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Determination of Some Biochemical Parameters of Acromegalic Patients with Type 2 Diabetes Mellitus.

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Abstract

Background: Because of the disturbance in the pituitary gland, growth hormone (GH) secretion will be increased and, as a result, insulin-like growth factor 1 (IGF-1) secretion will be increase as well, leading to a chronic and rare disease called acromegaly disease. One of the most serious complications of acromycaly is diabetes. Insulin resistance, which causes diabetes, occurs in the body because of increased growth hormone secretion

Objective: The aim of this work is to estimate some biochemical parameters. These parameters were not studied extensively in the literature such as BALP and LOX and the possibility of using LOX as a new biomarker for acromyalgic patients with diabetic.

Patients and Methods: The study was performed on (25) male as patients with active acromegaly and those with type 2 diabetes mellitus, aged between (40–60) years, and (25) male aged between (40–60) years as control group. Blood was collected and serum was separated. Enzyme-linked immune sorbent assay (ELISA) technique was used to determine the GH, IGF-1, BLAP, and LOX. By using enzymatic colorimetric method (Glucose oxidase-peroxidase), fasting serum glucose (FSG) was estimated. MDA and TAC were estimated by colorimetric methods as well.

Results: The results showed that there were significant differences among GH, IGF-1, FSG, BLAP, LOX, and MDA when compared between patients and control group, while TAC showed a significant decrease between patients and healthy group ($p < 0.05$).

Conclusion: A conclusion could be obtained from the above data that the increase in GH, IGF-1, BLAP, LOX, and LPO can be associated with active acromegaly.

Key words: Acromegaly**,** GH**,** Lysyl Oxidase, Lipid Peroxidation, IGF-1.

INTRODUCTION

Acromegaly is a chronic disease caused by pituitary adenoma; lead to increase secretion of the growth hormone . The high concentration of growth hormone stimulates the liver to secrete of insulin-like growth factor-1 IGF-1, which in turn unacceptable changes in the shape of the patient and changes in the body as well as abnormalities in the skeleton [1].

Growth hormone plays an important role in inhibiting the work of insulin, such as inhibiting the phosphorylation of insulin receptors, which is one of the most important signs of the function of insulin. As a result, insulin sensitivity of the cells will decrease, in the periphery in stimulating peripheral glucose uptake and to increased resistance to insulin's ability to suppress gluconeogenesis. Therefore, the increase in the secretion of growth hormone leads to the mobilization of free fatty acids and inhibits insulin stimulated glucose oxidation leading to further deterioration of insulin resistance leading to diabetes [2].

Alkaline phosphatase (ALP) is an enzyme from the zinc-based group of proteins that cleave the phosphate end of the organic phosphate ester. Many of causes lead to ALP activity, including liver obstruction and metabolic bone disease. Elevation serum BALP concentration may provide good diagnostic information on the symptoms of acromegaly [3].

Lysyl oxidase is an enzyme that does not work without copper and works through the association of collagen and elastin by stimulating the deletion of the oxidation group of alpha- amino groups of lecine and hydroxyline residues .The mechanism of lysyl oxidase occurs via modification of the ε-amino group of a lysine side chain[4]. The lox can be divided into two parts depending on the structure. The first part includes lox and lox1 and the other part lox2 and lox4 respectively. Lox and lox1 are more compatible in terms of composition than lox2 and lox4[5].

Reactive oxygen species (ROS) plays a major role in the pathogenic of many disorders including cancer, diabetes, brain edema and acromegaly [6].

The blood antioxidant system is impaired in patients with active acromegaly, which indicates the development of oxidative stress. When extracellular fluid is attacked by free radicals, the TAC acts as the first line of defense because it has a number of anti-oxidants with low molecular weight [7].

MATERIAL AND METHODS

25 male patients with diabetic acromegaly were selected from Baghdad Teaching Hospital during 2017. All patients were diagnosed by physicians and administrated octreotide treatment which is use to lowering GH as well as IGF-1 concentrations in acromegalic patients[8]. As control, 25 men were also used in this study. Patients and control were aged 40 – 60 years.

5ml of blood was collected from each individual subjected to this study. Blood samples were centrifuged at 3000 rpm. The separated sera were kept into plain tubes and froze until the required tests were accomplished.

