Correlation Between Insulin Resistance and Obesity in Normoglycemic Obese Syrian Subjects

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ABSTRACT
Insulin resistance is a pathophysiologic link to development of several metabolic disorders in obese subjects. The aim of this study is to evaluate the association between obesity and insulin resistance using HOMA-IR index in normoglycemic obese subjects and to compare the results with the result of healthy non obese subjects. The importance is to identify the subjects in risk for developing preventive strategies before the manifest disease as type 2 diabetes. A total 45 obese subjects (25 men and 20 women) and 45 lean subjects (25 men and 20 women) were enrolled to evaluate obesity by body mass index BMI, waist circumference, waist to hip ratio WHR and insulin resistance measured by HOMA-IR index. The results demonstrate that HOMA-IR is significantly higher in obese groups, males and females, compared with the control group of the same sexes and was positively correlated with the elevated values of body mass index, waist circumference, and waist to hip ratio in the tow sex.

Key words: Obesity, Insulin Resistance, HOMA-IR index.

INTRODUCTION
Obesity is a public health problem and the increasing prevalence of overweight and obesity is reaching global epidemic status. According to the World Health Organization (WHO), there is about 2.3 billion overweight people aged 15 years and above, and over 700 million people expected to be obese worldwide in 2015. There is a difference geographic in the distribution of obesity which is attributed to changes in lifestyle, dietary habits, physical activity and the social and cultural environment.

Obesity especially abdominal obesity is an important risk factor for several diseases due to its pathophysiological link to the development of type 2 diabetes and cardiovascular abnormalities.

Obesity has been strongly associated with insulin resistance in normoglycemic persons and in individuals with type 2 diabetes. Obese individuals develop resistance to the cellular actions of insulin, characterized by an impaired ability of insulin to inhibit glucose output from the liver and to promote glucose uptake in fat and muscle and consequently decreased insulin sensitivity.

The relationship between obesity and insulin resistance is likely a cause-and-effect relationship based on studies conducted on human and animal. As a result, insulin resistance is used as a predictor of type 2 diabetes development even in individuals with normal glucose tolerance. Therefore it is important to recognize and to determine the insulin resistance in the period of pre-disease when therapeutic intervention is likely to be more successful in prevention before the development of manifest disease.

The homeostasis model assessment of insulin resistance (HOMA-IR), first described by Matthews et al., is a simple method to evaluate insulin sensitivity, calculated from fasting plasma glucose level and insulin. HOMA-IR is an index of insulin resistance which reflect hepatic insulin sensitivity and basal hepatic glucose production. HOMA-IR can be used for evaluation of insulin resistance in normoglycemic persons and is frequently used in clinical research and in population screening.

Anthropometric measures using waist circumference and waist/hip ratio have been used as measures of central obesity (where visceral adipose tissue is stored), and body mass index (kg/m2) has been used as a measure of general obesity. The aim of this study was to evaluate homeostasis model assessment of insulin resistance (HOMA-IR) and its relationships with obesity and anthropometric parameters in sample of obese normoglycemic syrian population.

MATERIALS & METHODS
Subjects: 45 obese subjects (25 men and 20 women) were recruited from several medical clinics in Damascus and 45 lean subjects (25 men and 20 women) had been included as a healthy reference population. Subjects who gave informed consent to participate were included in the data collection. Samples were collected during 12 months from 1 April 2013 to 1 April 2014. Mean (X) and Standard Deviation (SD) for ages in males (X± SD: 43±4.12) years.
Table1. Characteristics and Profiles of the study population

<table>
<thead>
<tr>
<th></th>
<th>Obese subjects</th>
<th>Lean subjects</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose (mg/dl) - males</td>
<td>104.5 ±4.12</td>
<td>93.4 ±2.09</td>
<td>0.06</td>
</tr>
<tr>
<td>Fasting Glucose (mg/dl) - females</td>
<td>101.67 ±5.06</td>
<td>94.3 ±3.34</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI (kg/m²) - males</td>
<td>32.22 ±2.56</td>
<td>24.8 ±1.8</td>
<td>0.0008</td>
</tr>
<tr>
<td>BMI (kg/m²) - females</td>
<td>33.64 ±1.61</td>
<td>22.69 ±2.03</td>
<td>0.002</td>
</tr>
<tr>
<td>Fasting insulin μIU/ml - males</td>
<td>29.11 ±3.9</td>
<td>8.64 ±2.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting insulin μIU/ml - females</td>
<td>27.91 ±5.03</td>
<td>9.04 ±3.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HOMA -IR - males</td>
<td>7.51 ±0.92</td>
<td>2.1 ±0.87</td>
<td>0.002</td>
</tr>
<tr>
<td>HOMA -IR - females</td>
<td>7 ±0.64</td>
<td>21 ±0.87</td>
<td>0.003</td>
</tr>
<tr>
<td>Waist circumference cm - males</td>
<td>110.25 ±1.43</td>
<td>93.12 ±0.23</td>
<td>0.0003</td>
</tr>
<tr>
<td>Waist circumference cm - female</td>
<td>99.94 ±0.76</td>
<td>80.16 ±0.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHR - males</td>
<td>1.07 ±0.91</td>
<td>0.9 ±0.18</td>
<td>0.001</td>
</tr>
<tr>
<td>WHR - females</td>
<td>1.03 ±0.34</td>
<td>0.83 ±0.76</td>
<td>0.005</td>
</tr>
</tbody>
</table>

and in females (X ±SD: 44±2.31) years. Each participant was interviewed to obtain a detailed medical history. All subjects don’t use any drugs which affect the studied parameters. Subjects with any other chronic illness like tuberculosis, malignancy, hepatitis, hypercholesterolemia, hyperlipidemia, hypertension, renal diseases, hormonal derangements like Cushing’s syndrome, hypothyroidism etc, pregnancy, alcoholism were excluded.

