**Yuzvenko T. Lipids profile and thyroid parameters in patients with type 2 diabetes mellitus. Journal of Education, Health and Sport. 2016;6(3):227-232. eISSN 2391-8306. DOI http://dx.doi.org/10.5281/zenodo.55173**
**http://ojs.ukw.edu.pl/index.php/johs/article/view/3569**

**The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part B item 755 (23.12.2015).**
**755 Journal of Education, Health and Sport eISSN 2391-8306 7**

**The authors declare that there is no conflict of interests regarding the publication of this paper.**
**Received: 05.03.2016. Revised 20.03.2016. Accepted: 23.03.2016.**

# LIPIDS PROFILE AND THYROID PARAMETERS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

**T. Yuzvenko**

**Ukrainian Research and Practice Center of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues, Health Ministry of Ukraine, Kyiv**

## Abstract

**Background** Higher level of thyroid-stimulating hormone (TSH) and lower thyroid hormone levels within the euthyroid range may adversely affect atherosclerosis.

**The aim of this study** was to investigate the potential association between thyroid parameters and lipids profile in a cohort of euthyroid diabetic patients.

**Methods.** Two hundred and thirty-one euthyroid patients with type 2 diabetes mellitus (151 males and 80 females) were consecutively recruited. Clinical and anthropometric data was collected from all participants. Whole blood samples were drawn in the morning after an overnight fasting for the measurement of serum TSH, free thyroxine ($fT_4$), free triiothyronine ($fT_3$), anti-thyroid peroxidase antibody (TPO-Ab) levels, as well as lipid concentrations and glucose.

**Results** TSH was higher in females than males. Stratified by TSH, high-density lipoprotein cholesterol (HDL-c) level increased in subjects with TSH ≥2.5 uIU/mL (p = 0.003). In females, total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-c) level was significant lower in subjects with TSH <2.5uIU/mL. TSH was significantly associated with TC and LDL-c. In a multiple linear regression analysis (stepwise), TSH was positive associated with TC and LDL-c. Among all patients 49 (21.2%) were TPO antibody positive. The blood pressure and lipid levels were lower in TPO-Ab positive patients, however, the differences were not significantly.

**Conclusions.** TSH was positively associated with serum TC and LDL-c in euthyroid women with type 2 DM. Analysis in the subgroup having TPO antibody assays demonstrating non-significantly lower TC levels among seropositive subjects was consistent with the above stated consideration for women as a whole. Further investigations are needed to understand the intimate mechanisms of lipid metabolism in type 2 diabetes with respect to thyroid function.

**Key words: type 2 diabetes mellitus, thyroid parameters, lipids profile.**

## Background

Thyroid hormones were recognized as catabolic hormones and they regulated various processes of metabolism, including the synthesis, mobilization, and breakdown of lipids. Hypothyroidism had been reported to be associated with an increased risk for dyslipidemia and atherosclerotic cardiovascular disease [4, 11]. The concept was emerging nowadays that effects of low thyroid function on atherosclerosis susceptibility might extend into the euthyroid range [6]. Several studies reported an association between higher thyroid-stimulating hormone (TSH) and lower thyroid hormone levels that were still within the normal range and lipids profile in the euthyroid population [8, 10]. Diabetes mellitus (DM), in particular type 2 diabetes, which was mostly associated with lipoid abnormalities, was also known to dramatically increased risk of cardiovascular diseases [1, 7]. Thyroid dysfunctions were more frequent in diabetic patients than in the general population [2]. The association between circulating TSH levels and cardiovascular diseases risk factors seemed to be amplified by the degree of insulin-resistance [3, 9], and it might be particularly relevant in type 2 DM. Recently, several studies had reported that even relative low thyroid functions that were still within normal range were more frequent and might be more dangerous in people with diabetes [5, 8]. And in most of these studies, free triiodothyronine ($fT_3$), free thyroxine ($fT_4$) and TSH were not measured together.

**The aim** of this study was to investigate the potential association between TSH and thyroid hormones levels within the normal range and lipids profile in a cohort of euthyroid patients with type 2 DM.

