Negative associations of Diurnal Cortisol Levels with Visceral obesity in Adults
Male and Female

Nour Shakir Rezaieg 1*

1 General Directorate of Education in Anbar, Gifted Guardianship Committee, Ministry of Education in Iraq, Anbar, Iraq

Abstract

Adipose tissue is considered an endocrine organ and but excess compromises the immune response and the metabolism of hormones and increase cortisol synthesis. The purpose of this study was to check cortisol level in obese individuals, And the detection of relationships between cortisol and other parameters. The study was done in a hospitals in Anbar governorate, Iraq from April 2021 to September 2021. Eighty male and female volunteers participated in this study, and they were divided according to BMI into two groups (40 obese and 40 non-obese individuals). Serum level of Cortisol, Vitamin D3, Zn, Ferritin Insulin and lipid profile were estimated. Anthropometric measurements were measured by a special formula. There was a significant (P< 0.05) increase in the levels of cortisol, insulin, ferritin, total cholesterol (TC), triacylglycerol (TAG), low-density lipoprotein cholesterol (LDL-C), WC and Fat% in obese groups as compared to non-obese groups (P-value < 0.05). While there was a significant (P< 0.05) decreased in the level of Zn, Vitamin D3, high-density lipoprotein cholesterol (HDL-C) in obese groups compared with non-obese groups. Also, the results noticed that there is a significant positive correlation between the levels of cortisol and each of BMI and insulin, while there was a significant negative correlation between cortisol level with Zn. Changes in levels of cortisol hormone, as observed in obese individuals contribute to the show of related disorders such as decrease in Zn levels and insulin resistance. Keywords: Cortisol, Zn, Vitamin D3, Ferritin, Visceral obesity.

Introduction

Obesity is characterized as an excess of body fat that can harm health and raise death rates. This condition raises the chance of developing a number of diseases, including type 2 diabetes, cardiovascular disease and various cancer [1]. Many factors contribute to the rise in obesity, including the widespread availability and relatively low cost of high-calorie foods, increased use of sugars, sugar substitutes, preservatives, and sugar sweetened beverages, altered eating patterns, and the promotion of sedentary lifestyles. Also, genetic, biological and social factors all play a major role in obesity[2].

Obesity occurs as a result of energy imbalance, that is, when the energy input from calories is higher than the energy expended as a result of physical activity, thus, the body stores these calories as fat [3]. Two forms of obesity can be distinguished based on the
location of adipose tissue deposition: android/apple obesity (adipose tissue accumulation primarily around the abdomen) and gynoid /pear obesity (adipose tissue accumulation primarily in the femoral region) [4].

Visceral obesity is related with changes hypothalamus–pituitary–adrenal (HPA) axis functioning which leads to development of visceral obesity by First, many DNA polymorphisms connected to HPA axis functioning are contributed to the increase of obesity. Second, chronic high of circulatory glucocorticoid levels results in increased abdominal adiposity. Third, visceral obesity is linked with a decreased capacity of cortisol to suppress its secretion [5].

The hypothalamus–pituitary–adrenal (HPA) axis is a neuroendocrine system contributed into the stress-response, through adjusting the excretion of cortisol hormone. The cascade of the HPA axis beholds that first the hypothalamus products and release corticotropin releasing hormone (CRH) [6], which then induces the stimulates and release of adrenocorticotropic hormone (ATCH) of the anterior pituitary. ACTH is produced from a larger precursor namely the proopiomelanocortin (POMC) protein, and stimulates the synthesis and release of cortisol by the adrenal cortex[7].

Cortisol is a steroid hormone that has an important role in weight control and also has an important effect on lipolysis, meaning it helps break down fats, but under some situations, cortisol may slightly suppress lipolysis [8]. Cortisol action to raise blood sugar through gluconeogenesis. As well, it help in metabolism of fat, protein, and carbohydrates [9].

