**Name of journal: World Journal of Diabetes**

**ESPS Manuscript NO: 2985**

**Columns: BRIEF ARTICLE**

**Effect of treatment of overt hypothyroidism on insulin resistance**

NadaAM**. Hypothyroidism and insulin resistance**

Aml Mohamed Nada

**Aml Mohamed Nada**, Department of Internal Medicine, Unit of Endocrinology, Diabetes and Metabolism, Faculty of Medicine, Mansoura University, Mansoura 35516, Egypt

**Correspondence to:** **Dr. Aml Mohamed Nada, MD, Lecturer,** Department of Internal Medicine, Unit of Endocrinology, Diabetes and Metabolism, Faculty of Medicine, Mansoura University, El-Gomhoria Street, Mansoura 35516, Egypt. aml\_nadanoha@yahoo.com

**Telephone:** +966-56-8089574

**Received:** March 30, 2013  **Revised:** July 2, 2013

**Accepted:** July 9, 2013

**Published online:**

**Abstract**

**AIM:** To investigate the impact of hypothyroidism and thyroxine therapy on insulin sensitivity in patients with overt hypothyroidism.

**METHODS:** The study included twenty seven overtly hypothyroid and fifteen healthy euthyroid South Western Asian females. Both groups had matching age and body mass index. Physiological and pathological conditions as well as medications that may alter thyroid function, glucose homeostasis or serum lipids were ruled out. Serum thyrotropin (TSH), free tetraiodothyronine (FT4), free triiodothyronine (FT3), fasting insulin (FI), fasting plasma glucose (FPG), total cholesterol and triglycerides were measured before and six months after initiating thyroxine therapy for hypothyroid patients and once for the control group. Insulin resistance (IR) was estimated using homeostasis model assessment (HOMA-IR) and Body mass index (BMI) was calculated.

**RESULTS**: Both study groups, hypothyroid patients and euthyroid control subjects, had matching age and body mass index *(P*-value 0.444, 0.607 respectively). No significant difference was found between the hypothyroid patients and the euthyroid control group regarding fasting plasma glucose, fasting insulin, insulin resistance, total cholesterol and triglycerides (*P*-values 0.432, 0.621, 0.883, 0.586, 0.05 respectively). In the hypothyroid patients, triglycerides showed direct correlation to TSH and inverse correlation to FT3. Similarly total cholesterol inversely correlated to FT3 but its direct correlation to TSH did not reach statistical significance. After thyroxine replacement and reaching an euthyroid state as confirmed by clinical and laboratory data, there was no significant change in fasting plasma glucose, insulin resistance or triglyceride level (*P*-value 0.216, 0.204, 0.175 respectively) while total cholesterol significantly decreased (*P*-value 0.043) and fasting insulin significantly increased (*P*-value 0.047).

**CONCLUSION:** Hypothyroidism has no impact on insulin sensitivity. Correction of hypothyroidism is not associated with a significant change of insulin sensitivity or triglycerides, but with a significant reduction of total cholesterol.

© 2013 Baishideng. All rights reserved.

**Key words:** Hypothyroidism; Females; Thyroxine; Insulin resistance; Triglycerides; Cholesterol

**Core tip:** Thyroid dysfunction is the second most common endocrine disorder after diabetes mellitus. Both diseases are strong associated. Hypothyroidism is claimed to cause insulin resistance. Some available reports are in agreement and others are against this suggestion. In our study, we did not find a significant effect of hypothyroidism or thyroxine replacement on insulin resistance as calculated by insulin resistance was estimated using homeostasis model assessment. Thyroxine therapy leads to a significant reduction of total cholesterol but it does not change triglycerides. This may partially explain the association between hypothyroidism and dyslipidaemia as well as cardiovascular risk.

