



A comparative study for GLP-1 levels in Iraqi diabetic patients with hyper & hypothyroidism

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Abstract:

The current study aimed to determine GLP-1 levels in hyper and hypothyroidism disease with diabetic and compared the results with a control group. The study also aimed to find the relationship for GLP-1 with (TSH, T3 and insulin) in patients groups. The study involved 30 subjects with hyperthyroidism and diabetic as group 1 (G1), and 30 subjects hypothyroidism patients with diabetes as group 2 (G2) to 30 healthy controls as group 3 (G3). The subjects were matched aged of (40-65 years). Serum used in determination T3, TSH, FBG and insulin in the control and patients groups, the BMI and IR were also calculated. Results showed highly significant increase in T3 levels in G1 contrast to G3 while there are no significant decreasing was found in G2 contrast to G3. Results in this study revealed highly significant decreasing in TSH levels in G1 contrast to G3 with highly significant increase in G2 comparing to G3. Results illustrate levels of FBG in all studied groups, which showed highly significant increase in FBG in G1 and G2 comparing to G3. Results showed highly significant increase in insulin levels in G1 contrast to G3 while there are no significant different observed in G1 contrast to G2. Results, also, showed highly significant increasing in GLP-1 in G1 and G2 when compared to G3. Correlation relation of GLP-1 with T3, TSH and insulin were studied. Result revealed significant positive correlation between GLP-1 and T3 in G3 ($P \leq 0.05$, $r = 0.350$) while a significant negative correlation was observed in G1 and G2 ($P \leq 0.05$, $r = -0.047$, $r = -0.55$). Results revealed significant positive correlation in G3 between TSH and T3 ($P \leq 0.05$, $r = -0.55$) while a significant negative correlation ($P \leq 0.05$, $r = -0.047$, $r = -0.386$) was observed in G1 and G2. Study also showed the correlation relation between GLP-1 and insulin there are no significant positive relation was seen in G3 ($P > 0.05$, $r = 0.083$), while showed highly significant positive correlation in G1 and G2 ($r = 0.55$, $r = 0.344$). It is Concluded from this study that GLP-1 can be used as a marker in diagnostic and monitoring the development in diabetes to its complication in these patients.

Keywords: GLP-1, hypo and hypothyroidism, diabetic patients.

INTRODUCTION

Diabetes and thyroid dysfunction illustrate effect on each other and linked between them (1) via hyperthyroidism (2, 3). Decreasing in rate of glucose synthesis in liver is seen in hypothyroidism lead to lower in insulin requirement in hypothyroid diabetic patients. Hypoglycemic events are the important signs for the progressive of hypothyroidism in patients with type 1 diabetes (4).

Glucagon like peptide-1 (GLP-1) is an insulinotropic hormone with 42 amino acids derived from the transcription product of the [proglucagon](#) gene in the [intestinal L cell](#) (5), and is secreted into the blood stream when food containing fat, protein (6). Recent report demonstrated that perfusion of a normal rodent or human pancreas would yield significant amounts of bioactive GLP-1 in the perfusate (7).



It is demonstrated that GLP-1 restores the glucose sensitivity of pancreatic β -cells, with the mechanism including the elevation in expression of glucose transporters 2 ([GLUT-2](#)) and [glucokinase](#) (8).

The present study aimed to estimate the GLP-1 levels in hyper and hypothyroidism with diabetic and contrast the results with control group. The study also aimed to found the relationship for GLP-1 with (TSH, T3 and insulin) in patients groups.

MATERIALS AND METHODS:

The current study involved 30 subjects with hyperthyroidism as group 1 (G1) and 30 subjects with hypothyroidism as group 2 (G2) and 30 healthy subjects as control group 3 (G3). Type of research is case control study that subjects were matched by age (40-65 years). Blood samples were collected from healthy controls and patients after 12-14 hours of fasting in February to October 2017 at Specialized Center for Endocrinology and Diabetes / Baghdad the T3, TSH, FBG, insulin and GLP-1 were determined in all subjects in serum. BMI was calculated using below formula (9).

$$\text{BMI} = \frac{\text{weight(kg)}}{\text{height}^2 \text{ (m)}}$$

Enzymatic colorimetric method was used in determination of glucose which bases (10).

