

A PROSPECTIVE STUDY ON NEUTROPHIL LYMPHOCYTE RATIO AND PLATELET LYMPHOCYTE RATIO AS EARLY PREDICTOR OF NECROSIS IN ACUTE PANCREATITIS

Suryasish Sengupta¹, Joydeep Ghosh², Nikhil Agrawal³, Md. Waheduzzaman⁴

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Corresponding Author:

Dr. Nikhil Agrawal,

Email: agrawalnikhil6687@gmail.com

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¹Assistant Professor, Department of General Surgery, Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, 99 Sarat Bose Road, Kolkata, India.

²Assistant Professor, Department of General Surgery, Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, 99 Sarat Bose Road, Kolkata – 700026

³Assistant Professor, Department of General Surgery, Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, 99 Sarat Bose Road, Kolkata – 700026

⁴2nd Year PGT General Surgery, Department of General Surgery, Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, 99 Sarat Bose Road, Kolkata, India.

Abstract

Background: Acute pancreatitis (AP) is a rapidly growing pancreatic inflammatory illness that varies in severity and clinical presentation. It is one of the most common disorders of the gastrointestinal system. Between 4.9 and 73.4 cases of AP are reported globally for per 100,000 individuals. The study aims to investigate the Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) can serve as early predictors of necrosis in patients with acute pancreatitis. **Materials and Methods:** The present study was a Comparative study. This Study was conducted for 1 year at Multi Speciality hospitals in Kolkata. Total 100 patients were included in this study. **Result:** In Mild group, the mean NLR (mean±s.d.) of patients was 1.30 ± 0.42 . In Severe, the mean NLR (mean±s.d.) of patients was 10.15 ± 2.41 . Distribution of mean NLR with Severity of AP was statistically significant ($p < 0.001$). In Mild group, the mean PLR (mean±s.d.) of patients was 125.38 ± 21.51 . In Severe, the mean PLR (mean±s.d.) of patients was 180.89 ± 51.12 . Distribution of mean PLR with Severity of AP was statistically significant ($p < 0.001$). In Mild group, the mean Hospital stay (days) (mean±s.d.) of patients was 10.23 ± 2.31 . In Severe, the mean Hospital stay (days)(mean±s.d.) of patients was 17.63 ± 4.12 . Distribution of mean Hospital stay (days) with Severity of AP was statistically significant ($p < 0.001$). **Conclusion:** In conclusion, this prospective study demonstrates the potential of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as early, accessible, and cost-effective predictors of necrosis in patients with acute pancreatitis. By identifying patients at higher risk for complications early in the disease course, these markers could help guide more aggressive monitoring and management strategies, potentially improving patient outcomes. Further research with larger cohorts and diverse populations is warranted to validate these findings and better integrate NLR and PLR into clinical practice for acute pancreatitis.

INTRODUCTION

Acute pancreatitis (AP) is a rapidly growing pancreatic inflammatory illness that varies in severity and clinical presentation. It is one of the most common disorders of the gastrointestinal system. Between 4.9 and 73.4 cases of AP are reported globally for per 100,000 individuals. While most patients with AP have a reasonable prognosis and a mild state, 15% to 20% of them have a severe clinical course with higher rates of morbidity and death.^[1]

Gallstones and alcohol addiction are the primary risk factors for AP, along with medicines, trauma, ischemia, neoplasms, infections, endoscopic retrograde cholangiopancreatography (ERCP), pharmaceuticals, and genetic factors. The numerous different etiological elements that lead to an AP attack are caused by uncertain processes.^[2]

Early identification of those at risk for severe acute pancreatitis (SAP) is essential for timely treatment and therapy optimization. A variety of severity grading methods have been proposed and accepted in

order to assess and classify the severity of AP in the modern world. The most often utilized ones in routine clinical practice are the Bedside Index for Severity in Acute Pancreatitis (BISAP) score, Ranson criteria, and APACHE II system.^[3]

Among several serum biochemical markers, serum procalcitonin (>1.8 ng/mL) and C-reactive protein (CRP) ≥ 150 mg/L at 48 hours post-admission have been adopted as prognostic factors for the management of AP. Also, serum levels of the inflammatory mediators interleukin (IL) 6, 8, and IL-10 have been found to be accurate for predicting persistent organ dysfunction in AP patients.^[4]

These serum indicators, however, are costly, difficult to obtain, and unable to accurately predict the course or severity of AP. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are two recently suggested widely available indicators that offer a quick assessment of the degree of inflammation in patients with AP. secondary to the lack of information regarding the usage of PLR and NLR in SAP prediction in our community. The purpose of this study is to determine if patients with acute pancreatitis can benefit from using the Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) as early indicators of necrosis.

