

# Evaluation of Thyroid Dysfunction in Type 2 DM in Duhok Governorate

## SEFAR MOHAMAD AL HAJ \*, BAYAR AHMED QASIM \*\*.

## Abstract Background and Objectives

Thyroid diseases and Diabetes are the most common endocrinal disorders seen in clinical practice. As a result it is common for an individual to be affected by both thyroid diseases and diabetes. Most studies show increased incidence of thyroid dysfunction in type 2 DM than general population. The unrecognized thyroid dysfunction not only worsens the metabolic control but also impede the management of diabetes.

The aim of this study is to estimate the frequency and characteristics of thyroid dysfunction among type-2 diabetic patients in Duhok Governorate.

## **Patients and Methods**

The study population consisted of a total 101 randomly sample Type II diabetic patients from 1st January to 30th November 2013 at Duhok Diabetic center .The patients were interviewed and examined, and their blood samples taken for lipid profiles, Thyroid function tests and at least 2 fasting blood sugars were checked .

## Results

The study population consisted of a total 101 Type II diabetic patients (33 males and 68 females) with mean age of  $53.73 \pm 9.07$  and  $51.97 \pm 11.93$  respectively. 74 out of 101 patients were euthyroid. The remaining 27 patients had thyroid dysfunction. Subclinical hypothyroid being commonest 14.9% followed by overt hypothyroidism constituting 7.9%.

## Conclusions

Thyroid dysfunction is common among Type 2 DM and it is more common in females than males. Of thyroid dysfunction subclinical hypothyroidism was the most common type followed by overt hypothyroidism.Dyslipidemia was significantly higher in hypothyroid group than euthyroid group specifically athergenic LDL. Glycemic control was poor significantly in hypothyroid and hyperthyroid groups than euthyroid so unidentified thyroid dysfunction could negatively impact glycemic control.

## Key words

Thyroid, Diabetes

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#### Introduction

Thyroid diseases and Diabetes are the most common endocrinal disorders seen in clinical practice <sup>1</sup>.Diabetes is an important health problem affecting major population worldwide<sup>2</sup>. The prevalence of diabetes is increasing rapidly; the WHO has predicted, the number of adults with diabetes will have almost doubled worldwide from 285 million in 2000 to 435 million by 2030, with the greatest increase in developing countries such as India and China. The life time risk of developing diabetes is 1 in 10, with most cases being diagnosed after age of 40 years <sup>3,4</sup>. It is common for an individual to be affected by both thyroid diseases and diabetes <sup>5</sup>. The first reports showing association between diabetes and thyroid dysfunction was published in 1979 6. Since then a number of studies have estimated the prevalence of thyroid dysfunction among diabetes patients to be varying from 2.2 to 17%. The most common disorder being subclinical hypothyroidism. However, few other studies have also estimated much higher prevalence of thyroid dysfunction in diabetes e.g 31% and 46.5% <sup>5</sup>. Thyroid function tests are especially recommended in patients with clinical suspicion and / or unexplained changes in diabetic metabolic control or serum cholesterol and weight gain because thyroid dysfunction can produce significant metabolic disturbance <sup>5,7</sup>. The treatment of hypothyroidism helps better control of other associated `conditions 5. so American association of clinical endocrinologists(AACE) 2002<sup>8</sup> and American Thyroid Association(ATA) guidelines for detection of thyroid dysfunction<sup>9</sup> recommend ((Thyroid palpation and TSH at diagnosis and at regular intervals))<sup>10</sup> while the British Thyroid Association(BTA) and Association of Clinical Biochemistry Guidelines, 2006<sup>11</sup> recommend TFT at the time of diagnosis of DM.

Diabetes may affect the thyroid function to variable extent and undiagnosed thyroid dysfunction worsens the metabolic control and impede the management of diabetes. Studies have suggested that type 2 diabetic patients with subclinical hypothyroidism are at risk of complications like nephropathy and cardiovascular events. Therefore, diabetic patients need to be screened for thyroid dysfunction <sup>12</sup>.

## Effect of Thyroid hormone (TH) on glucose Metabolism

Thyroid hormones can produce different effects on metabolism of glucose. These effects include changes in insulin levels, counter regulatory hormones, absorption of carbohydrates, gluconeogenesis and glucose utilization by peripheral tissues<sup>13</sup>. TH act differently in liver, skeletal muscles and adipose tissue, these are the main targets of insulin action. In the liver, TH antagonizes insulin action by stimulating gluconeogenesis and glycogenolysis <sup>14,15</sup>. on the other hand they act synergistically with insulin in peripheral tissues by increasing expression of GLUT4 and thus increase glucose utilization figure 1<sup>16,17</sup>.

