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Original Research Article

Serial neutrophil-to-lymphocyte ratio and disease severity in acute biliary pancreatitis: a prospective observational study

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ABSTRACT

Background: The neutrophil-to-lymphocyte ratio (NLR) is an inexpensive marker of systemic inflammation, but its prognostic performance varies with timing and population. This study assessed the association of NLR measured at admission and 48 hours with final severity of acute biliary pancreatitis.
Methods: This prospective observational study was conducted at Lady Hardinge Medical College and Associated Hospitals, New Delhi, from January 2021 to June 2022. Thirty adults with acute biliary pancreatitis were included. NLR was assessed within 6 hours of presentation and repeated at 48 hours. Severity was classified using the Revised Atlanta Classification. Group comparisons and exploratory receiver operating characteristic (ROC) analyses were performed.
Results: The cohort included 30 patients (mean age 38.2±11.8 years; 21 [70.0%] women). Final severity was mild in 18 (60.0%), moderately severe in 8 (26.7%) and severe in 4 (13.3%); no in-hospital deaths occurred. Median admission NLR was 9.70 (interquartile range [IQR], 5.68–21.76) in severe disease and 3.52 (IQR, 2.92–7.50) in mild/moderately severe disease (p=0.061). At 48 hours, corresponding values were 6.17 (IQR, 5.17–7.70) and 2.90 (IQR, 2.14–4.33; p=0.002). ROC area under the curve was 0.798 at admission and 0.947 at 48 hours. At exploratory thresholds of >4.65 and >4.67, sensitivity was 100% at both time points, while specificity was 61.5% and 84.6%, respectively.
Conclusions: In this small cohort, 48-hour NLR was associated with final disease severity, whereas the admission comparison did not reach statistical significance. Thresholds are exploratory and require external validation.

Keywords: Acute biliary pancreatitis, Neutrophil-to-lymphocyte ratio, Disease severity, Prognosis, Receiver operating characteristic curve

INTRODUCTION

Acute pancreatitis ranges from a self-limited illness to severe disease complicated by persistent organ failure. The Revised Atlanta Classification defines severe acute pancreatitis by organ failure persisting for more than 48 hours and provides a standard framework for severity assessment.[1] Early identification of patients at risk of deterioration is important, although commonly used scoring systems require multiple clinical and laboratory variables. The neutrophil-to-lymphocyte ratio (NLR), calculated from a routine differential blood count, is a readily available but nonspecific marker of systemic inflammation. Previous studies have examined its association with severity and adverse outcomes in acute pancreatitis.[2-5] Studies published in International Surgery Journal have also evaluated NLR in unselected acute pancreatitis cohorts.[6,7] Studies focused on gallstone pancreatitis and large observational cohorts add to this evidence base.[8,9] A recent systematic review found that NLR performance varies by measurement time, outcome definition and patient population; a single universal

threshold is not supported by the available evidence.[10] Evidence specifically focused on acute biliary pancreatitis and serial NLR measurements remains limited. This study evaluated the association between NLR measured at admission and 48 hours and final severity of acute biliary pancreatitis. The analysis was exploratory and was not designed to establish a definitive clinical decision threshold.

METHODS

Study design and participants

This prospective observational study was conducted in the Department of General Surgery, Lady Hardinge Medical College and Associated Hospitals, New Delhi, India, between January 2021 and June 2022. Adults aged 18–65 years presenting with acute biliary pancreatitis were eligible. Acute pancreatitis was diagnosed when at least two of the following were present: characteristic abdominal pain; serum amylase and/or lipase at least three times the upper limit of normal; or characteristic findings on ultrasonography, computed tomography or magnetic resonance imaging. Biliary aetiology was established by imaging evidence of gallstones.

Exclusion criteria were chronic liver or lung disease, malignancy, previous pancreatic surgery, presentation more than 48 hours after symptom onset, chemotherapy during the preceding month, steroid or antibiotic use, blood transfusion during the preceding month, and signs or symptoms of infection in another organ system. Thirty patients were included. The thesis protocol estimated a sample size of 42; the final cohort was smaller than this target.

