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RESEARCH ARTICLE
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NEUTROPHIL-TO-LYMPHOCYTE RATIO AS AN INFLAMMATORY MARKER IN PATIENTS WITH ACUTE PANCREATITIS: A PROSPECTIVE STUDY FROM A TERTIARY CARE CENTRE IN CENTRAL INDIA.

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Abstract

Background: Early prediction of severity in acute pancreatitis (AP) guides triage, monitoring and resource allocation, especially in resource-limited settings. Neutrophil-to-lymphocyte ratio (NLR) is an inexpensive inflammatory marker that may aid early risk stratification.

Methods: This prospective observational study included 100 adult patients with a first episode of AP admitted to Index Medical College, Indore, from January 2021 to December 2021. Severity was classified according to the revised Atlanta criteria. Admission NLR was calculated from complete blood counts. Patients were grouped as mild versus moderately severe/severe AP. Associations of NLR with severity, ICU admission, local complications, length of stay and in-hospital mortality were assessed. Receiver operating characteristic (ROC) analysis evaluated the diagnostic performance of NLR for predicting moderately severe/severe AP.

Results: Mean age was 42.5 ± 13.2 years; 58% were male. Gallstones (46%) and alcohol (32%) were the commonest etiologies. Mild AP occurred in 68%, and moderately severe/severe AP in 32%. Mean admission NLR was 4.3 ± 2.1 in mild AP and 9.5 ± 3.9 in moderately severe/severe AP ($p<0.001$). Patients with higher NLR had significantly greater ICU admission (43.8% vs 5.9%), local complications (56.3% vs 8.8%), longer hospital stay (11.5 ± 4.6 vs 5.9 ± 2.3 days) and mortality (18.8% vs 0%; all $p<0.01$). ROC analysis showed an area under the curve of 0.84; an NLR cut-off of 5.0 predicted moderately severe/severe AP with 84.4% sensitivity and 79.4% specificity.

Conclusion: Admission NLR was significantly associated with severity and adverse short-term outcomes in acute pancreatitis. As a simple, low-cost parameter, NLR may serve as a useful adjunctive inflammatory marker for early risk stratification in AP in tertiary centres in India.

Keywords: acute pancreatitis; neutrophil-to-lymphocyte ratio; severity.

Introduction

Acute pancreatitis is an acute inflammatory disease of the pancreas, with clinical manifestations that range from mild, self-limiting illness to severe disease with organ failure and death .[1] The revised

Atlanta classification stratifies AP into mild, moderately severe and severe based on presence of organ failure and local or systemic complications.[2]

It is necessary to take steps such as enhanced fluid resuscitation, close monitoring and transfer to higher levels of care, which should begin early in patients with identification SAP risk.[3]

Many prognostic scoring systems have been developed including Ranson's score, APACHE II, BISAP, CT severity index (CTSI), C-reactive protein (CRP), and blood urea nitrogen (BUN) .[4] Although these scores are useful, many require multiple variables, are quite complex or have their best predictive capacity 48–72 h after admission, limiting their use in the emergency setting, especially when resources are limited .[5] It is ideal to have simple and affordable biomarker easily available in that environment.

The routine complete blood count reflects the neutrophil-mediated innate immune activation and lymphocyte-mediated adaptive immunity balance. NLR is a well-accepted marker for systemic inflammation and stress in various conditions for sepsis, malignancy and cardiovascular disease.[6]Similarly higher NLR at admission has been shown to correlates with the severity of the disease, organ failure, local complications, length of hospital stay and mortality in case of AP in multiple studies and systematic reviews.[7-9]Reported admission NLR cut-offs to predict any severe outcome common ranged from 4 to 9 with moderate to high sensitivity and specificity.[10-12]The data on NLR in AP in India are still evolving, while India Central has limited reports where mixed urban-rural population and differentetiological patterns could influence NLR. With this presentation, we wish to examine the performance of NLR in our busy public sector teaching hospital. This study was done to study admission NLR as an inflammatory marker in patients with acute pancreatitis managed at a tertiary care centre in Indore and to determine its association with severity and short-term outcomes.

Materials and Methods

Study design and setting

This was a prospective observational study conducted in the Departments of General Medicine at Index Medical College Hospital and Research Centre, Indore, Madhya Pradesh, India, from January 2021 to December 2021. The hospital is a tertiary care teaching institution serving predominantly urban and semi-urban populations.

