Original Article

The ANGPTL8 Levels as An Important a Biochemical Markers for The Women with T2DM

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Abstract

Background: The metabolic syndrome including type 2 diabetes mellitus(T2DM), insulin resistance(IR), obese, hypertension, and dyslipidemia, is an increasing health burden. In the last decade, various metabolic hormones have been noticed to significantly role obese and associated complications. for example of this, the adipokines or hepatokines secreted proteins from hepatocyte and adipocyteare correlate with metabolic syndrome. Angiopoietin-like protein 8 (ANGPTL8) has a novel hepatokine or adipokine, which is mostly expressed in the adipose tissue, and liver stimulates the β-cell proliferation as a pancreatic in an insulin resistance state. It's a recently discovered the endocrine regulator associated with glucose homeostasis, IR, and metabolism of lipid.

Patients and Methods: Ninety women participated in this study, comprising sixty patients with diabetes mellitus type-2 and thirty healthy (sex and age - matched) as a control group. ELISA was used to assess ANGPTL8 and insulin. Standard procedures were used to measure fasting blood glucose, lipid profile, and glycated hemoglobin(HBA1c) in a certified laboratory.

Results: Diabetes patients had higher levels of ANGPTL8 than the control group. The blood ANGPTL8 level in the Type-2 diabetes group varied from 4432.89±1171.09 pg/ml, while the control group's level was 2892.11±537.91pg/dl ($p<0.0001$). ANGPTL8 level that only was a negatively significant determinant ($r = -0.343$; and $r = -0.293$), with TC and LDL. Serum ANGPTL8 levels a positively correlated with age, BMI, insulin, HBA1c, HOMA-IR, HOMA-B, QUICKI, and HDL in T2DM group, and negatively correlated with FBG, TC, TG,LDL, and VLDL in the T2DM patients group.

Conclusion: ANGPTL8 levels were found to be considerably higher in type two diabetes individuals, and they continued to rise in tandem with the decline in beta cell function. ANGPTL8 level that only was a negatively significant with total cholesterol (TC) and LDL. As a result, the level of serum ANGPTL8 may have a role in the etiology and diagnosis of Type 2 Diabetes Mellitus.

Keywords: Angiopoietin-like protein 8, Lipid profile, Insulin resistance, HBA1c, Diabetes mellitus type-2.

INTRODUCTION

Diabetic and obesity are global public health issues, and it's especially vital to look into prospective treatments that focus on diabetes causes, reduced pancreatic-cell function, and insulin resistance (IR) [1].

ANGPTL8, also known as refeeding-induced fat and liver, betatrophin, and lipasin is 198-amino-acid, secreted protein that is predominantly produced in the adipose tissues and liver [2]. It's a newly discovered endocrine regulator linked to glucose metabolism, lipid, and IR, all of which are considered to have a role in T2DM etiology [1], [2]. It was found that ANGPTL8 directly correlates with triglyceride levels in animals. Triglyceride levels were lower in ANGPTL8-deficient condition than in the control group [3], but ANGPTL8 overexpression resulted in an increased in TG levels[4]. ANGPTL8 may be a novel identified member of the angiopoietin-like protein (ANGPTL) family and is additionally referred to as CD26, and C19 or f80 [5], [6]. it's induced upon feeding in liver and fat both brown (BAT), and white fat (WAT) whereas fasting suppresses its expression [4], [5], [7], [8]. They have been identified as the key players involved in the metabolic conversion of fasting to refeeding [4], [7], [8]. It has been shown to play an important role in triglyceride metabolism by regulating postprandial lipid traffic through inhibition of lipoprotein lipase activity [5], [9]. The mechanism demonstrated by Zhang (2015) concordant with LPL as a hydrolytic enzyme that generates free fatty acids (FFA) from TG hydrolysis for subsequent uptake by memory, skeletal muscle, and WAT [8], ANGPTL8 inhibits the postprandial LPL activity of cardiac and skeletal muscles which allows the uptake of FFA by WAT for storage.

