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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

PANKREATİTLİ ÇOCUKLARDA HEMATOLOJİK PARAMETRELERİN KLİNİK ÖNEMİ

CLINICAL SIGNIFICANCE OF HEMATOLOGICAL PARAMETERS IN CHILDREN WITH PANCREATITIS

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ÖZET

AMAÇ: Bu çalışmada, akut pankreatit (AP) ve akut rekürren pankreatit (ARP) tanısı alan çocuklarda akut pankreatitin inflamatuar sürecinde tanıda yeni hematolojik parametrelerin önemini retrospektif olarak değerlendirmeyi amaçladık. Bu çalışma pankreatitli çocuklarda yeni hematolojik parametreleri; (eritrosit dağılım genişliği (RDW), eritrosit dağılım genişliği kalsiyum oranı (RDWCaR), nötrofil lenfosit oranı (NLR), lenfosit monosit oranı (LMR), trombosit lenfosit oranı (PLR), eritrosit dağılım genişliği trombosit oranı (RDWPR), ortalama trombosit hacmi (MPV))'ni retrospektif olarak değerlendiren literatürdeki ilk çalışmadır.

GEREÇ VE YÖNTEM: Ocak 2014 - Aralık 2019 tarihleri arasında hastaneye başvuran ve AP ve ARP tanısı alan 55 hastanın tıbbi kayıtları geriye dönük olarak incelendi. 0 ve 48. saatlerde RDW, RDWCaR, MPVPR, NLR, LMR, RDWPR ve PLR değerleri geriye dönük olarak değerlendirildi. Grup 1 akut pankreatit, Grup 2 akut rekürren pankreatit hastalardan oluşmaktadır. İstatistiksel olarak p<0,05 değeri anlamlı kabul edildi.

BULGULAR: Grup 1 ve Grup 2'nin RDW_{48h} değerleri, RDW_{0h} değerlerinden anlamlı derecede düşük bulundu (sırasıyla p<0,001 ve p=0,006). Her iki grupta da $RDWCaR_{48h}$ değerleri de $RDWCaR_{0h}$'den anlamlı derecede düşük bulundu (sırasıyla p= 0,003 ve p= 0,012). Grup 1'de NLR_{48h} değeri NLR_{0h}'den düşük saptandı (p= 0,004). Ayrıca Grup 2'de $RDWPR_{48h}$ değeri $RDWPR_{0h}$'ye göre daha düşük bulundu (p=0,041).

SONUÇ: Bu çalışmada AP ve ARP'li çocukların tanı ve takibinde ilk 48 saat içindeki RDW, RDWCaR, NLR ve RDWPR değerlerinin önemli olduğunu belirledik.

ANAHTAR KELİMELER: Eritrosit dağılım genişliği, Pankreatit, Çocuk.

ABSTRACT

OBJECTIVE: In this study, we aimed to retrospectively evaluate the significance of new hematological parameters in the diagnosis of the inflammatory process of acute pancreatitis in children diagnosed with acute pancreatitis (AP) and acute recurrent pancreatitis (ARP). This is the first study in the literature assessing new hematological parameters (Red cell distribution width (RDW), red cell distribution width to calcium ratio (RDWCaR), neutrophile to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), platelet to lymphocyte ratio (PLR), Red cell distribution width to platelet ratio (RDWPR) and mean platelet volume (MPV)) in children with pancreatitis retrospectively.

MATERIAL AND METHODS: The medical records of 55 patients, who were admitted to the hospital between January 2014 and December 2019 were diagnosed with AP and ARP, were examined retrospectively. RDW, RDWCaR, MPV, NLR, LMR, RDWPR and PLR values at 0 and 48 hours were evaluated retrospectively. Group 1 consists of patients with acute pancreatitis, Group 2 consists of patients with acute recurrent pancreatitis. A p value of <0.05 was considered statistically significant.

RESULTS: RDW_{48h} values of Group 1 and Group 2 were found to be significantly lower than RDW_{0h} values (p<0.001 and p=0.006, respectively). $RDWCaR_{48h}$ values in both groups were also found to be significantly lower than $RDWCaR_{0h}$ (p= 0.003 and p= 0.012, respectively). NLR_{48h} value was detected to be lower than NLR_{0h} in Group 1 (p= 0.004). Moreover, the $RDWPR_{48h}$ value was found to be lower compared to $RDWPR_{0h}$ in Group 2 (p=0.041).

