Original Article

Investigating the association between the severity of acute pancreatitis and red blood cell distribution width and platelet distribution width in patients diagnosed with acute pancreatitis referred to Imam Khomeini Hospital in Ahvaz from 2018 to 2021

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Abstract

Introduction and Aim: Acute pancreatitis (AP) is an inflammatory disease that causes significant morbidity and mortality. Red blood cell distribution width (RDW) and platelet distribution width (PDW) are commonly used and easily measurable indicators that provide valuable information about an individual's inflammatory condition. This study aimed to evaluate the diagnostic value of RDW and PDW in comparison with other scoring systems for predicting the severity of AP. **Method:** The present study with a retrospective cross-sectional design was conducted on 115 patients admitted to Imam Khomeini Hospital in Ahvaz from 2018 to 2021. The variables that were measured included demographic characteristics, comorbidities, hospitalization, laboratory parameters, prognostic scoring systems (Ranson and bedside index for severity in acute pancreatitis (BISAP)), and mortality rates. A comparison was made between various parameters in patients diagnosed with mild and severe AP. The prognostic value of RDW and PDW in determining the severity of AP was determined using the receiver operating characteristic (ROC) curve. **Results:** Severe AP patients exhibited higher Ranson and BISAP scores ($P < 0.01$) and experienced a longer duration of hospital stay ($P < 0.01$) compared with AP patients. PDW was found to be significantly elevated in AP patients compared to those with mild AP (17.77 ± 25.11 vs. 14.8 ± 1.67; $P = 0.02$). There were no statistically significant differences in the RDW in mild and severe AP patients (14.0 ± 3.59 versus 14.19 ± 5.9; $P = 0.90$). **Conclusion:** The findings of the study suggest that utilizing PDW as an indicator of inflammation can serve as a valuable approach to evaluating the progression of AP. However, RDW does not offer significant assistance in the early prediction of AP severity. Nonetheless, it is crucial to conduct future prospective studies with larger sample sizes, including all pancreatitis cases.

Keywords: Acute pancreatitis (AP), platelet distribution width (PDW), red blood cell distribution width (RDW), severity

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Introduction

Acute pancreatitis (AP) stands out as a significant source of abdominal pain[1] and a prevalent digestive disorder, characterized by the rapid onset of an inflammatory response that may lead to diverse localized and systemic complications.[1,2] While the majority of AP cases exhibit a mild course and recover without significant consequences, offering a favorable prognosis, it is important to note that 10%–20% of AP patients experience a severe form of the disease, characterized by elevated rates of mortality and morbidity.[3,4]

Given the potential for severe organ damage and the occurrence of life-threatening complications, it becomes imperative to evaluate the severity of the disease to establish appropriate treatment approaches.[2] To assess the severity of AP, a range of techniques are employed, including the utilization of serum biomarkers, imaging modalities, and various scoring systems such as Ranson, Atlanta bedside index of severity in acute pancreatitis (BISAP), Balthazar, EWS2, APACHE II, and Glasgow and Imrie scores.[5,6] However, each of these approaches has its disadvantages. Many of them involve a multitude of parameters, making their routine and daily calculation in clinical practice challenging. Additionally, certain methods require significant financial and time investments.[5,7,8]

The complete blood count is a simple and readily available routine laboratory examination, encompassing numerous parameters capable of indicating the inflammatory condition observed in AP cases.[7,9,10] Red blood cell distribution width (RDW) is a metric that evaluates alterations in the size of circulating red blood cells.[8] Recent findings have indicated a notable association between RDW and several inflammatory indicators, such as C-reactive protein and fibrinogen.[11] In recent studies, the potential of RDW in diagnosing and monitoring individuals with AP has been explored. However, the precise correlation between RDW and the severity indicators of the disease remains somewhat ambiguous, with conflicting outcomes reported in this area.[9,12,13]

