Süleyman Demirel Üniversitesi
Sağlık Bilimleri Dergisi
Cilt 13, Sayı 2, 212 - 217, 2022

Suleyman Demirel University
Journal of Health Sciences
Volume 13, Issue 2, 212 - 217, 2022

Elevated Level of RDW is Associated with Cholelithiasis

Artmış RDW Değeri ile Kolelitiazis İlişkisi

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ABSTRACT

Objective: Red cell distribution width (RDW) ,an index of heterogenity of circulating red blood cell, has recently been found to be associated with multiple diseases and used as a marker to predict outcome in these patients. In the present study we aimed to investigate if RDW value is associated with cholelithiasis and symptoms of the disease.

Material- Method: A total of 204 women (101 with cholelithiasis and 103 without the disease) were included to the study. The demographic and the laboratory data of the routine complete blood cell parameters including RDW values were recorded. Women with cholelithiasis were divided into symptomatic or non-symptomatic group according to presence of biliary colic or pain. The patients were compared in terms of their demographic and laboratory characteristics.

Results: Age and BMI were similiar between groups in the study population. In our study population mean RDW value was significantly higher in women with cholelithiasis than without disease. However in subgroup analysis there was no significant difference of RDW value between symptomatic group and nonsymptomatic group

Conclusion: In conclusion we demonstrated an association between serum RDW level and cholelithiasis in our study but not with disease symptom. However further studies are needed to understand the role of RDW in patients with cholelithiasis and if this simple , inexpensive and routinely reported parameter can be used for prognostic information in this disease.

Keywords: Red Cell Distribution Width, Cholelithiasis, Inflammation

Alınış / Received: 12.01.2022 Kabul / Accepted: 25.08.2022 Online Yayınlanma / Published Online: 31.08.2022

DOI: 10.22312/sdusbed.1056712
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ÖZET

Amaç: Kırmızı hücre dağılım genişliği (RDW) , kırmızı kan hücrelerinin hacmin değişkenliğini göstermekte olup yakın zamanda yapılan çalışmalarda birçok hastalıkla ilişkili bulunmuştur ve bu hastaların hastalıklarının gidişatını öngörmede belirteç olarak kullanılabileceği gösterilmiştir. Biz de bu çalışmamızda serum RDW değeri ile *kolelitiazis hastalığı ve semptomları arasında ilişki olup olmadığını saptamayı amaçladık.*

Materyal-Metot: Toplam 204 kadın hasta (101 kolelitiazis ve 103 kontrol) çalışmaya dahil edildi. Hastaların demografik özellikleri ve RDW içeren rutin kan sayımı parametreleri kayıt edildi. Kolelitiazis hastaları semptomatik olup olmadıklarına göre iki gruba ayrıldı. Hasta grupları demografik ve laboratuar parametreleri açısından karşılaştırıldı.

Bulgular: Gruplar arasında demografik özellikler açısından fark izlenmedi.Çalışma grubumuzda ortalama RDW değeri kolelitiazis grubunda kontrol grubuna göre yüksek bulundu. Subgrup analizinde semptomatik grup ve semptomatik olmayan grup arasında RDW açısından fark bulunamadı.

Sonuç: Sonuç olarak çalışmamızda serum RDW değeri ile kolelitiazis hastalığı arasında ilişki saptandı. Fakat kolelitiazis hasalığında RDW değerinin rolü olup olmadığı ve bu basit ve rutin olarak değerlendirilen parametrenin hastalığın prognozunu öngörmede kullanılıp kullanılamayacağına dair gelecekte çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Kırmızı hücre dağılım genişliği, kolelitiazis, enflamasyon

1. Introduction

Cholelithiasis that refers to the formation of gallstone is one of the most common disease of digestive system and one of the most commmon cause of hospital admission in Europe [1] . The prevalance of the disease increases with age and nearly 20 % of adults have gallstones in developed countries [2]. The disease is more common in women and 20% of patients have symptoms defined as biliary colic or pain [3].

The exact pathogenesis of cholelithiasis is unclear and genetic and environmental factors have role in pathogenesis of the disease. Differences in cholesterol production in liver, gallbladder function, cholesterol absorption and bile acids are all possible factors in the formation of gallstone[3]. Association between diseases such as diabetes mellitus, dyslipidemia, metabolic syndrome and atherosclerosis with cholelithiasis have been demonstrated in many studies in the literature [4,5]. Increased inflammation in gallbladder site and systemic inflammation may also be involved in the etiology of the formation of the disease [6].