NLR measurement and outcome definition

Differential leukocyte counts were recorded within 6 hours of presentation and repeated 48 hours after admission. NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count, or equivalently from the percentages when both were derived from the same differential count. Patients were followed during admission and classified as having mild, moderately severe or severe disease according to the Revised Atlanta Classification.[1] Severe disease was defined by persistent organ failure lasting more than 48 hours. For severe-versus-nonsevere analyses, mild and moderately severe cases were combined.

Statistical analysis

Categorical variables are presented as counts and percentages; continuous variables are summarised as mean and standard deviation or median and interquartile range (IQR), as appropriate. Kruskal–Wallis tests were used for comparisons across three severity categories, and Mann–Whitney U tests for severe-versus-nonsevere comparisons. Fisher exact tests assessed associations at the thesis-reported NLR thresholds. Two-sided exact permutation p values were used for Mann–Whitney U comparisons. ROC analysis was used to estimate discrimination; AUC confidence intervals were calculated using the DeLong method. Confidence intervals for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using exact binomial methods. Analyses were exploratory because only four patients developed severe disease. Reporting was guided by the STROBE recommendations for observational studies.[11] A $p<0.05$ was considered statistically significant.

Ethics

The study was approved by the Institutional Ethics Committee of Lady Hardinge Medical College and Associated Hospitals (LHMC/IEC/2020/PG Thesis/61; 29 December 2020). Written informed consent was obtained from all participants. Patients received standard departmental care.

RESULTS

Participant characteristics and clinical course

Thirty patients were included. Mean age was 38.2±11.8 years; 21 (70.0%) were women and 9 (30.0%) were men. Final disease severity was mild in 18 (60.0%), moderately severe in 8 (26.7%) and severe in 4 (13.3%) patients. No in-hospital deaths were recorded. Median hospital stay was 4 days (Table 1).

NLR at admission and 48 hours

Median NLR at admission was 3.38 in mild, 4.27 in moderately severe and 9.70 in severe disease; the difference across the three groups was not statistically significant (Kruskal–Wallis p=0.161). At 48 hours, the respective medians were 3.17, 2.39 and 6.17, with a significant difference across severity categories (p=0.009; Table 2). When severe disease was compared with the combined mild/moderately severe group, median admission NLR was 9.70 (IQR, 5.68–21.76) versus 3.52 (IQR, 2.92–7.50; p=0.061). At 48 hours, corresponding values were 6.17 (IQR, 5.17–7.70) versus 2.90 (IQR, 2.14–4.33; p=0.002; Table 3).

Exploratory threshold and ROC analyses

At the admission threshold of NLR>4.65, all four severe cases were above the threshold, as were ten nonsevere patients; 16 nonsevere patients had NLR≤4.65 (Fisher exact p=0.037). At 48 hours, an NLR threshold >4.67 classified all four severe cases and four nonsevere cases above the threshold; 22 nonsevere patients had NLR≤4.67 (Fisher exact p=0.003). The reported ROC AUC was 0.798 at admission and 0.947 at 48 hours (Table 4). These estimates are imprecise because only four severe outcomes occurred.

Table 1: Baseline characteristics and final severity.

Characteristic	Result
Number of participants	30
Age, mean±SD, years	38.2±11.8
Women, N (%)	21 (70.0)
Men, N (%)	9 (30.0)
Final mild acute pancreatitis, N (%)	18 (60.0)
Final moderately severe acute pancreatitis, N (%)	8 (26.7)
Final severe acute pancreatitis, N (%)	4 (13.3)
In-hospital death, N (%)	0 (0)
Hospital stay, median days	4

Abbreviations: SD, standard deviation.

Table 2: NLR by final severity category.

Final severity	N	Admission NLR, median (IQR)	NLR at 48 h, median (IQR)
Mild	18	3.38 (2.92–7.33)	3.17 (2.50–4.67)
Moderately severe	8	4.27 (2.69–11.06)	2.39 (2.07–3.46)
Severe	4	9.70 (5.68–21.76)	6.17 (5.17–7.70)
Kruskal–Wallis p value	—	0.161	0.009

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; IQR, interquartile range.