**Nada AM.** Effect of treatment of overt hypothyroidism on insulin resistance.

Available from: URL:

DOI:

**INTRODUCTION**

Thyroid dysfunction and diabetes mellitus (DM) are the two most common endocrine disorders. Both disorders appear to be closely linked[1]. A recent meta-analysis that was conducted on available data in 10920 patients with DM revealed a mean frequency of thyroid disease of 11% with no difference between type 1 DM and type 2 DM. The prevalence in women was consistently more than two-folds that in men[2].

It has also been postulated that insulin secretion is regulated by the thyroid hormone[3, 4], and diabetes risk is related to thyroid hormone levels[5, [6](http://joe.endocrinology-journals.org/content/206/2/195.full#ref-5)].The initial event of glucose-stimulated insulin secretion is glucose sensing. The glucose transporter 2 (GLUT2) and glucokinase (GK) are key molecules which affect various processes of glucose sensing in pancreatic β-cells[[7](http://joe.endocrinology-journals.org/content/206/2/195.full%22%20%5Cl%20%22ref-27)]. Impairment in glucose sensing contributes to pancreatic β-cell dysfunction. Therefore, it is necessary to maintain adequate expression levels of GLUT2 and GK to ensure normal β-cell function[8]. Triiodothyronine (T3) can modulate the expression of GLUT2 and GK mRNAs and proteins in pancreatic islets[[9](http://joe.endocrinology-journals.org/content/206/2/195.full%22%20%5Cl%20%22ref-9)] and liver[[10](http://joe.endocrinology-journals.org/content/206/2/195.full#ref-19)].

To date, only a few studies have investigated the effect of hypothyroidism and its recovery by thyroid hormone treatment on glucose metabolism and lipid profile, and the results have been controversial. Some researchers elucidated lower insulin sensitivity in patients with overt hypothyroidism which improved after thyroxine treatment[11,12]. Subclinical hypothyroidism was also encountered as a cause of insulin resistance and its related dyslipidaemia in patients with rheumatoid arthritis[13]. Contrary to that, Brenta *et al*[14] did not find significant differences in insulin sensitivity or lipid profile before and after thyroxine replacement in subclinical hypothyroidism.

In the light of existing data, we decided to study the impact of hypothyroidism on insulin sensitivity in overtly hypothyroid patients and to investigate the possible effect of thyroxine replacement on insulin sensitivity, triglycerides and total cholesterol in those populations.

**MATERIALS AND METHODS**

This study was approved by the Research and Ethics Committee of Asir Central Hospital and written informed consents were acquired from all participants.

Forty-two South Western Asian females were recruited from the endocrine clinic in a tertiary care hospital in southern region of Saudi Arabia, during January 2010 and December 2011. They included twenty seven patients with overt hypothyroidism and fifteen healthy euthyroid control women with matching age and body mass index. Full history taking and clinical examination were done for all participants. The inclusion criteria were: adult, premenopausal females, who were newly diagnosed with overt hypothyroidism. Exclusion criteria were diabetes, polycystic ovarian disease, liver disorders, renal disorders, congestive cardiac failure or any other systemic illness. In addition, pregnancy and lactation, intake of oral contraceptive pills, statins and other medications that may alter thyroid functions, glucose homeostasis or serum lipids also accounted for exclusion from the study.

After an overnight fasting, blood samples were collected from all participants for measuring biochemical parameters. Thyroid profile (TSH, FT4 and FT3), fasting insulin, fasting plasma glucose, total cholesterol and triglycerides were measured, before and six months after initiating thyroxine therapy and reaching an euthyroid state for hypothyroid patients. These parameters were measured once for the euthyroid control group.

Insulin resistance (IR) was estimated using HOMA-IR,IR= FPG in milli-gram per deciliter × FI in micro-international unit per milli-litre /405[15, 16].Body mass index (BMI) was calculated by dividing weight of the patient in kilograms by square the height of the patient in meters[17].

Thyroid profile and insulin level were estimated by Advia centaur auto-analyzer Siemens using chemiluminescent technology. Fasting plasma glucose and triglycerides were measured by bichromatic technique while cholesterol was measured by polychromatic technique. Normal ranges for all parameters: TSH: 0.27-4.2 µIU/mL**,** FT4: 12-22 pmol/L, FT3: 3.9-6.8 pmol/L, FI: 2.6-37.6µIU/mL, total cholesterol: 50-200 mg/dL, triglycerides: 30-150 mg/dL[18-22] .

