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Red Cell Distribution width (RDW) and Neutrophil-to-lymphocyte Ratio (NLR) as Predictors of Outcome in Acute Pancreatitis

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Abstract:

Background: *Acute pancreatitis is a commonly encountered emergency in children. It has always been tough to predict accurately among the patients who will become systemically unwell. Simple prognostic markers, such as red cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR), could identify such patients. This study was done to assess the usefulness of those markers.*

Methods: *This cross-sectional study was conducted from July 2018 to June 2020 at department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka. Thirty-one children with abdominal pain diagnosed as acute pancreatitis were included by purposive sampling in the study.*

Results: *The mean age of the pediatric patients was 11.19 (±3.45) years. The mean red cell distribution width was 14.99 (±2.96) and mean neutrophil-to-lymphocyte ratio was 4.49 (±3.99). Total thirty patients (97%) were recovered and one patient (3%) died in hospital stay. Thirteen patients (41.9%) developed complications among which ascites was more common (12, 38.7%). NLR> 5 was observed in higher proportion in the study subjects with complications (46.2%) than without complications (16.7%) without any statistically significant difference. RDW e"14 was found in 53.8% study subjects with complications and 50% without complications. However, no statistically significant difference was found. Length of hospital stay was longer in patients with NLR >5 than with NLR d"5. RDW <14 was associated with longer hospital stay than RDW e"14. There was no statistically significant difference.*

Conclusion: *It was found that elevated RDW and NLR on admission had unfavorable clinical outcomes for pediatric patients with acute pancreatitis although statistical significance could not be established. Further multicenter studies with larger sample size are required for making some clinically applicable inference.*

Key words: *Acute pancreatitis, predictors, outcome, NLR, RDW*

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Introduction:

Acute pancreatitis (AP) is a commonly encountered emergency in children and the incidence has 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 two of the following criteria: sudden onset of abdominal pain compatible with acute pancreatitis, elevation of serum amylase and/or lipase more than three times of the upper limits of normal and

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characteristic imaging findings compatible of acute pancreatitis [6]. Characteristic findings 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 [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 the upper limit of normal [10]. Also in AP, serum lipase is usually increased within 6 hours of symptoms; serum levels 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. Several clinical scoring systems for predicting severity, e.g., Ranson and Glasgow modified scores, 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].

Red cell distribution width (RDW) is a laboratory parameter routinely reported in our institution as part of the full blood count, which is a measure of erythrocyte anisocytosis – the variation in the size of circulating red blood cells. A higher RDW implies a greater degree of anisocytosis. Elevated RDW has been shown to predict poor outcome in septic shock, acute myocardial infarction and in critically ill patients in general [13]. It has previously been identified as a potential biomarker for the prediction of morbidity and mortality in acute pancreatitis[14,15]. It has been suggested that RDW increases in severe acute pancreatitis because the systemic inflammatory response suppresses haematopoiesis and erythrocyte maturation, leading to increased levels of circulating immature reticulocytes, which are larger in size [14].

Neutrophil-to-lymphocyte ratio (NLR) is a simple measure of systemic inflammation, calculated on the basis of parameters usually 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 elevated red cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR) on admission as predictors of poor clinical outcomes for the patients with acute pancreatitis.

Materials and methods:

This cross-sectional study was carried out in the Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka, Bangladesh. From July 2018 to June 2020. Patients aged bellow 18 year who got admitted as a case of acute pancreatitis, among them 31 were selected purposively fulfilling the inclusion and exclusion criteria were included in this study. 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, red cell distribution width (RDW) etc. from department of hematology of BSMMU. Neutrophil-to-lymphocyte ratio (NLR) was measured manually by using the absolute value of neutrophil and lymphocyte. NLR was considered normal up to 5 and RDW considered normal when the value is <14 (as per reference value given by Haematology department of BSMMU). Outcomes of acute pancreatitis were observed as proportion of complications and mortality. Overall length of in-patient stay (LOS) was assessed as a secondary outcome. Data was analyzed by SPSS for Windows

(using version 25.0). All continuous variables were presented as mean. Statistical significance was determined by Chi-square (or Fisher Exact test where applicable) and Student's t-test. For all statistical tests $p < 0.05$ was considered as statistically significant.

Ethical issues:

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:

Table-I

Summary of patient characteristics.

Characteristics	
Total number of patients	31
Male	14(45%)
Female	17(55%)
Mean age	11.19(±3.45) years
Age range	3.8 years- 15 years
Mortality	1(3%)

A total of 31 patients were included in this study. The mean age of the pediatric patients was 11.19 (±3.45) years. 20 (64.51%) patients aged >10 years. Total thirty patients (97%) were recovered and one patient (3%) died. (Table I). The mean red cell distribution width was 14.99 (±2.96) and mean neutrophil-to-lymphocyte ratio was 4.49 (±3.99).

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

Most of the patients (14, 45.2%) were suffering from colicky type of pain while six patients (19.4%) experienced diffuse pain. Epigastric region was the main location of pain (21, 67.7%) while six patients (19.4%) had pain in hypochondriac region.

Most (29, 93.5%) of the respondents were suffering from vomiting. Fever was present in 20 patients (64.5%). Loss of appetite was present in 20 (64.5%) patients as well as eleven patients (35.5%) gave history of fatty food intake and six patients (19.4%) gave history of drug intake. Abdominal distension was reported in five cases (16.1%).

Among the studied patients 13 (41.9%) developed complications among which ascites was most frequent found in 12 (38.7%). Pleural effusion found in 7 patients (22.7%) and pancreatic pseudocyst / cyst found in 2 (6.5%) patients (Table II).