Cortisol also affects the metabolism of micronutrients like zinc, making it a an important regulator of endocrine function [10]. Cortisol stimulates the gene expression of metallothionein and the zinc transporter Zip14, allowing plasma zinc to be redistributed to diverse tissues such as hepatic and adipose, resulting in Hypozincemia in obesity [11].

Most cortisol (95%) is transported through the circulation bound to plasma proteins ( 80% bound to cortisol binding protein, 15% attached to albumin) and 5% is free and functional. Free cortisol is a physiologically astir hormone that is not attached to plasma protein therefore can act straightly on tissue locale [12].

Also, cortisol hormone (stress hormone) affects our body in both physical and mental ways that can be detrimental to our overall health. Some of the effects of stress can be due to our genes, while some effects can be due to external environmental factors[13].

The purpose of this study is investigate the effect of obesity on cortisol and other biochemical parameters.
Materials and Methods

Participants

From April 2021 to September 2021, the comparative cross-sectional study was conducted at AL Ramadi Teaching Hospital for Maternity and children, in Ramadi, Anbar, Iraq. This study included 80 subjects between the ages of 40 to 45. According to their BMI, they were separated into two groups: Group I: Obese subjects (male n=20 and female = 20), Group II: Non-obese subjects (male n=20 and female n=20). Secondary hypertension, diabetes mellitus, pregnancy, and liver and renal illness were among the exclusion criteria. Prior to being enrolled in the study, each person signed a consent form to participate in the study.

Anthropometric measurements

These included the height (m), weight (kg), and the waist circumference (cm). Body mass index (BMI) was calculated by dividing the weight (kg) by height square (m$^2$) according to below formula:

\[
\text{BMI} = \frac{\text{weight (kg)}}{\text{square height (m}$^2$)}
\]
Subjects were classified into groups depending on the World Health Organization (WHO) body mass index (BMI) Classification as shown in the table below:

**Table 1: WHO body mass index (BMI) Classification.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5-24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25-29.9</td>
</tr>
<tr>
<td>Obesity class I</td>
<td>30-34.9</td>
</tr>
<tr>
<td>Obesity class II</td>
<td>35-39.9</td>
</tr>
<tr>
<td>Obesity class III</td>
<td>≥40.0</td>
</tr>
</tbody>
</table>

The Waist Circumference (WC) estimate is based on measuring the level of the umbilicus at the horizontal level around the center with a flexible, non-stretchable tape measure. Then asked from each subject to rest while he's exhaling in order to get the most exact measurements. The waist circumference of 88 cm for women and 94 cm for men is considered as discriminator value of central obesity.

**Biochemical measurements**

Venous blood samples were obtained collected into test tubes containing separator gel. Then serum was separated, within one hour after drawing of the blood, by centrifugation at 3000 rpm for 10 minutes. The samples were kept on −20°C for biochemical analysis.

Total cholesterol (TC), Triacylglycerol (TAG), Low density lipoprotein cholesterol (LDL-C), and High density lipoprotein cholesterol (HDL-C) were estimated by using laboratory kits (Bio Systems, Spain). While, serum Cortisol, Vitamin D3, Zn and Insulin were estimated by using Enzyme Linked Immune Sorbent Assay (ELISA) kit according to the manufacturer's instructions.

**Statistical Analysis**

All data analysis was done by using SPSS, and data are shown as mean ± SD. ANOVA was used to compare between means. p value ≤ 0.05 was considered statistically significant.

**Results**

Results in table 2 summarized the demographic characteristics of all groups. There was significant increase in BMI, WC and fat% in obese groups compared with non-obese groups.
Table 2: Comparison of demographic characteristics between obese and non-obese groups.

