Estimation The Trace Elements And Their Association With Insulin Resistance In Obese Adults.

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ABSTRACT
Background: Trace elements are essential micronutrients in the development of the metabolic complication of obesity, arterial hypertension, dyslipidemia, and insulin resistance or diabetes. According these it is important to know and measure the trace elements status in obesity.

Aim of the study: A study was performed to estimate serum levels trace elements status Sodium (Na⁺), Potassium (K⁺), Calcium (Ca²⁺), and Chloride (Cl⁻) in the adults obese comparison with normal weight controls, and to evaluate their potential association with insulin resistance.

Material and Methods: Eighty obesity with Body Mass Index (BMI) 35–39.5 Kg/m² and twenty healthy person with (BMI) 18 - 24.5 Kg/m² as control group aged 20-40 years were assessed the serum levels trace elements and also were evaluated the insulin resistance in the obesity and control groups, according to Homeo-static Model Of Assessment for Insulin Resistance (HOMA-IR) protocol.

Results: Compared to the control group Ca and K serum levels were significantly lower (all P<0.05) and Na and Cl serum levels were significantly higher (P< 0.05) in the adults obese group in all age groups. Also significant inverse correlation was found between HOMA-IR and Ca level.

Conclusion: Obese adults have higher mineral serum levels especially Na and Cl than control group in all age groups, and lower Ca and K which contributed with insulin resistance.

INTRODUCTION
The trace elements are sodium, copper, iron, magnesium, potassium, and zinc which have been identified as essential for human health (1). In these study we estimation the serum levels of the trace elements changes that include Na⁺, K⁺, Ca²⁺, and Cl⁻ in obesity compare with normal persons, and to evaluate their potential association with insulin resistance. Trace elements can be involved their production or in the protection against inflammation and peroxidation which are important key factors in the development of metabolic complication of obesity (2).

Dietary with high amounts of sodium, calories and fats considered one of the etiology of chronic disease, including obesity and high blood pressure (3). Many studies on animals indicated that a diet with high sodium may increase adipose tissue mass, and this is lead to alteration in insulin and glucose metabolism which promote fat accumulation (4). Obesity caused of restrict sodium excretion, which leads to elevated blood pressure. In a study on obese adolescents with age 10-16 years, increased blood pressure could directly be related with a volume dependent of increased stroke volume and which decreased with a low sodium diet (5). High levels of salt in the body may lead to increased circulatory volume, this can lead to increase fluid pressure on the blood vessel walls. This process can cause thickening of the blood vessel walls and leave less space for the blood flowing within the vessels (6).

Several mechanisms may contribute to the pathogenesis of obesity induced hypertension, these mechanisms are the sodium retaining effects of catecholamine and insulin, disorders in transmembrane fluxes of sodium and altered carbohydrate metabolism, also some of these mechanisms can alter the urinary excretion of sodium and that effect on the serum sodium level (7).

Potassium can be defined as intracellular cationic electrolyte which is essential for normal cellular function, also it was easily excreted by the kidneys instead of stored in the body and the average of potassium consumption was insufficient (8). Many studies showed that higher potassium can be reduced the obesity and meta – bolic syndrome risk (9).

Potassium contributed in the protein synthesis and carbohydrate metabolism later was excreted, in the urine instead of storage in the body, the human body requires a constant quantity of potassium, also it has important role in insulin secretion from pancreatic beta cells (10). Potassium consumption can be alterable to the activation of the renin – angiotensin system (RAS) in response to the volume contraction, promoted potassium exchange with sodium in the distal tubule when potassium enters the cell lead to diuretic-induced alkalosis, the (RAS) activation can be considered an important system contributes to hypertension in obese individuals, sodium retention in the body and volume expansion can be enhanced sympathetic activity, also high levels of circulation components of (RAS) were observed in obese subjects, which had shown a reduction in weight loss (11). In insulin – resistance obese patients an elevated Na⁺/K⁺ ratio was found in skeletal muscles, pointing to reduction pump ability, also the same study showed a positive association between skeletal muscle Na⁺/K⁺ and BMI (12).

