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GLYCEMIC CONTROL, THYROID HORMONES AND OTHER BIOCHEMICAL PARAMETERS IN TYPE 2 DIABETES PATIENTS

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ABSTRACT

With the increasing incidence of obesity and type 2 diabetes mellitus in the Iraq and abroad, we should focused on the molecules and pathways that regulate metabolic homeostasis with the hope of identifying a pharmacological target to limit obesity and diabetes, and/or its pathophysiological consequences. The study conducted to evaluate glycemic control and its relationship with other metabolic parameters including thyroid hormones and thyroid stimulating hormone in type 2 diabetic patients and to compare it with that in healthy non obese and overweight and obese subjects, to assess whether glycated hemoglobin measurement can predict diabetes in obese subjects in the future. So a case control study was conducted at the center of diabetes management and research between 1st of December 2019 to the 15th of May 2020. The study include 100 subjects, divided into three groups: group 1: included 20 (11 male and 9 female) apparently healthy individuals whose body mass index (BMI) below 25 kg/m^2, age range 30-60 years, group 2: included 20 (8 male and 12 female) healthy individuals whose BMI equal or above to 25 kg/m^2, age range 32-60 years, and group 3: included 60 (28 male and 32 female) newly diagnosed diabetic patients whose BMI equal or above to 25 kg/m^2, age range 35-66 years. From all participants, a fasting blood sample was taken for measurement of fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), lipid profile, thyroid hormones, thyroid stimulating hormone (TSH) and fasting insulin. Insulin resistance (IR), BMI and atherogenic index (AI) were calculated according to special equations. A comparison of biochemical parameters between group 1 and group 2 revealed a significant increase in fasting insulin and triglycerides, a significant decrease in high density lipoprotein cholesterol (HDL-c) in group 2, with a significant increase in level of HbA1c, IR and AI, while there was no significant differences were detected in FPG, total cholesterol, low density lipoprotein cholesterol (LDL-c), TSH and thyroid hormones. A comparison of biochemical parameters between group 1 and group 3 showed a significant increased differences in FPG, HbA1c, triglycerides, AI, fasting serum insulin and IR, with a significant increased differences in the total cholesterol and LDL-c in group 3. There was a significant increased differences in TSH and a significant decrease in both thyroid hormones. A comparison of biochemical parameters between group 2 and group 3 showed a highly significant increased differences in FPG, HbA1c and IR, with a significant increased differences in AI and TSH. A significant decreased differences in HDL-c in group 3, with no significant differences in the fasting serum insulin, total cholesterol, triglycerides and LDL-c. The healthy subjects suffering from obesity are at a high risk of developing diabetes in the future. Thyroid stimulating hormone show high level and a low levels of thyroid hormones in diabetic and obese participant compare with that of non obese group.

KEYWORDS: Diabetes, insulin resistance, obesity, thyroid stimulating hormone.

INTRODUCTION

Diabetes mellitus is characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Two major forms of diabetes were identified; type 1 and type 2. Lack of or severe reduction in insulin secretion due to autoimmune or viral destructions of β-cells is responsible for type1 diabetes, which accounts for 5-10% of diabetic patients. The more prevalent form, type 2 diabetes, accounts for more than 90% of cases. Type 2 diabetes usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to reduce it.

Lack of insulin action and/or secretion in type 2 diabetes induces hepatic glucose output by inhibiting glycogen synthesis and stimulating glycogenolysis and gluconeogenesis then increased rates of hepatic glucose production result in the development of overt hyperglycemia, especially fasting hyperglycemia. In such conditions, Ketone bodies are produced, and are found in large quantities in ketosis, the liver converts fat into fatty acids and ketone bodies which can be used by the body for energy. In addition, excess fatty acids in serum of diabetics are converted into phospholipids and cholesterol in liver. These two substances along with excess triglycerides formed at the same time in liver may be discharged into blood in the form of lipoproteins.

Thyroid hormones play a very important role in controlling the body's metabolism, that is, the rate at which the body uses energy, by stimulating divers metabolic activates most tissue, leading to an increase in basal metabolic rate one consequence of this activity is to increase body heat production.

Aim of the study

This study intended to assess and study correlation between glycemic control parameters and thyroid hormones in diabetic and obese patients.

