

Red Cell Distribution Width as a Predictor of Severity of Acute Pancreatitis

Thapa P¹, Gautam S², Pun H³, Sharma A⁴

ABSTRACT

Introduction: Acute pancreatitis (AP) is a disorder featured by local and systemic inflammatory response, which manifests as mild, self-limited disorder to severe and sometimes fatal disease. Red cell distribution width (RDW) is reflective of systemic inflammation and has been shown to be effective at predicting severity. This study was aimed to investigate the association between Red cell distribution width as coefficient of variation (RDW -CV) on admission and severity of acute pancreatitis. **Method:** This was a hospital based prospective study conducted in the Department of Surgery, Nepalgunj Medical College Teaching Hospital for a period of 2 years from July 2017 to June 2019. The patients with acute pancreatitis were categorized into mild, moderate and severe acute pancreatitis. The value of RDW-CV on admission was correlated with the severity of acute pancreatitis. **Results** : RDW-CV on admission was significantly correlated with the severity of AP (p value <0.001). Receiver Operating Characteristic (ROC) analysis showed that RDW has very good discriminative power for severe acute pancreatitis [Area Under curve (AUC) 0.963, 95% CI, 0.919 to 1.007, p-value <0.001] but not useful to predict mild AP (AUC 0.157, 95% CI, 0.063 to 0.250, p value 0.14) and moderate AP (AUC 0.397, 95% CI, 0.252 to 0.541, p value 0.234). The maximum sensitivity and specificity of detecting severe AP was 95.7% and 91.5% respectively. The positive predictive value (PPV) and negative predictive value (NPV) was 84.6% and 97.7% respectively. **Conclusion:** RDW-CV width on admission is a predictor of severity in patients with severe acute pancreatitis.

Keywords: *Acute pancreatitis, Red cell distribution width as coefficient of variation, Severity*

1. Dr. Pradip Thapa
2. Dr. Subodh Gautam
3. Dr. Hemanta Pun
4. Dr. Anup Sharma

Address for Correspondence:

Dr. Pradip Thapa
Lecturer
Department of surgery
Nepalgunj Medical College & Teaching Hospital
Kohalpur, Banke

INTRODUCTION

Acute pancreatitis (AP) is one of the common gastrointestinal causes of hospital admissions worldwide. Clinical manifestation and effects of AP range from a mild, self-limited disease to severe and sometimes fatal disease¹. However, reported mortality from AP is about 1% but this risk increases with age, co-morbidities and development of complications, and varies from 7–42% in severe disease². AP is often complicated with systemic inflammatory response syndrome and multiple organ failure³. Early identification of these patients who are at high risk of mortality in emergency room can help us with rational use of more aggressive treatment leading to decreased mortality rate. In previous studies, several AP scoring systems and laboratory tests have been developed to estimate the prognosis of AP, such as Ranson's score, Balthazar score, BISAP score and SIRS score, C-reactive protein (CRP) titre and procalcitonin levels⁴. However, there are multiple disadvantages associated with score systems such as hassle of calculation, need for ordering specific tests and testing parameters are expensive, operation trival, and not conducive to clinical implementation⁴. This also has brought up a need for finding a simple and easily available predictor of severity of acute pancreatitis.

Red blood cell distribution width (RDW) is an easily obtained, inexpensive, routinely reported parameter as a part of the complete blood count test⁵. It is the laboratory parameter which measures the variability in size of circulating erythrocytes. Higher values indicate greater variation in size of circulating erythrocytes, i.e. anisocytosis. Normal reference range of Red cell Distribution width as coefficient of variation (RDW-CV) in human red blood cells is 11-15% and normal Red cell distribution width as standard deviation (RDW-SD) is 39-46 fL⁶.

To date, multiple studies have investigated the usefulness of RDW in determining the prognosis of AP at the time of admission, but the results have not been consistent. RDW value has scarcely been investigated as a potential biomarker of AP. Therefore, the aim of this study is to investigate whether RDW is associated with the severity and mortality of AP.