The T3 and TSH were estimated by a one-step enzyme immunoassay sandwich kit with a final fluorescent detection (ELFA) (11).

The enzyme-linked immunosorbent assay (ELISA) kit was purchased from (Mybiosource) and used for determination of the levels GLP-1 levels Sandwich ELISA format was employed and performed as per the manufacture's instructions (12).

The insulin were determined by electrochemiluminescence immunoassay (ECLIA) in intended for use on Elecsys and cobas e immunoassay analyzers. (13)

Insulin resistance calculated by equation of homeostasis model assessment (HOMA):

$$\text{IR (HOMA)} = \text{F1} * \text{FG} / 405 \text{ (14)}.$$

Statistical Analysis:

The results are expressed as mean \pm SD. Student's t-test was used to compare the significance of the variation between thyroid dysfunction and control groups. The p -values ($p < 0.05$), were considered statistically significant, and respectively. The correlation coefficient (r) test was used for describing the association between the different studied parameters.

Result and Discussion:

The Table (1) display levels of BMI, T3, TSH and FBG in G1, G2, and G3 as descriptive parameters.



Table (1): Descriptive parameters of G1, G2 and G3

parameters	G1 hyperthyroidism	G2 hypothyroidism	G3 control	p.value G1and G2	p.value G1 and G3
	mean ±SD	mean ±SD	mean ±SD		
BMI kg/m ²	24.379 ± 4.854	27.098 ± 5.082	23.422 ± 4.981	S	HS
T3(nmol)	2.966 ± 0.477	1.471 ± 0.689	1.7 ± 0.217	HS	NS
TSH(mu/L)	0.068 ± 0.003	27.324 ± 8.312	2.606 ± 0.44	HS	HS
FBG	10.976 ± 3.812	9.980 ± 3.833	5.290 ± 0.851	HS	HS

As per our knowledge this is the first study to determine the levels of GLP-1 in hypo and hyperthyroidism patients with diabetes, as well as to find the relationship for GLP-1 with T3, TSH, and insulin.

Results showed a significant increase in T3 levels in G2 ($P < 0.01$) when contrast to G1 while there are no significant decreasing was observed in G3 ($P > 0.05$) when compared to G1.

Table (1) also showed a significant ($P < 0.01$) decreasing in TSH levels in G2 comparing to G1 ($P < 0.01$) and a significant ($P < 0.01$) elevation in G3 comparing to G1 was seen.

Results in table (1) display levels of FBG in all studied groups, which showed highly significant ($P < 0.01$) elevation in G2 and G3 (10.976, 9.980) comparing to G1 (5.290). These results revealed that G2 and G3 have diabetic mellitus as a complication with hyper and hypothyroidism respectively.

The absolute increases in the prevalence of hypothyroidism and positive TPO Ab status linked to autoimmune diabetes were identical in women and men. Hence, the impact of diabetes-associated autoimmunity on autoimmune hypothyroidism appears gender neutral, a notion that agrees with type 1 diabetes being similar in women and men (15). This suggests that the autoimmune mechanisms behind the added risk of hypothyroidism in autoimmune diabetes differ from those governing the female preponderance of hypothyroidism. It has been suggested that, elevated in transcription of enzyme involved in lipid production in spite of. Impedance via insulin inhibitory effect on gluconeogenesis (16, 17). study revealed that T3 elevated led to glucose production elevation through sympathetic projection to the liver (18).

Table (2) display levels of insulin, IR and GLP-1 in G1, G2 and G3. Results revealed highly significant elevation in insulin levels in G2 comparing to G1, while there are no significant elevation was found in G3 comparing to G1.



Table (2): Insulin and IR and GLP-1 for G1, G2 and G3.

parameters	G1	G2	G3	p.value G1and G2	p.value G1 and G3
	mean ±SD	mean ±SD	mean ±SD		
Insulin(mu/L)	14.446 ± 3.01	79.270 ± 14.243	80.134 ± 8.635	HS	HS
HOMA (IR)	35.964 ± 10.55	25.645 ± 19.465	3.396 ± 1.300	HS	HS
GLP-1	27.678 ± 3.321	23.492 ± 1.934	24.216 ± 2.315	HS	HS

Table (2) also display levels of GLP-1 in studied groups. Results showed a significant elevation in GLP-1 levels in G2 and G3 (23.492, 24.216) comparing to G1 (27.678).