## Material and Methods

Two hundred and thirty-one euthyroid patients with type 2 diabetes mellitus (151 males and 80 females) were consecutively recruited in this cross-sectional study from patients of Department of Preventive Endocrinology in Ukrainian Research and Practice Center of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues, Health Ministry of Ukraine. Euthyroidism was defined as TSH, $fT_3$, and $fT_4$ levels within their normal reference ranges. Exclusion criteria: type 1 diabetes, latent autoimmune diabetes of the adults, gestational diabetes, and other type of diabetes, pregnancy, neoplasms, liver, kidney, and heart failure. In particular, subjects with a previous history of thyroid diseases, such as overt hyper/hypothyroidism, thyroid cancer, were excluded. Subjects taking medications affecting thyroid hormone levels (such as thyroid supplementation and antithyroid agents, amiodarone, lithium, corticosteroids, etc.) and lipids profile (such as statins, fenofibrate, etc.) were also excluded. Informed consent was obtained from all participants. The present study was approved with the Institutional Ethnics Committee in Ukrainian Research and Practice Center of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues, Health Ministry of Ukraine, Kyiv.

Clinical data was collected from all participants. Whole blood samples were drawn in the morning after an overnight fasting for measurements of the study parameters. Serum TSH, $fT_3$, and $fT_4$ levels were measured using chemiluminescence tests. Anti-thyroid peroxidase antibody (TPO-Ab) was measured in all patients with agreement, with reference values between 0 and 50 U/L. Fasting plasma glucose (FPG) and lipid concentrations (total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C)) were assayed using enzymatic methods.

The data analysis was performed using SPSS version 12.0. All data was expressed as means ± standard deviation (SD). All subjects were divided into two groups by sex or TSH (≥2.5 uIU/mL and <2.5 uIU/mL). Student's *t* test or Mann-Whitney U test, depending on the shape of the distribution curves, was used for evaluation of differences between the two groups. The Pearson correlation test was applied in order to assess for the existence of any significant interdependence between numerical parameters. Partial correlation analyses were performed to evaluate the association of thyroid parameters with major cardiovascular risk factors (blood pressure and lipid concentrations), adjusted for age, sex, duration of diabetes, FPG, and BMI. We performed a multiple linear regression analysis to confirm the association, with cardiovascular risk factors as dependent variables, independent variables as follows: age, sex, BMI, duration of diabetes, FPG, $fT_3$, $fT_4$, TSH. Males and females

were analyzed separately. Subjects with data of TPO-Ab were divided into two groups: TPO-Ab positive (TPO-Ab >50U/L) and TPO-Ab negative (TPO-Ab <50U/L), and differences between the two groups were compared by *t* tests.

**Results**

The mean age of type 2 DM patients was 53.38 ± 11.72 years (range 28 to 79), and the mean BMI was 29.83 ± 3.96 kg/m$^2$ (range 23.5 to 39.2). Age and TSH level were higher in females, and BMI, diastolic blood pressure (DBP), and $fT_3$ were lower. No difference was found in $fT_4$ or duration of diabetes.

Stratified by TSH, HDL-C level increased in subjects with TSH ≥2.5 uIU/mL ($p = 0.003$). TSH was associated with HDL-C in a Pearson correlation test ($\beta = 0.085$, $p = 0.037$). In females, TC and LDL-C level was significant lower in subjects with TSH <2.5 uIU/mL. TSH was significantly associated with TC and LDL-C, even in a partial correlation analysis ($p = 0.004$ and 0.014, respectively. In a multiple linear regression analysis TSH was positive associated with TC ($\beta = 0.204$, $p = 0.004$) and LDL-C ($\beta = 0.148$, $p = 0.02$). In males, no difference was found in lipids profile or BP between subjects with TSH ≥2.5 uIU/mL and TSH <2.5 uIU/mL group.

Among all patients 49 (21.2%) were TPO antibody positive. In TPO-Ab positive patients, SBP, DBP, $fT_3$, TC, TG, HDL, LDL levels were lower than TPO-Ab positive patients.

**Discussion**

Thyroid dysfunction was a risk factor for cardiovascular disease mediated by the effects of thyroid hormones on lipids metabolism and blood pressure [2, 8], yet most subjects at risk for cardiovascular disease were euthyroid in the clinical setting. The relationship between thyroid hormones and atherosclerosis in the euthyroid population had garnered much interest recently.

In our study, we demonstrated that TSH was higher in females than males, which was in agreement with previous studies [6, 11]. Furthermore, we found that in diabetic females, TC and LDL-C level was significant lower in subjects with TSH <2.5 uIU/mL. TSH was significantly associated with TC and LDL-C, even in a partial correlation analysis. In a multiple linear regression analysis TSH was positive associated with TC and LDL-C. TSH levels within the reference range had been reported to be associated with serum lipid concentrations previously. Higher TSH was reported to confer increased plasma cholesteryl ester transfer in the context of chronic hyperglycemia [10]. All these suggested that

relatively low but clinically normal thyroid function, as inferred from higher TSH in normal range, could also influence lipids profile and atherosclerosis susceptibility in type 2 DM.