Table-III

Cross tabulation between RDW and complications (n=31)

RDW	Complications		*p*-value*
	Yesn (%)	Non (%)	
<14	6 (46.2)	9 (50.0)	0.833
e"14	7 (53.8)	9 (50.0)	
Total	13 (100.0)	18 (100.0)	

* Chi squared test

Cross tabulation between RDW and complications is presented in Table V. Six patients (46.2%) with RDW<14 had complications while seven patients (53.8%) with RDW e"14 had complications. Nine patients with RDW<14 did not have any complications while an equal number of patients with RDW e"14 had no complications. However, these differences were not statistically significant. (Table III)

Table-IV

Cross tabulation between NLR and complications (n=31)

NLR	Complications		*p*-value*
	Yesn (%)	Non (%)	
d"5	7 (53.8)	15 (83.3)	0.114
>5	6 (46.2)	3 (16.7)	
Total	13 (100.0)	18 (100.0)	

*=Fisher's Exact test

Seven patients (53.8%) with NLR d"5 had complications while six patients (46.2%) with NLR >5 had complications. More than 83% patients with NLR d"5 did not have any complications while only 16.7% with NLR >5 had no complications. (Table IV)

Table-V

Comparison of length of hospital stay with NLR and RDW

Variables	Cut-off	Frequency	Mean± SD	p-value
NLR	≤5	22	9.32±3.85	0.749
	>5	9	9.78±2.77	
RDW	<14	15	9.8±3.52	0.604
	e”14	16	9.13±3.63	

SD= Standard deviation

Mean length of hospital stay (LOS) for NLR<5 group was 9.32 days while that mean was 9.78 days for e”5 NLR group. On the other hand, mean Length of hospital stay (LOS) for RDW <14 group was 9.8 days while that of the RDW e”14 group was 9.13 days. (Table V)

There was only one death in the study population. Age of the patient was 12 years, hospital stay 11 days, NLR 10.8 and RDW was 16.3.

Discussion:

In the present study, the mean age of the pediatric patients was 11.19 (±3.45) years. The age range was 3.8-15 years and 20 (64.51%) patients were aged > 10 years. Several studies have reported an increasing incidence of acute pancreatitis in all pediatric age groups over the past two decades [16,17]. 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 [17].

Pancreatitis causes substantial morbidity in the pediatric population. It is estimated that 2–13 new cases occur annually per 100,000 children. 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 [17,18]. According to a study, the mean inpatient length of stay for children with pancreatitis in 2009 was 4 days [17]. In the current study the mean inpatient length of stay was higher i.e. 9 days. Lack of skilled manpower, adequate beds and diagnostic facilities could be causes for such discrepancy.

Most of the patients (14, 45.2%) were suffering from colicky type of pain and six patients (19.4%) had diffuse type of pain. Epigastric region was the main location of pain for 21 patients (67.7%). Several studies have reported abdominal pain is an important early symptom in children with AP [19,20]. A study from Bangladesh also reported similar findings of main location of pain [21].

Most (29, 93.5%) of the respondents were suffering from vomiting. Fever was present in 20 patients (64.5%). Eleven patients (35.5%) gave history of fatty food intake and six patients (19.4%) gave history of drug intake. A study has reported vomiting, abdominal discomfort, tachycardia, fever, and hypotension, jaundice and back pain as other important sign symptoms of acute pancreatitis in paediatric patients [22].

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%). A study on acute pancreatitis in 50 pediatric patients from BSMMU showed that 6% patients had pancreatic pseudocyst and pancreatic necrosis was observed in 2% cases [21]. They also found hypocalcemia in 22 (38%) patients, but in the current study four patients (12.9%) had hypocalcemia.

The mean red cell distribution width (RDW) was 14.99 (±2.96) % and mean neutrophil-to-lymphocyte ratio (NLR) was 4.49 (±3.99). A study from Egypt reported a mean RDW% of 15.03 for non-survivors and a mean RDW% of 12.5 for survivors (p<0.05) [23].

Patients were categorized in to two groups on the basis of NLR score. Seven patients (53.8%) with NLR d”5 had complications while six patients (46.2%) with NLR > 5 had complications. More than 83% patients with NLR d”5 did not have any complications while only 16.7% with NLR > 5 had no complications. However, these differences were not statistically significant. A study

from Ireland reported similar finding that NLR above 5 is associated with poorer prognosis in patients with acute pancreatitis[13]. In the study, seventeen 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 [24-26]. Recent studies found that RDW for predicting mortality were used in cardiovascular diseases, acute dyspnoea and pulmonary diseases [27-29]. In the current study patients were also categorized in to two groups on the basis of RDW%. Six patients (46.2%) with RDW<14 had complications while seven patients (53.8%) with RDW e"14 had complications. Nine patients with RDW<14 did not have any complications while equal number of patients with RDW e"14 had no complications. However, these differences were not statistically significant. *Wang et al.* examined the RDW values in 120 AP patients and found that the mortality rate was significantly higher in patients with RDW >13.4% than those with RDW <13.4%.[15] In the current study only one death was observed who had a NLR >5 and RDW >14.

Conclusion:

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

Limitations:

The current study has some limitations. It was a cross-sectional, single-center study with small sample size. It focused on the predictive role of NLR and RDW only on admission. Changes of these markers over time and their effects on outcome could not be assessed. These methods of risk prediction were not directly compared with established clinically used criteria, such as Glasgow-Imrie, Ranson or APACHE II.

Recommendation

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

Conflict of interest:

We have no conflict of interest to declare

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