Republic of Iraq
Ministry of higher education
and scientific research
University of Diyala
College of Medicine

:A Review article

(Thyroid disease and diabetes mellitus)

Submitted to the council of the collage

Of medicine , Diyala

University, in partial fulfillments of

Requirements for the bachelor degree

In medicine

Submitted by

Hussein majid shukir

Supervised by

DR.Zeina farooq

2020-2021

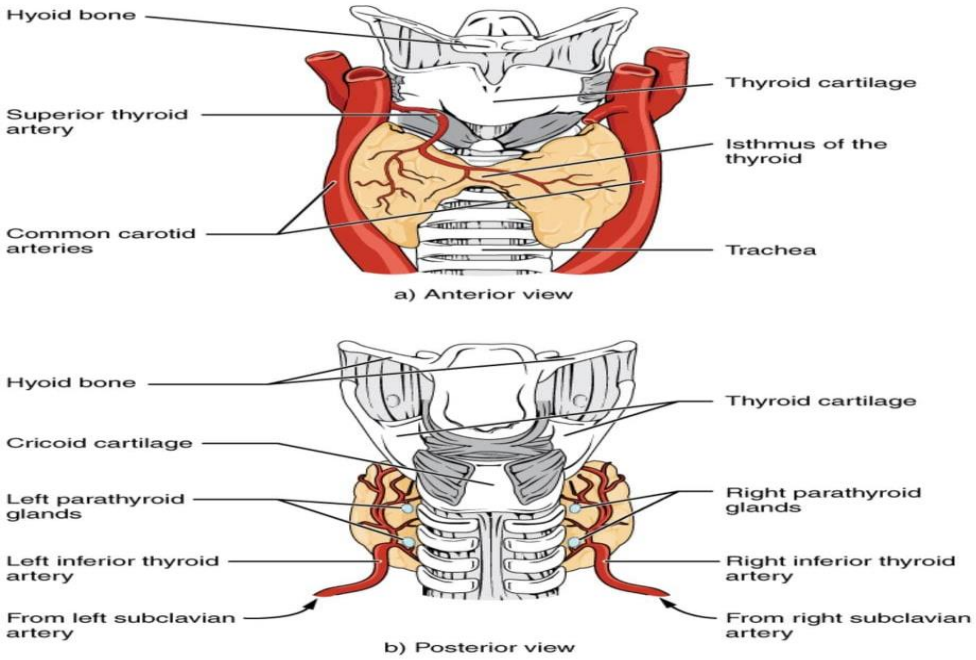
Abstract

Both diabetes mellitus and thyroid disorders are most encountered in general population. Both the disorder have complex biochemical pathophysiology along with hormonal and genetic malfunction , thyroid hormone important for regulators of carbohydrate and lipid metabolism .diabetes affects functioning of thyroid hormones. Thyroid dysfunction associated with insulin resistance . both of hyperthyroidism and hypothyroidism are reported to be associated with diabetes mellitus .researches that investigated the potentiality of thyroid hormone analogues to alleviate obesity ,diabetes , and atherosclerosis are also being conducted in clinical practice .

INTRODUCTION

Thyroid is a butterfly shaped organ . located anterior to the trachea just inferior to the larynx . the median region called isthmus is flanked by wing shaped left and right lobe . each of the thyroid lobe is embedded with parathyroid gland primary on their posterior surfaces the tissue of thyroid gland is composed mostly of thyroid follicles . the follicle are made up of central cavity filled with fluid called colloid . the colloid is the center of thyroid hormone production . the thyroid produce hormones called thyroid hormones T3 (tri iodothyronine) and T4 (tetra iodothyronine) that are involved in various cellular metabolic process and functions .growth and development . since the thyroid hormone affect the metabolism and it also affect blood sugar regulation that's increase the risk of diabetes or glycemic control . the presence the risk of insulin resistance alson increase the risk of thyroid disorder

Previous studies reported that changes in level in thyroid hormone associated with diabetes . hypothyroidism and hyperthyroidism associated with hyperglycemia . Autoimmune is to be the primary of thyroid disorder in diabetes mellitus .



