

Association of Total Serum Calcium Level with Obesity Markers (Body Mass Index and Waist Circumference) among Healthy Young Saudis

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ABSTRACT

Background & Objective: The pathophysiology of obesity and comorbid diseases may be associated with the levels of intracellular and extracellular calcium. This study aimed to investigate the association between overweight/obesity measures and the total serum calcium level in young Saudis.

Methods: This was a cross-sectional observational study that involved 121 healthy young Saudi participants of both genders. Venipuncture was performed to obtain blood samples of 4 ml. Serum specimens were extracted and aliquoted into Eppendorf tubes, then preserved at a temperature of -20°C until the time of analysis. Anthropometric Measures (BMI and WC) were measured. SPSS software was used for statistical analysis. The measurement of total serum calcium was conducted through the utilization of a Human Diagnostics kit (Wiesbaden, Germany) on a hospitex Diagnostics Eos-bravo Autoanalyzer. The statistical analysis was conducted using the SPSS software.

Results: The sample population consisted of 87.6% males, 27.3% smokers, 57% students, and 66.9% individuals with a university degree or higher. Nearly 50% of participants were 15–23 years old. Obese subjects had considerably lower total serum calcium than normal weight subjects. BMI and WC inversely correlated with calcium levels.

Conclusion: The present study confirms the inverse relationship between total serum calcium level and obesity in the Saudi healthy population. Calcium supplementation could lower obesity-related chronic disease mortality and morbidity and hence reduce healthcare expenses and increases healthy life years.

Keywords: calcium; obesity; overweight; waist circumference; body mass index; Saudi Arabia.

INTRODUCTION

The Kingdom of Saudi Arabia (KSA) underwent a notable modernization process during the past three decades that resulted in the advancement and transformation of its society. Furthermore, it is noteworthy that approximately 83% of the Saudi population resides in urban areas, indicating a level of urbanization that surpasses that of certain Western European nations [1]. A significant proportion of Saudis currently show a preference for American fast food, which relies on ultraprocessed foods despite the fact that the quality of much of it is poor. These products have a significant commercial advantage over minimally processed or fresh and whole foods because they are more accessible, convenient, appetizing or tasty, and energy dense [2]. Combined with the reduced physical activity and a significant surge in sedentary behaviors, such a cultural shift has contributed in escalating rates of obesity within the Saudi Arabian population [1]. According to the Ministry of Health in Saudi Arabia, the prevalence of overweight and obesity in 2019 was estimated to be 38% and 20%, respectively. A more recent estimate suggests that the prevalence of obesity in Saudi Arabia may be as high as 36% [3]. The economic ramifications of overweight and obesity in KSA have been determined to incur a direct cost of \$3.8 billion, which is equivalent to 4.3 percent of the country's health expenditures and 0.1 percent of its GDP in the year 2019 [4]. Obesity has been found to have a negative impact on life expectancy, resulting in a reduction of approximately 6-7 years. The presence of a body mass index (BMI) ranging from 30 to 35 kg/m² has been found to result in a reduction of 2 to 4 years in an individual's life expectancy. Conversely, an individual with a BMI exceeding 40 kg/m² may experience a decrease in life expectancy by as much as 10 years [5].

The increasing prevalence of obesity appears to have been primarily influenced by non-genetic factors, with genetic factors playing a relatively minor role. It is probable that the primary factors contributing to the rise in adiposity were environmental influences on diet and physical activity [6]. The scientific community has conducted research on the mechanisms that impact adipose tissue with the aim of identifying diverse therapeutic approaches for obesity. The potential correlation between intracellular and extracellular calcium and the pathophysiology of obesity and comorbid diseases may be

attributed to these mechanisms [7]. Inadequate consumption of calcium is regarded as a potential contributor to various conditions, such as osteoporosis, hypertension, cancer, insulin resistance, and the metabolic syndrome [8].

The present research endeavors to examine the correlation between the serum total calcium level and overweight/obesity measures among young healthy Saudis.