MATERIAL AND METHODS

This was a prospective hospital based study conducted in the Department of Surgery, Nepalgunj Medical College Teaching Hospital from July 2017 to June 2019. All patients with Acute pancreatitis (AP) were included, the diagnosis is based on the 2 out of following 3 criteria: 1) Abdominal pain

characteristic of Acute Pancreatitis 2) Elevated serum amylase and/or lipase levels by at least threefold that of normal range 3) Characteristic findings of Acute Pancreatitis on abdominal ultrasonography and/or CT scan. The patients with presence of malignant tumor, active infections, respiratory diseases and serious cardiovascular disease, known chronic liver and/or kidney diseases, immune system disease, patients with recent transfusion history, recurrent AP, chronic pancreatitis and pregnant patients were excluded.

A detailed history was taken including history of pain on epigastric or periumbilical region that radiates to the back. Detailed physical examination of patient including abdominal examination was done. Demographic data, etiology of pancreatitis, organ failure, metabolic disorder, hospitalization time, and the following laboratory measures was obtained from each patient record on admission: serum amylase, RDW, white blood cell (WBC) count, platelets, hemoglobin, ABG, blood glucose, electrolytes, creatinine.

The value of RDW on admission was measured by automated cell counter, BeneSphera Avantor Model H33s Hematology Analyzer, in the Pathology Department Laboratory at NGMC, Kohalpur.

USG abdomen/pelvis was done to differentiate between biliary and non-biliary pancreatitis. The patients were categorized into 3 groups as per severity of acute pancreatitis: mild, moderate and severe according to the 2012 revised Atlanta criteria (Table I) ⁷. Organ dysfunction is defined by Modified Marshall scoring system (Table II). The patients were followed up regularly to monitor vital signs and severity assessment done every 48hrs till discharge or in-hospital mortality

Severity	Criteria
Mild	No organ failure. No local or systemic complications
Moderate	Organ failure that resolves within 48 hrs (transient organ failure) and/or Local or systemic complications without persistent organ failure
Severe	Persistent organ failure (>48hrs)

Table I: Revised Atlanta criteria Definition of Severity in Acute Pancreatitis

Organ system	SCORE				
	0	1	2	3	4
Respiratory (PaO ₂ /FiO ₂)	>400	301-400	201-300	101-200	<=101
Renal (Serum Creatinine μmol/L)	<=134	134-169	170-310	311-439	>439
Cardiovascular (systolic blood pressure, mm Hg, off inotropic support)	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH<7.3	<90, pH<7.2

Table II: Modified Marshall Scoring System for Organ Dysfunction

A score of 2 or more in any system defines the presence of organ failure. After that, the value of RDW-CV on admission was correlated with the severity of acute pancreatitis. In addition, RDW-CV was also correlated with the etiology of pancreatitis. Furthermore, various demographic and clinical parameters were correlated with the severity of acute pancreatitis.

Data Analysis

All the data collected was processed and analyzed by using statistical package for social science (SPSS) version 21 using appropriate statistical tools like Analysis of Variance (ANOVA), Pearson's chi-squared test (χ^2) test, Student's t test, Receiver operating characteristic curves (ROC curve). A $P < 0.05$ was considered as statistically significant.

RESULT

A total of 70 cases of Acute Pancreatitis were included over a period of 2 years. There were 48 (69%) males and 22 (31%) females. The mean age was 47.06 ± 16.56 (20-95 years). Acute pancreatitis was most common in the age of 31-40 years with the least incidence at the extremes of age group [Figure 3]. Out of 23 patients with severe pancreatitis 20 (28%) were males and there was statistical difference in proportion of severity of acute pancreatitis in male and female (p -value 0.045) [Table III].

Parameters	Mild	Moderate	Severe	p-value
Age (in years)	49.52 ± 20.42	48.43 ± 14.85	42.70 ± 9.69	0.303
Sex (Male/Female)	21/12	7/7	20/3	0.045
Etiology (Biliary/Non-biliary)	12/21	8/6	7/16	0.253

Table III: Comparison of demographic and clinical parameters in AP

In our study, the etiology of Acute pancreatitis was classified into two group as Biliary AP and Non-biliary AP. The majority of cases in this study were non-biliary AP. There was no statistically significant difference in the severity of acute pancreatitis in biliary and non-biliary etiology (p value 0.253) [Table III]

The majority of cases 33 (47%) in this study were mild acute pancreatitis, 14 (20%) were moderate pancreatitis and 23 (33%) were severe pancreatitis. The mean duration of hospital stay was 6.21 ± 3.49 days.

