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Red Cell Distribution Width and Red Cell Distribution Width to Total Serum Calcium Ratio as Predictors of Severity and Mortality in Acute Pancreatitis

Dr. Vasista Palnati[1], Dr. Praveen Papineni[2], Dr. Tavva Sravya Ravali[3], Dr. Girish Kumar Pati[4], Dr. Ayaskanta Singh[5]
[1]Assistant Professor, Department of Medical Gastroenterology and Hepatobiliary Sciences, NRI Academy of Sciences, Mangalagiri, Andhra Pradesh, India
[2]Assistant Professor, Department of Medical Gastroenterology and Hepatobiliary Sciences, NRI Academy of Sciences, Mangalagiri, Andhra Pradesh, India.
[3]Senior Resident, Department of Medical Gastroenterology and Hepatobiliary Sciences, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India.
[4]Professor, Department of Medical Gastroenterology and Hepatobiliary Sciences, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India
[5]Professor, Department of Medical Gastroenterology and Hepatobiliary Sciences, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India

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Corresponding Author
Dr. Vasista Palnati,
Assistant Professor, Department of Medical Gastroenterology and Hepatobiliary Sciences, NRI Academy of Sciences, Mangalagiri, Andhra Pradesh, India
Email: *vasistapalnati10edu@gmail.com*

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ABSTRACT

Background: Acute Pancreatitis (AP) is a common cause of acute severe abdomen with clinical spectrum ranging from mild self-limiting disease to severe acute pancreatitis (SAP) with multi-organ failure and mortality. Early identification of high-risk patients remains crucial. This study aims to evaluate Red Cell Distribution Width (RDW) and RDW-to-Total Serum Calcium (RDW/TSC) ratio as early predictors of severity and mortality in AP.

Methods: This Prospective Observational study was conducted at the Department of Medical Gastroenterology & Hepato-Biliary Sciences, IMS & SUM Hospital, Bhubaneswar, from December 2021 to May 2023. A total of 241 patients diagnosed with AP according to Revised Atlanta Classification 2012 were enrolled. Clinical details, laboratory parameters, and prognostic scores including BISAP, CTSI, and Ranson's score were recorded. RDW, total serum calcium (TSC), and RDW/TSC ratio were analyzed for predicting severity and in-hospital mortality. Receiver operating characteristic (ROC) analysis and multivariate regression analysis were performed.

Results: Of the 241 patients, 46% had mild AP, 22% moderately severe AP, and 31% severe AP. Multivariate regression identified RDW and RDW/TSC ratio as independent predictors of severity and mortality. Median RDW values increased significantly with disease severity (13.2%, 15.45%, and 16.1% in mild, moderately severe, and severe AP respectively; $p<0.001$). RDW >14.85% predicted SAP with 88% sensitivity and 71.1% specificity. Median RDW/TSC ratio also increased significantly with severity (1.52, 2.02, and 2.23 respectively; $p<0.001$). A cutoff >1.88 predicted SAP with 93.3% sensitivity and 69.8% specificity. For mortality prediction, the RDW/TSC ratio demonstrated good diagnostic accuracy with an AUROC of 0.883, showing superior predictive performance compared to BISAP, CTSI and Ranson's score.

Conclusion: RDW and RDW/TSC ratio are inexpensive, rapidly available, and reliable biomarkers for early prediction of severity and mortality in AP. Among them, RDW/TSC ratio showed superior prognostic performance and may serve as a practical tool for early risk stratification in acute pancreatitis

Key Words: *Acute Pancreatitis, Red cell Distribution Width, Total Serum Calcium,Red cell Distribution Width to Total Serum Calcium ratio, CTSI score, Ranson's score, BISAP score*

INTRODUCTION

Acute Pancreatitis (AP) is the sudden onset severe inflammation of the pancreatic parenchyma, induced by activated pancreatic enzymes due to a variety of pathogenesis.[1,2] It is a common cause of severe acute abdomen and is one of the most frequent gastrointestinal causes of hospital admission.[3] Gall stones and alcohol lead to more than 70 % of all causes of AP[4].

Prognosis of AP depends on its severity, currently classified as Mild AP, Moderately Severe AP and Severe AP, according to the revised Atlanta classification (RAC) 2012,[5] which emphasises the presence of local or systemic complications and persistent organ failure using the modified Marshall (MM) score.[3]The clinical spectrum varies from a mild, self-limiting form to a serious disease with severe local and systemic complications that may lead to multi-organ failure and death.[6]. The diagnosis of Moderately Severe AP and Severe AP at admission is difficult to predict because the local complications cannot be precisely discerned through imaging at the early stage while the systemic complications are a result of pre-existing comorbidities exacerbation that often occurs after hospitalisation.[7]Therefore, early identification of patients at increased risk of severe and fatal AP is crucial to improve prognosis through a prompt medical or endoscopic treatment and admission to a specialised intensive care unit.

