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Association Between Obesity Severity and Inflammatory Markers in Obese Children

Obez Çocuklarda Obezite Şiddeti ile Enflamatuvar Belirteçler Arasındaki İlişki

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Abstract

Objective: Childhood obesity is associated with chronic low-grade inflammation. This study aimed to evaluate the association between obesity severity and inflammatory hematologic parameters in children with obesity.

Method: This retrospective cross-sectional study included 88 pediatric patients with obesity aged 5-17 years who presented to the outpatient clinics of a tertiary pediatric training and research hospital. Patients were classified into obese and severely obese groups according to body mass index standard deviation score. Hematologic inflammatory parameters including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio (MLR) and hemoglobin levels were evaluated and compared between groups.

Results: A significantly greater proportion of participants were female in the severely obese group (p=0.016), whereas hemoglobin concentrations were higher among those with obesity (p=0.026). Among inflammatory hematologic ratios, only the MLR was significantly elevated in the obese group (p=0.003). In age- and sex-based subgroup analyses, an unadjusted difference in NLR was observed only in boys aged 5-9 years (p=0.016); however, this difference did not remain statistically significant after Bonferroni correction (adjusted p=0.064).

Conclusion: Inflammatory hematologic markers did not show a consistent relationship with obesity severity in children. Although MLR was lower in children with severe obesity and remained

Öz

Amaç: Çocukluk çağı obezitesi kronik düşük dereceli enflamasyon ile ilişkilidir. Bu çalışmada, obezite şiddeti ile obez çocuklardaki enflamatuvar hematolojik parametreler arasındaki ilişkinin değerlendirilmesi amaçlanmıştır.

Yöntem: Bu retrospektif kesitsel çalışmaya, üçüncü basamak bir çocuk eğitim ve araştırma hastanesinin polikliniklerine başvuran, yaşları 5-17 arasında değişen obezitesi olan 88 pediatrik hasta dahil edildi. Hastalar beden kitle indeksi standart sapma skoruna göre obez ve ağır obez gruplarına ayrıldı. Nötrofil-lenfosit oranı (NLR), trombosit-lenfosit oranı, monosit-lenfosit oranı (MLR) ve hemoglobin düzeylerini içeren hematolojik enflamatuvar parametreler değerlendirildi ve gruplar arasında karşılaştırıldı.

Bulgular: Ağır obez grubunda kadın cinsiyet oranı anlamlı olarak daha yüksek bulundu (p=0,016), buna karşın hemoglobin düzeyleri obez grubunda daha yüksekti (p=0,026). Enflamatuvar hematolojik oranlar arasında yalnızca MLR obez grupta anlamlı olarak daha yüksekti (p=0,003). Yaş ve cinsiyete göre yapılan alt grup analizlerinde, yalnızca 5-9 yaş arası erkek çocuklarda NLR açısından düzeltilmemiş analizde farklılık saptandı (p=0,016); ancak bu farklılık Bonferroni düzeltmesi sonrasında istatistiksel anlamlılığını korumadı (düzeltilmiş p=0,064).

Sonuç: Enflamatuvar hematolojik belirteçler çocuklarda obezite şiddeti ile tutarlı bir ilişki göstermemiştir. MLR ağır obez çocuklarda daha düşük bulunmuş ve yaş ile cinsiyete göre düzeltme sonrasında da obezite şiddeti ile anlamlı ilişkisini korumuşken, NLR çoklu karşılaştırma düzeltmesi sonrasında anlamlı bir ilişki göstermemiştir.

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Abstract

significantly associated with obesity severity after adjustment for age and sex, NLR showed no significant association after correction for multiple comparisons. These findings suggest that inflammatory hematologic markers should be interpreted with consideration of age, sex, and obesity severity.

Keywords: Childhood obesity, inflammatory markers, obesity severity

Öz

Bu bulgular, enflamatuvar hematolojik belirteçlerin yaş, cinsiyet ve obezite şiddeti dikkate alınarak yorumlanması gerektiğini düşündürmektedir.

