

Original Research Article

Prognostic value of neutrophil to lymphocyte ratio in acute gall stone and alcoholic pancreatitis

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ABSTRACT

Background: Acute pancreatitis (AP) is associated with increased mortality. Many scoring systems have been used to predict the severity of acute pancreatitis but they are either time consuming or done after 48 hours of admission. The aim of the study was to evaluate the prognostic value of Neutrophil to lymphocyte ratio (NLR) in acute gall stone and alcoholic pancreatitis.

Methods: 240 patients with acute pancreatitis were prospectively enrolled from December 2017 to December 2019 from the department of general surgery and gastroenterology at St. John's Medical College, Bangalore. NLR obtained at admission were compared with other known prognostic scoring systems.

Results: A total of 240 patients were studied with an etiology of gall stone (N=131) and alcohol (N=109). NLR (17.6 ± 18.3 vs 8.7 ± 8.4 , $p < 0.001$) were significantly high in gall stone pancreatitis group whereas high NLR were not related to severe AP in alcoholic AP. For gall stone pancreatitis group NLR demonstrated a predictive value and not in alcoholic AP.

Conclusions: NLR can be used as a predictor of severity of acute pancreatitis, at the time of initial diagnosis. Our study demonstrated that NLR can predict the severity in gall stone pancreatitis.

Keywords: Acute pancreatitis, Neutrophil to lymphocyte ratio, Gall stone pancreatitis, Severity

INTRODUCTION

Acute pancreatitis (AP) is one of the most common cause of emergency admissions in our country. AP is an acute inflammatory process of the pancreas that starts with local acinar cell injury with variable involvement of other regional tissues or remote organ system.¹ Although the majority of the acute pancreatitis cases are mild and self-limiting, severe cases can be accompanied by complications such as acute pancreatitis (SAP), high mortality rates of up to 50% have been reported. The severity of acute pancreatitis is related to extra pancreatic organ failure secondary to the patient's systemic inflammatory response, and a poor prognosis of SAP is

thought to be the result of uncontrolled systemic inflammatory response syndrome.^{2,3}

White blood cell count (WBC) are non-specific markers of systemic inflammation that can be measured using routine serum haematological tests. In addition, the WBC count is correlated with poor prognosis as a compositional element of Ranson's criteria, Glasgow score, Acute physiology and chronic health evaluation- II (APACHE- II), and bedside index of severity. However total WBC count can fluctuate based on various physiological and pathological conditions including hydration status, stress, and how the blood specimen is handled.^{4,5} Neutrophils and lymphocytes reflect the immune response better than the total WBC count. 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.

The objectives of this study were (a) to assess the clinical usefulness of the NLR to predict severe acute pancreatitis at an early stage and; (b) to evaluate the adverse outcomes in severe AP by incorporating NLR as a scoring tool.

METHODS

This prospective observational study was conducted from December 2017 to December 2019 in department of General Surgery and Gastroenterology at St. Johns' Medical College Hospital. We included the patients who visited our hospital for the primary visit and patients referred from other centers were excluded. Written consent was obtained from all patients.

The diagnosis of AP requires 2 of the following 3 criteria: typical abdominal pain; serum amylase or lipase elevation ≥ 3 times the upper limit of normal; and characteristic findings of AP on contrast-enhanced computed tomography, magnetic resonance imaging, or abdominal ultrasonography.⁶ Etiologies other than gallstone and alcohol were excluded.

All patients were followed until discharge from the hospital. Data collected included: demographic details, symptoms, vitals at admission, comorbidities, laboratory investigations and NLR at admissions were noted. Ethical committee clearance was taken prior to this study.

Data collection

Blood samples for hematological and biochemical data were obtained within 1 hour of admission. NLR were defined as the quotient of absolute neutrophil count to absolute lymphocyte count. Ranson score, Computed tomography scoring index (CTSI), and BISAP score were also calculated upon admission.