Calcium constitutes about 1.5% - 2% of total body weight and mostly found in bones and teeth (13), also calcium is the most abundant in the human body, which participated in many physiology processes such as muscle contraction, hormones, and neurotransmitters release, glycogen metabolism, cell proliferation and differentiation, nerve impulse transmission and structural support of the skeleton (14).

Calcium concentration controlled by three hormones; parathyroid hormones, calcitriol, and calcitonin hormones, these hormones work to increase calcium concetration by interaction with kidneys, intestines, and bones (13). Many data have proved the regulation of...
of adipocyte energy storage can be controlled by intracellular Ca\(^{2+}\) which lead to increase circulating calcitrophic hormones and/or parathyroid hormone and low Ca\(^{2+}\) diets induce adipocyte Ca\(^{2+}\) flow and thereby increase lipid storage (15).

Loos et al. (2004) showed an association between fat-free mass and calcium intake in black women and also indicated that lower Ca\(^{2+}\) intake can be linked with higher adiposity (16). In a study performed on Chinese women showed that calcium is inversely associated with BMI, weight change, waist to higher ratio, and fat mass, they also indicate when dairy calcium is increased, the risk for abdominal obesity was significantly decreased (17).

Trace elements is involved in the pathogenesis of obesity and obesity-related disease, we tried to assess trace elements status (Na, K, Ca, and Cl) serum levels and insulin resistance in obese adults compare to the control group.

**MATERIAL AND METHODS**

**Subjects**: This study conducted between July 2020 continued through September 2020 in Al-Diwaniah Teaching Hospital. The study included 100 individuals, subjects with history of chronic medication use, history of chronic disease, drug use and other disorder were excluded from this study. The total samples 100 blood samples were taken from men in this study which divided according BMI into control group (20 sample) which BMI 18-24.5Kg/m\(^2\) and obesity group (80 sample) which BMI 35-39.5 Kg/m\(^2\) and according to age divided into four groups (20-25 year), (26-30 year), (31-35 year), and (36-40 year). Obese male groups examined to estimate the serum trace elements levels and evaluated the insulin resistance according to the (HOMA-IR) protocol and compare with control group. The hospital ethical committee approved the human study, control and obese were told about the importance, and other detail of research and explain the aim of this study and protocol of ethics. Many of subjects refused to give the blood samples.

**Blood Collection**: Blood were collected by vein puncture at 8 - 10 am after overnight fast. Separated into 3 ml untreated gel tube for serum and 2 ml EDTA treated tube for plasma. The serum were frozen at -20°C in two replicate until thawed for assay.

**Trace Elements Measurements**: Trace elements levels in the serum (Na, K, Ca, Cl) were detected for all subjects and control by using Opti - Lion analyzer (Optimedical, U.S.A.) by using available cassette which taken the serum 200 microliter, after 2 minutes, the result was given in mol/L.

**Glucose and Insulin Resistance Measurements**: Fasting glucose level was estimated by using Reflotron plus automated analyzer (Roche, Germany). Plasma insulin was determined by immunoradiometric assay (DIA-Source Immunoassays S.A. Nivelles, Belgium).

The diagnosis of insulin resistance was determined by Homeostasis Model Assessment index for Insulin Resistance (HOMA-IR) protocol, which the product of fasting insulin (µIU/ml) and fasting glucose (mmol/L) divided by 22.5. Insulin resistance was defined when P values were above 3.16 (18).

Data are shown as mean ± SD, all calculations and statistics were performed using analyzed Statistical Package for the Social Science (SPSS), version 20. Comparisons between groups were carried out using the Mann–Whitney U test. Simple correlations between variable were calculated as the Spearman Coefficient of correlation at P Value <0.001 was regarded as significant.

**RESULTS**

One way ANOVA analysis showed significant increased (P <0.05) the Na serum level in obese compare with the control group in all age groups. Statistical analysis demonstrated no significant difference (P < 0.05) between obesity and control group k serum level in age group (20-25 year), while significant decrease (P <0.05) K serum level in obesity compared with control group in age groups (26-30 year), (31-35 year), and (36-40 year).

