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# The Effects of ANGPTL8 Levels and Correlated with Lipid Profiles and Insulin Resistance in Iraqi Patients with Overt and Subclinical Hypothyroidism

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**ABSTRACT**

Hypothyroidism is a disease that is characterized by abnormally low thyroid hormone production and excretion by the thyroid gland T3 , T4 ,these Hormones regulate the body's metabolism, Angiopoietin-like peptide-8 is a glycoprotein-structured adipokine synthesized in adipose tissue and the liver. It paly a role in energy metabolism by inhibiting lipoprotein lipase, the key enzyme in the hydrolysis of plasma lipoproteins. Also , thyroid hormones play an important role in energy metabolism, therefore, the aim of the present study was to explore serum Angptl8 and its correlation with lipid profile and insulin resistance in hypothyroidism patients .

A case control study comprised of 90 eligible participants were included and divided into three groups including (overt hypothyroidism group = 32 ),( subclinical hypothyroidism group =28 ), ( healthy group = 30 ). were age-matched to the patient . ranged from (20 – 50 yrs.) Also , included females, with 55.5% of the participants being female and 44.5% of the participants being male. To if serum ANGPTL8 levels were significantly higher in patients with overt and subclinical hypothyroidism compared with control group. The level of ANGPTL8 is an indicator risk of hypothyroidism when the level of ANGPTL8 rises, patients experience hypothyroidism complications.

The study's findings The means levels of the BMI, serum TSH, FSG, Insulin, TG, cholesterol, VLDL-C, LDL-C, and Angptl 8 and HOMA- IR were significantly higher in all hypothyroidism patients group , except in a sub clinical group HOMA-β have a non-significantly when compared with healthy control group .while The means levels serum of the T3 , T4 , TG, Tc, and Angptl 8 were higher significantly in overt hypothyroidism when compared with subclinical hypothyroidism as shown in in **table ( 1 ) ,** In overt hypothyroidism angiopoietin like 8 significant positive correlation with BML , TSH ,FSG ,insulin , HOMA IR , TC , LDL , VLDL and TG As وfor negative correlation HOMA-β and HDL.

while In sub clinical hypothyroidism angiopoietin like 8 significant (positive )correlation with FSG , TG ,T4 , LDL -C, and VLDL _Cو ,As for significant negative correlation with HDL.

**Conclusion :** serum circulating ANGPTL8 levels are increased in patients with hypothyroidism and associated with change in lipids profile and HOMA-IR. the elevated levels of ANGPTL8 in hypothyroidism especially in subclinical hypothyroidism patients high light their potential involvement , their potential role as predicator marker for metabolic disorder ,T2DM their role in regulating the activity of lipoprotein lipase , a key enzyme in metabolism of lipoprotein .

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***Key words :****overt and subclinical hypothyroidism disease Angptl8, HOMA IR. with Lipid profiles*