CONCLUSIONS: In this study, we determined that RDW, RDWCaR, NLR and RDWPR values within the first 48 hours were important in the diagnosis and follow-up of children with AP and ARP.

KEYWORDS: Red cell distribution width, Pancreatitis, Children.

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INTRODUCTION

Childhood pancreatitis has been diagnosed with an increasing frequency in the past 20 years. While life-threatening complications develop in nearly 20% of childhood pancreatitis, the mortality rate is less than 5% (1 - 3). Acute pancreatitis (AP) is a disease in which reversible structural and functional alterations are characterized by the presence of inflammatory cells, interstitial edema, and various degrees of necrosis (1). The number and distribution of leukocytes are associated with the immunological status of the patient and the etiology of the infection (4). The changes in the distribution of blood cells during the infection, inflammation, and malignant diseases may alter complete blood count (CBC) parameters (5). Red cell distribution width (RDW) is a marker characterized by the changes in the size of red blood cells found in the circulation and it is routinely included in CBC. The upper limit of RDW is 15.5% (6). High RDW levels in AP patients are considered to be associated with the suppression of hematopoiesis as a response to systemic inflammation and the transition of big-sized immature red blood cells into the peripheral blood (7). High neutrophile to lymphocyte ratio (NLR) indicates mortality risk in patients with sepsis and trauma (8). In recent analyses, the normal range of NLR was found as 0.78-3.53 (9). Increased NLR is an indicator of poor prognosis for pancreatitis (10).

Platelet to lymphocyte ratio (PLR) is a parameter used in the follow up of cardiovascular events, sensorineural hearing loss, and rheumatoid arthritis-associated interstitial lung disease (11 - 16). In a retrospective and cross-sectional study including 301 children, it was found that mean platelet volume (MPV), NLR and PLR were significant markers in the differential diagnosis of diseases that progress with inflammation such as acute appendicitis, mesenteric lymphadenitis and familial mediterranean fever (17). MPV is included in the CBC as an assessment of platelet functions, and it is used for the diagnosis of some inflammatory diseases. MPV is the marker of active platelets. While high MPV levels in diseases such as diabetes mellitus, cardiovascular diseases and cerebrovascular diseases indicate that the inflammatory process is mild, low MPV levels were found in diseases such as ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis and familial mediterranean fever (FMF) (18). In this study, we aimed to investigate the significance of new hematological parameters at 0 and 48 hours in the diagnosis by reviewing the medical records of the patients diagnosed with AP and ARP.

MATERIALS AND METHODS

This study was carried out retrospectively by examining the medical records of 55 patients who were diagnosed with AP and Acute Recurrent Pancreatitis (ARP) in the pediatric clinic of Afyonkarahisar Health Sciences University Faculty of Medicine Department of Pediatrics between January 2014 and December 2019. Patients in the study were divided into 2 groups: those with AP were in group 1 and those with ARP were in group 2. The cases in both groups had mild pancreatitis based on Atlanta criteria (1). Etiology, demographic characteristics, hospitalization time and abdominal pain duration were evaluated in the patients with AP (group 1) and ARP (group 2). Red cell distribution width (RDW), red cell distribution width to platelet ratio (RDWCaR), MPVPR, neutrophile to lymphocyte ratio (NLR), lymphocyte to monocyte ratio (LMR), RDWPR, and PLR of the cases were evaluated at 0 and 48 hours of admission. Patients with a diagnosis of chronic pancreatitis and a lack of records were excluded from the study. The diagnosis of AP and ARP was made based on INSPPIRE criteria. AP is characterized by the presence of two of three criteria including abdominal pain compatible with pancreatitis, amylase or lipase levels three times higher than normal and imaging records compatible with pancreatitis. The diagnosis of ARP was made by the occurrence of AP attacks at two different times, the presence of painless periods for ≥1 month, or normal levels of amylase and lipase between the attacks (1).

Ethical Committee

The ethics committee approval for the study was obtained from the Clinical Research Ethics Committee of Afyonkarahisar Health Sciences University, Faculty of Medicine, with the decision number of 2019/3.

Statistical Analysis

Data were analyzed by using the SPSS 20.0 statistical package program. Categorical variables were given as percentage and frequency, and

continuous variables were expressed as mean and standard deviation. Patients were grouped as AP (group 1) and ARP (group 2); and accordingly, data were analyzed. Categorical variables were tested by chi-square test while continuous variables were compared by Mann-Whitney U test and Wilcoxon signed-rank test. P value of <0.05 was accepted as statistically significant.

