International Journal of Biotechnology and Biochemistry
ISSN 0973-2691 Volume 14, Number 2 (2018) pp. 85-93

http://www.ripublication.com

Correlation between Glycemic Control and Thyroid Status in Patients with Type 2 Diabetes Mellitus

Dr. Asmabi Makandar D[1], Dr. Amit D. Sonagra[2]*, Dr. Tousif Imdad[3], Dr. Shylaja T.V.[4]

[1 & 4.] Assistant professor, Department of Biochemistry, East Point College of medical science, Bangalore India.

[2.] Assistant Professor, Department of Biochemistry, G.M.E.R.S. Medical College, Dharpur-Patan, Gujarat India.

[3.] Senior Registrar, Health Care Global Cancer Hospital, Bangalore India.

[2]Corresponding Author*

Abstract

Introduction: There is a complex inter relationship between diabetes mellitus and thyroid disorders which involves biochemical, genetic, hormonal and pathophysiological mechanisms. The present study was conducted to find the correlation between glycemic control and levels of thyroid hormones in patients with type 2 diabetes mellitus.

Objectives: To find out the correlation between glycosylated haemoglobin (HbA_{1c}) and the levels of thyroid hormones namely tri iodotyronine (T_3), tetra iodotyronine (T_4), and thyroid stimulating hormone (TSH).

Materials and Methods: A prospective cross sectional study was carried out including 100 clinically diagnosed cases of type 2 diabetes mellitus. The parameters measured are Fasting blood sugar (FBS), HbA_{1c}, T_3, T_4 and TSH. Based on HbA_{1c} level diabetic cases are divided into two groups. Group 1 having HbA_{1c} <8% and Group 2 having HbA_{1c} > 8%. FBS, T_3 T_4 and TSH levels are compared among these two groups.

Results: Among 100 diabetic cases, 27% have hypothyroidism, 15% cases have hyperthyroidism and 58% cases show normal levels of thyroid hormones. Mean levels of T_3 are significantly low in Group 2 as compared to group 1, mean levels of T_4 do not show any significant difference among the group 1 and 2, whereas the mean levels of TSH are significantly high in group 2 as compared to group 1.

Conclusion: Determining thyroid status in type 2 DM is helpful for the better management and its prognosis.

Keywords: Diabetes mellitus, Glycosylated haemoglobin, Hypothyroidism, Hyperthyroidism, Thyroid hormones.

INTRODUCTION:

Diabetes mellitus is an important health problem affecting major population worldwide.[1] According to the Indian Heart association 2015, India is the Diabetic Capital of the World with a projected 109 million individuals with diabetes by 2035.[2] Thyroid disorders are also very common in the general population and it is second only to diabetes as the most common condition to affect the endocrine system. As a result it is common for an individual to be affected by both thyroid diseases and diabetes.[3,4] Diabetes affects thyroid function at various levels and thyroid hormones influence carbohydrate metabolism and pancreatic functions to variable extents.[5] Various studies have estimated the prevalence of thyroid disorder in diabetic patients, in few studies higher prevalence in diabetes has been estimated.[6,7]

In a patient with diabetes, the most common type of thyroid dysfunction is hypothyroidism. It results in reduced hepatic glucose production which means a reduced insulin dose is required in a patient with hypothyroid diabetics. On the other hand impaired insulin stimulated glucose utilization in peripheral tissues has been reported in both clinical and subclinical hypothyroidism which accounts for insulin resistance. So, hypothyroidism predisposes to hypoglycemia, and at the same time, causes insulin resistance.[8] Also in patients with T2DM, hyperthyroidism is reported to be more common compared to normal people. In many patients, uncontrolled hyperthyroidism may be the reason for poor glycemic control and recurrent diabetic ketoacidosis. In response to hyperthyroidism gut absorption of glucose is increased along with endogenous glucose production.[9] Several studies have been conducted to find out the prevalence of thyroid dysfunction in diabetic patients but only few studies have compared the levels of thyroid hormone with glycemic status in diabetic patients. Present study is carried out to find out the inter relation between the glycemic status and levels of thyroid hormones in type 2 DM.

MATERIALS AND METHODS

A cross sectional study was carried out on 100 diabetic patients. Consent was taken from all the patients and was informed about the objectives of the study and what roles they were expected to play. This study was approved by institutional ethical committee.