20–30% of severe cases may be initially misclassified based on clinical, biochemical and imaging findings alone[8]. Although several prognostic scoring systems, including Ranson's, BISAP, APACHE II, Glasgow-Imrie and SOFA, are used for risk stratification, they have limitations related to delayed availability, complexity and time-consuming calculations[9]. Ranson's criteria require 48 hours for completion, while APACHE II and SOFA are more suitable for intensive care settings. Similarly, contrast-enhanced CT, although useful for assessing disease severity, is generally performed 48–72 hours after symptom onset and may be unsuitable in patients with acute renal dysfunction. These limitations highlight the need for simple, inexpensive and readily available biomarkers for early prediction of severity and mortality in AP.

Several simplified single serum markers such as WBC count, Hematocrit(PCV), Serum Creatinine, Serum Calcium, Arterial Lactate, C-Reactive Protein(CRP), Blood Urea Nitrogen(BUN), Serum Procalcitonin, Interleukin-6 and Interleukin-8, Interleukin-10 and Tumor Necrosis Factor-Alpha, have also been evaluated to estimate the prognosis or severity of the AP.[8,10] Most of these currently available markers are not routinely use, associated with significant additional costs and their results have been inconsistent and unrelated to the severity of the disease.[8] Few of them are non-validated in the clinical arena, and not readily available.

Few newer biomarkers that are easily available and can reliably predict the prognosis of acute pancreatitis are Red cell Distribution Width (RDW), RDW to Total Serum Calcium Ratio (RDW/TSC), Neutrophil to Lymphocyte Ratio (NLR), Platelet to Lymphocyte Ratio (PLR) and Lymphocyte to Monocyte Ratio (LMR). The severity and poor prognosis of AP have been linked to these markers[11].

RDW is a routinely measured, inexpensive and readily available parameter of complete blood count that reflects erythrocyte size variability (anisocytosis)[12]. It has been associated with inflammatory markers such as CRP, IL-6 and fibrinogen and has emerged as an independent prognostic marker in several inflammatory, cardiovascular, pulmonary and malignant conditions. In AP, systemic inflammation and oxidative stress may increase RDW by impairing erythrocyte maturation and survival, promoting the release of immature erythrocytes and causing structural alterations to RBCs[13]. Similarly, hypocalcemia is associated with increased disease severity and mortality in AP, possibly due to pancreatic fat necrosis, wherein free fatty acids bind circulating calcium, resulting in calcium saponification[14]. Although both RDW and Total Serum Calcium (TSC) are routinely available parameters associated with the inflammatory and metabolic disturbances of AP, their individual predictive performance may be limited. Combining these parameters as the RDW/TSC ratio may provide additional prognostic information. However, its clinical utility in predicting AP severity and mortality has been evaluated in only a limited number of studies.

Therefore, in our study, we try to evaluate RDW and RDW/TSC ratio as early predictors of severity and mortality in patients with AP.

AIM:

My study aims to evaluate Red Cell Distribution Width and Red Cell Distribution Width to Total Serum Calcium ratio as early predictors of severity and mortality in patients with Acute Pancreatitis.

OBJECTIVES:

Primary:

1) To assess the utility of RDW and RWD-to-TSC ratio for early prediction of AP severity.
2) To assess the utility of RDW and RWD-to-TSC ratio for early prediction of AP mortality.
3) To determine an optimal cut-off value that would allow identification of those patients who are at risk of SAP and mortality.

Secondary:
To compare RDW and RDW-to-TSC ratio with AP specific prognostic scoring systems, namely Ranson's, BISAP and CTSI.

Primary End Points:
The primary endpoints were severity and in-hospital mortality associated with AP.

MATERIAL &METHODS:
This was a single-centre, prospective, observational study conducted from December 2021 to May 2023 at the Department of Medical Gastroenterology and Hepato-Biliary Sciences, Institute of Medical Sciences and SUM Hospital, Bhubaneswar. The study included 241 patients diagnosed with acute pancreatitis. Consecutive sampling was employed for patient recruitment.

This study was conducted after obtaining approval from the Institutional Ethics Committee, and all procedures were performed in accordance with the Declaration of Helsinki. All patients admitted with AP during the study period were enrolled. AP and its severity were defined according to the RAC 2012, based on the presence of transient (<48 hours) or persistent organ failure (>48 hours) and/or local complications. Organ failure included respiratory, renal, and cardiovascular failure.

