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General Medicine

THE PROGNOSTIC SIGNIFICANCE OF RED CELL DISTRIBUTION WIDTH (RDW) AND NEUTROPHIL–LYMPHOCYTE RATIO (NLR) IN ACUTE PANCREATITIS: IDENTIFICATION OF AN OPTIMAL VALUES

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ABSTRACT

Introduction: "Acute pancreatitis" is usually a self-limiting disease; however, severe form of the disease developed in 25 % of patients & it is associated with a mortality of up to 50 %. Currently available gold standard scoring system for assessment of acute pancreatitis' is the "Acute Physiology and Chronic Health Evaluation" (APACHE II)

Aims and Objectives: The aim of the current study is to investigate the validity of RDW and NLR in predicting outcome, and to determine an optimal cut-off value that would allow division of patients in to mild (MAP) and severe acute pancreatitis (SAP) groups.

Results: NLR is increased in patients with severe compared to mild acute pancreatitis

Conclusion: Elevation of the NLR during the first 48 h of admission is significantly associated with severe acute pancreatitis and is an independent negative prognostic indicator in AP"

KEYWORDS : acute pancreatitis, NLR, neutrophil, RDW

INTRODUCTION

"Acute pancreatitis" is usually a self-limiting disease; however, severe form of the disease developed in 25 % of patients & it is associated with a mortality of up to 50 %. Available Scoring system's aim is to stratify the severity of the AP, and this in turn guides the management with improving outcomes.

Currently available gold standard scoring system for assessment of 'Acute pancreatitis' is the "Acute Physiology and Chronic Health Evaluation" (APACHE II), is labor intensive and is not widely adopted for patients with acute pancreatitis outside of the intensive care setting. Other scoring systems such as the "Sequential Organ Failure Assessment" (SOFA) have been developed but are still suitable only in the intensive care setting and not for routine use in all patients presenting with acute pancreatitis.

As such, they are not suitable for stratifying patients at the time of admission or shortly thereafter Simplified tests using serum markers such as procalcitonin, interleukin-6, and interleukin-8 have been said to be able to predict the severity of AP, but these are expensive, non-validated in the clinical arena, and not readily available.

Red cell distribution width is an independent prognostic marker, it has been used in many pathological conditions, such as CVS diseases, respiratory diseases, RA and progressive inflammatory status, and even in malignancy

The white blood cell count (WBC count) is a routinely performed, easily available haematological test that is already added in many of the current scoring systems. Components of the total WBC count include 'neutrophils' & 'lymphocytes' both can be used individually as markers of inflammation. Poor outcome is due to an uncontrolled systemic inflammatory response syndrome (SIRS), it leads to progression of acute pancreatitis to multi-organ dysfunction syndrome (MODS).

Indeed, the WBC count is one of the criteria in scoring of the SIRS. Neutrophils increased in SIRS and lymphocyte depletion occurs in severe sepsis, both are associated with a poor outcome of acute pancreatitis. The neutrophil–lymphocyte ratio (NLR) is a measure of the divergence of these two WBC components, and may be more accurate than the total WBC count or individual neutrophil/ lymphocyte counts in predicting poor outcome in benign and malignant surgical conditions.

AIMS AND OBJECTIVES

The aim of the current study is to investigate the validity of RDW and NLR in predicting outcome, and to determine an optimal cut-off value that would allow division of patients in to mild (MAP) and severe acute pancreatitis (SAP) groups based on NLRs & RDW within the first 48 h of hospitalization.

MATERIALS AND METHODS

STUDY POPULATION:

This study is to be conducted among 30 patients with acute pancreatitis attending the Department of Medicine & Department of Medical gastroenterology, Govt. Rajaji Hospital, Madurai.

Inclusion criteria:

- Patients with features of acute pancreatitis
- Age > 12 years
- patients with recurrent pancreatitis (only on first admission)

Exclusion criteria

- Age less than 12 years
- Traumatic / Autoimmune pancreatitis
- Diabetes mellitus
- Tumor or liver failure

ANTICIPATED OUTCOME

The RDW & NLR can simply be determined from an element of the routine work-up of patients with AP and therefore accumulates no additional cost, and appears to correlate with outcome. Continuous RDW & NLR monitoring on each day of admission provides a dynamic reflection of the variable course of AP, with optimal NLRs varying with changes in patient status.

Aim of this study is to optimize the RDW & NLR and investigate if incorporation in to current AP prognostic scoring systems increases the accuracy of current methods.

DATA COLLECTION:

A Brief history with detailed clinical examination

LABORATORY INVESTIGATIONS:

- White cell count (WBC), RBC count, RDW, platelet count, hemoglobin level, MCV and mean platelet volume (MPV)
- Serum Amylase, creatinine , total protein, albumin, total calcium, total bilirubin, glucose, lactate dehydrogenase, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities levels.
- ULTRASOUND & CT ABDOMEN

	Type of Pancreatitis	
	Mild Acute Pancreatitis (n=22)	Severe Acute Pancreatitis (n=8)
	Median (IQR)	Median (IQR)
NL ratio at 0 hours	6.6 (5.0, 7.5)	10.5 (9.9, 11.0)
p-value	<0.001 (Significant)	

STUDY PROTOCOL:

- A diagnosis of Acute Pancreatitis required two of three features:

(1) Prolonged abdominal pain characteristic of AP

(2) Threefold elevation of serum amylase and/or lipase levels above the normal range

(3) Characteristic findings of AP on abdominal ultrasonography and/or CT scan.

