

## The Correlation of Serum Calcium Level and Obesity; Is There any Explanation?

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### Abstract

**Background:** Obesity is caused by several factors while sedentary lifestyle and excessive energy intake are the most important ones. Obesity could be due to abnormal calcium metabolism, and a high calcium intake may prevent obesity. Studying serum calcium level, albumin, and triglyceride concentrations, we searched for probable correlation between serum calcium level and anthropometric data of the participants. **Materials and Methods:** This cross-sectional study was performed in 2011 in Shiraz Endocrine and Metabolism Research Center on 468 participants. Anthropometrics and serum levels of calcium, albumin, and triglyceride levels were measured, recorded, and analyzed by SPSS statistical software. **Results:** 329 participants were female (70.3%) and the remaining were male (29.7%) with mean age of  $46.08 \pm 15.22$  years old. Corrected plasma concentration of calcium based on albumin level had a significant relation with weight, BMI, and triglyceride levels. **Conclusion:** It is assumed that obesity induces the production of inflammatory cytokines which stimulates bone absorption by osteoclasts that might subsequently lead to a higher serum calcium level in obese people who have a high level of triglyceride at the same time. [GMJ. 2013;2(1):26-31]

**Keywords:** Obesity, Serum level, Calcium, Albumin, Triglyceride

### Introduction

Obesity, having a body mass index  $\geq 30$  kg/m<sup>2</sup> is caused by several environmental factors such as sedentary life-style and excessive energy intake.<sup>1,2</sup> According to previous reports, obesity could be due to abnormal calcium metabolism, and a high calcium intake may prevent obesity.<sup>3,4</sup> Intracellular calcium plays a key role in mod-

ulating the regulatory factors involved in hypertension, insulin resistance and obesity.<sup>3</sup> Intracellular calcium is regulated by calcitrophic hormones, such as parathyroid hormone (PTH) and 1, 25-hydroxy vitamin D. PTH and 1, 25-hydroxy vitamin D levels are increased by low dietary calcium intake, which consequently stimulates high levels of intracellular calcium in adipocytes. High levels of calcium in adipocytes stimulate lipogenesis and inhibit

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lipolysis. Levels of PTH and 1, 25-hydroxy vitamin D are decreased by dietary calcium intake, so it lowers intracellular calcium, inhibits lipogenesis, and stimulates lipolysis.<sup>5,6</sup> An obesity gene expressed in human adipocytes called "agouti" helps to understand the anti-obesity effect of dietary calcium. Agouti protein stimulates calcium influx<sup>7,8</sup> and causes energy storage in human adipocytes by stimulating the expression and activity of fatty acid synthase and inhibiting lipolysis; Calcium channel agonists mimicked this action of agouti and it was inhibited by calcium channel antagonists.<sup>9,10</sup> Moreover, using a calcium channel antagonist (ex. nifedipine) for four weeks, in transgenic mice over-expressing agouti, resulted in significant decreases in lipogenesis and in adipose tissue mass.<sup>11</sup>

Polymorphism of Vitamin D receptor gene is associated with susceptibility to obesity in patients with early onset type II diabetes<sup>12</sup>, and circulating 1,25-(OH)<sub>2</sub>-D levels are elevated in obese individuals.<sup>13-18</sup>

In a survey conducted in Norway, PTH and BMI were shown to have a significant correlation with each other<sup>19</sup>, yet in other studies it was revealed that serum ionized calcium level and PTH had a significant correlation.<sup>20-22</sup> Renal hydroxylation of 25-hydroxy vitamin D to its active form is stimulated by PTH<sup>23</sup>, and activated vitamin D in turn elevates the calcium influx into adipocytes.<sup>3</sup> Increased intracellular calcium increases lipid storage<sup>24</sup> and also might activate phosphodiesterase 3B, which then reduces catecholamine-induced lipolysis. Both these effects promote lipid storage in fat tissue.<sup>25</sup> Other studies have shown that PTH has a direct correlation with BMI, since 25-hydroxy vitamin D is inversely related to PTH levels; this suggests that hyperparathyroidism develops as a consequence of reduced levels of 25-hydroxy vitamin D.<sup>26</sup>

It seems that obesity affects bone metabolism in different ways. Since adipocytes and osteoblasts are derived from a mutual stem cell, Obesity could lead to decrease in bone formation while increases adipogenesis.<sup>27,28</sup> It was shown in other studies that agents that inhibit adipogenesis stimulate osteoblast differentiation<sup>28,29</sup> and vice versa.<sup>31</sup> There is elevated oxidative stress and increased pro-

duction of pro-inflammatory cytokines in obese people.<sup>1,30</sup> Subsequently, more production of pro-inflammatory cytokines in obese people could stimulate osteoclast activity and then might increase serum calcium level in them<sup>32,33</sup> Moreover, osteogenesis or bone resorption might be affected directly by more leptin secretion or a reduction in adiponectin production in obesity.<sup>34-36</sup>

Based on the results of the previous studies which have not all shown a similar outcome, we are to find the possible correlation between serum calcium, albumin, and triglyceride levels and anthropometrics of the participants in this survey.

