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Research Article

THE IMPACT OF INCREASED PLATELET COUNT ON ERYTHROCYTE AGGREGATION IN OBESE INDIVIDUALS WITHOUT CARDIOVASCULAR DISEASE

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ABSTRACT

Introduction: Although obesity raises the risk of cardiovascular illnesses, it is an important issue for public health. Platelets play important role in thrombosis and inflammation, and elevated number of platelets has been noted in obese individuals. The erythrocyte aggregation process involves the clumping of red blood cells, is influenced factors, including platelet activation. This study aimed to investigate the relationship amongst platelet levels and erythrocyte aggregation in obese individuals without cardiovascular disease.

Methods: Anthropometric measurements of obese individuals (n=101) and non-obese controls (n=37) were recorded. Erythrocyte aggregation parameters, such as aggregation index (AI%), aggregation half-time (t1/2), and aggregation amplitude (AMP), were measured using a laser-based aggregometer. Platelet counts were determined by automated hematology analyzer. We examined the relationship between anthropometric parameters, platelet counts, and erythrocyte aggregation measures.

Results: Obese individuals had significantly higher BMI, fat percentage, fat mass, and fat-free mass versus non-obese controls. In the obese group, Fat mass, increasing fat percentage and BMI, were associated with decreased AMP and t1/2 values, and increased AI% values. Platelet counts were also significantly elevated in the obese group and were inversely correlated with AMP and t1/2 values. No significant associations were observed between anthropometric parameters, platelet counts, and erythrocyte aggregation measures in the non-obese group.

Conclusion: There was strong association between elevated platelet levels and altered erythrocyte aggregation in obese individuals. Findings suggest that obesity-induced increases in platelet count may contribute to increased erythrocyte aggregation, potentially leading to an elevated risk of thrombotic events. Targeting platelet-related pathways may be a promising therapeutic strategy to mitigate cardiovascular complications in obese individuals.

Keywords: Obesity; Anthropometric Measurements; Platelets; Erythrocyte Aggregation

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INTRODUCTION

Obesity is a long-term, multisystem illness that is becoming more widespread across the globe (1). Obesity is recognized by the increase of the of the adipose tissue and the presence of a persistent inflammatory response (2). The increase in adipose tissue activates inflammatory mechanisms, resulting persistent inflammation (1). Considering obesity is a long-term illness, the possibility of developing complications is elevated. Cerebrovascular and cardiovascular complications are frequently observed and affect quality of life (3). Studies on obesity have shown that the emergence of complications is linked to persistent inflammation, hyperlipidemia, hypertension, diabetes, and increased whole blood and plasma viscosity (4-8), It is conceivable that any condition disrupting blood flow affects tissue perfusion. Changes in blood cells also influence flow properties. An increase in the aggregation of erythrocytes, the most abundant cells in circulating blood, can reduce tissue perfusion and oxygen delivery to tissues, leading to ischemia (9). Investigations has indicated that enhanced erythrocyte aggregation plays a role in vascular complications in obesity (10). Identifying factors that enhance aggregation becomes crucial. While various studies have been conducted in this area, research is increasingly focusing on how inflammation in obesity contributes to increased aggregation (11). In obesity, there is also an increase in platelet count along with increased adipose tissue (12), and it has been shown that inflammation in obesity enhances prothrombotic events, leading to arterial and venous thrombosis (13). It is believed that platelets can trigger inflammation, with platelet activation increasing in inflammatory diseases and contributing to atherothrombotic events (14). While previous researches have established a link between obesity, inflammation, and increased erythrocyte aggregation, the specific role of platelets in this process remains relatively unexplored. Furthermore, studies have investigated the connection between obesity, inflammation, and platelet activation, the direct impact of increased platelet count on erythrocyte aggregation in obese individuals has not been comprehensively examined.

To address this gap, we investigated the connection amongst anthropometric measurements, erythrocyte aggregation, and platelet counts in obese and non-obese individuals. By exploring this connection, we seek to enhance understanding of the mechanisms underlying vascular complications in obesity and potentially identify novel therapeutic targets.

Despite, previous studies have shown that inflammation and platelet count increase in obesity, but our study is one of the few to directly correlate platelet count with erythrocyte aggregation parameters. Understanding the interplay between obesity, platelets, and erythrocyte aggregation can provide valuable insights into the pathophysiology of obesity-related cardiovascular complications and inform the progression of the targeted interventions.

This study aims to investigate whether increased platelets in obesity affect erythrocyte aggregation, Figure 1.

