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The effect of insulin resistance on inflammation markers in individuals with obesity

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ABSTRACT

Objective: Obesity has recently been recognized as a chronic low-grade inflammation condition. We aimed to compare the predictive values of insulin resistance and inflammatory indices in individuals with obesity.

Materials and Methods: 124 people who had a health check for obesity-related risk factors in our hospital between June 2018 and September 2019 were included in the study. Inflammatory markers of the patients were evaluated.

Results: The study group consists of a total of 224 people, and we compared the demographic data and laboratory parameters of the individuals. C-reactive protein (CRP) levels of obese individuals were statistically higher than those with normal body mass index ($p < 0.001$). There was no statistically significant difference between the groups in terms of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) values, among other inflammation markers. A positive and statistically significant correlation was found between body mass index and CRP level ($r = 0.334$, $p < 0.001$). There was no significant correlation between body mass index and NLR and PLR.

Conclusion: As a result, CRP levels of obese individuals were statistically higher than individuals with normal body mass index. No statistically significant difference was found between the groups in terms of NLR and PLR values among other inflammation markers.

Keywords: Obesity, insulin resistance, neutrophil / lymphocyte ratio, platelet / lymphocyte ratio

INTRODUCTION

The number of patients diagnosed with obesity increases significantly around the world regardless of the economic structure of the society. The World Health Organization (WHO) predicted that society would face serious problems in terms of obesity in the 21st century (**1**). In its simplest definition, obesity is excessive fat accumulation in the body. Body fat is between 15-20% in men with average body weight and 25-30% in women. Since it is not easy to determine the percentage of body fat, obesity is defined as being overweight rather than excessive fat. WHO defines overweight individual and obese individual according to body mass index (BMI = Weight [kg] / Height [m2]) (**2**).

It has been shown that mild inflammation in the chronic process has a balancing role in various metabolic diseases and diseases with physiological and pathophysiological mechanisms. Although obesity is considered an inflammatory process, it causes many chronic diseases (**3**). Excessive accumulation of fat in the human body causes the production of numerous pro-inflammatory chemokines and cytokines by activating macrophages (**4**). Consequently, obesity-induced adipose tissue remodeling may lead to metabolic dysfunctions such as insulin resistance, hyperlipidemia, and hypertension (**5**). Inspired by this, measuring a person's inflammation level can enable us to diagnose health problems caused by obesity and prevent complications that may be encountered in the later life of those in this disease group (**6**).

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Insulin resistance; in normal concentration in the circulation defined as a reduced response to insulin.

This definition includes the biological response to insulin, as well as the metabolic effects of insulin (related to carbohydrate, protein, lipid metabolism) as well as its mitogenic effects. In order for insulin to exert its biological effect, it must be secreted from the pancreatic beta-cell. It must be included in the systemic circulation through the portal, pass from the circulation to the interstitium and reach the target tissues, and bind to the receptors on the cell surface of these tissues. Insulin, which binds to the receptor, enters the cell and initiates a series of post-receptor events that will carry out the effect of the hormone. A disruption that may occur in one or more of these steps ultimately results in the organism's subnormal response to insulin (**7, 8**).

In short, insulin resistance can be defined as a condition in which the amount of insulin required for the disruption of the normal biological response to both endogenous and exogenous insulin or the quantitative normal response of the cell, tissue or organism is higher than normal (**9, 10**).

At normal glucose concentrations, it is significantly correlated with cardiovascular complications such as hyperinsulinemia, left ventricular hypertrophy, intima-media thickening of the arteries, silent coronary-cerebral infarctions. Increased insulin levels increase cell proliferation and inflammatory response in the artery wall and accelerate atherogenesis (**11**).

In our study, we aim to investigate the possible roles of inflammation markers by determining the relationship between the levels of hematological markers in routine hemogram tests, which are easily accessible and cheap, and insulin resistance in patients with obesity.