## Materials and Methods

This cross-sectional study was performed in endocrine and metabolism research center of Shiraz University of Medical Sciences located in Namazi Hospital at 2011. The target population of this study was 468 participants from Shiraz. The essential inclusion criteria were to be a resident of Shiraz city and not having any major disease (e.g. CVA, MI, endocrine diseases). In selection of participants one person from each family was chosen randomly based on 8 areas of Shiraz city considering postal codes (if the last digit was an even number). 100 families were selected from each area which means a total number of 800 people, thereafter the subject of the study was discussed to them by an expert and informed consent forms were filled by the patients. Finally, from a total of 513 cases who were present at Endocrine and Metabolism Research Center, 468 persons had completed profiles of anthropometric information, demographic characteristics, and biochemistry data and they were included as the control group.

In order to record the data of the people in the study a demographic form was designed that included age, sex and anthropometric characteristics. Weight was measured by a digital scale (100 grams accuracy) with light clothing and barefoot; height was measured by a wooden tape-meter with an accuracy of 0.1 cm. Waist circumference was measured to the nearest millimeter and taken midway between the lower limit of the rib cage and iliac crest

at the end of normal expiratory phase using a non-stretchable nylon tape in a fasting setting. Hip circumference was measured by a tape-meter in the largest part with no compression. All these data were collected by an expert person. Body Mass Index (BMI) was also calculated.

A blood sample of 5cc was collected from a peripheral vein in forearm. All of the samples were collected between 8 and 9 AM in a fasting condition. Serum total calcium (using Colorimetric kit), albumin (using AssayMax Human Albumin ELISA), and triglyceride (using MaxDiscovery kit) were measured in Shiraz Endocrine and Metabolism Research Center.

Statistical analyses were carried out using SPSS software for Windows, version 19 (SPSS, Chicago, IL, USA). Data were expressed as means  $\pm$  SD. Statistical significance was determined by using the t-tests and Mac Pearson correlation test. Significant difference was accepted when P-values were less than 0.05.

## Results

This cross-sectional study was conducted on 468 participants, randomly selected based on 8 areas of Shiraz city. From the 468 participants 329 (70.3%) were females and 139 (29.7%) were males. Mean age of all of the participants was 46.08 years.

In this study serum albumin and calcium levels were measured and then serum level of ionized calcium was corrected according to serum albumin concentration; the mean  $\pm$  SD level of the corrected calcium level was  $9.88 \pm 0.93$  mmol. Anthropometric data of the patients and chemical profiles of the participants are shown in table 1.

Data analyses showed that serum albumin level had a direct significant correlation with serum calcium level, weight and height of the participants; while it had a negative correlation with their age and abdominal circumference ( $P < 0.05$ ) (Table 2).

Serum calcium and corrected serum calcium (adding 0.8 mmol to serum calcium for each 1mg/dl that albumin level is below 4 g/dl) both had a significant direct correlation with

**Table 1.** Anthropometric and biochemical data

Data	Average $\pm$ SD
Age	46.08 $\pm$ 15.22
Weight	68.96 $\pm$ 12.78
Abdominal circumference	88.63 $\pm$ 13.53
Pelvic circumference	98.43 $\pm$ 12.77
Body mass index	23.79 $\pm$ 4.64
Abdominal/pelvic circumference ratio	0.90 $\pm$ 0.07
Serum calcium level	9.84 $\pm$ 0.95
Serum albumin level	4.48 $\pm$ 0.58
Corrected serum calcium level	9.88 $\pm$ 0.93
Serum triglyceride level	157.34 $\pm$ 47.2

BMI, weight, and serum triglyceride level ( $P < 0.05$ ). Using the t-test in SPSS software we found no significant difference in serum calcium level or corrected calcium level in males and females.