Thyroid hormone disorder

Change in the level of thyroid hormone lead to disorder of the thyroid (hyper and hypothyroidism) . hyperthyroidism is elevation level of circulating thyroid hormone the most common causes are Graves disease,multinodular goiter and toxic adenoma the level of T3 and T4 increase while the TSH level is decrease in hyprtthyroidism . and in case of hypothyroidism its common condition of thyroid hormone deficiency T3 and T4 while TSH level is high . incidence of thyroid dysfunction is high in pregnant women with high risk of gestational diabetes . postbirth thyroid dysfunction is found in 25% of women with type 1 diabetes mellitus

Effect of hyperthyroidismon in glucose homeostasis

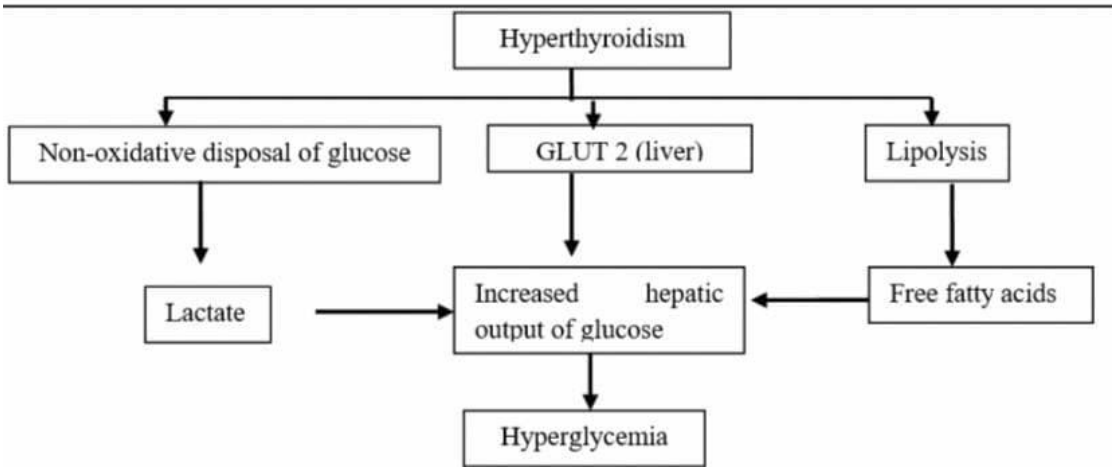
Hyperthyroidism has long been recognized to promote hyperglycemia . During hyperthyroidism, the half-life of insulin is reduced most likely secondary to an increased rate of degradation and an enhanced release .of biologically inactive insulin precursors

In untreated Graves' disease, increased proinsulin levels in response to a meal . In addition, untreated hyperthyroidism was associated with a reduced C-peptide to proinsulin ratio suggesting an underlying defect in proinsulin processing. Another mechanism explaining the relationship between hyperthyroidism and hyperglycemia is the increase in glucose gut absorption mediated by the excess thyroid hormones

Endogenous production of glucose is also enhanced in hyperthyroidism via several mechanisms. Thyroid hormones produce an increase in the hepatocyte plasma membrane concentrations of GLUT2 which is the main glucose transporter in the liver, and consequently, the increased levels of GLUT-2 contribute to the increased hepatic glucose output and abnormal glucose metabolism . Additionally, increased lipolysis is observed in hyperthyroidism resulting in an increase in FFA that stimulates hepatic gluconeogenesis. The increased

release of FFA could partially be explained by an enhanced catecholamine-stimulated lipolysis induced by the excess thyroid hormones . Moreover, the nonoxidative glucose disposal in hyperthyroidism is enhanced resulting in an overproduction of lactate that enters the Cori cycle and promotes further hepatic gluconeogenesis. The increase in GH, glucagon and catecholamine levels associated with hyperthyroidism further contributes to the impaired glucose tolerance

