Monoamine Oxidase activity in Iraqi patients with metabolic syndrome

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Abstract
Monoamine oxidase is an enzyme responsible for the oxidative deamination of monoamines. As neurotransmitters, monoamines mediate the neural control on glucose metabolism by inhibiting insulin secretion. Hence, glucose levels in metabolic syndrome may be affected by monoamine oxidase activity. Consequently, this work aims to assess the role of MAO in metabolic syndrome. The activity of monoamine oxidase was simultaneously determined with the levels of glucose and insulin in sera samples from 100 volunteers with metabolic syndrome and the other 30 healthy controls. The result showed that all three variables were significantly higher in metabolic syndrome patients as compared to the control group. These data suggest that the observed overactivity of MAO might play a role in the pathogenesis of the metabolic syndrome.

Key words: Monoamine oxidase, insulin, metabolic syndrome

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Introduction
Metabolic syndrome is a cluster of biochemical and physiological disorders characterized by some disturbances including increased waist circumference, hypertension, hyperglycemia, high serum triglycerides, and low serum high-density lipoprotein (HDL), the presence of at least three of these signs constitutes a clinical diagnosis [1].

Monoamine oxidases are a group of enzymes located in the mitochondrial outer membrane, they catalyze the oxidative deamination of monoamines, generating hydrogen peroxide and the corresponding aldehyde, and either ammonia or a substituted amine [2]. Thus MAO reactions have been demonstrated to be substantial sources for oxidative stress and its numerous complications [3]. In this context, MAO has also been shown to play important roles in tumorigenesis [4], diabetes [5], cardiovascular disease [6] and obesity [7]. Among these disorders, obesity has been pointed out as the most pivotal factor in the development of insulin resistance and the consequent hyperglycemia in metabolic disorders [8]. Furthermore, several studies have suggested that insulin secretion might be controlled by MAO via regulating monoamines store in islet beta cells [9, 10]. In this study, the activity of MAO, insulin and glucose levels were determined in sera of Iraqi patients with metabolic syndrome and healthy controls in an attempt to shed light on the potential role played by MAO in the emergence of metabolic syndrome.

Materials and Methods
Blood samples were collected by venipuncture from 100 males aged between 40-55 years who have been diagnosed with metabolic syndrome through the determination of at least three out of five symptoms; high blood pressure, hyperglycemia, high waist circumference, and abnormal cholesterol or triglyceride levels. In addition, 30 healthy volunteers were also included as age and sex-matched control group. The samples were collected during the period from October 2018 to May 2019. Glucose levels were determined using the enzymatic colorimetric method [11], by the protocol of the diagnostic kit provided from Randox Company, UK. Insulin level was determined in sera of
patients and controls using Elisa kit (LDN, Nordhorn, Germany), whereas insulin resistance was calculated using the following mathematical relationship: 

$\text{IR} = \frac{\text{Fasting glucose (mg/dL)} \times \text{Fasting Insulin (μU/mL)}}{405}$

Serum MAO activity was determined according to McEwen and Cohen [13] with benzylamine as the substrate. The assay and control reaction was incubated in open test tubes at 37°C for 3 hours. The assay tube contained 600μL of serum, 700 μL of 0.1 M phosphate buffer (pH 7.2) and 200 μL of 6 mM benzylamine hydrochloride. At the end of the incubation time, 200 μL of 50% perchloric acid was added to stop the reaction. In the control tube, the substrate was added just before the perchloric acid. 1500 μL of cyclohexane was added to each tube, the assay tubes were then shaken for 15 minutes, then centrifuged (2000 rpm) for 10 minutes. Then, the absorbance of cyclohexane extract was read at 242 nm. Enzyme activity was measured through aldehyde formed in 3 hours by reading the absorbance of the test tube against the control tube.

**Results and Discussion**

Insulin and glucose concentrations were determined in sera samples from patients and controls, the results of those tests are shown in table (1) and figure (1).

**Table (1):** The mean ± SD and P-value of Insulin and glucose in sera of Mets patients and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group IMets</th>
<th>Group IIControls</th>
<th>*p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl) mean±SD</td>
<td>463.97±15.72</td>
<td>85.10±14.01</td>
<td>0.0001</td>
</tr>
<tr>
<td>Insulin μU/ml mean±SD</td>
<td>47.15±41.18</td>
<td>29.46±15.43</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*significant at p≤0.05.

**Figure (1):** The mean ± SD value of glucose levels in sera of Mets patients and controls.

The pathophysiology of metabolic syndrome is not completely understood and whether elevated FBS and insulin resistance are its causes or consequences is still a field of ongoing scientific research; however, some studies have stated that insulin resistance in metabolic tissues is mainly initiated by obesity [14]. High fasting blood glucose level has long been considered as one of the major signs to diagnose people with metabolic syndrome along with a large waistline, high blood pressure and impaired lipid profile [15]. The obtained results revealed a highly significant elevation (p <0.001) in FBS in group I as compared to controls which can be greatly attributed to decreased glucose uptake by adipocytes, hepatocytes, and myocytes as a result of insulin resistance condition in those individuals who become unable to utilize glucose in their bodies leading to its accumulation in blood.

On the other hand, insulin concentrations also showed a significant increase in group I in comparison with controls as shown in table (1)and figure (2), this result could be regarded as a consequence for the condition of insulin resistance where the beta cells of pancreas overproduce insulin to make up that defect of responding to the hormone in a condition called compensatory hyperinsulinemia.

Monoamine oxidase activity was determined by using the method described by McEwen and Cohen. The results of MAO activity indicate a significant increase (p <0.001) of its level in sera of metabolic syndrome patient in comparison to its level in the control group as shown in table (2) and figure (3).

Table (2): The mean±SD and P-value of MAO and IR in sera of Mets patients and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group IMets</th>
<th>Group IIControls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAO (µmol/L) mean±SD</td>
<td>44.75±7.6</td>
<td>40.14±5.24</td>
<td>0.003</td>
</tr>
<tr>
<td>IR</td>
<td>57.09±61.8</td>
<td>6.15±3.2</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

To a certain extent, glucose metabolic pathways have been shown to be affected by the autonomic nervous system via a not fully understood connection to insulin-producing beta cells of the pancreas [16]. The occurrence of monoamine neurotransmitters such as dopamine, serotonin, and norepinephrine in the pancreatic islets of various mammalian species has earlier been reported [17]. The neural control on glucose metabolism is notably mediated by such monoamine neurotransmitters which act as potent inhibitors for insulin secretion. In view of the role played by MAO in degrading various biogenic monoamines [18], it can be suggested that the high activity observed in this work...
reflects the overexpression of MAO as a response to increasing demand for insulin, hence, the much the needs to insulin the more the activity exhibited by MAO.

On the other hand, MAO is unequivocally known as a prominent producer of one of the most prevalent reactive oxygen species, namely H2O2, as this enzyme is responsible for electron transport process at the outer mitochondrial membrane by which electrons are transported from various monoamines to oxygen resulting in the production of H2O2 [19, 20], which in turn, largely contributes to the development of mitochondria-related oxidative stress in metabolic syndrome and/or diabetes mellitus.

It could, therefore, be said that MAO overactivity is obviously associated with mitochondrial abnormalities as a major factor in promoting metabolic disorders. However, the current data remain inconclusive about the involvement of MAO in the pathophysiology of metabolic syndrome (and then diabetes) as further evidence is still required to ascertain whether MAO overactivity is a cause or a result of the disease.

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References