Association between Red Blood Cell Distribution Width and Acute Pancreatitis

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Data Collection **B**
Statistical Analysis **C**
Data Interpretation **D**
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Background: We aimed to determine whether there are any alterations in red blood cell width in patients diagnosed with acute pancreatitis.

Material/Methods: This was a retrospective study of records of patients treated in emergency units and diagnosed with acute pancreatitis between January 2011 and April 2013. Records were investigated regarding patient age, sex, and causes of acute pancreatitis. Red blood cell width and amylase values obtained from the patients during diagnosis and after a full recovery from acute pancreatitis were added to the records.

Results: Recorded red blood cell width and amylase values of 104 patients diagnosed with acute pancreatitis were statistically compared according to the time of sample collection. Samples were collected in the post-diagnostic period and after full recovery. Values of red blood cell width and amylase were found to be significantly higher in samples collected during hospital admission in comparison to those obtained from patients after fully recovering from acute pancreatitis (p<0.05).

Conclusions: An increase in red blood cell width value is a marker of acute pancreatitis; therefore, we suggest that red blood cell width can be used as a tool for the early diagnosis and assessment of disease progression.

MeSH Keywords: **Abdomen, Acute • Erythrocyte Volume • Inflammation • Pancreatic alpha-Amylases**

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Background

Acute pancreatitis (AP) occurs due to the auto-digestion of the pancreas by the intrapancreatic activation of digestive enzymes. AP is an acute inflammatory disease of the pancreas characterized by severe abdominal pain that may be located in the epigastric region or spread to the back. Local or systemic symptoms may also be associated with the disease [1]. Pancreatic enzymes normally remain inactive. Activation of these enzymes by various etiological factors results in the auto-digestion of pancreatic tissues. Thus, AP leads to inflammation of the pancreas and may consequently result in local or systemic complications [2].

Patients are diagnosed with AP with the consideration of a combination of positive findings obtained from a history of pancreatitis, the physical examination of patient, serological markers, and radiological images [3]. Nevertheless, the diagnosis of AP can be difficult when patients are admitted to the emergency unit, due to the variable clinical properties of AP and factors that may restrict the diagnostic approaches to AP.

Moreover, a number of different parameters are still used for the diagnosis and management of AP. Increases in blood and urinary amylase, serum enzymes (including lipase, elastase 1, trypsin and phospholipase 2), C-reactive protein (CRP), interleukin 6–8 (IL-6–8) and procalcitonin levels are used to confirm the diagnosis of AP [4].

Furthermore, there is still no consensus on the diagnosis and (especially) the treatment of AP, which has a heterogeneous distribution ranging from mild interstitial edematous pancreatitis to necrotizing pancreatitis with a 20% mortality rate [5]. Therefore, early diagnosis and treatment of AP is crucial. No criterion standard for the diagnosis of AP has been developed. The first approach to the diagnosis of AP is to check the level of serum amylase and lipase; however, the specificity and sensitivity of these enzymes is low. Computerized tomography (CT) is the most reliable tool in the diagnosis of AP and the determination of its severity. The high cost-effectiveness, restricted availability of CT, and the potential adverse effects of using contrast chemicals are the disadvantages of CT use [6].

RDW refers to an evaluation of the sizes of the red blood cells (RBCs) circulating in the vasculature, demonstrating the width of distribution of RBCs based on their sizes. It is a component of the complete blood cell (CBC) test. It is calculated by dividing the histogram width of 68.26% of RBCs by the mean corpuscular volume (MCV), then multiplying the result by 100. RDW values are also affected in other of diseases, including celiac disease, pulmonary embolism, and coronary artery disease [7–9]. In addition, elevated levels of RDW were determined in inflammatory and infectious bacteriemia, severe sepsis, and septic shock [10].

This study aimed to determine whether there was a difference in RDW levels and amylase on admission to emergency units, compared to the levels obtained from patients who had fully recovered from AP. Moreover, the role and association of these markers with the early diagnosis of AP was evaluated. Also, we tried to determine whether there were any permanent alterations (either increase or decrease) in RDW values in the post-recovery period.

Material and Methods

We included 104 patients diagnosed with AP in the emergency unit of Baskent University Konya Training and Research Hospital between January 2011 and April 2014 were included in this retrospective analysis. Clinical and laboratory examinations, in addition to radiological methods, were performed for the diagnosis of AP in patients on admission to the emergency department. Patients were excluded if they had any history of oncologic pathologies, iron deficiency anaemia, thalassemia, metabolic disorders, or inflammatory bowel disease. The Ranson criteria were used for the classification of AP severity. Patients who died or had severe necrotizing pancreatitis were also excluded from the study (n=63). Only patients with mild or moderate AP (edematous or interstitial) were included into the study.

