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Associations Between Body Mass Index and Hematological Parameters in Obese and Normal-Weight Adolescents: A Cross-Sectional Study

Obez ve Normal Ağırlıklı Adölesanlarda Beden Kitle İndeksi ve Hematolojik Parametreler Arasındaki İlişkiler: Kesitsel Çalışma

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ABSTRACT Objective: Although many studies are showing that obesity is an inflammatory condition, to our knowledge, there are few studies showing the effects of obesity on erythrocyte indices and thrombotic risk in adolescence. This study aimed to investigate the impact of obesity on these hematological parameters in an adolescent cohort. **Material and Methods:** This is a cross-sectional study in which 52 obese (body mass index (BMI)>30) and 60 normal-weight (BMI=20-25) adolescents aged 10-19 participated. Weight, height, BMI, and blood count parameters were included in the study. The obese and control groups were matched for age and gender (p=0.08, p=0.26). **Results:** The mean age of the obese group was 14±3.7 years, and the normal-weight group was 15±2.42. While the male/female ratio in the obese group was 34/18, in the control group this ratio was 33/27. When we examined the blood count parameters between the 2 groups, significant differences were found between the Red Blood Cells (RBC), mean corpuscular volume (MCV), Platelet Distribution Width (PDW), and neutrophil to lymphocyte ratio (NLR) parameters, respectively. (p=0.009, p=0.038, p=0.03, p=0.02). In the correlation analysis between blood count parameters and BMI, it was seen that the positive correlation with RBC was significant and the negative correlations with MCV and NLR were significant. (p=0.006, p=0.01, p=0.03). In multivariate binary regression analysis, the independent negative association between RBC and obesity was significant (p=0.028). **Conclusion:** The significant relationship between BMI and RBC, MCV, PDW, and NLR in the adolescent age group in our study indicates that obesity may be associated with thrombosis and vascular disease, which are shown by hematological parameters in adolescence. Future studies using blood count parameters and indices in this age group should take into account the participants' BMI.

Keywords: Adolecents; hematological parameters; obesity

ÖZET Amaç: Obezitenin bir inflamasyon durumu olduğunu gösteren fazlaca çalışma olmasına rağmen, bildiğimiz kadarıyla adölesan dönemde obezitenin eritrosit indeksleri ve trombotik risk üzerindeki etkilerini gösteren az sayıda çalışma bulunmaktadır. Bu çalışma ile adolesan bir kohort üzerinde obezitenin bu hematolojik parametreler üzerindeki etkilerinin araştırılması amaçlandı. **Gereç ve Yöntemler:** Bu çalışma, 10-19 yaşlarındaki 52 obez (beden kitle indeksi (BKİ)>30) ve 60 normal kilolu (BKİ=20-25) adölesanın katıldığı kesitsel bir çalışmadır. Çalışmaya ağırlık, boy, BKİ ve kan sayımı parametreleri dâhil edildi. Obez ve kontrol grupları yaş ve cinsiyet açısından eşleştirildi (p=0,08, p=0,26). **Bulgular:** Obez grubun yaş ortalaması 14±3,7, normal kilolu grubun yaş ortalaması ise 15±2,42 idi. Obez grupta erkek/kadın oranı 34/18 iken kontrol grubunda bu oran 33/27 idi. İki grup arasındaki kan sayımı parametrelerini incelediğimizde sırasıyla kırmızı kan hücresi [red blood cells (RBC)], ortalama hücre hacmi [mean corpuscular volume (MCV)], trombosit dağılım genişliği [platelet distribution width (PDW)] ve nötrofil lenfosit oranı [neutrophil to lymphocyte ratio (NLR)] parametreleri arasında anlamlı farklar tespit edildi (p=0,009, p=0,038, p=0,03, p=0,02). Kan sayımı parametreleri ile BKİ arasındaki korelasyon analizlerinde RBC ile pozitif korelasyonun anlamlı, MCV ve NLR ile negatif korelasyonun anlamlı olduğunu görüldü (p=0,006, p=0,01, p=0,03). Çok değişkenli ikili regresyon analizinde ise RBC'nin obezite ile bağımsız negatif ilişkisi anlamlıydı (p=0,028). **Sonuç:** Çalışmamızda adölesan yaş grubunda BKİ ile RBC, MCV, PDW ve NLR arasında anlamlı ilişki bulunması, obezitenin ergenlik döneminde hematolojik parametrelerle gösterilen tromboz ve vasküler hastalıklarla ilişkili olabileceğini göstermektedir. Araştırmada kullanılan yaş grubunda kan sayımı parametreleri ve indekslerinin kullanıldığı gelecekteki çalışmalarda katılımcıların BKİ'leri dikkate alınmalıdır.