MATERIAL and METHODS

This study was conducted with the ethics committee approval from Fırat University Scientific Research Projects Coordination Unit (Number:19-08, Date: 22/11/2018). First group consisted of 124 participants between the ages of 18-60 with obesity and no other comorbidities. In the control group; It was formed from 100 healthy individuals of similar age and sex without obesity and no comorbidities. Patient group: It was formed based on the evaluation of patients who applied to Fırat University, Faculty of Medicine, Department of General Internal Medicine outpatient clinic and clinic. Demographic information was recorded for the whole study group. Body mass indexes (BMI) were calculated in kg/height (m^2); It was obtained by dividing the body weight in kg by the body surface area in m^2. Patients with a BMI of> 30 were considered obese. Routine biochemistry samples of the patients were studied in the central biochemistry laboratory of our hospital. HbA1c, AST, ALT, urea, creatinine, Lipid levels, CRP, CBC results were obtained from the records of routine examinations.

HOMA-IR (Homeostasis model assessment-insulin resistance) formula from insulin resistance, fasting insulin, and fasting glucose levels; It was calculated as follows based on the formula reported by Matthews et al. (**12**), and those with a HOMA value above 2.5 were considered insulin resistance.

HOMA-IR = [Fasting insulin (µU/ml) x Fasting glucose (mg/dl)] /405

The criteria for participation in the study:

1- Patients in the age range of 18-65 with a BMI of> 30 and no other comorbidities

Exclusion criteria from the study:

1- Those diagnosed with Type 1, Type 2 DM
2- Patients under the age of 18, over the age of 65
3- Patients diagnosed with hypertension, heart failure, renal failure, liver disease, acute infection, hypothyroidism
4- Patients with malignancies

Statistical analysis

We performed the statistical analysis of the data with IBM SPSS 23 program. Shapiro-Wilk test was used to determine the normal distribution of the data. Descriptive statistics of the data are expressed as Mean ± SD and [Median (quarter 1-quarter 3) for continuous data, frequency and percentage [n (%)] for categorical variables.

In the comparison of independent groups, Kruskal-Wallis test or Anova test was used according to the distribution of data. Bonferroni test was used for post hoc analysis. The Pearson correlation coefficient was used to evaluate the relationship between the two continuous data. Statistical significance was set at $P < 0.05$.

RESULTS

Average age of 224 participants was 35.68 ± 7.99 years. 78.6% (n = 176) of the participants were women. 16.1% of the participants were normal, 29.9% overweight and 54.0% obese. Age, gender, body fat weight, body lean mass weight, body fluid weight, and fasting blood glucose were statistically different between the groups.

The distribution of demographic characteristics of the participants according to the body mass index classification is presented in **Table 1**.

CRP levels of obese individuals were statistically higher than those with normal body mass index ($p < 0.001$). No statistically significant difference was found between the groups in terms of NLR and PLR values among other inflammation markers (**Table 2**).

A positive and statistically significant correlation was found between body mass index and CRP level ($r = 0.334$, $p < 0.001$). There was no significant correlation between body mass index and NLR and PLO ratios (**Table 3**).

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Table 1. Distribution of demographic and biochemical parameters of the participants

Variables	Normal (n=36) median±SD	Overweight (n=67) median±SD	Obese (n=121) median±SD	P value	
Age(years)	31,97±8,35[1]	34,57±8.68[2]	37.40±7.02[3]	0.001	1-3:0.001 1-2<0.001
Fasting glucose(mg/dl)	85.86±12.86[1]	90.19±10.54[2]	93.54±13.85[3]	0.005	1-3:0.005
Insulin (mIU/L)	14,43(12.42-16.47)	13,82(9.17-17.65)	16,53(9.72-17.50)	0.691	
HOMA–IR index	2,99(0.57-3.69)	3,08(1.90-4.00)	3,90(2.32-4.19)	0.537	
Serum 25(OH) D (ng/mL) (ng/mL)	18,78(11.05-25.12)	17,06(10.60-20.50)	17,62(8.90-23.50)	0.453	
TSH(ng/dl)	1,97(1.02-2.69)	2,03(0.97-2.81)	2,01(1.16-2.55)	0.850	
LDL-C (mg/dl)	143.08±33.05	155.73±35.18	152.02±33.28	0.241	
HDL-C (mg/dl)	48.47±9.63	49.24±10.47	49.99±10.22	0.749	
Triglycerides (mg/dl)	218.83±38.69	212.46±34.46	221.04±42.34	0.375	
SBP (mmHg)	120.06±9.51	120.58±12.85	119.74±10.91	0.889	
DBP (mmHg)	71.81±8.02	71.21±7.39	70.29±7.62	0.507	