ANGPTL8 levels in the blood were found to be significantly higher in patients than in control subjects [10]. Other studies have also found that ANGPTL8 levels are increased in patients with T2DM [2], [11]–[16]. Furthermore, in patients, several studies have found a link between blood glucose, (HOMA-IR), and ANGPTL8 [12], [17].

T2DM that is usually characterized by hyperinsulinemia and hyperglycemia [7], [15]. it's gave to affect 642 million human by 2040 consistent to the International Diabetes Federation [18]. The reason are well studied and encompass lipid homeostasis and uncontrolled glucose involving effect of hormone and substrate [19]. However, the suboptimal effectiveness of current diabetic drugs to regulate glycemic conditions necessitates the identification of new molecular players in the regulation of glucose homeostasis, and lipid [9]. Some studies show ANGPTL8 as a unique secondary target for the treatment of T2DM and related metabolic and organic disorders thanks to its unique nature in controlling both lipid and glucose metabolism. [14]. Also, fasting lowers ANGPTL8 expression and inhibits LPL activity in cardiac and skeletal muscles, allowing them to take up FFA for energy expenditure. Thus, ANGPTL8 has a significant role in adipose tissue lipid metabolism and lipid breakdown consistent with dietary levels. ANGPTL8 is essential in certain lipid metabolic pathways including lipogenesis and autophagy [7]. ANGPTL8's role in glucose metabolism was studied in several studies [5], [20], [21]. However, Guo etal., showed the mechanism of ANGPTL8 for glucose regulation via FOXO/AKT and AKT/GSK3beta of insulin hormone pathway [21]. FOXO/AKT and AKT/GSK3beta signaling control inhibition or the activation to gluconeogenesis and glycogen synthesis, respectively. Despite the new research, there is still a large amount of data that remains to be investigated regarding the functions of ANGPTL8 and its physiological mechanism and regulation.

In present, a controversial scientific discussion on whether and the way ANGPTL8 level regulate IR and glucose has been ongoing. Interestingly, several in vitro and in vivo studies have suggested the complex roles of ANGPTL8 level in IR and T2DM. Data resulting from studies in human individuals involving the influence of ANGPTL8 on the event of diabetes were controversial.

As a result, the current study aimed to intend to assess the Angiopoietin-like protein 8 concentration and its association with age, BMI, HBA1c, serum insulin, insulin resistances, and the lipid profile in Iraqi women with type-2 diabetes and in healthy controls, summarize currently clinical study to take advantage of whether the ANGPTL8 might be applied for clinical biomarker to predict type-2 diabetes, and answer the following questions: (1) Is a rise in (ANGPTL8) level in the bloodstream linked to T2DM? (2) Whether (ANGPTL8) levels in the blood are elevated in T2DM patients.

MATERIALS AND METHODS

Materials

A total of 90 women were chosen to participate in this study from 2021 to 2022 at Al-Sader teaching hospital's medical examination diabetes and endocrinology center. The subjects were then divided into two groups: (1) healthy people (n = 30); (2) type 2 diabetics (n = 60).

The following were the criteria for exclusion: (1) Subjects who were taking any drug that was known to alter lipid metabolism or insulin sensitivity as a control group. (2) Treatment with angiotensin-receptor blockers, insulin, or angiotensin-converting enzyme inhibitors. (3) Use of known TG medications for more than two months or at any time in the six months prior to sampling. (4) any symptoms of acute infections and cardiac disorders, cancer, diabetes complications, liver, respiratory failure, or renal. (5) Participants who did not provide all of their information.

The work was authorized by the hospital's ethics committee. After being fully told about the study's aim and nature, each participant gave written informed consent.