**Introduction :**

Hypothyroidism is characterized by the thyroid gland producing insufficient thyroid hormone. It can be primary (abnormality in the thyroid gland itself) or secondary/central (abnormality elsewhere in the body) (as a result of hypothalamic or pituitary disease). The term "subclinical hypothyroidism" refers to a type of primary hypothyroidism in which TSH levels are elevated despite normal serum free thyroxine (T4) and triiodothyronine (T3) levels. **(Usuda, Takagi et al. 2020).** In about 2–5% of cases each year, subclinical hypothyroidism progresses to overt hypothyroidism. TSH levels greater than 10mIU/L should be treated in all patients with overt hypothyroidism and subclinical hypothyroidism. Hypothyroidism manifests itself in a variety of ways, including neuropsychiatric issues like depression, memory and cognitive disorders, and poor motor coordination,. It is more common in older people, especially women, with a 10% overall incidence. **(Khandelwal and Tandon 2012)** . Obesity is associated with hypothyroidism. However, it is debatable whether they are causally linked. Overt hypothyroidism is associated with slight weight gain, but subclinical hypothyroidism is unknown. Changes in thyroid-stimulating hormone (TSH) may be secondary to obesity, according to a new theory. **(Sanyal and Raychaudhuri 2016).** Hypothyroidism has numerous etiologies and manifestations. The most common clinical manifestations are weight gain, hair loss, cold intolerance, lethargy, constipation, dry skin, and voice change. The signs and symptoms of hypothyroidism differ according to age, gender, severity of the condition, and a few other factors. **(Alam, Quamri et al. 2020)** If left untreated, hypothyroidism increases morbidity and mortality. Patients with DM-II were at increased risk of developing hypothyroidism (**Alsolami, Alshali et al. 2018)** High prevalence of overt hypothyroidism can lead to hyperlipidemia, which could be accountable for the increased risk of coronary artery disease (CAD) **(Grais and Sowers 2014)**.The most common cause of hypothyroidism is autoimmune thyroid disease (Hashimoto thyroiditis), but a lack of iodine in the diet is the most common cause worldwide. ,Simple blood tests can now be used to diagnose hypothyroidism, which can then be treated with exogenous thyroid hormone. **(Patil, Rehman et al. 2020).** Angiopoietin-like proteins (Angptls) share protein domains with angiopoietins, a secreted glycoprotein family expressed in the liver. The Angptls family is subdivided into eight subtypes, Angptl1–8. Angptl3, Angptl4, and Angptl8**(Kersten 2017).,(Ren, Kim et al. 2012).** lipoprotein lipase (LPL) physiological inhibitors that play an important role in lipoprotein and triglyceride metabolism in response to nutritional cues. ANGPTL8 has been given various names in different studies and has been assigned various functions at the systemic and cellular levels **(Abu-Farha, Ghosh et al. 2020)**. in addition to its role in beta cell proliferation, ANGPTL8 influences the lipid profile by regulating VLDL secretion from the liver, inhibiting lipoprotein lipase activity, and interacting with angiopoietin like protein 3. (ANGPTL3) **(Yi, Park et al. 2013).**

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## Materials and Methods:

**Subjects**: the study was designed as a case-control It was performed in specialized center for endocrinology and diabetes at Al sadr Medical City in Al-Najaf province Iraq during the period from October 2020 and February 2021, in formation of histories of subjects were taken anthropometric measurements included (Ages , gender weight , height and body mass index ) . hormonal parameters were evaluated ,The study included 90 subjects sixty patients who were dignsed as having overt and subclinical hypothyroidism and healthy individuates aged between (20 – 50 years) divided into three groups: 32 diagnosed overt hypothyroidism(OH) patients, 28 subclinical hypothyroidism (SCH )patients, and thirty healthy adults as the control group. Diagnosis of patients OH ,SCH hypothyroidism was made on the basis of TSH levels higher than the normal range and values of T4 , T3 were defined as subclinical patients with higher serum TSH and low serum T4 and T3 levels were defined as overt hypothyroidism . patients with history of thyroidectomy and cancer anemic or has an obvious systemic disease or any chronic diseases. Among the taking any drug that could possibly affect lipid metabolism were excluded from the study.

The Body mass index (BMI) was calculated by dividing an individual's weight in kilograms by their height in meters2: BMI = (weight in kg) / (height in meters2) (Nuttall 2015). After 12 hours of fasting, samples were obtained by venipuncture and collected into tubes. Centrifugation at 3000 Xg for 15 minutes at 4o °**C** yielded serum, which was separated and stored at -20 °**C** until use. ELISA KIT( Melsin Medical Co Company, China) was used to measure serum Thyroid stimulating hormone (TSH), total triiodothyronine (T3), total tetraiodothyronine (T4), Angptl8, and insulin . While , The enzymatic method was used to determined Fasting serum glucose levels HDL, total cholesterol, and triglycerides (kits BIOLABO , France) The insulin resistance index (HOMA-IR, Homeostatic model assessment-insulin resistance) was estimated as follows: HOMA IR = [glucose (mg/dl) * insulin (U/ml) / 405 HOMA percentage =360 insulin/ ( Glucose - 63) (**DeUgarte, Bartolucci, et al. 2005).** Low density lipoprotein cholesterol (LDL-C) was measured by the indirect method using Friedewald equation(Friedewald, Levy et al. 1972).

LDL-C= total cholesterol – (HDL-cholesterol + VLDL cholesterol).