It is well known that diabetic patients with hyperthyroidism experience worsening of their glycemic control and thyrotoxicosis has been shown to precipitate diabetic ketoacidosis in subjects with diabetes



Effect of hypothyroidism in glucose homeostasis

As for hypothyroidism, glucose metabolism is affected as well via several mechanisms. A reduced rate of liver glucose production is observed in hypothyroidism

and accounts for the decrease in insulin requirement in hypothyroid diabetic patients. Recurrent hypoglycemic episodes are the presenting signs for the development of hypothyroidism in patients with type 1 diabetes and replacement with thyroid hormones reduced the fluctuations in blood glucose levels . In a case control study involving type 1 diabetic patients, those with subclinical hypothyroidism experienced more frequent episodes of hypoglycemia during the 12 months prior to the diagnosis of hypothyroidism compared to euthyroid diabetics. On the other hand, both clinical and subclinical hypothyroidisms have been recognized as insulin resistant states . In vivo and in vitro studies have shown that this is due to impaired insulin stimulated glucose utilization in peripheral tissues . A recent study involving subjects from a Chinese population found a higher TSH level in patients with metabolic syndrome compared to that in the nonmetabolic syndrome group suggesting that subclinical hypothyroidism may be a risk factor for metabolic syndrome . More recently, Erdogan et al. found an increased frequency of metabolic syndrome in subclinical and overt hypothyroidism compared to healthy controls Therefore, it seems prudent to consider hypothyroidism in newly diagnosed metabolic syndrome patients. This raises the issue whether routine screening for thyroid disease in all patients newly diagnosed with metabolic syndrome will be cost effective.Furthermore,

an increased risk of nephropathy was shown in type 2 diabetic patients with subclinical hypothyroidism which could be explained by the decrease in cardiac output and increase in peripheral vascular resistance seen with hypothyroidism and the resulting decrease in renal flow ,and glomerular filtration

reported that treating hypothyroidism improved renal function in diabetic patients . As for retinopathy, Yang et al. demonstrated recently that diabetic patients with subclinical hypothyroidism have more severe retinopathy .than euthyroid patients with diabetes

The increased risk of retinopathy and nephropathy observed in diabetic patients with subclinical hypothyroidism provides evidence in favor of screening patients with type 2 diabetes for thyroid dysfunction and treating when present

.