Methods

All subjects were given a standard questionnaire to record clinical and demographic data. For at least three days before to the assessment, participants were instructed to maintain their normal physical activity and nutrition. Blood samples were taken after a 10-hour or longer overnight fast to assess ANGPTL8, HbA1c, blood lipids, fasting blood glucose (FBG), and fasting insulin. A concentrations of ANGPTL8 and insulin in the blood were measured using an ELISA. T2DM is preceded by insulin resistance. HOMA2 calculator software was used to calculate beta-cell activity, Insulin resistance, QUICKI, and insulin sensitivity from fasting insulin and fasting blood glucose (FBG). Also, LDL, and VLDL from cholesterol, TG, and HDL were used to calculate in (60) patients, and (30) controls as previously reported [22], [23].

Analytical Statistics

SPSS 16.0 software was used for statistical analysis. Before statistical analysis the parameters (ANGPTL8, HbA1c, insulin, fasting blood glucose, triglyceride(TG), HDL, Total cholesterol(TC), LDL, VLDL, HOMA % B, HOMA % S, QUICKI, and HOMA-IR) were converted to means ± standard deviation whilst continuous variables were reported. The student t-tests were

compared using characteristics of the groups. The estimate of correlation coefficients between the variables was investigated using correlation analysis.

RESULTS AND DISCUSSION

laboratory and Clinical Characteristics:

Comparison of demographic between a T2DM patients and controls:

The results are presented in table.1, for demographic data in controls and T2DM patients, showed a nonsignificant difference (p-value = 0.185 and 0.288) in age and BMI in patients compared with a control.

Table 1. Demographic data of the healthy controls and a T2DM subjects

Parameters		Control N=30	Patients N=60	p-value
Age	Yrs.	51 ± 10	55 ± 11	0.185
BMI	kg/m2	32.318± 4.365	33.409± 4.919	0.288

Non significant (p-value ≥ 0.05); BMI: body mass index.

In the current research, our data that values are given in Table 1, are agreement with other studies in T2DM group as compared with controls [1], [11], [15].

Comparison of a clinical between T2DM patients and controls:

The results are presented in table.2, for a biochemical markers in controls and T2DM patients. A significant increase (p<0.0001) in table.2, were showed in Angiopoietin-like Proteins 8 level in patients (4432.89±1171.09 pg/dl) in comparison with the controls (2892.11±537.91 pg/dl); A significant increase (p<0.0001) in HbA1c level in patients (7.639 ± 1.495) in comparison with the controls (5.135 ± 0 .718); A significant increase (p<0.0001) in Insulin level in patients (21.04±9.87 uIU/ml) in comparison with the controls group (9.38±3.66 uIU/ml); A significant increase (p<0.0001) in FBG level in patients (177.73± 39.61mg/dl) in comparison with the controls (88.66± 10.05mg/dl), and HOMA-IR in patients (p<0.0001) (9.39±5.14) in comparison with the controls (2.06±0.81).

There is a significant increase (p<0.0001) in TC level (220.40±44.21 VS154.73±31.63 mg/dl) , TG level (275.42±102.31 VS 126.07±50.39 mg/dl) ,LDL (128.8±44.84 VS 81.81±31.37 mg/dl) , and VLDL(55.08±20.46 VS 25.21±10.07 mg/dl) in patients compared with the controls group.

There is a significant decrease (p<0.0001) in HDL level (36.51±7.79 VS 47.71±12.02 mg/dl), HOMA-B (62.46±37.97 VS 114.18±38.79), HOMA-S (40.28±19.05 VS 95.48±37.17), and QUICKI (0.43±0.02 VS 0.50±0.01) in patients compared with the controls group.