Enzyme-linked immune sorbent assay ELISA kit which use to determined many parameters used to estimate G H , IGF-1, BLAP, and LOX [9]. It is possible to use immune radiometric assay (IRMA) technique to determined BALP [10].

We used the enzymatic reaction to estimate blood glucose levels in blood. After enzymatic oxidation of glucose oxidase [11] .To estimate the serum level (MDA), we used the Buege & Aust method; one of the methods that relies on enzymatic reactions[12].

On the other side, TAC serum was measured with hydrogen peroxide. The serum antioxidant eliminated a certain amount of hydrogen peroxide. By an enzymatic reaction, the remaining amount of hydrogen peroxide was measured using the chromatic method [13].

Statistical Analysis

Statistical analysis program (SPSS) version 21 was utilized in this study. To compare the results of the studied groups. As we mentioned in the tables, we applied mean and standard deviation (Mean±SD) to express the results. Significant level was considered at $P < 0.05$.

RESULTS AND DISCUSSION

Data in table (1) and Fig (1) summarize diagnostic parameters in patients and healthy subjects. GH level increases significantly compared to control group $p < 0.05$. One of studies found that GH level in acromegaly patients was higher than the normal value. On the other hand, study found a significant increase in GH concentration in the acromegalic patients groups compared to the control group, that agreement with present study[14].

Table (1) also shows that IGF-1 levels among acromegalic patients group significantly than those in control group $p < 0.05$.

GH increases in parallel with IGF-1, since IGF-1 production is released under GH stimulation effect. Therefore, GH levels in present study are associated with high IGF-1 levels. Another study has measured GH and IGF-1 levels in acromegalic patients and the result showed an increase in GH levels associated with an increase in IGF-1 levels. Many studies have showed elevated IGF-1 levels, which reflect that the GH elevation can be associated with several biochemical changes[15].

The present study shows a significant increase in FSG level compared to control group $P < 0.05$. Insulin resistance plays an important role in the increase in blood glucose levels in acromegalic patients. The increase in insulin resistance in diabetes mellitus type 2 is associated with elevated body fat, which induces hypothalamic somatostatin harmony with disorder growth hormone secretion[16].

Our results are in agreement with results that found by Piniewska-Hulas *et.al*. This group showed that from 22 acromegalic patients of unknown blood glucose levels 40.90% of them when measured glucose levels later showed impaired glucose tolerance [17].

Table (2) and Fig (2) shows noticeable differences $P<0.05$ in BALP level between control and patients groups.

The level of bone isoenzyme of ALP can be an indication of bone disease. However, the loss minerals in bone is not always considered as a complication of diabetes. The results in the present study are similar to that concluded by Gul OZ. *et.al*., who showed that bone formation markers were decreased in diabetic patients who are not susceptible to the reabsorption of bone. This low bone resorption can result in a slow rate of bone loss and elevate the bone density. The endocrine and metabolic alterations in diabetes mellitus can cause a disorder in calcium homeostasis, skeletal metabolism and bone mass [18].

Table -1: Serum Levels of GH, IGF-1and FSG in Patients and Healthy Individuals.

Parameters	Groups Studied		*P*-Value
	Control	Patients	
GH (ng/ml)	2.53 ±0.109	12.3±2.18	< 0.05
IGF-1 (ng/ml)	260.5±11.22	654.9±48.15	< 0.05
FSG(mg/dl)	85.25±6.5	188.54±17.80	< 0.05

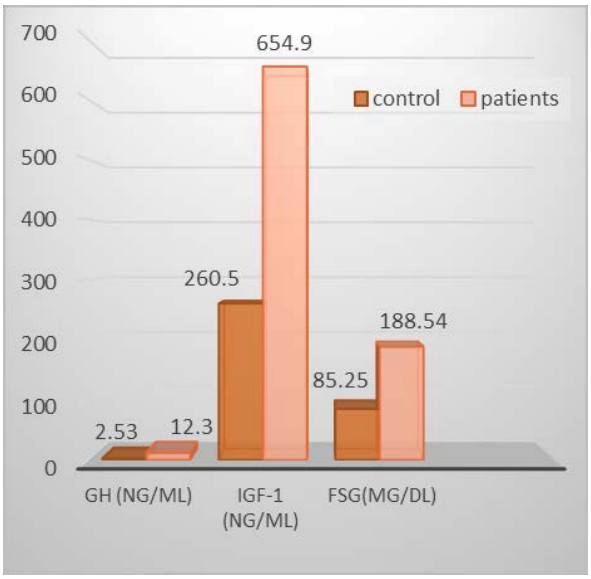

Figure-1: Levels of GH, IGF-1and FSG in Control and Patients Groups.