Nutritional influences, like high-fat diets, were also important which alter the effects of thyroid hormones on insulin resistance. It is suggested that both clinical hypothyroidisms which lead to insulin resistant by impaired insulin induced glucose utility in peripheral tissues. *In vivo* and *In vitro* studies (19, 20). Studies revealed a lowering in glucose stimulation insulin secretion related to β -cells that response to glucose or catecholamine is elevated in hyperthyroidism (21, 22).

A study in healthy suggests euthyroid male noticed positive correlations in TSH, endothelial dysfunction and IR and improving relationship among thyroid status, insulin resistance and CVD risk. The close interactions for thyroid disorder and metabolic control favors close monitoring of thyroid function are patients T1DM patients (23).

It was reported that hyperthyroidism is link to insulin resistance, and lowered insulin sensitivity appear in different effects of thyroid hormones in hepatic and peripheral tissues (15, 24).

Studies in response of insulin in adipocytes and skeletal muscle of mature rats rendered hypothyroid noticed that glycogen which produce from glucose was inhibited partially as well as the glycolytic flux indication via insulin was frustrated totally. The reduced in insulin sensitivity happened without any defect in membrane insulin effector system (25). An authors illustrated decrease insulin-stimulated glucose transport and/or phosphorylation in addition these studies also revealed that the effects of hypothyroidism in muscle were not associated with an interference of insulin receptor (26, 27). Research showed that glucose in hypothyroid patients and control that uptake in muscle and tissue was explored after the consumption of a mixed meal in the anterior abdominal subcutaneous adipose tissue and the forearm muscles (28).

(GLP-1) receptor agonists activate the glucagon-like peptide-1 receptor, increasing insulin secretion dependent on blood glucose levels, suppressing glucagon secretion and slowing gastric emptying (29). They also prevent weight gain or promote weight loss. The use of GLP-1 agonists led increase in clinical practice inspite the availability of three oral sodium glucose co-transporter 2 inhibitors with the same useful weight may slow this progression (30).

Studies are agreement with research that noticed that GLP-1 receptor expression in thyroid carcinomas which using of GLP-1 receptor (31).



Studies showed that GLP-1 receptor activation in C cells (when present) does not causes C cell hyperplasia in the short term, that adjudged by calcitonin levels found in thyroid comparing between with humans and nonhuman main animals (4), that result agreement with data revealed that calcitonin have significant role in the control of calcium levels in rodents contrast to primates (32, 33).

Table (3) illustrated correlation coefficient of GLP-1 with T3, TSH and insulin. The correlation relation between GLP-1 and T3 showed a significant positive correlation in G1 ($r = -.055$) as show in table (3) and figures (1, 2, 3). While a significant negative correlation ($P \leq 0.05$, $r = -.047$, $r = .386$) was observed in G2 and G3 as display in table (3) and figures (1, 2, 3). Results revealed significant negative correlation in G1 between GLP-1 and TSH ($r = -.153$) while a significant positive correlation ($r = .034$, $r = .157$) was observed in G2 and G3 as display in table (3) and figures (4, 5, 6). Study also showed the correlation relation between GLP-1 and insulin there are non-significant positive relation was seen in G1 ($P > 0.05$, $r = 0.083$), while showed highly significant positive correlation in G2 and G3 ($r = 0.55$, $r = 0.344$) as display in table (3) and figures (7, 8, 9). It is concluded from this study that GLP-1 can be used as a marker diagnostic and monitoring the development in diabetes to its complication in these patients.