Table 2. Comparison of the serum biochemical markers levels between T2DM patients and controls:

Biomarker	**Control N=30**	**Patients N=60**	**p-value**
ANGPTL8 (pg/dl)	2892.11±537.91	4432.89±1171.09	<0.0001
FBG mg/dl	88.66± 10.05	177.73± 39.61	<0.0001
HbA1c %	5.135 ± 0 .718	7.639 ± 1.495	<0.0001
Insulin (uIU/ml)	9.38±3.66	21.04±9.87	<0.0001
HOMA-IR	2.06±0.81	9.39±5.14	<0.0001
HOMA-B	114.18±38.79	62.46±37.97	<0.0001
HOMA-S	95.48±37.17	40.28±19.05	<0.0001
QUICKI	0.50±0.01	0.43±0.02	<0.0001
TC(mg/dl)	154.73±31.63	220.40±44.21	<0.0001
TG (mg/dl)	126.07±50.39	275.42±102.31	<0.0001
HDL-C(mg/dl)	47.71±12.02	36.51±7.79	<0.0001
LDL-C(mg/dl)	81.81±31.37	128.8±44.84	<0.0001
VLDL-C(mg/dl)	25.21±10.07	55.08±20.46	<0.0001

Highly significant(p-value < 0.0001); ANGPTL8: Angiopoietin-like Proteins 8; FBG: fasting blood glucose; HbA1c: glycated hemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance; HOMA-β: homeostasis model assessment of β; QUICKI: Quantitative Insulin sensitivity Check Index; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; VLDL: Very low-density lipoprotein cholesterol.

ANGPTL8 levels in the blood has been studied in the T2DM patients in the past, however, the results have been mixed [11], [21], [24]. ANGPTL8 levels in a female with T2DM was found to be constant in some investigations, while they were shown to be elevated or lowered in others[25], [26]. This variation could be related to differences in sample size, study design, medication status, race, ELISA kit use, and blood sample handling. All published data on ANGPTL8 levels and the T2DM found that patients have higher circulating level of ANGPTL8 [10], [11]. Our findings consistently showed in table.2, that serum level of ANGPTL8 in a female with T2DM patients were significantly higher than in controls. We also discovered that female patients' (poor HBA1c) and serum levels of ANGPTL8 were considerably higher than a female withT2DM patients with (good HBA1c). Furthermore, ANGPTL8 levels in the T2DM individuals was found to be favorably connected with age, BMI, and insulin. The negatively correlated with HDL, total cholesterol, and triglyceride in a group.

Summary Therefore, with a dual role in triglyceride metabolism and glucose homeostasis, elevated ANGPTL8 levels in obese type 2 diabetics provide a potential mechanism to explain hyperglycemia in these two conditions.

Our results showed a positive relationship between triglycerides and cholesterol and a negative relationship with ANGPTL8 [26], [27]. In animals lacking ANGPTL8 exhibited significantly lower TG [28].

Our research, show in the table.2, The present results showed that (poor HBA1c) for T2DM, high levels of TG, and ANGPTL8 were all significantly associated with risk of obesity in female patients. In addition, ANGPTL8 levels had the highest BMI and HBA1c risk among these parameters above, implying that ANGPTL8 could be a novel biochemical marker for T2DM. Although most other researchers have found a positive correlation between age, TG, and ANGPTL8 in healthy, unaffected subjects [2], [29], one work found that ANGPTL8 level was a positively related to age but not related to triglyceride level. It should be seen that there is a lack of association between ANGPTL8 level in blood and triglyceride level in healthy also age [30]. The inconsistencies are unknown from a cause, it is most likely due to differences in age groups, ethnicity, sample collection (serum vs. plasma), and sample size. Future study is needed to note this topic further.

Comparison of parameters in current study between overweight (BMI<30 kg/m2) and obesity (BMI>30 kg/m2) in T2DM patients

Results in the table .3, showed a significant increase (p=0.0001) in BMI only in obesity (BMI>30 kg/m2) group (37.98±3.36 kg/m2) in comparison with the overweight (BMI<30 kg/m2) group (29.90±2.35 kg/m2). There are no significant differences of interest between the two groups above for the rest of the parameters measured under this study.

