A comparative Study of Adiponectin and Oxidative Stress (malondialdehyde and peroxynitrite) levels in Iraqi Patients with Acromegaly

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ABSTRACT
The aim of this study is to find a relationship between oxidative stress and adiponectin in Iraqi patients with acromegaly. The present study included 30 patients with acromegaly disease attending at Al-Yarmuk teaching hospital, and 30 healthy individuals as a control group. The two groups with ages ranging (30-55) years. The results revealed a highly significant elevation in all parameters (GH, IGF-1, adiponectin, malondialdehyde, and peroxynitrite) levels in sera of patients when compared with healthy control. It can be concluded that oxidative stress (malondialdehyde and peroxynitrite) may be valuable in detecting of endocrine diseases like acromegaly.

INTRODUCTION
Acromegaly is due to excessive production of growth hormone (GH), generally by a pituitary GH-secreting adenoma. Its prevalence is estimated at 40-130 cases per million inhabitants [1]. It is characterized by slowly progressive acquired somatic disfigurement (mainly involving the face and extremities) and systemic manifestations. The diagnosis is confirmed by elevated serum GH concentrations that cannot be suppressed by an oral glucose load, and by increased levels of insulin-like growth factor 1 (IGF-1) [2].

Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) most definitely play essential roles in growth in childhood, and continue to have important metabolic actions in [3].

It, as its name suggests, is implicated in postnatal growth. It is also used in replacement therapy for GH deficient children to induce linear growth. Indeed, it is well proven that pituitary GH deficiency or a defect in tissue GH receptor (GHR), result in dwarfism, whereas an excess of pituitary GH secretion results in gigantism in juveniles, or acromegaly in adults. The GH and insulin-like growth factor-I (IGF-I) axis is not only involved in the regulation of somatic growth, but also in glucose metabolism [4].

Adiponectin is exclusively secreted adipose tissues, and it plays a role in the suppression of the metabolic that may result in type 2 diabetes, obesity, atherosclerosis and an independent risk factor for metabolic syndrome [5]. Adiponectin, an adipocyte-derived hormone, possesses insulin-sensitizing [6].

Oxidative stress can be identified as an imbalance between the oxidant materials (free radical and their metabolism outputs) and antioxidants. The cells contain oxidant materials more than antioxidants, which is lead to destroy the big vital molecules of the body. Oxidative stress happens when the level of oxidant compounds exceed the ability of antioxidants on removing it [7]. The formation of peroxynitrite is very toxic harmful for biomolecules and cells as it is interact with thiol leading
to lipid peroxidation [8], and attach cells membranes such as fat, lipids, proteins, and nuclear acids causing many damages to different cells tissue and increases the oxidative stress [9].

Malondialdehyde (MDA) is reactive species which occurs naturally and it is used as a biomarker to measure the level of oxidative stress in an organism. [10]. Malondialdehyde (MDA) is an end product of lipid peroxidation. Reactive oxygen species degrade polyunsaturated fatty acid, forming Malondialdehyde (MDA). This compound is a reactive aldehydes and is one of the many reactive electrophilic species that causes toxic stress in cells and form covalent protein addicts which are referred to as advanced lipoxidation end products (ALE).[11].

Aim of study
This study aimed to find a relationship between oxidative stress and adiponectin in Iraqi patients with acromegaly.

Materials & Methods:
Subjects
Serum samples were obtained from 30 patients (18 women and 12 men) with non diabetic acromegaly disease and 30 healthy individuals as a control group(16 women and 14 men) with ages ranging from (30-55) years. The patients were diagnosed by GH,IGF, and abnormal growth of the hands and feet. This study was conducted in AL- Yarmuk teaching hospital, Baghdad, Iraq between January and June, 2014. Serum samples were frozen at -20°C for subsequent analysis.

Determination of Serum GH, and IGF-1 (ng/ml)
Serum growth hormone and insulin-like growth factor-I levels were measured using immunoradiometric assay for the in vitro determination in human serum and plasma (GH IRMA kit, a Beckman Coulter Company, English).

Estimation of Serum Adiponectin Level (ng/ml)
Human adiponectin ELISA kit supplied by Human company is a solid-phase ELISA assay designed to measure the amount of total human adiponectin in cell culture separates, serum and plasma.

Estimations of Serum Peroxynitrite Level (μmol/L)
Serum peroxynitrite level was measured using the modified method of (vanuuffelen.,1998) [12]. The principle of this determination is the radical peroxynitrite (ONOO−) mediate nitration of phenol resulting in formation of nitrophenol which is detected spectrophotometrically at (412 nm). Concentration of nitrophenol refers to serum peroxynitrite level.