#### Effect of Thyrotoxicosis on glucose metabolism:

Thyrotoxicosis associated with impaired glycemic control in diabetic patients both FPG and postprandial glucose secondary to increased intestinal absorption of glucose and increased gluconeogenesis.while it is associated with increased glucose uptake by peripheral tissues <sup>18</sup> figure 2. Insulin levels in thyrotoxicosis could be normal ,increased or decreased <sup>19,20</sup>.the major cause of poor glycemic control in thyrotoxic diabetic patients is secondary to beta cell apoptosis induced by high levels of TH as suggested by recent studies <sup>19,21</sup>.

Effect of Hypothyroidism on glucose metabolism:

In hypothyroid diabetic patients there is decrease in gluconeogenesis and glycogenolysis ,in addition to decrease in intestinal glucose absorption and result in decrease in hepatic glucose production and resulted in decrease in plasma glucose level figure 3<sup>22,23</sup>.Decrease in insulin levels accounts for better beta cell function .on the other hand there is decrease in peripheral tissue uptake of glucose reflecting a decrease in GLUT4 expression <sup>13</sup> figure 3.

### Effect of Subclinical Hypothyroidism on glucose metabolism :

Insulin resistance has been reported in subclinical hypothyroidism <sup>24</sup>. This may explain increased cardiovascular risk in subclinical hypothyroidism. The presence of hypothyroidism is particularly risky if associated with insulin resistane(IR).In both diabetic and nondiabetic hypothyroid patients ,the presence of IR associated with more astherogenic effect on lipid profile than in absence of IR <sup>25,26</sup> (figure 4).

## **Patients and Methods**

This cross sectional study was conducted at Diabetes Center in Duhok City from January 2013 to November 2013 .The majority are outpatients attending the diabetes center . All patients were already diagnosed and registered. The study population consisted of a total 101 Type II diabetic patients (33 males and 68 females) with mean age of  $53.73\pm$ 9.07 and  $51.97\pm11.93$  respectively. Randomly selected diabetic patients were subjected to biochemical evaluation. The diagnosis of DM was based on American Diabetes Association(ADA) criteria for diagnosis of type 2 DM(2011) table 1 <sup>27</sup>. If they are asymptomatic the tests done on 2 separate occasions.

Inclusion criteria include presence of at least one of the ADA criteria for diagnosis of Diabetes mellitus on two separate occations. All patients currently or previously were on oral hypoglycemic agents.

Exclusion Criteria include any factors alter TFT <sup>28</sup> these are; pregnancy as increase in TBG production by liver leads to increase in total T4 ,Drugs like estrogen-containing oral contraceptives ,amiodarone ,phenytoin and steroids, liver and renal disorders ,previous Thyroid disorders or family history of thyroid diseases,smoking,History of recent surgery as concentration of total and free T3 decreases after surgery and returns to normal after several days <sup>29</sup> and History of acute illness as critical illness is often associated with alterations in thyroid hormone concentrations in patients with no previous intrinsic thyroid disease <sup>30-32</sup>

The following guidelines for detection of thyroid dysfunction were considered 4 ;euthyroidism ,when T3, T4 and TSH were within the reference range. Primary hypothyroidism ,when TSH is more than 5.0 mIU//L and, T3, T4 are less than the reference range. Primary hyperthyroidism , when TSH is less than 0.3 mIU/L and T3, T4 are more than reference range. Subclinical hypothyroidism , when TSH is more than 5.0 mIU/L and T3, T4 are at the lower end of the reference range. Subclinical hyperthyroidism ,when TSH is less than 0.3 mIU/L and T3, T4 are at the upper end of the reference range.

Dyslipidemia cut points based on AACE guidelines <sup>33</sup> which include; total cholesterol: desirable < 200 mg/ dl, Borderline high 200- 239, High > 239 mg/dl.High density lipoprotein -cholesterol: dyslipidemic Low < 40 mg/dl in males, < 50 mg/dl in females.Low density lipoprotein -cholesterol: Optimal < 100 mg/dl, near optimal 100–129 mg/dL, Borderline high 130-159 mg/dl, High 160 -189 mg/dl, very high > 189 mg/dl.Triglyceride: Normal < 150 mg/d, High 150-199 mg/dl, Hypertriglyceridemic 200-499 mg/dl, very high > 499 mg/dl. The Glycemic control(GC) was assessed by the average values of 2 readings of their fasting plasma glucose(FPG) levels at least 6 weeks apart in the last 3 months .The GC graded according to ADA criteria as "good" if FPG  $\leq$  130 mg/dl and "poor" if FPG >130  $mg/dl^{34}$ .

A specially-designed questionnaire was used to obtain information from participants.Information include gender,age,weight (recorded to nearest kilogram using an electronic scale)and height ((recorded to the nearest centimeter using the Center of Disease Control (CDC) measuring board)) and residence .Data on personal health including family history of thyroid diseases, history of chronic illnesses, mode of diabetes treatment, and any other drugs patient currently receiving it.All participants underwent a routine medical history & physical examination including examination of thyroid gland as clinically relevant.