Results showed significant decreased (P < 0.05) the Ca serum level in obesity in all age groups compare with control groups. Studied reveal significant increased (P < 0.05) in Cl serum concentration level in obesity compare with control group in all age groups (Table 1).

<table>
<thead>
<tr>
<th>Subject</th>
<th>Parameter</th>
<th>Mean ± SD(age groups)</th>
<th>L.S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI 35-39.9 Kg/m(^2) N=80</td>
<td>Na m mol/L</td>
<td>20 - 25 Year N=20</td>
<td>140.62±1.789”</td>
</tr>
<tr>
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<td>K m mol/L</td>
<td>26 - 20 Year N=20</td>
<td>142.31±2.074”</td>
</tr>
<tr>
<td></td>
<td>Ca m mol/L</td>
<td>31- 35 Year N=20</td>
<td>4.240±0.409</td>
</tr>
<tr>
<td></td>
<td>Cl m mol/L</td>
<td>36 - 40 Year N=20</td>
<td>1.021±0.036</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>104.22±2.831</td>
</tr>
<tr>
<td>Obesity BMI 35-39.9 Kg/m(^2) N=80</td>
<td>20-25 Year N=5</td>
<td>105.20±2.864</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>26-20 Year N=5</td>
<td>106.20±2.550</td>
</tr>
<tr>
<td></td>
<td></td>
<td>31-35 Year N=5</td>
<td>140.61±1.303”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>36-40 Year N=5</td>
<td>143.71±3.032”</td>
</tr>
</tbody>
</table>
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**Table 1:** Comparison mean ±SD trace elements serum levels in obesity and control in different age groups.

In present study we found significant increase (P < 0.001) insulin resistance in obesity as represent by HOMA-IR indices, serum insulin and glucose concentration levels compare with the control group in all age groups (Table 2, Table 3) Also result indicate significant correlation between obesity and poor trace elements Ca and K with control group in all age groups.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Parameter</th>
<th>Mean ± S.D (age groups)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>Glucose (m mol/L)</td>
<td>20 – 25 Year N = 20</td>
</tr>
<tr>
<td>BMI 35-39.9 Kg/m² N=80</td>
<td>90.860±5.409*</td>
<td>97.920±3.091*</td>
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<td></td>
<td>14.3±3.4*</td>
<td>16.8±4.8*</td>
</tr>
<tr>
<td>Control</td>
<td>Glucose (m mol/L)</td>
<td>20 – 25 Year N = 5</td>
</tr>
<tr>
<td>BMI 18-24.9 Kg/m² N=20</td>
<td>81.800±5.611</td>
<td>84.610±2.590</td>
</tr>
<tr>
<td></td>
<td>8.1±6.1</td>
<td>9.2±5.2</td>
</tr>
</tbody>
</table>

*Significant (P<0.05)

**Table 2:** The comparison mean ±SD fasting Glucose and Insulin concentration in obesity and control in different age groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Obesity N=80</th>
<th>Control N=20</th>
<th>P</th>
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<tbody>
<tr>
<td>Glucose (m mol/L)</td>
<td>100.89±5.577*</td>
<td>84.25±5.080</td>
<td>P&lt;0.001</td>
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<tr>
<td>Insulin (µUI/ml)</td>
<td>14.725±4.025*</td>
<td>8.775±4.5</td>
<td>P&lt;0.001</td>
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<tr>
<td>HOMA-IR</td>
<td>66.026±1.7*</td>
<td>32.858±0.58</td>
<td>P&lt;0.001</td>
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</tbody>
</table>

*Significant (P<0.001)
Table 3: Comparison mean ± SD Glucose, insulin concentration and, insulin resistance level in the obesity and control groups.

The mean ± SD HOMA-IR was significantly higher (P < 0.01) in obesity with Ca and K deficiencies as well as correlation analyses showed significant invert relation between Ca serum level in obesity with HOMA-IR (P < 0.01) (Table 4).