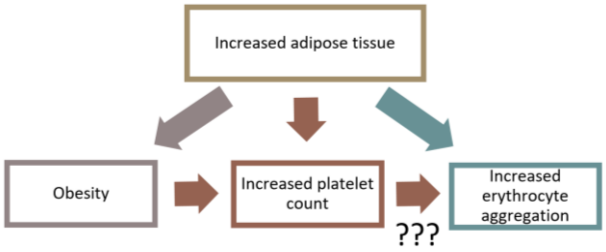

Figure 1. The central research question addressed in the study, focusing on the relationship between anthropometric measurements, erythrocyte aggregation, and platelet counts in obese and non-obese groups.

MATERIALS AND METHODS

Ethical Approval

This study was approved by the Clinical Research Ethics Committee of Haydarpaşa Numune Research and Training Hospital (Number: HNEAH-KEAK2022/136).

Participants

Individuals between the ages of 18 to 65 with body mass index (BMI) of 25 were recruited from the Endocrinology outpatient clinic at Haydarpaşa Numune Training and Research Hospital. Participants with a history of malignancy, infection, pregnancy, drug use, or any other significant medical conditions were excluded. Height was recorded in centimeters with participants standing barefoot on a flat surface using a stadiometer. Body composition analysis was conducted via a Tanita-BC418 (bioimpedance device) which assessed BMI, weight, mass body fat percentage, fat-free mass and fat mass. Pregnant participants those with certain conditions were omitted from the study by the conditions that elevate blood viscosity. Also, the healthy individuals in the control group had no previous diagnosis of blood or heart disorders. Hematological and biochemical parameters, electrocardiogram, transthoracic echocardiography, carotid and vertebral artery color Doppler ultrasonography were evaluated by an expert physician to

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make election of participants in the clinics of the university hospital.

Blood Sample Collection

Samples were taken from participants in a 10 mL purple-capped tube. Routine blood biochemistry tests were performed on a separate blood sample. Samples of blood were drawn from the antecubital vein and stored in K_2-EDTA purple tubes (1.8 mg/dl K2EDTA, BD Vacutainer) and analyzed in the Hemorheology Laboratory of our Faculty, within a maximum of 4 hours. All measurements related to hemorheology were performed at 37 °C.

Aggregation Measurement of Erythrocytes

The aggregation of erythrocyte (EA) was assessed in the Hamidiye Medical Faculty. The erythrocyte aggregation properties of the samples were also evaluated with a laser echocytometer (RR Mechatronics, Hoorn, Netherlands; Laser-assisted Optical Rotational Cell Analyzer LORCA). The aggregation measurement principle is as mentioned previously (15), (16). Undiluted whole blood is used for this measurement. Since the amount of HbO_2 (oxyhemoglobin) in the blood, Since it could affect aggregation parameters, oxygenation is routinely applied to all samples before measurement (15). For oxygenation, the whole blood sample is kept in a tube with a volume at least 10 times its volume for 10 minutes (for contact with oxygen in the air). During this time, the sample is gently turned upside down to bring it into contact with oxygen. Aggregation index (AI) (aggregation index in percentage, %)): Percentage of erythrocyte aggregation in stasis, Aggregation amplitude (AMP) (aggregation magnitude parameter in arbitrary units, au): The total alteration in the signal of aggregation, Half-time of aggregation (t½) (half-time of aggregation in seconds, sec): Taken as the duration needed for the aggregation signal to reduce to half of the maximum change, Figure 2.

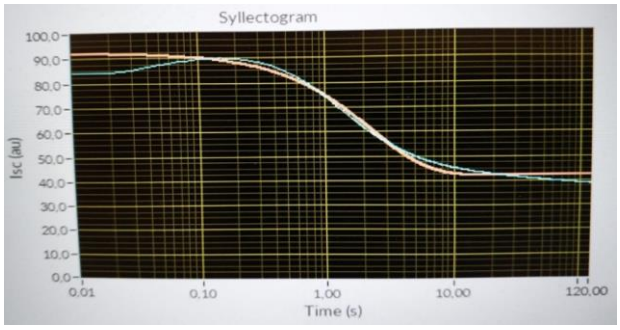

Figure 2. Syllectogram of obese subjects

The parameters AMP, AI, and t1/2, which are examined when evaluating erythrocyte aggregation, are obtained from the sedimentation curve. Accordingly, AMP, representing the aggregation amplitude, is the distance between the peak point of the shape correction phase and the point where the formation of three-dimensional aggregates ends. AI (aggregation index) is obtained by dividing the area A indicated on the graph by the sum of areas A and B. It expresses both the aggregation amplitude and the kinetics of aggregation. The t1/2 parameter determines the required time for the amplitude to diminish half of the peak point (I1/2), Figure 3.