Based on a previously reported AP incidence rate of 33.74 cases per 100,000 person-years and using the formula $N = Z^2 \times P(1-P)/d^2$with 80% power, 95% confidence interval, and 1.2% precision, the minimum required sample size was calculated as 90. A total of 241 patients were included in the study.

Detailed medical history, demographic characteristics, comorbidities, etiology of AP, physical examination findings, organ failure(OF), local/systemic complications, duration of hospital stay, and mortality data were recorded at admission. Laboratory investigations included WBC count, hematocrit, hemoglobin, platelet count, liver function tests, blood urea nitrogen, creatinine, INR, albumin, lactate dehydrogenase, serum glucose, amylase, lipase, C-reactive protein, arterial lactate, arterial blood gas analysis, D-dimer, total serum calcium (TSC), and red cell distribution width (RDW). Additionally, RDW-to-TSC Ratio(RDW/TSC) was calculated. RDW and RDW/TSC ratio were further compared with established prognostic scoring systems including Ranson's score, BISAP score, and CTSI.

Inclusion Criteria:
1) Age ≥ 18 years.
2) A minimum hospital stay of 24 hours
3) A diagnosis of AP (RAC 2012) - at least two out of three criteria:
- Typical clinical presentation including acute persistent prolonged upper abdominal pain.
- Serum Amylase and /or Lipase ≥ 3 times the upper limit of normal (100 IU/L).
- Characteristic findings on abdominal ultrasonography and/or contrast enhanced computed tomography.

Exclusion Criteria:
1) Age < 18 years.
2) Lack of enough data.
3) Chronic Pancreatitis.
4) Conditions affecting RDW (Infections, Abdominal trauma, Active Malignancy, Pregnancy, Recent transfusion history, Immunosuppressive condition/therapy, Chronic use of erythropoietin).
5) Conditions affecting the TSC Levels (parathyroid disorders, the use of thiazides, or granulomatous disorders such as sarcoidosis).
6) Diseases affecting hematologic system (lymphoma, leukemia, and bone marrow malignancies).
7) Chronic inflammatory diseases (including tuberculosis, Henoch-Schönlein purpura & any autoimmune disorders).
8) Patients with time from onset of disease to presentation in the ED greater > 5 days.

Statistical Analysis
Data was entered into Microsoft Excel. Statistical analysis was carried out using social package for social sciences version 22.0 for Windows (SPSS Inc., Chicago, IL, USA). Normality of data distribution was assessed with Kolmogorov-Smirnov or Shapiro-Wilk test. Continuous data were expressed as mean and standard deviation(SD) or median and interquartile range(IQR) based on the normality of distribution. Groups were compared using Student's t-test or MannWhitney test. Categorical variables were expressed as frequency and percentage and compared using X2-test or Fisher's exact test. All tests were two-tailed and the level of significance was set at p value less than 0.05. All significant factors on univariate analysis were considered for inclusion in multiple regression analysis to predict AP severity and AP related in-hospital mortality. The receiver operating characteristic (ROC) curves were plotted to measure and compare the performance of

different parameters to determine severity and mortality risk and to select the best cutoff point in terms of sensitivity and specificity, positive (PPV) and negative (NPV) predictive values.

RESULTS:

A total of 241 patients with AP were included in the study to evaluate the utility of RDW and RDW/TSC ratio in predicting severity and mortality. The mean age of patients was 40.25 (SD: 13.07 years),with a median age of 38 years (IQR: 30–48 years). Males constituted 75.1% (181) of the study population, with a male-to-female ratio of 3.01:1. Alcohol was the most common etiology (56%), followed by biliary causes (22%), hypertriglyceridemia (11.2%), and idiopathic causes (10.8%). Most of the cases 33.2% (80) presented on day 3 of symptoms, followed by day two in 29% (70) and 6.6% (16) on day 1. According to the RAC 2012, 46%(112) of patients had Mild AP (MAP), 22%(54) had Moderately Severe AP (MSAP), and 31%(75) had Severe AP (SAP). Organ failure (OF) was present in 48.9%(118) of cases. 43 patients had transient OF (< 48 hours), while 75 patients had persistent OF(> 48 hours) with respiratory failure being the most common, followed by renal and cardiac failure. 91% (220) of the cases were discharged following clinical improvement. In hospital mortality was seen in 9% (21).

