Study Of Thyroid Parameters In Type 2 Diabetic Patients By Using Recent ECL Assay

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Abstract

Background: The two endocrines dysfunction: thyroid problem and diabetes complication has gained great attention for endocrinologist. These two endocrines are a common metabolic clutter, and critical cause of dismalness and health threats worldwide. Patients with diabetes have the next predominance of thyroid disarranges when compared with common population. Several studies make attention that altering thyroid function complicates the management of diabetes and associated consequences.

Aim of research: The objective of the current research was to discovery the predominance of thyroid problem (dysfunction) in subjects with type 2 diabetes mellitus (T2DM) and correlated with high risk of type2 diabetes.

Materials Methods and subjects: Across sectional study was conducted from October 2019 to January 2020 at the center which is specialized for endocrinology and Diabetes. 220 patients diagnostic with Type 2 DM or recently detected cases were included and compared with 60 apparently healthy groups in this work.

All the patients were evaluated for thyroid dysfunction by examines thyroid hormones "triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH)". These parameters were analyzed by Electrochemiluminescent assay (ECLassay).The advantages of this system include high sensitivity, large dynamic range, non-toxic , stable conjugate 12 month and precisely controlled. The relationship of predominance of thyroid clutter with sex male/female distribution, age (30>70) distribution, hemoglobin A1C, duration of diabetes, family history of diabetes, body mass index(BMI), usage of oral antiglycemic agents and insulin, and thyroxin for hypothyroid and Neomecazol for hyperthyroid patients. The interpretations were taken and measurably analyzed.

Results: The patients in this study range in age from 30 to 70 years old. Thyroid indicators were abnormal in 26.35 percent of Type 2 DM patients in our study. Hypothyroidism was the most common condition (19.54 percent), followed by hyperthyroidism (6.8%), with 162 euthyroid patients. Thyroid abnormalities were

found to be more common in females (19.44 percent) than in males (6.86 percent), with a significant Pvalue <0.05. The results of this investigation revealed a significant relationship between hypothyroid parameters and BMI, with a pvalue of 0.05. In T2DM compared to control groups, there was no significant association between thyroid hormones and diabetes duration (Pvalue >0.05)
.**Conclusion:** Thyroid disorder has a higher predominance and can occur in type 2 diabetic patients, implying that people with type 2 diabetes should have their thyroid function evaluated on a regular basis.
Keyword: Thyroid parameters, Type2 diabetic, hemoglobin A1C, ECL analyzer

دراسة معلمات الغدة الدرقية في مرضى السكري من النوع 2 باستخدام مقايسة ECL الحديثة

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خلاصة

الخلفية: حظي خلل الغدد الصماء: مشكلة الغدة الدرقية ومضاعفات مرض السكري باهتمام كبير لأخصائي الغدد الصماء. هذان النوعان من الغدد الصماء هما من الفوضى الأيضية الشائعة ، وسبب حاسم للكآبة والتهديدات الصحية في جميع أنحاء العالم. مرضى السكري لديهم الغلبة التالية لاضطرابات الغدة الدرقية عند مقارنتهم بالسكان العاديين. تركز العديد من الدراسات على أن تغيير وظيفة الغدة الدرقية يعقد إدارة مرض السكري والعواقب المرتبطة به.

هدف البحث: كان الهدف من البحث الحالي هو اكتشاف غلبة مشكلة الغدة الدرقية (اختلال وظيفي) في الأشخاص المصابين بداء السكري من النوع 2 (T2DM) والمرتبط بارتفاع مخاطر الإصابة بمرض السكري من النوع 2. طرق المواد والموضوعات: أجريت دراسة مقطعية شاملة من أكتوبر 2019 إلى يناير 2020 في المركز المتخصص في أمراض الغدد الصماء والسكري. تم تضمين 220 مريضًا تم تشخيص إصابتهم بالنوع 2 DM أو الحالات المكتشفة حديثًا ومقارنتها بـ 60 مجموعة تبدو سليمة في هذا العمل.

