

Research Article

The comparison of inflammatory hematological parameters in obese and non-obese children

Obez ve obez olmayan çocuklarda inflamatuvar hematolojik parametrelerin karşılaştırılması

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Abstract

Introduction: Obesity is an increasing health problem in the whole world, and it has an important inflammatory component related to the insulin resistance (IR), hypertension, atherosclerosis and some cancers. This study aims to evaluate the inflammatory hematological parameters in childhood obesity.

Methods: Sixty-four obese and 50 normal weight cases were included in the study. The physical examination features and laboratory data of the patients were evaluated retrospectively from the patient's files. Laboratory tests, hematological parameters, gender were compared between the groups. Correlations between Homeostasis model evaluation for insulin resistance (HOMA-IR) and other laboratory parameters in the obese group were examined.

Results: The leukocyte, neutrophile, monocyte, lymphocyte, thrombocyte and MPV values of the obese group were found to be statistically higher than the control group (p: 0.006, p:0.015, p:0.014, p:0.001, p<0.001). There was no statistically significant difference between the two groups for Neutrophile/Lymphocyte ratio (NLR), Monocyte/Lymphocyte ratio (MLR) and Platelet/Lymphocyte ratio (PLR) (p:0.642, p:0.989, 0.982). Also, there was no statistically significant correlation between Homa IR and age, BMI, Neutrophil, Lymphocyte, Monocyte, Thrombocyte, Neutrophil/Lymphocyte, Monocyte/Lymphocyte and Thrombocyte/Lymphocyte values.

Conclusion: The current study showed that there was no significant difference between obese and controls in terms of NLR, PLR, and MLR values. However, the leukocyte, neutrophile, monocyte, lymphocyte, thrombocyte and MPV values were statistically higher in obese group than controls. Nevertheless, these findings can point relation between obesity and inflammation.

Keywords: obesity, children, inflammation, hematological parameters

Öz


Giriş: Obezite, tüm dünyada giderek artan bir sağlık sorunudur ve insülin direnci (İD), hipertansiyon, ateroskleroz ve bazı kanserlerle ilgili önemli bir inflamatuvar faktöre sahiptir. Bu çalışma, çocukluk çağı obezitesindeki inflamatuvar hematolojik parametreleri değerlendirmeyi amaçlamaktadır.

Yöntem: Altmış dört obez ve 50 normal kilolu olgu çalışmaya dahil edildi. Hastaların fizik muayene özellikleri ve laboratuvar verileri dosyalarından geriye dönük olarak değerlendirildi. Gruplar arasında laboratuvar testleri, hematolojik parametreler, cinsiyet dağılımı karşılaştırıldı. Obez grupta insülin direnci (HOMA-IR) için Homeostasis modeli değerlendirmesi ile diğer laboratuvar parametreleri arasındaki korelasyonlar incelendi.

Bulgular: Obez grubun lökosit, nötrofil, monosit, lenfosit, trombosit ve MPV değerleri kontrol grubuna göre istatistiksel olarak yüksek bulundu (p: 0,006, p:0,015, p:0,014, p:0,001, p<0,001). Nötrofil/Lenfosit oranı (N/L), Monosit/Lenfosit oranı (M/L) ve Trombosit/Lenfosit oranı (T/L) açısından iki grup arasında istatistiksel olarak anlamlı fark yoktu (p: 0,642, p:0,989, 0,982). Ayrıca Homa IR ve yaş, VKİ, Nötrofil, Lenfosit, Monosit, Trombosit, Nötrofil/Lenfosit, Monosit/Lenfosit ve Trombosit/Lenfosit değerleri arasında istatistiksel olarak anlamlı bir ilişki bulunmamıştır.

Sonuç: Çalışmamızda obez adolesan grubunun N/L, P/L, M/L değerleri kontrol grubu ile benzerdi. Bununla birlikte, obez grubundaki lökosit, nötrofil, monosit, lenfosit, trombosit ve MPV değerleri, istatistiksel olarak kontrol grubundan daha yüksekti. Ancak bu bulgular, HOMA-IR'den bağımsız olarak obezite ve inflamasyon arasında bir ilişkiye işaret etmektedir.

