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Original Research Article

Neutrophil to lymphocyte ratio (NLR) in acute pancreatitis as an early predictor of severity and outcome

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ABSTRACT

Background: The management of Acute Pancreatitis (AP) is determined by an accurate assessment of severity of the disease. Numerous severity indicators have been described till date, most of which require reassessment after admission and resuscitation. We propose a novel indicator, the Neutrophil to Lymphocyte ratio (NLR), as a predictor of severity of acute pancreatitis at the initial time of diagnosis. NLR may have a role in predicting the length of hospital stay and ICU admission and also to predict adverse manifestations of Severe Acute Pancreatitis (SAP) including organ failure.
Methods: A retrospective analysis was performed of 107 patients diagnosed with acute pancreatitis based on Atlanta 2012 definitions, who were admitted and treated between August 2017 and November 2017. The patients were grouped according to severity of acute pancreatitis and organ failure occurrence and a comparative analysis was performed to compare the NLR between groups. NLR was also compared with the modified Marshall score as a standard predictor of organ failure in acute pancreatitis.
Results: Median NLR among the severe group is significantly higher compared to mild and moderate group (P <0.001). NLR significantly correlated with length of hospital stay (p 0.004) and also had a statistically significant correlation with ICU stay (p < 0.001). We found in our study that NLR at admission correlated significantly with the modified Marshall score in predicting the organ failure (p <0.001) in patients with acute pancreatitis. The receiver operator characteristic (ROC) curve analysis showed a cut-off values of NLR >8.5 at admission correlated with adverse outcomes in patients with acute pancreatitis.
Conclusions: Neutrophil to Lymphocyte ratio (NLR) can be used as a predictor of severity of acute pancreatitis, right at the time of initial diagnosis. Further it may predict adverse outcomes, need for ICU care as well as length of hospital stay. NLR can be used as a tool to refer at risk patients to tertiary center needing ICU admission.

Keywords: Acute pancreatitis, Neutrophil to Lymphocyte ratio, Organ failure, Severe Acute Pancreatitis

INTRODUCTION

Acute pancreatitis, accounts for the most common causes of emergency hospital admissions in India. Yet, no prevalence data are available from India. The clinical presentation varies widely from no symptoms to systemic inflammatory response syndrome (SIRS), persistent organ failure (POF) and death.[1] The management of patient with acute pancreatitis is determined by an accurate assessment of severity of the disease.

A series of scoring systems have been designed to stratify the severity of acute pancreatitis. As it is important to recognize those patients, who are at risk to progress to

severe acute pancreatitis (SAP) at the earliest, as the overall mortality due to SAP is 15-20%.[2,3] Numerous severity indicators have been described till date, require assessment at admission and reassessment after resuscitation. In patients with Acute Pancreatitis, a large number of unnecessary investigations are done which increase the financial burden, thus not feasible in the rural Indian set up. However, prediction of severity during the early stage remains challenging.

The objectives of the study included (a) to determine the severity of acute pancreatitis at an early stage using the Neutrophil to Lymphocyte ratio (NLR) and correlate with other established severity indices like Revised Atlanta Classification (b) to demonstrate the usefulness of NLR in predicting the length of hospital stay and ICU admission (c) to predict manifestation of SAP(Severe acute pancreatitis) and organ failure in the early stages (d) to determine an optimal cut-off value for the prediction of adverse outcomes.

METHODS

This retrospective observational cohort was conducted from August 2017 to December 2017 in department of General Surgery and Gastroenterology at St. Johns' Medical College Hospital. The study included all patients aged above 18 years as diagnosed case of acute pancreatitis based on clinical/laboratory/ radiological diagnosis as per Revised Atlanta criteria.[4] Exclusion criteria's included patients aged below 18 years of age, patients diagnosed as acute on chronic pancreatitis and in patients with incomplete investigations or missing medical records. Ethical committee clearance was taken prior to study.

Definitions: Patients were diagnosed with acute pancreatitis if more than 2 of the following conditions were satisfied: (1) abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back); (2) serum amylase and/or lipase level at least 3 times greater than the upper limit of the normal value; and (3) characteristic manifestation of acute pancreatitis on contrast-enhanced computed tomography, magnetic resonance imaging, or transabdominal ultrasonography.[4]

Acute pancreatitis was categorized into mild acute pancreatitis (MAP), moderately severe acute pancreatitis, and severe acute pancreatitis (SAP) in accordance with the revised Atlanta classification.[4] Data collected included demographics, symptoms, vitals at admission, laboratory investigations and NLR at admission was noted.

During the course of hospitalization, outcomes of the disease including organ failure, duration of hospital stay was noted. Modified Marshall score for all patients was noted. In subset, patients with other severity indices (BISAP, APACHE) if documented was also noted.