Anahtar kelimeler: Çocukluk çağı obezitesi, enflamatuvar belirteçler, obezite şiddeti

Introduction

Childhood obesity represents a growing global public health concern and is associated with metabolic, inflammatory, endocrine, and hematologic alterations throughout childhood and adolescence (1). Excess adipose tissue functions not only as an energy storage organ but also as an active endocrine organ that secretes various adipokines and proinflammatory cytokines. Increased adipose tissue accumulation, adipokine imbalance, oxidative stress, and dysregulation of immune system activation contribute to the development of chronic low-grade inflammation in children with obesity (2,3).

Recent studies have demonstrated that obesity-related inflammation may play an important role in the pathogenesis of insulin resistance, metabolic syndrome, cardiovascular disease, and endothelial dysfunction beginning from early life (4,5). Therefore, identifying simple and accessible inflammatory biomarkers in children with obesity has gained increasing clinical importance.

Inflammatory hematological ratios derived from routine complete blood count parameters are inexpensive, practical, and easily accessible markers for evaluating systemic inflammation. Among these, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been associated with inflammation and metabolic risk in pediatric obesity; however, findings regarding their relationship with obesity severity remain inconsistent (6-8).

The monocyte-to-lymphocyte ratio (MLR) has been evaluated in a limited number of studies in obese children, and its association with obesity severity is still unclear. Previous studies have suggested that inflammatory hematological ratios may indicate the presence of obesity-related inflammation but may not increase linearly with increasing obesity severity (9-11). In addition, inflammatory responses and hematological parameters may vary according to age and sex (12).

Accordingly, this study aimed to evaluate the relationship between obesity severity and inflammatory hematological ratios, including NLR, PLR, and MLR, in children with obesity while taking age and sex differences into consideration.

Materials and Methods

This single-center cross-sectional observational study was conducted at the Department of Pediatrics of University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital. Pediatric patients aged 5-17 years with obesity who presented to the outpatient clinics between April 1, 2025, and December 1, 2025, were evaluated. All eligible patients who met the predefined inclusion criteria during the study period were included in the study.

Inclusion criteria were age between 5 and 17 years, body mass index-standard deviation score (BMI-SDS) ≥2, and availability of complete blood count data. Exclusion criteria were chronic kidney disease, chronic liver disease, malabsorption syndromes, congenital heart disease, diabetes mellitus, hypothyroidism, Cushing's syndrome, other endocrine disorders, any medication use or supplementation (including vitamin B12, folate, or vitamin D), and the presence of acute or chronic infection.

Ethical Approval

Ethical approval for the study was obtained from the Scientific Research Ethics Committee of University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital on June 25, 2025 (decision no: 2025/231). The extension of the retrospective study period was subsequently approved by the same Ethics Committee at its meeting held on January 14, 2026, under the same study approval (decision no: 2025/231). All procedures were conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

Anthropometric and Clinical Measurements

Height was measured using a stadiometer with participants wearing light clothing and no shoes. Body weight was measured using a calibrated digital scale. BMI was calculated as weight (kg) divided by height squared (m^2). BMI-SDS values were calculated using the ÇEDD Çözüm/TPEDS Metrics software based on age- and sex-specific reference values for Turkish children reported by Neyzi et al. (13). Obesity was defined as BMI-SDS ≥2 to <3, while severe obesity was defined as BMI-SDS ≥3 according to World Health Organization criteria (14).

Laboratory Assessments

Complete blood count results from venous blood samples collected in the morning after an overnight fast (8-12 hours) were retrospectively retrieved from the hospital information system. Complete blood count parameters were recorded for analysis.

NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. PLR was calculated as the absolute platelet count divided by the absolute lymphocyte count. MLR was calculated as the absolute monocyte count divided by the absolute lymphocyte count. All parameters were derived from complete blood count analysis.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as median (minimum-maximum), and categorical variables as number and percentage [n (%)]. Percentages were calculated within each study group.

Participants were classified into two groups based on BMI-SDS values: Obese (BMI-SDS ≥2 to <3) and severely obese (BMI-SDS ≥3.0). Comparisons were performed between obese and severely obese groups.

Intergroup comparisons were performed using the Mann-Whitney U test for continuous variables and Pearson's chi-square test for categorical variables. To evaluate the association between obesity severity and MLR independently of potential confounding factors, a multivariable linear regression analysis was performed with MLR as the dependent variable and obesity severity group, age, and sex as independent variables.