Platelet distribution width (PDW), a hematological parameter routinely assessed, provides insights into the diversity of platelet sizes found within organs, exhibiting a range spanning from 8.3% to 56.6%. According to a study, it has been documented that serum PDW levels upon hospital admission can serve as a valuable prognostic indicator for AP.[3] Although changes in PDW levels have been documented in response to inflammatory reactions and clinical conditions, the precise association between PDW and the severity of AP remains uncertain.[3,10] Since AP is a systemic inflammatory response and affects different organs, platelets undergo a range of modifications during the inflammatory process, with various platelet indices serving as potential indicators of these processes.[14] Given the absence of a singular and optimal approach for evaluating the severity of AP,[15] as well as the significance of promptly assessing severity for timely treatment and preventing subsequent risks, and the scarcity of accurate and cost-effective diagnostic markers readily available for rapid calculation in this context, this study aimed to investigate the correlation between hematological parameters (including RDW and PDW) and the severity of AP (as determined by Ranson criteria and BIASAP scoring).

Methods

A cross-sectional descriptive study was undertaken at Imam Khomeini Hospital in Ahvaz during 2017–2019, focusing on patients who were diagnosed with AP. Upon receiving approval from the Research Ethics Committee of Jundishapur University of Medical Sciences, Ahvaz (Ethical code: IR.AJUMS.HGOLESTAN.REC.1401.058), this study was performed. In all stages of this study, adherence to the ethical guidelines outlined in the Helsinki Declaration and the principles of maintaining patient information confidentiality was ensured.

A sample size of 115 individuals was determined for this study, taking into account previous studies. Random selection was employed to include patients diagnosed with AP who were above 18. The diagnosis of AP was established by evaluating clinical, laboratory, and imaging findings, requiring a minimum of two of the following criteria: 1) sudden severe abdominal pain spreading to the back; 2) serum amylase and lipase levels least higher than three times the normal range; 3) abdominal imaging findings (sonography and computed tomography (CT) scan) indicating AP; and 4) exclusion of alternative causes for abdominal pain. The exclusion criteria encompassed individuals with pre-existing chronic pancreatitis and malignant pancreatic conditions, as well as those with underlying ailments such as diabetes, renal failure, pulmonary issues, congestive heart failure, and peripheral vascular disease. Additionally, patients with hematological disorders, acute or chronic inflammatory conditions, cancer, liver diseases, or incomplete laboratory investigation results were also excluded.

The questionnaires for this research project were completed by examining the clinical files of the patients to gather relevant information. The desired data encompassed age, gender, etiology of pancreatitis, comorbidities, duration of hospital stay, and the retrieval of pertinent laboratory parameters. The laboratory parameters that were examined encompassed white blood cells (WBC), aspartate aminotransferase (AST), alanine aminotransferase (ALT), platelet count (PLT), blood urea (BUN), creatinine (Cr), mean platelet volume (MPV), red blood cell distribution width (RDW), blood PDW, lactate dehydrogenase (LDH), amylase, lipase, glucose, hemoglobin (Hb), and mean corpuscular volume (MCV). The evaluation of AP severity involved the utilization of both the Ranson scoring system and BISAP criteria. Ranson criteria include five parameters which are measured upon admission and hospitalization, while an additional six parameters are evaluated 24 h following the hospitalization (8). The parameters considered at the time of referral include age over 55 years, WBC >16,000/μL, blood glucose level >200 mg/dL, serum LDH level >350 IU/L, and

AST >250 IU/L. Classification criteria within the initial 24-h period involve a drop <10% in hematocrit since admission, an increase >8 mg/dL in BUN, an increase in serum calcium of less than 8 mg/dL, arterial partial pressure of oxygen (PaO2) below 60 mmHg, a decrease in base greater than 4 mEq/L, and estimated fluid retention exceeding 6 L. Mild AP is diagnosed if one to three of these criteria are present, while severe pancreatitis is diagnosed when four or more criteria are met.

The BISAP criteria for the diagnosis of AP comprise five parameters: BUN >25 mg/d, mental status disorder, SIRS >2 OF 4, age >60, and pleural effusion, where BISAP score ≥3 is considered as severe pancreatitis.