Study population

All consecutive adult patients (≥18 years) admitted with a diagnosis of acute pancreatitis during the study period were screened. AP was diagnosed by the presence of at least two of the following: (i) characteristic upper abdominal pain; (ii) serum amylase and/or lipase ≥3 times the upper limit of normal; and/or (iii) typical findings of AP on ultrasonography or contrast-enhanced CT scan, according to the revised Atlanta criteria.

Inclusion criteria

- Age ≥18 years
- First episode of acute pancreatitis
- Presentation within 72 hours of onset of abdominal pain
- Availability of complete blood count at admission prior to major intervention

Exclusion criteria

- Chronic pancreatitis or acute-on-chronic pancreatitis
- Known hematological malignancy or chronic inflammatory/autoimmune disorder
- Ongoing corticosteroid or other immunosuppressive therapy
- Active non-pancreatic sepsis or documented infection at admission
- Pregnancy

Sample size

A total of 100 eligible patients who fulfilled inclusion and exclusion criteria and provided written informed consent were included. The sample size was based on feasibility and is comparable with several previous NLR studies in AP.

Data collection

Data were recorded using a structured proforma. Baseline variables included age, sex, presenting symptoms, etiology (gallstones, alcohol, hypertriglyceridemia, post-ERCP, idiopathic, others) and comorbidities. Laboratory parameters at admission included complete blood count, serum amylase, lipase, liver function tests, renal function tests, serum electrolytes and random blood sugar as clinically indicated.

Absolute neutrophil and lymphocyte counts were obtained from automated hematology analyzer reports at admission. NLR was calculated as:

$$\text{NLR} = \frac{\text{Absolute neutrophil count}}{\text{Absolute lymphocyte count}}$$

All patients underwent abdominal ultrasonography; contrast-enhanced CT was performed where indicated. Severity of AP (mild, moderately severe, severe) was classified using the revised Atlanta criteria based on organ failure (transient/persistent) and presence of local or systemic complications.

Patients were followed during hospital stay for development of local complications (acute necrotic collection, peripancreatic collection, pseudocyst, walled-off necrosis), ICU admission, length of hospital stay and in-hospital mortality.

Outcome measures

The main outcome of interest was the association between admission NLR and severity of AP (mild versus moderately severe/severe). Secondary outcomes were the association of admission NLR with ICU admission, occurrence of local complications, length of hospital stay and in-hospital mortality.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using standard statistical software. Continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range) depending on distribution; categorical variables were presented as frequencies and percentages.

Comparisons between mild and moderately severe/severe groups were done using independent t-test or Mann–Whitney U test for continuous variables and chi-square test or Fisher's exact test for categorical variables. ROC curve analysis was performed to assess the diagnostic performance of admission NLR for predicting moderately severe/severe AP, and area under the curve (AUC) was calculated. An optimal cut-off value was derived considering the best trade-off between sensitivity and specificity. A p-value <0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee of Index Medical College Hospital and Research Centre. Written informed consent was obtained from all participants. Patient confidentiality was maintained.

Results

Of the 100 patients included, the mean age was 42.5 ± 13.2 years (range 18–78 years). Males accounted for 58% (n=58) and females for 42% (n=42). Gallstones were the most common etiology (46%), followed by alcohol (32%), hypertriglyceridemia (8%), post-ERCP pancreatitis (5%) and idiopathic/other causes (9%).

Table 1. Baseline demographic and etiological profile (n=100)

Variable	Value
Mean age (years)	42.5 ± 13.2

Male, n (%)	58 (58.0)
Female, n (%)	42 (42.0)
Gallstones, n (%)	46 (46.0)
Alcohol, n (%)	32 (32.0)
Hypertriglyceridemia, n (%)	8 (8.0)
Post-ERCP, n (%)	5 (5.0)
Idiopathic/others, n (%)	9 (9.0)

As per revised Atlanta classification, 68 patients (68%) had mild AP, 22 (22%) moderately severe AP and 10 (10%) severe AP. For further analysis, moderately severe and severe AP were combined into one group (n=32).

Overall, 18 patients (18%) required ICU admission. Local complications occurred in 24 patients (24%). Mean length of hospital stay was 7.8 ± 4.1 days. Six patients (6%) died during hospitalization; all deaths occurred in the severe subset.

Table 2. Severity and outcomes of acute pancreatitis (n=100)

Parameter	Mild AP (n=68)	Mod. severe/severe AP (n=32)
Mean age (years)	40.8 ± 12.6	46.1 ± 13.7
Male, n (%)	36 (52.9)	22 (68.8)
ICU admission, n (%)	4 (5.9)	14 (43.8)
Local complications, n (%)	6 (8.8)	18 (56.3)
Mean hospital stay (days)	5.9 ± 2.3	11.5 ± 4.6
In-hospital mortality, n (%)	0 (0)	6 (18.8)

Differences in ICU admission, complications, length of stay and mortality between groups were statistically significant (all $p<0.01$).

