



## **Determination of Ibuprofen in Pharmaceutical Formulations Using Differential Pulse Polarography**

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### **Abstract**

Study aimed to determination of chitotriosidase-1 levels in Iraqi diabetic and diabetic patients with thyroid disorder. Also, study aimed to found relation correlation for chitotriosidase-1 with FSG, T3, T4 and TSH. Ninety subjects were including in this study, first group consisted of (30) healthy individuals who have no history of any thyroid disorders or diabetes mellitus as control group. Second group (G2) (n=30) patients with diabetic and hyperthyroidism as association disease, and third group (G3) (n=30) include patients with diabetic and hypothyroidism as association disease. Serum used in (FSG, T3, T4, TSH, and Chitotriosidase-1) determination. Results showed a significant elevation in patients' groups (G2, G3) comparing to control group in FSG. In addition to a significant elevation in G3 compared to G2. Results, also, revealed a significant elevation in T3 and T4 levels in G2 when comparing with G1 and G3. While there is significant decrease in these parameters in G3 compared to G1 and G2. Results revealed a significant decrease in G2 in TSH levels comparing to G1 and G3. While there is significant increase in TSH level in G3 compared to G1 and G2. Results revealed a significant increase in Chitotriosidase-1 levels in G2 comparing to G1 and G3. Results, also, showed a significant decrease in G3 comparing to G2 and a significant increase was found in G3 comparing to G1. Conclusion could be drowning from this study that chitotriosidase-1 may be helpful in monitoring and early diagnosis of thyroid disorder in these patients.

**Keywords:** Chitotriosidase-1, Iraqi Diabetic mellitus with thyroid disorder.

### **1. Introduction**

Diabetes mellitus (DM) and thyroid dysfunction are two endocrine disorders affect each other in a variety of ways. Thyroid hormones contribute to the regulation of carbohydrate metabolism and pancreatic function [1, 2]. Reasonable mechanism for advancement of T2DM in thyroid disorder patients may be related to disturbed genetic expression of genes in conjunction with physiological aberrations leading to impaired glucose consumption by the

augmented hepatic glucose output, muscles, and glucose absorption elevation from intestine [3]. Chitotriosidase-1 is known as an enzyme involved with N-terminal triose phosphate isomerase catalytic groove. The C-terminal chitin-binding domain linked by a short hinge region [4,5]. Chitotriosidase-1 are hydrolytic enzymes that break down glycosidic bonds in chitin that found in two forms, 50 KD the dominant form in blood and a 39 KD the dominant form in tissues [4]. Chitotriosidase-1 is necessary in chitin digestion by hydrolyzing its  $\beta$ -1, 4 glycoside linkages like a defensive action and/or utilization of chitin as a source of carbon and energy [6]. Enzymatically active mammalian chitinases cleave chitin polymers into oligosaccharides of varying sizes (endochitinase activity) and release glucosamine monosaccharides from the end of a chitin polymer (exochitinase activity) [7]. Chitotriosidase-1 has highly affinity binding to substrate in addition to its responsible for the transglycosylation activity of the enzyme even in the absence of highly substrate concentrations, causing chitotriosidase-1 complete independent chitinolytic machinery [8-10]. Study are focused on chitotriosidase-1 effects through the processes of chitin recognition, antigen presentation, stimulation of cell mediated immunity and synergistic effects with proteases to kill various kinds of cancer cells [11]. Chitotriosidase-1 has been implicated in the pathogenesis of many human diseases by improper stimulation of faulty tissue remodeling and inflammation like nonalcoholic fatty liver disease, chronic obstructive pulmonary disease and neurodegenerative disorders like Alzheimer's disease and amyotrophic lateral sclerosis [12-14]. The aim of the present study was to determine the chitotriosidase-1 levels in Iraqi diabetic patients with thyroid disorders, and the study aimed to found relation correlation for chitotriosidase-1 with T3, T4 and TSH.

## **2. Materials and Methods**

A prospective study was conducted on three groups of subjects during the period from June (2018) to August (2018) at the Specialized Center for Endocrinology and Diabetes / Baghdad. The age range of all subjects was (40-65) years. Ninety subjects were included 3 groups in this study that divided into control group G1) that consisted of (30) healthy individuals who have no history of any thyroid disorders or DM. Group (G2) (n=30) that consisted of diabetic patients and hyperthyroidism as associated disease, and group (G3) (n=30) include diabetic patients and hypothyroidism as associated disease.

### **2.1. Blood Sample Collection**

Five milliliters of peripheral veins blood were taken from all subjects in plain tubes. Serum obtained stored at (-20°C) until assay time for analysis of FSG, T3, T4, TSH and chitotriosidase-1.

### **2.2. Determination of Fasting Serum Glucose**

An enzymatic colorimetric method was used for determination of fasting serum glucose (FSG) based on Trinder hydrogen peroxide and the phenol and 4-aminoantipyrine. The quinine (complex) red-violet in colour, measured at 505 nm, 510nm with the intensity of the colour being in proportion to the glucose concentration [15].

### **2.3. Determination of Triiodothyronine (T3), Thyroxine (T4), and Thyroid Stimulating Hormone (TSH)**

The T3, T4 and TSH were determined by Enzyme linked Fluorescent Immunoassay (ELFA) competition method with a final detection [16].

## 2.4. Determination of Chitotriosidase-1

Sandwich enzyme linked immune sorbent assay (ELISA) technique was used for determination of chitotriosidase-1 by ready kit from my bio source, Cat.No.: MBS765849.

## 3. Statistical Analyses

The results were expressed as mean  $\pm$ SD. Students t-test was applied to compare the significant of the difference among the groups. P-value ( $P \geq 0.05$ ), ( $P \leq 0.05$ ), ( $P \leq 0.01$ ) were considered statically non-significant, significant, and highly significant respectively. The correlation coefficient test used for illustration the association between the various parameters that studied.

