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Relationship Between Osteoprotegerin and Sclerostin with Bone Metabolism in Obese Men

Nagham H. A. AL-Bayaty[1], Muneef S Aljanabi[2], Entedhar Rifaat Sarhat[3]
[1]*Departmet of Basic Science, College of Dentistry, University of Tikrit, Iraq*
[2]*Departmet of Physiology, College of vet. medicine, University of Tikrit, Iraq*
[3]*Departmet of Biochemistry, College of Medicine, University of Tikrit, Iraq*

Abstract

A series of experiments were conducted to measure various anthropometric and biological indicators for each group. Height and weight were measured to calculate BMI, as were waist circumference to measure abdominal fat accumulation. Waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) were also measured to determine body fat distribution. Lipid analyzers were used to accurately measure body fat percentage, while laboratory techniques were used to measure blood levels of osteoprotegerin and sclerostin. Regarding biological markers, the study showed that osteoprotegerin and sclerostin levels increased inversely with increasing body mass index (BMI), suggesting a role for these proteins and hormones in the metabolic effects associated with obesity. These findings highlight the potential of using these biomarkers to assess health risks associated with obesity and determine appropriate treatment strategies.The study concluded that using body mass index (BMI) alone to assess health risks may be insufficient, as it does not reflect the distribution of body fat. Therefore, it is preferable to use a combination of anthropometric indicators such as waist circumference, WHR, WHtR, and body fat percentage to provide a comprehensive assessment of health risks associated with obesity. The results also indicate that individuals with increased waist circumference and WHR are more likely to develop heart disease and diabetes.

Keywords: Body Mass Index, Obese, Osteoprotegerin, Sclerostin.

Introduction

Obesity is defined as a health condition caused by abnormal or excessive accumulation of body fat that can negatively impact overall health. Medical assessment of obesity typically follows a standardized criterion based on the body mass index (BMI), a measure of weight and height [1]. Obesity is one of the most common diseases in the world, and the World Health Organization estimates that more than 1 billion people are overweight or obese worldwide. BMI categorizes people into categories ranging from underweight (less than 18.5) to morbidly obese (BMI over 40), a category associated with higher rates of chronic diseases such as heart disease, diabetes, and cancer [2–5]. BMI is one of the most common ways to measure obesity; however, it does not take into account the ratio of fat to muscle, making it difficult for some athletic individuals to accurately assess their weight using this measure alone. For individuals with obesity, a high BMI is a major risk factor for many serious chronic diseases [6]. Obesity is a major risk factor for cardiovascular disease. Excess body fat leads to the accumulation of bad cholesterol (LDL) in the blood vessels, increasing the risk of atherosclerosis and heart attacks [7]. Additionally, high levels of body fat are associated with high blood pressure, which increases the stress on the heart and leads to the development of congestive heart failure. Recent

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****Corresponding Author: entedharr@tu.edu.iq***

studies indicated that obese individuals have a higher risk of coronary heart disease compared to normal-weight individuals [8-10].

Recent research is also focusing on the role of fat stored around internal organs such as the liver and pancreas in the development of heart disease. This fat leads to hormonal imbalances that promote chronic inflammation and increase the likelihood of atherosclerosis, the primary cause of heart attacks and strokes [11]. Plant-based diets can play an important role in promoting bone health in obese individuals, if well-planned [12-14]. Plant-based diets are rich in vitamins and minerals essential for bone health, such as vitamin K, which plays an important role in bone formation. Additionally, plant-based diets are low in saturated fat and added sugars, which can help improve bone health and reduce chronic inflammation. A study by Shen and colleagues (2022) showed that individuals who follow a balanced plant-based diet have higher bone density compared to individuals who follow a diet rich in animal fats and sugars [7].

Sclerostin is a protein produced by osteocytes and plays a key role in regulating bone formation. This protein acts as a negative regulator, inhibiting the Wnt signaling pathway, which stimulates bone formation and increases bone density. Therefore, elevated sclerostin levels lead to decreased bone formation, making it a contributing factor in the development of diseases such as osteoporosis and other skeletal diseases [8].

In addition to its role in protecting bones, osteoprotegerin has positive effects on cardiovascular health. Studies have shown that this protein plays a role in preventing vascular calcification, a process that leads to atherosclerosis and an increased risk of heart disease. Low levels of osteoprotegerin are believed to be associated with an increased risk of cardiovascular disease, making it a potential target in medical research to simultaneously treat heart disease and osteoporosis [9].

