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Platelet Activation is a Risk Factor for Obesity

Trombosit Aktivasyonu Obezite İçin Bir Risk Faktörüdür

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Abstract

Objective: Obesity is known to be a triggering factor for many chronic diseases. Blood parameters, especially platelet (PLT)-related factors, have gained importance for a better understanding of obesity. In this study, we investigated the correlation between PLT-related parameters and bodily factors to enhance our knowledge of this important area of research. **Material and Methods:** Consenting volunteers between 18 and 65 years were included in the study. Their heights, weights, body mass indices (BMI), fat percentages, fat masses (FM), and fat-free masses (FFM) were determined. Fat mass index (FMI=fat mass/height m^2) and fat-free mass index (FFMI=fat free mass/height m^2) were calculated. Blood samples were taken to determine the parameters such as PLT, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT). **Results:** In males, PLT increased with weight, fat percentage, FM, and FMI. However, there was no change in PCT values with these parameters. In females, PLT decreased with age, increased with weight, BMI, fat percentage, FM, FFM, and FMI. PCT increased with weight, BMI, fat percentage, FM, FFM, and FMI. **Conclusion:** A significant relationship between PLT activation and body fat content was observed in both genders in the present study. Thus, these blood parameters can be a useful tool for investigating inflammation-related complications in obese individuals. It is speculated that obese individuals may be encouraged toward becoming thrombocyte apheresis donors to reduce their PLT counts, which may lead to a decrease in the risk of obesity-related inflammation in such individuals.

Keywords: Obesity; fat mass; fat mass index; platelet; plateletcrit

Özet

Amaç: Obezitenin birçok kronik hastalığı tetiklediği bilinmektedir. Kan parametrelerinden özellikle trombositler [platelets (PLTs)] ile ilgili olan parametrelerin obeziteyle ilişkisi üzerine yapılan çalışmalar önem kazanmaya başlamıştır. Bu çalışmada amacımız, obezitede yağ dokusu artışının PLT parametreleri ile ilişkisini ortaya koymaktır. **Gereç ve Yöntemler:** Polikliniğimize obezite nedeni ile başvuran 18-65 yaş arası bireyler çalışmaya dahil edildi. Çıplak ayakla boy uzunlukları ölçüldükten sonra biyoimpedans cihazı ile yağ analizi yapılarak kilo, beden kitle indeksi (BKİ), yağ yüzdesi,yağ ağırlığı ve yağsız ağırlık tespit edildi. Yağ ağırlığı indeksi [fat mass index (FMI)/height m^2] ve yağsız ağırlık indeksi [fat free mass (FFMI)/height m^2] hesaplandı. Kan bulgularına ulaşılarak PLT, ortalama trombosit hacmi [mean platelet volume (MPV)], trombosit dağılım genişliği [platelet distribution width (PDW)] ve "plateletcrit (PCT)" değerleri belirlendi. **Bulgular:** Trombosit sayısının erkeklerde kilo, yağ yüzdesi, yağ ağırlığı ve FMI ile arttığı fakat PCT'nin değişmediği tespit edildi. Kadınlarda ise PLT sayısının yaşla orantılı azaldığı, ancak kilo, BKİ, yağ yüzdesi, yağ ağırlığı, FFM ve FMI ile orantılı olarak arttığı tespit edildi. PCT'nin kilo, BKİ, yağ yüzdesi, yağ ağırlığı, FFM ve FMI ile arttığı tespit edildi. **Sonuç:** Her iki cinste PLT aktivasyonu ile vücut yağ dokusu arasında bir ilişkinin olduğunun tespit edilmiş olması, kolaylıkla ulaşılması mümkün olan kan parametrelerinin obezitenin inflamasyonla ilişkili komplikasyonlarının takibinde kullanılabileceğini düşündürmektedir. Ayrıca obez kişileri PLT aferez vericisi olarak yönlendirme ve cesaretlendirmenin de PLT sayısını azaltarak inflamasyonla ilişkili komplikasyonları önlemede etkili olabileceği yönünde düşünülebilir.