Table 3: NLR in severe versus non-severe disease.

Measurement	Severe (n=4), median (IQR)	Mild/moderately severe (n=26), median (IQR)	P value
At admission	9.70 (5.68–21.76)	3.52 (2.92–7.50)	0.061
At 48 hours	6.17 (5.17–7.70)	2.90 (2.14–4.33)	0.002

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; IQR, interquartile range.

Table 4: Exploratory performance at thesis-reported NLR thresholds.

Metric	Admission NLR >4.65	NLR at 48 h >4.67
True positive / false positive	4 / 10	4 / 4
False negative / true negative	0 / 16	0 / 22
Sensitivity, % (exact 95% CI)	100 (39.8–100)	100 (39.8–100)
Specificity, % (exact 95% CI)	61.5 (40.6–79.8)	84.6 (65.1–95.6)
Positive predictive value, % (exact 95% CI)	28.6 (8.4–58.1)	50.0 (15.7–84.3)
Negative predictive value, % (exact 95% CI)	100 (79.4–100)	100 (84.6–100)
Fisher exact p value	0.037	0.003
ROC AUC (95% CI)	0.798 (0.527–0.933)	0.947 (0.787–0.989)

Abbreviations: CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio; ROC AUC, area under the receiver operating characteristic curve. Estimates are exploratory and imprecise because only four patients had severe disease.

DISCUSSION

In this prospective single-centre cohort of 30 patients with acute biliary pancreatitis, 48-hour NLR was associated with final disease severity, whereas the admission NLR comparison between severe and nonsevere groups did not reach statistical significance. The ROC AUC was numerically higher at 48 hours than at admission. These findings suggest that serial NLR may reflect the evolving inflammatory course, but the study does not establish a validated prediction rule or demonstrate that NLR adds value beyond established clinical assessment.

The results are consistent with earlier studies reporting associations between NLR and acute pancreatitis severity or adverse outcomes.[2-7] NLR is appealing because it can be derived from a routine blood count without additional testing. However, it is nonspecific and may be influenced by concurrent infection, medications, physiological stress

and other inflammatory conditions.[12] The 2026 systematic review by Chooklin and Chuklin highlighted variation in thresholds and substantial heterogeneity across studies, supporting the use of NLR as an adjunct rather than a stand-alone decision rule.[10] The apparent 100% sensitivity at both thresholds should be interpreted cautiously because only four participants developed severe disease. At the admission threshold, PPV was 28.6%; at 48 hours, PPV was 50.0%. Thus, high sensitivity in this small cohort did not establish a high probability of severe disease among patients with a positive result. Predictive values also depend on the prevalence of severe disease. Thresholds were assessed in the same cohort in which their performance was evaluated, which may overestimate accuracy. The 48-hour measurement requires additional caution. Persistent organ failure for more than 48 hours is part of the definition of severe acute pancreatitis.[1] Depending on the exact timing of blood sampling and onset or resolution of organ failure, the 48-hour NLR may partly reflect the clinical course used to classify severity rather than provide an independent early prediction. Future studies should prespecify outcome timing and evaluate whether NLR adds predictive information to established scores and routine clinical variables.

Limitations

Limitations include the small sample size, only four severe outcomes, single-centre design, assessment of thresholds in the same cohort, and absence of external validation. The study was not powered to assess mortality, and no in-hospital deaths occurred. No multivariable model or formal assessment of incremental value over established severity scores was performed. Because the 48-hour measurement coincides with the period used to define persistent organ failure, it may partly reflect evolving severity rather than independent prediction. The reported statistics should be checked against the original patient-level dataset before submission.

CONCLUSION

In this small prospective cohort, 48-hour NLR was associated with final severity of acute biliary pancreatitis, while the admission comparison did not reach statistical significance. The proposed thresholds and their apparent diagnostic performance are exploratory and should not guide clinical decisions without validation. Larger prospective studies with prespecified outcomes, adequate numbers of severe cases and independent validation are required.

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