Neutrophil-to-lymphocyte ratio as Predictor of outcome in Acute Pancreatitis

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Abstract

Background : Acute pancreatitis (AP) is a commonly encountered emergency in children. It has always been tough to predict accurately among the AP patients who will become progressively unwell. Simple prognostic marker such as neutrophil-to-lymphocyte ratio (NLR) could identify such patients. This study was done to assess the usefulness of this marker in case of clinic AP.

Methods : This Cross-sectional descriptive study was conducted from July 2018 to June 2020 at the department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Thirty-one children with abdominal pain aged between 3-15 years diagnosed as acute pancreatitis as per INSPPIRE criteria were included in this study.

The detailed clinical history, physical examination findings and investigation reports were recorded in a predesigned standard data sheet. Complete blood count (CBC) report from each patient on admission was obtained which included white blood cell (WBC) count with differentials, Neutrophil-to-lymphocyte ratio (NLR) was measured manually by using the absolute value of neutrophil and lymphocyte. Outcomes of acute pancreatitis were observed in terms of cure or survival or mortality. Data was analyzed by SPSS version 25. All continuous variables were presented as mean. For all statistical tests $p < 0.05$ was considered statistically significant.

Results : The mean age of the patients was 11.19 (±3.45) years. The mean neutrophil-to-lymphocyte ratio (NLR) was 4.49 (±3.99). Total thirty patients (97%) were recovered and one patient (3%) expired during hospital stay. Thirteen patients (41.9%) developed complications among which ascites were most common, present in 12(38.7%). Eighteen patients had no complications among them 15 patients were with NLR < 5. A total of 9 patients had complications among them 6 (46.2%) were with NLR ≥ 5. Mean length of hospital stay (LOS) for NLR < 5 group was 9.32 days while that mean was 9.78 days for ≥ 5 NLR group.

Conclusion : It was found that elevated NLR on admission had an unfavorable clinical outcome for pediatric patients with acute pancreatitis (AP) although statistical significance could not be established. Therefore, multicenter studies with larger sample size are required for making some clinically applicable inference.

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Introduction

Acute pancreatitis is a common acute emergency in children. The incidence has been increased in the last two decades,[1] ranging from 3.6 to 13.2 cases per 100,000 children [2,3]with a mortality rate between 4% and 10%.[4,5] Acute pancreatitis in children is diagnosed in the presence of at least 2 of the following criteria: 1) sudden onset of abdominal pain compatible with acute pancreatitis 2) Elevation of serum amylase and/or lipase more than three times of the upper limits of normal and 3) characteristic imaging findings compatible of acute pancreatitis.[6] Characteristic findings in imaging include pancreatic edema, fat stranding, peripancreatic fluid collections on abdominal imaging.[7] In infants and toddlers, symptoms may be subtle, vomiting, irritability and abdominal distension may suggest AP.[8]

The serum amylase has been the universal laboratory test used to establish the diagnosis of acute pancreatitis(AP).[9] The specificity for a serum amylase in determining acute pancreatitis can be increased by using a cutoff of more than 2 to 3 times of the upper limit of normal.[10] Also in AP, serum lipase is usually increased within 6 hours of symptoms, serum levels reached to peak at 24 to 30 hours and can remain elevated for

more than 1 week. Some advocate that serum lipase without serum amylase is sufficient to diagnose AP, as lipase is a more sensitive and specific marker of AP (87%–100% and 95%–100%, respectively).[6]

Up to 25% of AP cases in children have complications. [11] At present, there are several clinical scoring systems for predicting severity of AP. Ranson and Glasgow modified scores 11 have been adopted based on studies in adult populations; consequently, their validity in pediatric patients is limited. The Pediatric Acute Pancreatitis Severity Score (PAPS) was the first severity prediction score designed with data obtained from children, with a sensitivity of 70%.[11]Later,developed a scale for the Japanese pediatric population (JPN), obtaining a sensitivity of 80%.[12]

Neutrophil-to-lymphocyte ratio (NLR) is a simple measure of systemic inflammation, calculated from the parameters supplied with a full blood count report. NLR assesses two complimentary immunological pathways. Neutrophils activate non-specific immune cascades and have been shown to play an important role in the pathogenesis of acute pancreatitis in animal models. An elevated NLR has been shown to be associated with poorer outcomes in acute stroke, acute coronary syndrome and colorectal cancer. An elevated NLR has also been suggested as a simple haematological predictor of adverse outcome in acute pancreatitis.[13]

So, the aim of this study was to assess the usefulness of neutrophil-to-lymphocyte ratio (NLR) on admission, independently and in combination, as predictors of severity and poorer clinical outcomes for the patients with acute pancreatitis, especially in children.