MATERIALS AND METHODS

Study Area: Multi Speciality hospitals in Kolkata, India

Study Design: Comparative study

Study Period: 1 year

Inclusion criteria

- Patients diagnosed with acute pancreatitis based on clinical symptoms (e.g., abdominal pain) and confirmed by imaging (e.g., CT scan, MRI) or elevated pancreatic enzymes (amylase/lipase).
- Adults aged 18 years and above.
- Patients (or legal guardians, if applicable) must provide informed consent to participate in the study.
- Patients without a history of chronic pancreatitis, pancreatic cancer, or previous pancreatic surgery.

Exclusion criteria:

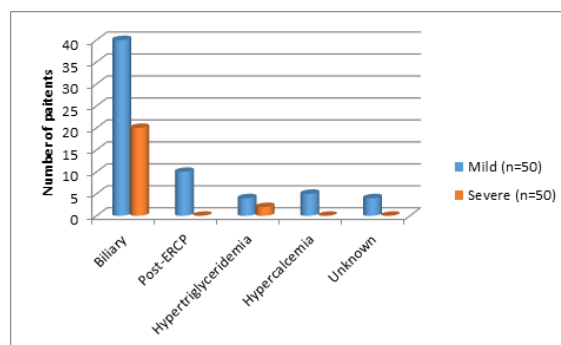
- Patients with chronic pancreatitis.
- Patients with hematological disorders (e.g., leukemia, lymphoma).
- Patients on immunosuppressive therapy (e.g., steroids, chemotherapy).
- Pregnant women and Pediatric patients

Sample Size: A total of 100 samples have been included in this study.

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests, which

compare the means of independent or unpaired samples, were used to assess differences between groups. Paired t-tests, which account for the correlation between paired observations, offer greater power than unpaired tests. Chi-square tests (χ^2 tests) were employed to evaluate hypotheses where the sampling distribution of the test statistic follows a chi-squared distribution under the null hypothesis; Pearson's chi-squared test is often referred to simply as the chi-squared test. For comparisons of unpaired proportions, either the chi-square test or Fisher's exact test was used, depending on the context. To perform t-tests, the relevant formulae for test statistics, which either exactly follow or closely approximate a t-distribution under the null hypothesis, were applied, with specific degrees of freedom indicated for each test. P-values were determined from Student's t-distribution tables. A p-value ≤ 0.05 was considered statistically significant, leading to the rejection of the null hypothesis in favour of the alternative hypothesis.

RESULTS



In Mild, 20(40%) patients had Diabetes mellitus, 8(16%) patients had Ischaemic heart disease and 16(32%) patients had Chronic kidney disease In Severe, 2(4%) patients had Diabetes mellitus, 10(20%) patients had Ischaemic heart disease and 21(42%) patients had Chronic kidney disease. Association of Comorbidities with Severity of AP was not statistically significant ($p=0.25$). In Mild, 40(80%) patients had Biliary, 10 (20%) patients had Post-ERCP, 4 (8%) patients had Hypertriglyceridemia and 5 (10%) patients had Hypercalcemia In Severe, 20 (40%) patients had Biliary and 2(4%) patients had Hypertriglyceridemia. Association of Aetiologies with Severity of AP was not statistically significant ($p=0.18$).

In Mild group, the mean Age (year) (mean \pm s.d.) of patients was 50.59 ± 8.79 . In Severe, the mean Age (year) (mean \pm s.d.) of patients was 46.95 ± 6.84 . Distribution of mean Age (year) with Severity of AP was not statistically significant ($p=0.22$). In Mild group, the mean Hemoglobin (g/dl) (mean \pm s.d.) of patients was 11.56 ± 1.23 . In Severe, the mean Hemoglobin (g/dl) (mean \pm s.d.) of patients was 12.09 ± 0.67 . Distribution of mean Hemoglobin (g/dl) with