Statistical analysis

Statistical analysis was conducted using SPSS version 21 (SPSS Inc., Chicago, IL, U.S.A.). The data was described using measures such as the mean, standard deviation, frequency, and percentage. The normality of data distribution was measured using the Kolmogorov–Smirnov test. For the univariate analysis and comparison of quantitative variables between groups, statistical methods such as the Mann–Whitney test and Spearman's correlation were employed. To assess the prognostic value of RDW and PDW in determining the severity of AP, the analysis involved utilizing area under the receiver operating characteristic (AUROC) analysis. A significance level of 0.05 was employed for the tests.

Results

Over three consecutive years (2018–2021), a total of 115 eligible patients diagnosed with AP were admitted to Imam Khomeini Hospital in Ahvaz. Out of the total, 78 individuals (67.83%) were diagnosed with mild AP, while severe AP was observed in 37 individuals (32.17%) (refer to Table 1). Based on the outcomes of univariate analysis, no significant association was found between RDW and Ranson's criterion ($P = 0.7$), nor between PDW and Ranson's criterion ($P = 0.1$). Moreover, no statistically significant correlation was observed between RDW and BISAP criteria ($P = 0.8$), and between PDW and BISAP criteria ($P = 0.4$). Furthermore, the analysis revealed no significant association between PDW and the duration of hospitalization ($P = 0.9$). However, there was a significant correlation between RDW and the length of hospital stay ($P < 0.01$).

Furthermore, the findings indicated a significant association between the severity of pancreatitis and various factors, including the duration of hospitalization, PDW index, AST, BUN, LDH, amylase, and glucose levels, as well as Ranson and BISAP criteria ($P < 0.05$). However, no significant association was observed between the severity of pancreatitis and other variables, including RDW (refer to Table 2). The AUROC analysis outcomes revealed that RDW exhibited limited efficacy in predicting the severity of AP, as per Ranson's criterion (AUROC: 0.58; $P = 0.31$). At the cut-off point of 5.6, a sensitivity of 100% and specificity of 97% were attained. However, when considering Ranson's criterion, the diagnostic capability of PDW demonstrated a moderate performance (AUROC: 0.66; $P = 0.04$). At the cut-off point of 5.1, the analysis revealed a sensitivity of 100% and a specificity of 99% [Figure 1]. Regarding the diagnostic accuracy of RDW compared with the BISAP criterion, at the cut-off point of 5.6, the analysis yielded a sensitivity of 100% and specificity of 98% (AUROC = 0.56; $P = 0.30$). Conversely, for PDW at the cut-off point of 5.1, the specificity was determined as 100% and the sensitivity as 96% (AUROC = 0.50; $P = 0.93$) [Figure 2]. Besides, concerning the prediction of the duration of hospitalization, RDW exhibited a sensitivity of 100% and specificity of 99% at the cut-off point of 5.6 (AUROC = 0.90; $P = 0.016$). On the other hand, PDW demonstrated a sensitivity of 100% and specificity of 97% at the cut-off point of 5.1 (AUROC = 0.36; $P = 0.64$) [Figure 3].

Discussion

The findings of the present study demonstrated that severe pancreatitis patients exhibited higher average values for the

Table 1: Basic characteristics and age distribution of examined patients with AP

Variable	Group	Frequency (%)	Age, year (Mean±Standard deviation)
Severity of pancreatitis	Mild	78 (67.83)	49.23±12.19
	Severe	27 (32.17)	64.24±13.54
Gender	Male	52 (45.22)	49.37±14.83
	Female	63 (54.78)	49.27±17.5
Etiology	Bile	103 (89.57)	50.27±163.4
	Alcohol	6 (5.22)	43.83±13.73
	Hyperlipidemia	6 (5.22)	38.33±14.21
Disease outcomes	Pleural fusion	16 (13.91)	67.5±10.66
	Death	9 (7.83)	69.89±8.16
Organ failure	Organ failure	8 (6.96)	62.13±9.39
	Pancreatic necrosis	15 (13.04)	63.47±16.62
Underlying disease	High blood pressure-hyperlipidemia	12 (10.43)	57.83±15.19
	Hyperlipidemia	19 (16.52)	48.42±14.54
	High blood pressure	28 (24.35)	44.31±15.28