Statistical analysis

Data was analysed using SPSS (V21). Number and percentages were used for the categorical variables. Mean and standard deviation (SD) were calculated for the normally distributed continuous variables. Median, 25th and 75th percentiles were calculated for non-normally distributed continuous variables. Chi-square test was used to test the association between categorical variables. Analysis of variance was used to compare the normally distributed variable between the three categories of SAP, multiple comparison using Bonferroni correction.

Kruskal Wallis test was used to compare the non-normally distributed variable between the three categories of SAP, 2 group Correlation coefficients was used to assess the reliability between NLR with other scores. ROC curve was done to arrive a cut off for NLR ratio. P value <0.05 was considered as statistically significant.

RESULTS

A total of 107 patients were studied (n = 107). Mean age 39.5 years with male-to-female ratio of 5:1. All these patients presented with pain abdomen (100%). Time duration between onset of pain abdomen and hospital admission had median of 2 days (IQR 1, 4). Other associated symptoms included nausea and vomiting (77.5%), Fullness of abdomen (33%), Dyspnea (12.3%).

Most common etiology in our study was found to be Alcoholism (65.8%) followed by Gall stones (13.1%). Others causes also included post ERCP (4.7%), Hypertriglyceridemia (3.8%), Hypercalcemia (0.9%), Trauma (2.8%), Idiopathic (8.9%).

Table 1: Severity as per revised Atlanta classification.

Severity of pancreatitis	No.	(%)
Mild	51	47.7
Moderate	24	22.4
Severe	32	29.9

Severity of pancreatitis among 107 patients as per the Revised Atlanta classification were noted (Table 1) and median NLR in each of the mild, moderate and severe groups were studied (Table 2).

Table 2: Median NLR in each of the groups.

	Mild N=50	Moderate N=24	Severe N=32	P value
Median NLR	5.94	7.17	11.9	<0.0001
25th, 75th percentiles	2.97, 9.94	6.04, 10.0	8.84, 15.7	

We found in the present study that median NLR among the severe group is significantly higher compared to mild and moderate group (p<0.001). Although the median

NLR is higher among moderate group compared to mild group, it was not statistically significant (p=0.06).

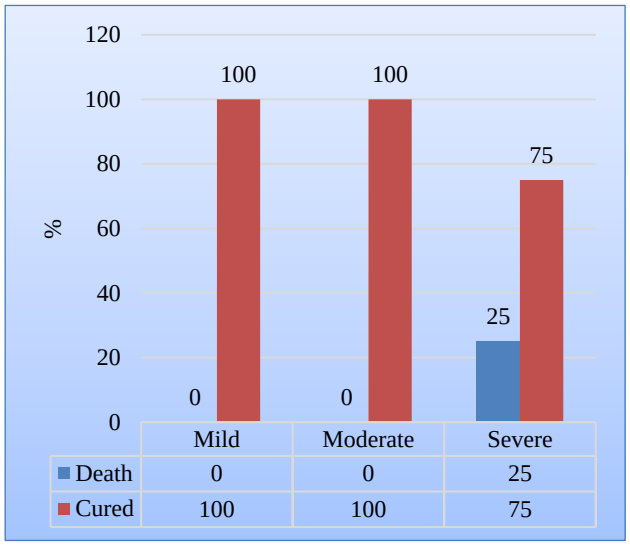

Figure 1: Association between severity of disease with mortality.

We also found in our study that NLR at admission significantly correlated to total duration of hospitalization (r=0.28, p value 0.004) and ICU stay (r =0.40, p value <0.001) among these patients. 36.4% of these patients were in SIRS at admission. 31.8% of these patients developed MODS during the course of hospitalization. Outcome was cured in 92.5% of patients and 7.5% mortality was noted. Median NLR was higher among death group as compared to cured group (Figure1).

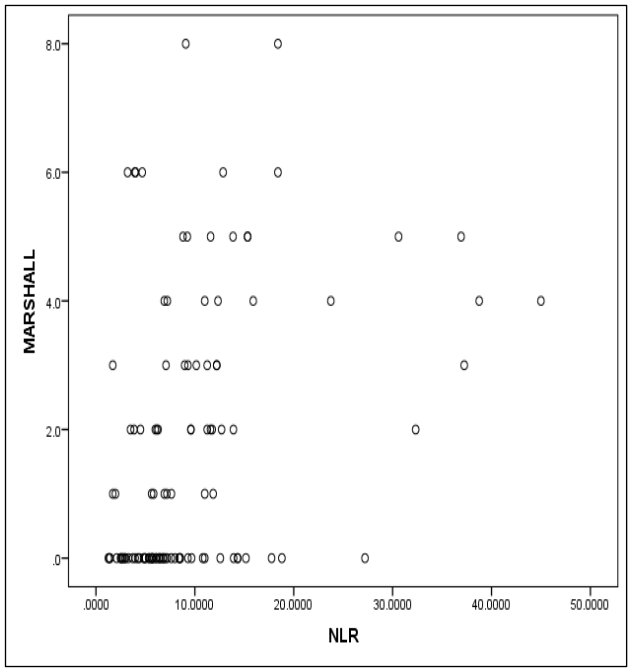

Figure 2: Scatter plot showing correlation of organ failure between NLR at admission and modified Marshall score.