For analysis, the height and weight measurement for each subject was used to calculate the BMI as a weight (Kg) divided by height (m2). Subjects with BMI 18.5-24.9 were consider normal, while those with BMI 25-29.9 were considered overweight and those BMI  $\geq$  30 were considered obese <sup>35</sup>.Participants were instructed to attend the Lab-unit of Diabetes center in the morning after overnight fasting for 12-14 hours and avoiding heavy physical activity for more than 2 hours before the examination. Then the serum was processed immediately for measuring serum TSH,total T4, total T3,cholesterol, serum TGs, HDL-Ch, blood sugar by clinical chemistry analyzer Lisa.Xs (open,automated,discreate,random access).Two readings of TFT done on separate occasions in cases of abnormal initial result.

All data were analyzed using the Statistical Package for Social Science (SPSS); paired student t- test was calculated to assess differences in serum analyte among groups. Significance of association between various risk factors was assessed using Chi-square test. Level of statistical significance was set at < 0.05

#### Results

The median age of participants was 52.54±11 .Females constitutes around two thirds of the study sample. 76% of participants were overweight (figure 6) .51% of participants had poor glycemic control and 45.5% were dyslipidemic.74 out of 101 patients were euthyroid. The remaining 27 patients had thyroid dysfunction. Subclinical hypothyroid being the commonest(14.9%) followed by overt hypothyroidism constituting 7.9%(Figure 5). 81.2% of patients were taking oral hypoglycemic agents as shown in (table 2 and figure 7). Regarding the gender difference of participants; the average BMI in females was slightly higher in the average in males (30.77kg/m2 vs. 30.55 kg/m2). Average HDL cholesterol level in females was significantly higher than the average HDL cholesterol level in males (49.34 mg/dl vs. 41.96 mg/dl, p = 0.002)this reflect the difference in normal range between both gender . Mean fasting blood sugar was slightly higher in females than in males (146.03 mg/dl vs. 144.72mg/dl). Average TSH level was slightly higher in females than in males (6.57 nmol/L vs. 4.65 nmol/L) as shown in table 3.

There was significant difference between euthyroid and hypothyroid groups regarding both Dyslipidemia and GC (P value < 0.001 and <0.014 respectively) table 4 .Those patients with hypothyroid have significantly higher average LDL and total cholesterol than those with Euthyroid (p < 0.001, 0.034 respectively). FBS was higher in hypothyroid than euthyroid group but p value was 0.087 which is not significant, that is to the fact some FBS readings were very high in euthyroid group. There was no significant difference between both groups regarding Age and BMI(P value 0.855 and 0.076 respectively). Mean TSH level was significantly higher in subjects with hypothyroid than those with Euthyroid (19.14 nmol/L vs. 2.15 nmol/L, p < 0.001). Average total T4 level was significantly lower in those with hypothyroid than those with Euthyroid (64.14 nmol/L vs. 86.62 nmol/L, p < 0.001). Also average total T3 level was significantly lower in those with hypothyroid than those with Euthyroid (1.07nmol/L vs. 1.48 nmol/L, p < 0.001)as shown in table 5. Poor glycemic control (GC) and Dyslipidemia in both Subclinical hypothyroid and overt hypothyroid groups in comparison with euthyroid group .Hypothyroid group were mainly females. While overt hyperthyroid and subclinical hyperthyroid groups show poor glycemic control (GC) and no dyslipidemia in comparison to euthyoid group as shown in table 6. The frequency of hypothyroidism does not increase with increase in the age and it was statistically not significant (p value = 0.075) table 7. About 82 % of euthyroid diabetics and 78.3% of hypothyroid diabetics treated with OHA, while 9.5 % of euthyroid diabetics and 17.4% of hypothyroid diabetics treated with insulin. There was statically no significant difference regarding type treatment of DM between two groups (the P value 0 .508) table 8.

#### Discussion

The prevalence of thyroid dysfunction as represented by hyperthyroidism, hypoyhyroidism ,and suclinical hypothyroidism ,was examined in adult population in the Wickham Survey ,and was reported to be 6.6% <sup>36</sup>.Early in 1968 it was reported that there exists the association of hypothyroidism in diabetic patients. Later studies in 1979 emphasized the importance of screening of diabetic patients to identify hypothyroidism 12. In UK ,The Smithson (1998) found the prevalence of thyroid dysfunction in type 2 DM of 10.8% while Radaideh et al (2004) in Jordan found to be higher than  $12.5\%^{-37}$ .