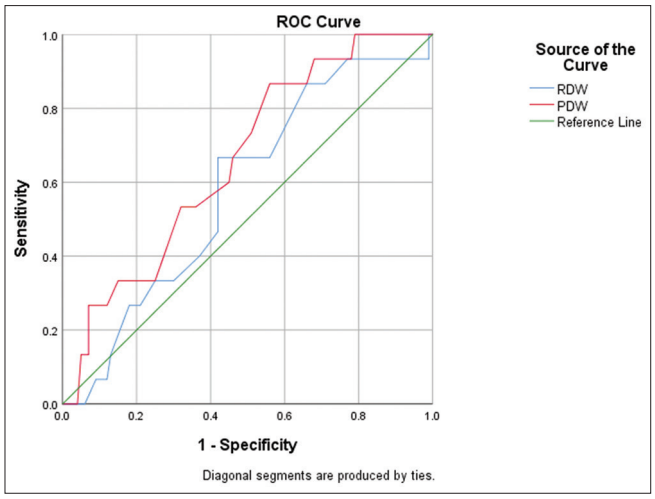

Figure 1: The specificity and sensitivity of RDW and PDW values in determining the severity of acute pancreatitis compared to Ranson's criteria

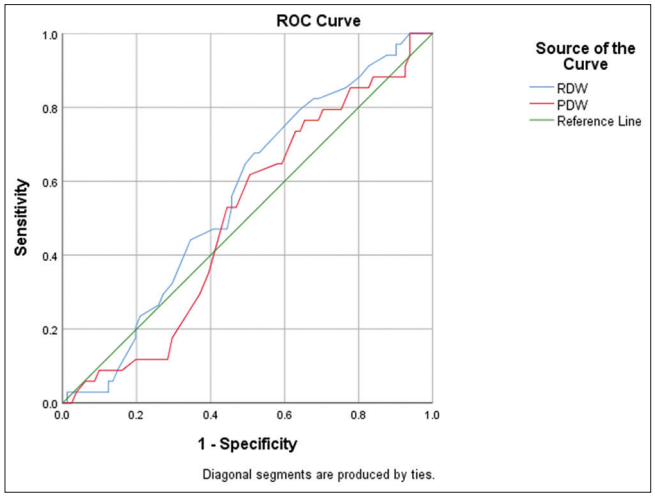

Figure 2: Specificity and sensitivity of RDW and PDW values in determining the severity of acute pancreatitis compared to the BISAP criteria

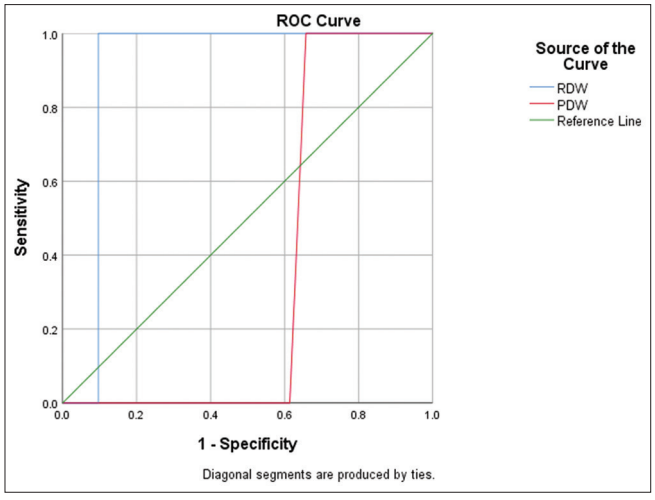

Figure 3: The specificity and sensitivity of RDW and PDW values in determining the duration of hospitalization in acute pancreatitis patients

Table 2: Comparing the mean and standard deviation of different variables based on AP severity