RESULTS

Demographic characteristics and duration of abdominal pain and length of hospital stay were shown in **Table 1**.

Table 1: Demographic Characteristics of the Patients

	Mean age	p value	Sex	p value	BMI (Z score)	p value	Abdominal pain duration/ days	P value	Hospitalization time/days	p value
Grup 1 (n=43)	9.9± 4.46	P=0.919	23E (53.5%)	P=0.422	-0.12 ±1.23	P=0.312	2.5±1.6	P=0.428	7.3±3.6	P=0.521
Grup 2 (n=12)	10.03± 4.98		8E (66.7%)		-0.61±1.54		2.8±2.5		7.40±3.8	

In terms of the etiology of the cases, there were idiopathic (88.5%), stone (2.3%), trauma (2.3%), infections (4.6%) and coledochal choledochal cyst (2.3%) in group 1; and idiopathic (50%), congenital abnormalities of the pancreatic duct (8.3%), allergy (8.3%), autoimmunity (8.3%) and genetic causes (25%) in group 2.

RDW_{0h} was 15.37±2.63 in group 1 and 15.93±2.84 in group 2; and RDW_{48h} was 13.15±0.93 in group 1 and 12.77±0.62 in group 2. No statistically significant differences were found between both groups in RDW_{0h} and RDW_{48h} values (p=0.575 and p=0.274, respectively). It was found that the RDW_{48h} value of group 1 was significantly lower compared to the RDW_{0h} value (p<0.001). Also, the RDW_{48h} value of group 2 was significantly lower than the RDW_{0h} value (p=0.006).

In group 1, $RDWCaR_{0h}$ was 1.57±0.28 and $RDWCaR_{48h}$ was 1.38±0,11 whereas $RDWCaR_{0h}$ was 1.63±0.31 and $RDWCaR_{48h}$ was 1.34±0.11 in group 2; and there was not a statistically significant difference between groups for RDWCaR0h (p=0.571), Also, $RDWCaR_{48h}$ was not significantly different between the groups (p=0.126). It was also found that the $RDWCaR_{48h}$ value was significantly lower than the $RDWCaR_{0h}$ value in group 1 (p=0.003). In group 2, the $RDWCaR_{48h}$ value was found to be significantly lower compared to the $RDWCaR_{0h}$ value (p= 0.012). In Group 1, NLR_{0h} was 3.98±3.36 and NLR_{48h} was 2.41±2.34 whereas they were 3.92±3.28 and 3.30±2.30 respectively in group 2. No statistically significant difference was found in NLR_{0h} and NLR_{48h} between both groups (p=0.823; p=0.070). It was found that NLR_{48h} values were significantly lower than NLR0h in group 1 (p=0.004). In group 2, no statistically significant difference was found between NLR values at 0 and 48 hours (p=0.130).

In group 1, LMR_{0h} was 5.07±2.93 and LMR_{48h} was 5.93±3.39; and they were 4.51±2.26 and 5.89±4.23 respectively in group 2. There was no statistically significant difference between the groups in terms of LMR at 0 and 48 hours (p=0.684; p=0.721). Moreover, no statistically significant difference was found between the LMR_{0h} and LMR_{48h} values of group 1 and group 2 (p=0.181; p=0.692). PLR_{0h} and PLR_{48h} values were 175.94±100.31 and 142.84±59.99, respectively in Group 1. In group 2, PLR_{0h} was 177.22±115.41 and PLR_{48h} was 150.81±85.68. There was not a statistically significant difference between the PLR values of both groups at 0 and 48 hours (p=0.887; p= 0.919). Besides, no statistically significant differences were found between PLR values at 0 and 48 hours in group 1 and group 2 (p=0.131; p=0.431). In group 1, mean the platelet volume to platelet ratio $(MPVPR)_{0h}$ was found as 0.03±0.007 and $MPVPR_{48h}$ was found as 0.03±0.017. These values were found to be 0.03±0.012 and 0.03±0.007 in group 2, respectively. No statistically significant difference was found in $MPVPR_{0h}$ and $MPVPR_{48h}$ between both groups (p=0.289). $MPVPR_{48h}$ values in group 1 and group 2 were not found to be statistically significant (p=0.338). Besides, no significant difference was detected between MPVPR values at 0 and 48 hours in group 1 (p=0.362). Moreover, the difference between MPVPR values at 0 and 48 hours was not statistically significant in group 2 (p=0.692).