Table 3. Comparison of parameters in current study between overweight (BMI<30 kg/m2) and obesity (BMI>30 kg/m2) in T2DM patients

Parameters	**Overweight (BMI<30 kg/m^2) N=34**	**Obesity (BMI>30 kg/m^2) N=26**	**p-value**
Age Yrs.	54.56±11.82	55.58±10.08	0.720
BMI kg/m^2	29.90±2.35	37.98±3.36	0.0001
ANGPTL8 (pg/dl)	4199.57±1101.62	4738.01±1209.89	0.077
FBG mg/dl	183.35±38.58	170.38±40.49	0.211
HbA1c %	10.56±2.41	11.12±2.71	0.403
Insulin (uIU/ml)	22.69±9.92	21.58±9.59	0.665
HOMA-IR	10.36±5.34	9.32±4.99	0.445
HOMA-B	64.41±7.63	66.97±6.74	0.802
HOMA-S	36.13±3.09	38.24±3.23	0.643
QUICKI	0.43±0.02	0.44±0.02	0.259
TC(mg/dl)	223.88±50.83	215.85±34.10	0.490
TG (mg/dl)	303.38±17.08	277.69±17.36	0.303
HDL-C(mg/dl)	35.44±8.05	37.91±7.36	0.221
LDL-C(mg/dl)	127.76±8.24	122.39±7.30	0.639
VLDL-C(mg/dl)	60.67±3.41	55.53±3.47	0.303

Highly significant(p-value < 0.0001); Non-significant (p-value ≥ 0.05) BMI: body mass index; ANGPTL8: Angiopoietin-like Proteins 8; FBG: fasting blood glucose; HbA1c: glycated hemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance; HOMA-β: homeostasis model assessment of β; QUICKI: Quantitative Insulin sensitivity Check Index; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; VLDL: Very low-density lipoprotein cholesterol.

In the current study, no association was observed in the fasting state between ANGPTL8 and triglycerides, whether in a disordered state of factors affecting glucose metabolism or due to BMI due to looking at the association between ANGPTL8

levels and lipids, ideally, we should note in the group of subjects enjoying the two characteristics. The following two are:

1- A relatively wide range of lipid profile values.

2- Without confounding factors, i.e. similar glucose levels and BMI.

When the women with T2DM patients were compared to the controls group, serum ANGPTL8 level was shown to be considerably increased in women patients. Furthermore, in table.3, the study found a positive association and strong between level of ANGPTL8 and HBA1C, also ANGPTL8 and insulin, the level of ANGPTL8 in blood was associated with higher triglyceride (TG) and total cholesterol (TC) in female patients, show in table.4, implying that ANGPTL8 level could be a novel biochemical markers for a women with T2DM.

Some studies have come to unsupportive conclusions, ie that T2DM is not associated with ANGPTL8 or decreased in T2DM, many studies support the conclusion that ANGPTL8 is increased in T2DM. More detailed data analysis showed that ANGPTL8 was significantly associated with insulin resistance, fasting blood glucose and HbA1c, and this supported the conclusion confirming the association between T2DM and ANGPTL8. However, our study showed in Table 3, that ANGPTL8 levels were significantly higher in subjects with T2DM, regardless of their weight and age, leading to the consideration that other associated factors may be related to the enrolled diabetic patients. In the study presented by Guo et al, it was shown that the concentration of ANGPTL8 in the blood of obese diabetic patients may need to be reduced.[21].

The correlation between biochemical markers and demographic characteristics of subjects.

The correlation analysis for ANGPTL8 level and other biochemical markers for the T2DM patients group was show in table(.4and 5), showed all results for ANGPTL8 level that only was a negatively significant determinant (r = -0.343; and r = -0.293), with TC and LDL. Serum ANGPTL8 levels a positively correlated with age, BMI, insulin, HBA1c, HOMA-IR, HOMA-B, QUICKI, and HDL in T2DM group. The negatively correlated with FBG, TC, TG,LDL, and VLDL for the T2DM patients group.