In our study we found the prevalence of thyroid dysfunction to be 26.7% (of which 21.8% had hypothyroidism and 4% had hyperthyroidism) and 73.3% showed normal thyroid function. it is in agreement with many other reports among the Indian, the most recent Vinu Vij et al published in international Biological journal oct. 2012, the prevalence thyroid dysfunction was 28.75% (of which 22.50% had hypothyroidism and 6.25% had hyperthyroidism) and 71.25% showed normal function 5. In Punjab population the prevalence was 30%(23.75% were hypothyroid and 6.25% were hyperthyroid)<sup>3</sup>8. while Ghazali and Abbiyesuku (2010)studied thyroid dysfunction in Nigerian type 2 DM found , the prevalence of thyroid dysfunction was 29.7% <sup>37</sup> and the other study from India /Manipur shows prevalence of 31.2% <sup>39</sup>.

The reason for high prevalence of thyroid dysfunction selected group of diabetics in Edinburgh.table 9 and in our study may be explained by the following: table-10

Type 2 DM tends to occur late in life ,as the age increase the incidence of thyroid dysfunction increased 4.
Possibly to the fact that some type 2 DM patients actually have type 1 DM of very slow-onset, and so it has the same genetic predisposition towards autoimmune disease as patients with type 1 diabetes <sup>38</sup>.

Hypoglycemic agents like sulphonylureas are known to suppress the level of FT4 and T4, while causing raised levels of TSH. Some of the type 2 diabetic were on oral hypoglycemic agents alone and some were on both insulin injections and oral hypoglycemic agents 38. These situations may explain thyroid dysfunction.
It is known that insulin ,an anabolic hormone enhances the level of FT4 while it suppresses the level of T3 by inhibiting hepatic conversion of T4 to T3 and may suppress TSH <sup>38</sup>.

• Poor Glycemic control(GC) suppresses TSH 37. In our study 53.46 % of randomly selected samples had poor GC. In addition 73.9% of hypothyroid group have poor GC VS 44.6% in Euthyroid group. This result is similar to Ghazali and Abbiyesuku (2010) studied thyroid dysfunction in Nigerian type 2 DM, in which hypothyroid group with poor GC 66.7% VS 40% in Euthyroid group 37.So the prevalence of poor GC increased in hypothyroid group.while hyperthyroid group have very poor GC.

The thyroid dysfunction was more common in female than males, this agree with all other studies mentioned above. Dyslipidemia was significantly higher in hypothyroid in comparison to euthyoid group especially the atherogenic LDL (P value <0.001). This agree with what found in previously mentioned studies.

While there was no significant difference of BMI between Hypothyroid and Euthyroid group this agree with what found in Ghazali and Abbiyesuku (2010) and this may reflect the prevalence of obesity in our sample. The study done by P.Perros and his colleague in Royal Infirmary, Edinburgh <sup>36</sup> they compare the prevalence and annual incidence of thyroid dysfunction in general population (Wickham's study) and among randomly selected group of diabetics in Edinburgh.table 9 and table-10

So they come to a conclusion that there is significant higher incidence and prevalence of thyroid dysfunction among diabetics in comparison to general population and the annual testing of TFT in diabetic patients is a worthwhile clinical excersise which is cost effective <sup>36</sup>. If we compare the prevalence of TD in type 2 DM in our study to the royal infirmary study as shown in table 11:

We put all overt hypothyroidism and hyperthyroidism on the appropriate treatment .while we recommend those patients with subclinical hyperthyroidism to repeat their TFT in 3-6 months and then annually <sup>40</sup>. for those 15 patients with subclinical hypothyroidism,12 of them were also dyslipidemic so we start thyroxine treatment 25-50micrograms/day. The remaining three patients with no dyslipidemia we did Anti-TPO for them and all of them were negative so we advice them to repeat TFT 3-6 months later and then annually <sup>40</sup>. That is according to the following indications for treatment of subclinical hypothyroidism(MKSAP 16)<sup>41</sup>:

• Any time TSH> 10 mIU/L.

- Dyslipidemia.
- Any time Symptoms developed
- Pregnancy or planning for pregnancy
- Positive anti-TPO antibodies .

## Conclusions

•Thyroid dysfunction is common among Type 2DM and it is more common in females than males . Among cases of thyroid dysfunction subclinical hypothyroidism was the most common type followed by overt hypothyroidism.

•Dyslipidemia was significantly higher in hypothyroid group than euthyroid group specifically the athergenic LDL. Glycemic control was significantly poor in both hypothyroid and hyperthyroid groups than euthyroid group.

•Routine screening of type 2 DM for TFTs is indicated upon diagnosis and annually latter on.

Failure to recognize thyroid dysfunction may have bad consequences on glycemic control. If dyslipidemia is identified in subclinical hypothyroidism, treatment with thyroxine is indicated to prevent cardiovascular complications .Larger scale studies are needed to define more precisely the frequency of thyroid dysfunction among type 2 diabetic patients. Prospective follow up studies are needed to identify annual incidence of thyroid dysfunction in diabetic patients.

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## REFERENCES

1. Shabbir B, Qadir H, Shafi F, Mahboob F. Thyroid Dysfunction in Diabetes Mellitus. Pakistan Journal of Medical and Health Sciences 2012;6(1).