The effect of growth hormone on bone in patients with acromegaly is demonstrated by elevating of ALP concertation. We found that effect in 27% of patients under study, while bone isoenzyme action is increased in 84% of patients [19].

There was a significant increase in lysyl oxidase levels in acromegalic patients when compared with control group $p<0.05$ as showed in table (2) and Fig (2).

Many studies have shown that diabetic patients exhibit an increase in collagen fibres due to the big changes in the collagen structure. This is demonstrated by non-enzymatic contact of residues of lecithin and hydroxylycin with glycosyl. There are many types of collagen cross-bonds mild lysyl oxidase cross-bonds and developed glycation end-products . Lysyl oxidase catalyzes the end known enzymatic step required for collagen and elastin cross-bonding. A cross-bonded collagenous extracellular matrix is required for bone formation [20,21].

Table -2: Serum Levels of BALP, LOX, MDA and TAC in Patients and Healthy Individuals.

Parameters	Groups Studied		*P*-Value
	Control	Patients	
BALP (ng/ml)	8.4±0.46	24.34±1.88	< 0.05
LOX (ng/ml)	3.5±0.12	6.875±0.87	< 0. 05
MDA(µmol/L)	2.88±0.11	6.14±0.85	< 0. 05
TAC(mmol/L)	0.77±0.32	0.26±0.45	< 0. 05

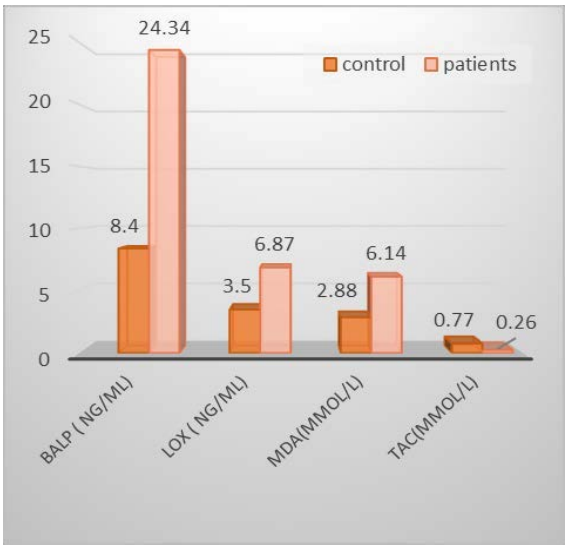

Figure -2: Levels of BALP, LOX, MDA and TAC in Control and Patients Groups.

Table (2) and fig (2) also show that MDA level showed significant increase in patients group when compared to control group P<0.05.

We suggest that the elevated levels of MDA in acromegalic patients is a marker of increased oxidative stress or LPO due to the excessive production of GH, which inhibits glucose uptake and oxidation of free fatty acids (FFA) initiate an up-stream and then increase level of free radical. Malondialdehyde MDA, one of the most popular markers, consider a biomarker for oxidative stress and was designed to indicate lipid peroxidation.

We observed a significant decrease in levels of malondialdehyde and growth hormone after taking octreotide treatment[22].

Table (2) and Fig (2) show that TAC level showed significant decrease in patients group when compared to control group P<0.05.

The plasma TAC in patients was on the average 20% lower than in the control subjects. These results confirm the imbalance in the antioxidant system of blood at acromegaly patients, which leads to the development of oxidative stress in these patients, these result are agreement with our present study. The sharp drop in TAC serum level and the high level of ROS production lead to an imbalanced and reduced TAC ability to attack free radicals and as a result, the TAC is ineffective. This imbalance can lead to deterioration of the functional system cells. We suggest that impair antioxidant system in acromegalyic patients so leading to reduce MDA comparing to control group [23].

CONCLUSION

In the current study, we found that elevated levels of GH, IGF-1, FSG, BALP, LOX, and MDA sera, whereas TAC was low in patients compared to healthy individuals. Serum LOX level was significantly increased in acromegalic patients when compared with control. Therefore, LOX may be used as a new biomarker in the diagnostic of acromegalic patients.

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