LDL-C = total cholesterol - (HDL-cholesterol + TG/5)

## Statistical Analysis:

Statistical Evaluation. For normally distributed variables, means and standard deviations (S.D.) were used; for nonnormally distributed variables, medians with interquartile ranges were used; and for categorical variables, frequencies were used.Normally distributed variables were compared among study groups using one-way ANOVA, followed by Bonferroni correction in paired comparisons. Variables that failed the normality test were assessed using Kruskal-Wallis one-way ANOVA for ranks in groups and the Mann-Whitney rank sum test for pairwise comparisons. Pearson's Chi-square test was used to compare sex ratios, and Pearson correlation or Spearman rank correlation analysis was used for correlation analysis. Multiple linear regression analyses were run to identify independent relationships and to account for the effects of covariates.). All P values calculated were two-sided, and P values less than 0.05 were considered statistically significant. SPSS software was used for all statistical analyses (version 20.0).

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## Results

In table 1, the base line characteristics of the study are presented. That included the data of study groups compared between patients with OH, SCH, and healthy controls : Age, sex were not different. ,The means levels of the FSG , insulin ,BMI, serum TSH, FSG, Insulin, TG, cholesterol, VLDL-C, LDL-C, and Angptl 8 and HOMA- IR were higher significantly in all hypothyroidism patients group , except sub clinical group the HOMA-β index has a non-significantly difference when compared with healthy control group .while The means levels serum of the T3 , T4 , TG, Tc, and Angptl 8 were higher significantly in overt hypothyroidism when compared with subclinical hypothyroidism group.

**Table 1: Clinical parameters compared means between patients (overt and subclinical hypothyroidism groups )with control group**

| **Parameters** | **Control group1 No=30 Mean±SD** | **Patients No =60** | | **P_value** |
|---|---|---|---|---|
| | | **OH group 2 No=32 Mean±SD** | **SCH group 3 No=28 Mean±SD** | |
| Total Age (yrs )<br>Age: males<br>Age: Females | 35.314± 4.500<br>37.125± 5.00<br>33.503± 4.00 | 35.066± 5.000<br>36.123± 6 .000<br>34.010± 4.00 | 36.010± 2.15<br>38.008±2.10<br>35.012±2.2 | _____ |
| **Sex F/M** | 15 /15 | 20 /12 | 15 /13 | _____ |
| BMI ($Kg/m^2$ ) | 23.023± 1.448 | 27.72±1.58 | 26.210± 1.180 | $^{a}p = 0.000$<br>$^{b}p = 0.000$<br>$^{c}p = 0.05$ |
| SBP ( mmHg )Total | 120 ± 0.28 | 127±0.32 | 123± 0.53 | $^{a}p = 0.000$<br>$^{b}p = 0.000$<br>$^{c}p = 0.000$ |
| DBP ( mmHg) | 80 ± 1.5 | 86± 1.9 | 84± 2.11 | $^{a}p = 0.000$<br>$^{b}p = 0.000$<br>$^{c}p = 0.000$ |
| **TOTAL T3 nmol/l** | 1.533±0.507 | 0.766± 0.430 | 1.033± 0.182 | $^{a}p = 0.000$<br>$^{b}p = 0.000$<br>$^{c}p = 0.011$ |
| **TOTAL T4 nmol/l** | 85.233±26.23 | 42.766± 42.766 | 71.517± 6.092 | $^{a}p = 0.000$<br>$^{b}p = 0.01$<br>$^{c}p = 0.000$ |