2. Al-Wazzan H, al e. Prevalence and associated factors of thyroid Dysfunction among Type 2 diabetic patients.

Alexandria Journal of Medicine 2010;46.2:141-148.

3. Ghosh S, Collier A. Epidemiology in type 2 DM. Churchill's Pocketbook of Diabetes, Elsevier Health Sciences. 2nd ed,Edinburgh,2012p25.

4. Holt R, Hanley N. Epidemiology of type 2 DM and Thyroid gland. Essentail Endocrinology and Diabetes. 6 ed2012. p 286 and p174.

5.Vij V. Evaluation Of Thyroid Dysfunction Among Type II Diabetic Patients. International Journal of Pharmacy and Biological Sciences (IJPBS) 2012;2(4):150-155.

6. Papazafiropoulou A, Sotiropoulos A, Kokolaki A, Kardara M, Stamataki P, S. P. Prevalence of Thyroid Dysfunction Among Greek Type 2 Diabetic Patients Attending an Outpatient Clinic. J Clin Med Res 2010;2(2):75–78.

7. Wu P, al. e. Thyroid Disease and Diabetes. CLINI-CAL DIABETES 2000;18.

8. Baskin HJ. AACE guidelines for clinical practice for evaluation and treatment of hyperthyroidism and hypothyroidism. ENDOCRINE PRACTICE 2002;8 457-469.

9. Ladenson PW, Singer PA, Ain KB. American thyroid association guidelines for detection of thyroid dysfunction. Archives of Internal Medicine 2000;160:1573-1575.

10. C. W. The Relationship between Type 2 Diabetes Mellitus and Related Thyroid Diseases. Journal of Diabetes Research 2013:47-51.

11. Association BT. 2006 The UK guidelines for the use of thyroid function tests. The Association for Clinical Biochemistry.

12. Swamy, Kumar, Srinivasa, Manjunath, al. e. Evaluation of hypothyroidism as a complication in Type2 Diabetes Mellitus. Biomedical Research 2012;23(2):170-172.

13. Brenta G. Diabetes and thyroid disorders. British Journal of Diabetes & Vascular Disease 2010;10:172-177.

14. Raboudi N, Arem R, Jones RH. Fasting and postabsorptive hepatic glucose and insulin metabolism in hyperthyroidism. Am J Physiol 1989;256:159-66. 15. Weinstein SP, O'Boyle E, Fisher M, Haber RS. Regulation of GlUT2 glucose transporter expression in liver by thyroid hormone: evidence for hormonal regulation of the hepatic glucose transport system. Endocrinology 1994;135:649-54.

16. Viguerie N, Millet I, Avizou S. Regulation of human adipocyte gene expression by thyroid hormone. J Clin Endocrinol Metab 2002;87:630-4.

17. Clément K, Viguerie N, Diehn M. In vivo regulation of human skeletal muscle gene expression by thyroid hormone. Genome Res 2002;12:281-91.

18. Potenza M, Via MA, Yanagisawa RT. Excess thyroid hormone and carbohydrate metabolism. Endocr Pract 2009;15:254-62.

19. S. l, Bailey CJ. Thyroid hormones, gonadal and adrenocortical steroids and the function of the islets of langerhans. Endocr Rev 1984;5:411-34.

20. Ortega E, Koska J, Pannacciulli N. Free triiodothyronine plasma concentrations are positively associated with insulin secretion in euthy-roid individuals. Eur J Endocrinol 2008;158:217-21.

21. Ximenes HM, lortz S, Jörns A, lenzen S. Triiodothyronine (T3) mediated toxicity and induction of apoptosis in insulin-producing INS-1 cells. Life Sci;80:2045-50.

22. Okajima F, Ui M. Metabolism of glucose in hyper and hypothyroid rats in vivo. Glucose turnover values and futile cycle activities obtained with 14 C and 3H labelled glucose. Biochem J 1979;182:565-75.

23. McCulloch AJ, Nosadini R, Pernet A. Glucose turnover and indices of recycling in thyrotoxicosis and primary thyroid failure. Clin Sci 1983;64:41-7.

24. Maratou E, Hadjidakis DJ, Kollias A. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol 2009;160:785-90.

25. Bakker SJ, Maaten JC, Popp-Snijders C. The relationship between thyrotropin and low density lipoprotein cholesterol is modified by insulin sensitivity in healthy euthyroid subjects. J Clin Endocrinol Metab 2001;86:1206-11.

26. Chubb SA, Davis WA, Davis TM. Interactions among thyroid function, insulin sensitivity, and serum

lipid concentrations: The Fremantle Diabetes Study. J Clin Endocrinol Metab 2005;90:5317-20.

27. Powers AC. Diabetes Mellitus. Harrison's principle of internal medicine. 18 ed,McGraw-Hill,Newyork,2012,Volume 2 ,Chapter 344.p2970.

