow early stratification of patients in alignment with established studies. The Ranson score was computed at admission and again after 48 hours; a score of 3 or more indicated severe illness.

OpenEpi version 3.01 was used to compute the sample size based on a 21.7% prevalence of severe acute pancreatitis, a 95% confidence level, and a 5% margin of error. The computed minimum sample size was 264 patients, with an adjustment of 10% inflation of the sample size for non-responses. Finally, 288 patients were recruited, sufficient for subgroup analyses.

SPSS version 24.0 was used to analyze the data. Quantitative variables were reported as means ± standard deviation or medians ± interquartile ranges, whereas categorical variables were reported as frequencies and percentages. Normality was assessed with the use of the Shapiro-Wilk test. Regarding the distribution of data groups, the independent t-test or Mann-Whitney U test was used to compare the means of continuous variables, and the Chi-square test was used to compare the means of categorical variables.

SPSS version 24.0 was used to create receiver operating characteristic (ROC) curves to evaluate the diagnostic effectiveness of NLR, LMR, and PNI in predicting severe acute pancreatitis (SAP) using the Ranson score as a reference standard. Sensitivity, specificity, PPV, NPV, accuracy, and area under the ROC curve (AUC) were then computed for each biomarker. The cut-offs of NLR

(>11.36), LMR (<1.43), and PNI (<41.1) were adopted from published literature that validated the cut-off values of these cut-offs for predicting early occurrence of SAP, and were not derived from an existing dataset. Multivariate binary logistic regression was conducted to control for potential confounding factors, including age, gender, NLR, LMR, and PNI. Statistically significant variables were defined as those with p-values of 0.05 or less.

NLR, LMR, and PNI were evaluated for their ability to predict severe acute pancreatitis using the Ranson score as the reference standard. Each marker was calculated for sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and area under the ROC curve (AUC). An age- and gender-stratified analysis was carried out, with p-values ≤ 0.05 considered statistically significant.

Although patients were recruited through purposive sampling from a tertiary care hospital, the demographic and clinical profiles of participants reflect the typical spectrum of adult acute pancreatitis cases presenting to similar urban tertiary care centres in Pakistan.

RESULTS

A total of 288 patients with acute pancreatitis were recruited for this study. From the 288 participants, 55.2% were females, followed by 44.8% males, and their average age was 41.1±11.1 years. According to the Ranson score, 33% (95/288) of patients were classified as having severe acute pancreatitis (SAP). **Table I** represents the detailed descriptive statistics of significant clinical and laboratory variables.

Table I: Descriptive statistics of patient characteristics

Variables	Mean	SD	Median	IQR
Age (years)	41.1	11.1	40	20
Ranson score (at admission)	2.4	1.5	2.0	1
Neutrophil-to-Lymphocyte Ratio (NLR)	7.9	3.8	6.3	6.8
Lymphocyte-to-Monocyte Ratio (LMR)	4.5	3.1	5.0	5.7
Prognostic Nutritional Index (PNI)	45.3	8.4	45.8	9.9

To assess the usefulness of inflammatory markers in determining the severity of AP, we compared their diagnostic accuracy with that of the Ranson score, the gold standard. The highest diagnostic accuracy was indicated in Neutrophil to Lymphocytes ratio (NLR), NLR 90.97%, followed by PNI 85.42% and LMR 80.03%. The most significant area under the curve (AUC) was observed for NLR (0.88), indicating substantial predictive value for SAP. These results are tabulated in **Table II**.

Table II: Diagnostic accuracy of inflammatory markers compared to Ranson score in the overall cohort (n = 288)

Inflammatory Marker	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
NLR (>11.36)	81.1%	95.9%	90.6%	91.1%	90.97%	0.88
LMR (<1.43)	74.7%	88.6%	76.3%	87.7%	80.03%	0.82
PNI (<41.1)	70.5%	92.7%	82.7%	86.5%	85.42%	0.81

Further stratification was performed to obtain patient data by gender and age group. In male patients (n = 129), NLR was the best predictor of severe AP, with 93.7% accuracy and an AUC of 0.94. In contrast, LMR and PNI were also valid predictors, with accuracies of 91.4% and 87.5%, respectively (**Table III**).