تم تقييم جميع المرضى لضعف الغدة الدرقية عن طريق فحص هرمونات الغدة الدرقية "ثلاثي يودوثيرونين (T3)، هرمون الغدة الدرقية (T4) ، وهرمون الغدة الدرقية (TSH)". تم تحليل هذه المعلمات بواسطة مقايسة اللمعان الكهربائي (ECLassay) وتشمل مزايا هذا النظام الحساسية العالية ، والمدى الديناميكي الكبير ، والمقارن غير السام ، والمستقر لمدة 12 شهرًا والتحكم فيه بدقة. علاقة غلبة فوضى الغدة الدرقية بتوزيع الجنس بين الذكور والإناث ، وتوزيع العمر (30> 70) ، والهيموجلوبين A1C ، ومدة مرض السكري ، والتاريخ العائلي لمرض السكري ، ومؤشر كتلة الجسم (BMI) ، واستخدام الأدوية المضادة للسكر عن طريق الفم والأنسولين ، و هرمون الغدة الدرقية لقصور الغدة الدرقية ونيوميكازول لمرضى فرط نشاط الغدة الدرقية. تم أخذ التفسيرات وتحليلها بشكل قابل للقياس.

النتائج: تتراوح أعمار المرضى في هذه الدراسة من 30 إلى 70 عامًا. كانت مؤشرات الغدة الدرقية غير طبيعية في 26.35 بالمائة من مرضى النوع DM 2 في دراستنا. كان قصور الغدة الدرقية هو الحالة الأكثر شيوعًا (19.54 في المائة) ، يليه فرط نشاط الغدة الدرقية (6.8 في المائة) ، مع 162 مريضًا بالغدة الدرقية. تم العثور على تشوهات الغدة الدرقية لتكون أكثر شيوعًا عند الإناث (19.44٪) منها عند الذكور (6.86٪) ، مع قيمة Pvalue كبيرة <0.05. أظهرت نتائج هذا البحث وجود علاقة معنوية بين متغيرات الغدة الدرقية ومؤشر كتلة الجسم بقيمة 0.05. في T2DM مقارنة بمجموعات التحكم ، لم يكن هناك ارتباط كبير بين هرمونات الغدة الدرقية ومدة مرض السكري(Pvalue> 0.05)

الخلاصة: اضطراب الغدة الدرقية له غلبة أعلى ويمكن أن يحدث في مرضى السكري من النوع 2 ، مما يعني أن الأشخاص المصابين بداء السكري من النوع 2 يجب أن يتم تقييم وظائف الغدة الدرقية لديهم على أساس منتظم.

الكلمات الرئيسية: معلمات الغدة الدرقية ، السكري من النوع 2 ، الهيموغلوبين A1C ، محللECL

1- Introduction

Diabetes mellitus (DM) is a multi-complicated disease marked by a persistent increase in blood glucose levels. It occurs when the body is unable to create enough insulin to meet its own requirements, either due to impaired insulin production, insulin action, or both. Diabetes affects 450 million individuals worldwide, and its prevalence is rising. [1]. Chronic high blood glucose has a number of risky effects on the body, including neuropathy (nerve damage), nephropathy (kidney illness), and retinopathy (eye disease) [2]. Type 2 diabetes affected over 90% of those surveyed. Furthermore, type 2 diabetes already kills 5 million people each year, largely from cardiovascular illnesses, and by 2030, it will be the seventh leading cause of death worldwide. [3].The thyroid is a butterfly-shaped gland in the neck that is found right below the Adam's apple and above the collarbone. [4]. Thyroxine (T4) and triiodothyronine (T3) are two hormones produced by the thyroid gland that enter the bloodstream and regulate the metabolism of the heart, liver, muscles, and other organs. [5] The thyroid gland works as part of a feedback mechanism concerning the hypothalamus, a region of the brain, and the pituitary gland, which is located within the brain [6,7]. Hypothyroidism (underactive thyroid gland) and hyperthyroidism (overactive thyroid gland) are the two most common thyroid disorders [8]. Thyroid problems are more common among diabetics. Thyroid disorders affect about 6% of the general population. Thyroid disorders, on the other hand, are more common in patients with diabetes, with rates ranging from 10% to 25%. [9].This difference in results promotes overproduction thyroid hormone leads to increased glucose synthesis in the liver, fast glucose absorption through the intestines, and insulin resistance. In hypothyroidism, liver glycogen secretion and breakdown both

decrease, resulting in increased glycogen levels and a range of irregularities in blood lipid levels. [10,11]. Thyroid hormones are insulin antagonists; both insulin and thyroid hormones are involved in cell metabolism, and changes in one can lead to a functional deficiency in the other. [12,13].