Biochemical analyses: For all kinds of measurements, fasting venous blood was collected after a 12 hours overnight fasting. Plasma glucose levels were measured by the glucose oxidase-peroxidase method and plasma insulin levels were measured by Electro Chemiluminiscence Assay (ECLIA) using Elecsys 2010 Roche Kite, HOMA-IR was defined using the following formula (Fasting Insulin μIU/mL x Fasting Glucose mg/dl) / 405.

Anthropometry: Height and weight were measured using standard techniques while the subject was wearing light clothes and bare-footed. Height was measured to the nearest 0.1 cm and weight to the nearest 0.1 kg. The body mass index was calculated as weight in kilograms divided by the square of height in meters. The waist circumference was measured midway between the lower rib and the iliac crest, and the hip circumference at the level of the great trochanters, the waist to hip ratio (WHR) was calculated as the ratio between the waist and the hip circumferences.

According to the World Health Organization criteria, a body mass index (BMI) of 25—30 kg/m² indicates overweight, and ³0 kg/m² indicates obesity 1.

Statistical analyses: All statistical analyses were performed using the SPSS-PC program (version 7.5, Chicago, IL, USA). Adopted t-Test for the Significance of the Difference between the Means. Also, Pearson correlation coefficient was used to study the correlation between the studied parameters. P < 0.05 was considered statistically significant.

RESULTS
The values of clinical and medical characteristics between lean and obese subjects are shown in table 1. The obese subjects were heavier and exhibited significantly higher waist circumference, as well as BMI and WHR. The concentrations of fasting glucose did not differ between groups (obese/lean, male/female). In contrast the concentrations of fasting insulin were significantly higher in obese subjects (male/female) than lean subjects. HOMA-IR is higher and statistically significant in obese groups, males and females, compared with the control group of the same sexes.

Male subjects
HOMA-IR was positively correlated with body mass index (R=0.31 P=0.003), waist circumference (R=0.38, P=0.001), and waist to hip ratio (R=0.15, P<0.001).

Female subjects
HOMA-IR was positively correlated with body mass index (R=0.23, P<0.001), waist circumference (R=0.12, P=0.001), and waist to hip ratio (R=0.32, P=0.002).

DISCUSSION
These findings suggest that obesity is closely correlated with lower insulin sensitivity in normoglycemic subjects namely before the development of any alteration in glucose metabolism. An association between obesity and insulin resistance has been reported in adults and children 5,16. Several studies suggested that weight loss is associated with a decrease in insulin concentration and an increase in insulin sensitivity in adults including reduction in incidence of type 2 diabetes 17,18. However, this study showed that fasting glucose level was not a specific indicator to development of insulin resistance because in the first stage of metabolic abnormalities the determination of fasting insulin level is more important than fasting glucose level to evaluate the insulin resistance as a risk factor for type 2 diabetes 19. However, this study showed that fasting glucose level was not a specific indicator to development of insulin resistance because in the first stage of metabolic abnormalities the determination of fasting insulin level is more important than fasting glucose level to evaluate the insulin resistance as a risk factor for type 2 diabetes. This is can be explained by the hypothesis that glucose intolerance may develop latter than other metabolic abnormalities 19. These data also suggest that insulin resistance (measured by HOMA-IR ) are significantly associated with higher values of BMI, Waist Circumference and WHR in the two sex. This finding showed that BMI, WC, and WHR were equally predictive risk of type 2 diabetes and CVD. This result is in agreement with the results from a 2007 meta-analysis 20 that suggested that measures of general obesity (BMI) and measures of central obesity (WHR and WC) performed equally well in predicting the incidence of type 2 diabetes. Unlike to other studies that have been shown that WHR was a better predictor than body mass index of
hypothesis, diabetes, and dyslipidemia. As visceral adipose tissue is known to generate diabetogenic substances and may be more informative than total fat as a risk factor for diagnostic evaluation the development of type 2 diabetes. In conclusion, these results indicate that insulin resistance measured by HOMA-IR index was positively correlated to obese subjects evaluated by BMI and other anthropometric measures and may contribute to development of several metabolic abnormalities. Taking in our account that the screening for metabolic abnormalities in obese subjects using blood glucose level alone is not sufficient to determine the abnormalities in glucose homeostasis. Fasting measures of glucose and insulin levels are more specific in screening for the abnormalities in glucose homeostasis associated with insulin resistance. The major role of the insulin sensitivity index seems to be a clinical prediction of the development of metabolic disorders (Type 2 diabetes and CVD) in obese normoglycemic subjects. The clinical value of HOMA-IR index is for early detection of obese subjects who are at risk for the application of preventive interventions including lifestyle changes in increasing physical activity and decreasing caloric consumption and weight loss. Finally, the present study has several limitations. First, it was a cross sectional design which does not allow to make causal relationship between insulin resistance and life style habits and other hormone abnormalities (like leptin and adiponectin etc). Second, the results of this pilot study including a small sample size clearly have to be validated in large populations in the future, to be representative of the general population.

REFERENCES
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