Table 4. Correlation between ANGPTL8 and all biochemical markers and demographic characteristics of subjects.

Parameters	**Correlation Coefficient with ANGPTL8 (pg/ml)**
Age (year)	0.211
BMI(kg/m2)	0.106
Insulin (µIU/mL)	0.090
HBA1C	0.028
FBG (mg/dl)	-0.166
HOMA-IR	0.001
HOMA-B	0.224
HOMA-S	-0.066
QUICKI	0.180
TC (mg/dl)	-0.343**
TG (mg/dl)	-0.158
HDL (mg/dl)	0.073
LDL (mg/dl)	-0.293*
VLDL (mg/dl)	-0.158

Correlation is significant at the 0.05 level.; Correlation is significant at the 0.01 level.

BMI: body mass index; ANGPTL8: Angiopoietin-like Proteins 8; FBG: fasting blood glucose; HbA1c: glycated hemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance; HOMA-β: homeostasis model assessment of β; QUICKI: Quantitative Insulin sensitivity Check Index; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; VLDL: Very low-density lipoprotein cholesterol.

Table 5. The correlation between the some biochemical markers and the demographic characteristics of subjects.

Parameter	**Age(year)**	**BMI(kg/m2)**	**ANGPTL8 (pg/ml)**	**HBA1C**	**Insulin (µIU/mL)**	**TC (mg/dl)**	**TG(mg/dl)**	**HDL(mg/dl)**
Age (year)	1	0.027	0.211	0.220	0.065	-0.312*	-0.313*	-0.011
BMI(kg/m2)		1	0.106	0.181	-0.074	0.009	-0.148	0.112
ANGPTL8 (pg/ml)			1	0.028	0.090	-0.343**	-0.158	0.073
HBA1C				1	0.157	0.246	-0.251	0.036
Insulin (µIU/mL)					1	-0.185	-0.024	0.036

TC (mg/dl)	1	0.284*	0.026
TG (mg/dl)		1	0.023
HDL (mg/dl)			1

**: Correlation is significant at the 0.01 level.

*: Correlation is significant at the 0.05 level.

BMI: body mass index; ANGPTL8: Angiopoietin-like Proteins 8; HbA1c: glycated hemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance; HOMA-β: homeostasis model assessment of β; QUICKI: Quantitative Insulin sensitivity Check Index; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol.

In women with T2DM, shown in Table 4, our current work and previous evidence showed that serum ANGPTL8 level is significantly and negatively associated with TG, and TC. [31], [32]. However, other studies were not find this significant association in T2DM [33]. This inconsistency could because some participants in other research have been treated with insulin and lowering drugs of triglyceride, which would affect blood triglyceride. When showing that triglycerides (TG) have played a role in mediating this strong relationship. Although ANGPTL8 has been linked to glucose and cholesterol metabolism [26], [28], in our findings revealed that there was nonsignificant association between HDL-C and ANGPTL8.

Previous studies have looked into the correlates among ANGPTL8, insulin resistance, and glucose metabolism[10], [34], [35]. Insulin resistance and hyperglycemia have long been thought to be risk factors for developing the diabetes mellitus disease [36]. Hu et al, discovered the ANGPTL8 was positively correlated with FBG in a newly diagnosed T2DM patients [17], and the results of this study and other study both proved the ANGPTL8 level was a positively correlated with IR in a novel diagnosed female with T2DM patients [21], [30]. However, nonsignificant correlations were identified in ANGPTL8, FBG, and HOMA-IR for treated T2DM patients in our investigation; our findings were consistent with Fenzl et alfindings.'s [37]. Therefore, it is hypothesized that the antidiabetic drugs may play a role in the correlation for ANGPTL8, glucose metabolism, and IR in T2DM. Lipid metabolism abnormalities have previously been correlate with a development of its, in addition to IR, and hyperglycemia [38].