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| | | | | |
|---|---|---|---|---|
| **TSH µIU/ml** | 2.466±1.008 | 18.366±18.555 | 12.800±5.880 | [a]p = 0.000<br>[b]p =0.001<br>[c]p =0.058 |
| FSG (mg/dL) | 89.666±7.94 | 111.76± 12..040 | 107.233±11.58 | [a]p = 0.000<br>[b]p =0.000<br>[c]p =0.071 |
| Insulin(µU/ mL) | 7.066± 2.765 | 13.366± 3.518 | 12.733± 3.117 | [a]p = 0.000<br>[b]p =0.000<br>[c]p =0.438 |
| HOMA IR | 1.549±0.605 | 3.969±1.028 | 2.960±1.038 | [a]p = 0.000<br>[b]p =0.000<br>[c]p =0.222 |
| HOMA-β | 156.050±35.425 | 111.045±35.150 | 110.74±31.670 | [a]p = 0.01<br>[b]p =001<br>[c]p =0.31 |
| TG (mg/dl) | 113.740±32.03 | 188.327±32.35 | 171.473±33.45 | [a]p = 0.000<br>[b]p =0.000<br>[c]p =0.048 |
| TC (mg/dl) | 187.449±25.624 | 221.74± 24.03 | 210.148±38.855 | [a]p = 0.000<br>[b]p =0.042<br>[c]p =0.07 |
| LDL-C (mg/dl) | 117.66±10.472 | 135.568±34.896 | 130.962±22.898 | [a]p = 0.000<br>[b]p =0.000<br>[c]p =0.305 |
| VLDL-C (mg/dl) | 29.09±7.541 | 41.580±13.323 | 34.293±6.693 | [a]p = 0.004<br>[b]p =0.04<br>[c]p =0.348 |
| HDL-C (mg/dl) | 38.933± 7.342 | 22.433± 7.463 | 23.700± 6.292 | [a]p = 0.000<br>[b]p =0.000<br>[c]p =0.438 |
| angiopoietin like 8( ng/mL) | 6.089±1.028 | 9.800± 2.62 | 7.625±1.795 | [a]p= 0.001<br>[b]p=0.037<br>[c]p =0.04 |

[a]p =significantly difference between values in group 2 and group 1. [b]p =significantly difference between values in group 3 and 1. [c]p =significantly difference between values in group 3 and 2 BMI: body mass index, , FBG: fasting blood glucose, HOMA-IR: hemostasis model assessment-Ins resistance assessment, HOMA-β%: hemostasis model assessment-beta cell percentage. TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low-density lipoprotein-cholesterol, Data represented as Mean ±SD: standard deviation,

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NS= non- significantly differences at (P>0.05). *=significantly differences at (P≤ 0.05, ,OH :OVERT hypothyroidism , SCH : subclinical hypothyroidism No: number patients

The results of the correlation analysis between serum Angptl8 levels and other parameters are summarized in table 2 and figure 1. There was a positive correlation between betatrophin levels with participants, they are BMI ,TSH, FSG , insulin ,HOMA-R ,TG , ,LDL-C ,VLDL-C and TC. A negative correlation was found between Angptl8 levels of with participants and total T3, T4 , HOMA-β and HDL serum levels

***Table 2: The Univariate Analysis of serum angiopoietin like 8 level chemerin with the Investigated Parameters in the Enrolled Patients(overt hypothyroidism)***

| Parameters | r | P-Value |
|---|---|---|
| Age ( years) | 0.082 | 0.437 |
| BMI ($Kg/m^2$ ) | 0.618 | 0.000 |
| TOTAL T3 nmol/l | -0.336 | 0.001 |
| TOTAL T4 nmol/l | -0.488 | 0.001 |
| TSH µIU/ml | 0.314 | 0.002 |
| FSG (mg/dL) | 0.583 | 0.001 |
| Insulin(µU/ mL) | 0.391 | 0.001 |
| HOMA IR | 0.460 | 0.001 |
| HOMA-β | -0.261 | 0.012 |
| TG (mg/dl) | 0.478 | 0.001 |
| TC (mg/dl) | 0.347 | 0.001 |
| LDL-C (mg/dl) | 0.333 | 0.001 |
| VLDL-C (mg/dl) | 0.348 | 0.001 |
| HDL-C (mg/dl) | -0.259 | 0.013 |

p-vale =significantly difference between values in group(OH) 2 and group (CONTROL) 1.Thyroxine (T4) , tri-iodothyronine (T3) and Thyroid Stimulating Hormone (TSH) ,OH :OVERT hypothyroidism , FSG: fasting serum glucose,: HOMA-IR: hemostasis model assessment-insulin resistance, HOMA-.β%: hemosta- sis model assessment-beta cell percentage,, TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol VLDL.C: Very Low-Density Lipoprotein- Cholesterol, TC: total cholesterol

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in Table 3, the following the a positive correlation significantly are found between serum Angptl8 levels and other parameters are FSG , TG , LDL-C and VLDL-C وWhile A negative correlation was found between Angptl8 levels of with participants and TSH HOMA-β and HDL serum level