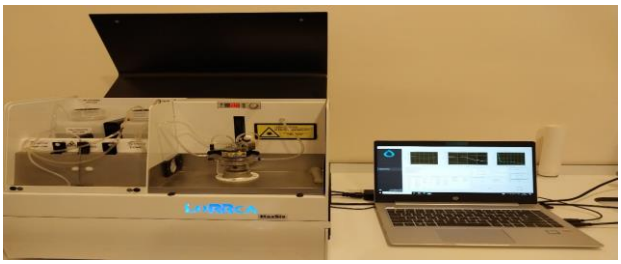

Figure 3. Data was collected using LORCA, a laser-based ektacytometer. Basic instrument (left) computer screen (right) presents disaggretion curve, syllectogram, ilteration curve, measurement parameters etc. *The laser ektacytometer images were obtained at the Hemorheology Research Laboratory, University of Health Sciences, Hamidiye Faculty of Medicine.*

Statistics

To summarize characteristics of the patient's descriptive statistics as the mean and standard deviation were performed using software (GraphPad Prism 6). All continuous variables were tested for normality using the Shapiro-Wilk test. For normally distributed data, Student's t-test and Pearson's correlation were used; otherwise, non-parametric equivalents Mann-Whitney U, were applied. Equality of variances was tested using Levene's test. Age differences between groups were significant ($p < 0.001$), and age was included as a covariate in multivariate analyses where appropriate. ANOVA (Analysis of Variance) was utilized to compare means across more than two grouped data groups in order to determine if there were statistically significant differences. To determine the direction and strength of the linear link between two or more continuous variables, correlation analysis was performed using the Pearson correlation coefficient. $p<0.05$ is noted for statistical significance.

RESULTS

The statistical analysis of the demographic and anthropometric data showed that the obese group exhibited substantially higher values (mean ± SD) than the non-obese group (Table 1).

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Table 1. The comparison of demographic and anthropometric data between the obese (n=101) and the non-obese group (n=37). The values are reported as mean ± SD (Standard deviation). All comparisons show statistically significant differences amongst the groups, with p-values less than 0.001.

Variables	Obese Group (n=101)		Non-obese Group (n=37)		p value
	Mean	SD	Mean	SD	
Age (year)	45.3	1.2	33.7	2	0.001
Height (cm)	160	0.8	167.4	1.2	0.001
Weight (kg)	90.9	2.1	61.4	1.3	0.001
BMI (kg/ m²)	35.2	0.6	21.8	0.3	0.001
Fat (%)	37.9	0.6	23.1	1	0.001
Fat mass (kg)	34.9	1.1	14.2	0.7	0.001
Fat free mass (kg)	56	1.3	47.2	1.2	0.001

In the obese group, AMP value decreased with BMI and fat mass, and AI (%) value increased statistically significantly with weight, BMI, fat percentage, fat mass. t1/2 value decreased statistically significantly with BMI, fat percentage, fat mass (Table 2).

Table 2. The correlations between erythrocyte aggregation parameters and anthropometric measurements in the obese group. The parameters analyzed include AMP (aggregation magnitude parameter in arbitrary units, au), AI (aggregation index in percentage, %), and t1/2 (half-time of aggregation in seconds, sec). The correlation coefficients (r) and their corresponding p-values (p) are provided for each anthropometric measurement. (* noted as p< 0.05).

Obese Group	AMP (au)		AI (%)		t 1/2 (sec)	
	r	p	r	p	r	p
Age (year)	0.04	0.62	0.07	0.46	-0.12	0.21
Height (cm)	0.03	0.75	-0.15	0.11	0.12	0.19
Weight (kg)	-0.15	0.22	0.1	0.039*	-0.16	0.09
BMI (kg/m²)	-0.19	0.041*	0.36	0.0001*	-0.29	0.001*
Fat (%)	-0.18	0.05	0.43	<0.0001*	-0.39	<0.0001*
Fat mass (kg)	-0.21	0.025*	0.38	<0.0001*	-0.32	0.0007*
Fat free mass(kg)	-0.04	0.61	0.06	0.48	-0.06	0.53

In the obese group, the platelet value positively correlated with BMI, % fat, fat mass and T1/2, while AMP values negatively correlated with platelet and platelet A (%) values (Table 3). In the non-obese group, AMP value decreased statistically significantly with fat percentage, fat mass, AI (%) and t1/2 values were not affected by anthropometric parameters (Table 4). In the non-obese group, platelet value was not affected by anthropometric parameters and erythrocyte aggregation parameters. (Table 5).