The relationship between Red cell distribution width on admission (RDW-CV) and severity of acute pancreatitis was analyzed. Fig 1 is a scatter plot showing relationship of RDW-CV on admission and severity of AP. When the value of RDW-CV on admission was correlated with the severity of acute pancreatitis, it was found to be statistically significant (p value <0.001).

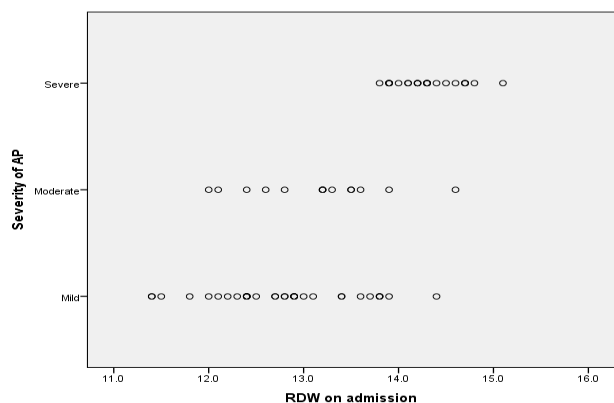


Figure 1: Scatter plot of RDW-CV on admission against severity of acute pancreatitis

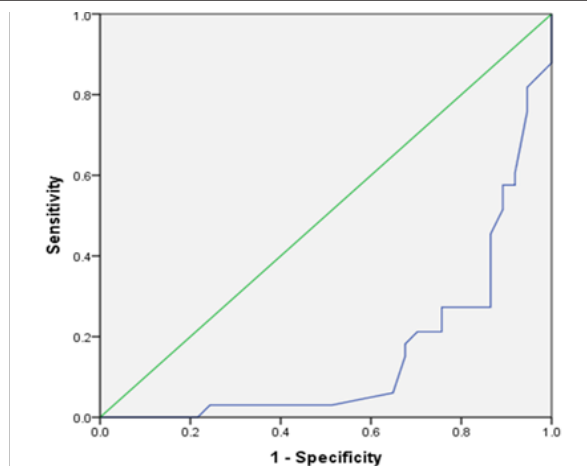


Figure 3: ROC curve for detecting Mild AP

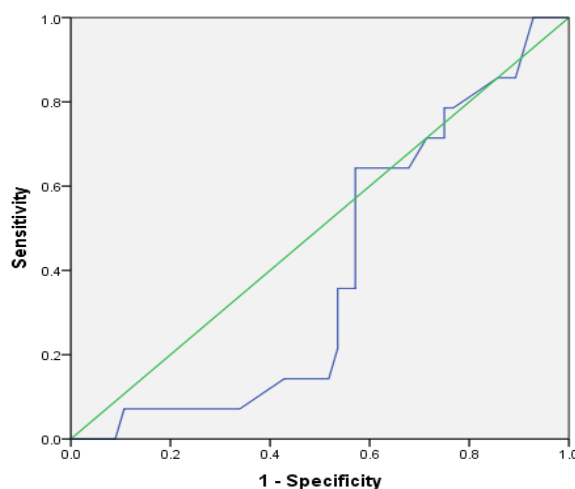


Figure 4: ROC curve for detecting Moderate AP

Receiver-operating characteristics (ROC) analysis was done to measure the accuracy of RDW-CV on admission to detect severity of acute pancreatitis. For severe pancreatitis, area under the curve was 0.963 (95% CI, 0.919 to 1.007, p-value <0.001), which was statistically significant. The maximum sensitivity and specificity of RDW-CV on admission to assess severe acute pancreatitis was 95.7% and 91.5% respectively with a cut off value of 13.85 [Figure 2]. Similarly, the positive predictive value (PPV) and negative predictive value (NPV) of RDW-CV on admission in identifying severe AP was 84.6% and 97.7% respectively.

Furthermore, out of 70 patients there were two cases of severe acute pancreatitis who died eventually. In both these patients, the value of RDW-CV on admission was high (13.9 and 14.3).