$RDWPR_{0h}$ and $RDWPR_{48h}$ values of group 1 were 0.05±0.015 and 0.004±0.021, respectively. In group 2, they were 0.06± 0.019 and 0.04± 0.010, respectively. When $RDWPR_{0h}$ and $RDWPR_{48h}$ values were compared between both groups, no statistically significant difference was found (p=0.121; p=0.639). Moreover, no statistically significant difference was seen between $RDWPR_{0h}$ and $RDWPR_{48h}$ values in group 1 (p=0.074). In group 2, $RDWPR_{48h}$ value was found to be

significantly lower than $RDWPR_{0h}$ (p=0.041). A comparison of laboratory values of children with pancreatitis was is shown in **Table 2**.

Table 2: Comparison of the laboratory values of pancreatitis patients

Parameters		GROUP 1	GROUP 2	p value (0-48 hours)	p value (Group 1) (0-48 hours)	p value (Grup 2) (0-48 hours)
RDW	0 hour	15.37±2.63	15.93±2.84	0.575	**<0.001**	**0.006**
	48 hour	13.15±0.93	12.77±0.62	0.274		
RDWCaR	0 hour	1.57±0.28	1.63±0.31	0.571	***0.003***	**0.012**
	48 hour	1.38±0.11	1.34±0.11	0.126		
NLR	0 hour	3.98±3.36	3.92±3.28	0.823	***0.004***	0.130
	48 hour	2.41±2.34	3.30±2.30	0.070		
LMR	0 hour	5.07±2.93	4.51±2.26	0.684	0.181	0.692
	48 hour	5.93±3.39	5.89±4.23	0.721		
PLR	0 hour	175.94±100.31	177.22±115.41	0.887	0.131	0.431
	48 hour	142.84±59.99	150.81±85.68	0.919		
MPVPR	0 hour	0.03±0.007	0.03±0.012	0.289	0.362	0.690
	48 hour	0.03±0.017	0.03±0.007	0.338		
RDWPR	0 hour	0.05±0.015	0.06±0.019	0.121	0.074	***0.041***
	48 hour	0.04±0.021	0.04±0.010	0.639		

DISCUSSION

Some simple hematological prognostic markers were used to determine the diagnosis, severity and mortality of adult pancreatitis. RDW, which is one of the hematological parameters, is included in the complete blood count panel. It measures the RDW in the circulation and is generally used in the differential diagnosis of anemia. RDW is a common blood test parameter that measures the degree of red blood cell heterogeneity and has the benefits of being precise, easy to measure, and quantitative. According to several research studies, RDW is an early prognostic marker linked to fatalities in AP patients, and when the RDW > 13.55%, patients were considerably more likely to be admitted to the ICU (19). In the study by O'Connell et al. which was carried out with 185 adult AP patients, RDW level was reported to be above the upper limit in 23 (%12) of the patients and it was associated with hospitalization in the intensive care unit. Even though RDW has been the subject of numerous investigations, it is still unknown how RDW increases in AP (6). According to some researchers, the production of numerous inflammatory mediators and cytokines that inhibit red blood cell maturation may be the reason for high RDW in severe AP (7). High RDW is thought to be associated with the suppression of hematopoiesis and erythrocyte maturation as a result of systemic inflammatory response (6, 7).

Yılmaz et al. reported that RDW was a beneficial marker for determining prognosis in 264 patients with AP (20). In our study, no statistically significant difference was found between groups in terms of RDW levels In the study by Senol et al., it was reported that high RDW levels at the time of diagnosis were an independent risk factor for mortality in adult patients with AP (7). Also, Zhang et al. determined that RDW was a more valuable prognostic factor in 42 patients with AP based on APACHEII and SOFAS scores (19).

In a retrospective case-control study involving 301 hospitalized patients with AP from China, Wang et al. reported that the Mild AP group had lower levels of RDW than the severe AP group (21). In our study in both groups, RDW_{48h} values were found to be significantly lower compared to RDW_{0h} values (p<0.001 in group 1 and p=0.006 in group 2). Low RDW_{48h} values can be considered as an indicator of response to treatment.