Table III: Diagnostic accuracy of inflammatory markers in male patients (n = 129) and female patients (n = 159)

Inflammatory Marker	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
Male patients (n = 129)						
NLR (>11.36)	91.4%	95.8%	94.6%	93.2%	93.7%	0.94
LMR (<1.43)	89.7%	93.0%	91.2%	91.7%	91.4%	0.91
PNI (<41.1)	81.0%	93.0%	90.4%	85.7%	87.5%	0.87
Female patients (n = 159)						
NLR (>11.36)	64.9%	95.9%	86.8%	87.5%	86.2%	0.82
LMR (<1.43)	60.3%	86.5%	70.6%	80.4%	75.2%	0.76
PNI (<41.1)	68.9%	91.7%	81.0%	84.6%	83.0%	0.80

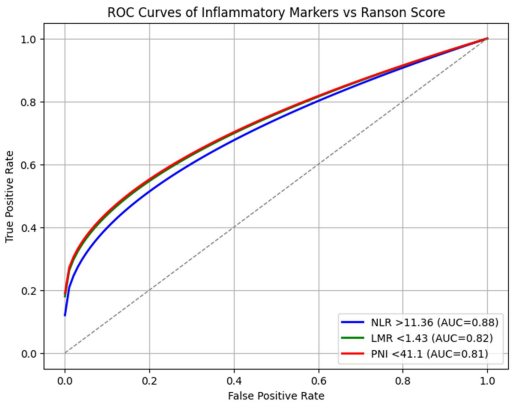
However, female patients (n = 159) had a lower NLR sensitivity of NLR (64.9%) but a higher specificity (95.9%). The total accuracy of NLR in female capillary fluids was 86.2, and the AUC reached 0.82. As shown in **Table IV**, PNI demonstrated stable performance with 83% accuracy, and LMR demonstrated the lowest diagnostic accuracy of 75.2% in females. Also, age-stratified results validated the performance of NLR in younger patients, with an accuracy of 95.6%. Still, the variations between markers were lower in elderly patients aged 50 years or older, where NLR (79.5%), LMR (80.7%), and PNI (78.3%) performed similarly.

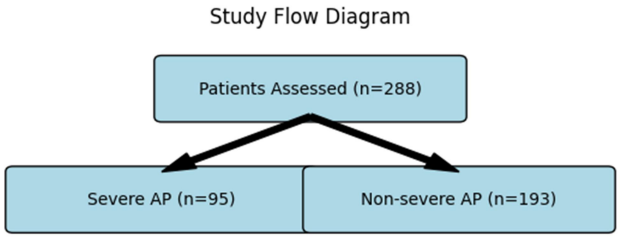
Table IV: Multivariate Binary Logistic Regression for Predictors of Severe Acute Pancreatitis

Variable	AOR (95% CI)	p-value
Gender		
Male (Ref)	1.00	
Female	0.803 (0.300 – 2.150)	0.662
Age (years)	1.066 (1.017 – 1.118)	0.007
PNI	0.844 (0.780 – 0.913)	<0.001
NLR	1.952 (1.564 – 2.437)	<0.001
LMR	1.516 (1.072 – 2.144)	0.019

Females had 0.803 times reduced odds of getting Severe Acute Pancreatitis (SAP) compared to males. With a per-year increase in age, the odds of SAP were 1.066 times higher (95% CI: 1.0171.118), and this was a significant finding (p = 0.007). Such a finding adds to the sensitivity of older adults when it comes to the progression of the disease. The odds of PNI were 0.844 (95% CI: 0.780–0.913) times lower in SAP, which was highly significant (p < 0.001). This indicates that PNI is protective against severe disease. The odds of NLR were OR = 1.952 (95%

CI: 1.564–2.437) for an increase in SAP, which was statistically significant ($p < 0.001$). This finding identifies systemic inflammation as one of the powerful indicators of disease severity. The higher LMR was associated with 1.516 times (95% CI: 1.072, 2.144) greater odds of SAP, with the results of statistical significance ($p = 0.019$). The increased LMR can be an indication of an immune response that is adjusted to more severe cases.