Table (3) Correlation relation of GLP-1 with T3, TSH and insulin:

parameters	G1 GLP-1		G2 GLP-1		G3 GLP-1	
	r	P-Value	r	P-Value	r	P-Value
T3 (nmol)	.350	$P > 0.05$	-.047	$P > 0.05$	-.055	$P > 0.05$
TSH (mu/L)	-.153	$P > 0.05$.034	$P > 0.05$.157	$P > 0.05$
Insulin	.083	$P > 0.05$.550**	$P < 0.01$.344*	$P < 0.01$

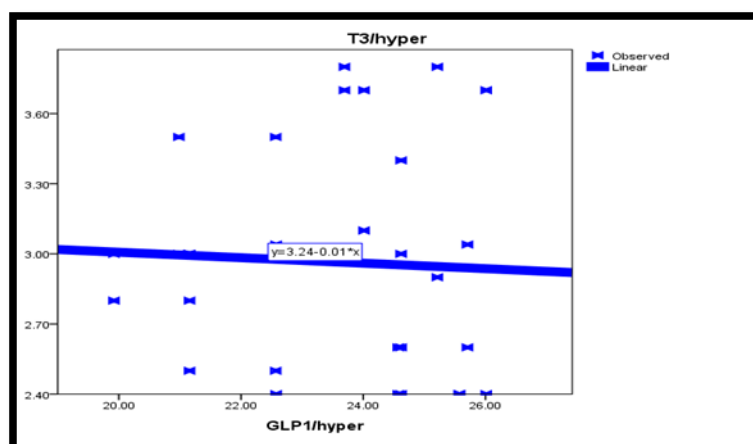


Figure (1) correlation between (GLP-1 and T3) in G1