Table 1: Baseline laboratory parameters of the cases

Parameter	Mean	SD	Median	IQR
RDW	14.70	1.84	14.80	13.25 – 16.0
TSC	7.97	0.87	7.90	7.30 – 8.63
RDW/TSC Ratio	1.88	0.40	1.86	1.53 – 2.13
CTSI Score	5.19	2.48	6	4.0 – 8.0
BISAP score	1.39	1.21	1.0	0.0 – 2.0
Ranson's score	2.68	2	2.16	1.0 – 4.0

Diagnostic accuracies of Red Cell Distribution Width, Total Serum Calcium and Red Cell Distribution Width to Total Serum Calcium ratio with severity of Acute Pancreatitis:

The Median RDW of the study population was 14.8% (IQR: 13.25-16.0). It increased significantly with disease severity, measuring 13.2%, 15.45%, and 16.1% in mild, moderately severe, and severe AP, respectively ($p < 0.001$). An RDW cutoff value of >14.85% predicted severe AP with 88% sensitivity, 71.1% specificity, PPV of 57.8%, and NPV of 92.9%.

The Median TSC of the study population was 7.90 mg/dL. (IQR: 7.30-8.63). It decreased significantly with increasing severity of AP, with values of 8.6 mg/dL, 7.6 mg/dL, and 7.2 mg/dL in mild, moderately severe, and severe AP, respectively ($p < 0.001$).

The Median RDW/TSC ratio of the study population was 1.86 (IQR: 1.53-2.13). The ratio increased progressively with disease severity, measuring 1.52, 2.02, and 2.23 in mild, moderately severe, and severe AP, respectively ($p < 0.001$). An RDW/TSC ratio cutoff of >1.88 predicted severe AP with 93.3% sensitivity, 69.8% specificity, PPV of 58.3%, and NPV of 95.8%.

In the present study, the median CTSI, BISAP and Ranson's scores showed a progressive increase with increasing severity of AP, with statistically significant differences across the three severity groups. The median CTSI scores were 4, 6 and 8; BISAP scores were 1, 1 and 2; and Ranson's scores were 1, 3 and 5 in mild, moderately severe and severe AP, respectively. A CTSI cut-off of >5 predicted severe AP with 82.6% sensitivity and 62% specificity, while a BISAP cut-off of >1.5 showed 57.3% sensitivity and 99.1% specificity. A Ranson's score cut-off of >1.5 demonstrated the highest sensitivity (86.6%), with a specificity of 56%. The corresponding PPV and NPV were 49.6% and 88.7% for CTSI, 45.74% and 78.2% for BISAP, and 47.1% and 90.2% for Ranson's score, respectively.

Table 2: Comparison of predictive performance for Severe Acute Pancreatitis

Parameter	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
RDW	>14.85%	88.0	71.1	57.8	92.9
RDW/TSC ratio	>1.88	93.3	69.8	58.3	95.8
CTSI	>5	82.6	62.0	49.6	88.7
BISAP	>1.5	57.3	99.1	45.74	78.2
Ranson's score	>1.5	86.6	56.0	47.1	90.2

The regression analysis of the study data demonstrated that patients with severe AP had significantly higher RDW, RDW/TSC ratio, CTSI, BISAP and Ranson's scores, along with lower total serum calcium levels, compared with patients with mild and moderately severe AP. RDW (adjusted OR: 2.31) and RDW/TSC ratio (adjusted OR: 2.33) showed positive associations with severe disease, whereas TSC showed an inverse association (adjusted OR: 0.294). Overall, these findings suggest that RDW and RDW/TSC ratio may serve as useful independent markers for identifying patients at increased risk of severe acute pancreatitis.

Figure 1: ROC curve of RDW, RDW/TSC ratio, BISAP, CTSI &Ranson's score for the Severity of AP