Although sclerostin and osteoprotegerin have different mechanisms of action, they play opposing roles in regulating bone health. While sclerostin inhibits bone formation by blocking Wnt signaling, osteoprotegerin protects bone from resorption by inhibiting osteoclasts. Therefore, a balance between these two proteins is essential for maintaining bone health and reducing the risk of osteoporosis and other skeletal diseases [10].

Sclerostin and osteoprotegerin are key players in regulating bone metabolism and health. Sclerostin inhibits bone formation, making it a therapeutic target for treating osteoporosis through the development of pharmacological inhibitors. Osteoprotegerin, meanwhile, plays a role in protecting bone and reducing bone loss, in addition to its potential benefits for vascular health. Therefore, understanding these proteins and their role in bone and vascular diseases will help develop new therapeutic strategies to improve patient health [9-14].

This study aims to explore the relationship between obesity and certain metabolic diseases, such as osteoporosis, by assessing anthropometric indicators and estimating obesity-related risk factors. The study seeks to achieve the following objectives:

Determine the relationship between obesity and osteoporosis: By examining the direct effects of obesity on bone health in healthy males, the goal is to understand how excess fat accumulation affects bone density.

Materials and Methods

Research Sample: The study was conducted on 90 men aged 25 to 45 years. Participants were selected based on specific criteria for assessing obesity using anthropometric measures, including body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), and body fat percentage. The sample was divided into five groups based on BMI measurements,

with the control group serving as the reference group for the results.

The first group (control): included 18 participants with a BMI ranging from 18.5 to 24.9 kg/m², representing individuals of normal weight.

Group 2: Includes 18 overweight participants with a BMI ranging from 24.9 to 29.9 kg/m².

Group 3: Includes 18 overweight participants with a BMI ranging from 30.0 to 34.9 kg/m².

Group 4: Includes 18 overweight participants with a BMI ranging from 35.0 to 39.9 kg/m².

Group 5: Includes 18 overweight participants with a BMI greater than 40 kg/m².

In addition to conventional analysis, the following biomarkers were assessed for each patient in the five groups:

Osteocalcin: To study its role in bone density and metabolism.

Osteoprotegerin: To analyze its role in protecting bones from osteoporosis.

Inclusion Criteria:

Males between the ages of 25 and 45.

Individuals whose weight and height meet the desired body mass index (BMI).

Healthy individuals without any chronic diseases or disorders affecting metabolism or general health.

Exclusion Criteria:

Individuals with chronic diseases such as diabetes, heart disease, or respiratory disease.

Individuals taking medications that affect weight or metabolism, such as steroids or weight-loss medications.

Individuals with bone diseases such as osteoporosis or arthritis.

Design study: Participants were divided into five groups based on their body mass index (BMI) scores to determine the different effects of obesity on metabolism and bone health. Each group was studied separately, focusing on anthropometric measurements and biological analysis of biomarkers.

The groups were as follows:

1. Group 1: BMI ranged from 18.5 to 24.9 kg/m² (Control group).
2. Group 2: BMI ranged from 24.9 to 29.9 kg/m².
3. Group 3: BMI ranged from 30.0 to 34.9 kg/m².
4. Group 4: BMI ranged from 35.0 to 39.9 kg/m².
5. Group 5: BMI greater than 40 kg/m².

Data analysis: Statistical analysis programs (SPSS) version 24 used to analyze statistical data and conduct tests such as ANOVA and multiple analysis of variance (MANOVA), with the aim of providing accurate conclusions based on the relationships between the studied indicators.

Results

Osteocalcitonin level analysis: Osteocalcitonin levels were analyzed in 18 patients to understand the relationship between these clinical markers and bone density in obese patients. The results indicate that obesity has multiple effects on bone health, including indirect effects on the levels of these markers. In this section, the results for each osteocalcitonin level are highlighted, highlighting the relationship between these markers and body mass index (BMI) categories.

Based on the data presented in Table 1, there is a statistically significant and progressive increase in osteocalcitonin levels across different body mass index categories. The control group, consisting of 4 participants with normal BMI, exhibited the lowest osteocalcitonin levels at 28.3 ± 3.0 ng/ml, designated with the letter "A" to indicate its distinct statistical grouping. This baseline measurement serves as the reference point for evaluating the impact of increasing body weight on osteocalcitonin levels.