Inclusion criteria: This study includes 100 cases of Diabetes mellitus. All the patients are confirmed diabetics who had fasting blood glucose levels >126mg/dl on more than two occasions based on the American Diabetes Association (ADA) criteria

for diagnosis of DM, and who are receiving treatment such as insulin, or oral hypoglycaemic drugs.

Exclusion criteria: The study excluded the patients having history of type 1 diabetes mellitus, those with known history of thyroid dysfunction and patients with liver disease, renal disease, hypertension and pregnancy.

Data collection: After taking the informed consent, the study subjects were subjected to medical examination and blood investigations. General health characteristics such as age, sex, smoking status, menopausal status, alcohol consumption, and dietary habits (particularly as related to preference) were investigated by a self-administered questionnaire.

Biochemical investigation: A fasting blood sample of about 5 ml was drawn from all the study subjects. 3ml of blood was subjected to centrifugation, separated serum was used for the estimation of FBS and thyroid hormones. 2ml of blood was used for the estimation of HbA1c.

Methods of estimation: FBS is measured by Glucose oxidase (GOD-POD) method [10]. Serum T_3, T_4 and TSH are estimated by Chemiluminescence Immunoassay Method (CLIA) in CLIA analyzer [11]. HbA1c is estimated by Cation-Exchange resin method and the kit was purchased from Euro diagnostics Bangalore [12]. FBS and HbA1c are measured in fully automated analyser ERBA MANNHEIM EM 200. Classification of the values into high, low, or normal thyroid hormone level was based on the following criteria. Subjects classified as having high levels of thyroid hormones had T_3 values >2ng/ml, T_4 value > 12μg/dl or TSH< 0.2 μIU/ml or both. Those classified as having hypothyroidism had T_3 values < 0.5 ng/ml, T4 values < 4.8 μg/dl or TSH values >5.4 μIU/ml or both. Subject grouped as euthyroid had T_3, T_4 and TSH values within the range of 0.5 – 2.0 ng/ml, 4.8 – 11.6 μg/dl and 0.28 – 5.45 μIU/ml respectively.

STATISTICAL ANALYSIS

The quantitative variables are expressed as mean ± SD. Prevalence of thyroid dysfunction was expressed as percentage with 95% confidence interval (CI). Unpaired *t*-test was used for two-group comparison. The *p*-value of <0.05 was considered for statistical significance for all the test results.

RESULTS: Among the 100 diabetic cases studied, 58% have normal levels of thyroid hormones, 15% cases have high levels of thyroid hormones (hyperthyroidism) and 27% cases have low levels of thyroid hormones (Hyperthyroidism) figure 1.

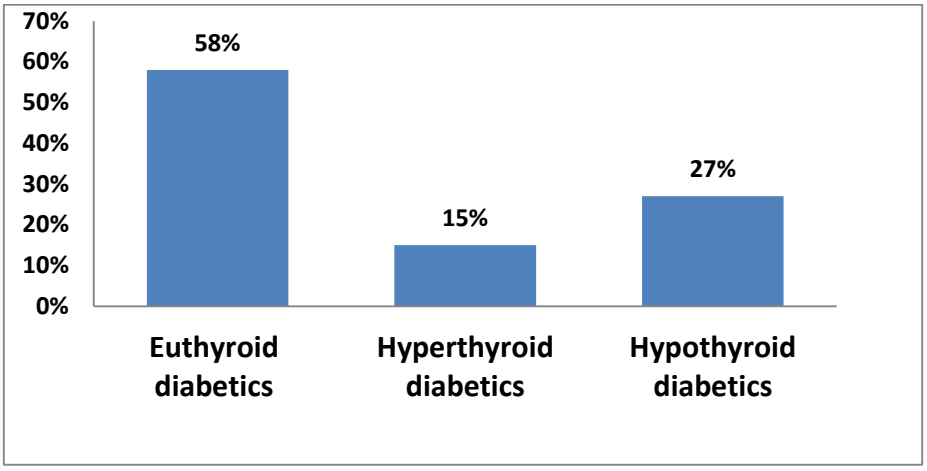

Figure 1: shows prevalence of thyroid dysfunction among 100 diabetic cases.

After analysing all the parameters, diabetic patients are divided into two groups based on the levels of HbA1c as an indicator of Glycemic status in diabetics.