To evaluate the levels of RDW and amylase, blood samples were collected from 104 patients diagnosed with AP on admission.. Patients were then hospitalized in clinics for AP treatment. Standard AP treatment included intravenous fluid resuscitation, electrolyte replacement, and the use of analgesics. Nasogastric drainage was applied to protect patients with nausea and vomiting from respiratory aspiration. Patients were given nutritional support [total parenteral nutrition (TPN)] and antibiotics to protect them from septic complications. Patients were also exposed to specific procedures, including endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP), to reduce mortality rates caused by pancreatic parenchymal injury and complications. Patients started to be fed via oral nutrition after about 5–10 days. The patients were observed to improve, based on clinical, radiological, and laboratory findings. To evaluate the values of RDW and amylase, blood samples were collected from 104 patients who had recovered from AP.

Lab assessment

For the evaluation of RDW, an electronic blood cell counting device was used (Cell-Dyne 3700, Abbott, Abbott Park, IL, USA). A routine biochemical kit was used to assess amylase values.

Table 1. Demographic properties and RDW/ Amylase values at two time periods;early phase AP and post-recovery AP.

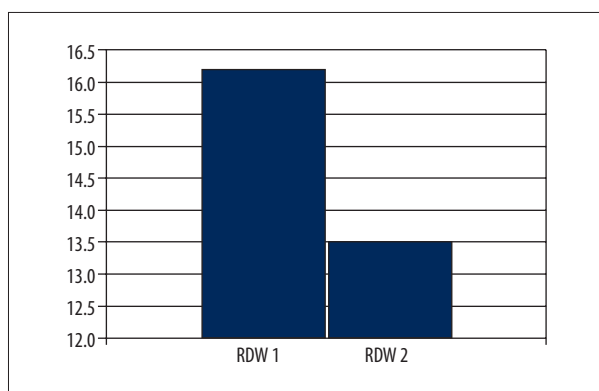|	Early phase AP (n=104)	Post-recovery phase AP (n=104)	p
Male/female	53/51	53/51	P>0.05
Age	56.5±1.55	56.5±1.55	P>0.05
Amylase (U/L)	1004.7±126	124.3±42	P=0.00
RDW(%)	16.2±1.29 (14.1–18.7)	13.5±1.1 (11.3–15.6)	P=0.00

Figure 1. Graphical comparison of RDW values obtained from AP patients at both early phase (RDW1) and recovery (RDW2) period of the disease.
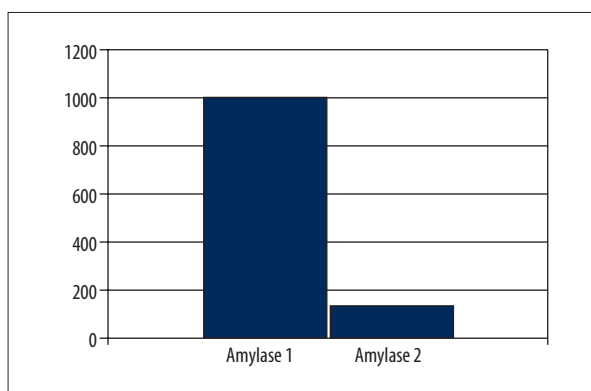

Figure 2. Graphical comparison of amylase values obtained from AP patients at both early phase (Amylase 1) and recovery (Amylase 2) period of the disease.

Table 2. Analysis of correlation between RDW1 and RDW2.

parameters	Correlation coefficient (r)	P value
RDW1-RDW2	−0.069	0.489

Statistically assessment

Collected data were recorded on previously prepared forms. In data analysis, SPSS software was used. Analysis of normalization to common distribution was performed. The t test and paired t test (t test for dependent groups) were performed. The numerical values were presented as mean ± standard deviation (SD). A p value less than 0.05 ($p<0.05$) was accepted as indicating a statistically significant difference between 2 groups.

Results

The study included 104 patients hospitalized with the diagnosis of AP on emergency admission to Baskent University Konya Training and Research Hospital between January 2011 and April 2013. The sex distribution of patients was 51 males (49%) and 53 females (51%). The mean age was 56.5±1.55 years. There were 17 patients (16.3%) over age 70 years. The major etiological factor was determined to be biliary disorders in 82 patients (79%).