Specific Objectives

- Comparison between healthy people (thin and obese) and diabetic patients according to level of fasting glucose levels and glycated hemoglobin.
- To assess the correlation between thyroid function and serum lipids in newly diagnosed type 2 diabetes and healthy thin and obese subjects.
- To assess whether HbA1c measurement can predict diabetes in obese subjects or not.

Literature review

Diabetes is a complex, chronic illness requiring continuous medical care with multi-factorial risk-reduction strategies beyond glycemic control. Ongoing diabetes self-management education and support are critical to preventing acute complications and reducing the risk of long term complications.[1] According to the American Diabetes Association 2020, diabetes can be classified into the following general categories: Type 1 diabetes, Type 2 diabetes, Gestational diabetes mellitus and specific types of diabetes due to other causes.[2]

In type 2 diabetes, hyperglycaemia is the result, initially, of the inability of the body's cel s to respond ful y to insulin, a situation termed 'insulin resistance.[3] During the state of insulin resistance, the hormone is ineffective and, in due course, prompts an increase in insulin production.[4] Over time, inadequate production of insulin can develop as a result of failure of the pancreatic beta cells to keep up with demand. Type 2 diabetes is most commonly seen in older adults, but is increasingly seen in children and younger adults owing to rising levels of obesity, physical inactivity and inappropriate diet.[3,4]

Diabetes is a major health issue that has reached alarming levels: today, nearly half a billion people are living with diabetes worldwide.[5] It is one of the major health priority of the 21st century causing 1.5 million deaths in 2012[6] and 4.2 million deaths resulting from diabetes and its complications in 2019.[3] So this pathology will move up to the seventh leading cause of death worldwide.[7] Diabetes is recognized as a well-known risk factor for cardiovascular diseases, responsible for about a twofold excess risk for various vascular diseases such as coronary heart diseases, strokes, and other vascular deaths.[8]

Globally, the prevalence of type 2 diabetes is high and rising across all regions. This rise is driven by population aging, economic development and increasing urbanization leading to more sedentary lifestyles and greater consumption of unhealthy foods linked with obesity.[9]

It is estimated that 79.4% live in low- and middle-income countries. the estimated 463 million adults aged 20–79 years are currently living with diabetes. This represents 9.3% of the world's population in this age group. The total number is predicted to rise to 578 million (10.2%) by 2030 and to 700 million (10.9%) by 2045.[3]

The estimated number of adults aged 20–79 years with impaired glucose tolerance is 374 million (7.5% of the world population in this age group). This is predicted to rise to 454 million (8.0%) by 2030 and 548 million (8.6%) by 2045.[3]

Type 2 diabetes has also become a concern in children and young people as a result of an increasing prevalence of obesity.[10] Females are more commonly affected by type 2 diabetes in all groups.[11]

A data available on 20 Arab countries with about 20.5 million were having diabetes and 13.7 million with prediabetes.[12] Diabetes in developed countries is a disease of the elderly while in Arab countries, its disease of younger age <60 year, which is the most productive age, making the problem of diabetes even worse.[12] Screening for diabetes in developing countries is not easy because of limited resources, blood tests may be difficult, and one needs to rely on the less expensive bedside tests available to predict high risk subjects for the development of diabetes.[13]

In Iraq data from 2003-2010, the overall overweight and obesity affects 55.1% of the population (54.7% of women and 45.3% of men). The prevalence of overweight alone was 31.3% (50.2% of them men and 30.9% of women) and obesity was 23.8% (61.1% of them women and 18.6% of men). 31 Obesity is a prominent risk factor for type 2 diabetes, and with global

obesity rates rising, the ensuing burden of type 2 diabetes looks set to worsen.[14]

The presentation of type 2 diabetes is much less dramatic and the condition may be completely symptomless. Also, the exact time of the onset of type 2 diabetes is usually impossible to determine.[15] As a result, there is often a long pre-diagnostic period and as many as one-third to one-half of people with type 2 diabetes in the population may be undiagnosed. When unrecognised for a prolonged time, complications such as retinopathy or a lower-limb ulcer that fails to heal may be present at diagnosis.[15] The causes of type 2 diabetes are not completely understood but there is a strong link with overweight and obesity, and increasing age, as well as with ethnicity and family history. Type 1 diabetes and type 2 diabetes results from a combination of multi-gene predisposition and environmental triggers.[3]