Red cell distribution width (RDW) that shows variation of red blood cell size is an index of heterogenity of circulating red blood cell. It is evaluated in routine complete blood count (CBC) test [7] and used for detecting and differential diagnosis of anemia [8]. Although RDW is used for differential diagnosis of anemia, recent studies reported that RDW is also associated with multiple diseases related with inflammation as cardiovascular diseases [9,10], hypertension [11], stroke [12], and pulmonary hypertension [13]. RDW is also found to be a prognostic factor for liver disease [14] and high RDW

value is thought to be independent risk factor for death in the general population [15]. The purpose of this study is to investigate the relationship between RDW value and cholelithiasis and with symptoms of the disease.

2. Material and Method

This study was performed at in Giresun University, Clinics of General Surgery. Medical records of all women patients diagnosed with cholelithiasis and prepared to surgery between 2018-2020 were systematically evaluated. Healthy women volunteers admission to hospital within the same period for check-up were constituted the control group. Patients who had chronic systemic disease (such as dibetes mellitus, hypertension,malignancy), active infection and with blood transfusion 4 months prior to admission were not included into the study. All the patients in our study had abdomial ultrasonography and cholelithiasis was proved by ultrasonography method. Symptomatic cholelithiasis was defined as patients with biliary colic or pain, asymptomatic cholelithiasis was defined as gallstones which are not obstructive and do not cause any symptom [3] . Acute cholecystitis, choledocholithiasis, cholangitis, and gallstone pancreatitis were referred as complicated gallbladder disease [3] and patients with complicated gallbladder disease were not included into study.

Demographic data, including age, body mass index (BMI) and the laboratory data of the CBC parameters and serum liver enzyme profiles, [creatinine, glucose, sodium (Na) and potassium concentrations performed before surgical treatment in cholelithiasis group and control group were obtained from the patient records. Patients with cholelithiasis were grouped as symptomatic and nonsymptomatic according to the presence of biliary colic or pain. The patients were compared in terms of their demographic and laboratory characteristics.

Statistical Package for Social Sciences, Windows version 20.0 (SPSS, Chicago, IL, USA) was used for data analysis. Descriptive statistics were expressed as mean and standard deviation for numerical variables. Kolmogorov-Smirnov test was used to asses normality of the data distribution .T-test was used to compare the groups with normal distribution and non-parametric tests such as the Mann–Whitney U test or the Fisher Exact tests were used for parameters with non-normal distribution. A p value less than 0.05 was considered as statistically significant.

3. Results

204 women (101 women with cholelithiasis and 103 healthy women) were included to the study. BMI and age were similiar between groups. There were no statistically significant difference in mean hemoglobin and hematocrit concentration, white blood cell count (WBC) and serum liver enzymes between groups. Mean platelet count was significantly lower in control group. Demographic characteristics data and laboratory parameters of cholelithiasis and healthy group are depicted in Table 1.

Table 1. Demographic and laboratory characteristics of cholelithiasis and control group

Variable	Cholelithiasis Group (n=101)	Control Group (n=103)	P value
Age[years]	52.1±14.4	51.2±8.0	0.57
BMI [kg/m2]	27.6±3.43	28.4±3.5	0.11
Hemoglobin [g/dL]	12.9±1.1	12.5±0.7	0.07
Hemotocrit [%]	35.7±2.7	35.3±2.7	0.35
WBCx10^3mL	7.5±2.3	7.3±2.1	0.60
Plateletsx10^3mL	267.2±71.0	246.2±62.3	0.02*
Glucose [mg/dL]	93.7±8.1	90.6±17.7	0.11
Serum creatinine [mg/dL]	0.9±0.2	0.8±0.4	0.06
ALT[U/L]	22.2±12.3	21.3±13.2	0.62
AST[U/L]	19.9±18.8	24.6±29.2	0.16
Serum Na [meq]	137.5±3.9	136.5±2.8	0.05
Serum K [meq]	4.2±0.5	4.1±0.4	0.28
RDW[%]	14.4±1.1	13.7±1.4	0.0001*

Abbreviations: BMI, Body Mass Index; WBC, White Blood Cell Count; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; RDW, Red Cell Distribution Width. * indicates statistical significance.

Mean age and BMI were also similiar in symptomatic and non-symptomatic group. There were no significant difference between hemoglobin and hematocrit concentration, WBC and platelet count between groups. Demographic data and laboratory parameters of symptomatic and nonsymptomatic cholelithiasis groups are presented in Table 2.