Table 2. Comparison of inflammatory parameters between groups

Variables	Normal (n=36)	Overweight (n=67)	Obese (n=121)	P value*
CRP	4,07±1.91[1]	3.67±0.94	6,21±4.89[2]	**<0.001**
NLR	2,11±0.72	2,23±1.44	2,15±0.79	0.831
PLR	140,33±47.18	132,32±46.65	129,66±42.75	0.454

P value*: multiple comparison p value **1-2 p value**: 0.008 (comparison between groups)
NLR: neutrophil lymphocytes ratio, PLR: platelet lymphocytes ratio

Table 3. Correlation between BMI and inflammation markers

Variables	BMI	Liquid mass
CRP	r=0.334 p=**<0.001**	r=0.329 p=<0.001
NLR	r=0.023 p<0.723	r=0.15 p=0.825
PLR	r=-0.065 p=0.336	r=-0.021 p=0.760

r: correlation coefficient; p:statistical significance value

DISCUSSION

We aimed to investigate the possible roles of inflammation markers by determining the relationship between the levels of hematological markers in routine hemogram tests and insulin resistance, which are easily accessible and cheap in patients with obesity. The NLR recommended as a biomarker of subclinical inflammation has been shown to be associated with prognosis in both CAD and cardiac failure (**13, 14**). Again, the PLR was found to be an important marker of inflammation. Recent studies have shown that the PLR has a strong relationship with significant cardiovascular adverse outcomes and atherosclerosis (**15, 16**). There are studies showing that there is a significant relationship between endocrinological diseases and these indexes and rates (**17, 18**). As in many known chronic diseases, inflammatory processes have an important role in the pathophysiology of diabetes mellitus (**19**). Studies have shown that the N/L ratio is a strong systemic marker of inflammation. In addition, it has been shown that the N/L ratio is an important marker in predicting short and long-term cardiovascular mortality and showing prognosis in cancer patients (**20, 21**). In a study evaluating inflammation markers in obese individuals, while leukocyte and hs-CRP were useful markers in showing inflammation in individuals with obesity and metabolic syndrome without diabetes, N/L ratio and P/L ratio did not have the same feature (**22**). In another study, it was shown that the number of neutrophils increased and the N/L ratio increased with the rate of obesity (**23**).

In our study, when looking at the N/L ratio and P / L ratio, there was no statistically significant difference in obese and overweight patients compared to normal weight. CRP was significantly higher in obese individuals compared to non-obese individuals (<0.001).

Acute phase proteins such as CRP and interleukin-6 is increase in patients with visceral obesity. Tumor necrosis factor-alpha (TNF-alpha), a pleiotropic cytokine involved in many metabolic responses, has been shown to have a central role in modulating energy expenditure, fat accumulation, and insulin resistance in obesity (**24**). In obesity, fasting plasma insulin level increases, there is a significant decrease in the stimulation of peripheral glucose use with large decreases in hepatic and peripheral insulin sensitivity. In parallel, the higher the waist-hip ratio, the lower the sensitivity to insulin (**25**).

CONCLUSION

In our study, insulin levels, HOMA index, FPG were found to be higher in obese participants compared to non-obese participants, but it was not statistically significant. As a result, CRP levels of obese individuals were statistically higher than individuals with normal body mass index. No statistically significant difference was found between the groups in terms of N/L ratio and P/L ratio values, among other inflammation markers. Considering that obesity may be a major risk factor

in the initiation of the pro-inflammatory process by causing comorbid diseases, prospective randomized controlled studies with a large number of patients are needed.

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