METHODS

Study design & Subjects: The present investigation was a cross-sectional observational study that was carried out at the Biochemistry Laboratory, which is situated in the Department of Medical Laboratories, College of Applied Medical Sciences. This study involved the participation of 121 young subjects of both genders from Saudi Arabia. The study participants' age ranged from 15 to 54 years, with a calculated mean value of 25.5 years and a standard deviation of 7.2 years.

Samples Collection & Preparation: Blood samples of 4 ml were obtained via venipuncture from the median cubital vein situated in the antecubital fossa of each participant as per the Clinical and Laboratory Standards Institute (CLSI) document [9]. The samples were collected in plain vacutainers and transported to the Biochemistry laboratory in an ice box insulated container, where they were processed according to a designated protocol to produce serum.

The serum samples were obtained from each participant's blood through centrifugation at 3000 RPM for 5 minutes using a NUVEFUGE-CN180 centrifuge, following the completion of clotting within a 30-minute timeframe. Samples of serum were aliquoted into Eppendorf tubes and subsequently stored at a temperature of -20°C until the time of analysis.

Assessment of Anthropometric Measures: The weight of the subjects was determined with precision up to the nearest 0.1 kg, utilizing a calibrated scale (Proton Digital Scale, Model PHC 309 MD), while they were attired in light clothing and were barefoot. The measurement of height was conducted by utilizing a Portable Height Scale (Mentone Educational, Model PE087, Australia). The calculation of body mass index involved the division of weight in kilograms by the square of height in meters, utilizing a computer program known as "BMI Calc Chart." Subjects were categorized as

normal if BMI < 25 kg/m², overweight if BMI between 25-29.9 kg/m², and obese if BMI ≥ 30 kg/m² based on WHO criteria [10].

The waist circumference (WC) was assessed through the utilization of a conventional tape measure, measuring the narrowest region below the rib cage and above the umbilicus. In brief, the measuring tape was positioned against the participant's abdomen, specifically above the umbilicus, and subsequently secured in situ. The measuring tape was utilized to encircle the waist of the participant until it intersects with the opposite end that is being held above the umbilicus. The waist circumference (WC) of each participant was represented by the measurement in centimeters where the two ends meet.

Laboratory Analysis: The quantification of total serum calcium was measured using Human Diagnostics kit (Wiesbaden, Germany), on an hospitex Diagnostics Eos-bravo Autoanalyzer. Briefly, the reaction between the cation and appropriate chromogenic agents, o-cresolphthalein complexone, in an alkaline medium, resulting in the formation of a purple colored complex. The intensity of the colour proportional with the concentration of calcium in the sample.

Statistical analysis: Statistical analyses were performed using SPSS software, version 23.0 (SPSS Inc®, Chicago, IL, USA). Descriptive statistics, including mean ± standard deviation (SD) or number (percent) were used for numerical and categorical data, respectively. Total calcium was compared between groups of overweight or obesity (BMI ≥ 25 kg/m²) to the group of normal weight (BMI < 25 kg/m²) using an independent t-test. The Pearson's correlation test was used to assess the relationship between serum calcium and BMI and WC. P 0.05 was regarded statistically significant on a two-sided basis.

Ethical Consideration: The present study was conducted in accordance with the Helsinki Declaration guidelines. Prior to the commencement of the study, the objectives were comprehensively explained to each participant and verbal consent was subsequently obtained. Voluntary participation was ensured, and confidentiality was maintained among all participants as no personal identification information was solicited.

RESULTS

Characteristics of participants: One hundred twenty-one healthy participants enrolled in this study with mean age of 25.5±7.2 years with mean BMI almost equal to 26.1±5.9 Kg/m², which reflects that most of the participants were obese or overweight. The study's sample population was predominantly male, comprising 87.6% of the participants. A significant proportion of the sample, 27.3%, reported being smokers. Additionally, 57% of the participants identified as students, while 66.9% of the sample had attained a university degree or higher. Nearly 50% of the participants fell within the youthful age range of 15 to 23 years (table 1).