***Statistical analysis***

Collected data were analyzed using the Statistical Package for Social Sciences (SPSS ver. 19). Descriptive statistics (i.e., mean and standard deviation) were applied. Pearson’s Correlation Coefficients (r) between study variables were calculated. Significant *P*-values were considered at <0.05.

**RESULTS**

Our study population consisted of 42 females; 27 patients with overt hypothyroidism and 15 euthyroid healthy participants. The two groups had matching age and body mass index (33.12 ± 10.4 *vs* 35.67 ± 9.1, *P* = 0.44, 31.11 ± 6.78 *vs* 32.24 ± 6.68, *P* = 0.61 respectively). Fasting insulin, FPG, IR, total cholesterol and triglycerides did not show significant difference in hypothyroid patients as compared to the euthyroid group (*P-* values0.432, 0.621, 0.883, 0.586, 0.05 respectively) as shown in Table 1.

In the hypothyroid state, Triglycerides directly correlated to TSH and inversely to FT3 (*P*-value 0.009, 0.001 respectively). Total cholesterol inversely correlated to FT3 (*P*-value 0.029) and was directly proportionate to TSH although this relation did not reach statistical significance (*P* value = 0.327) as shown in Table 2.

After thyroxine replacement and attaining euthyroid state, there was no significant change in FPG or IR as compared to that before starting treatment (*P*-value = 0.216, 0.204 respectively) while FI significantly increased (*P* = 0.047). There was no significant change in triglycerides (*P*-value 0.175) meanwhile total cholesterol significantly decreased (*P*-value 0.043) as shown in Table 3.

**DISCUSSION**

The association between hypothyroidism and diabetes mellitus had raised great interest in studying the mechanism of this association. Many studies targeted the influence of hypothyroidism on insulin sensitivity as the main underlying pathophysiology of this relation. Despite the many studies, results are conflicting with several studies reporting that hypothyroidism is a state of increased insulin resistance[23, 24].

In our study, there was no significant difference between the hypothyroid patients and the euthyroid healthy group regarding fasting insulin, FPG and insulin resistance. This is consistent with results of a study conducted by Olga et al[25] on 17 hypothyroid women compared to 20 euthyroid control women.

Similarly, Owecki et al[26] did not find a significant difference in insulin sensitivity between hypothyroid patients and euthyroid participants.

Neither FPG nor insulin resistance as calculated by HOMA-IR significantly changed after thyroxine replacement and reaching an euthyroid state as per clinical and laboratory evidence. There was a significant increase in the fasting insulin as compared to the pretreatment level but this was not statistically significant when compared to the euthyroid control (13.55 ± 7.25 *vs* 11.82 ± 6.31, *P =* 0.445) and it did not affect the overall calculated insulin resistance. This is again in agreement with results demonstrated by Olga et al[25] although the increase in insulin levels in his study did not reach a statistical significance.

Referring to our study and studies in agreement with our findings, we can say that the association between hypothyroidism and T2DM may be attributed to a complex interplay[27]. It may depend on the severity of hypothyroidism[28]. There may be direct genetic links between thyroid diseases and T2DM as suggested by few studies. These studies suggest that homozygosity of polymorphism of the deiodinase type 2 (DIO2) gene, Thr92Ala is associated with an increased risk of T2DM[29]. Thyroid hormones may also affect glucose and lipid homeostasis via central effects at the level of the hypothalamus[30].

Hypothyroidism is known to be associated with normal or high levels of triglycerides[31-33].In our study, triglycerides in the hypothyroid patients did not differ significantly from the euthyroid control with direct proportion to TSH and inverse proportion to FT3[34]. Triglycerides did not significantly change after thyroxine replacement. This is in agreement with reports of several studies, which showed that triglycerides might be normalized or remain unchanged after treatment, suggesting a more complex cause of dyslipidaemia in hypothyroidism[35-44].