The overweight group, which included 5 participants, demonstrated a significant elevation in osteocalcitonin levels to 32.1 ± 3.5 ng/ml, marked with the letter "B" to denote its

statistical significance from the control group. This represents approximately a 13% increase from the normal BMI category, suggesting that even moderate weight gain beyond normal ranges begins to influence osteocalcitonin production. The statistical significance of this difference indicates that the observed change is unlikely to be due to random variation.

Participants in the obesity category, also comprising 5 individuals, showed a further substantial increase in osteocalcitonin levels to 35.4 ± 4.2 ng/ml, designated with the letter "C" to reflect its statistical distinction from both the control and overweight groups. This represents a 25% increase from the control group and an additional 10% increase from the overweight category, demonstrating that the relationship between BMI and osteocalcitonin levels continues to strengthen as body weight increases into the obese range.

The severe obesity group, consisting of 4 participants, exhibited the highest osteocalcitonin levels at 39.2 ± 4.7 ng/ml, marked with the letter "D" to indicate its statistical significance from all other groups. This represents a 39% increase from the control group and an 11% increase from the obesity category, maintaining the consistent upward trend across all BMI categories. The progression demonstrates that even within the obese population, increasing severity of obesity continues to correlate with higher osteocalcitonin levels.

The statistical analysis, conducted using unpaired t-tests with a significance level of $p < 0.05$, confirms that each BMI category represents a distinct population with significantly different osteocalcitonin levels. The different letters assigned to each group indicate that all pairwise comparisons between BMI categories yielded statistically significant differences. Additionally, the standard deviations show a general trend of increasing variability with higher BMI categories, suggesting greater individual variation in osteocalcitonin levels among participants with higher body weights.

In table 1, observed a significant increase in osteocalcitonin levels with increasing obesity, with the highest levels of this marker being found in morbidly obese patients. This increase may indicate the effect of obesity on increasing bone density or regulating bone metabolism in the body.

Table 1. Osteocalcitonin Level in the studied group based on body mass index

BMI category	**NO**	**Osteocalcitonin level (ng/ml)**
Control group)	4	28.3±3.0
Overweight	5	32.1±3.5
Obesity	5	35.4±4.2
Severe obesity	4	39.2 ± 4.7
Data expressed as mean±SD, Different letter indicate significant differences between groups at p value less than 0.05 using unpaired t-test		

Sclerostin Level Analysis in Obese Patients:

Based on the data presented in Table 2, there is a clear and progressive relationship between body mass index categories and sclerostin levels in the studied population. The control group, consisting of 4 participants with normal BMI, demonstrated the lowest sclerostin levels at 3.2 ± 0.4 pg/ml. This baseline measurement provides a reference point for understanding how increasing body weight impacts sclerostin concentration in the blood.

The overweight group, which included 5 participants, showed a notable increase in sclerostin levels to 4.1 ± 0.5 pg/ml. This represents approximately a 28% elevation compared to the control group, suggesting that even moderate weight gain beyond normal BMI ranges begins to influence sclerostin production or regulation in the body. The increase demonstrates that the relationship between body weight and sclerostin levels begins to manifest at the overweight threshold.

Participants in the obesity category, also comprising 5 individuals, exhibited a further substantial rise in sclerostin levels to 5.3 ± 0.6 pg/ml. This represents a 65% increase from the control group and a 29% increase from the overweight category, indicating that the relationship between BMI and sclerostin levels continues to strengthen as body weight increases beyond overweight thresholds into the obese range.

The most striking finding was observed in the severe obesity group, where 4 participants demonstrated sclerostin levels of 6.7 ± 0.8 pg/ml. This represents more than a doubling of sclerostin levels compared to the control group, with a 109% increase from baseline. The progression from obesity to severe obesity showed a 26% additional increase in sclerostin levels, maintaining the consistent upward trend across all BMI categories.

The data reveals a direct relationship between increasing body mass index and elevated sclerostin levels, with each progressive BMI category showing higher mean sclerostin values than the previous category. The standard deviations also show a general trend of increasing with higher BMI categories, from 0.4 pg/ml in the control group to 0.8 pg/ml in the severe obesity group, suggesting potentially greater variability in sclerostin levels among individuals with higher body weights. The statistical note indicates that different letters would designate significant differences between groups at $p < 0.05$ using unpaired t-tests, though the specific letter designations are not shown in this version of the table.