Anahtar kelimeler: Obezite; yağ dokusu; yağ dokusu indeksi; trombosit, plateletkrit

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Introduction

The incidence of obesity continues to rise throughout the world (1). Obesity can be considered as a low-grade inflammation since increased body fat is known to trigger inflammation (2). These inflammatory processes initiate several chronic diseases such as atherosclerosis, cardiovascular diseases, and diabetes (3). Therefore, the impact of obesity on the body needs to be investigated further. The changes in blood parameters in obesity, especially related to platelets, have recently been assessed. These studies have shown that obesity is associated with platelet activation and an increase in platelet-related cytokines. This may be due to the established role of platelet in hemostasis and the development of inflammation (4).

Moreover, it has been asserted that the platelet-related changes in obesity may increase risks for inflammation and cardiovascular problems (5). Similarly, it has been shown that the number and activation of platelets are associated with metabolic syndrome and insulin resistance (6). A high number of platelets in women with metabolic syndrome suggest that inflammation and thromboembolic events may lead to an increase (6). Furthermore, it has been shown that platelet counts are associated with triglyceride and HDL-cholesterol (HDL-C) in women, which was thought to increase insulin resistance (7).

Although several studies emphasize the relationship between obesity-related problems and platelet activation, only a small number of studies are available on the association between body fat content and platelet counts in obesity. This study aimed to investigate the link between platelet-related parameters and body weight, BMI, fat percentage, fat mass (FM), fat-free mass (FFM), fat mass index (FMI), and fat-free mass index (FFMI) in obese subjects to increase our understanding on this important area of research.

Material and Methods

The study subjects were outpatients of our clinic aged between 18 and 65 years. Written informed consent was obtained before their inclusion in the study. The study protocol was approved by the institutional Ethics committee (Ethics committee decision number: 09.2019.369). The subjects were positioned barefooted with their backs touching a wall, and then their heights were measured. The weight, body mass index (BMI), fat percentage, FM and FFM, were determined using Bio-impedance analyzer device (Tip-BC-418-MAIII, Tanita Body Composition Analyzer; Tokyo, Japan) and FMI (FM/height m^2) and FFMI (FFM/height m^2) were calculated. Blood samples were taken to determine the biochemical parameters such as platelet (PLT), mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW).

Statistical Analysis

Values were expressed as mean±standard deviation. Pearson's correlation test was used to evaluate the relationship between continuous variables. A two-tailed t-test was used to compare the values between genders. $p<0.05$ was considered statistically significant for both tests.

Results

The study variables of all patients are shown in Table 1. While men were found to be taller ($p<0.05$) and heavier ($p<0.001$) than women, fat percentage ($p<0.001$) and FMI ($p<0.001$) of women were higher than men (Table 1). PLT, MPV, PCT, and PDW values were not significantly different according to gender (Table 2). PLT decreased with age but increased with weight, BMI, fat percentage, FM, FFM, FMI, and FFMI. MPV values decreased with height but did not change with other parameters. PCT values decreased with age and height but increased with weight, BMI, fat percentage, FM, FMI, and FFMI. PDW values increased with age but decreased with weight, BMI, fat percentage, FM, and FMI (Table 3).

In males, PLT increased with weight, fat percentage, FM, and FMI. PDW values decreased with weight, BMI, fat percentage, and FM (Table 4). In females, PLT decreased with age, but increased with weight, BMI, fat percentage, FM, FFM, FMI, and FFMI. PDW values increased with age but decreased with weight, BMI, fat percentage, and FM (Table 5).

Table 1. Mean±SD values of anthropometric measurements according to gender.

	Male (n=87)	Female (n=432)	
	Mean±SD	**Mean±SD**	**P value**
Age	39.7±13.2	39.9±11.9	p>0.05
Height	173.9±7.7	159.5±6.3	**p<0.001**
Weight	120.7±31.4	105.1±26.3	**p<0.001**
BMI	39.7±9.6	41.2±10	p>0.05
Fat%	34±7.6	44.6±6.7	p<0.001
FM	42.9±20.6	48.2±17.9	p>0.05
FFM	78.1±13.9	56.9±9.8	p>0.05
FMI	14.2±6.8	18.9±7	**p<0.001**
FFMI	25.8±3.7	22.3±3.7	p>0.05

Table 2. Mean±SD values of platelet parameters according to gender.