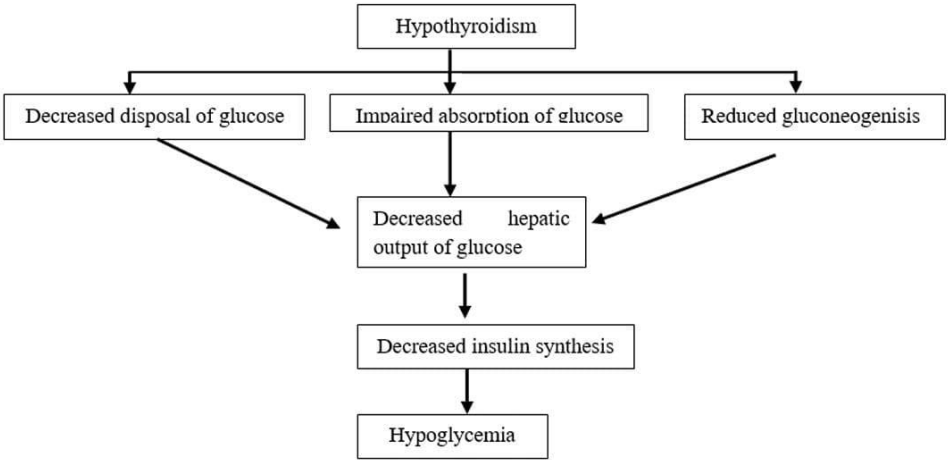


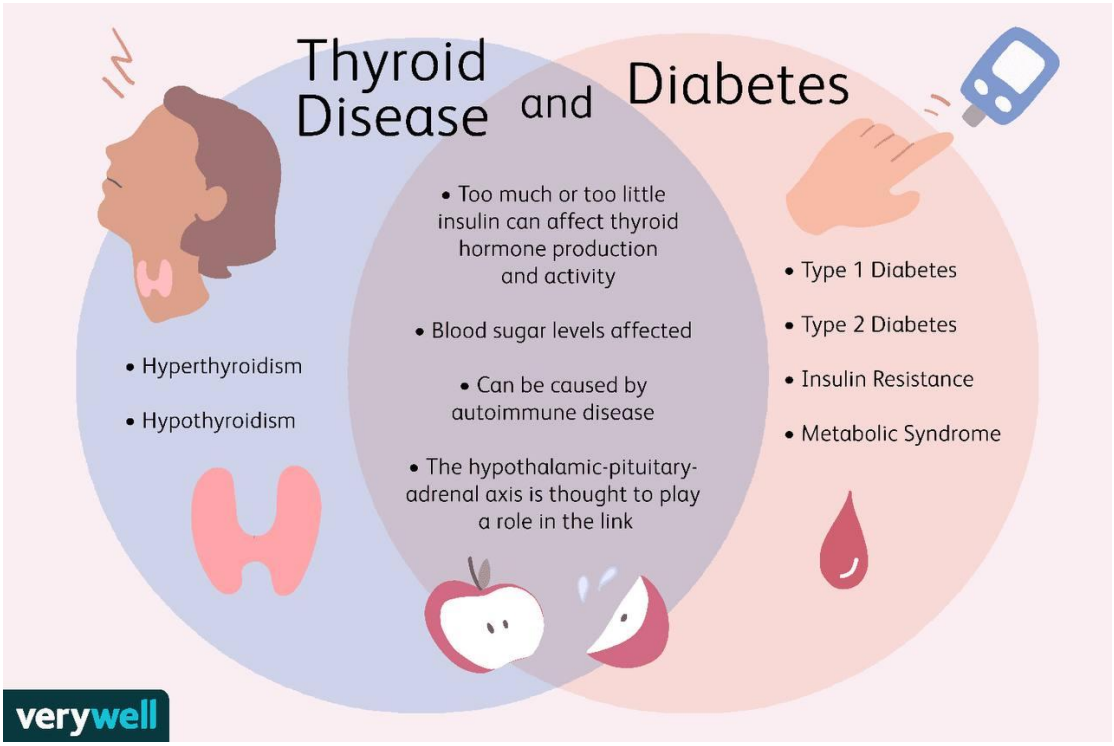
Fig. 1: Hypothyroidism and glucose metabolism

Effect of diabetes on thyroid hormone

Diabetes mellitus affects thyroid function by altering the thyroid stimulating hormone (TSH) level and impairing the conversion of thyroxine (T4) to triiodothyronine (T3) in peripheral tissue that normalizes with improvement in glycemic control . high level of circulating insulin associated with insulin resistance have shown effect on thyroid tissue leading to enlargement of the size of thyroid with increase formation of the nodule .

Table 1: Mutual association between diabetes and thyroid

Clinical profile	Influence on glycemia	Effect on thyroid function or thyroid disorder
Diabetes mellitus (euthyroid individuals)	-	T3↓, rT3↑ ↓ Response of TSH to TRH Impairment in nocturnal TSH peak
Diabetes mellitus (hyperthyroid individuals)	Poor control of glycemia	↑ dysthyroid optic neuropathy
Hyperthyroidism (normoglycemic individuals)	Glucose intolerane (50% of cases)	-
Hyperthyroidism (diabetic individuals)	Deteriorates control of diabetes	-
Hypothyroidism (diabetic individuals)	Predisposes recurrent hypoglycaemia	-
Autoimmune (T1DM)	-	↑ incidence of disease