T2DM shows hyperinsulinemia, hyperglycemia, and hypertriglyceridemia. In people without diabetes, nutrition raises blood sugar and this stimulates pancreatic insulin secretion, which leads to increased synthesis of triglycerides, glycogen and fatty acids within the liver and inhibits gluconeogenesis. IR is associated with failure to inhibit gluconeogenesis, but is associated with hypertriglyceridemia, rather than impaired TG synthesis. [39]–[41].

Because ANGPTL8 inhibits LPL and thereby suppresses TG clearance and increases TG [42], [43], the increased the ANGPTL8 in patients with T2DM play a task in explaining the hypertriglyceridemia in T2DM.

Our results showing that ANGPTL8 is increased in T2DM and its levels are positively correlated with FBG suggest that the glucose may play a task in control ANGPTL8 expression[1], [44], see the table.5. it's been well established that in a mice ANGPTL8 mRNA is induced by fed [27], [42]; According to the current observation because nutrition raises blood sugar. In previous studies, the prevalence of obesity has grown to an epidemic level and this obesity may be the main reason for the prevalence of T2DM because 85% of T2DM is due to obesity. [45]. A distinguishing indicator of obesity is elevated TG levels, as evidenced by both clinical trials [46]. It is well established that ANGPTL8 mainly contributes to the regulation of triglyceride metabolism [26], [28]. It has been shown that exposure of ANGPTL8 KO mice leads to low levels of TG in the blood and significantly increases their secretion of TG levels. [47], [48]. We also show here that ANGPTL8 is increased in obese cases, which leads to an increase in ANGPTL8 being also a co-factor in increasing TG levels in obesity.

Our work's limitations should as well as be discussed. First, the our research from addressing the correlation between obesity and ANGPTL8 level in a female with T2DM. Second, because our work's sample size is modest (especially in T2DM group) and there is no mechanistic basis, more work is needed to confirm our findings. Third, the link between a ANGPTL8 level and HBA1c could be due to more than one parameter (TC and TG level); more study is needed to identify additional potential mediator parameters. Fourth, our study do not the first to reveal that ANGPTL8 has a role in the progression of a female with T2DM; ANGPTL8 is significantly increased in type two diabetic with various stages of obesity [30], [49], in this work, we also highlighted the possible role of a TG, TC, LDL, and IR in the relationship between a ANGPTL8 level in blood and women with T2DM.

ANGPTL8 levels are directly and significantly correlated with HbA1c level, and not related to blood glucose during prolonged fasting or no eating. This result drew our attention to the fact that ANGPTL-8 may be related to the long-term glycemic control represented by HbA1c, as an alternative to the short-term glycemic control represented by FBG. It has been determined that HbA1c, may be a reliable measure of glycemic status and has a direct relationship with the incidence of diabetes-related complications as demonstrated by several previous studies. [49]. Penno et al. has shown that HbA1c can predict renal disorder with DM but do not retinopathy [50]. Hou etal., concluded in their study supported this observation and

considering the association between ANGPTL8 and HBA1c [51], The aspect of research examining the role of ANGPTL8 in predicting diabetes complications, in particular diabetic kidney disorder, can be addressed.

Conclusion

We discovered that ANGPTL8 level was considerably a higher in the women withT2DM patients; and, our findings revealed that a ANGPTL8 level was a positively connected for age, insulin, BMI, and FBG. ANGPTL8 level may play a role as an important biochemical markers in a women with T2DM, according to our findings.

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AUTHOR CONTRIBUTIONS

Manal F. AL-Khakani aided in the design and conception of the research, also, as the execution and planning of the statistical analysis. Aws Safaa Fadhel gave the data. The authors committed to being responsible for all parts of the research, including ensuring that any questions about the accuracy or integrity of any component of the study are handled and appropriately investigated.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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