Table 1: Demographic characteristics of participants (n=121)

	Number (%)	mean±SD
Gender:		
Males	106 (87.6%)	
Females:	15 (12.4%)	
Age years:		25.5±7.2
15-23	56 (46.3%)	
24-33	49 (40.5%)	
34-44	12 (9.9%)	
45-54	4 (3.3%)	
Body weight (kg)		75.5±18.2
Body height (cm)		169.1±10.8
BMI (kg/m ²)		26.1±5.9
< 18.5	8(6.6)	
18.5-24.9	48(39.7)	
25-29.9	39(32.2)	
30-34.9	15(12.4)	
35-39.9	8(6.6)	
≥ 40	3(2.5)	
Waist circumferences (cm)		88.4±17.9
Level of education:		
None /Primary	05 (4.1%)	
Intermediate	7 (5.8%)	
Secondary	28 (23.1%)	

University/higher	81 (66.9%)	
Occupation:		
Student	69 (57.0%)	
Private/Gov Job	31 (25.6%)	
Health Professional	6 (5.0%)	
Housewives	7 (5.8)	
Retired/jobless	8 (6.7%)	
Current status of smoking:		
Yes	33 (27.3%)	
No	80 (66.1%)	
Quitted	08 (6.6%)	

Data presented as mean±standard deviation & number (percent)

Abbreviations: SD = standard deviation, yr = years, Kg = kilograms, cm = centimeters, BMI = body mass index

Total serum calcium level among different BMI categories:

Statistical analysis showed that there were significant differences in total serum calcium concentration (mg/dl) in different categories of BMI related to obesity when compared to normal weight (table 2).

Table 2: serum calcium concentration (mg/dl) among different BMI categories of study participants

BMI category	Total serum calcium level (mg/dl)	P-value
18.5-24.9 (n=56)	8.82±0.28	
25-29.9 (n=39)	8.03±0.26	.048*
30-34.9 (n=15)	7.57±0.53	.030*
35-39.9 (n=11)	7.25±0.82	.032*

Correlation between total serum calcium level (mg/dl) and BMI/WC among different BMI categories: We performed Pearson correlation analysis between serum concentrations of calcium (mg/dl) and BMI. Our findings showed that serum concentration of calcium was negatively correlated to BMI (r = -0.393*, p = .003), WC (r = -0.352*, p = .008) Fig a & b

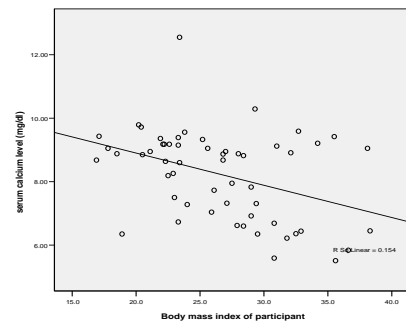


Fig 1-a: Relationship between serum calcium concentration (mg/dl) and BMI in the study participants.

r = -0.393*, p = .003; * correlation is significant at the 0.05 level (2-tailed)

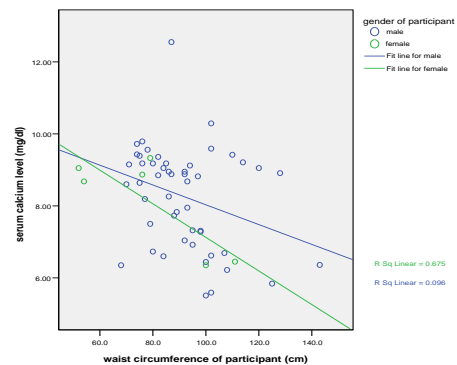


Fig 1-b: Relationship between serum calcium concentration (mg/dl) and WC in the study participants.