Severity of AP was statistically significant ($p=0.08$). In Mild group, the mean Platelets (103/ul) (mean \pm s.d.) of patients was 245.56 ± 51.98 . In Severe, the mean Platelets (103/ul) (mean \pm s.d.) of patients was 215.98 ± 56.32 . Distribution of mean Platelets (103/ul) with Severity of AP was not statistically significant ($p=0.65$). In Mild group, the mean Leucocytes (103/ul) (mean \pm s.d.) of patients was 6.98 ± 1.11 . In Severe, the mean Leucocytes (103/ul) (mean \pm s.d.) of patients was 7.88 ± 1.71 . Distribution of mean Leucocytes (103/ul) with Severity of AP was not statistically significant ($p=0.56$). In Mild group, the mean Albumin (mg/dl) (mean \pm s.d.) of patients was 39.58 ± 3.45 . In Severe, the mean Albumin (mg/dl) (mean \pm s.d.) of patients was 28.78 ± 4.44 . Distribution of mean Albumin (mg/dl) with Severity of AP was statistically significant ($p<0.001$). In Mild group, the mean Alanine transmarine (u/L) (mean \pm s.d.) of patients was 46.87 ± 10.31 . In Severe, the mean Alanine transmarine (u/L) (mean \pm s.d.) of patients was 49.09 ± 10.58 . Distribution of mean Alanine transmarine (u/L) with not Severity of AP was statistically significant ($p=0.76$). In Mild group, the mean Aspartate transaminase (u/L) (mean \pm s.d.) of patients was 51.45 ± 5.55 . In Severe, the mean Aspartate transaminase (u/L) (mean \pm s.d.) of patients was 50.50 ± 12.43 . Distribution of mean Aspartate transaminase (u/L) with not Severity of AP was statistically significant ($p=0.3$). In Mild group, the mean Creatinine (mg/dl) (mean \pm s.d.) of patients was 1.09 ± 0.1 . In Severe, the mean Creatinine (mg/dl) (mean \pm s.d.) of patients was 2.01 ± 0.41 . Distribution of mean Creatinine (mg/dl) with Severity of AP was statistically significant ($p<0.001$). In Mild group, the mean C-reactive protein (mg/dl) (mean \pm s.d.) of patients was 15.67 ± 3.63 . In Severe, the mean C-

reactive protein (mg/dl) (mean \pm s.d.) of patients was 30.87 ± 4.21 . Distribution of mean C-reactive protein (mg/dl) with Severity of AP was statistically significant ($p<0.001$). In Mild group, the mean RDW (%) (mean \pm s.d.) of patients was 11.11 ± 2.61 . In Severe, the mean RDW (%) (mean \pm s.d.) of patients was 15.32 ± 0.96 . Distribution of mean RDW (%) with Severity of AP was statistically significant ($p=0.03$). In Mild group, the mean APACHE-II score (mean \pm s.d.) of patients was 4.88 ± 0.95 . In Severe, the mean APACHE-II score (mean \pm s.d.) of patients was 10.14 ± 2.21 . Distribution of mean APACHE-II score with Severity of AP was statistically significant ($p<0.001$).

In Mild group, the mean NLR (mean \pm s.d.) of patients was 1.30 ± 0.42 . In Severe, the mean NLR (mean \pm s.d.) of patients was 10.15 ± 2.41 . Distribution of mean NLR with Severity of AP was statistically significant ($p<0.001$). In Mild group, the mean PLR (mean \pm s.d.) of patients was 125.38 ± 21.51 . In Severe, the mean PLR (mean \pm s.d.) of patients was 180.89 ± 51.12 . Distribution of mean PLR with Severity of AP was statistically significant ($p<0.001$). In Mild group, the mean Hospital stay (days) (mean \pm s.d.) of patients was 10.23 ± 2.31 . In Severe, the mean Hospital stay (days)(mean \pm s.d.) of patients was 17.63 ± 4.12 . Distribution of mean Hospital stay (days) with Severity of AP was statistically significant ($p<0.001$). In Mild, 10 (20%) patients had ICU admission. In Severe, 15(30%) patients had ICU admission Association of ICU admission with Severity of AP was statistically significant ($p<0.001$). In Mild, 1 (2%) patient was Mortality. In Severe, 8 (16%) patients had Mortality. Association of Mortality with Severity of AP was statistically significant ($p<0.001$).