2- Aim of study

The current study's goal is to discover the predominance of thyroid dysfunction in patients with type 2 diabetes mellitus and conjointly the impact of the type 2 diabetes on other biochemical factors among diabetic patients.

3- Subjects, Material and Methods:

This cross-sectional study was conducted on a group of 220 patient's diagnosed type2 diabetes mellitus whose ages ranged between (30-70) years with maximum 80 years at Baghdad city. At a specialized center for endocrinology and diabetes, blood samples were collected. During the period from October 2019 to January 2020.Patients in this study were recruited and underwent investigation for thyroid function [total thyroxin (TT4), total triiodothyronine (TT3),and thyroid-stimulating hormone (TSH)]. Those patients were being treated for both diabetes and co-existing illnesses. All of the patients gave their written informed consent for the study. Pregnant women and those on glucocorticoids or amiodarone were excluded. One hundred and sixty two apparently euthyroid individuals with compared with case study. Sixty healthy subjects no previous history of thyroid disorders or any diabetic disease was selected as a control group. Their age and gender matched that of the patients group. Brief bio-data collection, clinical history and physical examination were performed and recorded on proforma designed for this study. Clinical and analytical tests were performed on all patients. Gender, age (years), DM duration (years), and body mass index were all recorded as clinical factors (BMI). For the determination of glucose levels in the fasting state, For the determination of glucose levels in the fasting state, venous blood samples were taken after a 12-hour fast. Estimation of glucose levels was carried by auto analyzer assay [13]. About 5 mL of venous blood was sucked with a disposable syringe, 2 mL was transferred to an EDTA container tube, and the blood was gently agitated with a blood shaker to prevent clotting. Whole blood was used for estimation of HbA1c using an automated clinical chemistry analyzers. Fasting plasma sugar ≥126 mg/dl, postprandial blood sugar ≥200 or Glycated hemoglobin [HbA1c] ≥ 6.5%. After allowing blood samples to coagulate, they were centrifuged at 3000 RPM for 10 minutes to separate serum, which was then transferred to another tube and frozen at (-20c) for thyroid profile analysis., serum thyroixine (TT4), triiodothyronine (TT3) and thyroid stimulating hormone (TSH) these

parameters were measured by using Electrochemiluminescent assay(ECLassay)[14]. This assay is technique depend on electro generated chemiluminesence that mix the two advantages of electrochemical and photoluminescence analysis [15]. The advantages of this system include high sensitivity, large dynamic range, non-toxic, stable conjugate 12 month and precisely controlled [16]. Ethics committee was taken from ministry of health. We excluded pregnant women and patient taking amiodarone . Results were analyzed using SPSS ver. 18.00 and Microsoft excel micro soft office (2010) for *T* test and The significance between the means was determined using the chi-square test, with a P-value of 0.05 considered significant. The findings of continuous measures were provided as a mean standard deviation, whereas categorical measurements were presented as a number (N) and a percentage (%).

4- Results

The subjects in this present study were 220 Iraqi type 2 diabetic patients compared with 60 apparently non diabetic health subjects. In this current study, the socio-demographic and clinical data are reported.

. Figure (1) explain the total prevalence of thyroid dysfunction were 58(26.34%) and hypothyroid was 43(19.54%) while hyperthyroid recorded 15(6.8%).