**Table 3:** ***The Univariate Analysis of serum angiopoietin like 8 level chemerin with the Investigated Parameters in the Enrolled Patients(subclinical hypothyroidism)***

| Parameters | r | P-Value |
|---|---|---|
| Age ( years) | 0.036 | 0.847 |
| BMI ($Kg/m^2$ ) | 0.296 | 0.112 |
| TOTAL T3 nmol/l | 0.0416 | 0.8269 |
| TOTAL T4 nmol/l | 0.028 | 0.881 |
| TSH µIU/ml | -0.122 | 0.5193 |
| FSG (mg/dL) | 0.3439 | 0.029 |
| Insulin(µU/ mL) | 0.029 | 0.874 |
| HOMA IR | 0.128 | 0.498 |
| HOMA-β | -0.0877 | 0.644 |
| TG (mg/dl) | 0.404 | 0.026 |
| TC (mg/dl) | 0.325 | 0.079 |
| LDL-C (mg/dl) | 0.367 | 0.045 |
| VLDL-C (mg/dl) | 0.405 | 0.026 |
| HDL-C (mg/dl) | -0.388 | 0.033 |

p-vale =significantly difference between values in group(SCH) 3 and group (CONTROL) 1. , Thyroxine (T4) , tri-iodothyronine (T3) and Thyroid Stimulating Hormone (TSH) ,SCH :Subclinical hypothyroidism , FSG: fasting serum glucose,: HOMA-IR: hemostasis model assessment-insulin resistance, HOMA-.β%: hemosta- sis model assessment-beta cell percentage,, TG: triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: low density lipoprotein-cholesterol VLDL.C: Very Low-Density Lipoprotein- Cholesterol, TC: total cholesterol

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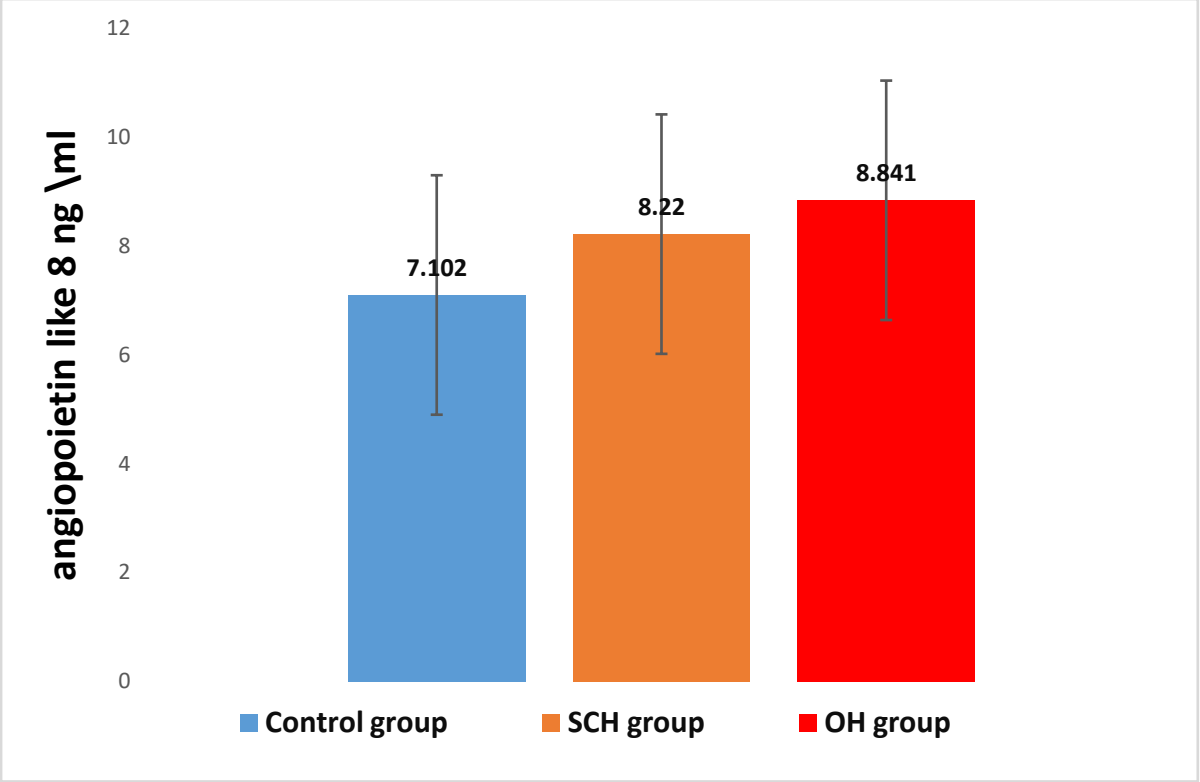