Table 3. The correlations between platelet count and various anthropometric measurements, as well as erythrocyte aggregation parameters in the obese group. The correlation coefficients (r) and their corresponding p-values (p) are provided for each variable (* noted as p<0.05, ** noted as p<0.01, ***p<0.001).

Obese Group	Platelet	
	r	p
Weight (kg)	0.18	0.068
BMI (kg/m²)	0.228	0.021*
Fat (%)	0.202	0.041*
Fat mass (kg)	0.246	0.012*
Fat free mass (kg)	0.015	0.879
aggregation half-time (t 1/2)	-0.348	<0.001**
Aggregation index (AI (%))	0.416	<0.0001***
Aggregation amplitude (AMP; arbitrary units, au)	-0.431	<0.001**

Table 4. The correlations between erythrocyte aggregation parameters and anthropometric measurements in the non-obese group. The parameters analyzed include AMP (aggregation magnitude parameter in arbitrary units, au), AI (aggregation index in percentage, %), and t1/2 (half-time of aggregation in seconds, sec). The correlation coefficients (r) and their corresponding p-values (p) are provided for each anthropometric measurement. (* noted as p< 0.05).

Non-obese group Variables	AMP (au)		AI (%)		t 1/2 (sec)	
	r	p	r	p	r	p
Age (year)	0.04	0.81	0.21	0.20	-0.17	0.30
Height (cm)	0.16	0.32	-0.09	0.57	0.08	0.62
Weight(kg)	0.02	0.88	0.04	0.78	-0.04	0.79
BMI (kg/m2)	-0.14	0.40	0.1	0.35	-0.13	0.41
Fat percentage (%)	-0.36	0.025*	0.15	0.34	-0.11	0.48
Fat mass (kg)	-0.33	0.042*	0.4	0.38	-0.10	0.51
Fat free mass(kg)	0.22	0.17	-0.02	0.86	0.01	0.94

Table 5. The correlations between platelet count and various anthropometric measurements, as well as erythrocyte aggregation parameters in the non-obese group. The correlation coefficients (r) and their corresponding p-values (p) are listed for each variable. None of the correlations were statistically significant, as indicated by p-values greater than 0.05.

Non-obese Group Variables	Platelet r	Platelet p
Weight (kg)	0.032	0.848
BMI (kg/m2)	0.08	0634
%Fat	0.121	0.163
Fat mass	0.116	0.482
Fat free mass (kg)	-0.038	0.819
t 1/2	-0.027	0.873
AI (%)	0.014	0.933
AMP	0.093	0.579

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DISCUSSION

In this study, our hypothesis was that increased platelet levels in obesity could enhance erythrocyte aggregation. Our findings support this hypothesis, revealing that elevated platelet levels in obesity indeed increase erythrocyte aggregation.
What could be the mechanism by which platelets enhance erythrocyte aggregation?

Secretion of Adhesion Molecules by Platelets

Adhesion molecules from the selectin family, such as P-selectin secreted by platelets, facilitate the developing of platelets cumulation on endothelial cells and their aggregation with leukocytes. This rolling interaction initiates the effect of platelets on target cells (17) and promotes leukocyte rolling on the endothelium (18). Subsequently, the secretion of intercellular adhesion molecules results in a tighter adhesion process among leukocytes. P-selectin primarily initiates interactions with monocytes (19), and the resulting monocyte-platelet complex has pro-inflammatory properties, contributing to atherosclerosis (20). The leukocytes adhesion to the endothelium, triggers the inflammatory process, increasing vascular reactivity (21), and the development of the platelet-monocyte complex leads to further endothelial disruption, which can enhance erythrocyte adhesion and accelerate aggregation processes. Our study indicates that in the obese group, increased platelet and erythrocyte aggregation parameters are proportional to fat tissue, a change not observed in the non-obese group. This suggests the importance of understanding the implications of increased platelets in obesity and potential secondary complications.