## 3. Results & Discussion

Descriptive parameters were presented in **Table 1**. Which display the levels of FSG, T3, T4 and TSH for all studied groups. **Table 1**. Showed a highly significant elevation in patients' groups (G2, G3) comparing to control group in FSG levels. In addition, a significant elevation in G3 compared to G2 was found.

**Table 1.** Levels of FSG, T3, T4 and TSH and chitotriosidase-1 for G1, G2, G3.

Parameters	Mean $\pm$ SD (G1)	Mean $\pm$ SD (G2)	Mean $\pm$ SD (G3)	T-Test G1 vs G2	T-Test G2 vs G3	T-Test G1 vs G3
FSG (mmol/L)	4.356 $\pm$ 0.76	10.607 $\pm$ 2.533	11.091 $\pm$ 2.935	$P \leq 0.01$	$P \leq 0.05$	$P \leq 0.01$
T3(nmol/L)	1.66 $\pm$ 0.384	2.78 $\pm$ 0.170	1.09 $\pm$ 0.068	$P \leq 0.05$	$P \leq 0.05$	$P \leq 0.05$
T4(nmol/L)	82.3 $\pm$ 9.450	145.21 $\pm$ 27.90	48.71 $\pm$ 15.507	$P \leq 0.05$	$P \leq 0.05$	$P \leq 0.05$
TSH(nmol/L)	2.15 $\pm$ 0.411	0.154 $\pm$ 0.06	21.43 $\pm$ 4.827	$P \leq 0.01$	$P \leq 0.01$	$P \leq 0.01$
Chitotriosidase-1 ( ng/mL )	0.045 $\pm$ 0.003	0.597 $\pm$ 0.072	0.09 $\pm$ 0.005	$P \leq 0.01$	$P \leq 0.01$	$P \leq 0.01$

\*G1: control group. G2: diabetic group. G3: diabetic neuropathy group.

Results, also, revealed a significant increase in levels of T3 and T4 in G2 when comparing with G1 and G3. While there is significant reduction in these parameters in G3 compared to G1 and G2. Results revealed a highly significant decrease in G2 in TSH levels comparing to G1 and G3. In addition, there are highly significant increase in TSH level in G3 compared to G1 and G2.

Diabetic patients seem to influence thyroid function in level of hypothalamic control of TSH release and at peripheral tissue by converting T4 to T3. High levels of glucose lead to decrease in deiodinase enzyme concentration in liver, decreased concentration of T3, elevation levels of reverse T3 and low, normal, or high level of T4 [17].

Results in **Table 1**. Revealed a highly significant increase in chitotriosidase-1 levels in G2 comparing to G1 and G3. Results, also, showed a highly significant decrease in G3 comparing to G2 and a significant increase was found in G3 comparing to G1.

Activity of chitotriosidase-1 elevated in patients with newly diagnosed, untreated, and uncomplicated type 2 DM which is positively linked to glucose levels, age, and asymmetric dimethylarginine (ADMA) levels of those patients. Increased ADMA levels inhibit nitric oxide production in addition to impair endothelial function [18,19].

Evidence from experimental studies illustrated increase in chitotriosidase-1 levels in pathological conditions, like atherosclerosis, coronary artery disease, cerebrovascular dementia and complications of DM [20].

It has been display that increased in chitotriosidase-1 levels may be associated with inflammatory status [21]. Study assumed that chitotriosidase-1 have role in the development of atherosclerosis, which forms association with type 2 diabetes patients [22].

Correlations of chitriosidase-1 were examined with the other parameters and r- coefficients demonstrate in **Table 2.** with p-value.

**Table 2.** R- coefficient and p-value of chitriosidase-1 with TSH, T3 and T4.

parameters	Chitotriosidase-1 (ng/mL) $r_1$	T-Test	Chitotriosidase-1 (ng/mL) $r_2$	T-Test	Chitotriosidase-1 (ng/mL) $r_3$	T-Test
<b>TSH</b> (nmol/L)	-0.265	$p \leq 0.05$	0.100	$p \leq 0.05$	-0.224	$p \leq 0.05$
<b>T3</b> (nmol/L)	0.033	$p \leq 0.05$	-0.260	$p \leq 0.05$	-0.012	$p \leq 0.05$
<b>T4</b> (nmol/L)	0.218	$p \leq 0.05$	-0.167	$p \leq 0.05$	- 0.159	$p \leq 0.05$

A significant negative correlation was observed between chitotriosidase-1 and TSH in G1 and G3 ( $p \leq 0.05$ ,  $r_1 = -0.265$ ,  $r_3 = -0.224$ ), while a significant positive correlation was found in G2 ( $p \leq 0.05$ ,  $r_2 = 0.100$ ) as shown in **Table 2.**

**Table 2.** revealed a significant positive correlation was found between chitotriosidase-1 and T3 in G1, while a significant negative correlation in G2 and G3 ( $p \leq 0.05$ ,  $r_1 = +0.033$ ,  $r_2 = -0.260$ ,  $r_3 = -0.012$ ). A significant positive correlation was found between chitotriosidase -1 and T4 in G1 ( $p \leq 0.05$ ,  $r_1 = 0.218$ ), but there was a significant negative correlation in G2 and G3 ( $p \leq 0.05$ ,  $r_2 = -0.167$ ,  $r_3 = -0.159$ ).

#### 4. Conclusion

Conclusion could be drowning from this study that chitotriosidase-1 levels were changed in patients' groups that may be used in monitoring and early diagnosis of thyroid disorder in these patients depending on the significant relation for chitotriosidase-1 with T3, T4 and TSH.

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