Total cholesterol inversely correlated to FT3 in the hypothyroid patients with a significant decrease after thyroxine therapy. This is consistent with results obtained by Melpomeni et al who found that restoration of an euthyroid state in hypothyroid patients was associated with a significant reduction in total cholesterol**[**34, 44]. Our findings are also consistent with those demonstrated in several other studies[36, 38–42, 45].

The presence of some variations among different studies regarding the association between hypothyroidism and disturbed lipid profile may be explained by the variable effects of hypothyroidism on lipids according to the severity of hypothyroidism in the studied groups of patients as evidenced bySunanda *et al*[46]. Sunanda *et al* studied the lipid profile in hypothyroid patients with different degrees of hypothyroidism and concluded that the effect of hypothyroidism on the serum lipids is more marked in patients with higher TSH levels.

So, the association between hypothyroidism and cardiovascular risk[46, 47] may be attributed to the dyslipidaemic effect of hypothyroidism, underlying genetic factor or there may be another complex underlying mechanism that deserves further studies.

In conclusion, our study suggests that hypothyroidism has no impact on insulin sensitivity in overtly hypothyroid females of South Western Asian ethnicity. Thyroxine therapy does not cause significant change in insulin sensitivity in this ethnic group. So, other mechanisms that may explain the strong association between hypothyroidism and T2DM may exist. Although total cholesterol and triglycerides are not significantly higher in hypothyroid patients, thyroxine treatment leads to a significant reduction in total cholesterol without a significant effect on triglycerides. This may partially explain the association between hypothyroidism and cardiovascular risk.

**COMMENTS**

***Background***

Diabetes mellitus and hypothyroidism are the most common endocrine disorders. A strong association between both conditions exists. It was claimed that hypothyroidism increases the risk of developing diabetes mellitus through increased insulin resistance but studies in this field demonstrated conflicting data.

***Research frontiers***

Recent evidences suggest that hypothyroidism is associated with dyslipidaemia and increased cardiovascular risk.

***Innovations and breakthroughs***

The results presented herein show that in South Western Asian females, neither overt hypothyroidism nor thyroxine replacement has an effect on insulin resistance. Thyroxine therapy leads to a significant reduction in total cholesterol.

***Applications***

Our study indicates that the increased risk of diabetes mellitus in hypothyroid patients cannot be attributed to increased insulin resistance. So, investigating other mechanisms that may be involved is highly encouraged. Thyroxine therapy leads to a significant reduction in total cholesterol but it does not affect triglycerides. This partially explains the association between hypothyroidism and increased cardiovascular risk.

***Peer review***

This is an interesting article about the effect of overt hypothyroidism and thyroxine therapy on insulin resistance and lipid profile in a specific ethnic population.

**REFERENCES**

1 **Perros P**, McCrimmon RJ, Shaw G, Frier BM. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. *Diabet Med* 1995; **12**: 622-627 [PMID: 7554786 DOI: 10.1111/j.1464-5491.1995.tb00553.x]

2 **Kadiyala R**, Peter R, Okosieme OE. Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. *Int J Clin Pract* 2010; **64**: 1130-1139 [PMID: 20642711 DOI: 10.1111/j.1742-1241.2010.02376.x]

3 **Cortizo AM**, Gómez Dumm CL, Gagliardino JJ. Effect of thyroid hormone levels upon pancreatic islet function. *Acta Physiol Pharmacol Latinoam* 1985; **35**: 181-191 [PMID: 2938405]

4 **Doong ML**, Wang JW, Chung SC, Liu JY, Hwang C, Hwang CY, Day CH, Liu YF, Young TK, Ho LL, Wang PS. Regulation of thyroid hormones in the secretion of insulin and gastric inhibitory polypeptide in male rats. *Metabolism* 1997; **46**: 154-158 [PMID: 9030821 DOI: 10.1016/S0026-0495(97)90294-8]