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Parameter</th>
<th>R</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(20-25 year)</td>
<td>(26-30 Year)</td>
<td>(31-35 Year)</td>
</tr>
<tr>
<td>Obesity</td>
<td>Ca-HOMA-IR</td>
<td>0.347*</td>
<td>0.469*</td>
</tr>
<tr>
<td></td>
<td>Significant( P&lt;0.01)</td>
<td>R (Spearman Coefficient)</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Significant correlation between Ca trace element in obesity relation with HOMA-IR in different age groups.

DISCUSSIONS

Our data showed that sodium serum level was increased in obese adult individuals compared with control group. The insulin resistance can increased the activity of central sympathetic nervous system which increased the peripheral resistance and increased the reabsorption of sodium in the kidney tubules (19). The increasing risk factors of blood pressure and cardiovascular diseases related with the consumption of salt which increasing in the risk of stroke and renal diseases which associated with obesity (20).

Our study reveal that potassium serum level were decreased in obese indivi-duals in age groups (26 - 30 year), (31 - 35 year), and (36 -40 year), so that our suggestion about the decreased of potassium in these age groups may be related with the reduction of muscle mass or increase the glucose metabolism in those individuals, while no significant differences potassium level in obese age group (20-25 year) compare with control may be related with high dietary of potassium. Cai et al. (2016) showed that potassium intake was related to metabolic syndrome and also performed a protective influence of potassium intake on metabolism syndrome and obesity, sodium to potassium ratio was considered a sensitive marker to obesity. We finding significant differences in calcium serum level between obese and control group in all age groups, while no significant differences between age groups in control an obesity groups. Our suggestion that the decrease of calcium level in obesity groups may be related with many factors such as affected in the future with hypertension, diabetes type II, insulin resistance, high cholesterol levels and other complications of obesity as well as increasing cytokines and interleukins and deficien-cy of Vitamin D. The mechanism which explain the influence of calcium on the body weight alteration that calcium was considered a regulatory for lipid metabolism because the increasing levels of intracellular calcium can stimulate the activity of lip-ogenic enzyme and inhibit the lipolysis with elevated the accumulation of fat (16).

May study confirm with our result data, calcium intake as calcium only or in the dairy food was related with weight loss (21), also Huang et al. (2011) showed that dietary calcium intake, but not calcium supplement was negatively related with abdominal obesity and body composition. The absence of some micronutrients were associated with fat accumulation and obesity, such as overweight and obese individual had lower levels of minerals and vitamins compared with non-overweight and non-obese individuals (21).

In the cross sectional study, elevated the degree of obesity higher BMI and weight were associated with higher sodium intake and low calcium (22).

Our data demonstrated a significant differences in glucose concentration in obese individual compare with control group in all age groups, our suggestion about increasing levels of glucose in obese may be related with their insulin resistance and dyslipidemia which increasing the risk factors of obesity and metabolic syndrome. The increasing of plasma insulin is associated with increasing obesity and with incre-increasing the decline of insulin sensitivity, while the glucose levels not raised in the men with BMI >25 without metabolic syndrome, but the levels of insulin elevated in the men with metabolic syndrome (23-24).

The elevated levels of fatty acids in the liver lead to increase triglycerides, hepatic gluconeogenesis and the synthesis of Very Low Density Lipid (VLDL) which can cause the abnormalities in glucose metabolism (25).

Obesity, metabolism syndrome and the risk factor of cardiovascular disease was increased when the blood glucose increased (26). The immunoassay of serum insulin was caused a con-foundering results about insulin secretion in individuals with abnormalities of glucose tolerance, so that many researchers showed that glucose induced insulin can release in mild diabetes while others showed that it was increased in obesity (27-28).

CONCLUSIONS

Obese adult individuals were have significant increased Na and Cl serum levels, and significant decreased Ca and K mineral compare with control in all age groups, also invert correlation between Ca and K serum levels deficiencies with insulin resistance.

REFERENCES

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