Diagnosis and treatment of thyroid in diabetes

Diabetes affects thyroid function at two level

>first level at hypothalamus which control the secretion of TSH .in DM response of TSH to TRH impaired
>second level at the peripheral tissue 80% of T4 is converted to T3

Measurement of T3 ,T4 and TSH in the presence of hyperglycemia maybe impaired

So its need to measurement of TSH and thyroperxidase antibody in all diabetic patients

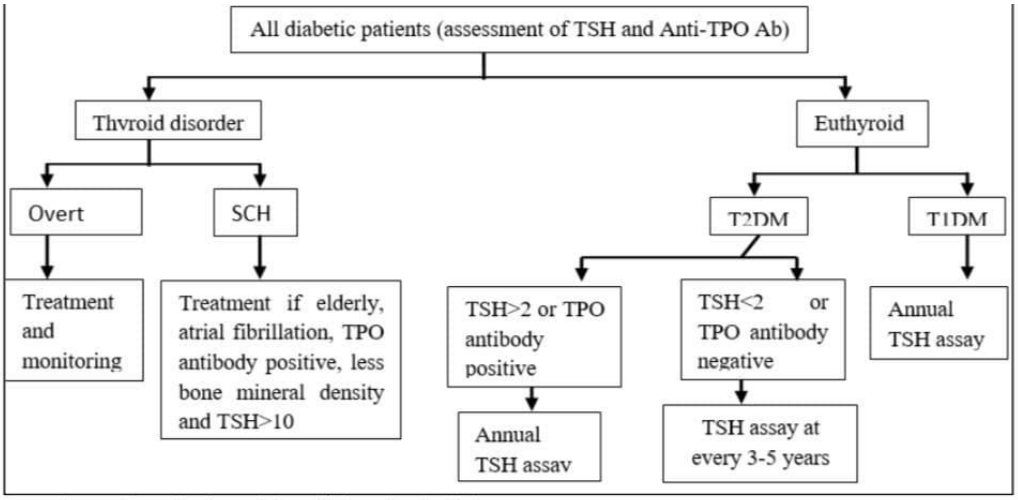


Fig. 3: Screening and monitoring of thyroid function in diabetes

Metformin the most widely used antidiabetic drug for DM type 2 . common anti diabetic drug suppress the secretion of TSH in hypothyroid patient .

Conclusion

Thyroid disorders are common in diabetic patients. Though the efforts are being increasingly made to unravel the pathophysiological mechanisms involved, there is still a requirement of further in-depth studies. Thyroid dysfunctions if untreated can impair metabolic processes and further increase CVD risk in diabetes. SCH is the most commonly observed thyroid disorder in diabetes and confers greater risk of associated complications. Thus it is very important to diagnose thyroid disorder in diabetic patients and screening should also be recommended in routine practice in diabetic care. It is necessary from the part of clinician to identify the high-risk diabetic groups and manage the thyroid abnormalities if present as early as possible to minimize the risk of further complications

References

1.Radaideh AR, Nusier MK, Amari FL, Bateiha AE, El-Khateeb MS et al. Thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. Saudi Med J

2.Mishra M, Sotto MR, Panta R, Miyares M, Solanki R. Association of Diabetes Mellitus and Thyroid Disorders: A Metabolic Prospective. Asian Pac J Health Sci

3. Wang C. The Relationship between Type 2 Diabetes Mellitus and Related .Thyroid Diseases. J Diabetes Res 2013;2013:390534

4.Monaco F. Classification of thyroid diseases: suggestions for a revision. J Clin Endocrinol Metab

5.Nazir. s., Sharma p., itagappa M, kumar p, Sharma R evaluation of metabolic

Syndrome as complication in thyroid patient in

6.Reilly DS. Thyroid function test time for reassessment . BMJ 2000,320(7245)