## Discussion

The results of this study revealed that serum calcium level of the participants had a significant correlation with their BMI, weight, and serum triglyceride levels. In previous studies it was shown that abnormal calcium metabolism is related to obesity. Similar to this study in some other studies a direct significant correlation between serum ionized calcium level and BMI was mentioned.<sup>20-22</sup> Yet some other surveys showed a significant association between PTH and BMI.<sup>19,26</sup> In most of the previous investigations obesity and serum levels of vitamin D and PTH were studied and the etiology of reduced levels of 25-hydroxy vitamin D in obese people is not known yet, but is unlikely to be due to malabsorption or inadequate intake of vitamin D. One possibility is that morbid obese patients have less exposure to sunlight than normal subjects. An alternative explanation could be that 25-hydroxy vitamin D is sequestered in fat tissue, so it has less bioavailability. It was further postulated that the increased PTH represents end-organ resistance of the bone to PTH as a consequence of increased skeletal mass. The increased level of 25-hydroxy vitamin D would be secondary to the increased PTH,

Table 2. correlations of demographic and biochemical data

Pearson correlation P value	Alb	Height	Weight	Abd. Cir.	Pel. Cir.	BMI	Serum Ca	Age	Abd/Pel	Cor. Ca
<b>Alb</b>	1	0.14** 0.00	0.12** 0.00	-0.09* 0.04	-0.05 0.23	0.03 0.42	0.19** 0.00	-0.12** 0.00	-0.07 0.12	0.14** 0.00
<b>Height</b>	0.14** 0.00	1	0.42** 0.00	0.03 0.50	-0.06 0.16	-0.19** 0.00	0.03 0.46	-0.15** 0.00	0.16** 0.00	0.03 0.48
<b>Weight</b>	0.12** 0.00	0.42** 0.00	1	0.63** 0.00	0.65** 0.00	0.80** 0.00	0.08 0.06	-0.00 0.96	0.12** 0.00	0.09* 0.03
<b>Abd. Cir.</b>	-0.09* 0.04	0.03 0.50	0.63** 0.00	1	0.83** 0.00	0.66** 0.00	-0.01 0.80	0.32** 0.00	0.49** 0.00	0.00 0.89
<b>Pel. Cir.</b>	-0.05 0.23	-0.06 0.16	0.65** 0.00	0.83** 0.00	1	0.76** 0.00	0.00 0.91	0.28** 0.00	-0.05 0.23	0.02 0.67
<b>BMI</b>	0.03 0.42	-0.19** 0.00	0.80** 0.00	0.66** 0.00	0.76** 0.00	1	0.07 0.09	0.10* 0.03	0.02 0.63	0.09* 0.04
<b>Serum Ca</b>	0.19** 0.00	0.03 0.46	0.08 0.06	-0.01 0.80	0.00 0.91	0.07 0.09	1	-0.02 0.58	-0.04 0.38	-----
<b>Age</b>	-0.12** 0.00	-0.15** 0.00	-0.00 0.96	0.32** 0.00	0.28** 0.00	0.10* 0.03	-0.02 0.58	1	0.13** 0.00	-0.01 0.70
<b>Abd/Pel</b>	-0.07 0.12	0.16** 0.00	0.12** 0.00	0.49** 0.00	-0.05 0.23	0.02 0.63	-0.04 0.38	0.13** 0.00	1	-0.03 0.48
<b>Cor. Ca</b>	0.14** 0.00	0.03 0.48	0.09* 0.03	0.00 0.89	0.02 0.67	0.09* 0.04	-----	-0.01 0.70	-0.03 0.48	1

Alb:Albumin, Abd.Cir:Abdominal Circumference, Pel.Cir: Pelvic Circumference, BMI:Body Mass Index, Abd/Pelv: Abdominal Circumference/ Pelvic Circumference, Cor.Ca: corrected calcium level

\*\* Correlation is significant at the 0.01 level (2-tailed)

\* Correlation is significant at the 0.05 level (2-tailed)

which may in turn result in negative feedback on 25-hydroxylase, resulting in lower levels of 25-hydroxy vitamin D.

In this study in order to be able to have a look on all the aspects we also measured serum triglyceride level of the participants. Obesity induces an increase in pro-inflammatory cytokines<sup>1,30</sup> which leads to osteoclasts activity and bone resorption<sup>31,32</sup>; subsequently serum calcium level in obese people is higher while at the same time serum triglyceride level is higher in them and this two indicators might be not directly linked to each other.

Studying serum leptin and insulin level on serum calcium in obesity we can have a better conception of the mechanism that alters serum calcium level in obesity. In future studies we could also study the effects of vitamin D and PTH on serum calcium level in a larger group of obese people.

## Conclusion

Serum calcium level is significantly higher in obese participants and probably has no relation to high level of triglyceride in obese subjects.

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