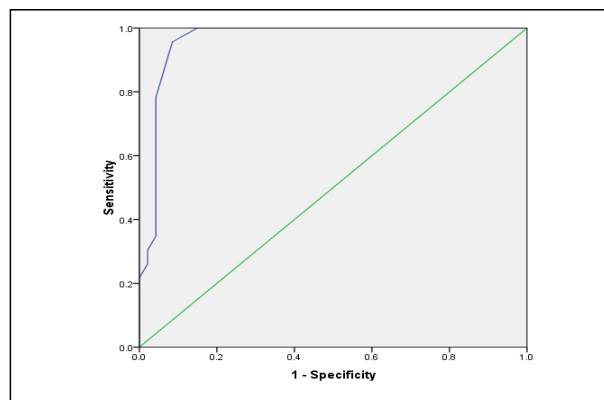


Figure 2: Receiver operating characteristics (ROC) curve for detecting severe AP

Similarly, (ROC) analysis was done to measure the accuracy of RDW-CV on admission to detect mild and moderate acute pancreatitis. For mild AP, the area under the curve was 0.157 (95% CI, 0.063 to 0.250, p value 0.14) which was statistically not significant [Figure 3]. In addition, for moderate AP the area under the curve was 0.397 (95% CI, 0.252 to 0.541 p value 0.234) which also was statistically not significant [Figure 4]. Therefore, RDW-CV was useful to predict severe AP but not useful to predict mild and moderate AP.

DISCUSSION

The pathophysiologic mechanisms for the association between higher RDW and mortality in AP are unclear. Inflammation may help explain the underlying association of RDW with mortality. Inflammation influences bone marrow function and iron metabolism, suppress erythrocyte maturation, accentuated with sepsis, allowing newer, immature, larger reticulocytes to enter the circulation, which is associated with RDW increase⁸. High oxidative stress can also lead to elevated RDW by reducing red blood cell (RBC) survival and increasing release of large premature RBCs into the peripheral circulation. In addition, inflammation alters RBC membrane glycoproteins and ion channels, contributing to the change of RBC morphology^{9, 10}. Previous studies have mostly focused on the ability of RDW to predict mortality and not on predicting severity of AP. This study focused mainly on the role of RDW at predicting severity of AP.

The result of this study revealed that RDW-CV on admission was significantly correlated with the severity of AP. ROC analysis revealed that RDW-CV was useful to predict severe AP but not useful to predict mild and moderate AP. The maximum sensitivity and specificity of detecting severe AP was 95.7%

and 91.5% respectively with a cut off value of 13.85 which is within the normal laboratory range 11-15% but at the upper limit of normal range.

The result in this study is similar to previous studies in which higher RDW level at the upper half of normal range were associated with unfavorable outcomes.

Karabulut et al (2014) who did a retrospective study comparing RDW at the time of diagnosis and after full recovery of the patient with acute pancreatitis. Further, red blood cell width and amylase values were statistically compared according to the time of sample collection. They concluded that an increase in red blood cell width value is a marker of acute pancreatitis and suggested that red blood cell width can be used as a tool for the early diagnosis and assessment of disease progression¹¹.

Wang et al (2015) who conducted a retrospective study in Guangzhou, China found that RDW was a good prognostic predictor of death in AP patients with a cut-off RDW value of 14.35 with a sensitivity of 88.2% and a specificity of 91.8 similar to this study¹². In addition in the study conducted by Yao et al (2017), the cut off value of RDW-CV for predicting mortality in AP was 14.2%, which was also at the upper half of normal range. Their study also revealed patients with AP with the highest RDW tertiles had the highest mortality and the non-survivors of AP had higher RDW values when compared with survivors¹³. Goyal et al (2017) and Moharamzadeh et al (2018) found that RDW can be used as a biomarker for predicting in-hospital mortality in pancreatitis^{14,15}.

In addition, this study also revealed that RDW-CV on admission is not accurate in predicting mild and moderate AP and is not able to differentiate mild from moderate AP. The reason for similar RDW-CV between mild and moderate AP may be because systemic inflammatory process has not reached to a level that could affect and suppress bone marrow function.

Furthermore, this study revealed that the etiology of acute pancreatitis (Biliary and Non-biliary) was not a predictor of severity of acute pancreatitis. Lastly, the duration of hospital stay progressively increased with increase in severity of acute pancreatitis with severe AP associated with a longer duration of hospital stay.

CONCLUSION

This study has revealed that Red cell distribution width (RDW-CV) on admission which is an easily obtained, inexpensive, routinely reported parameter as a part of the complete blood count test, was useful to predict severe AP with a cut-off value of 13.85, which is within the normal laboratory range 11-15% but at the upper limit of normal range. However, it was not useful to predict mild and moderate AP.

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