Anahtar Kelimeler: Adölesanlar; hematolojik parametreler; obezite

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Changing life conditions over time, a high-calorie diet, and physical inactivity, are responsible for the recent development of obesity, a disease that has reached epidemic proportions in human evolution. The World Health Organization says that more than 1 billion adults worldwide are overweight (about 1 in 8 people) and 300 million people are clinically obese, and have a body mass index (BMI) of 30 kg/m^2 or more.[1] It is stated that childhood obesity has increased 10-fold worldwide in recent years and has arrived at epidemic proportions and has now become a serious public health problem.[2]

Excess body fat causes low-level chronic systemic inflammation and is responsible for a miscellaneous of associated comorbidities. Moreover, expanded adipose tissue exhibits prothrombotic and proatherogenic properties that may affect hematological parameters' physiological functions, size, and morphology. Despite being simply accessible and low-cost indicators, few studies evaluate hematological parameters such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), red blood cell distribution width (RDW), etc. in children and adolescents.[3] In the overweight pediatric ages, where low-grade inflammation is prominent, these markers may be indicators of comorbidities such as insulin resistance and cardiovascular events over time. Various platelet function abnormalities have been described in obese individuals, including increased adhesion and activation *in vitro* and *in vivo* and reduced sensitivity to physiologic agonists.[4,5] It is also well documented that obesity and metabolic syndrome (MetS) are characterized by the asset of a prothrombotic state resulting from a unity of increased thrombin production, increased platelet activity, and reduced fibrinolysis.[6,7] Additionally, many studies have demonstrated that high RDW is related to MetS, but there are still many inconsistencies in the relationship between RDW and obesity.[8-10]

Since children have not yet reached their final adult height, definitions vary to meet age and gender criteria rather than absolute threshold values. Therefore, age and gender should be considered in the definition of obesity determined during adolescence. In addition, data from some studies on identical twins and adopted siblings also support the strong genetic impact of obesity. Some ethnic groups (e.g., Hispanics and South Asians) appear to tend to be overweight. For these reasons, the effects of adolescent obesity are still unclear in many areas of our population.[11-14] Parameters such as RDW, increased cell counts, etc. can be easily applied, inexpensive, and powerful predictors for monitoring comorbidities (acute coronary syndrome, diabetes, etc.) that may develop in adolescent individuals with increasing BMI.

Previous studies on hematological changes in obesity have mainly focused on adults, and population studies in adolescents are limited. This study aimed to compare the hematological parameters of overweight adolescents (BMI>30) with those of normal weight and verify the associations of these values with BMI.

MATERIAL AND METHODS

This study is a cross-sectional study that included 52 obese (BMI>30) adolescents aged 10-19 years and 60 normal weight (BMI=20-25) healthy individuals grouped as a comparison group according to age and gender. The study was conducted in S.B.U. İstanbul Training and Research Hospital patients, who had been admitted to the outpatient clinics and met the criteria, were recruited for the study. Patients in the specified age group who had any chronic disease data (hypothyroidism, polycystic ovary syndrome, etc.) and overweight adolescents with BMI values between 25-30 were not included in the study. The hospital-based data was collected in a period between 2022 and 2024. Blood samples were obtained in the morning hours, after at least 8 hours of fasting. Whole blood K2EDTA (Becton Dickinson, USA) tubes were used for hematological parameters. Mindray BC6800 hematology analyzer (Mindray Bio-Medical Electronics. Shenzhen, China) which is a cellular analysis product line was used to determine hematological analyses. The instrument speed is 125 tests per hour in CBC+Diff (Complete blood counts with leukocyte differential counts) mode and the sample volume required for analysis is 200 µl in automatic mode. BMIs (kg/m^2) were calculated using the formula "weight (kg)/height (m)^2".[15] All participants in this research informed consents were obtained. The

study was conducted by the Principles of the Declaration of Helsinki. The study was approved by the Clinical Research Ethics Committee of S.B.U. İstanbul Training and Research Hospital with decision no. 96 on October 18, 2024.

STATISTICAL ANALYSIS

The data was analyzed using SPSS version 26.0 (IBM Corp. Armonk, NY, US). The data distribution was assessed by the Kolmogorov-Smirnov test. Skewed distributed variables were given as median (25^{th} percentile-75^{th} percentile) and compared by the Mann-Whitney U test. The chi-square test was used for qualitative variables. Pearson correlations were applied to test the correlations between the study parameters examined. The effects of other variables (age and gender) were examined with binary logistic regression analysis. A p value of 5% or less is considered statistically significant.