Group 1: HbA_{1c} level < 8% and are considered as patients with controlled diabetes mellitus.

Group 2: HbA_{1c} level >8% and are considered as patients with uncontrolled diabetes mellitus. The mean levels of FBS, T_3, T_4 and TSH are compared among group 1 and 2.

Table 1: Showing Mean levels of FBS, HbA_{1c}, T_3, T_4 and TSH

Parameters	Group 1 HbA_{1C} <8	Group 2 HbA1c >8	p value
Age	54.88±6.5	56.12 ±6.2	0.326
FBS	147.9±11.6	190.9 ±23.4	<0.001
HbA1c	7.6±0.4	10.9 ±1.2	<0.001
T_3	1.2 ±1.3	0.8±0.4	<0.05
T_4	8.0±2.1	8.0 ±7.0	0.99
TSH	2.1±1.6	23.6± 33.2	<0.001

Table 1 shows that the mean age between group 1 and group 2 did not show significant difference (p-0.32). The mean levels of FBS are significantly high in group 2 as compared to the group 1($p<0.001$). The mean levels of T_3 are significantly low in group 2 as compared to group 1($p<0.04$), but the mean levels of T_4 did not differ significantly between group 1 and group 2(p-0.99). The mean levels of TSH are significantly high among group 2 as compared to group 1($p<0.001$).

Table 2: Shows correlation between HbA1c and thyroid hormone levels in all the patients with diabetes mellitus.

Parameters	T_3		T_4		TSH	
	r	P	R	P	R	P
HbA_{1c}	-0.207	<0.05	0.076	>0. 05	0.38	<0.001

