Original Article
Internal Medicine
DOI: 10.56016/dahudermj.1567959

DAHUDER
Medical Journal
e-ISSN: 2791-9250

Impact of obesity severity on hepatic steatosis and systemic inflammatory markers: a comparative analysis across obesity classes

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ABSTRACT

Objectives: Obesity has become a global health issue, with its prevalence steadily increasing. It is closely linked to several metabolic disorders, cardiovascular diseases, non-alcoholic fatty liver disease, and chronic low-grade inflammation and can progress to more severe liver conditions. This study evaluates the relationship between obesity and inflammatory markers in individuals with different obesity levels.

Methods: A cross-sectional study was conducted among 50 patients categorized into three obesity classes based on body mass index (BMI). Blood samples were taken to evaluate inflammatory and metabolic markers, including white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein (CRP). Results: There were no statistically significant differences in inflammatory markers such as WBC, NLR, or CRP; a trend toward higher CRP levels was observed in Class 3 obesity.

Conclusion: In our study, no statistically significant association was observed between inflammatory markers and the degree of obesity. Although the sample size was relatively small, it is essential to acknowledge that obesity is a multifaceted condition, and genetic variations may play a role in these results.

Keywords: Obesity, inflammation, the neutrophil-to-lymphocyte ratio, the C-reactive protein

Obesity is a global health concern, with its prevalence continuing to rise significantly over the past decades. Obesity is strongly associated with metabolic complications such as type 2 diabetes mellitus (T2DM), cardiovascular diseases, and hepatic steatosis, mainly non-alcoholic fatty liver disease (NAFLD). Hepatic steatosis, which refers to the excessive accumulation of fat in the liver, often manifests as part of the metabolic syndrome in obese individuals. The pathogenesis of NAFLD is multifactorial, mainly driven by insulin resistance, central obesity, and systemic inflammation, which contributes to the progression of simple steatosis to more severe liver conditions such as non-alcoholic steatohepatitis (NASH) and cirrhosis.[1, 2]

Chronic low-grade inflammation plays a crucial role in obesity-related metabolic dysfunction and the development of hepatic steatosis. Several inflammatory markers, including C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII), have been identified as critical indicators of metabolic dysregulation in obese individuals. Recent studies have demonstrated a strong association between elevated inflammatory

Received: *October 17, 2024;* ***Accepted:*** *October 25, 2024;* ***Published Online:*** *October 29, 2024*

How to cite this article: *Uyar S, N Koca, Oral A, Zorlu Görgülügil G. Impact of obesity severity on hepatic steatosis and systemic inflammatory markers: a comparative analysis across obesity classes. DAHUDER MJ 2024,4(4):77-82. DOI: 10.56016/dahudermj.1567959*

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Available at http://dergipark.org.tr/en/pub/dahudermj

markers and both hepatic steatosis and cardiovascular risk in obese populations.[1, 3]

The relationship between obesity, inflammation, and liver health is of increasing interest due to the rising incidence of NAFLD in parallel with the obesity epidemic. Emerging evidence suggests that central obesity and insulin resistance are primary drivers of both hepatic fat accumulation and systemic inflammation, contributing not only to liver disease but also to an increased risk of cardiovascular morbidity and mortality.[2, 4]

This study aims to explore the differences in demographic, metabolic, and inflammatory profiles among individuals with varying degrees of obesity and hepatic steatosis, providing further insights into the interplay between obesity-related inflammation and liver health.

METHODS

Study Design and Population

This cross-sectional study evaluated and compared demographic characteristics and laboratory parameters among 50 patients with Class 1, Class 2, and Class 3 obesity. The study population consisted of individuals who presented to the outpatient clinic for routine health examinations and were diagnosed with obesity based on their body mass index (BMI) values. The inclusion criteria were adults aged 18 and older with a BMI ≥30 kg/m². Patients with any history of chronic liver disease, active infection, autoimmune disorders, or malignancy were excluded from the study.