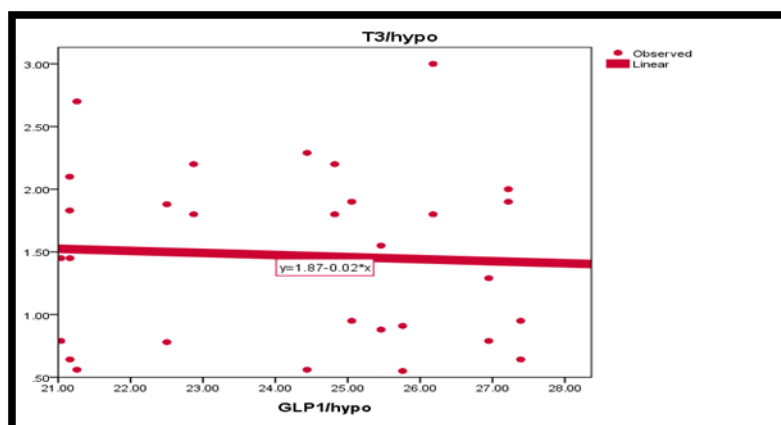


Figure (2) correlation between (GLP-1 and T3) in G2

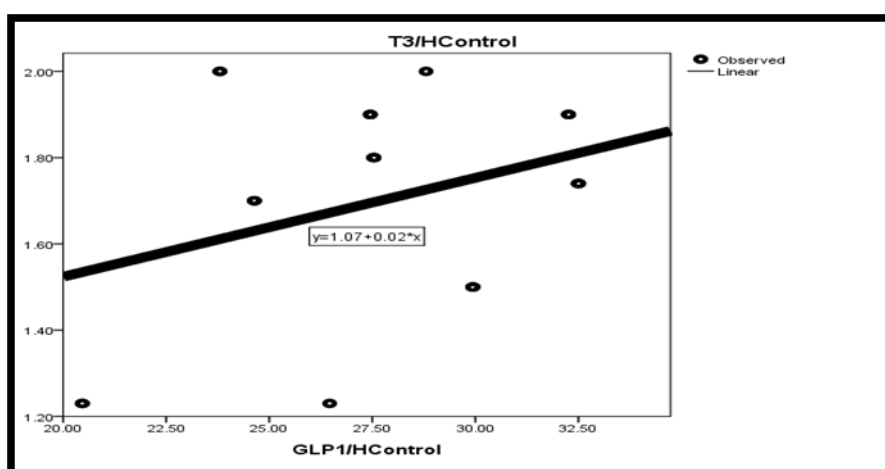


Figure (3) correlation between (GLP-1 and T3) in G3

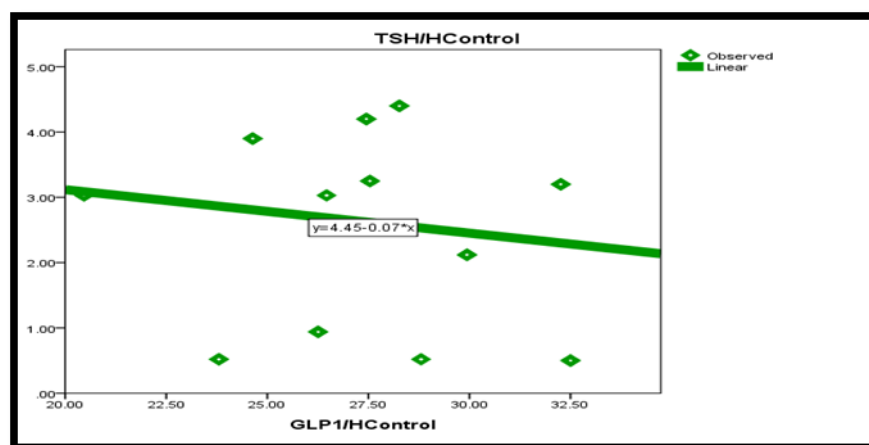


Figure (4) correlation between (GLP-1 and TSH) in G1

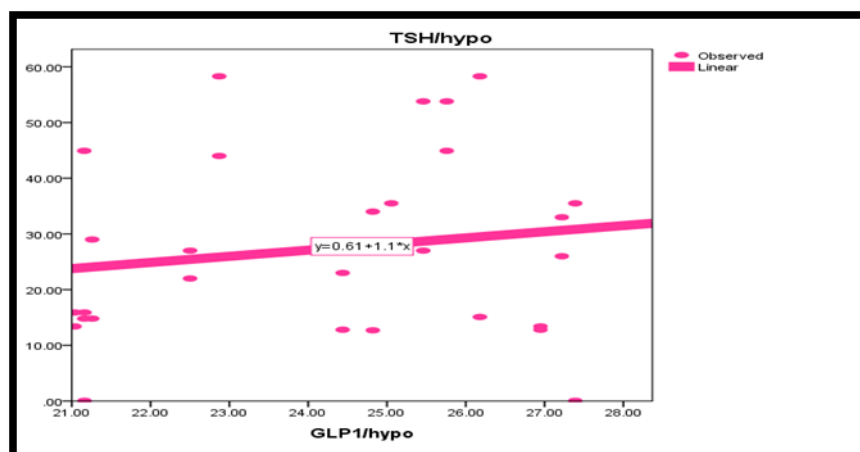


Figure (5) correlation between (GLP-1 and TSH) in G2

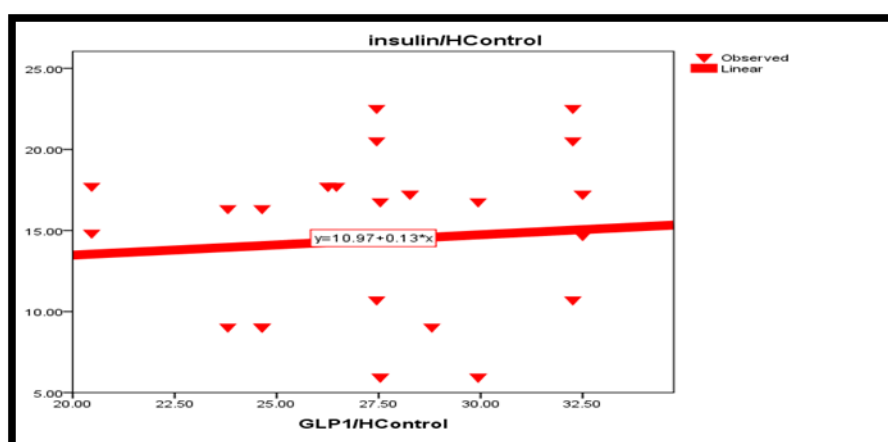