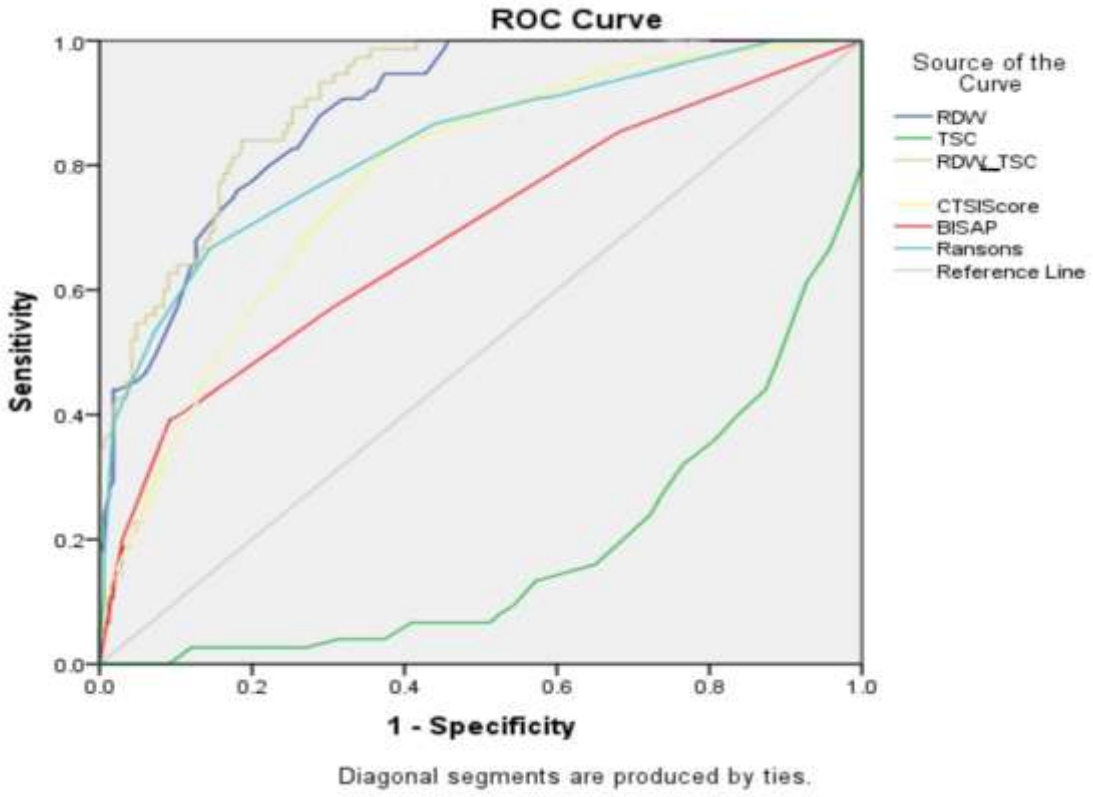


Table 3: ROC curve of RDW, RDW/TSC ratio, BISAP, CTSI &Ransons score for the Severity of AP

	AUROC	P value	95% CI	Cut-off	Sensitivity	Specificity
RDW	0.886	< 0.001	0.84 – 0.92	14.85	88%	71.1%
TSC	0.180	< 0.001	0.12 – 0.23	7.25	49.3%	10.8%
RDW/TSC ratio	0.907	< 0.001	0.87 – 0.94	1.88	93.3%	71.1%
CTSI score	0.782	< 0.001	0.72 – 0.84	5.0	82.7%	62.0%
BISAP Score	0.687	< 0.001	0.61 – 0.76	1.5	57.3%	69.3%
Ransons score	0.829	< 0.001	0.77 – 0.88	1.5	86.7%	56%

The ROC curve analysis demonstrated that the RDW/TSC ratio had the highest predictive accuracy for severe acute pancreatitis (AUROC: 0.907), followed by RDW (AUROC: 0.886). At optimal cut-offs of 1.88 and 14.85, respectively, their sensitivities and specificities were 93.3% and 71.1% for RDW/TSC ratio and 88% and 71.1% for RDW. Among conventional scoring systems, the AUROC values were 0.829 for Ranson's score, 0.782 for CTSI and 0.687 for BISAP, indicating better discriminatory performance of RDW and RDW/TSC ratio.

Diagnostic accuracies of Red Cell Distribution Width, Total Serum Calcium and Red Cell Distribution Width to Total Serum Calcium ratio with mortality of Acute Pancreatitis:

With respect to outcomes, median RDW values were significantly higher in non-survivors compared to survivors (16.9% vs 14.3%, $p < 0.001$). An RDW cutoff of >15.55% predicted mortality with 80.9% sensitivity and 69% specificity, 20% PPV & 94.7% NPV.

The Median TSC values were significantly lower among non-survivors (7.1 mg/dL) compared to survivors (8.0 mg/dL) ($p < 0.001$).

The median RDW/TSC ratio was significantly higher in non-survivors than survivors (2.50 vs 1.80, p < 0.001). An RDW/TSC ratio cutoff of >2.11 predicted mortality with 80.9% sensitivity, 78.1% specificity, PPV of 26.1%, and NPV of 97.7%.

In the present study, the median CTSI, BISAP and Ranson's scores were significantly higher among non-survivors compared with survivors. The respective median scores in survivors and non-survivors were 4 and 8 for CTSI, 1 and 3 for BISAP, and 2 and 7 for Ranson's score, demonstrating a significant association between higher prognostic scores and mortality in AP. The optimal RDW threshold for predicting mortality was >15.55%, yielding 80.9% sensitivity, 69% specificity, 20% PPV and 97.4% NPV. For the RDW/TSC ratio, a cut-off of >2.11 provided 81.1% sensitivity, 78.1% specificity, 26.1% PPV and 97.7% NPV. A CTSI score exceeding 5 demonstrated 90.4% sensitivity, 51.8% specificity, 15.2% PPV and 98.2% NPV, while a BISAP score above 1.5 showed 90.4% sensitivity, 65.4% specificity, 20% PPV and 98.6% NPV. A Ranson's score exceeding 4.5 yielded 95.2% sensitivity, 85.4% specificity, 38.4% PPV and 99.4% NPV for mortality prediction in AP.