Determination of Serum Malondialdehyde (MDA) (μmol/L)
Serum level of malondialdehyde (MDA) was determined by the reaction of MDA with thiobarbituric acid (TBA) to form a color product of MDA-TBA, which is determined at 532 nm according to the modified method described by( Schmedes and Holmer.,1989) [13].

Statistical Analysis
Data were expressed as mean ± SD. The comparison between patients and control groups were analyzed using student t-test. Pearson’s correlation coefficient. P-value of < 0.001 and < 0.05 were considered highly significant and significant respectively.

Results & Discussion:
The levels of diagnostic parameters in patients and control groups are summarized in table (1). The results which expressed as (mean ± SD), showed a highly significant elevation (p<0.001) in serum levels of GH and IGF of acromegaly patients when compared with control group.

Acromegaly is an endocrine diseases characterized by increased circulating growth hormone (GH) and insulin – like growth factor (IGF-1) levels, usually resulting from pituitary adenoma [14]. Growth hormone causes the production of IGF-1. Together, excessive GH and IGF-1 can cause metabolic changes and soft tissue, bone, and organ enlargement. GH, or somatotropin, is responsible for the growth of almost all cells and tissues. [15].

The somatic growth and metabolic dysfunction associated with acromegaly result from excess secretion of GH and subsequent elevation of circulating and locally produced insulin-like growth factor-1 (IGF-1). In healthy individuals, GH secretion is under the dual regulation of growth hormone-releasing hormone (GHRH) and somatostatin, with variations in the secretion of somatostatin being the primary mode of regulation [16].

The collective results of the measured biochemical parameters are summarized in table (2). The result showed a highly significant increase (p<0.001) in serum level of adiponectin, peroxynitrite and malondialdehyde of acromegaly patients compared to healthy subjects. These results are agree with the finding of previous study [17-18]. But they disagree with the results obtained by [19], who found that the serum levels of adiponectin was lower in acromegalic patients when compared to the control group. The difference in adiponectin levels in acromegalic patients depend on degree of insulin resistance in those subjects [20].

Patients with active acromegaly have hypoadiponectinemia, which is reversible with GH-lowering therapies. Because adiponectin is known to have beneficial effects on insulin sensitivity, atherogenesis, and inflammation of the arterial wall, this reduction in adiponectin expression may contribute to the increased cardiovascular risk in patients with acromegaly. [21]. Acromegalic patients present hypoadiponectinemia and a favorable bone marker profile. It has been reported that adiponectin and visfatin
could be a link between fat mass and bone in acromegaly. [22].

It has been found that the increased levels of IGF-I are associated with enhanced oxidative stress in rats and humans. In addition, increased ROS may play an important role in the complications and premature death in acromegaly. Some studies have shown increased oxidative stress and reduced antioxidant status in acromegaly [23].

Acromegaly is associated with increased levels of oxidative stress coupled by diminished antioxidant capacity and endothelial dysfunction indicated by the presence of decreased NO levels [24].

In fact, this is the first study which found the elevation of oxidative stress (peroxynitrite and malondialdehyde levels) in patients with acromegaly disease, which is a hormonal disorder that results from producing excessive growth hormone. [23].

Oxidative stress and reduced antioxidant status in acromegaly. [22].

Finally, we can conclude that oxidative stress (malondialdehyde and peroxynitrite) as toxic molecule and biological marker of oxidative stress. Physiol.Rev.,87(1):315-342,2007.


Meenaaksi, T; and Dinesh, J; Adenosine Deaminase and Malondialdehyde Levels in Type-2 Diabetes Mellitus – a Short Study, Global Journal of Medical research, 14(4):758-787, 2014.


Lam,K.S., Xu A.,Tan K.C., Wong LC, Tiu SC, Tam S.,Serum adiponectin is reduced in...


Table (1): levels of diagnostic parameters in acromegaly patients and control groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>AC Patients</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH (ng/ml)</td>
<td>2.77±0.67</td>
<td>25.70±1.22</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>IGF (ng/ml)</td>
<td>319.60±71.31</td>
<td>817.00±153.90</td>
<td>p&lt;0.001</td>
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</tbody>
</table>

Table (2): Levels of adiponectin, peroxynitrite, and malondialdehyde in acromegaly patients and control groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>AC Patients</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD (ng/ml)</td>
<td>9.66±0.65</td>
<td>38.10±0.94</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Peroxynitrite (mol/L)</td>
<td>42.74±17.77</td>
<td>109.50±5.52</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>MDA (mol/L)</td>
<td>5.13±0.70</td>
<td>12.00±0.44</td>
<td>p&lt;0.001</td>
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