In their study with 312 patients with AP (including 92 with severe AP), Gravito Soares et al. reported an RDW_{0h} value > 13.0 and an $RDWCaR_{0h}$ >1.4; and concluded that they were reliable markers in determining the severity of pancreatitis. RDWCaR was 2.0±0.3 in pancreatitis resulting in mortality and it was found as 1.6±0.3 in the survived ones; and no statistically significant difference was found between both (p=0.001). They also reported that $RDWCaR_{0h}$> 1.4 was a good marker and >1.7 was a better marker for the determination of pancreatitis severity (22). In our study, $RDWCaR_{0h}$ was found as 1.57±0.28 in group 1 and 1.63± 0.31 in group 2. Although the ratio in group 2 was found to be higher than in group 1, the difference was not statistically significant (p=0.57). $RDWCaR_{48h}$ was found as 1.38±0.11 in group 1 and 1.34±0.11 in group 2. No statistically significant differences were found between groups 1 and 2 in terms of $RDWCaR_{0h}$ and $RDWCaR_{48h}$ (p=0.13). While a high RDWCaR was found to be important in determining mortality in the study by Gravito Soares, it was also indicated in our study that RDWCaR was higher in the patients with ARP.

Azab et al. found that a high NLR was more significant in determining the clinical course of pancreatitis in patients with acute pancreatitis (23). In addition, Binnetoglu et al. indicated that the prognostic value of NLR might be controversial since antibiotic use may affect leukocyte count by alleviating the inflammatory process in AP patients (24). Gulen et al. also showed that NLR and RDW were not effective in determining mortality within the first 48 hours in 322 adult patients with AP (25). Also, O'Connell et

al. found intensive care admission rates as high in AP patients whose NLR was above 5. Moreover, they reported that the mortality rate was significantly increased in the patients whose RDW and NLR were high at the same time (RR 9.9; P=0.04) (6). In our study, NLR_{48h} value was found to be significantly lower than the NLR0h in group 1 consisting of patients with AP (p= 0.004). However, no statistically significant difference was found in group 2 including patients with ARP (p=0.130). Jain et al reported that an increase in serial NLRs is associated with a poorer prognosis in patients with severe pancreatitis (26). In our study, NLR at 0 hour was found to be higher than the ratio at 48 hours in children with AP; and this was evaluated in favor of inflammation. In our study, the lower NLR_{48h} values can be interpreted as a prognostic factor for good prognosis. Cho et al. found NLR and PLR values as 13.8+15.3 and 269.5+246.6, respectively in their study including 243 patients with APs who had a history of gallstones and alcohol use in their etiology. They reported that NLR and PLR were significantly high in AP associated with gallstones and they were important in determining the severity of disease (27).

PLR has been suggested to be a predictor of thrombotic and inflammatory disorders. PLR was discovered to be an independent risk factor that affected survival in individuals with many different types of cancer, including pancreatic and colorectal cancer (28). Ilhan et al. found that NLR was significantly higher in 14 patients who experienced AP during pregnancy, and they showed that there was not a statistically significant difference between PLR and RDWPR In our study, $RDWPR_{48h}$ value in group 2 was found to be significantly lower than $RDWPR_{0h}$ (p=0.041), but no significant difference was found in group 1 (29).

PLR was not found to be significant in pancreatitis patients in our study. Zhou et al. reported that only RDW was reliable and suitable for the determination of severe AP and mortality in 406 patients with AP who were admitted to a tertiary hospital (30). Moreover, Cetinkaya et al. reported that the use of RDWPR was beneficial in the identification of mortality in 102 adult patients with AP (31). Zhang et al. reported that the RDW was higher in non-surviving severe acute pancreatitis (SAP) patients than in surviving SAP patients and had better prognostic value for SAP patients than APACHE II and SOFA scores. RDW may be associated with mortality of severe acute pancreatitis patients (32). In addition, Wang et al. reported that the RDW-albumin ratio could be an accurate biochemical indicator that can be compared with scoring systems such as BISAP, the Ranson score and MCTSI in their study of 212 adult patients with mild pancreatitis and 89 patients with severe pancreatitis (33). However, further multicenter studies are needed to confirm the appropriate diagnostic significance of the findings of this study.

Our study has some limitations such as its retrospective design and conduction in a single center. This is the first study in the literature evaluating RDW, RDWCaR, NLR, LMR, PLR and MPVPR children with AP. It is required to carry out more comprehensive and large studies on the parameters which have prognostic significance in the evaluation of the severity of AP in children.

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