Table 4: Comparison of predictive performance for mortality in Acute Pancreatitis

Parameter	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
RDW	>15.55%	80.9	69	20	97.4
RDW/TSC ratio	>2.11	81.1	78.1	26.1	97.7
CTSI	>5	90.4	51.8	15.2	98.2
BISAP	>1.5	90.4	65.4	20	98.6
Ranson's score	>4.5	95.2	85.4	38.4	99.4

The multivariable analysis showed that mean RDW and RDW/TSC ratio were higher among non-survivors than survivors. RDW (adjusted OR: 2.62; 95% CI: 0.56–4.04; p=0.002) and RDW/TSC ratio (adjusted OR: 3.21; 95% CI: 2.7–9.07; p=0.001) were significantly associated with mortality. Among conventional scoring systems, CTSI, BISAP and Ranson's scores were also significantly associated with mortality (p=0.004, 0.002 and 0.003, respectively), whereas TSC alone did not show a statistically significant association (p=0.568).

Figure 2: ROC curve of RDW, RDW/TSC ratio, BISAP, CTSI &Ranson's score for the Mortality of AP

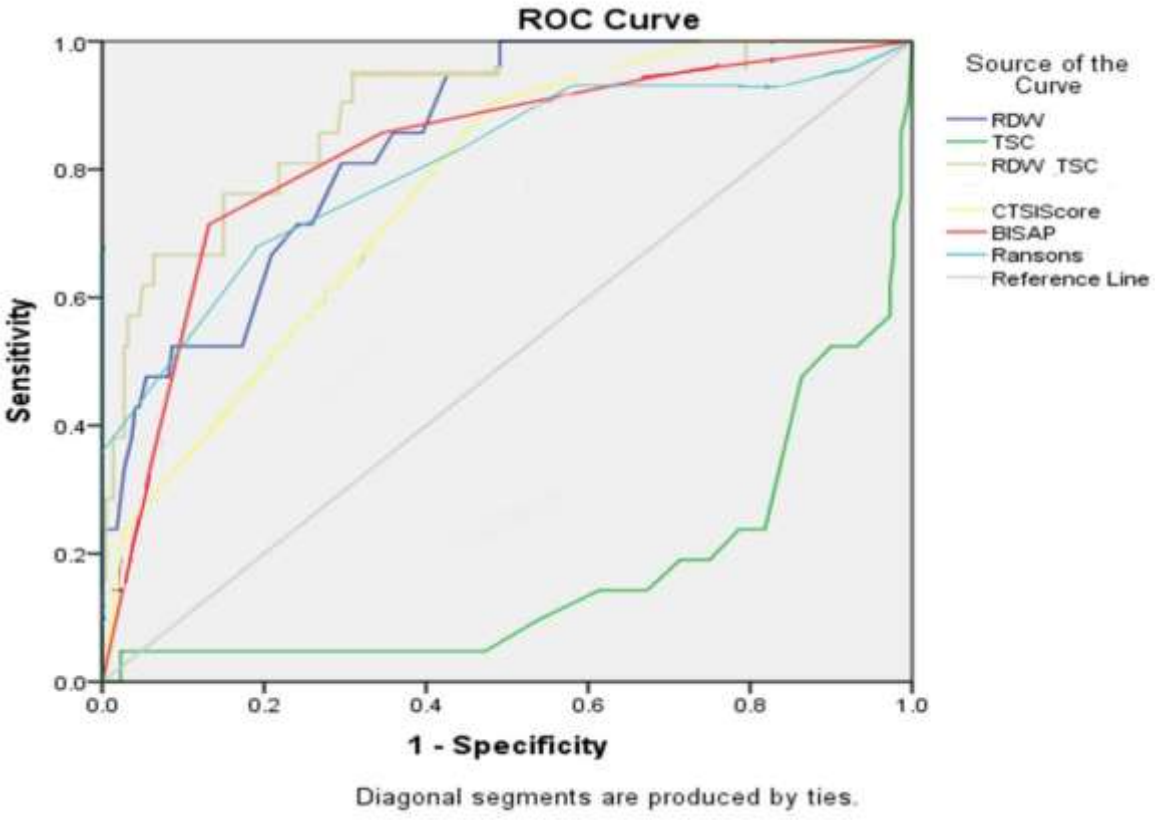


Table 5: ROC curve of RDW, RDW/TSC ratio, BISAP score, CTSI score and Ranson's score for the Mortality of AP