Table 2. Demographic and laboratory characteristics of symptomatic and non symptomatic-group

Variable	Symptomatic Group (n= 72)	Non-symptomatic Group (n=28)	P value
Age[years]	51.5±14.2	53.7±15.0	0.50
BMI [kg/m2]	27.3±3.16	28.6±3.9	0.08
Hemoglobin [g/dL]	12.9±1.1	12.9±1.3	0.67
Hemotocrit [%]	36.6±2.5	36.0±3.2	0.52
WBCx10^3mL	7.69±2.3	7.20±1.7	0.31
Plateletsx10^3mL	269.4±71.2	261.7±71.6	0.63
Glucose [mg/dL]	94.6±8.5	91.2±6.7	0.06
Serum creatinine [mg/dL]	0.72±0.13	0.8±0.3	0.50
ALT[U/L]	25.2±33.3	23.2±14.6	0.76
AST[U/L]	21.5±15.1	20.7±6.15	0.79
Serum Na [meq]	137.0±4.0	138.5±3.7	0.09
Serum K [meq]	4.2±0.47	4.07±0.37	0.16
RDW[%]	14.3±1.2	14.6±1.1	0.23

Abbreviations: BMI, Body Mass Index; WBC, White Blood Cell Count; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; RDW, Red Cell Distribution Width

RDW value was significantly higher in cholelithiasis group (14.4±1.1) than control group (13.7±1.4) (p=0.0001) (Table 1). However in subgroup analysis there was no significant difference in RDW value between symptomatic group (14.3±1.2) and nonsymptomatic group (14.6±1.1) (p=0.23) (Table 2) .

4. Discussion and Conclusion

In this study we found that RDW value was significantly higher in women with gallstones than women without the disease however there was no difference between symptomatic disease and nonsymptomatic disease. According to our knowledge there is no study in the literature about RDW level and cholelithiasis.

Cholelithiasis is a common health problem in the world .About 15% to 20 % of the population in developed countries had gallstones in their lifetime [4]. There is no general and standardized classification system for cholelithiasis however according to chemical composition, cholesterol gallstones accounts for 75% , pigment stones either black or brown made 25% of gallstones [2,17]. The exact pathogenesis of gallstones is not clear however both genetic and environmental factors may have role in the pathogenesis of the disease. While obesity is more associated with choleterol gallstones, biliary infections and hemochromatosis are more related with pigment stones [3].

Association between disease and inflammation also has been previously reported in the literature. Histopathologic changes related with inflammation in the gallbladder wall with choleterol gallstones have been showed in the studies [6,17]. Inflammation related diseases such as obesity, diabetes and infections are known to be associated with risk of gallstone disease [18,19]. Although the role of inflammation on gallstone formation is not clear, inflammation may cause change in the cholesterol and bile acid metabolism and increase bile salt levels and this may cause the formation of gallstones. Shengelia et al found increased macrophage inflammatory cytokine levels in menopausal women with cholelithiasis than control women in their study [20]. Liu et al also found that higher Interleukin levels were related with gallstone disease [6].

RDW is a CBC marker and shows red blood cell size heterogenity and usually used for cause of anemia [21]. However in recent studies it is showed that systemic inflammation is associated with high RDW level, and RDW may be used as an inflammation marker in many diseases related with inflammation like cardiovascular disease, renal disease, and diseases with thrombosis [11,21]. It is reported that RDW is also related with prognosis of these diseases and mortality of these patients. [22, 23]. Although the mechanism how inflammation increases RDW is not known, release of inflammatory cytokines due to inflammation may cause red cell immaturation and lead to the release of immature

erythrocytes to blood. Inflammation impairs iron metabolism. This may explain the increased RDW level in inflammation process [24, 25].

In a recent study Hu Z et al. postulated RDW level is increased in different types of liver disease and RDW may be used as prognostic marker in these diseases [14]. Beyazit et al found that increased RDW value in malignant obstructive jaundice when compared with benign obstructive jaundice [26]. Wang et al showed that RDW was related with stage of primary biliary cirrhosis that patients with advanced stage disease had higher RDW values than patients with early stage disease [27]. In their study Wang et al showed that RDW may be used as a clical parameter for predicting liver fibrosis in chronic hepatitis patients [28]. Although there are studies about RDV value and liver diseases little is known about the association between RDW value and cholelithiasis. In our study we found increased RDW level in patients with gallbladder stones than control patients. However RDW values were similiar between symptomatic disease and nonsymptomatic disease. To best of our knowledge, this is the first clinical study that is about the role of RDW on the pathogenesis of gallstones. Association between obesity and diabetes mellitus and risk of cholelithiasis and RDW has been demonstrated in many studies however in our study we excluded the patients with endocrinological diseases and BMI was similiar between groups.

In conclusion in this study we found an association between incresed RDW level and cholelithiasis but not with disease symptoms. Although our study was cross-sectional, our finding suggests that RDW may a role of in the formation of gallstones but further studies with large sample sizes are necessary to understand role of RDW in cholelithiasis disease and if this simple, inexpensive and routinely reported parameter can be used for prognostic information in this disease.

Declaration of Ethical Code

In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.

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