Secretion of Aggregation Factors by Platelets

Platelets form the first line of defense in maintaining vascular endothelial integrity and play a role in inflammation and atherogenesis (22). Platelet glycoprotein receptors interact with aggregation factors, coagulation factors, other platelets, and the endothelial layer (23). In chronic conditions such as diabetes, hypertension, obesity, and in the diseases of cardiovascular, the role of platelets in atherosclerosis is significant (24 -27). The progress of lesion in atherosclerosis and increased platelet binding in these areas activate platelets, and cause the release of granules containing adenosine diphosphate, factor Va, thrombospondin, von Willebrand factor, fibronectin, fibrinogen, heparinase, and thromboxane A_2 (TXA_2), which stimulate the aggregation process (28). Fibrinogen, in particular, is a significant factor in increasing of the aggregation of erythrocytes (29), and it is expected that an increase in platelets will also enhance erythrocyte aggregation. Additionally, the disturbance in hemodynamics of vascular system might be the reason of improved erythrocyte aggregation.

Pro-inflammatory Effects of Platelets

Platelets has a role in the formation of inflammation (30). The chemokines (e.g., CXCL7, CXCL1, CXCL4, CXCL5) and cytokines (e.g., TNF-alpha, leukotrienes, thromboxane A2, interleukin-1) secreted by platelets can stimulate both inflammation and atherosclerotic plaque development (25, 31). Platelets act as receptors for bioactive molecules and proteins involved in inflammation and immunity, such as those contained in δ-granules, α-granules, and lysosomes (14). They also encompass Toll-like receptors that can detect pathogens like bacteria and viruses (32, 30), and they can activate neutrophils (33), which may trigger inflammation and subsequently increase erythrocyte aggregation. The increase in platelet count and platelet-neutrophil interactions in systemic inflammation process such as ulcerative colitis (34) and systemic lupus erythematosus (SLE) (35) underscores the importance of platelets in inflammatory processes. The observed increase in the number of platelets in obesity, which was proportional to fat tissue increase, further supports the connection between platelets and inflammation.

Effects of Platelets on Vascular Circulation

The relationships between endothelial cells and platelet or immune cells (36), such as platelet-monocyte interactions, facilitate in the formation of atherosclerotic processes (14). Increased atherosclerotic plaque formation due to platelets can cause stasis in vascular structures, reducing blood circulation (37) and indirectly leading to increased erythrocyte aggregation through rouleaux formation. Additionally, a rise in count of platelets could also slow circulation in the vascular bed and, in turn, increase erythrocyte aggregation. Hydrodynamic forces in blood vessels push platelets toward the vessel walls while erythrocytes remain in the central flow. An increase in platelet count enhances this pushing effect and increases the area occupied by platelets, leading to slower erythrocyte circulation and increased aggregation.

Limitations

Our findings highlight the potential role of platelets in obesity-related hemorheological changes. While several plausible biological mechanisms have been proposed—such as platelet-driven secretion of adhesion molecules, inflammatory mediators, and aggregation factors—our study is cross-sectional in nature. Thus, although

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significant correlations were observed, causality cannot be established. It remains unclear whether increased platelet count directly drives erythrocyte aggregation or whether both arise in parallel due to shared underlying processes like chronic inflammation or endothelial dysfunction in obesity. If future studies confirm a causal relationship, targeting platelet activity or count (e.g., via antiplatelet or anti-inflammatory therapies) may offer a novel approach to mitigating vascular complications in obese individuals—even those not yet diagnosed with cardiovascular disease. Furthermore, potential pathways should be explored. Future longitudinal or interventional studies will be needed to determine whether modulating platelet activity can alter erythrocyte aggregation profiles and reduce cardiovascular risk.

CONCLUSION

A Despite their lower numbers compared to other blood cells, platelets are complex functional cells that influence hemodynamics through mechanisms such as the secretion of adhesion molecules, stimulation of aggregation, promotion of inflammation, and effects on vascular blood flow. These findings underscore the importance of recognizing platelets not only as markers of inflammation but also as active contributors to vascular risk in obesity. While causality cannot be confirmed due to the cross-sectional design, the consistent associations observed point to platelet-related pathways as promising therapeutic targets. Interventions aimed at modulating platelet activity may offer a novel strategy to mitigate the early vascular complications of obesity—even in the absence of overt cardiovascular disease. These findings highlight the importance of addressing obesity can potentially improve cardiovascular health.

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None

Authorship contributions
Serpil Cecen: Writing– review & editing, Writing– original draft, Visualization, Validation, Resources, Methodology, Investigation, Resources, Data curation, Conceptualization. Zozan Guleken: Writing– review & editing, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization, Supervision.

Data availibity statement
Data will be made available on reasonable request from the corresponding author.

Declaration of competing interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Ethics
Ethical approval for this study was obtained from the Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (HNEAH-KEAK2022/136).

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