- Mild AP (MAP) is defined as an absence of organ failure and an absence of local or systemic complications.
- Moderately SAP (MSAP) is defined as no evidence of persistent organ failure, but the presence of local or systemic complications and/or organ failure that resolved within 48 hours.
- SAP is defined as persistent organ failure (>48 hours).
- The Red cell distribution width (RDW) & white cell differential count to be analyzed and the NLR determined by calculating the ratio between the absolute neutrophil and lymphocyte counts on days 0, 1, and 2, and correlated with severity
- Sensitivity, specificity, Positive predictive value, negative predictive value, diagnostic accuracy of both tests are calculated.

DESIGN OF STUDY:
Prospective analytical study

PERIOD OF STUDY:
April 2017 TO August 2017

INTERPRETATIONS

	Type of Pancreatitis	
	Mild Acute Pancreatitis (n=22)	Severe Acute Pancreatitis (n=8)
	Median (IQR)	Median (IQR)
NL ratio at 24 hours	5.4 (4.9, 6.1)	9.1 (8.5, 9.7)
p-value	<0.001 (Significant)	

	Type of Pancreatitis	
	Mild Acute Pancreatitis (n=22)	Severe Acute Pancreatitis (n=8)
	Median (IQR)	Median (IQR)
NL ratio at 48 hours	4.2 (3.8, 4.6)	4.8 (4.3, 5.2)
p-value	0.035 (Significant)	

	Type of Pancreatitis	
	Mild Acute Pancreatitis	Severe Acute Pancreatitis
RDW at 0 hours	13.4	15.2
	Type of Pancreatitis	
	Mild Acute Pancreatitis	Severe Acute Pancreatitis
RDW at 24 hours	13.4	15.5
	Type of Pancreatitis	
	Mild Acute Pancreatitis	Severe Acute Pancreatitis
RDW at 48 hours	13.5	15.6

Similarly NLR ratio is higher than the normal population in acute pancreatitis; more significant rise observed in initial presentation than in 24 & 48 hours.

RESULTS
NLR is increased in patients with severe compared to mild acute pancreatitis

	Type of Pancreatitis	**P VALUES**	
	Mild Acute Pancreatitis (n=22)	Severe Acute Pancreatitis (n=8)	
	Median (IQR)	Median (IQR)	
NLR at 0 hours	6.6 (5.0, 7.5)	10.5 (9.9, 11.0)	<0.001 (Significant)
NLR at 24 hours	5.4 (4.9, 6.1)	9.1 (8.5, 9.7)	<0.001 (Significant)
NLR at 48 hours	4.2 (3.8, 4.6)	4.8 (4.3, 5.2)	0.035 (Significant)

CONCLUSION
Elevation of the NLR during the first 48 h of admission is significantly associated with severe acute pancreatitis and is an independent negative prognostic indicator in AP"

DISCUSSION
Rise in RDW is associated with the inflammation status of the disease, which may explain why patients with higher RDW values have a higher mortality rate.

It has been proposed that inflammation promotes deaths of RBCs or inhibits the maturation of RBCs, which is associated with an increase in RDW. Some inflammatory mediators influence bone marrow function and iron metabolism and suppress erythropoietin-induced maturation of RBCs. Therefore, RDW values reflect the inflammation status of acute pancreatitis and thus, may be used for predicting the severity of AP.

The WBC is a marker of infection and inflammation, and is part of many Acute Pancreatitis prognostic scoring systems including Ranson, Imrie, APACHE II, and the Simplified Acute Physiology Score (SAPS II).

Neutrophils and lymphocytes are important components of the WBC count. Neutrophils propagate inflammation and tissue destruction in Acute pancreatitis via activation of a "cascade of inflammatory cytokines (IL-6, IL8, and TNF-α), proteolytic enzymes (myeloperoxidase, elastase, collagenase, and βglucoronidase), and oxygen free radicals"

A rise in neutrophil numbers corresponds with the development of SIRS and progression to MODS, which are hallmarks of severe acute pancreatitis. Lymphocyte numbers increase following the initial stress and mediate the subsequent inflammatory response.

The traditional view is that neutrophilia is the primary cause of an elevated NLR, SIRS, and poor prognosis, while lymphocyte count remains static. Lymphopenia with in 24h of admission and persistent lymphopenia beyond this period is just as much a contributor to increased NLR and poor prognosis as neutrophilia.

This is replicated in our study where persistent lymphopenia is an independent marker of progressive inflammation, bacteremia, or sepsis in emergency admissions and intensive care patients. Uncontrolled inflammation is thought to precipitate lymphopenia by lymphocyte redistribution and accelerated apoptosis, and lymphopenia is associated with a higher mortality in patients with septic shock. The extent of lymphopenia, as with neutrophilia, also correlates with the severity of the insult.

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