Materials and methods

This Cross-sectional descriptive study was carried out in the Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka, Bangladesh from July 2018 to June 2020. Children with abdominal pain aged between 3-15 years diagnosed as acute pancreatitis as per INSPPIRE criteria[14] were included in this study. Any other co-morbid condition except the consequences of acute pancreatitis, patient with chronic pancreatitis and patient with pain abdomen due to other causes were excluded. Total 31 cases were selected purposively from children presenting with abdominal pain diagnosed clinically as acute pancreatitis admitted at the Department of Pediatric Gastroenterology and Nutrition, BSMMU. During recruitment, objectives of the study were explained to the parents and written consent was obtained. The detailed clinical history, physical examination findings and investigation reports were recorded in a predesigned standard data sheet. Blood samples were collected in the department of Pediatric Gastroenterology and Nutrition for laboratory workup. Complete blood count (CBC) report from each patient on admission was obtained which included white blood cell (WBC) count with differentials, Neutrophil-to-lymphocyte ratio (NLR) was measured manually by using the absolute value of neutrophil and lymphocyte. Outcomes of acute pancreatitis were observed in terms of cure or survival or mortality. Overall length of in-patient stay (LOS) was assessed as a secondary outcome. Data was analyzed with SPSS version 25. All continuous variables were presented as mean. For all statistical tests $p< 0.05$ was considered as statistically significant.

The study did not involve any social, psychological or legal risk to patients and their family and the study was approved by Institutional Review Board (IRB), BSMMU.

Results

A total of 31 patients were included in this study. The mean age of the pediatric patients was 11.19 (±3.45) years, and female were predominant (55%). (Table-I).

Table I: Summary of patient characteristics (N-31)

Characteristics	
Total number of patients	31(100%)
Male	14(45%)
Female	17(55%)
Mean age	11.19(±3.45) years
Minimum age	3.8 years
Maximum age	14.4 years

Among the studied patients 13 patients developed multiple complications (41.9%) among which ascites was most frequently found (38.7%). Pleural effusion was found in 7 patient (22.6%), pancreatic necrosis and pancreatic fluid collection were found in 6(19.4%) and 5 (16%) patients respectively. (Table-II)

Table II: Outcomes of studied population (n-31)

Variables	Frequency	Percentage (%)
Recovery	30	97
Complications	13	41.9
Ascites	12	38.7
Pleural Effusion	7	22.6
Pancreatic necrosis	6	19.4
Pancreatic fluid collection	5	16
Hypocalcaemia	4	12.9
Shock	3	9.7
Pancreatic cyst/pseudocyst	2	6.5
Mortality	1	03

• Multiple Responses

In our Study 6 patients with NLR <5 developed ascites and 6 patients with NLR >5 also developed ascites (no difference), while 4 patients with NLR >5 developed pleural effusion (44.4%).(Table-III)

Table III: Correlation between complications and NLR (n-13)

	NLR		Fisher's Exact Test	p-value
	<5	≥5		
	n (%)	n (%)		
Ascites	6 (27.3)	6 (66.7)	4.171	0.056
Pleural effusion	3 (13.6)	4 (44.4)	3.468	0.150
Hypocalcaemia	2 (9.1)	2 (22.2)	.980	0.560
Pancreatic necrosis	5 (22.7)	1 (11.1)	.552	0.642
Shock	1 (4.5)	2 (22.2)	2.283	0.195
Pancreatic cyst	2 (9.1)	0 (0.0)	.875	1.00

In our study, 7 patients (53.8%) with NLR<5 had complications while six patients (46.2%) with NLR ≥5 had complications. More than 83% patients with NLR<5 did not have any complications while only 16.7% with NLR ≥5 had no complications. (Table IV)

Table IV: Cross tabulation between NLR and complications (n-31)