**Figure (1) Comparison of Angiopoietin like 8 levels means between overt , subclinical hypothyroidism Patients and Control Groups.**

**Discussion:**

Hypothyroidism have an underactive thyroid and the thyroid does not make enough thyroid hormone to keep the body normally ,but Low thyroid hormone levels cause the body's functions to slow down leading to general symptoms like fatigue , and loss of energy and consider of the one of most common diseases in women than men , and much more so in young women than young men . the risk of hypothyroidism is more develop at any age the risk for developing it increases with age (**Shankar,zhang etal 2020** ) . presentation of thyroid dysfunction is non-specific and often variable; therefore, the diagnosis of thyroid dysfunction is based primarily on biochemical abnormalities. The pituitary hormone thyrotropin (TSH) has a complex inverse relationship with the thyroid hormones thyroxine (T4) and tri-iodothyronine (T3) **(Leng and Razvi 2019).**

A negative feedback mechanism exists between TSH and thyroid hormones, which means that TSH levels are the most sensitive marker of thyroid status in an individual **(Hadlow, Rothacker et al. 2013).** Accordingly, overt hypothyroidism is defined as serum TSH concentrations above the reference range with low free T4 levels, while subclinical hypothyroidism is diagnosed when TSH levels are high and circulating T4 is normal **(Brown, Bremner et al. 2016)** .Thyroid hormones have well-known effects on carbohydrate metabolism, including insulin resistance (IR), which is caused by both hyperthyroidism and hypothyroidism **(Răcătăianu, Leach et al. 2017)**. Hypothyroidism, either Subclinical or overt hypothyroidism has been associated with increased risk of coronary artery disease **(Sun, Chen et al. 2020)** Insulin resistance is a state of glucose homeostasis in which insulin

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produces a less than expected biological effect at the liver, muscle, adipose tissue, and other body tissues **(Chen, Wu et al. 2016)**. insulin resistance (IR) is a key and early pathogenetic mechanism of cardiometabolic diseases, with a huge potential for disease burden reduction if detected and mitigated early **(Štěpánek, Horáková et al. 2021)** .

In the Current study have found that patients with SCH and OH have higher serum insulin levels than healthy subjects. Insulin resistance is a diabetes and cardiovascular disease risk factor that is defined as a condition in which the cells' response to insulin is impaired. An increased insulin resistance index in hypothyroid patients is very important, as is an increased risk of diabetes and metabolic syndrome in these patients **(Ebrahimpour, Vaghari-Tabari et al. 2018),** HOMA IR and insulin, Hypothyroidism is the second most common endocrine disease, affecting 5% of the global population, primarily females and those over the age of 70. The presence of high serum TSH levels, which indicate insufficient thyroid secretion, is required for the diagnosis of primary hypothyroidism **(Chen, Deng et al. 2020)**. Participants with SCH and OH have significantly higher LDL-C and lower HDL-C levels than the control group, there was significantly between the prevalence of dyslipidemia in hypothyroidism regardless of age or gender (P-value 0.000), but no difference in TC levels in patients group. Dyslipidemia is considered one of the most important cardiovascular risk factors in hypothyroidism **(Saif, Mousa et al. 2018).**

Triglycerides (TGs) are one of the most important substrates for energy supply. Compared to carbohydrates and proteins, TGs have lower metabolic cost **(Wilde and Chu 2011)** . Therefore, synthesis and storage of TGs are particularly important to maintain the body's energy balance. Lipoprotein lipase (LPL) is a key rate-limiting enzyme in catalyzing hydrolysis of circulating triglyceride in chylomicrons CM) and very-low-density lipoprotein (VLDL,( the major forms of triglycerides in plasma (Li 2006). Genetic and functional studies have shown that ANGPTL3, ANGPTL4, and ANGPTL8 play important roles in the regulation of LPL activity **(Dijk and Kersten 2016)** .ANGPTL8 (also called RIFL, lipasin, and betatrophin( consists of 198 amino acids and is about 22 kDa in size **(Ren, Kim et al. 2012)** .Here, we report that circulating Angptl8 was significantly increased in the OH and SCH groups compared to the control groups. In addition, we observed that serum betatrophin level was increased in correlation with increased severity of hypothyroidism (with increased TSH and decreased total T4). Also, serum Angptl8 concentrations were independently associated with TSH and TG. Since the incidences of metabolic diseases are increasing rapidly, more and more research interests are focused on **(Liu, Han et al. 2015)them (Zhang, Guo et al. 2013)**