Obesity Classification

Obesity was classified according to BMI into three categories: Class 1 (BMI 30.0–34.9 kg/m²), Class 2 (BMI 35.0–39.9 kg/m²), and Class 3 (BMI ≥40.0 kg/m²). These classes are consistent with the World Health Organization (WHO) criteria for obesity stratification.[5]

Data Collection

Demographic data, including age, gender, height, weight, and waist circumference, were collected through patient interviews and physical examinations. BMI was calculated by dividing the patient's weight (in kilograms) by the square of their height (in meters). Hepatic steatosis was assessed by ultrasound and graded into three categories: Grade 1 (mild), Grade 2 (moderate), and Grade 3 (severe) steatosis.

Laboratory Measurements

Blood samples were collected after an overnight fast to assess various laboratory parameters. The following parameters were measured using standard automated techniques:

- **White blood cell (WBC) count, neutrophil (Neu) count**, and lymphocyte (Lymph) count were measured as indicators of systemic inflammation.
- **Hemoglobin (Hb) and platelet (Plt)** counts were assessed to evaluate hematologic status.
- **Fasting blood glucose (FBG), aspartate aminotransferase (AST), and alanine aminotransferase (ALT)** were evaluated as markers of metabolic and liver function.
- **Thyroid-stimulating hormone (TSH)** levels were measured to assess thyroid function.
- **The neutrophil-to-lymphocyte ratio (NLR),** a marker of systemic inflammation, was calculated by dividing the neutrophil count by the lymphocyte count.
- **C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)** were measured as additional inflammatory markers.
- The **FIB-4 index,** an indicator of liver fibrosis, was calculated using the formula:

$$\text{FIB-4} = (\text{age} \times \text{AST}) / (\text{platelet count} \times \sqrt{\text{ALT}})$$

Ethical Consideration

This study followed the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Antalya Training & Research Hospital Institutional Review Board (IRB) before the initiation of the study (2024-15/21). The confidentiality and privacy of participants were strictly maintained, and all data were anonymized before analysis to ensure participant protection. Additionally, the study adhered to all local and national guidelines for human research ethics.

Statistical Analysis

Descriptive statistics were presented as mean ± standard deviation (SD) or median (range) for continuous variables and as frequencies (percentages) for categorical variables. The normality of distribution was assessed using the Shapiro-Wilk test. Comparisons between the three obesity classes were performed using one-way analysis of variance (ANOVA) for normally distributed continuous variables and the Kruskal-Wallis test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

A p-value <0.05 was considered statistically significant. All statistical analyses were conducted using SPSS (version 26).

RESULTS

Demographic Comparison Among Obesity Classes

The comparison of demographic characteristics among patients with Class 1, Class 2, and Class 3 obesity is summarized in Table 1. There was no significant difference in age among the three obesity classes (47.42±9.94 vs. 52.47±12.52 vs. 48.09±8.43, p=0.331). Additionally, the gender distribution did not differ significantly between the groups, with a female predominance observed in all classes (62.5% vs. 46.7% vs. 63.6%, p=0.567).

Participants' height was also comparable across obesity classes (166.38±9.9 cm vs. 164.33±8.89 cm vs. 164.09±8.4 cm, p=0.718). However, there were notable differences in weight, with individuals in Class 3 obesity having significantly higher body weight compared to those in Class 1 and Class 2 obesity (93.42±29.33 kg vs. 98.47±12.55 kg vs. 115.73±15.74 kg, p<0.001).

Waist circumference showed a progressive increase with increasing obesity class, significantly more prominent in Class 3 compared to the other two groups (110.54±8.73 cm vs. 115.6±7.47 cm vs. 126.45±4.89 cm, p<0.001). Similarly, BMI increased significantly across the obesity classes (32.08±1.3 kg/m² vs. 36.33±1.33 kg/m² vs. 43.3±2.14 kg/m², p<0.001).

Regarding hepatic steatosis, there was a statistically significant difference among the classes, with higher grades of steatosis being more prevalent in Class 3 obesity (Grade 1: 50% vs. 40% vs. 9.1%; Grade 2: 37.5% vs. 46.7% vs. 27.3%; Grade 3: 12.5% vs. 13.3% vs. 63.6%, p=0.010).