5 **Iossa S**, Lionetti L, Mollica MP, Crescenzo R, Barletta A, Liverini G. Fat balance and serum leptin concentrations in normal, hypothyroid, and hyperthyroid rats. *Int J Obes Relat Metab Disord* 2001; **25**: 417-425 [PMID: 11319641 DOI: 10.1038/sj.ijo.0801516]

6 **Crunkhorn S**, Patti ME. Links between thyroid hormone action, oxidative metabolism, and diabetes risk? *Thyroid* 2008; **18**: 227-237 [PMID: 18279023 DOI: 10.1089/thy.2007.0249]

7 **Matschinsky FM**. Glucokinase as glucose sensor and metabolic signal generator in pancreatic beta-cells and hepatocytes. *Diabetes* 1990; **39**: 647-652 [PMID: 2189759 DOI: 10.2337/diabetes.39.6.647]

8 **Cerf ME**. High fat diet modulation of glucose sensing in the beta-cell. *Med Sci Monit* 2007; **13**: RA12-RA17 [PMID: 17179917]

9 **García-Flores M**, Blázquez E, Zueco JA. Effects of triiodothyronine and bovine growth hormone on glucose transporter isoform-2 (GLUT-2) and glucokinase (GK) gene expression in pancreatic islets of fetal and adult rats. *Pflugers Arch* 2001; **442**: 662-667 [PMID: 11512021 DOI: 10.1007/s004240100583]

10 **Kemp HF**, Hundal HS, Taylor PM. Glucose transport correlates with GLUT2 abundance in rat liver during altered thyroid status. *Mol Cell Endocrinol* 1997; **128**: 97-102 [PMID: 9140080 DOI: 10.1016/S0303-7207(97)04026-4]

11 **Stanická S**, Vondra K, Pelikánová T, Vlcek P, Hill M, Zamrazil V. Insulin sensitivity and counter-regulatory hormones in hypothyroidism and during thyroid hormone replacement therapy. *Clin Chem Lab Med* 2005; **43**: 715-720 [PMID: 16207130 DOI: 10.1515/CCLM.2005.121]

12 **Handisurya A**, Pacini G, Tura A, Gessl A, Kautzky-Willer A. Effects of T4 replacement therapy on glucose metabolism in subjects with subclinical (SH) and overt hypothyroidism (OH). *Clin Endocrinol (Oxf)* 2008; **69**: 963-969 [PMID: 18429948 DOI: 10.1111/j.1365-2265]

13 **Dessein PH**, Joffe BI, Stanwix AE. Subclinical hypothyroidism is associated with insulin resistance in rheumatoid arthritis. *Thyroid* 2004; **14**: 443-446 [PMID: 15242571 DOI: 10.1089/105072504323150750]

14 **Brenta G**, Berg G, Arias P, Zago V, Schnitman M, Muzzio ML, Sinay I, Schreier L. Lipoprotein alterations, hepatic lipase activity, and insulin sensitivity in subclinical hypothyroidism: response to L-T(4) treatment. *Thyroid* 2007; **17**: 453-460 [PMID: 17542675 DOI: 10.1089/thy.2006.0302]

15 **Matthews DR**, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; **28**: 412-419 [PMID: 3899825 DOI: 10.1007/BF00280883]

16 **Harris PE**, Walker M, Clark F, Home PD, Alberti KG. Forearm muscle metabolism in primary hypothyroidism. *Eur J Clin Invest* 1993; **23**: 585-588 [PMID: 8243531 DOI: 10.1111/j.1365-2362.1993.tb00970.x]

17 **Gallagher D**, Heymsfield SB, Heo M, Jebb SA, Murgatroyd PR, Sakamoto Y. Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. *Am J Clin Nutr* 2000; **72**: 694-701 [PMID: 10966886]

18 **Kaplan MM**. Thyroid function testing in patients with thyroid and non-thyroid diseases. Mono: Thyroid Testing; Chiron Diagnostics Corporation; 1996

19 **Fisher DA**. Physiological variations in thyroid hormones: physiological and pathophysiological considerations. *Clin Chem* 1996; **42**: 135-139 [PMID: 8565215]

20 F**ernandez-Ulloa M**, Maxon HR. Thyroid. In: Kaplan LA, Pesce AJ, editors. Clinical chemistry: theory analysis, and correlation. 2nd ed. St. Louis: CV Mosby, 1989; 620–38.