ANGPTL8 and lipid profile. Fenzl's group suggested that betatrophin was positively correlated with atherogenic lipids in 19 morbidly obese individuals and 18 type 2 diabetic individuals **(Fenzl, Itariu et al. 2014)** . Hence, it is believed that betatrophin may have a dual role in mediating both triacylglycerol metabolism and glucose homeostasis and may have effects on multiple metabolic diseases. It has been well established that overt hypothyroidism is associated with metabolic syndrome such as atherosclerotic cardiovascular disease, obesity, insulin resistance/diabetes, and dyslipidemia **(Han, He et al. 2015).** However, subclinical hypothyroidism is relatively more common, occurring in 4–

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10% of the adult population **(Biondi and Cooper 2008**). In addition, it is estimated that 1 to 11% of all patients with dyslipidemia have subclinical hypothyroidism **(Pearce 2012)** .

ANGPTL8, are associated with increased plasma lipid content due to their role in regulating the activity of lipoprotein lipase, a key enzyme in metabolism of the lipoprotein in circulation. Dyslipidemia is a risk factor for hypertension development and in the present data shown that serum Angptl8 levels are elevated in overt and subclinical hypothyroid Iraqi patients and that Angptl 8 may serve as potential biomarkers of hypothyroid disease, Angiopoietin-like proteins (Angptls) also play important roles in biological processes, particularly lipid metabolism. The thyroid's functional state has a significant impact on human metabolism. As a result, the purpose of this study was to look into possible changes in serum Angptl 8 levels in hypothyroid patients, Triglyceride (TG) metabolism is regulated, among other things, by lipoprotein lipase (LPL), which hydrolyzes TGs on endothelial cells. In turn, the ANGPTLs family of proteins, such as ANGPTL8, inhibit LPL **(Yang, Yin et al. 2019) (Catalano-Iniesta, Sánchez Robledo et al. 2020).** the reason for elevated betatrophin in subjects with overt hypothyroidism and subclinical hypothyroidism is still unclear. Consistent with our study, many epidemiological studies demonstrated that subclinical hypothyroidism may worsen the serum lipid profiles. TG levels were found with higher levels in subclinical hypothyroid subjects than in euthyroid subjects in a study among 25,862 participants in Colorado **(Canaris, Manowitz et al. 2000).** Serum ANGPTL8 level negatively correlated with LPL levels in healthy Japanese adults. Regulation of ANGPTL8 could be a promising therapeutic target for **hypertriglyceridemia (Yamada, Kusaka et al. 2018)** .

The involved in hypothyroidism. Elevations in the LPL inhibitors apoC-III and ANGPTL8 may contribute to hypertriglyceridemia in lipodystrophy and may mediate metre leptin-induced reductions in circulating and hepatic triglycerides. As a result, these patients are excellent candidates for therapies to lower triglycerides (**Lightbourne, Wolska et al. 2020)** . ANGPTL8 level showed no correlation with body mass index (BMI), waist-hip ratio, and homeostasis model assessment of insulin resistance (HOMA-IR) or with adipose tissue-derived adiponectin and leptin levels. Further, ANGPTL8 showed no association with glucose and insulin levels after 75-g OGTT **(Yamada, Kusaka et al. 2018)**.

**Conciusion** : In the present study found a high prevalence of metabolic dysfunctions in patients with hypothyroidism Hence , screening for glycemic indices, ANGPTL8 levels and considering the relation ship between should preformed routing so as to recognize these dysfunctions to cause T2DM and CVDs early to help in improving the quality of life and reducing the morbidly rate in them and may give promising results as a therapeutic target .

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**Declaration of interest:**

The authors have no conflict of interest to declare

**ETHICAL CLEARANCE**

The Research Ethical Committee at scientific research by ethical approval of both environmental and health

and higher education and scientific research ministry in Iraq

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