For age- and sex-stratified NLR analyses, Bonferroni correction was applied to account for multiple comparisons. A p-value <0.05 was considered statistically significant.

Results

A total of 88 individuals with obesity in the pediatric age spectrum (5-17 years) were analyzed. Of these, 65 (73.9%) were classified as obese and 23 (26.1%) as severely obese. The median age of the entire group was 11 (5-17) years, with no significant age difference between groups (p=0.557).

Females constituted a significantly greater proportion of the severely obese group than of the obese group (73.9% vs. 44.6%, p=0.016).

Among hematological parameters, hemoglobin levels were significantly higher in the obese group than in the severely obese group (p=0.026). Basophil counts (p=0.038) and red cell distribution width (p=0.025) also differed significantly between the groups. No statistically significant intergroup differences were observed in neutrophil, lymphocyte, monocyte, platelet, eosinophil, total white blood cell, red blood cell, mean platelet volume, mean corpuscular volume, or plateletcrit values (all p>0.05) (Table 1).

Among inflammatory hematological ratios, MLR values were significantly higher in children with obesity than in those with severe obesity (p=0.003). In contrast, no significant differences were observed in NLR (p=0.176) or PLR (p=0.422). After adjustment for age and sex, greater obesity severity remained independently associated with lower MLR (B=-0.042, standardized β=-0.269, p=0.015) (Table 2).

In the age- and sex-stratified analysis of NLR, an unadjusted intergroup difference was observed among boys aged 5-9 years (p=0.016); however, this finding did not remain statistically significant after Bonferroni correction for multiple comparisons (adjusted p=0.064). No significant differences were observed in girls aged 5-9 years or in boys or girls aged 10-17 years after adjustment for multiple comparisons (Table 3). Sex distribution findings are shown in Figure 1.

Discussion

This study aimed to evaluate the relationship between obesity severity and inflammatory hematological markers in children with obesity, in the context of the well-established association between childhood obesity and low-grade chronic inflammation. Childhood obesity is recognized as a complex disease associated with increased adipose tissue accumulation, adipokine imbalance, oxidative stress, and chronic inflammation (1,2).

Table 1. Demographic and hematological characteristics of the study population

Parameter	Total cases n=88 Median (min-max)	Obese n=65 Median (min-max)	Severely obese n=23 Median (min-max)	p-value
Age, years	11 (5-17)	10.5 (5-16)	13 (5-17)	0.557[1]
Female sex, n (%)	46 (52.3)	29 (44.6)	17 (73.9)	**0.016**[2]
Hemoglobin (g/dL)	12.9 (10.5-16)	13 (10.5-16)	12.5 (10.9-14.3)	**0.026**[1]
Neutrophils (10^3/mm^3)	4.41 (1.47-11.13)	4.44 (1.47-11.13)	4.22 (2.43-8.04)	0.655[1]
Lymphocytes (10^3/mm^3)	2.76 (1.05-6.15)	2.62 (1.05-6.15)	2.9 (1.65-4.26)	0.093[1]
Platelets (10^3/mm^3)	309 (137-525)	309 (137-482)	309 (181-525)	0.525[1]
Monocytes (10^3/mm^3)	0.48 (0.22-1.1)	0.48 (0.22-1.1)	0.44 (0.23-0.65)	0.171[1]
Eosinophils (10^3/mm^3)	0.17 (0-1.05)	0.17 (0-1.05)	0.16 (0.03-0.87)	0.569[1]
Basophils (10^3/mm^3)	0.03 (0.01-0.22)	0.03 (0.01-0.22)	0.03 (0.01-0.06)	**0.038**[1]
Red cell distribution width (%)	13.85 (9-19.7)	13.7 (9-19.7)	14.5 (11.8-17.2)	**0.025**[1]
Mean corpuscular volume (fL)	79.7 (68-94.5)	79.8 (70.6-88)	79 (68-94.5)	0.409[1]
NLR	1.66 (0.46-4.1)	1.7 (0.46-4.1)	1.51 (0.66-3.44)	0.176[1]
PLR	117.33 (49.26-214.43)	119.9 (58.33-214.43)	110.06 (49.26-210.3)	0.422[1]
MLR	0.17 (0.09-0.41)	0.18 (0.11-0.41)	0.15 (0.09-0.36)	**0.003**[1]
Mean platelet volume (fL)	9.15 (7-12.2)	9 (7-12.2)	9.2 (7.3-11.8)	0.868[1]
White blood cells (10^3/mm^3)	7.71 (2.9-16.25)	7.75 (2.9-16.25)	7.5 (4.9-11.2)	0.906[1]
Red blood cells (10^6/mm^3)	4.9 (2.02-6.21)	4.9 (2.02-6.21)	4.89 (3.97-5.53)	0.812[1]
Plateletcrit (%)	0.28 (0.15-0.46)	0.28 (0.15-0.39)	0.26 (0.22-0.46)	0.604[1]