Mean RDW value of AP cases was 16.2±1.29% in the acute period (RDW1) and 13.5±1.1% in the post-recovery period (RDW2) (Table 1) and this difference was statistically significant ($p<0.05$) (Figure 1). However, no correlation was found between the parameters of RDW1 and RDW2 (Table 2).

The mean level of amylase in the acute period of AP was 1004.7±126 U/L and 124.3±42 U/L in the post-recovery period. There was a statistically significant difference between the amylase values of the 2 groups ($p<0.05$) (Figure 2).

Discussion

AP is an important clinical condition that should be considered in the differential diagnosis of acute abdominal pain in patients examined in emergency departments. The clinical symptoms and findings of patients with AP may differ according to their age or severity of AP attack. The severity of AP may vary from mild edematous condense necrosis to hemorrhage [11,12].

However, the diagnosis of AP at emergency departments may be difficult due to the variable clinical properties of the disease and factors such as limited diagnostic tools. Various parameters are used for the diagnosis and treatment of AP; hence, no specific biochemical markers have still been determined for the early definite diagnosis and etiological clarification of AP [13].

The clarification of secondary inflammation has been studied in AP patients; increases in blood and urinary amylase, serum lipase, elastase 1, trypsin and phospholipase A2, C-reactive protein (CRP), interleukin 6–8 and procalcitonin may be observed [11,14].

In this study, we aimed to assess the alterations in amylase levels, as well as RDW values, in patients newly diagnosed with AP and to compare these values to those of individuals who had recovered from AP. A search of the relevant literature reveals that the majority of AP cases have mild pancreatitis (80–85%), and 15–20% have severe pancreatitis. In contrast to previous studies, we included patients with mild (85.1%) and moderate (14.9%) AP and excluded patients with severe AP.

Amylase levels increased in the early phase of AP in 3/4 of patients and remained increased for 7–10 days. Therefore, in the conventional approach, checking amylase level for the diagnosis of AP is the criterion standard test. In AP patients, amylase reaches a peak level at between 12 and 72 hours. The formation of a pseudocyst or abscess should be considered if the level of amylase remains high 10 days or longer after an acute attack [15,16].

Although the sensitivity of amylase levels for AP diagnosis is high, the specificity of this test is low. Many clinicians still use an enhanced (3-fold) level of serum amylase and lipase as a diagnostic parameter for AP. The sensitivity of blood amylase level for the diagnosis of AP is 67–100% and the specificity is 85–98% [11,17]. Treacy et al. suggested that the sensitivity and specificity rates for serum amylase were 45% and 97%, respectively; 63% and 85% for urinary lipase; and, 67% and 97% for serum lipase [18].

We found amylase levels to be 3-fold higher in 94 patients (90.4%) in the early phase of AP compared to the recovery period.

RDW is used as a marker to reveal alterations in the number of RBCs. RDW as a parameter is a component of the routine complete blood cell count. The formulation of RDW includes standard deviation of RBC volume, which is divided by the mid-corpuscular volume (MCV) and multiplied by 100 [19]. The value of RDW may be increased due to hemolysis, deficiency of iron and folic acids, and in response to blood transfusion. In addition, the increased level of RDW may be seen in thrombotic thrombocytopenic purpura (TTP), inflammatory bowel disorders such as Crohn's disease, and pregnancy [20]. Moreover, RDW is also used as a tool for the differential diagnosis of microcytic anemia caused by common iron deficiency, thalassemia, or hemoglobinopathies [21].

Results of a study conducted to evaluate the association between mortality and RDW in AP patients suggested that RDW is an excellent marker for the assessment of AP prognosis. The patients with severe AP were included in the study [22], and RDW values were found to be significantly increased in these cases, compared to the normal range RDW values [22].

Unlike previous studies, we included only patients with a mild and moderate AP in our study and excluded cases with fatal and severe AP. We also determined elevated RDW values in cases with mild and moderate AP. We found that RDW values are higher in patients with severe AP as well as in patients with early AP. Moreover, we observed a decrease in the elevated level of RDW to normal, without any permanent alteration.

Conclusions

AP is an important medical challenge due to its high mortality and morbidity. Early determination of disease severity is essential to determine the need for intensive care, to start a feasible and adequate treatment, and to determine the efficiency of treatment. We suggested that RDW could play an important role in the early diagnosis of AP and evaluation of prognosis of the disease. Expanded clinical and experimental studies are required to verify this.

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