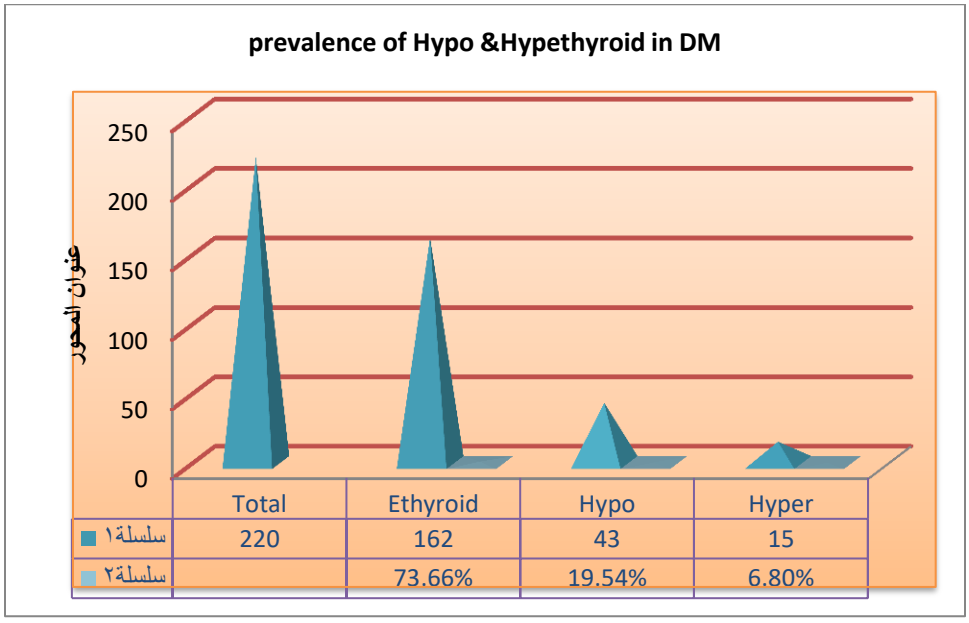

Figure (1) Prevalence Thyroid dysfunction among Type 2DM

Table (1) Comparison of studies- Thyroid dysfunction is common among diabetics.

Studies	Prevalence of Thyroid disease in T2DM	Hypothyroidism	Hyperthyroidism
Subhodip pramank etal.2018	26 %	23 %	3 %
Ashok K hurana etal.2016	16.5%	12 %	4.5 %
Madavarama Sreelatha etal .2017	12.2 %	10.12 %	2.8
Subekti etal.2017	9.9 %	7.59 %	2.31 %
Vikram Bvikhe etal.2013	30 %	22 %	8 %
Gorjeet Singh etal.2011	30 %	23.7 %	6.3 %
Present study	26.34%	19.54%	6.80

In comparison to the control group, Table (2) illustrates the connection between the two groups by age. There was a substantial difference at P≤0.05, according to the result. Regarding the age distribution of the two samples, Table (2) shows again the association between the two groups according to gender, the result had been indicated that there was a significant difference at P≤0.05 for the distribution of gender between the two samples. The association between BMI shows the different groups according to BMI, the result had been indicated that there was a significant difference at P≤0.05 for the distribution of BMI groups between the two samples. In the study group BMI ranged between (25-29.9) recorded high percent n=29(13.17%), compared with control BMI 60%.According to the duration of treatment of diabetes the result had been showed that there was a non-significant differences at P>0.05.The assessment of parameters TSH the high levels in diabetics with hypothyroid dysfunction was 14(6.36%) while hyperthyroid low levels was 8(3.6%) compared with euthyroid and diabetic control. Parameters T4 the low levels was 3(1.36%) and high levels was 2(0.9%). HbA1c values greater than 7.8 mmol/L showed glycemic control, whereas euthyroid levels were less than 7 mmol/L and control group HbA1c levels were less than 6.2 mmol/L and blood glucose levels were fewer than 126 mg/dl.