$r = -0.352^*$, $p = .008$; * correlation is significant at the 0.05 level (2-tailed)

DISCUSSION

The swift industrialization has brought about substantial modifications in lifestyles and surroundings, which have consequential effects on human health. The incidence of morbidity and mortality resulting from nutritional deficiencies and infectious diseases has experienced a significant decline, while the prevalence of obesity, hypertension, diabetes mellitus, and malignant tumors has markedly increased [11].

The findings from the present study revealed a noteworthy reduction in the total serum calcium concentration among individuals with obesity in comparison to those with normal weight. Nevertheless, the calcium concentration in individuals with obesity remains within the normal range. The precise regulation of calcium levels is attributable to various factors, including vitamin D, parathyroid hormone, and calcitonin. Consistent with the results of the current investigation, Jafari-Giv et al reported in a cross-sectional study of 908 participants enrolled in the Mashhad Stroke and Heart Atherosclerosis Disorder (MASHHAD) program that individuals with obesity exhibited a reduced concentration of serum calcium ($p < 0.05$), and that there existed a correlation between serum calcium levels and body mass index (BMI) [12]. Moreover, the findings of a case-control study involving 78 obese adolescents and 20 healthy volunteers between the ages of 12 and 18 years revealed a statistically significant decrease in serum calcium concentrations among the obese participants [13]. In a two – year prospective study of 54 normal weight women participating in an exercise intervention, the dietary calcium: energy ratio was a significant negative predictor of changes in both body weight and body fat; moreover increased total calcium and dairy calcium intakes predicted fat mass reductions independently of caloric intake for women at lower energy intakes (below the mean of 1.876 kilocalories per day) [14].

The correlation between increased dietary and overall calcium intake and reduced total body and truncal adiposity in young adults aged 18 to 28 years has been supported by the authors of another study involving a sample of 197 healthy Caucasian men and women. This relationship persisted even after controlling for physical activity levels. The authors encouraged for young adults to increase their total calcium intake to achieve or surpass the recommended daily allowance of 1000 mg/d [15]. Jacqmain et al. conducted a study comprising a sample of 470 individuals, consisting of 235 male and 235 female participants aged between 20 and 65 years. There exists a positive correlation between inadequate daily calcium consumption and increased adiposity, with a more pronounced effect observed in females. A correlation has been observed between increased calcium consumption and a plasma lipoprotein-lipid profile that is indicative of a reduced likelihood of developing coronary heart disease, as opposed to a decreased calcium intake [16].

In contrast to the results obtained in the present study, a positive correlation was observed between elevated total serum calcium levels and increased prevalence of overweight/obesity in a sample of 2,503 individuals from the Chinese population. The study revealed a significant correlation between the quartiles of total serum calcium levels and the prevalence of overweight/obesity subjects ($p < 0.001$). After controlling for sex and age ($p < 0.001$), the odds ratios (ORs) and 95% confidence intervals (CIs) for overweight/obesity in the second, third, and fourth quartiles compared to the lowest quartile were 1.407 (1.050–1.883), 1.543 (1.136–2.095), and 1.360 (0.995–1.859), respectively. The authors explained that the plausible mechanism entailed the noteworthy impact of dietary calcium on the anti-obesity effect. Additionally, the p38 MAPK pathway was deemed to potentially involved in calcium-mediated lipid accumulation and lipolysis in mouse preadipocytes [17]. An investigation was conducted on a sample of 82 Iranian women of reproductive age, ranging from 17 to 50 years, who were categorized into groups

based on their obesity status. The results of the study revealed a positive correlation between serum calcium concentrations and lipid profile. Subjects with higher serum calcium concentrations exhibited markedly elevated levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol in comparison to those with low and medium calcium concentrations. However, the study results indicate that there was no statistically significant variance in calcium concentration levels between the obese and non-obese groups (2.22 ± 0.18 vs. 2.20 ± 0.17 , $p = 0.459$) [18].