28 Jameson JL, Weetman AP. Disorders of the Thyroid Gland. Harrison's principle of internal medicine. 18 ed ,McGraw-Hill,Newyork,2012,Volume 2,Chapter 341.p2914-2915.and Konstantinos Tziomalos, Faidon Charsoulis.Endocrine Effects of Tobacco Smoking. Medscape.Clin Endocrinol. 2004;61(6)

29. Desborough JP. The stress response to trauma and surgery. Oxford Journals Medicine BJA 2008;85(1):109-117.

30. Farwell AP. Sick euthyroid syndrome in the intensive care unit. Irwin RS, Rippe JM, eds. Irwin and Rippe's Intensive Care Medicine. 5th ed2003. p 1205-1216.

31. DeGroot LJ. Non-thyroidal illness syndrome is functional central hypothyroidism, and if severe, hormone replacement is appropriate in light of present knowledge. J Endocrinol Invest 2003;26:1163-1170. 32. Adler SM, Wartofsky L. The nonthyroidal illness syndrome. Endocrinol Metab Clin North Am 2007;36:657-672.

33. Jellinger PS. AACE for management of Dyslipidemia and prevention of atherosclerosis guidelines. Endocrine practice 2012;18.

34. American Diabetes Association. Standards of medical care in diabetes—2013. Diabetes Care. 2013;36 (suppl 1):S11-S66.

35. Turner HE, Wass J. Diabetes. Oxford Handbook of Endocrinology and Diabetes. 2nd ed,Oxford university press,Oxford,2009. p 646.

36. Perros P, McCrimmon RJ, Shaw G, Frier BM. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. DIABETIC MEDICINE 1995;12(7):622-7

37. Ghazali SM, Abbiyesuku FM. Thyroid dysfunction in type 2 diabetics seen at the University College Hospital, Ibadan, Nigeria. Nig. J. Physiol. Sci. 2010;25:173-179. 38. Singh G, al. e. Evaluation of Thyroid Dysfunction Among type 2 diabetic Punjabi Population. Journal's URL 2011;2(2):03-09.

39. Demitrost L, Ranabir S. Thyroid dysfunction in type 2 diabetes mellitus. Indian J Endocr Metab

#### FIGURES AND TABLES

2012;16:334-5.

40. Turner HE, Wass JH. Diabetes. Oxford Handbook of Endocrinology and Diabetes. 2nd ed, Oxford university press,Oxford,2009. p 60.

41. Alguire PC. Endocrinology and metabolism.Subclinical hypothyroidism MKSAP 2012;16:34.

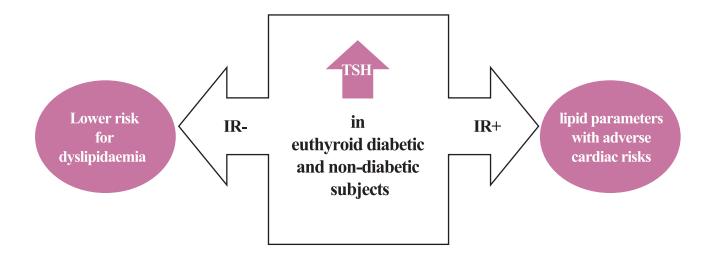


Figure 4: The interaction between insulin resistance and higher TSH. If TSH is increased especially in presence of insuresistance(IR), is associated with more atherogenic lipid profile13.

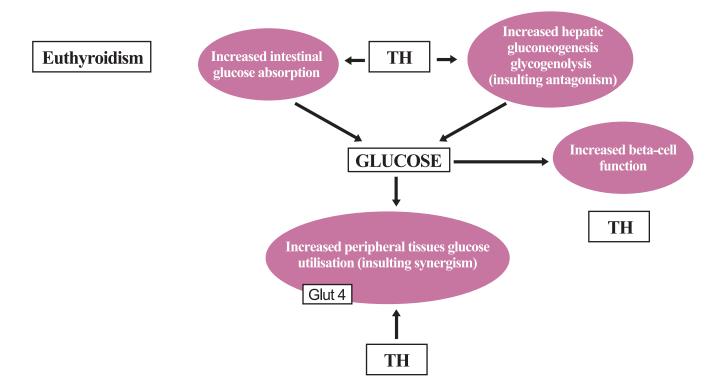


Figure 1: Effect of Thyroid Hormone on glucose metabolism in Euthyroidism13.