The cornerstone of type 2 diabetes management is the promotion of a lifestyle that includes a healthy diet, regular physical activity, smoking cessation and maintenance of a healthy body weight.[3] As a contribution to improving the management of type 2 diabetes, in 2017 International Diabetes Federation (IDF) issued the IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care.[16] If attempts to change lifestyle are not sufficient to control blood glucose levels, oral medication is usually initiated.[3]

Diabetes may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG) value or the 2-h plasma glucose (2-h PG) value during a 75-g oral glucose tolerance test (OGTT), or HbA1c criteria. Generally, FPG, 2-h PG during 75-g OGTT, and HbA1c are equally appropriate for diagnostic screening.[17] The same tests may be used to screen for and diagnose diabetes and to detect individuals with prediabetes.[18]

The causes of type 2 diabetes are not completely understood but there is a strong link with overweight and obesity, and increasing age, as well as with ethnicity and family history.[19]

Several risk factors have been associated with type 2 diabetes including obesity, unhealthy diet, lack of physical activity, pollutants and toxins, stress, exposure to enteroviruses causing damage to the immune cells, family history of diabetes and ethnicity. Attempts made so far target unhealthy diet and physical inactivity as the drivers of overweight and obesity, which are the most important modifiable risk factors for the development of type 2 diabetes.[20]

Type 2 diabetes is most commonly seen in older adults, but is increasingly seen in children and younger adults owing to obesity, physical inactivity and inappropriate diet.[15,16] In another word, a consequence of social trends toward higher energy intake and reduced energy expenditure.[2,21] Obesity is a rapidly growing health problem, conferring substantial excess risk for morbidity and mortality, especially from type 2 diabetes and atherosclerotic cardiovascular disease (CVD).[22] Obesity is a complex disorder, where genetic predisposition interacts with environmental exposures to produce a heterogeneous phenotype.[23] Body mass index (BMI) has consistently been associated with adverse health outcomes, but sub-phenotypes of obesity have been recognized that appear to deviate from the apparent dose-response relationship between BMI and its consequences.[22]

Among patients with both type 2 diabetes and overweight or obesity who also have inadequate glycemic, blood pressure, and lipid control and/or other obesity-related medical conditions, lifestyle changes that result in modest and sustained weight loss produce clinically meaningful reductions in fasting blood glucose to126 mg/dL, HbA1c to 6.5%, and triglycerides.[24,25] Greater weight loss produces even greater benefits, including reductions in blood pressure, improvements in LDL and HDL cholesterol, and reductions in the need for medications to control blood glucose, blood pressure, and lipids, and may result in achievement of glycemic goals in the absence of glucose-lowering agent use in some patients.[24,26]

The adipose tissue plays an important role in total energy homeostasis.[27] Glucose and lipid metabolism are regulated by complex interactions that occur within the adipoinsular axis.[27]

Thyroid hormones play a very important role in controlling the body's metabolism, that is, the rate at which the body uses energy, by stimulating divers metabolic activates most tissue, leading to an increase in basal metabolic rate one consequence of this activity is to increase body heat production.[28]

It has long been recognized that diabetes mellitus type 2 and thyroid disease, both common endocrine disorders, are closely related.[29] The underlying pathophysiological mechanisms of the repeatedly reported association between thyroid dysfunction and type 2 diabetes (T2DM) have not yet been fully elucidated.[29,30]

Thyroid hormones have a large impact on glucose homeostasis, and both high and low thyroid hormone levels are associated with peripheral insulin resistance.[31] Triiodothyronine (T3) has been shown to play a role in the protection of pancreatic island β-cells against apoptosis.[32] Furthermore, treatment of hypothyroidism may improve insulin sensitivity.[33] Contrarily, it has been found that patients with poor glycemic control in T2DM have higher risk of subclinical hypothyroidism.[34]

Various studies have shown a high prevalence of thyroid disorders (TDs) in patients with T2DM (12%–23%),

with hypothyroidism being the most common disorder.[35,36] Uncontrolled T2DM affects plasma triiodothyronine (T3) as well as thyroxine (T4) levels.[37] Existing evidence has demonstrated that the relationship of TSH and lipid levels was different between overweight and normal weight populations and between men and women.[38] Furthermore, the thyroid hormones play an important role in regulating lipid metabolism. Numerous studies have confirmed the presence of an inverse relationship between serum thyroxin and cholesterol levels.[39]

SUBJECTS, MATERIALS AND METHODS

A case control study was conducted between 1st of December 2019 to the 15th of May 2020 at Al- Wafaa center of diabetes management and research in Mosul city.