Table 1: Demographic variable data based on severity of AP.

	Variable	Severity of AP		P value
		Mild (n=50)	Severe (n=50)	
Comorbidities	Diabetes mellitus	20(40%)	2(4%)	0.25
	Ischaemic heart disease	8(16%)	10(20%)	
	Chronic kidney disease	16(32%)	21(42%)	
	Nothing	6(12%)	17(34%)	

Table 2: Mean baseline data of the studied based on severity of AP

Variable	Severity of AP		P value
	Mild (n=50)	Severe (n=50)	
Age (year)	50.59 ± 8.79	46.95 ± 6.84	0.22
Hemoglobin (g/dl)	11.56 ± 1.23	12.09 ± 0.67	0.08
Platelets (103/ul)	245.56 ± 51.98	215.98 ± 56.32	0.65
Leucocytes (103/ul)	6.98 ± 1.11	7.88 ± 1.71	0.56
Albumin (mg/dl)	39.58 ± 3.45	28.78 ± 4.44	<0.001
Alanine transmarine (u/L)	46.87 ± 10.31	49.09 ± 10.58	0.76
Aspartate transaminase (u/L)	51.45 ± 5.55	50.50 ± 12.43	0.3
Creatinine (mg/dl)	1.09 ± 0.1	2.01 ± 0.41	<0.001
C-reactive protein (mg/dl)	15.67 ± 3.63	30.87 ± 4.21	<0.001
RDW (%)	11.11 ± 2.61	15.32 ± 0.96	0.03
APACHE-II score	4.88 ± 0.95	10.14 ± 2.21	<0.001

Table 3: NLR and PLR based on severity of AP

Variable	Severity of AP		P value
	Mild (n=50)	Severe (n=50)	
NLR	1.30 ± 0.42	10.15 ± 2.41	<0.001
PLR	125.38 ± 21.51	180.89 ± 51.12	<0.001
Hospital stay (days)	10.23 ± 2.31	17.63 ± 4.12	<0.001
ICU admission	10 (20%)	15(30%)	<0.001
Mortality	1 (2%)	8 (16%)	<0.001

DISCUSSION

The clinical extent of AP varies widely from no symptoms to systemic inflammatory response syndrome (SIRS), persistent organ failure (POF), and death. The clinical presentation of AP is both unreliable and nonspecific and exhibits a sensitivity less than 40% for the prediction of adverse outcomes.^[5]

Furthermore, little is known about the underlying pathophysiology that leads from local pancreatic damage to SIRS. Multiple severity grading systems have been developed to assist doctors in triaging patients with acute pancreatitis (AP) and predicting their prognosis, owing to the varied presentations of AP and its unclear pathogenesis.^[6] Currently, there is widespread usage of the Ranson score, the Glasgow-Imrie criteria, the BISAP score, and the Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score. These methods involve a lot of variables, which makes them time-consuming and challenging to apply to patients outside of intensive care units. Furthermore, they are inappropriate for evaluating patients at the time of admission or soon after.^[7]

In a recent review by Shah et al,^[8] it was declared that the APACHE II scoring system had the highest accuracy for predicting severe AP when compared with other scoring systems. However, the APACHE II scoring system is exhaustive and cannot be widely adopted for AP patients outside the intensive care setting.

Also in a previous study, it was demonstrated that the APACHE II score had just a 67% PPV at 24 h after admission and was even less accurate for identifying patients with specific complications such as peripancreatic fluid collections or major organ failure.^[9]

In recent years, researchers have been interested in determining the most practical and accurate parameter indicative of the severity and prognosis of AP. Some researchers have found that no statistically significant pairwise differences were observed between the APACHE-II and the other scoring systems, including CRP value at 24 hours, BISAP, Ranson, and Balthazar scores.^[10]

In the current study, we aimed to assess the use of NLR and PLR in prediction of severity of SAP. The study enrolled 100 patients with AP. Out of those patients, based on the revised Atlanta Criteria, 10 (20%) patients had Post-ERCP in Mild group.

In Mild group, the mean Age (year) (mean±s.d.) of patients was 50.59 ± 8.79 In Severe, the mean Age

(year) (mean±s.d.) of patients was 46.95 ± 6.84 Distribution of mean Age (year) with Severity of AP was not statistically significant (p= 0.22).