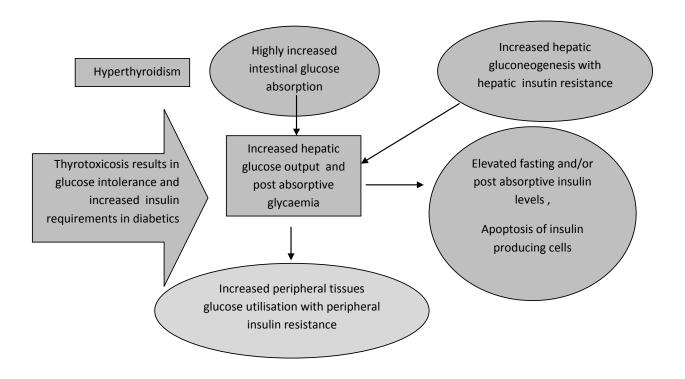
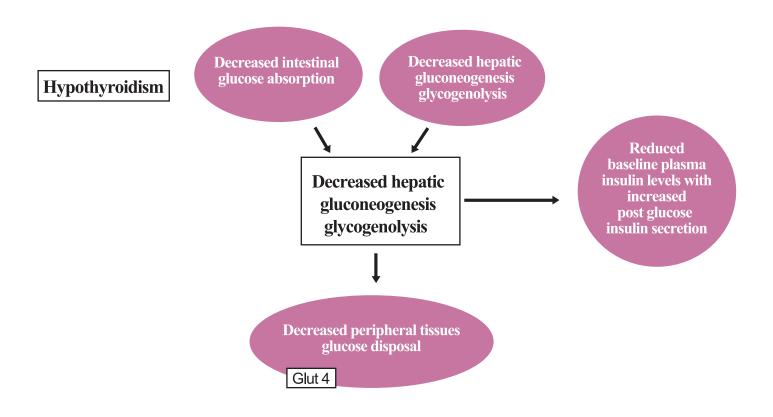
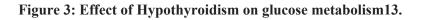
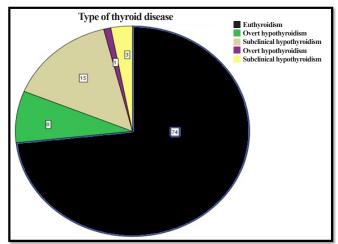
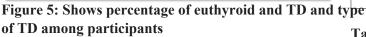


Figure 2: Effect of Thyrotoxicosis on glucose metabolism13.









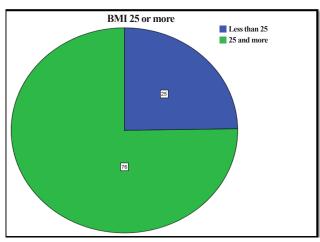


Figure 6: Shows BMI among participants

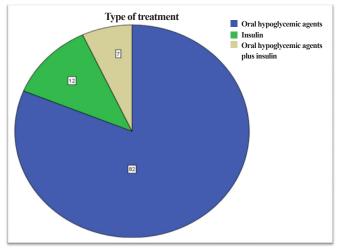


Figure 7: Shows type of treatment of DM among participants

#### Table 1: Criteria for the Diagnosis of Diabetes Mellitus

1.Symptoms of diabetes mellitus plus random blood glucose level  $\geq$ 11.1 mmol/L (200 mg/dL) or

2.Fasting plasma glucose lecel  $\geq$ 7.0 mmol/L (126 mg/ dL) or

3.HbA1C level  $\geq 6.5\%$  or

4.Two-hour plasma glucose level  $\geq$  11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test(OGTT).

Table 2: The characteristics of the participants

Variable	
Age (years)	52.54±11
Less than 50	37(36.6%)
50 and more	64(63.4%)
Gender(%)	
Male	33
Female	68
Thyroid dysfunction	
Male	7 (21%)

Thyroid dysfunction	
Male	7 (21%)
Female	20 (29%)
BMI	
Less than 25	25(24.8%)
25 and more	76(75.2%)
Glycemic control	
Good	47(46.53%)
Poor	54(53.46%)
Dyslipidemia	49(45.5%)
Euthyroid	74(73.3%)
Thyroid dysfunction	27(26.7%)
Subclinical hypothyroidism	15(14.9%)
Overt hypothyroidism	8(7.9%)
Subclinical hyperthyroidism	3(3%)
Overt hyperthyroidism	1(1%)
Type of treatment	
Oral hypoglycemic agents	82(81.2%)
Insulin	12(11.9%)
Oral hypoglycamic agants Plus	7(6.9%)

Oral hypoglycemic agents Plus insulin

Characteristics	Male(n33) Mean± SD	Female(n68) Mean± SD	P value (95% CI)		
Age(years)	53.73±9.070	51.97±11.939	0.457 *		
BMI	30.35±7.004	30.77± 6.69	0.771*		
TG(mg/dl)	153.67± 54.67	169.66± 110.97	0.436 *		
LDL Cholesterol (mg/dl)	119.37± 32.42	113.52± 32.35	0.397 *		
Total Cholesterol (mg/dl)	199.03± 41.42	192.12± 44.77	0.458 *		
HDL Cholesterol (mg/dl)	41.96± 8.45	49.34 ± 11.72	0.002 *		
Fasting blood sugar (mg/dl)	144.72± 29.17	146.03± 24.94	0.815 *		
TSH mIU/L	4.65± 9.96	6.57± 11.18	0.405 *		
Total T4 nmol/L	81.80± 21.23	83.21 ± 20.50	0.750 *		
Total T3 nmol/L	1.33±0.461	1.41±0.422	0.390*		