RESULTS

In total, 52 adolescents with BMI>30 and 60 other age and sex-matched normal weighted (BMI=20-25) subjects were included in the study as obese and normal-weight control groups, respectively. The clinical and biochemical characteristics of both groups are given in Table 1. While red blood cell count (RBC) counts were found to be significantly higher in the obese adolescent group than in the non-obese group (p=0.009), mean corpuscular volume (MCV), platelet distribution width (PDW), NLR levels were found to be significantly lower in the obese group (p=0.038, p=0.03, p=0.02). Figure 1 includes data comparison graphs for parameters that show significant differences. (RBC, MCV, PDW, NLR) There was no significant difference between the obese and control groups when other parameters were examined.

BMI showed significant positive correlation with RBC and negative correlations with MCV and NLR (p=0.006, p=0.01, p=0.03) (Table 2). We did not detect any significant correlation between BMI and other hematological parameters. The markers that were significantly associated with BMI in the correlation analysis (RBC, MCV, NLR) and the markers that showed significant differences between the 2 groups (RBC, MCV, NLR, PDW) were further tested for their possible independent association with obesity in the regression analysis. There was a significant positive association between obesity and RBC (p=0.008), and a significant negative association between obesity and MCV, NLR (p=0.016, p=0.034). Additionally, despite statistically equal gender and age distribution across subgroups, gender, and age were included as covariates in the multivariate binary

TABLE 1: Differences between the hematologic parameters of the groups

Test	BMI>30	BMI=20-25	p value
WBC (10^9/L)	8.23 (7.48-9)	8.2 (7.6-9.1)	0.79
RBC (10^{12}/L)	4.92 (4.75-5.14)	4.68 (4.44-4.89)	0.009
HGB (g/dL)	13.25 (12.8-13.5)	12.85 (12.08-13.3)	0.09
PLT (10^9/L)	320 (293-342)	289 (269-315)	0.11
MCV(fL)	80.1 (78.4-82.4)	82.2 (80.6-83.3)	0.038
MCH (pg)	27.25 (26.8 -27.8)	27.6 (27.1-28.3)	0.12
MCHC (g/dL)	34.1 (33.6-34.3)	33.85 (33.6-34.1)	0.53
RDWCV (%)	13.5 (13.3-13.7)	13.4 (13.2-13.6)	0.26
MPV (fL)	9.75 (9.3-10.2)	9.9 (9.6-10.3)	0.31
PDW (%)	15.7 (15.6-15.8)	15.9 (15.8-16)	0.03
NLR	1.77 (1.5-2.08)	2.25 (1.97-3)	0.02
PLR (%)	124 (109-137)	135 (115-154)	0.195
PCT (%)	0.31 (0.18-0.5)	0.3 (0.28-0.31)	0.444

BMI: Body mass index; WBC: White blood cell; RBC: Red blood cell; HGB: Hemoglobin; PLT: Platelet; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDWCV: Red cell distribution width- coefficient of variation; MPV: Mean platelet volume; PDW: Platelet distribution width; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; PCT: Plateletcrit

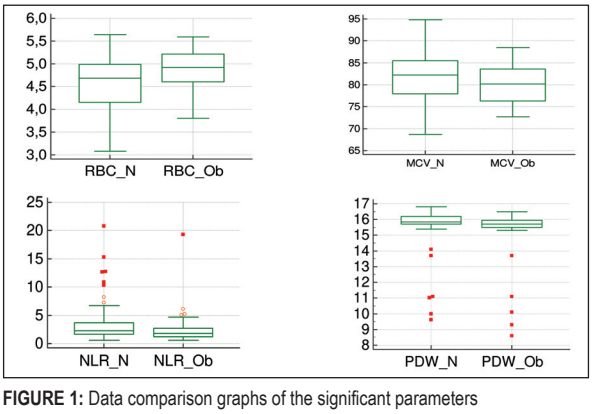

FIGURE 1: Data comparison graphs of the significant parameters
RBC_N: Red Blood Cell-Normal weight group RBC_Ob: Red Blood Cell-Obese group; MCV_N: Mean Corpuscular Volume-Normal weight group MCV_Ob: Mean Corpuscular Volume-Obese group; NLR_N: Neutrophil to lymphocyte ratio-Normal weight group NLR_Ob: Neutrophil to lymphocyte ratio-Obese group PDW_N: Platelet distribution width-Normal weight group PDW_Ob: Platelet distribution width-Obese group