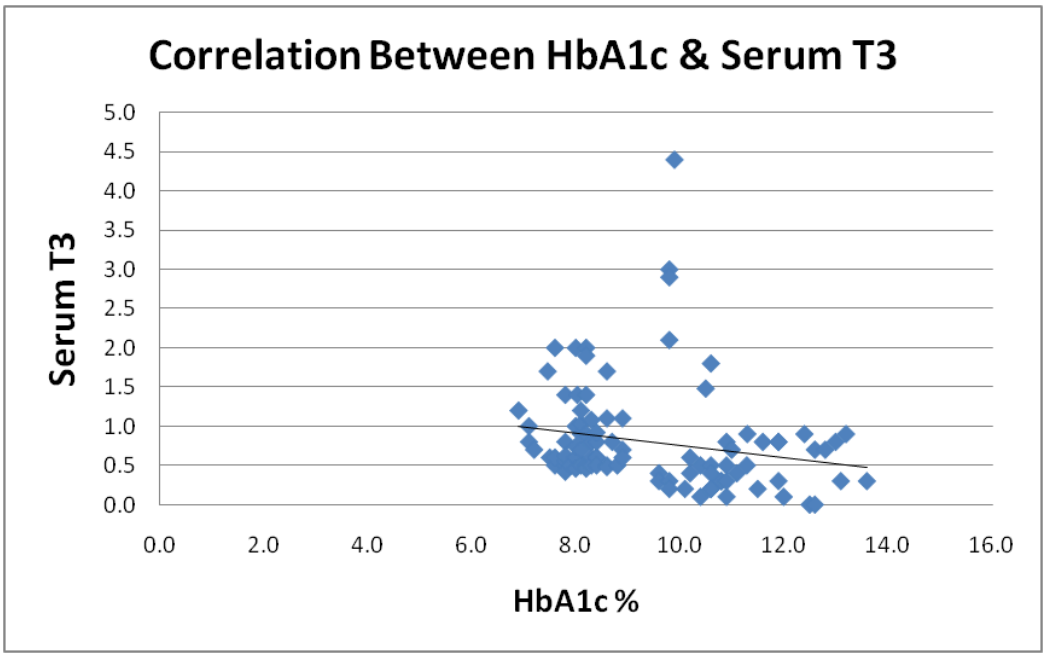

Figure 2. Shows correlation between HbA1c and T_3 levels

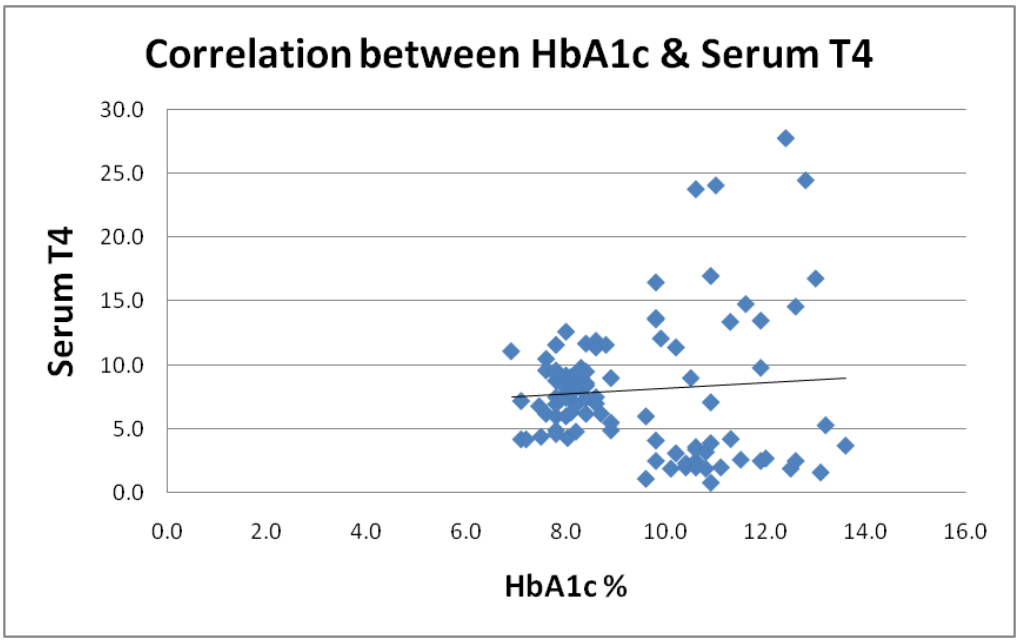

Figure 3. Shows correlation between HbA1c and T_4 levels

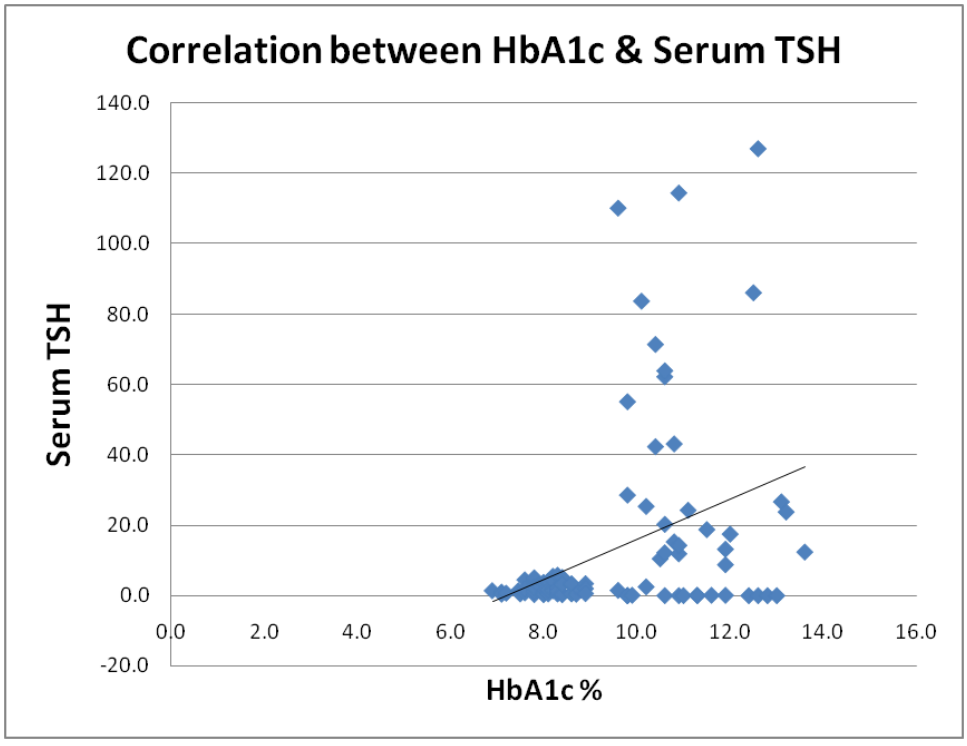

Figure 4. shows correlation between HbA1c and TSH levels

Table 2, Figure 2,3,4 shows that Serum T_3 ($p<0.05$) has a significant negative correlation with the levels of HbA1c and TSH ($p<0.001$) has significant positive correlation with HbA1c levels, whereas serum T_4 shows non significant positive correlation with HbA1c ($r= 0.07$; $p>0.05$).