Anahtar kelimeler: obezite, çocuk, inflamasyon, hematolojik parametreler

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Key Points

1. Obese children without additional complications, it is thought that the increase of neutrophil, lymphocyte, monocyte, and platelet counts could be a possible outcome of insulin resistance.
2. In this study the leukocyte, neutrophile, monocyte, lymphocyte, platelet and MPV values of the obese group were found to be statistically higher than the control group.
3. Increased leukocyte, platelet and MPV values in childhood obesity probably trigger atherogenesis.

Introduction

Obesity is an increasing health problem in the whole world. According to World Health Organization (WHO) it is defined as “abnormal or excessive fat accumulation that presents a risk to health” [1]. It is an important public health problem that affects 25-30% of children worldwide. Only 1-2% of childhood obesity develops from underlying diseases and syndromes whereas the great majority has exogenous obesity [2,3]. Studies indicate that 50% of obese adolescents are also obese in adulthood, this situation is associated with increased morbidity and mortality [4].

Obesity has an important inflammatory component related to insulin resistance (IR), hypertension, atherosclerosis and some cancers. The release of large amounts of inflammatory cytokines such as tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) from fatty tissue cause inflammation and trigger chronic inflammation [5,6]. It is shown in clinical studies that white blood cell (WBC) count, the number and ratio of lymphocytes, neutrophils are elevated in obesity and metabolic syndrome. Also, increased platelet count and platelet activation may occur as part of the chronic inflammation process in obesity [7]. Platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR) and monocyte/lymphocyte ratio (MLR) are defined as affordable and easily accessible indicators of degree of inflammation [8,9]. Studies conducted in adults display that these parameters are associated with body mass index (BMI), however different results are reported regarding their use in childhood obesity. This study aims to evaluate the inflammatory hematological parameters in childhood obesity.

Methods

This retrospective study included 64 obese pediatric patients who presented to the pediatric endocrinology and pediatric hematology outpatient clinic of Kartal Dr. Lutfi Kırdar City Hospital and pediatric hematology outpatient clinic at Acibadem Mehmet Ali Aydınlar University Hospital between July 2021 and February 2022. The control group comprised who did not have any disorder and who underwent a complete blood test for routine purposes, were retrospectively examined. Patients with infections, insulin-dependent diabetes, congenital metabolic disease, and hormonal disorders were excluded from the study.

According to World Health Organization (WHO) Growth Reference median values; obesity is defined as body mass index (BMI) for age greater than above two standard deviations (10). The patients wore light clothing and they were without shoes for weight measurement. Height was measured with a millimeter sensitive stadiometer without shoes. Each patient's weight in kilograms was divided by the square of his or every height in the mistress (kg/m²) as for BMI defined. A single pediatric endocrinologist made all anthropometric measurements.

All blood samples were taken by venous punctures after night fasting. Complete blood count (CBC) data of all subjects (obese + control) and blood glucose and insulin levels of patients in the obese group after 8 hours of fasting were recorded. Complete blood count parameters were measured by Abbott CELL-DYN Ruby hemogram analyzer with the help of laser flow cytometry technique. N/L ratio was calculated by dividing the number of neutrophils by the number of lymphocytes, the P/L ratio was calculated by dividing the number of platelets by the number of lymphocytes, and the M/L ratio was calculated by dividing the number of monocytes by the number of lymphocytes. Homeostasis model evaluation for insulin resistance (HOMA-IR); fasting insulin (IU/L) x fasting glucose (mg/dl)/405 was calculated [11].

Ethical approval, informed consent, and permissions

The study has been reviewed by the Ethics Committee of Acibadem University, Faculty of Medicine and has therefore been performed in accordance with the ethical standards laid down in an appropriate version of the Declaration of Helsinki (ethics approval number: 2022-15/11).

Informed consent

The approval of the local institutional review board was obtained before the study was begun (2022-15/11). Written informed consent for scientific use of data was provided by all parents or legal guardians of patients.

Statistical analysis

The data was evaluated in IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA) statistical package program. The descriptive statistics were denoted as number of units (n), percentage (%), mean \pm standard deviation, median (M), minimum (min), maximum (max) and interquartile range (IQR). Normal distribution of the numeric variables was examined with Shapiro Wilk normality test. Comparisons between groups in independent cases were performed with t test if they were normally distributed, Mann-Whitney U test was used in situations that are not normally distributed. Spearman correlation analysis tests were used for correlation analysis. $p < 0.05$ was considered statistically significant.

Results

Sixty-four obese and 50 normal weight cases were included in the study. Median age was 14 in the obese group, 13 in the control group. Boy to girl ratio was 0,56 in the obese group, 0,4 in the control group. There was no significant statistical difference between the age and gender of the groups.