	AUROC	P value	95% CI	Cut-off	Sensitivity	Specificity

RDW	0.845	<0.001	0.77 – 0.91	15.55	81%	70.5%
TSC	0.168	<0.001	0.06 – 0.26	8.05	48%	52.7%
RDW/TSC ratio	0.883	<0.001	0.80 – 0.96	2.11	80.9%	78.1%
CTSI score	0.769	<0.001	0.67 – 0.85	5.0	90.5%	51.8%
BISAP Score	0.828	<0.001	0.73 – 0.92	1.50	85.7%	65.5%
Ranson's score	0.838	<0.001	0.85 – 1.00	4.50	95.2%	85.5%

The ROC curve analysis demonstrated good predictive ability of RDW (AUROC: 0.845) and RDW/TSC ratio (AUROC: 0.883) for mortality prediction in AP. At cut-offs of >15.55% and >2.11, respectively, RDW showed 81% sensitivity and 70.5% specificity, while RDW/TSC ratio demonstrated 80.9% sensitivity and 78.1% specificity. Among conventional scoring systems, Ranson's score, BISAP and CTSI showed AUROC values of 0.838, 0.828 and 0.769, respectively. All parameters demonstrated statistically significant results.

DISCUSSION:

Acute Pancreatitis is a potentially life-threatening inflammatory condition with a variable clinical course. Although approximately 80–90% of patients experience mild disease, 10–20% develop severe complications, including pancreatic necrosis and transient or persistent organ failure. Early identification of patients at risk of severe disease and mortality is essential for appropriate risk stratification and timely intervention. Several scoring systems, including Ranson, BISAP, APACHE II and CT Severity Index (CTSI), are used for prognostication. However, limitations related to the time required for calculation, complexity and variable predictive accuracy highlight the need for simple, inexpensive and readily available biomarkers.

The present study included 241 patients with AP diagnosed according to the RAC 2012. The mean age was 40.25 ± 13.07 years, with a median age of 38 years (IQR: 30–48). This age distribution was comparable to previous studies by Zhang et al., Thapa et al. and Varun et al[15]. A significant difference in age was observed between survivors and non-survivors, with median ages of 37 and 51 years, respectively. This finding suggests that advancing age may be associated with increased severity and mortality in AP, consistent with the observations of the prior study done by Márta et al[16].

There was a male predominance in our study, with males accounting for 75.1% of cases and a male-to-female ratio of 3.01:1. Alcohol was the predominant etiology (56%), followed by biliary pancreatitis (22%), hypertriglyceridemia (11.2%) and idiopathic pancreatitis (10.8%). The higher proportion of males may be explained by the greater prevalence of alcohol consumption among men in our study population. However, gender was not significantly associated with either disease severity or mortality.

Based on the RAC, 46% of patients had mild AP, 22% had moderately severe AP and 31% had severe AP. In-hospital mortality was 8.7% (21 patients), comparable to the mortality rates reported in previous studies by Gravito-Soares et al.[17], Bidel et al.[18] and Varun et al[15]. Almost all deaths in our study occurred among patients with severe AP, emphasizing the importance of early identification of severe disease. Organ failure was observed in 48.9% of patients, with respiratory failure being the most common, followed by renal and cardiac failure. These findings were comparable to those reported by Gravito-Soares et al[17]. and Varun et al[15].

RDW reflects the variability in circulating erythrocyte size and is routinely available as part of a complete blood count. Although traditionally used in the evaluation of anemia, RDW has increasingly been recognized as a marker of systemic inflammation and oxidative stress. Inflammatory cytokines and oxidative stress can impair erythrocyte maturation, reduce red cell survival and promote the release of immature erythrocytes into circulation, resulting in increased RDW. Since AP is associated with an intense systemic inflammatory response, elevated RDW may reflect the magnitude of inflammation and its associated physiological disturbances.

In our study, RDW increased progressively with disease severity, with median values of 13.20%, 15.45% and 16.10% in mild, moderately severe and severe AP, respectively. It was significantly associated with severe AP, demonstrating an AUROC of 0.886 at a cut-off of 14.85%, with 88% sensitivity and 78.08% specificity. These findings are consistent with previous studies by Gravito-Soares et al.[17] and Varun et al.[15], which also demonstrated a significant association between elevated RDW and AP severity. The findings support the role of RDW as an easily accessible marker reflecting the systemic inflammatory burden in AP.