	Male (n=87)	Female (n=432)	
	Mean±SD	**Mean±SD**	**p value**
PLT	275.4±61.5	285±71	p>0.05
MPV	8.6±0.9	8.8±0.9	p>0.05
PCT	0.2±0.1	0.2±0.1	p>0.05
PDW	16.7±0.5	16.7±0.5	p>0.05

Discussion

There were several novel findings observed in this study. Firstly, we discovered that the PLT and PCT increased with weight, BMI, fat percentage, FM, FFM, FMI, and FFMI especially in females. However, a significant decrease was observed with increasing age. Secondly, there was a positive linear relationship between PLT and weight, fat percentage, FM, and FMI in males. Thirdly, in both genders, PDW decreased with weight, BMI, fat percentage, and FM. Also, in females, PDW increased with age but decreased with FMI.

Relationships Between Platelet, PCT and Obesity-Related Parameters

In the literature, a relationship between PLT and BMI has been asserted by several researchers (8). However, recently, body fat percentage and FM were also shown to be more important than BMI to indicate obesity (1). In our study, while PLT increased with FM, fat percentage, and FMI in both genders, it did not change with FFM in males. Hence, it is important to stress the positive

Table 3. Relationship between platelet activation values and anthropometric measurements in all patients.

n=519		**Age**	**Height**	**Weight**	**BMI**	**Fat%**	**FM**	**FFM**	**FMI**	**FFMI**
PLT	r	-0.13	-0.01	0.21	0.23	0.25	0.25	0.09	0.24	0.14
	p	**0.003**	0.82	**0.000**	**0.000**	**0.000**	**0.000**	**0.04**	**0.000**	**0.001**
MPV	r	0.08	-0.09	-0.08	-0.03	-0.015	-0.05	-0.08	-0.02	-0.03
	p	0.068	**0.040**	0.068	0.49	0.82	0.25	0.068	0.64	0.49
PCT	r	-0.09	-0.09	0.14	0.19	0.22	0.20	0.05	0.21	0.12
	p	**0.040**	**0.040**	**0.001**	**0.000**	**0.000**	**0.000**	0.25	**0.000**	**0.006**
PDW	r	0.12	-0.02	-0.15	-0.15	-0.17	-0.17	-0.06	-0.16	-0.05
	p	**0.006**	0.64	**0.000**	**0.000**	**0.000**	**0.000**	0.172	**0.000**	0.255

Table 4. Relationship between platelet activation values and anthropometric measurements for male subjects.

Male (n=87)		**Age**	**Height**	**Weight**	**BMI**	**Fat%**	**FM**	**FFM**	**FMI**	**FFMI**
PLT	r	-0.22	0.10	0.23	0.22	0.37	0.28	0.13	0.28	0.10
	p	0.04	0.35	**0.03**	0.04	**0.0004**	**0.008**	0.23	**0.008**	0.35
MPV	r	0.10	-0.08	-0.13	-0.1	-0.17	-0.15	-0.08	-0.14	-0:06
	p	0.35	0.46	0.23	0.35	0.11	0.16	0.46	0.19	0.58
PCT	r	-0.17	0.01	0.11	0.13	0.20	0.14	0.08	0.15	0.10
	p	0.11	0.92	0.31	0.23	0.06	0.19	0.46	0.16	0.35
PDW	r	0.19	-0.15	-0.22	-0.8	-0.23	-0.22	-0.19	-0.21	-0.14
	p	0.07	0.16	**0.04**	**0.0000**	**0.03**	**0.04**	0.07	0.05	0.19

Table 5. Relationship between platelet activation values and anthropometric measurements for female patients.

Female (n=432)		Age	Height	Weight	BMI	Fat%	FM	FFM	FMI	FFMI
PLT	r	-0.13	0.06	0.19	0.17	0.17	0.18	0.16	0.16	0.14
	p	**0.006**	0.21	**0.00007**	**0.0003**	**0.0003**	**0.0001**	**0.0008**	**0.0008**	**0.003**
MPV	r	0.07	-0.05	-0.04	-0.03	-0.04	-0.04	-0.03	-0.03	0.00
	p	0.14	0.29	0.40	0.53	0.4	0.4	0.53	0.53	1
PCT	r	-0.08	-0.04	0.18	0.20	0.18	0.18	0.14	0.18	0.17
	p	0.09	0.4	**0.0001**	**0.00002**	**0.0001**	**0.0001**	**0.003**	**0.0001**	**0.0003**
PDW	r	0.10	-0.03	-0.14	-0.14	-0.17	-0.15	-0.07	-0.15	-0.05
	p	**0.03**	0.5	**0.0003**	**0.003**	**0.0003**	**0.001**	0.14	**0.001**	0.29

association between platelet parameters and the adipose tissue.