The leukocyte, neutrophile, monocyte, lymphocyte, platelet and MPV values of the obese group were found to be statistically higher than the control group. There was no statistically significant difference between the two groups for Neutrophile/Lymphocyte ratio, Monocyte/Lymphocyte ratio and Platelet/Lymphocyte ratio (Table 1).

Table 1. The comparison of whole blood count parameters among study groups

Median (min-max)	Study groups		Test statistics	
	Obese (n=64)	Controls (n=50)	Test value	p value
Leukocyte	7815 (5150-16070)	7065 (4170-13340)	-2.744 ^ϕ	0.006
Neutrophil	3860 (2100-8450)	3425 (1350-10840)	-2.438 ^ϕ	0.015
Monocyte	855 (540-1590)	705 (440-2000)	-2.448 ^ϕ	0.014
Lymphocyte	2720 (1600-6160)	2490 (970-5300)	-2.033 ^ϕ	0.042
Platelet	324500 (192000-531000)	285000 (148000-403000)	-3.602 ^ϕ	0.001
Neutrophil/Lymphocyte	1.46 (0.71-2.68)	1.38 (0.34-7.97)	-0.465 ^ϕ	0.642
Monocyte /Lymphocyte	0.3 (0.15-0.69)	0.29 (0.13-0.84)	-0.014 ^ϕ	0.989
Platelet /Lymphocyte	113.55 (55.24-206.88)	111.44 (37.37-366.36)	-0.023 ^ϕ	0.982
MPV	10.34 ± 0.97	9.33 ± 1.38	4.388 [‡]	<0.001

^ϕ: Mann-Whitney U test (z), [‡]: Independent sample t test (t), Summary statistics are denoted as Median (min-max). Bold printed parts are statistically significant (p<0.05).

Descriptive statistics are shown in Table 2. Since blood samples were not evaluated for insulin and glucose from healthy children in the control group, these parameters and Homa IR were obtained only from the medical records of obese group.

Table 2. Descriptive statistics of study groups

	Study groups	
	Obese (n=64) Median (min-max)	Controls (n=50) Median (min-max)
Height (cm)	164.83 ± 9.95	147.21 ± 9.41
Height SDS	0.44 ± 1.09	-1.07 ± 0.65
Weight (kg)	92.92 ± 16.84	42.21 ± 8.13
Weight SDS	3.46 ± 1.03	-0.77 ± 0.61
BMI (kg/m ²)	33.99 ± 4.35	17.44 ± 5.42
BMI SDS	2.99 ± 0.56	-0.23 ± 0.56
Insulin	29.1 (10.1-67.6)	-
Glucose	85.66 ± 7.01	-
Homa IR	5.63 (2.06-14.06)	-

^ϕ: Summary statistics are mean ± standard deviation.

There is no statistically significant correlation found between Homa IR, Age, BMI, Neutrophil, Lymphocyte, Monocyte, Platelet, Neutrophil/Lymphocyte, Monocyte/Lymphocyte and Platelet/Lymphocyte values (Table 3).

Table 3. The correlation between HOMA-IR and other variables in obese group

	rho	p
Age	-0.136	0.284
BMI	0.225	0.073
Neutrophil	0.097	0.444
Lymphocyte	0.068	0.591
Monocyte	0.066	0.603
Platelet	0.187	0.138
Neutrophil/Lymphocyte	0.041	0.746
Monocyte / Lymphocyte	-0.007	0.954
Platelet/Lymphocyte	0.104	0.416

^ϕ: rho: Spearman Correlation Coefficient.

Discussion

In recent years, the prevalence of obesity has been increasing rapidly because of high fat diets and a sedentary lifestyle. Obesity plays a leading role in insulin resistance consisting of hyperinsulinemia, hypertension, hyperlipidemia, and type 2 diabetes and causes an increase in the risk of cardiovascular disease [12]. It is shown in studies that pathogenesis and associated risk factors of atherosclerotic cardiovascular disease extends to pediatric period [13].