7. Menon VU . sundaram KR unnikrishnan AG jayakumar RV.Nair V . Kumar high

Prevalence of undetected thyroid disorder in an iodine insuffient

8.Gupta G, Sharma preeeti , kumar P, Sharma, R cardiovascular risk in patients

With mild to severe subclinical hypothyroidism

9.Perros P , McCrimmon RJ, shaw G, Frier BM . Frequency of thyroid dysfunction

In diabetic patient

10.Kadiyala R, Peter R, Okosieme OE Thyroid dysfunction in patients with diabetes

11.Han C, He X, Xia X, Li Y , Shi X , Shan Z , Teng W sub clinical hypothyroidism and

Type 2 diabetes

12. Gerstein HC incidence of postpartum thyroid dysfunction

13..... H. R. Maxon, K. W. Kreines, R. E. Goldsmith , and H. C. Knowles, "Long-term observations of glucose tolerance in thyrotoxic patients," Archives of Internal .Medicine, vol. 135, no. 11, pp. 1477–1480, 1975

14..... N. M. O'Meara, J. D. Blackman, J. Sturis, and K. S. Polonsky, "Alterations in the kinetics of C-peptide and insulin secretion in hyperthyroidism," Journal of Clinical Endocrinology and Metabolism, vol. 76, no. 1, pp. 79–84, 1993

15……. G. Dimitriadis, B. Baker, H. Marsh et al., “Effect of thyroid hormone excess on action, secretion, and metabolism of insulin in humans,” The American journal of] .physiology, vol. 248, no. 5, pp. E593–E601, 1985

.

16... S. F. Beer, J. H. Parr, R. C. Temple, and C. N. Hales, “The effect of thyroid disease on proinsulin and C-peptide levels,” Clinical Endocrinology, vol. 30, no. 4, pp. 3

17…….. R. J. Levin and D. H. Smyth , “The effect of the thyroid gland on intestinal absorption of hexoses,” The Journal of physiology, vol. 169, pp. 755–769, 1963

18…. A.J. MattyandB.Seshadri, “Effect of thyroxine on the isolated rat intestine,” Gut, .vol. 6, pp. 200–202, 1965

19…... H.F.Kemp,H.S.Hundal,andP.M.Taylor,“Glucosetransport correlates with GLUT2 abundance in rat liver during altered thyroid status,” Molecular and Cellular Endocrinology, vol. 128, no. 1-2, pp. 97–102, 1997

20.. T. Mokuno, K. Uchimura, R. Hayashi et al., “Glucose transporter 2 concentrations in hyper-and hypothyroid rat livers,” Journal of Endocrinology, vol. 160, no. 2, pp. 285– .289, 1999

21…….M. Vaughan, “An in vitro effect of triiodothyronine on rat adipose tissue,” .Journal of Clinical Investigation, vol. 46, no. 9, pp. 1482–1491, 1967

22.N.Miki,M.Ono,N.Hizuka,T.Aoki,andH.Demura, “Thyroid hormone modulation of the hypothalamic growth hormone (GH)-releasing factor-pituitary GH axis in the rat,” Journal of Clinical Investigation, vol. 90, no. 1, pp. 113–120, 1992.
23.F.Tosi,P.Moghetti,R.Castello,C.Negri,E.Bonora, and M. Muggeo, “Early changes in plasma glucagon and growth hormone response to oral glucose in experimental .hyperthyroidism,” Metabolism, vol. 45, no. 8, pp. 1029–1033, 1996

24……..L. Sestoft, N. J. Christensen, and B. Saltin, “Responses of glucose and glucoregulatory hormones to exercise in thyrotoxic and myxoedematous patients before and after 3 months of treatment,” Clinical Science, vol. 81, no. 1, pp. 91–99, .1991

25…….E. Sol´a, C. Morillas, S. Garz´on, M. G´omez-Balaguer, and A. Hern´andez- . Mijares, “Association between diabetic ketoacidosis and thyrotoxicosis,” Acta Diabetologica,vol.39,no.4,pp. 235–237, 2002. [41] A. Bhattacharyya and P. G. Wiles,