Table (2) Distribution of studied sample according to clinical and socio-demographic characters

Variable	Thyroid dysfunction			
	Hypothyroidism n= 43(19.54) %	Hyperthyroidism n=15(6.8)%	DM control N= 60	Significant Pvalue
Gender				
Male	12(5.5)	3(1.36)	15(25)%	0.03
Female	31(14.0)	12(5.44)	45(75)%	s
Age				
30-40	4(1.80)	2(0.9)	38%	0.01
41-50	7(3.19)	1(0.4)	32%	
51-70	32(14.5)	8(3.6)	22%	S
71-80	0	4(1.8)	8%	
BMI				
<25	8(3.63)	11(5)	28%	0.04
25-29.9	29(13.17)	3(1.36)	60%	S
≥30	6(2.72)	1(0.4)	12%	
Duration of DM				
1-5 year	12(5.45)	6(2.72)	0	o.27
6-10 year	20(9)	5(2.26)	0	NS
>10 year	11(5)	4(1.8)	0	
Parameters Test				
TSH (0.025-5)µUl/ml	4.9±2.2	0.6±5.1		
Low	1(0.45)	8(3.6)		
Normal	28(12.72)	7(3.17)		
High	14(6.36)	0		
T4 (60-120) µUl/ml	85±9.5	145±15.5		
Low	3(1.36)	0		
Normal	38(17.26)	5		
High	2(0.9)	10		
HbA1c >7.0mmol/L	>7.8	>7.2		
Blood glucose (>126mg/dl) (≤6.5mmol/L)	>7	>7		

Table (3) shows the etiological diagnosis of thyroid gland removal of goiter which diagnosed by ultrasound the multi-nodular recorded n=11 for each hypo and hyperthyroid and single nodular recorded n=1 while diffuse was recorded n=2.Fine needle aspiration procedure detect colloid n=4 and hashimotos n=4 and gravies disease was recorded n=4.

Table (3) Characteristics of thyroid status regarding an etiological diagnosis

The aetiology	Thyroid status		
	Hypothyroidism	Hyperthyroidism	
Goiter removed			
Yes	11	0	
No	32	15	
Thyroidectomy	7		
Auto-Immune	27	3	
Nodular	9	12	
Ultrasound			
Multi-nodular goiter	11	11	
Single nodular	1	1	
Diffuse	2	3	
Normal	11	0	
Small size	5	0	
Not done	13	0	
Fine needle Aspiration			
Colloid	4	1 hyper-cellular	
Hashimotos	3	3 Graves disease	
Not done	36	11	

Table (4) shows the type of drug used for therapy of diabetic patients according to status of pancreas function and insulin production treatment by take oral anti-glycemic agent, insulin or combined drug. Hypothyroidism is treated by replacing the thyroid hormone that has been deficient. The most common form of thyroid hormone is a synthetic derivative, levothyroxine and for treatment of hyperthyroidism, dependent on the cause of the disorder; it must be checked for Long-term oral anti-thyroid medicines such as Neomercazol and propylthiouracil (PTU) are useful in regulating thyroid hormone production. Throughout the duration of treatment, blood tests must be performed regularly.

Table 4: Distribution of studied sample according to type of treatment

Thyroid status	**Medication in take**						
	OAA	insulin	Dietary	OAA Thyroxin	Insulin OAA	Insulin Thyroxin	Combined drug
Euthroid	93	46	23				
Hypothroid	15	7	2	2	8	6	3
Hyperthyroid	Neomercazol						

5- Discussion

Thyroid function is necessary for energy metabolism to function properly. and glucose homeostasis. In diabetes, aberrant thyroid function can have a big impact on blood glucose control. Both hyperthyroidism and hypothyroidism can affect the progression of diabetes, although their consequences vary depending on how well they are managed. [17] In this study, 162 (73.66 percent) of 220 diabetic individuals were found to be euthyriod i.e 43(19.54%) had hypothyroidism and 15(6.8%) had hyperthyroidism [18]. Thus a total of 58(26.34%) patients showed thyroid disorder. These data reveal that the diabetic population has a significant rate of aberrant thyroid hormone levels. which is supported by the various studies (Table 1) In a study by Subhodip pramank etal.2018[19] 23 % of patients had hypothyroidism and 3 % had hyperthyroidism a total of26%.Both studies Vikram Bvikhe and Gurjeet Singh et al. [20,21] showed maximum prevalence of a total prevalence 30% subclinical hypothyroidism (22%,23.7%) followed by hyperthyroidism (8 %,6.3%) respectively [22,23]. These studies are agreement with current study. Hypothyroidism is a less common thyroid condition among type 2 diabetics (12 percent vs. 7.59 percent) respectively totally of 16.5% and 9.9% in the studies of Ashok K hurana,and Subekti. [24,25]. Studies reported to the "National Health and Nutrition Examination Survey" (NHANES III Study), disorder of hypothyroidism and hyperthyroidism were illustrated in 4.6% and 1.3% of the total participants respectively[26].