Laboratory Parameter Comparison Among Obesity Classes

The comparison of laboratory parameters across the different obesity classes is summarized in Table 2. No statistically significant differences were observed in WBC count among the three classes (8.73±2.6 vs. 8.45±3.67 vs. 8.63±2.95 cells/µL, p=0.776). Similarly, the neutrophil count showed no significant variation (5.17±2.09 vs. 4.75±2.43 vs. 5.22±2.01 cells/µL, p=0.522), nor did the lymphocyte count (2.66±0.71 vs. 2.77±1.03 vs. 2.5±0.72 cells/µL, p=0.835).

Table 1. The comparison of demographics among the obesity classes

	Class 1 Obesity (n=24)		Class 2 Obesity (n=15)		Class 3 Obesity (n=11)		*p*
	Mean±SD	Median (Min-Max)	Mean±SD	Median (Min-Max)	Mean±SD	Median (Min-Max)	
Age	47.42±9.94	47.5(30-68)	52.47±12.52	55(24-72)	48.09±8.43	48(31-62)	0.331*
Gender, n (%)							0.567
Female		15 (62.5)		7 (46.7)		7 (63.6)	
Male		9 (37.5)		8 (53.3)		4 (36.4)	
Height, cm	166.38±9.9	165(150-184)	164.33±8.89	164(150-182)	164.09±8.4	164(155-183)	0.718*
Weight, kg	93.42±29.33	91.5(70-220)	98.47±12.55	99(80-130)	115.73±15.74	109(102-156)	<0.001
Waist Circumference, cm	110.54±8.73	112.5(95-128)	115.6±7.47	114(104-131)	126.45±4.89	128(119-133)	<0.001*
BMI, kg/m^2	32.08±1.3	31.9(30.1-34.9)	36.33±1.33	35.8(35-39.2)	43.3±2.14	43,7(40,2-46,6)	<0.001
Steatosis, n (%)							0.010
Grade 1		12 (50)		6 (40)		1 (9.1)	
Grade 2		9 (37.5)		7 (46.7)		3 (27.3)	
Grade 3		3 (12.5)		2 (13.3)		7 (63.6)	

BMI: body mass index
*: one-way ANOVA

The levels of Hb were consistent across the obesity classes (13.46±2 vs. 13.85±1.69 vs. 13.85±1.05 g/dL, p=0.727), as were Plt counts (291.75±70.09 vs. 287.27±74.91 vs. 271.55±90.09 cells/µL, p=0.766).

While FBG values varied among the obesity classes, these differences were not statistically significant (124.75±64.32 vs. 93.93±20.36 vs. 104.28±46.44 mg/dL, p=0.577). The liver enzymes AST and ALT also did not show significant differences among the groups (AST: 20.63±8.28 vs. 21.2±12.11 vs. 25.82±16.89 IU/L, p=0.678; ALT: 25.71±16.2 vs. 26.33±24.58 vs. 26.55±9.36 IU/L, p=0.304).

Regarding thyroid function, no significant difference was noted in TSH levels between the obesity classes (3.04±2.34 vs. 2.03±1.29 vs. 11.42±32.04 mIU/L, p=0.422). The NLR, an important marker of inflammation, showed no significant variation across classes (2.02±0.82 vs. 1.78±0.65 vs. 2.17±0.8, p=0.481).

Although CRP levels tended to increase with higher obesity class, especially in Class 3 (5.83±4.22 vs. 6.73±4.49 vs. 11.76±9.65 mg/L), this trend did not reach statistical significance (p=0.218). Similarly, the ESR comparison across the classes did not reveal any significant differences (16.61±10.56 vs. 18.13±10.18 vs. 13.43±8.98 mm/h, p=0.505).

Lastly, the FIB-4 index, a marker of liver fibrosis, was not significantly different among the obesity classes (0.72±0.32 vs. 0.74±0.33 vs. 1.06±0.72, p=0.367).