"Diabetic ketoacidosis precipitated by thyrotoxicosis," Postgraduate Medical Journal, .vol. 75, no. 883, pp. 291–292, 1999

26.F. Okajima and M. .,"Metabolism of glucose in hyper-and hypo-thyroid rats in vivo. Glucose-turnover values and futilecycle activities obtained with 14C-and 3H-labelled glucose," Biochemical Journal, vol. 182, no. 2, pp. 565–575, 1979

27……..K. S. Leong, M. Wallymahmed, J. Wilding, and I. MacFarlane, "Clinical . presentation of thyroid dysfunction and Addison's disease in young adults with type 1 .diabetes," Postgraduate Medical Journal, vol. 75, no. 886, pp. 467–470, 1999

28..G. Dimitriadis, P. Mitrou, V. Lambadiari et al., "Insulin action in adipose tissue and muscle in hypothyroidism," Journal of Clinical Endocrinology and Metabolism, vol. .91, no. 12, pp. 4930–4937, 2006

29.P. Cettour-Rose, C. Theander-CarrilloC. Asensio et al., "Hypothyroidism in rats decreases peripheral glucose utilisation, a defect partially corrected by central leptin .infusion," Diabetologia, vol. 48, no. 4, pp. 624–633, 2005

30…..E. Maratou, D. J. Hadjidakis, A. Kollias et al., "Studies of insulin resistance in patients with clinical and subclinical hypothyroidism," European Journal of Endocrinology, vol. 160, no. 5, pp. 785–790, 2009

31……..C. Rochon, I. Tauveron, C. Dejax et al., "Response of glucose disposal to hyperinsulinaemia in human hypothyroidism and hyperthyroidism," Clinical Science, vol. 104, no. 1, pp. 7–15, 2003

32……..G. Dimitriadis, M. Parry-Billings, S. Bevan et al., "The effects of insulin on transport and metabolism of glucose in skeletal muscle from hyperthyroid and hypothyroid rats," Europea

33……..M. Erdogan et al., "Metabolic syndrome prevelance in subclinic and overt hypothyroid patients and the relation among metabolic syndrome parameters," .Journal of Endocrinological Investigation. In press

34….H. S. Chen, T. E. J. Wu, T. S. Jap et al., "Subclinical hypothyroidism is a risk factor for nephropathy and cardiovascular diseases in Type 2 diabetic patients," Diabetic Medicine, vol. 24, no. 12, pp. 1336–1344, 2007

35……M. A. Singer, "Of mice and men and elephants: metabolic rate sets glomerular filtration rate," American Journal of Kidney Diseases, vol. 37, no. 1, pp. 164–178, 2001

36 ..J. G. Den Hollander, R. W. Wulkan, M. J. Mantel, and A. Berghout, “Correlation between severity of thyroid dysfunction and renal function,” Clinical Endocrinology, .vol. 62, no. 4, pp. 423–427, 2005

37……. .G. R. Yang, J. K. Yang, L. Zhang, Y. H. An, and J. K. Lu, “Association between subclinical hypothyroidism and proliferative diabetic retinopathy in type 2 diabetic patients: a case-control study,” Tohoku Journal of Experimental Medicine

38. …. Dora JM, Machado WE, Rheinheimer J, Crispim D, Maia AL. Association of the type 2 deiodinase Thr92Ala polymorphism with type 2 diabetes: case–control study .and meta-analysis. Eur J Endocrinol 2010;163(3):427-34

39..Gursoy NT, Tuncel E, Erturk E, Imamoglu S, Arinik A. The relationship between the glycemic control and the hypothalamus-pituitary-thyroid axis in diabetic patients. .Turk J Endocrinol Metab 1999;163-8

40…Ladenson PW, Singer PA, Ain KB, Bagchi N, Bigos ST, Levy EG, et al. American . Thyroid Association guidelines for detection of thyroid dysfunction. Arch Intern Med ,(2000;160(11