Our findings that PLT and PCT increase with body fat content in subjects with normal BMI (9) and in obese subjects with BMI over 30 (10) were in accordance with the previous studies. A significant decrease in PLT after bariatric surgery seems to support the association between obesity and PLT (11). In inflammatory diseases, a multifunctional proinflammatory factor, IL-6, is secreted from the adipose tissue (12), which increases the maturation of megakaryocyte precursors and may be the cause of increased PLT in obesity (13). Elevated platelet count may then increase the risk of venous thrombosis, which intensifies cardiovascular complications due to obesity (14).

PCT is the ratio of platelet volume to whole blood volume, indicating the percentage of platelet (PCT=PLT×MPV/10.000) (15). Increased levels of PCT were observed to be associated with the slow coronary flow and hence, could be a predictor of subclinical inflammation and slow coronary flow (16). Similarly, PCT was high in males and females with pulmonary tuberculosis, suggesting that this may be an important indicator of inflammation (17). Several other studies have reported that PCT gets elevated in cancers of the endometrium (18), lung (19), and papillary thyroid (20). There is continued research on the clinical importance of PCT as it is an easily accessible parameter. In our study, we found that PCT elevation was directly proportional to weight, BMI, fat percentage, FM, and FFM, especially in females. Besides the clinical conditions reported in the literature, these may be used as biomarkers for obesity. Since obesity is known to be a chronic inflammatory condition and is a precursor of several chronic diseases such as cancer, we suggest that elevated PCT can be used as a parameter for obesity. PCT, however, did not change in males indicating that it could be a gender-specific indicator for obesity.

Increased PLT and PCT due to an increase in the adipose tissue, especially in females, require a reinterpretation of changes in the body due to obesity. Blood viscosity is known to increase in obesity in both genders, and this may cause cardiovascular complications. While blood viscosity is affected by hematocrit level, plasma viscosity is affected by fibrinogen, albumin, and globulin levels (21). Blood viscosity is also affected by PLT (22). Previous studies have suggested that increased PLT will increase blood viscosity and hence slow the blood flow. However, there is not much literature to support these findings in obesity. In our study, we showed that PLT, PCT, and PDW increase with adipose tissue, especially in obese female individuals, which may also affect their risk of inflammation and speed of blood flow. These may cause complications like dilutional anemia (21) and obesity-related anemia (23).

Relationships Between MPV and Obesity Parameters

MPV is a marker of platelet reactivity and acts as an acute phase reactant. Higher MPV is an indicator of high-grade and lower MPV of low-grade inflammation (24). Higher MPV is observed in patients with diabetes (25) and hypertension (26). MPV is also an important biomarker for cardiovas-

cular diseases (27). A higher level of MPV increases mortality after myocardial infarction (28). Since obesity is a known low-grade inflammation, lower MPV values are expected. In this study, we showed that a decrease in MPV values was directly proportional to the increase in BMI and FM. This finding was not in accordance with the previous literature, as it was claimed that MPV either increased with BMI (29) or showed no change (30).

The relationship between MPV and PLT is not fully established as there are conflicting reports in the literature. While some studies showed a negative correlation between MPV and PLT (31), other studies did not observe such a relationship (32). In this study, there was no significant association found between MPV and FM, fat percentage, FMI, and as the result of these findings, MPV may not be suggested to be a reliable indicator for inflammation in obesity.

Relationships Between PDW and Obesity Parameters

PDW is an established parameter indicating platelet function (33) and was thought to be a risk factor for cardiovascular complications in patients with diabetes (34). In a study, a positive correlation was shown between PDW and HbA1c, and it was asserted that PDW may be an independent predictor for diabetes (35). In the current study, we showed that PDW decreased with an increase in weight, BMI, FM, and fat percentage in both genders. Thus, PDW may also be considered a negative factor for obesity. However, further studies are needed to consolidate this claim.

Limitations

The study group consisted of only obese people, and we did not have a control group of non-obese people.

Conclusion

Since there was a significant relationship between platelet activation and body fat content in both genders, it is suggested that these platelet parameters can be used for identifying and follow-up of inflammation-related complications in obese individuals. It is speculated that the obese individuals should be encouraged for thrombocyte apheresis donation to reduce their platelet levels and hence lower their risk of obesity-related inflammations.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

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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