ABSTRACT

Background: Obesity is a major health problem worldwide that increase risk for a wide range of diseases including diabetes mellitus and heart disease. As such, it increasingly important to understand how excess adiposity can perturb normal metabolic functions specially for glucose and lipid homeostasis.

Objectives: The study design to evaluate the effects of obesity on the glycosylation process and determine the effects of increase age and BMI on measured parameters.

Materials and Methods: This study was conducted during the period from October 2010 to September 2011 in the department of Clinical Pharmacy under approval of scientific and ethics committee. One hundred individuals were included in this work divided into 2 groups. The first group included fifty apparently healthy individuals (30 males and 20 females) with BMI (21±3.1 Kg/m2). The second group included fifty individuals (30 males and 20 females) with BMI (28.± 1.3 Kg/m2) whose defined as obese.

Results: The study demonstrated a significant elevation in serum glucose, mean blood glucose, serum fructosamin, measured and predicted HbA1c in obese individuals as compared with those of control individuals. Glycosylation gap showed a significant elevation in obese subjects when compared to control individual that mean significant elevation in intracellular glycosylation process. Regarding the relation between age and measured parameters, the study showed no significant correlation between age and measured parameters in the control group, while in obese group there were a significant correlation( r = 0.03) between ages and predicted HbA1c and BMI( p ≤ 0.05).Regarding the relation between BMI and measured parameters, the study showed significant correlation between measured parameters and BMI in obese individuals, while in control group only serum glucose and MBG were correlated to BMI ( r = 0.01) at ( p ≤ 0.05).

Conclusion: Obese subjects shows significant increase in glycosylation gap, so there is a significant intracellular glycosylation process that was related to many diseases process and their complication.

Keywords: Glycosylation gap, Obesity, HbA1c, Fructosamin.
Obesity is major health problem worldwide that increase risk for a wide range of diseases including diabetes mellitus and heart disease. As such, it increasingly important to understand how excess adiposity can perturb normal metabolic functions specially for glucose and lipid homeostasis. Glycosylation is a non-enzymatic process in which proteins react with reducing sugar molecules causing impair of their function and change of their characteristics. Glycosylation usually occurs in diabetes, aging and many other diseases where accumulation of glycosylation end products involve in pathogenesis of these diseases and their complications.

Glycated HbA1c result from non-enzymatic - concentration - dependent covalent bonding of glucose to Hb within the erythrocytes, thereby HbA1c is a good indicator for glycemic control over long period(2-3-months) and also its good indicator for intracellular glycation process.

The extracellular glycation process also can be evaluated using serum fructosamin, a glycated end product of serum protein. Fructosamin is a measure of average glycemic control over a shorter period (2-3 weeks) and its plasma concentration is much more stable than that of glucose itself and much more easier to measure than true mean blood glucose (MBG), which requires contagious blood glucose monitoring.

Glycosylation gap (GG) defined as the value that results from subtraction of direct measured HbA1c value minus the predicted HbA1c value obtained from equation using another indicator of glycemic control, fructosamin (FA). GG used as clinical research tool for evaluating physiological sources of variation that affecting glycemic control and it can also be used as a tool to define the direction of glycosylation process.
In the present work GG is considered as a corner stone of this study to evaluate the effects of obesity on the glycosylation process.

**Subjects and Methods**

This study was conducted during the period from October 2010 to September 2011 in the department of Clinical Pharmacy under approval of scientific and ethics committee.

One hundred individuals were included in this work divided into 2 groups. The first group included fifty apparently healthy individuals (30 males and 20 females) with BMI (21±3.1 Kg/m²). The second group included fifty individuals (30 males and 20 females) with BMI (28.7± 1.3 Kg/m²) which are defined as obese.