This study included 100 subjects; 40 non diabetic and 60 diabetic patients. Their age ranged between 30-66 years old. They divided into the following three groups: group (1): included 20 (9 females and 11 males), apparently healthy individuals, whose BMI < 25 kg/m^2, group (2): included 20 (12 females and 8 males), apparently healthy individuals, whose BMI ≥ 25 kg/m^2 and group (3): included 60 (32 females and 28 males), diabetic patients who were newly diagnosed (taking no anti-diabetic medications) and their BMI ≥ 25 kg/m^2. The study design was enrolled, age and sex were matched in the three groups, BMI was matched in group 2 and group 3. Group 3 included the newly diagnosed diabetes mellitus type 2 according to the ADA diagnostic criteria for T2DM.[10] Diabetes mellitus type 2 diagnosed by (Fasting ≥ 126 mg/dL or 2- hour PPG ≥ 200 mg/dL or HbA1c ≥ 6.5 %) and their BMI ≥ 25 kg/m^2 while patient with T1DM, diabetic patients on anti-diabetic medicine, pregnant and lactating women, smokers and alcoholic patients, patients with hepatitis, renal failure, liver disease, malignant disease and patients on chemotherapy were excluded.

The data was obtained directly from the participants by interviewing them, using a prepared questionnaire. The weight and the height were measured for each participant in the study using a medical scale machine.[2,3]

Ten ml of venous blood was drawn using disposable plastic syringes after an overnight fasting from the participants. The biochemical analysis was performed in a private clinical laboratory using MINI VIDAS compact multiparametric immunoanalyzer (ELFA), AIA 360 TOSOH, ELx800 universal microplate reader (ELISA) and Spectrophotometer to evaluate the result or HbA1c, serum insulin, FBS, serum lipid profile and thyroid function test.

The data obtained in the current study was analyzed using statistical package for social science (SPSS) program version 26. Different descriptive statistical methods were used to summarize and tabulate the data. ANOVA test were used to compare the mean difference of all parameters between the three groups. Duncan test were used to determine the non-homogenous group if the result of ANOVA test was significant. Furthermore independent 2 samples student t-test were used to compare the difference between each 2 groups. A P-value < 0.05 was considered statistically significant.

RESULTS

3.1. Demographic and clinical characteristics of the participants

The results of data analyzed are arranged according to the grouping of the subjects encountered inthis study is shown in table (3.1).

Table 3.1: Demographic and clinical characteristics of the participants.

characteristics		Group 1 (no. = 20)				Group 2 (no. = 20)					Group 3 (no. = 60)				
Age	mean± SD	44.0±8.3				45.0±7.0					47.5			±7.4	
	range	30-60				32-60					35-66				
GENDER		No.			%	No.				%	No.				%
male		11			55	8				40	28				46.6
female		9			45	12				60	32				53.3
M : F ratio			1.22 :	1			1	:	1.5			1	:	1.14	
Family history		No.			%	No.				%	No.				%
Presents		11			55	13				65	33				55
absent		9			45	7				35	27				45
BMI	mean± SD	22.4±1.7				34.2±5.3					32.9± 6.3				
	range	20.1-24.8				25.8-48.0					26- 50				

3.2. Biochemical parameters in the studied groups

Different biochemical parameters were measured in the participants, including: FPG, HbA1c, serum lipid profile, fasting s. insulin and HOMA-IR, TSH, fT3 and fT4 were measured. The results are presented as mean ± SD in table (3.2).

Table 3.2: Biochemical parameters in the studied groups.