Modified Marshall score was calculated in all these patients to predict the organ failure which was found to correlate significantly with NLR at admission with p value <0.001 (Figure 2).

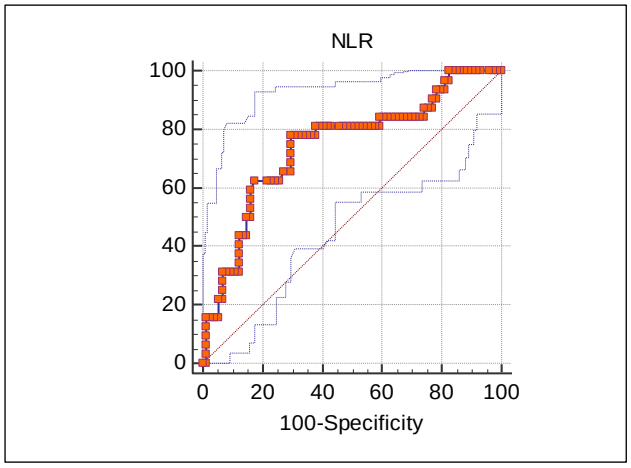

Figure 3: ROC to obtain optimal cut off value of NLR.

NLR at admission was found to be statistically significant in subset of patients with documented APACHE II (r=0.502, p value<0.0001) and BISAP (r=0.665, p value <0.0001).

NLR at admission of all patients were analyzed and its utility for predicting severity of acute pancreatitis was evaluated by receiver operator characteristic (ROC) curve analysis to obtain optimal cut off (figure 3), NLR >8.5 at admission, correlated with severity of acute pancreatitis, longer duration of hospital stay and ICU stay with sensitivity of 78.12% and a specificity of 70.27%.

DISCUSSION

Acute pancreatitis is an inflammatory process in which local pancreatic injury leads to systemic inflammation through cytokine cascade activation5. Due to varied presentations of acute pancreatitis, multiple severity scoring systems have been designed, to help clinicians in triaging acute pancreatitis patients and predicting their prognosis. 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 (SIRS) or multi-organ dysfunction syndrome (MODS).[4,6-8]

Ranson's score presents a great advantage to assess disease severity, its disadvantage being it requires 48 hours data. Similarly, although it is very easy to use, the Atlanta classification is unable to differentiate between moderately acute pancreatitis and severe acute pancreatitis within 48 hours of onset. Although Bedside Index of Severity in Acute Pancreatitis BISAP provides quick data, it is complicated, cumbersome, and with low sensitivity. In addition, the white blood cell (WBC) count

is correlated with poor prognosis as a compositional element of Ranson's criteria, Acute Physiology and Chronic Health Evaluation-II (APACHEII), and Bedside Index of Severity in Acute Pancreatitis (BISAP), which are the prognostic scoring systems of acute pancreatitis.[7,9] However, fluctuations have been noted in WBC count depending on the various physiological and pathological conditions including hydration status, stress, and pregnancy in addition to handling of blood specimen.[9] Neutrophils and lymphocytes reflect the immune response better than the WBC count.

As severity of acute pancreatitis, at the initial stage of manifestation is critical to improve the patient's prognosis.[6,10] Therefore, there is a need for a simple indicator that can easily predict the patient's prognosis within 24 hours of the manifestation of the disease.[6,10] The NLR was computed by calculating the ratio of the absolute neutrophil and lymphocyte counts, and the analysis was conducted using the NLR values on the day of hospitalization. This study demonstrated that the NLR was elevated in patients presenting with acute pancreatitis and that NLR can be used to classify patients according to disease severity and the presence of organ failure. NLR is predictive and can be assessed at the early stages which is repeatable, easily accessible and inexpensive. Drawbacks of this study included small sample size, also NLR is not specific for acute pancreatitis, as it is only measurable parameter of systemic inflammation. Also, this study needs further prospective validation cohort.

CONCLUSION

To conclude Neutrophil to Lymphocyte ratio (NLR) can be used as a predictor of severity of acute pancreatitis, right at the time of initial diagnosis. Further it may be predictive of risk of adverse outcomes, need for ICU care as well as length of hospital stay. NLR can be used as a tool to refer at risk patients to tertiary centre needing ICU admission.

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

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