Figure (6) correlation between (GLP-1 and TSH) in G3

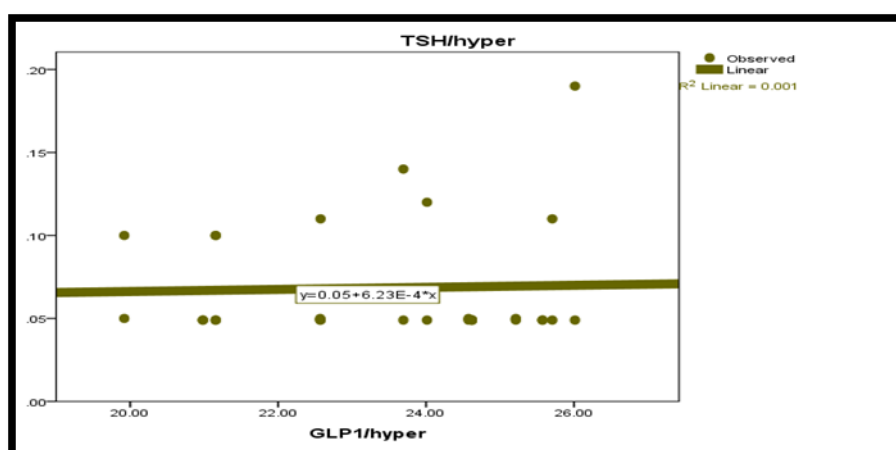


Figure (7) correlation between (GLP-1 and insulin) in G1

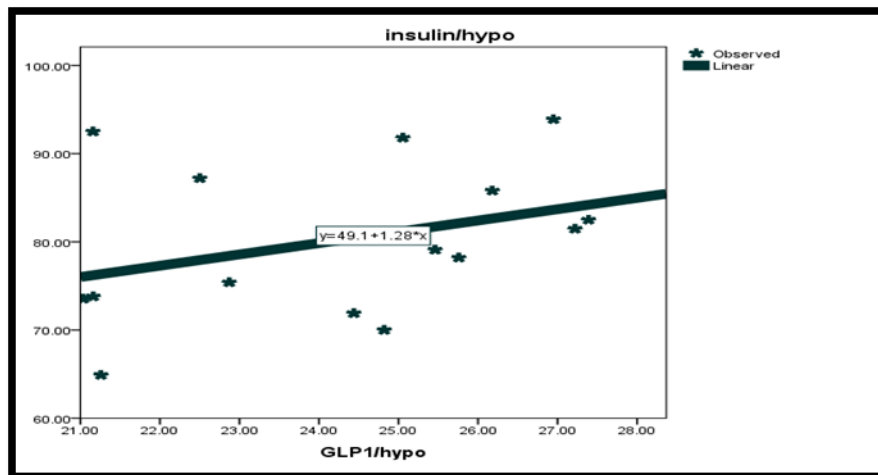


Figure (8) correlation between (GLP-1 and insulin) in G2

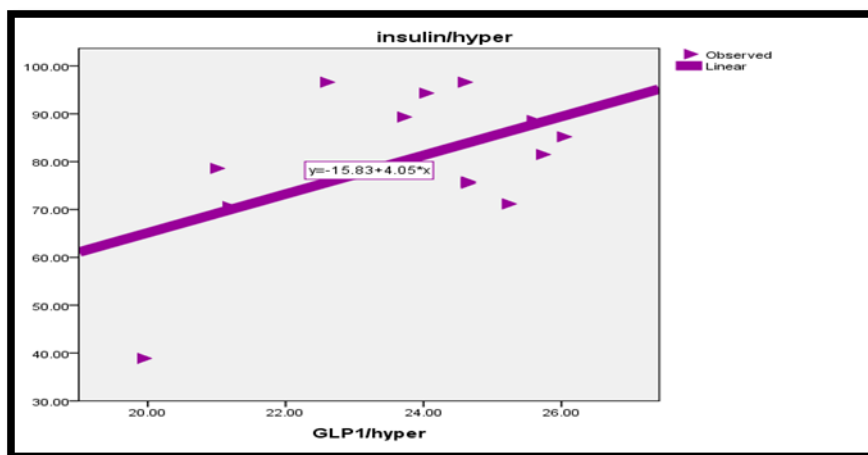


Figure (9) correlation relation between (GLP-1 and insulin) in G3

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