The presence of chronic inflammation is defined in obesity. For the indication of chronic inflammation, various parameters and their ratios in blood counts are used [14,15]. Leukocytes which are partly responsible for the relationship between obesity and inflammation, infiltrate fatty tissue can cause the release of inflammatory cytokines [16,17]. Previously meta-analyses indicated that obese patients have an increased number of leukocytes in circulation and are at elevated risk for type 2 diabetes [18]. Also, in diabetic individuals there is a relationship between leukocyte subgroups and insulin resistance [19]. It is thought that one of the major determinants of the significant relationship between high leukocyte number and obesity is the presence of insulin resistance [20]. However, in this study, even in the absence of insulin resistance, obese individuals have higher leukocyte numbers compared to the control group. Nevertheless, the absolute leukocyte count of obese individuals is in the normal range. These findings support the findings of previous studies that indicate a positive relationship between leukocyte count and BMI. Besides, the high number of neutrophils can be attributed to the chemokines produced by adipose tissue which plays a role in bone marrow hematopoiesis and limitation of intravascular neutrophils [21].

The role of platelets in systemic inflammation has been reported in numerous studies. The value of MPV has been found associated with low grade inflammation. Mean platelet volume also increases in some risk situations such as hypercholesterolemia, diabetes mellitus and hypertension. Even though the underlying mechanism for the increase seen in obese individuals is unknown, it is thought to be induced by adipocytokines such as leptin, adiponectin, resistin and PAI [22]. Despite positive correlations reported between platelet and leukocyte counts and the development of cardiovascular disease, studies about the relationship between these measurements and obesity as a risk factor for cardiovascular disease are deficient. In this study, platelet count and MPV value is statistically significantly higher in obese patient group compared to the control group.

Platelet activation is also a critical component of thrombogenesis, and platelet hyperactivity is recorded in obese individuals. Moreover, platelets isolated from obese individuals after aspirin treatment, are found to preserve reactivity more compared to non-obese individuals [23]. Aydin et al. reports higher NLR in obese adolescents compared to the control group [24]. Santoz et al. reports a positive relationship between NLR and BMI in a study with obese children [25]. Dilek et al. reported no difference between NLR values in obese adolescents when compared to the control group [26]. Another research done on obese patients obtained comparable results and emphasized that NLR is not a good indicator of inflammation [27].

Monocyte lymphocyte ratio is accepted as a new indicator appropriate for routine use to determine systemic inflammatory response. In a study, it is found that MLR is an independent risk factor for cardiovascular disease (CVD) presence and in patients with previous coronary artery disease and it is associated with the severity of lesion [28]. In another study, MLR is reported to be a strong and independent predictor of cardiovascular disease mortality [29].

Increasing PLR values are related with cardiovascular diseases and situations that increase cardiovascular diseases. When we examine studies conducted on obese children, Anik et al. reported that PLR is not different in obese adolescents compared to healthy controls [30]. Likewise, no difference was found in the study conducted by Yazaki et al. [31].

In this study high NLR, MLR, PLR values were not detected in the obese patient group, moreover no significant relationship was found with BMI. The reason for this is thought to be the increase of lymphocyte count among with the increase in neutrophil, monocyte and platelet count.

Obesity is an independent risk factor in children to have higher cell counts, especially leukocytes, neutrophils and platelets. In the current study it is detected that obese adolescents have higher leukocyte counts and subgroups, platelet counts and MPV compared to their healthy peers however no difference was detected in N/L, P/L and M/L among the two groups. Correlation was not found between HOMA-IR and these parameters. However, the increase of leukocyte parameters indicates a relationship between obesity and inflammation independent of HOMA-IR.

Limitations

The limitations of current study such as the cross-sectional design of current work, that only, complete blood count parameters and ratios were used to assess chronic inflammation and that a wider spectrum of inflammatory biomarkers, such as C-reactive protein, erythrocyte sedimentation rate, fibrinogen and IL-6 would have been desirable.

Conclusion

In this study of obese children without additional complications, it is thought that the increase of neutrophil, lymphocyte, monocyte and platelet counts could be a possible outcome of IR. Moreover, increased leukocyte, platelet and MPV values in childhood obesity probably trigger atherogenesis. For this reason, keeping obesity under control with diet changes and other treatment methods is important to decrease mortality and morbidity rates in adulthood. More comprehensive studies on this subject are needed.

Conflict of interest: There are no conflicts of interest.

Author Contributions		Author Initials
SCD	Study Conception and Design	FDY, ES, BBA
AD	Acquisition of Data	ES, BBA
AID	Analysis and Interpretation of Data	FDY, ES
DM	Drafting of Manuscript	FDY, ES
CR	Critical Revision	FDY, ES, BBA

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