The overall mean admission NLR was 6.1 ± 3.8. Patients with mild AP had significantly lower NLR (4.3 ± 2.1) compared to those with moderately severe/severe AP (9.5 ± 3.9; $p<0.001$).

Table 3. Admission NLR and its association with outcomes

Outcome category	Mean NLR ± SD	p-value
Mild AP	4.3 ± 2.1	<0.001*
Mod. severe/severe AP	9.5 ± 3.9	
No ICU admission	4.7 ± 2.4	<0.001*
ICU admission	10.2 ± 3.6	
No local complications	4.9 ± 2.6	<0.001*
Local complications	9.3 ± 3.8	
Survival	5.8 ± 3.4	0.002*
Non-survival	11.1 ± 4.1	

*Statistically significant

Higher admission NLR was significantly associated with increased severity, ICU requirement, local complications and mortality.

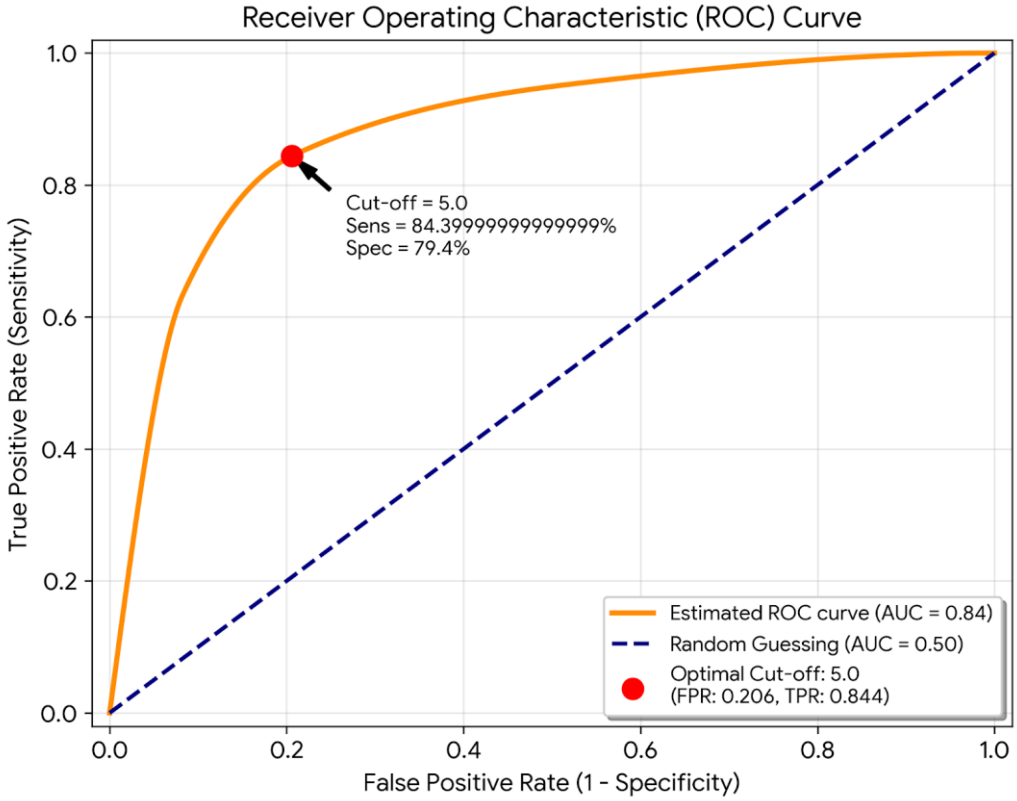
ROC curve analysis demonstrated good discriminative ability of admission NLR for predicting moderately severe/severe AP, with an AUC of 0.84. An NLR cut-off of 5.0 yielded sensitivity of 84.4% and specificity of 79.4% for identifying moderately severe/severe AP.

Table 4. Diagnostic performance of NLR cut-off 5.0 for predicting moderately severe/severe AP

Measure	Value

Area under ROC curve (AUC)	0.84
Optimal NLR cut-off	5.0
Sensitivity (%)	84.4
Specificity (%)	79.4
Positive predictive value (%)	69.1
Negative predictive value (%)	90.0

The ROC curve would show NLR on a continuum along the x-axis and sensitivity plotted against 1-specificity on the y-axis, with the curve bulging well above the diagonal "no-discrimination" line; the point closest to the upper left corner corresponds to the cut-off of 5.0 with the above sensitivity and specificity.