DISCUSSION

Acute pancreatitis (AP) is an inflammatory disease with a variable clinical course. Having failed organs or infected pancreatic necrosis often complicates severe cases, and they are the causes of death that dominate the list of fatalities in severe cases[12]. In this study, we assess the prognostic significance of various inflammation-based markers, i.e. the Neutrophil-to-Lymphocyte Ratio (NLR), Lymphocyte-to-Monocyte Ratio (LMR), Prognostic Nutritional Index (PNI), C-reactive protein (CRP) and Red Cell Distribution Width (RDW) as predictors of disease severity and mortality. NLR showed the highest predictive performance among them[13].

In our findings, NLR was 81.1%, specificity was 95.9% and total accuracy of 90.97% in AP severity measurement. The present results are consistent with a previous study by Bengi et al., which described NLR as the most useful of inflammation-based index for predicting mortality in AP[14]. To verify this, a single-centre study of a large Chinese population with biliary and hypertriglyceridemic AP demonstrated higher NLR values in biliary disease (9.1 vs. 6.9; $p < 0.001$) and that NLR was significantly associated with persistent organ failure regardless of etiology[15]. Likewise, another retrospective Chinese study in 300 patients found that on Admission, NLR was a significant predictor of severity (mean 2.18 in severe AP/1.23, 1.55 in the milder forms; $p<0.01$). Besides, the combination of CT severity index with NLR and procalcitonin resulted in higher prognostic accuracy (AUC 0.90) than NLR alone (AUC 0.81)[16].

The dynamic role of NLR was also outlined by a multicenter Turkish study (n=238), demonstrating that 24h levels performed best at predicting severity, followed by 48h levels predicting mortality and persistent organ failure [14]. Moreover, another study tested how well traditional scoring systems (e.g., Ranson, BISAP) predict critical illness compared to new inflammatory markers (e.g., NLR) and found a positive result, demonstrating that NLR is closely associated with illness severity and poor outcomes. They highlighted its utility as an early, convenient predictor of complications and mortality in AP[17].

These conclusions are strengthened by a study including 314 patients in the UK general hospital district, which demonstrated that NLR scores greater than 18.71 on day 0 identified mortality with 80% sensitivity and 90.2% specificity. NLR in the elevated range was also associated with higher ICU admissions and hospital length of stay, supporting its early prognostic significance[18].

The overall results of our male subgroup indicate that all three inflammatory markers, namely, NLR, LMR, and PNI, showed a better performance in predicting severe acute pancreatitis (AP), with NLR showing the highest predictive value (AUC 0.94; accuracy 93.7%). With slightly lower accuracy, LMR <1.43 demonstrated an outstanding sensitivity (89.7%) and specificity (93%) with an AUC of 0.91, which will make it useful as a screening tool. The accuracy and AUC of PNI <41.1 were 87.5% and 0.87, respectively, indicating the relevance of nutritional status in the pathogenesis of AP.

It should be noted that the biomarker performance of biomarkers in some populations can differ across populations due of differences in ethnicity, genetic factors, biliary versus alcoholic aetiology, nutrition, and access to healthcare facilities. The sample of our research represents an urban setting of South Asian tertiary care background, and the generalizability of these findings to other regions or ethnic groups requires further validation.

The result of our study is consistent with previous evidence. A prospective study in India involving 249 patients also demonstrated that day-1 LMR was significantly correlated with mortality and severity. However, its predictive value was similar to that of LMR and PNI within multivariate models[19]. Equally, a Chinese study found that PNI measured within 48 hours (in

addition to CRP and serum calcium) to be an independent predictor of severe AP, with an AUC of 0.87 [20]. These findings all demonstrate the usefulness of inflammatory and nutritional markers in supplemental risk stratification in the early stages.