Gezer et al,^[11] reported that regarding a variety of laboratory parameters, the NLR, PLR, RDW, glucose, and blood urea nitrogen (BUN) level of the SAP group were significantly increased compared to the MAP group on admission (P<0.001). The severity of AP increased as the NLR, SOFA, BISAP, and Ranson increased (P<0.01). The SAP group had significant lower albumin level compared to MAP group (P<0.001).

NLR showed the best discrimination ability for severe hypertriglyceridemia-induced AP, as shown by Wang et al.^[12] İlhan et al,^[13] looked at 30 healthy pregnant controls and 14 patients who acquired AP throughout their pregnancy. The results showed that there was no significant difference in PLR between the AP group and the controls, but there was a substantial increase in NLR.

Han et al,^[14] declared that NLR on admission within 48h had the highest AUC for predicting severe AP, with a cut-off value of 6.66, and NLR was also significantly positively correlated with the Ranson score and hospital stays.

CONCLUSION

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have the potential to be used as early, accessible, and affordable indicators of necrosis in patients with acute pancreatitis, as this prospective investigation has demonstrated. These indicators have the potential to improve patient outcomes by identifying individuals who are more susceptible to problems early in the course of the disease and guiding more aggressive surveillance and management techniques. To effectively integrate NLR and PLR into clinical management for acute pancreatitis and confirm these findings, bigger cohort and broad population research is needed.

REFERENCES

1. Tenner S, Baillie J, DeWitt J et al. (2013): American College of Gastroenterology guideline: management of acute pancreatitis. Official Journal of the American College of Gastroenterology, 108:1400-1415.
2. Boxhoorn L, Voermans R, Bouwense S et al. (2020): Acute pancreatitis. Lancet, 396:726-734. 5.
3. Tee Y, Fang H, Kuo I et al. (2018): Serial evaluation of the SOFA score is reliable for predicting mortality in acute severe pancreatitis. Medicine, Medicine (Baltimore), 97(7):e9654.

4. Brand M, Götz A, Zeman F et al. (2014): Acute necrotizing pancreatitis: laboratory, clinical, and imaging findings as predictors of patient outcome. *American Journal of Roentgenology*, 202:1215-1231
5. Banks P, Bollen T, Dervenis C et al. (2013): Classification of acute pancreatitis-2012. *Classification of acute pancreatitis. Gut*, 62(1):102-11.
6. Cho S, Jung S, Lee K et al. (2018): Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio can predict the severity of gallstone pancreatitis. *BMC Gastroenterology*, 18:1-6.
7. Pavlidis T, Pavlidis E, Sakantamis A (2010): Advances in prognostic factors in acute pancreatitis: a mini-review. *Hepatobiliary & Pancreatic Diseases International*, 9:482-486.
8. Shah A, Mourad M, Bramhall S (2018): Acute pancreatitis: current perspectives on diagnosis and management. *Journal of Inflammation Research*, 11:77- 82.
9. Larvin M, McMahon M (1989): APACHE-II score for assessment and monitoring of acute pancreatitis. *The Lancet*, 334:201-205.
10. Cho J, Kim T, Chung H et al. (2015): Comparison of scoring systems in predicting the severity of acute pancreatitis. *World Journal of Gastroenterology*, 21:2387-2394
11. Gezer N, Bengi G, Baran A et al. (2020): Comparison of radiological scoring systems, clinical scores, neutrophil-lymphocyte ratio and serum C-reactive protein level for severity and mortality in acute pancreatitis. *Revista da Associação Médica Brasileira*, 66:762-770
12. Wang Y, Fuentes H, Attar B et al. (2017): Evaluation of the prognostic value of neutrophil to lymphocyte ratio in patients with hypertriglyceridemia-induced acute pancreatitis. *Pancreatology*, 17:893-897
13. İlhan M, İlhan G, Gök A et al. (2016): Evaluation of neutrophil–lymphocyte ratio, platelet–lymphocyte ratio and red blood cell distribution width–platelet ratio as early predictor of acute pancreatitis in pregnancy. *The Journal of Maternal-Fetal & Neonatal Medicine*, 29:1476-1480.
14. Han C, Zeng J, Lin R et al. (2017): The utility of neutrophil to lymphocyte ratio and fluid sequestration as an early predictor of severe acute pancreatitis. *Scientific Reports*, 7:1-8.