Discussion

A study from tertiary care centre in central India shows that admission NLR is significantly associated with severity and short-term outcomes in acute pancreatitis. Patients with moderately severe/severe acute pancreatitis (AP) had more than double the mean neutrophil to lymphocyte ratio (NLR) of those with mild disease. Higher NLR correlated with increase in ICU admission, local complications, longer hospital stay and mortality. Such results have been reported by earlier studies from India and abroad which state NLR is a useful early prognostic marker in AP.

The mean NLR (neutrophil lymphocyte ratio) found to be 4.3 in mild AP and 9.5 in moderately severe/severe AP in our cohort is similar to that reported by Azab et al.,[6] Jeon et al.[7] and Dutta et al.,[8]where NLR was found to be higher in patients with severe disease than those with mild disease. According to Khanna et al.[2] study, higher admission NLR correlated with more severe disease, necrosis, and showed correlation with BISAP scores in the Indian population. According to a study conducted by Dutta et al. in 2021,[8] there is a significant association between NLR and ICU admission. According to Jeon et al., high NLR independently predicted persistent organ failure and intensive care unit admission. According to a systematic review by Suppiah et al.,[3] NLR and PLR are good inflammatory markers and were consistently elevated in patients with severe AP in a number of cohorts.

According to the study findings, it was reported that an admission NLR cut-off of 5.0 predicted moderately severe/severe AP with 84.4% sensitivity and 79.4% specificity. The cut-offs of 4 and 9 used in previous studies can be referred to as moderate to high in disease severity, organ failure, and mortality prediction accuracy. Researchers Azab et al.[13] proposed that the cut-off can be around 4.7 for adverse outcomes; several others have used 4 to 6 for differentiating mild and severe AP. According to Dutta et al.[8], and other Indian studies the threshold for predicting adverse outcome and ICU requirement was similar. Guo et al. [4] compared NLR with BISAP, CRP and BUN and observed that NLR has a comparable discriminative ability to these established markers and further, that the predictive ability of most was enhanced with the addition of clinical scores. As shown by Papachristou et al.[12] and Singh et al.[11] early systemic inflammatory response and higher prognostic scores predict organ failure and mortality; NLR seems to reflect a similar inflammatory burden in simpler form.

The underlying mechanism of NLR in acute appendicitis can be attributed to systemic inflammatory response and other immune dysregulation. Acute inflammation produces neutrophilia but lymphopenia is caused by stress mediated hormone and cytokine effect and lymphocyte apoptosis and redistribution. NLR is the ratio of these two cellular populations and serves as a straightforwardly measurable index of systemic inflammation and physiological stress. NLR is economical, readily available and does require any additional laboratory infrastructure since it is derived from routine complete venous blood counts, particularly advantageous in resource-limited settings.

In the current study, associations of higher NLR with ICU admission, complications and mortality were noted in cohort, similar to previous studies. The death rate for the severe group was eighteen point eight percent in the above study, which is comparable to other studies on SAP. The organizations advocate the conceivable value of using NLR as an early triage tool: patients presenting with NLR ≥5 may be considered at higher risk, warranting closer observation, early imaging and more vigorous supportive care.[14]

Limitations of the Study NLR is a non-specific marker and may be impacted by co-infections, chronic inflammatory diseases, blood disorders and medications such as corticosteroids. Many of these were excluded, but we cannot fully exclude subclinical diseases. The NLR measurement was only taken at first admission, but serial NLR should provide additional prognostic information.[2-4,7-9] Single centre design and modest sample size may limit generalizability. Also, long-term outcomes including readmission and late complications were not measured.

Notwithstanding these limitations, this study will be additional evidence for the NLR as a useful low-cost adjunct for early stratification of risk in AP patients from Indian tertiary centres. [2,3,6-9]. Larger multi-centre studies would validate optimal cut-off values, study serial trends of NLR and incorporate NLR into composite prognostic models along with scores like BISAP, APACHE II and CTSI along with biochemical markers like CRP, BUN, etc.[3,4,10-12]

Conclusion

Patients with moderately severe and severe acute pancreatitis had an elevated admission neutrophil-to-lymphocyte ratio, which correlated with an increased likelihood of ICU admission, local complications, prolonged hospital stay, and in-hospital mortality. A cut-off NLR of 5.0 showed a very good sensitivity and specificity for predicting more severe disease, comparable to literature values. Due to its simplicity, low cost and easy availability, NLR can be used as an adjunctive inflammatory marker for early risk stratification of patients with acute pancreatitis and in resource-limited settings.

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