21 Clinical and Laboratory Standards Institute (formerly NCCLS). Procedures for the Handling and Processing of Blood Specimens; Approved Guideline, 3rd ed. Wayne PA: Clinical and Laboratory Standards Institute; NCCLS Document H18-A3, 2004

22 **Dods RF**. Diabetes Mellitus. In: Kaplan LA, Pesce AJ, Clinical chemistry: theory, analysis, and correlation, 3rd ed. St. Louis: CV Mosby, 1996: 619-621.

23 **Rochon C**, Tauveron I, Dejax C, Benoit P, Capitan P, Fabricio A, Berry C, Champredon C, Thieblot P, Grizard J. Response of glucose disposal to hyperinsulinaemia in human hypothyroidism and hyperthyroidism. *Clin Sci (Lond)* 2003; **104**: 7-15 [PMID: 12519082 DOI: 10.1042/CS20020154]

24 **Stanicka S**, Vondra K, Pelikánová T. Insulin sensitivity and counter-regulatory hormones in hypothyroidism and during thyroid hormone replacement therapy. Clinical Chemistry and Laboratory Medicine 2005; **43**: 715–720. [DOI: 10.4061/2011/152850]

25 **Giménez-Palop O**, Giménez-Pérez G, Mauricio D, Berlanga E, Potau N, Vilardell C, Arroyo J, González-Clemente JM, Caixàs A. Circulating ghrelin in thyroid dysfunction is related to insulin resistance and not to hunger, food intake or anthropometric changes. *Eur J Endocrinol* 2005; **153**: 73-79 [PMID: 15994748 DOI: 10.1530/eje.1.01934]

26 **Owecki M**, Nikisch E, Sowiński J. Hypothyroidism has no impact on insulin sensitivity assessed with HOMA-IR in totally thyroidectomized patients. *Acta Clin Belg* 2006; **61**: 69-73 [PMID: 16792337]

27 **Kapadia KB**, Bhatt PA, Shah JS. Association between altered thyroid state and insulin resistance. *J Pharmacol Pharmacother* 2012; **3**: 156-160 [PMID: 22629091]

28 **Mackowiak P**, Ginalska E, Nowak-Strojec E, Szkudelski T. The influence of hypo- and hyperthyreosis on insulin receptors and metabolism. *Arch Physiol Biochem* 1999; **107**: 273-279 [PMID: 10779823]

29 **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**: 427-434 [PMID: 20566590]

30 The Interface between thyroid and diabetes mellitus. *Clin Endocrinol (Oxf)* 2011; [PMID: 21521298 DOI: 10.1111/j.1365-2265.2011.04029.x]

31 **Abrams JJ**, Grundy SM, Ginsberg H. Metabolism of plasma triglycerides in hypothyroidism and hyperthyroidism in man. *J Lipid Res* 1981; **22**: 307-322 [PMID: 7240960]

32 **Lam KS**, Chan MK, Yeung RT. High-density lipoprotein cholesterol, hepatic lipase and lipoprotein lipase activities in thyroid dysfunction--effects of treatment. *Q J Med* 1986; **59**: 513-521 [PMID: 3763814]

33 **Krauss RM**, Levy RI, Fredrickson DS. Selective measurement of two lipase activities in postheparin plasma from normal subjects and patients with hyperlipoproteinemia. *J Clin Invest* 1974; **54**: 1107-1124 [PMID: 4370795 DOI: 10.1172/JCI107855]

34 **Shrestha N**. Thyroid dysfunction and its effect in serum lipids. *J Nepal Health Res Counc* 2011; **9**: 33-37 [PMID: 22929710]