<table>
<thead>
<tr>
<th></th>
<th>Obese Males (n=20)</th>
<th>Non-obese Males (n=20)</th>
<th>P value</th>
<th>Obese Females (n=20)</th>
<th>Non-obese Females (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.15±2.37</td>
<td>43.08±6.85</td>
<td>N.S</td>
<td>41.91±6.28</td>
<td>42.19±2.92</td>
<td>N.S</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>34.91±7.41</td>
<td>24.76±2.93</td>
<td>0.0001*</td>
<td>33.98±9.63</td>
<td>23.01±7.13</td>
<td>0.0001*</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>112.01±3.40</td>
<td>93.37±6.09</td>
<td>0.0001*</td>
<td>99.51±1.27</td>
<td>86.72±0.65</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Fat %</td>
<td>34.76±2.65</td>
<td>29.54±6.23</td>
<td>0.0001*</td>
<td>36.13±3.11</td>
<td>27.43±1.04</td>
<td>0.0001*</td>
</tr>
</tbody>
</table>

P-value < 0.05 is significant, SE: Standard Division, N.S: Not–Significant

There was significant increase in cortisol hormone, Ferritin and Insulin levels in obese group in compared with non-obese group. While, there was significant decrease in Zn and vitamin D3 levels in obese group in compared with non-obese group as shown in Table 3.

Table 3: Comparison of Parameters studied between obese and non-obese groups.

<table>
<thead>
<tr>
<th></th>
<th>Obese males (n=20)</th>
<th>Non-obese males (n=20)</th>
<th>P value</th>
<th>Obese Females (n=20)</th>
<th>Non-obese Females (n=20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (ng/ml)</td>
<td>521.12±0.91</td>
<td>339.14±1.20</td>
<td>0.0001*</td>
<td>301.91±6.28</td>
<td>517.35±7.01</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Zn(µg/dl)</td>
<td>119.45±0.21</td>
<td>134.10±0.34</td>
<td>0.0001*</td>
<td>121.14±2.50</td>
<td>130.21±4.08</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Insulin (µU/ml)</td>
<td>18.53±2.67</td>
<td>10.30±2.42</td>
<td>0.0001*</td>
<td>17.22±3.59</td>
<td>9.62±3.22</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Ferritin(nɡ/ml)</td>
<td>48.90±0.23</td>
<td>30.82±1.26</td>
<td>0.0001*</td>
<td>41.41±0.19</td>
<td>37.43±5.06</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Vitamin D3 (nɡ/ml)</td>
<td>15.84±6.50</td>
<td>35.18±2.23</td>
<td>0.0009*</td>
<td>12.16±8.09</td>
<td>32.81±5.12</td>
<td>0.0006*</td>
</tr>
</tbody>
</table>

P-value < 0.05 is significant, SE: Standard Division, N.S: Not–Significant

Figure 2 summarized the levels of serum lipid profile of all groups. There was significant increase in Total cholesterol (TC), Triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) levels in obese groups in compared with non-obese groups. while, there was significant decrease in high-density lipoprotein cholesterol (HDL-C) levels in obese groups compared with non-obese groups.
Genetics, biological and other social variants share an increased susceptibility to obesity. Surprisingly, the obesity epidemic in our modern society is linked to a rise in factors that promote cortisol production, such as chronic stress, eating foods with a high glycemic index, and getting less sleep [14].

The results in our study showed high levels cortisol in individuals with greater BMI (fat mass) and waist circumference measurement, this results are in agreement with the study by [15] and his colleagues stating that ten (10) -kg/m² raise in Body Mass Index may raise produce cortisol to 2.5- fold in subcutaneous adipose tissue [16].

Cortisol in blood shows a diurnal rhythm with the highest levels in the morning and the lowest levels at night [15].

Also, the results of the study showed that the level of cortisol was higher in obese males compared to obese females in both groups, this may be due to the stress as a result their daily work in addition to the higher fat percentage in their bodies, so be cortisol produce as compensative technique devoted to stressful [17].

Cortisol is one of the most important hormones shared in the physiologic stress response. in addition, that the cortisol is a glucocorticoid (GC) hormone that works to redistribute of white adipose tissue to the ventral area, as well as an raise in hunger and a desire for tasty food (comfort food) [18].
Mezzullo [19] and his colleague mentioned that the stress associated cortisol levels play an important role in adipocyte biology and weight gain, potentially involve it as a main component in the evolution of obesity.