TABLE 2: Correlations between BMI and hematological parameters

Test	Correlation coefficients	p value
WBC (10^9/L)	-0.056	0.551
RBC (10^{12}/L)	0.257**	0.006
HGB (g/dL)	0.17	0.07
PLT (10^9/L)	0.156	0.09
MCV (fL)	-0.241*	0.01
MCH (pg)	-0.145	0.1
MCHC (g/dL)	0.133	0.159
RDWCV (%)	-0.143	0.130
MPV (fL)	-0.14	0.123
PDW (%)	0.160	0.09
NLR	-0,191*	0,03
PLR (%)	-0,128	0,178
PCT (%)	-0.09	0.32

**: Correlation is significant at the 0.01 level (2-tailed). *: Correlation is significant at the 0.05 level (2-tailed).
BMI: Body mass index; WBC: White blood cell; RBC: Red blood cell; HGB: Hemoglobin; PLT: Platelet; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDWCV: Red cell distribution width-coefficient of variation; MPV: Mean platelet volume; PDW: Platelet distribution width; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; PCT: Plateletcrit

regression model. When multivariate binary regression analysis was performed, only RBC maintained an independent negative association with obesity among the tested markers (p=0.028) (Table 3).

DISCUSSION

In this study, we aimed to compare erythrocyte and platelet indices between obese patients and healthy individuals in the adolescent group in Turkish society. Ultimately, we aimed to examine how these values, which vary according to community and age group, change in obese adolescent cohort and to what extent they should be taken into account in clinical decisions. Our findings showed that obese participants had higher RBC, Hemoglobin (HGB), Platelet (PLT), RDW (p=0.009, p=0.09, p=0.11, p=0.26 respectively) and lower MCV, Mean platelet volume (MPV), PDW, NLR, and PLR (p=0.038, p=0.31, p=0.03, p=0.02, p=0.195, respectively) values than those in the normal-weight group.

Obesity is associated with chronic inflammation, which contributes to the development of atherosclerosis and metabolic syndrome (MS). Since white blood cell (WBC) count increases in inflammation, WBC count is likely to be higher in obese individuals. However, in our study, we did not observe a significant difference between the 2 groups in terms of WBC. Inflammation is a key factor in the emergence of metabolic diseases, and RDW may play an important role in assessing the importance and prognosis of metabolic syndrome in obesity. RDW is a simple and inexpensive hematological parameter that reflects the dissimilarity of erythrocyte size in peripheral blood. Numerous studies conducted in recent years have demonstrated that increased RDW is an important marker in the prognosis of many chronic diseases such as cardiovascular diseases, diabetes, and cancer. In Vuong et al.'s study, RBC, WBC, and RDW increased with waist circumference, a change that may be associated with the low-grade inflammatory state that occurs with chronic immune system activation.[16] Kohsari et al. described a positive relationship between RDW and BMI in overweight/obese individuals due to increased secretion of free radicals and proinflammatory cytokines by adipose tissue.[17] These processes may alter the morphology and size of RBC and lead to anisocytosis with a compensatory increase in newly produced RBC. The reason why we did not

TABLE 3: Binary logistic regression analysis results for the obese adolescent group

Univariate regression (unadjusted)				Multivariate regression (adjusted)			
Parameter	Exp(B)	95% CI	p value	Parameter	Exp(B)	95% CI	p value
RBC(10^{12}/L)	2.877	1.324- 6.252	0.008	RBC*	2.953	1.125-7.752	0.028
MCV(fL)	0.912	0.847-0.983	0.016	MCV*	0.976	0.897-1.062	0.570
PDW(%)	0.867	0.670-1.122	0.278	PDW*	0.876	0.758-1.385	0.876
NLR	0.850	0.731-0.988	0.034	NLR*	0.896	0.772-1.041	0.15