[1]: Mann-Whitney U test, [2]: Pearson's chi-square test, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio

Table 2. Multivariable linear regression analysis of factors associated with MLR

Variable	B	Standardized β	p-value
Sex	-0.005	-0.035	0.756
Obesity severity group	**-0.042**	**-0.269**	**0.015**
Age, years	0.002	0.113	0.305

Dependent variable: MLR. Obesity severity group was coded as 1= obese and 2= morbidly obese. Sex was coded as 1= male and 2= female. B: Unstandardized regression coefficient; MLR: Monocyte-to-lymphocyte ratio

Table 3. Comparison of NLR values according to age group, sex, and obesity severity

Age group	Sex	Obese n	Obese Median (min-max)	Severely obese n	Severely obese Median (min–max)	p-value	Bonferroni-adjusted p
5-9 years	Male	**18**	1.53 (0.70-3.50)	**3**	0.91 (0.84-0.94)	0.016	0.064
	Female	**9**	1.31 (0.84-3.34)	**5**	1.50 (0.96-1.97)	0.841	1.000
10-17 years	Male	**18**	1.70 (0.98-3.80)	**3**	1.56 (0.66-1.58)	0.159	0.636
	Female	**20**	1.90 (0.46-4.10)	**12**	1.90 (1.12-3.44)	0.533	1.000

Bonferroni adjustment was applied for four subgroup comparisons. Adjusted p-values were calculated as p × 4 and capped at 1.000, NLR: Neutrophil-tolymphocyte ratio

Recent studies suggest that obesity-related inflammation begins early in life and may contribute to insulin resistance, endothelial dysfunction, and cardiovascular risk before clinically overt complications become apparent (2,3).

One notable finding of this study was the significantly greater proportion of females in the severely obese group, suggesting that sex-specific biological and hormonal differences may influence obesity severity during

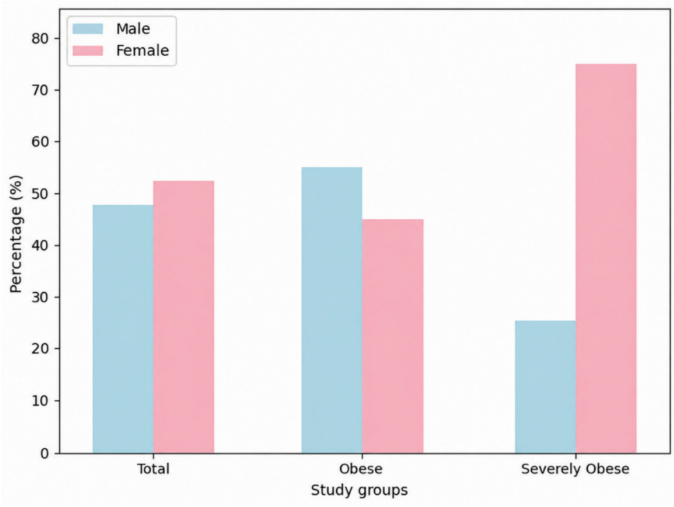

Figure 1. Distribution of sex by obesity severity

childhood and adolescence. Particularly during puberty, increased adipose tissue, elevated leptin levels, and hormonal changes in girls may contribute to more severe obesity (1). This finding is consistent with previous studies emphasizing sex as an important factor influencing obesity severity in pediatric populations (2).