DISCUSSION

Diabetes mellitus is a complex and multifactorial disease. The metabolic dysregulation associated with diabetes causes secondary pathophysiologic changes in multiple organ systems that impose a heavy burden of morbidity and mortality from macrovascular and microvascular complications.[1] A Cross sectional study was carried out on 100 diabetic patients to find the prevalence of thyroid dysfunction and correlation between thyroid hormones and glycemic control.

Among the 100 diabetic cases studied, 58% have normal levels of thyroid hormones, 27% cases have hypothyroidism and 15% cases have hyperthyroidism. Our study has shown a high prevalence of thyroid dysfunction ie 42%, our results are in accordance with the previous studies conducted by Singh et al.,[3] Pasupathi et al.,[6] Pimenta et al[7], Swamy et al.,[13] Mazin et al.,[14] Udiong et al(46%).,[15] and Bassyouni et al.,[16].

The presence of both raised and low levels of thyroid hormones in diabetic may be due to modified TRH synthesis and release.[1] The hyperglycaemia seen in type- 2 diabetics is known to have negative effect on thyroid function precisely blunting the pituitary TSH response to stimulation by hypothalamic TRH. This may be due to possible alteration of post translational glycosylation of TRH hence affecting its biological activity.[17] DM is associated with increased insulin level and C-peptide level. Insulin is an anabolic hormone known to enhance TSH turnover, which is protein in nature. Recently, C-peptide has been shown to enhance Na+/K+- ATPase activity, an action that may also increase protein synthesis. Such an action would induce increased turnover of TSH, a protein hormone.[16,18]

In our study we found that 27% of diabetic patients were suffering from hypothyroidism. Patients with uncontrolled diabetes HbA1c > 8 have low levels of T_3 when compared to patients with HbA1c < 8. But the levels of T_4 did not differ significantly among both the groups, these findings are in accordance with Uppal V et al,.[19] The low T_3 state may be due marked hyperglycaemia which reduced peripheral conversion of T_4 to T_3 via 5 monodeiodination reaction. It is known that insulin an anabolic hormone which inhibits the hepatic conversion of T_4 –T_3, enhances the levels of FT_4 while it suppresses the levels of T_3. [15,20] Hypothyroidism falsely raises HbA1c due to decreased erythropoiesis. Thyroid hormone replacement is associated with decrease in HbA1c level, which is influenced by increased erythropoiesis rather than by changes in glucose level.[21]

Our study reports negative correlation between T_3 and HbA1c and these findings are supported by various studies [20,22,23] who stated that dearrangement in glycemic control influences the thyroid hormone levels. Our result of positive correlation

between HbA1c and TSH is consistent with the results by vibha uppal et al and Velija-Asimi et al[24]. Vibha Uppal correlated the levels of insulin and HbA1c with thyroid hormones and reported that the levels of HbA1c have a positive and significant correlation with TSH level.

CONCLUSION

There is high prevalence of thyroid dysfunction among type 2 diabetic patients compared to the general population. The most common thyroid disorder is hypothyroidism followed by hyperthyroidism. There is significant association between the glycemic status and levels of thyroid hormones. So there is need for routine assay of thyroid hormones in diabetics which will help in the early detection, improving the management of diabetics and overall reduction morbidity and mortality.

Funds for study: Nil

Conflict of interest: None

REFERENCES

[1] Pasupathi P, Chandrasekar V and Kumar US. Evaluation of oxidative stress, antioxidant and thyroid hormone status in patients with diabetes mellitus. J Medicine. 2009; 10:60-66.

[2] Causes of Diabetes". National Institute of Diabetes and Digestive and Kidney Diseases. June 2014. Retrieved 10 February 2016.

[3] Singh G, Gupta V, Sharma AK, Gupta N. Evaluation of Thyroid Dysfunction Among type 2 diabetic Punjabi population. Advances in Bioresearch. 2011; 2(2): 3-9.

[4] Sathish R and Mohan V. Diabetes and thyroid Disease. Int J Diab Dev Countries. 2003; 23: 120-123.