In another study by McCleary-Gaddy [20] which mentioned that the etiology behind rise of cortisol hormone in obesity individuals is that the subcutaneous adipose tissue excrete cortisol hormone. Increased adipose tissue levels may be cause metabolic problems that increase the risk of cardiovascular disease and metabolic syndrome.

The studies mentioned there was changes in the metabolism of various minerals in obesity status like zinc. The results of our study also showed that there was a decrease of serum zinc in obese individuals, this may be associated with the development of several metabolic problems like oxidative stress, the chronic inflammation, and insulin resistance [10]. Also, cortisol promote activation of the metal-regulatory transcription factor 1 (MTF1) so, leads to excess the gene expression of metallothionein and Zip14, which decreases serum zinc levels [21].

Moreover, the variations in zinc homeostasis induced especially by cortisol may share to the evolution of insulin resistance in obese individuals because high concentrations of zinc affect insulin secretion and action, as show in our results there was a high levels of insulin in obese groups compared with non-obese groups [22].

Many possible mechanisms have been proposed to explain the negative effects of obesity, particularly visceral obesity, on glucose metabolism, including increase lipid supply via a mechanism known as lipotoxicity. When free fatty acids increased for an extended length of time, it directly affects the action of insulin in skeletal muscle tissue and the liver [23].

Obesity causes to rise circulating insulin levels over time, and thus lowering insulin sensitivity and thus impairing pancreatic-cell function [24].

The positive relation between BMI and cortisol and insulin in our results is in agreement with what was mentioned by other authors [25].

Results in the study showed a decrease in Vitamin D3 levels in obese group compared with non-obese group. This decrease may be due to the deficiency of exposure to sunlight among obese individuals as a result of their sedentary lifestyle and their less outdoor activity [26].

Also, vitamin D imprisonment in adipose tissue, and volumetric dilution of intake or cutaneous synthesized vitamin D3 in the large fat mass of obese individuals, all of them represent factors may contribute to low vitamin D in obese people [27].
Alkubaisi and colleagues, reported that vitamin D3 deficiency is associated with an increased risk of developing immune diseases such as rheumatoid arthritis, multiple sclerosis, type 1 diabetes mellitus and sensitivity to infections, in addition to infect with metabolic syndrome and cardiovascular disease [21].

Furthermore, some studies data have indicated that vitamin D decrease can leads to greater adiposity by stimulating increased levels of parathyroid hormone and increase flow of calcium into adipocytes, thereby increasing lipogenesis [26].

The previous studies revealed that serum ferritin levels rise in response to inflammation. Obesity is linked to low-grade inflammation of white adipose tissue (WAT) as a result of chronic innate immune system activation [28].

Inflammatory cytokines, such as tumor necrosis factor-α, which activates ferritin transcription, can be found in both WAT and infiltrating macrophages. As a result, serum ferritin levels in obese individuals high, as shown in our results [29].

Indeed, obesity is related with many alterations in lipid metabolism, included high serum levels of TC, LDL-C and TAG, and decrease in serum level of HDL-C [30].

Past study by () mentioned that the high levels of TAG is often related with decrease serum levels of HDL this may be refer to a possible metabolic interaction between TAG and HDL [31].

The main key to this relationship could be that increased fat deposition in obese people is linked to insulin resistance, which leads to raise produce of TAG-rich lipoprotein in liver, and thus causes changes metabolism of those particles. HDL particles that are high in TAG are hydrolyzed more quickly and causing lowering HDL levels [32].

**Conclusion**

The results of the current study showed that there was an increase in cortisol, Ferritin, insulin, lipid profile excepted HDL level in obese group. While there was a decrease in Vitamin D3, Zn, and HDL levels when compared with non-obese ones.

**References**


Exercise with Mental Stress on Cortisol and Alpha-Amylase Changes in Young Men, *Middle East Journal of Rehabilitation and Health Studies*, 7(1).