Statistical analysis

Continuous variables are presented as mean and standard deviation. Categorical variables are presented as frequency and percentage. Continuous variables in 2 groups were compared using Student's t-test, and categorical variables were compared using the chi-square test. P values less than 0.05 were considered statistically significant, and all statistical analyses were performed using SPSS software, version 21.

RESULTS

A total of 240 patients were enrolled (Table 1). The etiologies of acute pancreatitis were gallstone (N=131) and alcohol (N=109). Mean age was higher in the gallstone AP group, whereas the male-to-female ratio and proportion of smokers were lower. We found no significant difference in body mass index or proportion of patients with diabetes mellitus in the two groups. Hypertension and liver cirrhosis were more frequent in patients with alcoholic AP than in those with gallstone AP. According to the Atlanta classification, more patients with moderately severe and severe pancreatitis were classified into the alcoholic AP group. Mean Ranson and BISAP scores on admission did not differ between gallstone and alcoholic AP, but mean CTSI was significantly higher in the gallstone AP group. The mean duration of hospital stay did not differ between the two groups. However, the number of admissions to the Intensive care unit (ICU) and mortality were significantly higher in the alcoholic AP group.

We performed subgroup analysis according to AP etiology (Tables 2 and 3). For gallstone AP, NLR was significantly higher in severe pancreatitis, as defined by the revised Atlanta classification (32.4 ± 30.9 vs 17.1 ± 17.4 , $p=0.045$), Ranson score ≥ 3 (24.8 ± 19.6 vs 12.1 ± 15.1 , $p<0.001$), and BISAP score ≥ 3 (28.6 ± 20.7 vs 16.3 ± 17.6 , $p=0.012$) (Table 2). In the alcoholic AP group, higher NLR was significantly correlated only with Ranson score ≥ 3 (11.9 ± 10.9 vs 6.5 ± 4.7 , $p<0.001$) (Table 3).

Table 1: Baseline characteristics.

Characteristics	Overall (N=240)	Gall stones (N=131)	Alcohol (N=109)	P value
Age (year)	59.3 \pm 17.2	66.0 \pm 17.1	50.3 \pm 14.5	<0.001
Sex				
Male	166 (68.3%)	37 (27.6%)	94 (86.2%)	<0.001
Female	74 (31.7%)	60 (76.3%)	14 (23.7%)	<0.001
BMI (kg/m ²)	23.6 \pm 3.8	24 \pm 3.4	23.7 \pm 4.4	<0.001
Diabetes mellitus	62 (25.5%)	35 (26.1%)	27 (24.8%)	0.591
Hypertension	85 (35%)	56 (41.8%)	29 (26.6%)	0.810
Liver cirrhosis	21 (8.6%)	7 (5.2%)	14 (12.8%)	0.014
Smoking	114 (46.9%)	37 (27.6%)	77 (70.6%)	<0.001
Atlanta classification				
Mild	160 (66.2%)	106 (79.8%)	54 (54.5%)	<0.001
Moderate	56 (23.4%)	20 (15.7%)	36 (33%)	
Severe	24 (10.2%)	6 (4.4%)	18 (17.4%)	

Continued.

Characteristics	Overall (N=240)	Gall stones (N=131)	Alcohol (N=109)	P value
Scoring systems				
Ranson	2.4±1.7	2.4±1.5	2.4±1.8	0.998
CTSI	1.9±1.7	1.2±1.3	2.4±1.8	<0.001
BISAP	1.3±1.1	1.2±1.1	1.4±1.3	0.236
Laboratory data				
WBC (/mm ³)	11,936±5569	12,023±5172	11,828±6043	0.787
Neutrophil (/mm ³)	10.2±7.1	10.8±8.1	9.4±5.4	0.126
Lymphocyte(/mm ³)	1.2±1.0	1.1±1.0	1.5±0.9	<0.001
NLR	7.2±6.5	6.9±5.9	7.7±7.2	0.292
Hospital stay (day)	13.8±15.3	17.7±18.3	8.8±8.4	
ICU admission	51(21.4%)	14 (11.2%)	36 (33.9%)	<0.001

Note: BMI- Body mass index, CTSI- Computed tomography severity index, BISAP- Bedside index for severity in AP, WBC white blood count, NLR- Neutrophil to lymphocyte ratio.