Variable	Mild AP (*n*=78)	Severe AP (*n*=37)	*P**
Period of Hospitalization	7.35±1.711	12.86±5.6	<0.01
WBC	17635±25235	18248±5010	0.88
AST	64.74±50.63	122.7±157.4	<0.01
ALT	69±62.67	80±81	<0.30
PLT	317±118.5	295.3±106.4	<0.30
BUN	19.95±9.27	49.78±26.83	<0.01
Cr	2.32±12.39	6.60±30.93	<0.20
MPV	23.1±112.3	10.46±1.11	<0.50
RDW	14.0±3.59	14.19±5.9	<0.90
PDW	14.8±1.67	17.77±25.11	<0.02
LDH	484.5±228.4	717.9±291.8	<0.01
Amylase	1352.4±851.4	2141±3130	<0.03
Lipase	750.1±406.8	710.3±385.2	<0.60
Glucose	128.53±32.24	142.75±33.50	<0.03
Hb	13.03±1.36	13.12±1.48	<0.70
MCV	76.94±28.04	73.05±30.74	<0.50
Ranson Criteria	2.2±1.17	6.44±1.2	<0.01
BISAP Score	0.77±0.8	3.41±0.9	<0.01

*Mann–Whitney *U*-test and *P*<0.05 are statistically significant. WBC: White blood cells; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; PLT: Platelet count; BUN: Blood urea nitrogen; Cr: Creatinine; MPV: Mean Platelet Volume; RDW: Red blood cell distribution width; PDW: Platelet distribution width; LDH: Lactate dehydrogenase; Hb: Hemoglobin; MCV: Mean corpuscular volume; BISAP: bedside index for severity in acute pancreatitis

PDW index, as well as elevated levels of AST, BUN, LDH, amylase, glucose parameters, Ranson and BISAP criteria, and the duration of hospitalization, compared to patients with mild pancreatitis. However, there was no significant difference in the mean RDW index, as well as the WBC, ALT, PLT, MPV, Cr, lipase, Hb, and MCV parameters, between patients with mild and severe forms of pancreatitis. Consistent with our study, Gravito-Soares *et al.*[16] also found that patients with severe AP had higher levels of creatinine, BUN, LDH, amylase, Ranson criteria, and BISAP criteria compared to those with the mild form. However, no significant difference was observed in the levels of ALT, PLT, and hemoglobin between the two groups. According to the study conducted by Wang *et al.*,[17] it was found that LDH, BUN, creatinine, as well as Ranson and BISAP criteria, exhibited higher levels in individuals with the severe form of the disease, compared to those with mild AP. However, the severity of the disease did not show a significant effect on hemoglobin and WBC levels. On the other hand, contrary to our study findings, both studies[16,17] reported higher levels of RDW in the severe form of the disease compared to the mild form.

While the present study observed higher levels of AST and ALT in severe AP cases compared to the mild form, it is important to note that the difference in ALT levels between the two groups was not statistically significant. In the study conducted by Grau *et al.*,[18] similar findings were observed, indicating an elevation in ALT and AST levels in cases of severe AP. They further emphasized that the increased serum aminotransferase level plays a significant role in diagnosing AP caused by gallstones. Our

findings are consistent with these results in general. The elevation of liver enzymes in cases with severe AP can be attributed to various factors, such as the release of transaminases from blocked bile ducts into the liver sinuses, increased enzyme production, and the secretion of transaminases by liver cells in response to heightened pressure caused by AP.[19]

In the present study as well as other previous research,[16] it was observed that the level of amylase in severe AP was significantly elevated compared to mild pancreatitis. Among serum markers, the elevation of amylase level is considered the definitive standard for diagnosing AP cases. However, it should be noted that certain conditions like intestinal obstruction and renal failure can lead to a slight rise in serum amylase levels as well.[20] Muddana *et al.*[21] reported an elevation in BUN and creatinine levels in AP cases, suggesting that an increase in serum creatinine serves as an indicator of pancreatic necrosis in AP cases. It is important to note that both BUN and creatinine are recognized as markers for assessing kidney function. Changes from the initial state signify a reduction in intravascular volume. Compared to small changes in intravascular volume, creatinine levels exhibit lower sensitivity and are more effective in detecting and resolving visceral damage.