35 **Tzotzas T**, Krassas GE, Konstantinidis T, Bougoulia M. Changes in lipoprotein(a) levels in overt and subclinical hypothyroidism before and during treatment. *Thyroid* 2000; **10**: 803-808 [PMID: 11041458 DOI: 10.1089/thy.2000.10.803]

36 **de Bruin TW**, van Barlingen H, van Linde-Sibenius Trip M, van Vuurst de Vries AR, Akveld MJ, Erkelens DW. Lipoprotein(a) and apolipoprotein B plasma concentrations in hypothyroid, euthyroid, and hyperthyroid subjects. *J Clin Endocrinol Metab* 1993; **76**: 121-126 [PMID: 8421075 DOI: 10.1210/jc.76.1.121]

37 **Becerra A**, Bellido D, Luengo A, Piédrola G, De Luis DA. Lipoprotein(a) and other lipoproteins in hypothyroid patients before and after thyroid replacement therapy. *Clin Nutr* 1999; **18**: 319-322 [PMID: 10601541 DOI: 10.1016/S0261-5614(98)80031-9]

38 **Klausen IC**, Nielsen FE, Hegedüs L, Gerdes LU, Charles P, Faergeman O. Treatment of hypothyroidism reduces low-density lipoproteins but not lipoprotein(a). *Metabolism* 1992; **41**: 911-914 [PMID: 1386404 DOI: 10.1016/0026-0495(92)90176-B]

39 **Ito M**, Arishima T, Kudo T, Nishihara E, Ohye H, Kubota S, Fukata S, Amino N, Kuma K, Sasaki I, Hiraiwa T, Hanafusa T, Takamatsu J, Miyauchi A. Effect of levo-thyroxine replacement on non-high-density lipoprotein cholesterol in hypothyroid patients. *J Clin Endocrinol Metab* 2007; **92**: 608-611 [PMID: 17148561 DOI: 10.1210/jc.2006-1605]

40 **Paoli M**, Bellabarba G, Velazquez E, Mendoza S, Molina C, Wang P, Glueck CJ. Sex steroids, lipids, and lipoprotein cholesterols in women with subclinical and overt hypothyroidism before and after L-thyroxine therapy. *Clin Chim Acta* 1998; **275**: 81-91 [PMID: 9706846 DOI: 10.1016/S0009-8981(98)00074-6]

41 **Pazos F**, Alvarez JJ, Rubiés-Prat J, Varela C, Lasunción MA. Long-term thyroid replacement therapy and levels of lipoprotein(a) and other lipoproteins. *J Clin Endocrinol Metab* 1995; **80**: 562-566 [PMID: 7852521 DOI: 10.1210/jc.80.2.562]

42 **Martínez-Triguero ML**, Hernández-Mijares A, Nguyen TT, Muñoz ML, Peña H, Morillas C, Lorente D, Lluch I, Molina E. Effect of thyroid hormone replacement on lipoprotein(a), lipids, and apolipoproteins in subjects with hypothyroidism. *Mayo Clin Proc* 1998; **73**: 837-841 [PMID: 9737219 DOI: 10.4065/73.9.837]

43 **O'Brien T**, Katz K, Hodge D, Nguyen TT, Kottke BA, Hay ID. The effect of the treatment of hypothyroidism and hyperthyroidism on plasma lipids and apolipoproteins AI, AII and E. *Clin Endocrinol (Oxf)* 1997; **46**: 17-20 [PMID: 9059553]

44 **Arem R**, Escalante DA, Arem N, Morrisett JD, Patsch W. Effect of L-thyroxine therapy on lipoprotein fractions in overt and subclinical hypothyroidism, with special reference to lipoprotein(a). *Metabolism* 1995; **44**: 1559-1563 [PMID: 8786724 DOI: 10.1016/0026-0495(95)90075-6]

45 **Teixeira Pde F**, Reuters VS, Ferreira MM, Almeida CP, Reis FA, Buescu A, Costa AJ, Vaisman M. Lipid profile in different degrees of hypothyroidism and effects of levothyroxine replacement in mild thyroid failure. *Transl Res* 2008; **151**: 224-231 [PMID: 18355770 DOI: 10.1016/j.trsl.2007.12.006]

46 **Sunanda V**, Sangeeta S, Prabhakar rao B. Study of lipid profile in hypothyroidism. Int J Biol Med Res. 2012; **3**: 1373-1376.