Serum fasting glucose was assayed by glucose oxidase/peroxides colorimetric method, FA by NBT-spectrophotometric method and HbA1c% measured by Chromatographic–spectrophotometric method, while mean blood glucose (MBG) predicted HbA1c and Glycosylation gap were calculated using equations:

\[ \text{MBG} = 1.76 \times (\text{HbA1c}) - 3.67 \text{mmol/L} \]

\[ \text{P-HbA1c} = 0.017 \times \text{FA} + 1.61 \]

\[ \text{GG} = \text{M-HbA1c} - \text{P-HbA1c} \]

Data are presented as mean ±SD, 2-sample t-test was used to compare between measured parameters in test group and control group. The relationship between age or BMI and the measured parameters were determined by Pearson correlation.

**Result**

The study demonstrated a significant elevation in serum glucose, mean blood glucose, serum fructosamin, measured and predicted HbA1c in obese individuals as compared with those of control individuals.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control group (N=50)</th>
<th>Obese group (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycosylation gap</td>
<td>-0.05±0.23</td>
<td>1.07±0.31***</td>
</tr>
<tr>
<td>Measured HbA1C%</td>
<td>5.53±0.4</td>
<td>6.86±0.43**</td>
</tr>
<tr>
<td>Predicted HbA1C%</td>
<td>5.45±0.28</td>
<td>5.87±0.17***</td>
</tr>
<tr>
<td>Mean blood glucose</td>
<td>111±13.5</td>
<td>151.3±13.8***</td>
</tr>
<tr>
<td>Fructosamin (µmol/L)</td>
<td>227.2±17.4</td>
<td>248.12±8.16**</td>
</tr>
<tr>
<td>Serum glucose (mmol/L)</td>
<td>81.9±15.2</td>
<td>96.08±6.9**</td>
</tr>
</tbody>
</table>

* = p<0.05, **= p<0.01, ***= p<0.001
Glycosylation gap showed a significant elevation in obese subjects when compared to control individuals that mean significant elevation in intracellular glycosylation process.

Regarding the relation between age and measured parameters, the study showed no significant correlation between age and measured parameters in the control group, while in obese group there were a significant correlation ($r = 0.03$) between ages and predicted HbA1c and BMI ($p \leq 0.05$).

Regarding the relation between BMI and measured parameters, the study showed significant correlation between serum glucose, mean blood glucose, serum fructosamin, measured and predicted HbA1c and GG with BMI in obese individuals. While in control group only serum glucose and MBG shows significant correlation to BMI ($r = 0.01$) at ($p \leq 0.05$).

**Discussion**

The study demonstrated a significant elevation in serum glucose and MBG in obese subjects as compared to controls and this may be related to an increase in insulin resistance that in turn associated with intravascular hyperglycemia and hypertriglyceridemia that associated with obesity and agree with results described by Ruderman et al, Resnick and Boden et al.\(^{16-18}\)

Obesity Also associated with a significant reduction in the intracellular Mg$/$Ca ratio that interfere with normal insulin secretion and activity.\(^{19,20}\) Moreover, low intracellular Mg concentration will lead to increase adrenergic activity in obese subjects that will lead to increase in gluconeogenesis and glycogenolysis.\(^{16}\)

The significant elevation in serum fructosamin level in obese subjects can be related to sustained hyperglycemia and this result come in accordance with results obtained by Woo et al and Ardawi et al who describe the influence of obesity on plasma fructosamine concentration.\(^{21,22}\)

The high HbA1c value in obese individual can also related to sustained hyperglycemia that occur due to impaired glucose metabolism and this agree with results obtained by Power et al.\(^{11}\) The substantial increase in GG in obese subjects may be related to significant elevation of measured HbA1c value over the predicted HbA1c value that obtained from equation using serum fructosamin.

The study also revealed that with increasing age, predicted HbA1c will increase in obese subjects and this in consistence with results obtained by Martins et al and this may be due to the increase in the extracellular- intravascular glycation. BMI showed significant correlation with measured parameters in obese group and this is in consistence with results obtained by Power et al.\(^{11}\).

In conclusion obese subjects shows significant increase in glycosylation gap, so there is a significant intracellular glycosylation process which may be the underlying cause of many diseases process and their complication. Further studies are required to investigate the exact role of GG in clinical diagnosis.
References