The presence of both raised and low levels of thyroid hormones levels in diabetics may be due to treatment of diabetic patients. Because of variances in drug use, gender, and patient age, the prevalence of TD differs around the world. [27]. Thyroid disorder becomes more common as people get older all throughout the world, and women have a higher prevalence than men. This variable prevalence studies suggested that medication therapy by metformin drug had small size thyroid goiter and nodules with lower risk [28,29].

6- Limitations

A few limitations have to be recognized. Thyroid work categorization was based on biochemical characteristics. For about 25% of the members who were categorized as subclinical hypothyroid or hyperthyroid, we may not affirm subclinical thyroid brokenness owing to the nonattendance of FT4 estimation. This may have driven to a few misclassification. Another limitation of this of this cross-sectional study is needed to distinguish between T1 and T2 DM and necessary to extend of the examining sizes.

7-Conclusion;

In conclusion; thyroid disorder and Diabetes mellitus type2 they are frequently coexist and impact thyroid capacities. In this study the predominance of thyroid dysfunction was 26.35%. Hypothyroidism was more predominant disorder represented 19.54% than hyperthyroidism was 6.8%.Thyroid disorder are more in females (19.44%) than males (6.86%).Hormone TSH and blood HbA1c preferred test for diagnosis of thyroid dysfunction and screening of diabetic patients. This suggests that type 2 diabetics should have their thyroid evaluated.

8- Conflict of interest statement

The authors declare no conflicts of interest regarding the publication of this paper.

9- Acknowledgement

The researchers would like to thank all individuals who contributed to the completion of this work.

10- References

1. Petrosyan, L. Relationship between high normal TSH levels and metabolic syndrome components in type 2 diabetic subjects with euthyroidism. Journal of clinical & translational endocrinology 2, 110–113, https://doi.org/10.1016/j.jcte.2015.02.004 (2015).
2. Furukawa, S. et al. Association between subclinical hypothyroidism and diabetic nephropathy in patients with type 2 diabetes mellitus. Endocrine journal 61, 1011–1018 (2014).
3. American Diabetes, A.. 2. Classification and Diagnosis of Diabetes. Diabetes care 39(Suppl 1), S13–22, https://doi.org/10.2337/dc16-S005 (2016).
4. Zhou, Y. et al. Free Triiodothyronine Concentrations are Inversely Associated with Elevated Carotid Intima-Media Thickness in Middle-Aged and Elderly