Biochemicalparameters	Group 1	Group 2	Group 3	p-value
	mean± SD			
FPG	96.4±12.0	97.2±14.5	209 ± 53.1 [bc]	< 0.0001
HbA1c	4.9±0.3	5.3±0.4	8.97 ± 1.76 [bc]	< 0.0001
Fasting S.Insulin	6.5±2.3	13.2±9.0	14.2 ± 9.2	0.001
HOMA-IR	1.51±0.51	3.23±2.55 [a]	7.11 ± 4.14 [bc]	< 0.0001
T-c	164.0±25.7	179.7±44.7	187.1± 42.6 [b]	0.05
HDL- c	49.8±9.0	41.2±10.9 [a]	35.7 ± 8.9 [bc]	< 0.0001
LDL- c	93.6±24.5	106.4±36.6	117.1±37.0 [b]	< 0.05
Triglyceride	103.4±52.5	148.1±66.4 [a]	171.1± 59.6 [b]	< 0.0001
A.I.	3.4±1.0	4.2±1.2	5.6 ± 2.3 [b]	< 0.0001
TSH	2.31±0.99	4.51±2.55	7.1± 5.0 [bc]	0.01
f T4	1.09±0.28	1.2±0.35	1.54 ±0.71[b]	0.05
f T3	1.31±0.59	1.67±0.73	2.09±0.82 [b]	0.04

[a] = significant difference between group 2 and group 1 [b] = significant difference between group 3 and group 1 [c] = significant difference between group 3 and group 2.

3.3. Comparison of the biochemical parameters between group 1 and group 2

When different biochemical parameters in group 1 and group 2 were compared, there is significant decreased differences in HDL-c and a significant increased differences ($p< 0.01$) in the level of triglyceridesin group 2, with no significant differences ($p>0.05$) were detected in FPG, HbA1c, fasting insulin, total cholesterol, LDL-c, atherogenic index, TSH, free T3 and free thyroxine level.

Table 3.3: Comparison of the biochemical parameters between group 1 and 2.

Biochemical parameters	Group 1		Group 2		P- value
	mean ±SD	range	mean ±SD	range	
FPG	96.4±12.0	75-122	97.2±14.5	77-122	1.000
HbA1c	4.9±0.3	4.3-5.3	5.3±0.4	4.2-6.1	1.000
Fasting insulin	6.5±2.3	2.8-11.5	13.2±9.0	4.1-40.1	0.487
HOMA-IR	1.51±0.51	0.70-2.55	3.23±2.55	0.90-11.78	< 0.000
TC	164.0±25.7	112-210	179.7±44.7	112-295	0.235
HDL	49.8±9.0	30-65	41.2±10.9	20.0-62.0	0.047
LDL	93.6±24.5	34-139	106.4±36.6	42.0-194.0	0.106
TG	103.4±52.5	45-280	148.1±66.4	45.0-380.0	0.006
AI	3.4±1.0	2.0-6.6	4.2±1.2	2.0-7.0	1.0
TSH	2.31±0.99	0.87-4.00	4.51±2.55	0.66-9.10	0.342
f T4	1.09±0.28	0.85-2.00	1.2±0.35	0.76-2.00	1.00
f T3	1.31±0.59	2.70-5.01	1.67±0.73	2.49-4.76	0.84

3.4. Comparison of the biochemical parameters between group 1 and group 3

There was a highly significant increased differences ($p<0.001$) in FPG, HbA1c, insulin resistance, Tg and TSH levels and a highly significant decreased differences in HDL-c. There was a significant differences ($p< 0.01$) in the level of free T4 in group 3, with a significant differences ($p< 0.05$) were detected in fasting insulin level, free T3, total cholesterol, LDL-c and atherogenic index.

Table 3.4: Comparison of the biochemical parameters between group 1 and 3.