*Odds ratio adjusted for age and gender; OR: Odds ratio; CI: Confidence interval; RBC: Red blood cell; MCV: Mean corpuscular volume; PDW: Platelet distribution width; NLR: Neutrophil to lymphocyte ratio

find a significant difference in RDW in obese adolescents may be that they are at the beginning of the adipose tissue development process and have excess adipose tissue for a shorter period than adults. In contrast to all these studies, Klisic et al. found an independent negative association between lower red cell distribution width-coefficient of variation and BMI in overweight/obese adolescents.[18] There are conflicting data in the literature regarding the increased RDW values expected in obese individuals according to this theory. While Klisic et al. found low RDW findings in overweight/obese individuals, Furuncuoğlu et al. found an increase in RDW as BMI levels increased.[18,19] In our study, while there was a significant positive independent association between BMI and RBC (p=0.028), we could not detect a correlation between BMI and HGB, as well as BMI and RDW. However, the mean RDW value in obese individuals was higher than in normal-weight adolescents. The possible high RDW explanation could be an increase in insulin due to the metabolic syndrome that develops in obese individuals, as there are findings that insulin and insulin-like growth factors increase erythropoiesis.[16] In Abro et al.' mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration had statistically significant (p<0.001 and p=0.016) association with BMI.[20] Apart from these, Awad et al. reported no difference in RBC indices between individuals with obese and healthy groups.[21] The marker of mean red blood cell volume is MCV. In our study, we observed that MCV was lower in obese adolescents and was significantly negatively correlated with BMI. Inflammation resulting from obesity increases the hepatic output of the iron-regulating peptide hormone (Hepcidin). Raised hepcidin concentrations reduce the iron export to plasma by decreasing intestinal iron absorption and inadequate iron for erythropoiesis by acting as an inhibitor of the iron transporter ferroportin 1 in the duodenum. Hepcidin levels are increased in obese individuals, suggesting that hepcidin may be a factor in iron disorders in obesity.[22] Low MCV and increased RDW due to iron deficiency may be expected findings in obesity. In our study, MCV values were significantly lower in the obese group (p=0.038), but in the study by Farhangi et al, they reported that the difference in MCV values was not significant and the platelet count was significantly higher in the obesity group (p=0.047).[23] MPV is also a standard whole-blood parameter with an indicative role in the prognosis of diverse diseases. High MPV is an indicator of poor prognosis in acute thrombotic events. Findings in the meta-analysis study by Nkambule et al. suggest that mean platelet volume (MPV) may be an essential rapid parameter for monitoring and risk stratification of obese patients at risk of developing cardiovascular disease.[24] In Aslan et al.'s study, MPV was found to be significantly higher in obese adolescents than in their healthy peers.[25] We did not detect any significant difference in MPV values between the obese adolescent group and the normal-weight group. Our study demonstrated a significant difference between obese and normal-weight adolescent groups only in the PDW parameter in terms of platelet indices. As in our study, in the study of Erdal et al, although the PLT count was higher in the obese group, there was no significant difference in terms of MPV in both groups (p=0.815).[26] The NLR and PLR, measured by complete blood count, are considered effortless ways to demonstrate inflammation. In the study conducted by Aydın et al. with 187 children and adolescents (130 obese, 57 eutrophic) aged between 6 and 15 years, it was determined that NLR and C-reactive protein levels were significantly higher in the patient group than the healthy controls.[27] Yazaki et al, and Yu et al. found that the ratios were not different from the overweight and normal-weight groups.[28,29] In Koca's study, similar to our study, a negative correlation was found between NLR and BMI values, and lower NLR values were found in the obese group compared to the normal group.[30] Studies are showing that obesity is an independent risk factor for having higher cell counts in children.[31] It is predicted that this may indicate low-grade chronic inflammation. Studies showing the associations between increased cell counts and BMI in adolescence indicate that chronic inflammation can be managed by monitoring these lower-cost parameters in obesity treatment. Studies on obesity in adults have suggested that multiple comorbidities such as insulin resistance, diabetes, hyperlipidemia, and coronary vascular disease prevent the cause-effect association between obesity and in-

flammation from being revealed. This situation may also need to be considered for adolescent age groups. Therefore, one of the limitations of our study may be that comorbidities need to be taken into account. It is anticipated that this study will contribute to the clarification of controversial parameters and results that have emerged in the few studies conducted in adolescence to date. It is also believed that our study will guide future studies with larger numbers of individuals.

LIMITATIONS

Although adolescents with a BMI over 95th percentile according to age and gender are considered obese, we made this categorization using adult BMI diagnostic criteria. In addition, the insufficient number of obese adolescents can be perceived as a study limitation. The lack of some other simultaneous inflammatory markers may also cause the study results to remain uncertain.

CONCLUSION

In conclusion, with this study, in addition to previous studies on how obesity in adults can affect hematological parameters, we aimed to observe how obesity, which has been frequently seen in adolescents in recent years, affects hematological parameters. In this study, we observed that there is a positive independent association between BMI and RBC in the case of obesity developing in adolescence in Turkish society.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

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