A randomized study was conducted on 50 healthy overweight individuals, with a body mass index ranging from 25-35 kg/m² and an age range of 25-64 years. The subjects were randomly allocated to either a high dairy protein/high-calcium (DP) or high mixed protein/moderate calcium (MP) diet. The incorporation of higher levels of dietary calcium or dairy products within an energy-restricted, high-protein dietary regimen has no significant impact on weight loss or body composition. The findings of this study do not provide evidence in favor of the proposition that a high consumption of calcium from a diet restricted in energy leads to an increase in weight loss [19]. Another a randomized, double-blind, placebo-controlled design study was conducted on a sample of 100 premenopausal and postmenopausal women using to investigate the effects of a 1000 mg/d calcium supplementation. The results of the analysis indicated that there were no statistically significant distinctions between the placebo and calcium cohorts. The administration of calcium supplements did not yield a statistically significant impact on the quantity of weight or adipose tissue reduction among women who received counseling [20].

The basis for the potential impact of dietary calcium on reducing obesity derives from investigations into the mechanism of action of agouti, a gene associated with obesity that is manifested in human adipocytes. The agouti protein has been found to induce calcium influx and facilitate energy storage in human adipocytes. This is achieved through the coordinated stimulation of fatty acid synthase, a crucial enzyme in de novo lipogenesis, as well as the inhibition of lipolysis in a calcium-dependent manner [21]. Additionally, it is possible that the calcium sensitive receptor is involved in the regulation of adipocyte cellular activity. As per the model, the activation of calcium-sensitive receptors present in adipose tissue leads to an elevation in the levels of vitamin D in the bloodstream. The observed phenomenon can be attributed to the possible impact of heightened activation of lipogenic markers and reduced activation of lipolytic enzymes [8]. [7]. [22]. Hence, it can be inferred that the metabolism of triglycerides is stimulated by calcium ions (Ca^{2+}) through the coordinated regulation of lipolysis and lipogenesis. Additionally, proteins associated with Ca^{2+} , such as calcineurin, calreticulin, and the calcium receptor, have been documented to modulate adipogenesis in an opposite manner by controlling Peroxisome proliferator-activated receptor gamma (PPAR γ 2) [23].

One potential mechanism through which calcium may contribute to weight reduction is by diminishing the absorption of fat in the intestines and enhancing the excretion of fat through feces. Calcium has the ability to combine with fatty acids in the intestinal tract, resulting in the formation of insoluble calcium soaps. This process can potentially enhance the elimination of fecal fat, which may have implications for the regulation of body weight [24] [7]. In a randomized crossover study, three isocaloric 1-week diets were compared. These diets included a low calcium and normal protein diet, a high calcium and normal protein diet, and a high calcium and high protein diet. The study found that the consumption of calcium did not have any significant impact on 24-hour energy expenditure or fat oxidation. However, the excretion of fecal fat increased by approximately 2.5 times during the high calcium and normal protein diet in comparison to the low calcium and normal protein as well as the high calcium and high protein diets. This difference was statistically significant ($P < 0.05$), with fecal fat excretion rates of 14.2 g/day, 6.0 g/day, and 5.9 g/day, respectively. The diet that was high in calcium and normal in protein was observed to have a greater fecal energy excretion in

comparison to the diets that were low in calcium and normal in protein, as well as high in calcium and high in protein (1045 vs 684 and 668 kJ/day; $P < 0.05$). This observation may potentially provide insight into the mechanism behind the weight loss effects of a high-calcium diet, and it implies that the level of dietary protein may play a significant role in this interaction [25].

CONCLUSION & RECOMMENDATION

There is debate in the scientific literature on role of calcium in regulating adipocyte lipid metabolism and triglyceride storage and whether or not this has any association with obesity. Findings from the present study revealed a significant association of obesity measures (BMI and WC) and serum calcium level among the healthy Saudi population. Calcium supplements and other dairy product components affect body weight and obesity risk, therefore large-scale population-based clinical trials are needed.

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