Biochemical parameters	Group 1		Group 3		P- value
	mean ±SD	range	mean ±SD	range	
FPG	96.4±12.0	75-122	209 ± 53.1	142-390	< 0.000
HbA1c	4.9±0.3	4.3-5.3	8.97 ± 1.76	5.7-13	< 0.000
Fasting insulin	6.5±2.3	2.8-11.5	14.2 ± 9.2	3.4-65.0	0.031
HOMA-IR	1.51±0.51	0.70-2.55	7.11 ± 4.14	1.93- 26.64	< 0.000
TC	164.0±25.7	112-210	187.1± 42.6	109.0-322.0	0.048
HDL	49.8±9.0	30-65	35.7 ± 8.9	20.2-70.0	< 0.000
LDL	93.6±245	34-139	117.1±37.0	49.0-225.6	0.031
TG	103.4±52.5	45-280	171.1± 59.6	45- 459	< 0.000
AI	3.4±1.0	2.0-6.6	5.6 ± 2.3	2.6-16.4	0.033

TSH	2.31±0.99	0.87-4.00	7.1± 5.0	1.3- 27.0	< 0.000
f T4	1.09±0.28	0.85-2.00	1.54 ±0.71	1.04-2.48	0.008
f T3	1.31±0.59	2.70-5.01	2.09±0.82	2.33-5.43	0.05

3.5. Comparison of the biochemical parameters between group 2 and group 3

There was a highly significant increased differences (p<0.001) in FPG, HbA1c and TSH. There was a significant decreased differences (P< 0.05) in HDL-c and a significant differences (p< 0.05) in the insulin resistance in group 3. There was no significant differences (p>0.05) were detected in fasting insulin level, total cholesterol, LDL-c, Tg, atherogenic index and free thyroxin level.

Table 3.5: comparison of the biochemical parameters between group 2 and 3.

Biochemical parameters	Group 2		Group 3		P- value
	mean ±SD	range	mean ±SD	range	
FPG	97.2±14.5	77-122	209 ± 53.1	142-390	< 0.000
HbA1c	5.3±0.4	4.2-6.1	8.97 ± 1.76	5.7-13	< 0.000
Fasting insulin	13.2±9.0	4.1-40.1	14.2 ± 9.2	3.4-65.0	0.499
HOMA-IR	3.23±2.55	0.90-11.78	7.11 ± 4.14	1.93- 26.64	0.032
TC	179.7±44.7	112-295	187.1± 42.6	109.0-322.0	1.000
HDL	41.2±10.9	20.0-62.0	35.7 ± 8.9	20.2-70.0	0.043
LDL	106.4±36.6	42.0-194.0	117.1±37.0	49.0-225.6	1.000
TG	148.1±66.4	45.0-380.0	171.1± 59.6	45- 459	0.087
AI	4.2±1.2	2.0-7.0	5.6 ± 2.3	2.6-16.4	0.37
TSH	4.51±2.55	0.66-9.10	7.1± 5.0	1.3- 27.0	< 0.000
f T4	1.2±0.35	0.76-2.00	1.54 ±0.71	1.04-2.48	0.057
f T3	1.67±0.73	2.49-4.76	2.09±0.82	2.33-5.43	0.05

3.15. Correlation between BMI, glycemic control, thyroid hormone and other metabolicparameters in group 1

Table 3.10: Correlation between BMI, glycemic control, thyroid hormone and other metabolicparameters in group 1.

Characteristics	BMI		
	r	r^2	p
FPG	0.061	0.004	0.800
HbA1c	0.157	0.025	0.509
Fasting S. Insulin	0.033	0.001	0.891
HOMA-IR	0.015	0.000	0.951
TC	0.328	0.107	0.158
HDL	0.142	0.020	0.550
LDL	0.402	0.162	0.079
TG	0.013	0.000	0.958
AI	0.340	0.116	0.142
TSH	0.485	0.235	0.030
f T4	0.059	0.003	0.805
f T3	0.372	0.138	0.053

Correlation between BMI, glycemic control, thyroid hormone and othermetabolic parameters in group 2. there was a significant positive correlation between BMI level and glycemic control (FPG and HbA1c), lipid profile which indicating that an increase in BMI associated with increase in FPG, HbA1c and lipids. Table (3-11).

Table 3.11: Correlation between BMI, glycemic control, thyroid hormone and other metabolic parameters in group 2.

Characteristics	BMI		
	r	r^2	p
FPG	0.002	0.000	0.992
HbA1c	0.445	0.198	0.049
Fasting S. Insulin	0.078	0.006	0.744
HOMA-IR	0.103	0.011	0.664
TC	0.088	0.008	0.712
HDL	0.133	0.018	0.576

LDL	0.022	0.000	0.926
TG	0.084	0.007	0.725
AI	0.007	0.000	0.977
TSH	0.422	0.178	0.064
f T4	0.402	0.162	0.079
f T3	0.416	0.173	0.108

3.16. Correlation between BMI, glycemic control, thyroid hormone and other metabolicparameters in group 3

A positive correlation shown between BMI and glycemic control and lipids profile. There is apositive correlation between TSH and BMI. Table (3-12).