Consistent with our findings, numerous other studies[7,8,15-17,22] have reported that patients with severe AP experience a lengthier hospital stay compared to those with a mild form of the disease. Hence, it can be predicted that individuals diagnosed with severe AP will necessitate an extended duration of hospitalization. Therefore, identifying high-risk patients and delivering suitable treatment in the initial stages can effectively mitigate the morbidity and mortality rates associated with these individuals.[23] A notable discovery from this study was the significant yet moderate diagnostic accuracy of PDW in predicting the severity of AP using Ranson's criterion (AUROC = 0.66). However, PDW demonstrated efficacy as a reliable predictor for the duration of hospitalization, while its applicability to the BISAP criterion was not satisfactory.

Research has indicated that under specific conditions, the PDW level undergoes variations in comparison to healthy individuals.[24,25] Wang *et al.*'s[14] study findings, consistent with our current investigation, demonstrated that the serum PDW level upon hospital admission can serve as a valuable predictive factor for AP. Furthermore, this factor increases proportionally with the level of inflammation. Bilgic *et al.*[26] reported that in patients with severe AP, all platelet indices, such as PLT, MPV, and PDW, exhibited remarkably higher values compared to those with a mild form of the disease. Additionally, they observed a strong and significant correlation between all platelet indices and prognostic scoring systems.

Besides their critical role in maintaining hemostasis and managing thrombosis, platelets also contribute significantly to inflammatory processes.[27] Moreover, platelet indices are valuable indicators in the diagnosis and prognosis of various diseases.[28] PDW, a frequently used platelet index, serves as a dynamic indicator of platelet volume and increases in the presence of platelet anisocytosis. Furthermore, activated platelets experience alterations in their morphology in an inflammatory environment. Consequently, PDW can indicate the release of activated platelets, thereby providing insight into inflammatory conditions such as AP.[14] However, further studies are still required to explore their application and establish the most suitable cut-off for determining disease severity. In the present study, RDW did not demonstrate strong predictive capabilities for the Ranson and BISAP criteria. However, with an AUROC >0.9, RDW proved to be a reliable predictor for the duration of hospitalization in patients diagnosed with AP. In another study, it was reported that RDW serves as an independent indicator for both short-term and long-term prognosis among patients in the intensive care unit.[29] The investigations carried out by Yarkaç *et al.*,[7] Yilmaz *et al.*,[15] Donmez and Ayata,[22] and Jain *et al.*[30] collectively revealed that the RDW parameter exhibited limited predictive efficacy for severe AP. Hence, it appears that RDW does not offer assistance in the initial prediction of AP severity. To validate these findings, a prospective study with a larger sample size is required.

Conversely, in contrast to the findings of the present study, Wang *et al.*[17] demonstrated that RDW is capable of predicting the severity of AP based on the Ranson and BISAP criteria. Furthermore, as reported by Gravito-Soares *et al.*,[16] the RDW index proved to be a significant predictor of severe AP, with a cut-off value of 0.13. Additionally, it was identified as an independent prognostic factor for mortality among these patients. According to the findings of this study, RDW emerges as a simple, readily accessible parameter that can be used to predict the severity of AP. The difference in findings can be attributed to differences in sample size and the characteristics of the examined samples. Consequently, considering the conflicting results between the present study and previous research, it is advisable to assess alternative hematological parameters and diagnostic as well as prognostic tools to improve prognosis and determine the severity of AP.

The present study encountered limitations wherein our analysis relied solely on retrospective observations of patient record information, thereby potentially causing errors in our findings. On the other hand, randomized controlled trials are the most effective approach for exploring confounding factors.

Conclusion

The findings of this study indicated a significant elevation in PDW levels among individuals diagnosed with severe AP in comparison to those with mild AP. Furthermore, PDW demonstrated a moderate predictive capacity for determining the severity of AP based on Ranson's criteria. Therefore, utilizing PDW as a fundamental inflammatory marker can be a valuable approach to evaluating the progression of AP. There was no

significant difference in RDW levels between mild and severe cases of AP. However, RDW exhibited a significant association with the duration of hospitalization.

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Conflicts of interest

There are no conflicts of interest.

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