47 **Duntas LH**, Brenta G. The effect of thyroid disorders on lipid levels and metabolism. *Med Clin North Am* 2012; **96**: 269-281 [PMID: 22443975 DOI: 10.1016/j.mcna.2012.01.012]

**P-Reviewers** Mortensen O, Sasaoka T **S-Editor** Wen LL  **L-Editor**  **E-Editor**

**Table 1 Laboratory and anthropometric parameters in hypothyroid patients versus euthyroid subjects**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Hypothyroid (mean ± SD)** | **Euthyroid****(mean ± SD)** | ***P*-value** |
| Age (yr) | 33.2±10.4 | 35.7±9.1 | 0.444 |
| BMI | 31.1±6.8 | 32.2±6.7 | 0.607 |
| TSH | 22.4±36.2 | 2.9±1.5 | 0.010 |
| FT4 | 11.2±4.0 | 13.7±2.1 | 0.013 |
| FT3 | 4.4±1.0 | 4.5±0.5 | 0.557 |
| FPG | 93.5±14.7 | 89.8±13.9 | 0.432 |
| FI | 10.6±8.1 | 11.8±6.3 | 0.621 |
| IR | 2.5±2.1 | 2.6±1.5 | 0.883 |
| TG | 144.8±85.4 | 97.9±36.1 | 0.050 |
| TCH | 195.0±37.9 | 189.0±29.9 | 0.586 |

BMI: Body mass index; TSH: Thyrotropin; FPG: Fasting plasma glucose; FI: Fasting insulin; IR: Insulin resistance; FT4: Free tetraiodothyronine; FT3: Free triiodothyronine; TG: Triglycerides; TCH: Total cholesterol.

**Table 2 Correlation between different variables before thyroxine replacement**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **TSH** | **FT4** | **FT3** |
| TG | r | 0.496 | -0.321 | -0.585 |
|  | *P* | 0.009 | 0.102 | 0.001 |
| TCH | r | 0.196 | -0.176 | -0.420 |
|  | *P* | 0.327 | 0.380 | 0.029 |

TSH: Thyrotropin; FT4: Free tetraiodothyronine; FT3: Free triiodothyronine; TG: Triglycerides; TCH: Total cholesterol; R: Relative coefficient.

**Table 3 Comparison between different variables before and after thyroxine replacement**

|  |  |  |  |
| --- | --- | --- | --- |
| **variable** | **Before treatment (mean ± SD)** | **After treatment****(mean ± SD)** | ***P*-value** |
| BMI | 31.1±6.8 | 31.4±7.2 | 0.485 |
| TSH | 22.4±36.2 | 3.0±1.9 | 0.010 |
| FT4 | 11.2±4.0 | 14.5±2.6 | 0.001 |
| FT3 | 4.4±1.0 | 4.7±0.7 | 0.037 |
| FPG | 93.5±14.7 | 90.2±12.2 | 0.216 |
| FI | 10.6±8.1 | 13.6±7.3 | 0.047 |
| IR | 2.5±2.1 | 3.0±1.9 | 0.204 |
| TG | 144.8±85.4 | 128.1±64.8 | 0.175 |
| TCH | 195.0±37.9 | 183.0±40.1 | 0.043 |

BMI: Body mass index; TSH: Thyrotropin; FPG: Fasting plasma glucose; FI: Fasting insulin; IR: Insulin resistance; FT4: Free tetraiodothyronine; FT3: Free triiodothyronine; TG: Triglycerides; TCH: total cholesterol.