Table 3.12: Correlation between BMI, glycemic control, thyroid hormone and other metabolicparameters in group 3.

Characteristics	BMI		
	r	r^2	p
FPG	0.002	0.000	0.992
HbA1c	0.810	0.655	0.000
Fasting S. Insulin	0.001	0.000	0.993
HOMA-IR	0.032	0.001	0.811
TC	0.011	0.000	0.933
HDL	0.084	0.007	0.521
LDL	0.028	0.001	0.897
TG	0.017	0.000	0.897
AI	0.011	0.000	0.933
TSH	0.020	0.000	0.880
f T4	0.193	0.037	0.140
f T3	0.372	0.138	0.071

THE DISCUSSION

The present study provides a wide view on biochemical features in blood of type 2 diabetic patients and non diabetic obese. Diabetes is an important healthy problem since the incidence of diabetes is continuously increased. Greater than 50% of adult with type 2 diabetes mellitus have coronary artery disease (CAD).[40]

The mean age of type 2 diabetic patients who were participated in our study was (47.5±7.4) years, coincides with the fact that type 2 diabetes mellitus usually develops after age 40 years.[41]

The mean HbA1c of 8.97% observed in T2DM patients in this study is close to 8.3% reported by the Diabcare Nigeria study group and another study showed mean HbA1c of 7.8%.

However, this contrasted with findings in a study assessing quality of care for diabetes in the USA.[6,20,42]

The high HbA1c value in obese individual can also related to sustained hyperglycemia that occur due to impaired glucose metabolism and this agree with results obtained by Power et al[43], a cohort study done at 2011 where a 7855 participants, BMI and HbA1c for all were done, the result revealed an excessive BMI gain across the life span and earlier onset of overweight / obesity are associated with impaired glucose metabolism.[43]

In this study, there was a significant difference in HbA1c levels between the non diabetic groups and the diabetic group both had (p value <0.000). However this study could not find, a significant difference in HbA1c levels between non diabetic groups, the obese and non obese patients, although it was obviously lower in the non obese patients implying a better glycemic status in such patients. This results similar to the result of case control study conducted in Iraq 2008[44], involved 50 patients with T2DM with age range of 30 -70 years, and 30 healthy subjects (control group) of matching age and sex, and its results revealed highly significant differences in insulin resistance, Hb1AC and FPG (P<0.001) and significant differences in insulin (p<0.05).

Many previous studies mentioned that there is important relationship between the HbA1c and the obesity and lipid disturbances especially in diabetes patients like Liliana Zago, et al.[45]

Where they found that HbA1c showed a positive association with glucose. These events were more frequent in patients with obesity. Zehra Esra Önal, et al.[46] also showed a positive relationship between insulin resistance and serum HbA1c levels of obese. While, Unluer AN, et al.[47] study revealed that There

no difference between obese and non-obese groups in terms of HbA1c values as the result in this study.[47]

In the present study a highly significant difference in insulin resistance (HOMA) was observed in diabetic group as compared to non obese group, which was expected because of the increased level of fasting plasma glucose and high level of serum insulin in diabetic patients, and there was a highly significant difference in insulin resistance (HOMA) was observed in obese group as compared to non obese group which was expected due to high level of serum insulin in obese group which indicate the presence of insulin resistance in this group. The result show a significant difference in insulin resistance (p-value < 0.05) between diabetic and obese group. These results were agreement with a study conducted in AL-Mustansria University and AL– Yarmok Teaching Hospital Teaching 2017[48], on a total (120) individuals age range from (33-60) years. (80) patient type 2 diabetes nephropathy, (40) healthy controls. The enrolled patients were divided to three groups according to BMI, data collection about age, sex and BMI. The result revealed the mean FPG, HbA1c, C-Peptide level, fasting insulin level and HOMA-IR level show statistically significantly increased in diabetic patients when compared with control subjects.