#### Table 4: General characteristics of the participants by thyroid status :

Characteristics	Euthyroid(74) Mean(no.)	Percentage	Hypothyroid(23) Mean (no.)	Percentage	P value (95% CI)
Gender					
1- Male	26	35.1%	6	26.1%	
2- Female	48	64.9%	17	73.9%	0.420*
Age 50 or more	47	63.5%	13	56.5%	<0.547*
BMI 25 or more	56	75.7%	17	73.9	0.864*
Dyslipidemia	27	36.5%	19	82.6%	< 0.001 *
Glycemic control(GC)	41	55.4%	6	26.1	<0.014*

#### \* Chi-square test was used;

#### Table 5: Other Characteristics of the participants by thyroid status:

Characteristics	Euthyroid(74) Mean (no.)	SD	Hypothyr-oid(23) Mean (no.)	SD	P value (95% CI)
Age	53.32	10.58	48.61	12.28	0.076*
BMI	30.64	6.31	30.94	8.48	0.855*
TG (mg/dl)	165.57	105.30	166.52	71.47	0.968*
LDL(mg/dl)	110.01	30.49	137.96	27.62	< 0.001 *
HDL(mg/dl)	47.29	8.55	43.63	15.02	0.144*
T.Chol(mg/dl)	189.73	42.25	212.04	47.13	0.034*
FBS(mg/dl)	143.37	26.76	154.18	24.28	0.087*
TSH(mIU/L)	2.15	1.34	19.14	16.91	< 0.001*
Total T4(nmol)	86.62	14.42	64.14	23.79	< 0.001*
Total T3(nmol)	1.48	0.38	1.07	0.45	< 0.001*

Characterist-ics	Eu 74	Percentage	SCL Hypo 15	Percen- tage	overt hypo 8	Percen- tage	SCL Hyper (3)	Percen- tage	Overt hyper (1)	Percent- age
Gender										
1.Male	26	35.1%	4	26.7%	2	25%	1	33.3%	0	0%
2.Female	48	64.9%	11	73.3%	6	75%	2	66.7%	1	100%
Age ≥50	47	63.5%	7	46.7%	6	75.0%	3	100%	1	100%
BMI≥25	56	75.7%	10	66.7%	7	87.5%	2	66.7%	1	100%
Dyslipidemia	27	36.5%	12	80.0%	7	87.5%	0	0%	0	0%
Glycemic control(GC)	41	55.4%	4	26.7%	2	25%	0	0%	0	0%

#### Table 6: Characteristics of the participants by type of thyroid dysfunction:

Abbrevations;Eu=Euthyroid, SCL.Hypo=Subclinical hypothyroidism,Overt hypo=Overt hypothyroidism, SCL.Hyper= Subclinical Hyperthyroidism,Overt Hyper=Overt hyperthyroidism

 Table 7: Distribution of euthyroid and hypothyroid according to age group

 according to age group

Age(Year)	Total No.	Euthyroid (%)	hypothyroid (%)
< 40	14	7 (50%)	7 (50%)
40-49	24	20 (83.3%%)	4 (16.7%%)
50-59	31	23 (74.2%)	8 (25.8%)
60-69	21	19 (90.5%%)	2 (9.5%)
≥ 70	7	5 (71.4%)	2 (28.6%)
Total	74	23	97

#### Table 8: difference of treatment of DM between euthyroid and hypothyroid:

Type of treatment	Euthyroid	Hypoythyroid
OHA(oral hypoglycemic agents)	61(82.4%)	18(78.3%)
Insulin	7 (9.5%)	4(17.4%)
OHA(oral hypoglycemic agents) and insulin	6 (8.1%)	1 (4.3%)
Total	74 (100%)	23 (100%)

#### Table 9: Prevalence of thyroid dysfunction among general population, type 1 DM and type 2 DM.

Gender	Background Population	Type 1 DM	<b>Type 2 DM</b>
Female	-	31.4%	10.6%
Male	6.6%	12.4%	6.9%

#### Table 10: Annual incidence of thyroid dysfunction in background population ,type 1 DM and type 2 DM

Gender	Background Population	Type 1 DM	Туре 2 DM
Female	0.5%	10.5%	4.8%
Male	0.1%	6.5%	3.8%

## Table 11: Comparison between prevalence of thyroid dysfunction between our study (Duhok) and edinburgl study

Gender	Prevalence of TD in Duhok study	Prevalence of TD in Edinburgh Study
Female	19.8%	10.6%
male	6.9%	6.9%
Total	26.7%	17.5%