Table 2. The comparison of laboratory parameters among the obesity classes

	Class 1 Obesity (n=24)		Class 2 Obesity (n=15)		Class 3 Obesity (n=11)		*p*
	Mean±SD	Median (Min-Max)	Mean±SD	Median (Min-Max)	Mean±SD	Median (Min-Max)	
WBC, cells/mL	8.73±2.6	7.8(5.1-14.1)	8.45±3.67	7.6(5.7-20.5)	8.63±2.95	8.4(5.1-15.9)	0.776
Neu, cells/mL	5.17±2.09	4.52(2.66-9.8)	4.75±2.43	4.03(2.71-12.39)	5.22±2.01	5.12(2.95-10.46)	0.522
Lymph, cells/mL	2.66±0.71	2.56(1.24-3.85)	2.77±1.03	2.59(1.27-5.78)	2.5±0.72	2.5(1.05-3.61)	0.835
Hb, g/dL	13.46±2	13.2(9.4-17.2)	13.85±1.69	13.6(10.5-17.3)	13.85±1.05	14.1(12.1-15.9)	0.727*
Plt, cells/mL	291.75±70.09	279(188-436)	287.27±74.91	261(178-421)	271.55±90.09	235(181-475)	0.766*
FBG, mg/dL	124.75±64.32	97.5(70-323)	93.93±20.36	90(53-130)	104.28±46.44	102(3.1-191)	0.577
AST, IU/L	20.63±8.28	19(10-50)	21.2±12.11	19(12-64)	25.82±16.89	19(15-74)	0.678
ALT, IU/L	25.71±16.2	20(9-84)	26.33±24.58	21(9-113)	26.55±9.36	24(16-48)	0.304
TSH, mIU/L	3.04±2.34	2.95(0.62-11)	2.03±1.29	1.86(0.29-4.6)	11.42±32.04	1.6(0.8-108)	0.422
N/L Ratio	2.02±0.82	1.87(1.03-3.92)	1.78±0.65	1.61(0.81-3.23)	2.17±0.8	1.91(1.34-4.1)	0.481
CRP, mg/L	5.83±4.22	6.4(0.9-20.4)	6.73±4.49	7(1.2-16.9)	11.76±9.65	8.7(1.3-27.2)	0.218
ESR, mm/h	16.61±10.56	16.37(3-45)	18.13±10.18	19(2-35)	13.43±8.98	13(2-27)	0.505
FIB4 Score	0.72±0.32	0.65(0.31-1.45)	0.74±0.33	0.79(0.15-1.38)	1.06±0.72	0.89(0.38-2.89)	0.367

WBC: white blood cells, Neu: Neutrophils, Lymph: lymphocyte, Hb: hemoglobin, Plt: platelets, PBG: fasting blood glucose, AST: aspartate aminotransferase, ALT: alanine aminotransferase, N/L Ratio: neutrophils/Lymphocyte Ratio, CRP: c-reactive protein, ESR: erythrocyte sedimentation rate, FIB4: index for liver fibrosis
*: one-way ANOVA

DISCUSSION

In this study, we observed significant differences in both demographic and laboratory parameters among the three obesity classes. Specifically, higher obesity classes were associated with significantly increased body weight, waist circumference, and BMI, reflecting greater central adiposity. Notably, the prevalence of severe hepatic steatosis (Grade 3) increased significantly with higher obesity classes, indicating a strong relationship between adiposity and liver fat accumulation.

Obesity is strongly linked with heightened inflammatory activity, a relationship that can become detrimental over time. Chronic inflammation can trigger maladaptive immune responses, leading to tissue damage, including fibrosis and necrosis. This prolonged inflammatory state may ultimately result in organ dysfunction or failure.[6] A study conducted in the United States identified a positive association

between obesity and two specific inflammatory biomarkers: the systemic immune-inflammation index (SII) and the systemic inflammation response index (SIRI). These findings suggest that as obesity increases, so does the activity of these inflammatory markers, reinforcing the link between excess body weight and systemic inflammation.[1] Research has consistently demonstrated that as adipose tissue expands, it releases pro-inflammatory cytokines, contributing to chronic low-grade inflammation. This inflammatory state is linked to various metabolic disorders and contributes to the progression of obesity-related complications, such as insulin resistance and cardiovascular diseases. Another study demonstrated that as BMI increased, there was a corresponding rise in WBC, neutrophil, and lymphocyte counts. However, these elevated values decreased after weight loss, suggesting a link between obesity and heightened inflammatory activity, which can be mitigated by reducing body weight.[7]