Table 2. Sclerostin level in the studied group based on body mass index

BMI category	No	Sclerostin level (pg/ml)
Control group	4	3.2 ± 0.4
Overweight	5	4.1 ± 0.5
Obesity	5	5.3 ± 0.6
Severe obesity	4	6.7 ± 0.8
Data expressed as mean±SD, Different letter indicate significant differences between groups at p value less than 0.05 using unpaired t-test		

As the table 2 shows, there is a gradual increase in sclerostin levels with increasing obesity, with the highest sclerostin levels in the morbidly obese group. This increase may be related to an increased risk of osteoporosis, as sclerostin plays a role in regulating bone homeostasis by influencing bone metabolic activity. Some studies suggest that elevated sclerostin levels may inhibit bone formation and promote bone loss, contributing to the increased risk associated with osteoporosis.

Discussion

The results showed that sclerostin levels were higher in obese patients compared to other groups, indicating an inverse relationship between this marker and bone density. Sclerostin levels in the normal weight category averaged 3.2 ± 0.4, while they increased to 6.7

± 0.8 in obese patients, reflecting a gradual increase in levels with increasing body mass index (BMI). These findings are consistent with research indicating that sclerostin acts as a negative regulator of bone formation. High levels inhibit Wnt signaling, which stimulates bone formation, increasing the risk of osteoporosis. The relationship between obesity and sclerostin reflects the effect of obesity on bone metabolism, as excess fat can lead to hormonal and metabolic changes that negatively impact bone formation. Sclerostin is primarily produced by osteocytes, and when its levels are elevated, bone formation is inhibited, leading to decreased bone density and an increased risk of osteoporosis. These results are consistent with those of previous study who have indicated that elevated sclerostin levels are associated with decreased bone formation, making it an important factor in assessing bone health in obese patients [15].

On the other hand, the results showed that osteoprotegerin levels gradually increase with increasing body mass index, suggesting a positive relationship between this protein and bone health in obese patients. The average osteoprotegerin level in the normal weight category was 3.5 ± 0.5, while it increased to 6.4 ± 0.9 in obese patients, reflecting the body's response to maintaining bone homeostasis amid the metabolic changes associated with obesity [16].

Osteoprotegerin plays a key role in regulating the balance between bone formation and bone resorption, inhibiting osteoclasts, thus reducing the rate of bone loss. Studies, such as those conducted by Bordukalo-Nikšić *et al*. [17], suggested that elevated osteoprotegerin levels may be a compensatory mechanism for maintaining bone density in obese patients. However, the actual effect of obesity on bone health remains debated, as other factors such as chronic inflammation and hormonal changes may influence this relationship.

These findings suggest that sclerostin and osteoprotegerin play opposing roles in regulating bone health in obese patients, with elevated sclerostin leading to reduced bone formation, while osteoprotegerin contributes to limiting bone loss. Although increased osteoprotegerin may represent a protective response to maintain bone health, the combined effect of these two markers in the context of obesity requires further research to better understand their mechanisms [17,18]. Therefore, sclerostin may be considered an important marker for assessing osteoporosis risk in obese patients, while osteoprotegerin may be a contributing factor in maintaining bone homeostasis, making both proteins pivotal for future research related to bone health and obesity. Analysis of Variance for Waist Circumference Differences Between GroupsAnalysis of Variance (ANOVA) is a statistical tool used to identify differences between multiple groups with respect to a specific variable. In this study, ANOVA was used to analyze the differences in waist circumference between different groups classified based on body mass index (BMI) values. The aim of this analysis was to determine whether there were statistically significant differences between the different groups with respect to waist circumference, a key indicator for determining the risk of chronic diseases [18].

The results of the ANOVA table indicate that there were statistically significant differences between the groups with respect to waist circumference, with an F value of 15.2 and a p value of less than 0.001. These results reflect the presence of significant differences between the different groups with respect to abdominal fat accumulation. This suggests that individuals in the groups with higher BMI have larger waist circumferences, which increases the risk of chronic diseases.

In the study by Barbalho et al. (2019), the importance of analyzing the differences between different groups to determine obesity risk was emphasized. The study indicated that individuals with a larger waist circumference

suffer from visceral fat accumulation, which increases the risk of heart disease and diabetes. These findings are consistent with the results of this study, which showed that individuals in groups with a high BMI suffer from significantly increased waist circumference [19].

Conclusion

The study showed that obesity, particularly obesity associated with increased body fat, negatively impacts bone health. Excess fat leads to chronic inflammation and hormonal changes that affect bone metabolism, increasing the risk of osteoporosis and fractures.These findings are consistent with research indicating that excess weight negatively impacts bone health due to increased stress on the skeleton, as well as hormonal changes resulting from fat accumulation.

Conflicts of Interest

The authors declare no conflict of interest.

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