	Complications		Fisher's Exact Test	*p*-value
NLR	Yes	No		
	n (%)	n (%)		
<5	7 (53.8)	15 (83.3)	3.186	0.114
≥5	6 (46.2)	3 (16.7)		
Total	**13 (100.0)**	**18 (100.0)**		

Among the studied children, mean length of hospital stay for NLR<5 group was 9.32 days while that mean was 9.78 days for ≥ 5 NLR group.This association was not statistically significant (p>0.05).(Table V)

Table V: Comparison of length of hospital stay with NLR (n-31)

Variable	NLR	n	Mean	t-value	*p*-value
Length of hospital stay (days)	<5	22	9.32	-0.323	0.749
	≥5	9	9.78		

Discussion

In the present study, the mean age of the pediatric patients was 11.19 (±3.45) years.The minimum age of presentation was 3.8 years and 20 (64.51%) patients were aged > 10 years (maximum age was 14.4 years). Several studies have reported an increasing incidence of acute pancreatitis in all pediatric age groups over the past two decades.[15,16] In a study that included 55,012 children with acute pancreatitis, the disease was found to be more likely to occur in children older than 5 years old (median age, 17 years) and to occur slightly more frequently in girls than in boys.[16]

Pancreatitis causes substantial morbidity in the pediatric population. It is estimated that 2–13 new cases occur annually per 100,000 children.[17]Nearly one-quarter of children with acute pancreatitis develop severe complications, and the mortality rate is approximately 4–10% despite significant advances in the treatment of this disease.[16,18] According to a study, the median inpatient length of stay for children with pancreatitis in 2009 was 4 days.[16] In the current study the median inpatient length of stay was higher i.e. 9 days. Lack of skilled manpower and emergency diagnostic facilities could be causes for such discrepancy.

Out of 13 cases (41.9%) who developed complications, 12 patients (38.7%) developed ascites and 7 (22.8%) patients had pleural effusion. Three patients were presented with shock (9.7%). Among local pancreatic complications, pancreatic necrosis was found in 6 (19.4%) patients while pancreatic pseudocyst was found in only two patients (6.5%). In a study with 50 pediatric patients with acute pancreatitis from former BSMMU showed that 6% patients had pancreatic pseudocyst and pancreatic necrosis was observed in 2% cases.[19] They also found hypocalcemia in 38% patients,[19] but in our study only four patients (12.9%) had hypocalcemia.

Patients were categorized in to two groups on the basis of NLR score. Seven patients (53.8%) with NLR<5 had complications while 6 patients (46.2%) with NLR ≥5 had complications. More than 83% patients with NLR<5 did not have any complications while only 16.7% with NLR ≥5 had no complications. However, these differences were not statistically significant. O'Connell et al. (2018) reported similar finding that NLR above 5 is associated with poorer prognosis in patients with acute pancreatitis.[13]In his study, 17 patients (63.24%) had a NLR above 5 on admission of which 2 died, while no patient with a NLR below 5 died (p-0.278). Fourteen patients with elevated NLR on presentation required ICU or HDU admission (11.97%; RR 8.137, p-0.01), and the mean LOS was significantly longer in these patients (8.6 v 6.0 days; p-0.01).[13]

Early deaths (within the first week) due to severe AP is generally caused by massive inflammatory responses, which result in multiple organ failure, and late deaths (after 1–3 weeks) is caused by multiple organ dysfunction with infections and sepsis.[20,21]

Conclusion

Acute pancreatitis in children is an increasing health problem. The current study was done to assess the usefulness of neutrophil-to-lymphocyte ratio (NLR) as predictor of the in-hospital outcomes in patients with acute pancreatitis in children. It was found that elevated NLR on admission had an unfavorable clinical outcomes for patients with acute pancreatitis, although the statistical significance were not established.

Limitations of the study

The current study had the following limitations:

Small sample size.

Single center study.

A cross-sectional design and single mortality limiting the ability to

assess the sensitivity and specificity of NLR in predicting mortality of patients with AP.

It focused on the predictive role of this marker on admission, so any potential predictive value of changes in the NLR over time was not assessed. These methods of risk prediction were not directly compared with established clinically used criteria, such as Glasgow-Imrie, Ranson or APACHE II.[11]

Recommendation

Further multicenter well-designed, large sample-sized study should be done to establish the role for using NLR on admission to predict severity and outcomes for patients with pediatric acute pancreatitis.

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