However, many studies indicate that the correlation between obesity and inflammatory markers is inconsistent. In a survey conducted by Bahadır *et al*., a positive correlation was found between the degree of obesity and specific inflammatory markers, including WBC, lymphocyte, and CRP. However, the study did not observe any significant relationship between the levels of neutrophils and the NLR, suggesting that not all inflammatory markers increase consistently with obesity levels.[8] In a study conducted in Iran, a comparison was made between patients with metabolic syndrome and those without it. The results showed no significant difference in the NLR between the two groups, indicating that NLR may not be a distinguishing factor in the presence or absence of metabolic syndrome.[9]

In our study, while there were no significant differences in inflammatory markers such as WBC, NLR, or CRP levels, trends toward higher CRP levels in Class 3 obesity suggest a potential increase in systemic inflammation. The variation in findings between studies on the association between the degree of obesity and inflammatory markers suggest that the degree of obesity does not uniformly result in heightened levels of inflammation. In some cases, inflammatory markers remain stable or show minimal variation. This variability may be due to differences in individual metabolic responses, genetic predispositions, or varying degrees of adipose tissue activity across different populations.[10] Our study's limited number of patients may account for this discrepancy, and we recognize this as a potential limitation of our research. A larger sample size could have provided more robust data and increased the generalizability of our findings.

CONCLUSION

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Antalya Training & Research Hospital (IRB). (Decision number: 2024-15/21).

Authors' Contribution

Study Conception: SU, GZG; Study Design: NK; Supervision; AO; Materials: NK; Data Collection and/or Processing: GZG; Analysis and/or Data Interpretation: SU, GZG; Literature Review: SU; Critical Review: AO, NK; Manuscript preparing: SU.

REFERENCES

1. Zhou Y, Wang Y, Wu T, et al. Association between obesity and systemic immune inflammation index, systemic inflammation response index among US adults: a population-based analysis. Lipids Health Dis. 2024;23(1):245.
2. Semmler G, Balcar L, Wernly S, et al. Insulin resistance and central obesity determine hepatic steatosis and explain cardiovascular risk in steatotic liver disease. Front Endocrinol (Lausanne). 2023;14:1244405.
3. Yang H, Zhang T, Song W, et al. Dietary inflammatory potential is associated with higher odds of hepatic steatosis in US adults: a cross-sectional study. Public Health Nutr. 2023;26(12):2936-2944.
4. Li L, Shu X, Yi Y, et al. Dietary inflammatory impact on NAFLD development in obese vs. lean individuals: an analysis based on NHANES 2003-2018. Lipids Health Dis. 2024;23(1):127.
5. Consultation WHOE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004;363(9403):157-63.
6. Saltiel AR, Olefsky JM. Inflammatory mecha-

nisms linking obesity and metabolic disease. J Clin Invest. 2017;127(1):1-4.
7. Dixon JB, O'Brien PE. Obesity and the white blood cell count: changes with sustained weight loss. Obes Surg. 2006 ;16(3):251-7.
8. Bahadır A, Baltacı D, Türker Y, et al. Is the neutrophil-to-lymphocyte ratio indicative of inflammatory state in patients with obesity and metabolic syndrome? Anatol J Cardiol. 2015;15(10):816-22.
9. Omrani-Nava V, Moosazadeh M, Bahar A, et al. Neutrophil-to-lymphocyte, platelet-to lymphocyte and lymphocyte-to-monocyte ratios, any association with metabolic syndrome? Caspian J Intern Med. 2023;14(3):567-571.
10. Milano W, Carizzone F, Foia M, et al. Obesity and Its Multiple Clinical Implications between Inflammatory States and Gut Microbiotic Alterations. Diseases. 2022;11(1):7.