Obesity is associated with several deleterious changes in lipid metabolism, including high serum concentrations of total cholesterol, LDL, VLDL and TG, and reduction in serum HDL concentration.[49]

Previous studies showed that in all age groups, HDL levels were significantly lower in patients who had a high BMI. Hypertriglyceridemia is often associated with reduced levels of HDL suggesting a possible metabolic interaction between these two lipid fractions.[38,50]

The key to this relation may be that the increase in fat deposition in obese individuals is associated with insulin resistance, which will lead to increase synthesis of TG-rich lipoproteins in the liver. The increase of triglycerides in lipid particles changes their metabolism. Triglyceride- rich HDL particles are hydrolyzed more rapidly causing HDL level to fall.[49] By mean, the concentration of HDL is adversely altered in obesity, with HDL levels associated with both the degree and distribution of obesity.[51]

Darvall and his research team reported that increased levels of both triglycerides and free fatty acids are associated with obesity and insulin resistance.[52]

The results of serum lipid profile in this study show that, cholesterol, triglycerides and LDL-C levels were significantly increased in diabetic patients and obese controls when comparedto non obese controls whereas HDL-C level was significantly decreased in diabetics. Such findings are in concurrent with that declared in the literatures, a study from Gaza strip[53] and another conducted in India[54] on total of 100 subjects, with 50 diabetic patients and 50 controls, to study their HDL and LDL profile, results showed increased level of LDL in diabetic than controls and a decrement in the level HDL in diabetic than control subjects.

The abnormal levels of serum lipids in diabetics is due mainly to increase in the mobilization of free fatty acids from fat depots, since insulin inhibits the hormone sensitive lipase. Excess serum fatty acids are converted into triglycerides, phospholipids and cholesterol in liver which may be discharged into blood.[55]

Obesity as a cause of insulin resistance may play a role in thyroid dysfunction. There is evidence that low free T4 is associated with insulin resistance.[56] Solanki et al.[57] reported significant correlation between BMI and TSH in healthy adults and BMI was negatively associated with serum fT4 but had no association with serum fT3.[57]

There is a positive association between TSH and obesity (BMI) which is similar to the result shown in Chinese study[58] where they explain these result as an alterations in thyroid hormones activity or as a result of an alteration in the regulation of the hypothalamic-pituitary- thyroid axis, and our results agreed with a study conducted in Saudi 2017.[59]

In this study, the comparison of thyroid function between diabetic and the non obese group (table 3-4) show a highly significant differences in TSH and fT4 (p value < 0.01) and a (p value < 0.05) for fT3. There is also a highly significant differences in TSH between obese and diabetic groups. These result agreed with a case control study conducted in the Diabetes and Endocrine Center at Al-Husain Teaching Hospital, AL-Muthanna, Iraq 2015.[60]

In recent research has shown that excess weight can also influence thyroid function, with the presence of hyperthyrotropinemia, with or without changes in T3 and T4 concentrations, generally being observed in euthyroid obese subjects.[61,62]

In contrast, Manji et al.[63] and Figueroa et al.[64] found no correlation between BMI and serum levels of any of the thyroid hormones in euthyroid individuals. Moreover, Tarim[65] reported that fT3 and fT4 were normal in obese subjects.

CONCLUSIONS

On the bases of the results obtained in the present study, the following conclusions can be obtained: Healthy subjects

complaining from obesity are at a high risk of developing diabetes in the future concludedfrom the facts that their HbA1c and IR was significantly higher compared with thin healthy control andhighly significant difference in fasting serum insulin level. Thyroid stimulating hormone show high leveland a low levels of thyroid hormones in diabetic and obese participant compare with that of non obesegroup, i.e. TSH levels correlate with insulin resistance in obese patients.

Suggestions and Further Recommendations

Weight loss programs are particularly important for obese diabetic patients. Because of the high prevalence of their co-occurrence. Obesity, insulin resistance and thyroid dysfunction are common diseases, and consequently clinicians should be particularly alert to the possibility of thyroid dysfunction in obese patients. Patients with diabetes may need a screening for thyroid function. Further research should conduct to evaluate the response of obese or diabetic patient for weight loss programs by measuring insulin levels and thyroid function.

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