Among euthyroid patients with established diabetes, the stated variables might tend to normalize secondary to a decline in autoimmune processes and in the reduction of lipoprotein(a) levels. Some authors suggested that chronic autoimmune thyroiditis per se might be considered as a risk factor of atherosclerosis independent of thyroid function [4]. In this study, TPO-Ab was considered for the first time in the association of thyroid function and lipids profile and blood pressure in diabetic subjects. Along with higher TSH and lower $fT_3$ values in the seropositive group, lower lipid concentrations and blood pressure were observed, although the differences were not significantly. The result did not support autoimmune thyroiditis as a risk factor for atherosclerosis. Larger scale studies were needed to further confirm the role of thyroid antibodies in atherosclerosis.

Several methodological aspects and limitations of our study needed to be considered. First of all, the causal relationship could not be inferred from this study because it was cross-sectional in nature. Secondly, in type 2 DM patients, the relationship between thyroid hormones and cardiovascular disease risk might be influenced by other diabetes-related variables, such as metabolic control, co-morbidities, and/or hypoglycemic therapies.

**Conclusions**

TSH was positively associated with serum TC and LDL-C in euthyroid diabetic women. Analysis in the subgroup having TPO antibody assays demonstrating non-significantly lower TC levels among seropositive subjects was consistent with the above stated consideration for women as a whole. Further investigations are needed to understand the intimate mechanisms of metabolism in type 2 diabetes mellitus with respect to thyroid function.

**References**

1. Asvold B.O., Vatten L.J., Nilsen T.I., Bjøro T. The association between TSH within the reference range and serum lipid concentrations in a population-based study. The HUNT Study. // Eur J Endocrinol. – 2007. – Vol.156. – P.181-186.

2. Chamnan P., Simmons R.K., Sharp S.J. et al. Cardiovascular risk assessment scores for people with diabetes: a systematic review. // Diabetologia. – 2009. – Vol.52. – P.2001-2014.

3. Chubb S.A., Davis W.A., Davis T.M. Interactions among thyroid function, insulin sensitivity, and serum lipid concentrations: the Fremantle diabetes study. // J Clin Endocrinol Metab. – 2005. – Vol.90. – P.5317-5320.

4. Garduño-Garcia Jde J, Alvirde-Garcia U, López-Carrasco G, Padilla Mendoza M.E., Mehta R., Arellano-Campos O. et al. TSH and free thyroxine concentrations are associated with differing metabolic markers in euthyroid subjects. // Eur J Endocrinol. – 2010. – Vol.163. – P.273-278.

5. Giandalia A., Russo G.T., Romeo E.L. et al. Influence of high-normal serum TSH levels on major cardiovascular risk factors and Visceral Adiposity Index in euthyroid type 2 diabetic subjects. // Endocrine. – 2014. – Vol.47. – P.152-160.

6. Ichiki T. Thyroid hormone and atherosclerosis. // Vascul Pharmacol. – 2010. – Vol.52. – P.151-156.

7. Kadiyala R., Peter R., Okosieme O.E. Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. // Int J Clin Pract. – 2010. – Vol.64. – P.1130-1139.

8. Onat A., Can G., Murat S. et al. Aggregation of lipoprotein(a) to apolipoprotein A-I underlying HDL dysfunction as a major coronary risk factor. // Anadolu Kardiyol Derg. – 2013. – Vol.13. – P.543-551.

9. Roos A., Bakker S.J., Links T.P. et al. Thyroid function is associated with components of the metabolic syndrome in euthyroid subjects. // J Clin Endocrinol Metab. – 2007. – Vol.92. – P.491-496.

10. Taneichi H., Sasai T., Ohara M. et al. Higher serum free triiodothyronine levels within the normal range are associated with metabolic syndrome components in type 2 diabetic subjects with euthyroidism. // Tohoku J Exp Med. – 2011. – Vol.224. – P.173-178.

11. Triolo M., Kwakernaak A.J., Perton F.G. et al. Low normal thyroid function enhances plasma cholesteryl ester transfer in type 2 diabetes mellitus. // Atherosclerosis. – 2013. – Vol.228. – P.466-471.