Chinese Population. Journal of atherosclerosis and thrombosis 23, 216–224, https://doi.org/10.5551/jat.30338 (2016).
5. Qi, Q. et al. Association of Thyroid-Stimulating Hormone Levels with Microvascular Complications in Type 2 Diabetes Patients. Medical science monitor: international medical journal of experimental and clinical research 23, 2715–2720 (2017).
6. Garber, J. R. et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid: official journal of the American Thyroid Association 22, 1200–1235,
7. Gu, Y. et al. The Relationship Between Thyroid Function and the Prevalence of Type 2 Diabetes Mellitus in Euthyroid Subjects. The Journal of clinical endocrinology and metabolism 102, 434–442, https://doi.org/10.1210/jc.2016-2965 (2017).
8. Moura Neto, A. et al. Relation of thyroid hormone abnormalities with subclinical inflammatory activity in patients with type 1 and type 2 diabetes mellitus. Endocrine 51, 63–71, https://doi.org/10.1007/s12020-015-0651-5 (2016).
9. Pearce EN. Hypothyroidism is associated with increased mortality risk in individuals 65 years of age or older. Clin Thyroidol . 2018;30(8):350–352.
10. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, Okosieme OE. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol . 2018;14(5):301–316.
11. Garmendia Madariaga, A., Santos Palacios, S., Guillen-Grima, F. & Galofre, J. C. *The incidence and prevalence of thyroid dysfunction in Europe: a meta-analysis*. *J. Clin. Endocrinol. Metab.* **99**, 923–931 (2014).
12. Huang HK, Wang JH, Kao SL. Association of hypothyroidism with all-cause mortality: a cohort study in an older adult population. J Clin Endocrinol Metab . 2018;103(9):3310–3318.
13. Manish Mishra1*, Raju Panta2, Miguel Miyares1, Ranjan Solanki3. Association of Diabetes Mellitus and Thyroid Disorders: An Adipocytokines Prospective. J Endocrinol Thyroid Res. Volume 3 Issue 3 - April 2018.
14. Chen, K.; Liu, J.; Shu, G.; Yang, Y.; Zhu, Y.; Zhao, G. Electrochemiluminescence of terbium (III) complex and its potential application for the determination of bacterial endospores. J. Lumin. 2013, 141, 71–75. [CrossRef]]
15. Li, L.; Chen, Y.; Zhu, J.J. Recent advances in electrochemiluminescence analysis. Anal. Chem. 2017, 89, 358–371. [CrossRef].
16. Kurita, R.; Arai, K.; Nakamoto, K.; Kato, D.; Niwa, O. Development of electrogenerated

17. chemiluminescence-based enzyme linked immunosorbent assay for sub-pm detection. Anal. Chem. 2010, 82, 1692–1697. [CrossRef]
18. Hofman A, Brusselle GG, Darwish Murad S, van Duijn CM, Franco OH, Goedegebure A, Ikram MA, Klaver CC, Nijsten TE, Peeters RP, et al. The Rotterdam Study: 2016 objectives and design update. Eur J Epidemiol. 2015;30(8):661–708.
19. Ligthart S, Van Herpt TTW, Leening MJG, Hofman A, Stricker BHCH, Van Hoek M, Sijbrands E, Franco OH, Dehghan A. Lifetime risks for type 2 diabetes mellitus: the Rotterdam Study. Lancet Diab Endocrinol. 2016;4(1):44-51
20. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. Geneva: WHO; 2006
21. Dimitriadis G, Mitrou P, Lambadiari V, Boutati E, Maratou E, Panagiotakos DB, Koukkou E, Tzanela M, Thalassinos N, Raptis SA. Insulin action in adipose tissue and muscle in hypothyroidism. J Clin Endocrinol Metab. 2006;91(12):4930–7.
22. Roos A, Bakker SJ, Links TP, Gans RO, Wolffenbuttel BH. Thyroid function is associated with components of the metabolic syndrome in euthyroid subjects. J Clin Endocrinol Metab. 2007;92(2):491–6
23. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabet Endocrinol. 2015;3(11):866–75.
24. Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, Cooper DS, Kim BW, Peeters RP, Rosenthal MS, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. Thyroid. 2014;24(12):1670–751.
25. Subhodip Pramanik, Sujoy Ghosh, Pradip Mukhopadhyayet.al; Thyroid status in patients with Type 2 diabetes attending a Tertiary Care Hospital in Eastern India; J Endocr Metab 2018;22:112-5 Year : 2018 | Volume : 22 | Issue : 1 | Page : 112-115
26. Gurjeet Singh1, Vikas Gupta2 , Anu Kumar Sharma3 and Neeraj Gupta4 Evaluation of Thyroid Dysfunction Among type 2 diabetic Punjabi Population .Jof Advance bioresearch;vol2,Issue 2,2011.
27. Madavaram Sreelatha1, V Suresh Kumar1, G Chandra Shekar3, V Chandra Shekar4; Study of Thyroid Profle in Patients with Type 2 Diabetes Mellitus, International Journal of Scientifc Study | May 2017 | Vol 5 | Issue 2.
28. Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and

Nutrition Examination Survey (NHANES III) Journal of Clinical Endocrinology and Metabolism. 2002;87(2):489–499.

29. Kadiyala R, Peter R, Okosieme OE. Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. International Journal of Clinical Practice. 2010;64(8):1130–1139.