RDW was also significantly higher among non-survivors than survivors. It demonstrated an AUROC of 0.845 for predicting in-hospital mortality at a cut-off of 15.55%, with 80.9% sensitivity and 69% specificity. Similar associations between elevated RDW and mortality have been reported by Şenol et al.[19], Gravito-Soares et al[17]. and Varun et al[15]. The association may be explained by the greater inflammatory response, oxidative stress and physiological disturbances in patients with severe disease and adverse outcomes.

Hypocalcemia is a recognized biochemical abnormality in AP and has been associated with disease severity and mortality. One proposed mechanism is pancreatic fat necrosis, in which pancreatic lipase-mediated breakdown of adipose tissue releases free fatty acids that bind calcium, resulting in calcium saponification. Other mechanisms, including altered parathyroid hormone regulation, may also contribute.

In our study, total serum calcium decreased progressively with increasing disease severity, with median values of 8.60, 7.60 and 7.20 mg/dL in mild, moderately severe and severe AP, respectively. Similarly, non-survivors had significantly lower calcium levels than survivors (7.10 versus 8.00 mg/dL). These findings are comparable to those reported by Gravito-Soares et al.[17], Bidel et al.[18] and Varun et al.[15] However, isolated total serum calcium demonstrated poor predictive performance for both severity (AUROC: 0.180) and mortality (AUROC: 0.168) in our study. This suggests that although hypocalcemia is associated with disease severity, calcium alone may not adequately discriminate between patients with different clinical outcomes.

The RDW-to-total serum calcium ratio combines two parameters reflecting different aspects of the pathophysiological response in acute pancreatitis. RDW reflects systemic inflammation and oxidative stress, whereas reduced serum calcium may reflect pancreatic fat necrosis and metabolic disturbances associated with severe disease. Their combination may therefore provide a more comprehensive indication of disease severity than either parameter alone.

In our study, RDW/TSC ratio increased significantly with disease severity, with median values of 1.52, 2.02 and 2.23 in mild, moderately severe and severe AP, respectively. The ratio demonstrated the highest predictive performance for severe AP among the evaluated parameters, with an AUROC of 0.907 at a cut-off of 1.88 (sensitivity 93.3%, specificity 69.8%). These findings are comparable to those of Gravito-Soares et al.[17] and Varun et al.[15], who also demonstrated excellent predictive performance of the RDW/TSC ratio for severe AP.

Similarly, the RDW/TSC ratio was significantly higher among non-survivors than survivors (2.50 versus 1.80). It demonstrated an AUROC of 0.883 for predicting in-hospital mortality at a cut-off of 2.11, with 80.9% sensitivity and 78.1% specificity. These findings are consistent with previous studies demonstrating a strong association between an elevated RDW/TSC ratio and adverse outcomes in AP.

An important finding of our study was the superior predictive performance of RDW and RDW/TSC ratio compared with conventional prognostic scoring systems. RDW demonstrated better discrimination than Ranson, BISAP and CTSI for both severity and mortality. Furthermore, RDW/TSC ratio demonstrated the highest AUROC for predicting severe AP (0.907), followed by RDW (0.886). For mortality prediction, RDW/TSC ratio also performed better than RDW, Ranson's, BISAP and CTSI.

These findings suggest that routinely available hematological and biochemical parameters may provide valuable prognostic information during the initial evaluation of patients with AP. Their advantages include ease of measurement, low cost, wide availability and the possibility of early assessment without requiring complex scoring calculations or advanced imaging.

CONCLUSION:

Our study demonstrated a strong positive correlation between admission RDW levels and both severity and mortality in AP, with AUROC values of 0.886 and 0.845, respectively. Although TSC alone showed poor predictive performance (AUROC 0.180 for severity and 0.168 for mortality), the RDW/TSC ratio demonstrated excellent discriminatory ability, with AUROC values of 0.907 and 0.883, respectively. Both RDW and RDW/TSC ratio showed better predictive performance than conventional prognostic scores, including BISAP, Ranson's score and CTSI, even after adjustment for potential confounders. Among the evaluated parameters, RDW/TSC ratio demonstrated the highest predictive accuracy. RDW values of >14.85 and >15.55 and RDW/TSC ratios of >1.88 and >2.11 were identified as optimal cut-offs for predicting AP severity and mortality, respectively.

Hence, RDW & RDW-to-TSC ratio are simple, inexpensive, non-invasive, quantitative serum markers, and are convenient to perform as they are provided in a complete blood count test. The results are quickly available, with easy and reliable interpretation. Early identification of high-risk patients using these readily available markers may facilitate timely intensive management and improve clinical outcomes. Further large-scale multicentric studies are warranted to validate these findings and establish standardized cutoff values for broader clinical application.

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