One of the most striking findings of our study was that MLR values were higher in the obese group than in the severely obese group. Importantly, this association remained statistically significant after adjustment for age and sex, indicating that the association between obesity severity and MLR was independent of these potential confounding factors. This finding suggests that inflammation may not increase linearly with increasing obesity severity. While NLR and PLR have been widely investigated in pediatric obesity, data regarding MLR remain limited. Türkkan et al. (6) found no significant difference in MLR between obese adolescents and healthy controls and did not support the utility of inflammatory hematological ratios as biomarkers of adolescent obesity. In contrast, Bala and Bala (8) reported significantly higher MLR values in children with obesity than in normal-weight controls and demonstrated an association between MLR and bone mineral density in the obese group. These differing findings suggest that the relationship between MLR and pediatric obesity may be complex. The mechanisms underlying the lower MLR values observed in severe obesity in our study remain unclear and require further investigation.

Regarding NLR, our findings highlight the importance of considering age and sex when interpreting NLR in relation to obesity severity. Aydın et al. (9) reported that NLR reference ranges in children vary according to age and sex. Likewise, Aydin et al. (3) demonstrated that NLR may be influenced by age- and sex-related differences. In the present study, although an unadjusted difference in NLR was observed among boys aged 5-9 years, this finding did not remain statistically significant after Bonferroni correction for multiple comparisons. Therefore, this subgroup finding should be interpreted cautiously and does not provide sufficient evidence for an independent association between obesity severity and NLR.

The absence of significant differences in PLR, NLR, and most other hematological parameters according to obesity severity suggests that not all inflammatory hematological indices reflect obesity severity to the same extent. Previous studies have shown that although NLR and PLR may indicate increased inflammation in obese children, their ability to distinguish obesity severity remains limited (4,5). Additionally, mean platelet volume and platelet indices may change in obese children, but these changes are not always parallel to obesity severity (10,11).

Another important finding of this study was that hemoglobin levels were higher in the obese group than in the severely obese group. This finding suggests that hematological parameters may not change proportionally with increasing obesity severity. Previous studies have reported associations between obesity and alterations in hematological parameters in children (15,16). In addition, Furuncuoğlu et al. (7) demonstrated that BMI was associated with several complete blood count parameters, although hemoglobin levels did not differ significantly across BMI categories. Therefore, the lower hemoglobin levels observed in the severely obese group in our study may reflect differences in hematological profiles according to obesity severity; however, the underlying mechanisms remain unclear and require further investigation.

Study Limitations

Certain methodological constraints should be acknowledged. The single-center design and modest sample size may restrict the external validity of the results. Second, due to its cross-sectional design, causal relationships between obesity severity and inflammatory hematological parameters cannot be established. Third, inflammatory status was evaluated only through complete blood count-derived ratios, and additional inflammatory biomarkers such as high-sensitivity C-reactive protein or cytokine levels were not assessed. In addition, the absence of a healthy control group limited the ability to compare

inflammatory hematological parameters between obese and non-obese children. Finally, pubertal stage was not evaluated separately, although age- and sex-related differences were considered, which may have influenced the hematological parameters.

Conclusion

Obesity severity was not consistently associated with inflammatory and hematological markers in children with obesity. MLR was lower in children with severe obesity, and this association remained significant after adjustment for age and sex. In contrast, NLR did not differ significantly according to obesity severity after correction for multiple comparisons. These findings suggest that the associations between obesity severity and inflammatory hematological markers may vary across different markers and highlight the importance of considering age, sex, and potential confounding factors in their interpretation. Larger prospective studies are needed to clarify the underlying inflammatory mechanisms.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Scientific Research Ethics Committee of University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital on June 25, 2025 (decision no: 2025/231).

Informed Consent: The requirement for informed consent was waived due to the retrospective nature of the study.

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During the preparation of this manuscript, ChatGPT (OpenAI) was used as a language assistance tool. The authors reviewed and approved all content and take full responsibility for the final manuscript.

Footnotes

Authorship Contributions

Concept: A.B., Y.C., Ş.G., Design: A.B., Y.C., Ş.G., Data Collection or Processing: A.B., E.N.S., S.G.Ç., F.N.A.Ç., E.B.K.Ç., Analysis or Interpretation: A.B., F.N.A.Ç., Literature Search: A.B., E.N.S., S.G.Ç., E.B.K.Ç., Writing: A.B., E.N.S., S.G.Ç., F.N.A.Ç., E.B.K.Ç., Y.C., Ş.G.

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