The integration of NLR, LMR, and PNI into the existing clinical services workflow is possible because these biomarkers are based on complete blood count and serum albumin readings, which may be routinely performed during admission. They are affordable, available quickly and have low requirements in terms of resources, thus can be used in early triage where an advanced imaging or complex scoring mechanism may not be available at hand. Implementation can, however, be hampered by barriers such as lab processing delays, the inability to obtain timely serum albumin tests in peripheral centres, and disparities in laboratory calibration standards. These feasibility limits ought to be taken into account in the implementation of these biomarkers in various healthcare settings.

The strength of NLR is that it is simple, accessible, and cheap. Compared with imaging modalities or complex chemical testing, NLR can be obtained by performing a complete blood count, making it more convenient. Moreover, NLR has been reported in other inflammatory and malignant diseases as a marker of the overall burden of systemic inflammation and may have prognostic significance in AP. More importantly, we found that NLR is more helpful in younger male patients, suggesting possible demographic differences in the inflammatory process that warrant further examination.

It should be noted that the timing of blood sample collection may influence biomarker levels, as NLR, LMR, and PNI are dynamic markers. In this study, samples were collected on admission to provide an early assessment of inflammatory status, a clinically relevant approach for rapid risk stratification. However, serial measurements could provide additional insights into disease progression.

Still, our work also outlines the incorporation of single biomarkers of inflammation into multifactor scores. As an example of such a best skill, NLR demonstrated good performance when used by itself; it still ranks lower than a BISAP score as an independent predictor of AP severity. This is consistent with the existing body of literature indicating that NLR may have its most significant prognostic value when used with other multifactor prognostic scoring systems and in conjunction with multiple physiologic and laboratory parameters, such as BISAP or Ranson. Thus, instead of substitution, NLR, LMR, and PNI have the potential to be useful add-ons that enable clinicians to make early risk-stratification and management interventions, pending complete scoring outcomes. This has particular clinical implications. The timely recognition of patients with the risk of developing severe AP is vital to provide them with fast triage, aggressive fluid resuscitation, and close monitoring, which subsequently can reap dividends in terms of outcome. Given the limited availability of resources for imaging studies or serial biochemical testing, a simple hematologic index such as NLR can be a fair and adequate substitute.

STRENGTHS AND LIMITATIONS

The first strength of the study is a large sample size and the prospective nature of data capture in a tertiary care surgical unit, which enhances the internal validity of the results. The use of objective, accessible haematological markers and subgroup analyses stratified by age and gender further improves the clinical relevance of the results.

This research has several limitations. First, we could not assess the generalizability of our results to larger or more diverse populations due to the single-centre design. Second, because the

biomarker measurements were conducted at the time of admission, the study mainly reflects early inflammatory conditions and does not evaluate the effects of repeated measurements or the long-term impact of such measurements, such as mortality, recurrence, and complications. Third, purposive sampling allowed us to cover the full range of patient severity, but it could also be subject to selection bias. Also, not all patients had detailed etiological data and comorbidities, which limits the ability of fully adjust for potential confounders. Lastly, the long-term outcomes of patients were not evaluated in this study, and patients who suffered recurrent episodes of pancreatitis were excluded, thereby limiting the ability to assess the performance of the biomarkers over time.

Multi-centre studies with diverse ethnic and geographical populations should be conducted in future studies to enhance external validity. Serial measurements in NLR, LMR, and PNI can provide insights into the dynamic response of inflammation and its association with disease progression. Combining these biomarkers with established risk scores like BISAP or APACHE-II could improve predictive value and enable the creation of risk-stratification tools to be used early during the progression of acute pancreatitis.

CONCLUSION

The current literature indicates that the Neutrophil-to-Lymphocyte ratio (NLR) is a strong and independent predictor of severe acute pancreatitis (SAP). As well as Lymphocyte-to-Monocyte Ratio (LMR), Prognostic Nutritional Index (PNI), and age, a significant association of all of these factors with the disease severity was discovered. Compared with Ranson scoring, these markers can be used to assess risk earlier and enhance clinical decision-making because they are relatively easy to measure, accessible, and affordable. The integration into the regular process of testing is expected to increase the early detection and control of patients with concerns of severe outcomes.

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Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

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