[5] Shah SN. Thyroid disease in diabetes mellitus. JAPI. 2007; 32:1057-1059.

[6] Pasupathi P, Bakthavathsalam G, Saravanan G, Sundaramoorthi R. Screening for thyroid dysfunction in the diabetic / non-diabetic population. Thyroid Science 2008; 3(8): CLSI-6.

[7] Pimenta WP, Mazeto GM, Callegaro CF, Shibata SA, Marins LV, Yamashita S, et al. Thyroid disorders in diabetic patients. Arq Bras Endocrinol Metabol. 2005;49:234–40.

[8] Agarwal N and Gulati M. Study of Prevalence of Thyroid Dysfunction in Patients with Type 2 Diabetes Mellitus. International Journal of Contemporary Medical Research. 2016; 3(8):2212-2214.

[9] Wang C. The Relationship between Type 2 Diabetes Mellitus and Related

Thyroid Diseases, Journal of Diabetes Research. 2013;2013:1-9.

[10] Sack D. Carbohydrates. In: Brutis C, Ashwood E, Bruns D (Edts). Teitz Textbook of clinical chemistry and Molecular diagnostics, 4th ed. New Delhi: Elsevier. 2006; 868-875.

[11] Kricka L. Principles of immunochemical techniques. In: Burtis CA, Ashwood ER and Bruns DA, eds. Teitz Textbook of clinical chemistry and Molecular diagnostics, 4 th edn. New Delhi: Elsevier; 2006: 219-244.

[12] .Gowenlock AH, McMurray JR, McLauchlan DM. Tests in disorders of glucose metabolism. In: Weiner K edt. Practical clinical biochemistry. Chapter 25. 6th edn. CBS Publishers 1996: p.333-49.

[13] Swamy RM, Kumar N, Srinivasa K, Manjunath GN, Byrav DSP, Venkatesh G. Evaluation of hypothyroidism as a complication in Type II Diabetes Mellitus. Biomedical Research 2012; 23 (2): 170-172.

[14] Mazin Z, al-shabani.Diabetes Mellitus and thyroid disorders: Kufa Medical Journal. 2010; 13: 69-76.

[15] Udiong CEJ, Udoh AE, Etukudoh ME. Evaluation of thyroid function in diabetes mellitus in calabar, Nigeria. India J Clin Biochem. 2007; 22(2): 74-78.

[16] Bassyouni A, Ebrashy IE, Ismiel A, Amara I, Mahfouz M, and Halmy N. Profile of the thyroid function and ultrasound among patients with type-2 diabetes mellitus. Sci Med J. 2010; 22(2): 15-28.

[17] Suresh DR, Silvia CR and Murthy U K. Inter- relationship of glycemic control and thyroid status in type-2 diabetes mellitus. International journal of clinical and diagnostic research. 2014;2(4):V

[18] Shaikh AW, Memon AS, Sirichand. Frequency of hypothyroidism in type 2 diabetic patients. Pakistan J Med Health Sci 2009;2(4).

[19] Uppal V, Vij C, Bedi KV, Vij A and Banerjee BD. Thyroid Disorders in Patients of Type 2 Diabetes Mellitus. Ind J Clin Biochem. 2013; 28(4):336–341.

[20] Schlienger JL, Anceau A, Chabrier G, North ML, Stephan F. Effect of diabetic control on the level of circulating thyroid hormones. Diabetologia. 1982;22:486–8.

[21] Kim MK, Kwon HS, Baek K, Lee JH, Park WC, Sohn HS, et al. Effects of thyroid hormone on A1C and glycated albumin levels in nondiabetic subjects with overt hypothyroidism. Diabetes Care. 2010;33:2546–8.

[22] Bagchi N, Brown TR, Parish RF. Thyroid dysfunction in adults over age 55 years. A study in an urban US community. Arch Intern Med. 1990;150:785–7.

[23] Verga Falzacappa C, Panacchia L, Bucci B, Stigliano A, Cavallo MG, Bunetti E, et al. 3,5,30-Triiodothyronine is a survival factor for pancreatic beta cells undergoing apoptosis. J Cell Physiol. 2006;206:309–21.

[24] Velija-Asimi Z, Karamehic J. The effects of treatment of subclinical hypothyroidism on metabolic control and hyperinsulinemia. Med Arh. 2007;61:20–1.