Table 2: Neutrophil to lymphocyte ratio in gallstone pancreatitis

Parameters	NLR value	P value
Atlanta classification		
Mild/moderate	17.1±17.4	0.045
Severe	32.4±30.9	
Ranson		
<0.001		0.001
<3	12.1±15.1	
≥3	24.8±19.6	
CTSI		
<3	16.3±17.9	0.083
≥3	23.1±19.1	
BISAP		
<3	16.3±17.6	0.012
≥3	28.6±20.7	

Note: CTSI- Computed tomography severity index, BISAP- Bedside index for severity in AP, NLR- Neutrophil to lymphocyte ratio.

Table 3: Neutrophil to lymphocyte ratio in alcoholic pancreatitis.

Parameters	NLR value	P value
Atlanta classification		
Mild/moderate	8.7±8.3	0.606
Severe	9.8±8.8	
Ranson		
<3	6.5±4.7	0.001
≥3	11.9±10.9	
CTSI		
<3	7.5±7.8	0.107
≥3	10.1±8.7	
BISAP		
≥3	10.1±11.6	0.417

Note: CTSI- Computed tomography severity index, BISAP- Bedside index for severity in acute pancreatitis, NLR- Neutrophil to lymphocyte ratio, PLR- Platelet to lymphocyte ratio.

DISCUSSION

In this study, we evaluated the value of NLR as a predictive markers of AP severity. We found that NLR were well correlated with other scoring systems in patients with gallstone AP. However, in patients with alcoholic AP, NLR were not correlated with other scoring systems. NLR was first introduced as an easily measurable parameter

assessing systemic inflammation and stress in critically ill patients.^{7,8} The prognostic value of this parameter has been confirmed in a variety of clinical conditions, and was shown to be superior to NLR in certain cancers.⁹ AP is an inflammatory condition characterized by activation of both innate and adaptive immune responses. Activation and modulation of neutrophils and lymphocytes play a core role in establishing host defenses in settings of systemic

inflammation; however, excessive inflammatory response causes massive cell transmigration to the pancreas and subsequent release of aggressive defense molecules, resulting in destruction of the pancreas and organ failure.¹⁰⁻¹²

Therefore, we investigated the prognostic value of NLR in two distinct forms of AP. We excluded pancreatitis caused by factors other than gallstone and alcoholism. In alcoholic AP, NLR was a significant predictor. This can be explained by the different mechanism of alcohol AP. Alcoholic AP is usually associated with chronic liver disease. In our results, the number of liver cirrhosis patients was larger. Therefore, NLR can vary according to liver function as well as systemic inflammation. Although elevated NLR can be used as predictive biomarker in AP, interpretation should follow confirmation of the etiology.

Limitations

This study had few limitations. First, the number of patients enrolled were small, and this study was performed in a tertiary care center, which could have resulted in disproportionate inclusion of patients with severe disease status and tendency to progress to persistent organ failure. Such selection bias might have overestimated the predictive value of elevated NLR. Second, we did not compare NLR with other biochemical markers, such as procalcitonin and IL-6 or CRP. Despite these limitations, this study also has strengths. This prospective study investigated the predictive value of NLR in AP and the difference between it in two subgroups of AP. Also, all laboratory values were obtained within 1 hour of initial presentation, minimizing changes in WBC counts caused by hydration and medication.

CONCLUSION

In conclusion, NLR is a significant independent predictive marker in gallstone AP as compared to alcoholic AP. NLR can be used as an early diagnostic tool to predict the severity of acute pancreatitis and its adverse outcomes.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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