Endokrynologia Polska
DOI: 10.5603/EP.a2021.0016
Volume/Tom 72; Number/Numer 3/2021
ISSN 0423–104X, e-ISSN 2299–8306

The relationship between thyroid dysfunction during pregnancy and gestational diabetes mellitus

Vesselina Yanachkova[1], Zdravko Kamenov[2, 3]

[1]*Department of Endocrinology, Specialized Hospital for Active Treatment of Obstetrics and Gynaecology "Dr Shterev", Sofia, Bulgaria*
[2]*Department of Internal Medicine, Medical University — Sofia, Sofia, Bulgaria*
[3]*Clinic of Endocrinology, University Hospital "Alexandrovska", Sofia, Bulgaria*

Abstract

Introduction: Thyroid dysfunction and gestational diabetes (GDM) are the two most common endocrine disorders that can be observed during pregnancy. Thyroid function abnormalities can be associated with insulin resistance (IR) and changes in carbohydrate metabolism. In patients with type 1 diabetes, thyroid function is usually evaluated to rule out abnormalities within a second autoimmune disease. Patients with type 2 diabetes are tested for thyroid function in view of the associated weight gain, IR, and changes in metabolism. The question arises: Should we also look for thyroid dysfunction in patients with gestational diabetes? The aim of the study was to determine whether there are abnormalities in thyroid hormone levels in pregnant women with gestational diabetes.

Material and methods: A monocentric, retrospective study of the Dr Shterev Hospital electronic database was performed. We analysed the medical records of 662 pregnant women, divided in two groups — 412 with GDM and 250 with normal glucose tolerance, who gave birth in the period 2017–2019. Gestational diabetes mellitus in the study group was diagnosed with a 2-h, 75-g oral glucose tolerance test (OGTT) using the International Federation of Gynaecology and Obstetrics (FIGO) and American Diabetes Association (ADA) criteria. We analysed the mean serum concentrations of thyroid-stimulating hormone (TSH); free thyroxine (FT4), free triiodothyronine (FT3), FT3:FT4 ratio, fasting plasma glucose, age and body mass index in both groups. The groups were compared using the Mann-Whitney U-test.

Results: In patients who developed GDM, significantly higher concentrations of TSH ($p < 0.0001$) and FT3 ($p < 0.0001$), lower concentrations of FT4 ($p < 0.0001$), and higher FT3:FT4 ratios ($p < 0.0001$) were found.

Conclusion: The results of this pilot retrospective series reveal that high-normal to high concentration of TSH and low-normal to low concentration of FT4 as well as high FT3:Ft4 ratio could indicate increased risk of development of GDM. **(Endokrynol Pol 2021; 72 (3): 226–231)**

Key words: *thyroid dysfunction; pregnancy; insulin resistance; gestational diabetes mellitus*

Introduction

Thyroid disease and diabetes mellitus (DM) can be connected in a pathophysiological aspect [1–2]. These relationships have their significance and respective consequences related to insulin needs and insulin sensitivity. Unrecognized thyroid dysfunction may impair glycaemic control. A link has been established between thyroid hormones and the basal mechanisms controlling appetite and energy expenditure, and ultimately it is associated with changes in insulin sensitivity. Thyroid dysfunction is much more common in patients with DM [3–5]. The incidence of thyroid disorders in the diabetic population is 13.4%, being highest in women with type 1 diabetes mellitus (31%) and lowest in men with type 2 diabetes mellitus (6.9%) [1]. According to the data from the latest edition of the IDF Diabetes Atlas [6], the global prevalence of hyperglycaemia in pregnancy was 15.8%, i.e. 20.4 million live births were affected, in 2019. Data shows that 83.6% of cases were the result of gestational diabetes mellitus (GDM) [1, 3–5].

Both thyroid dysfunction and gestational diabetes could be connected with maternal complications like miscarriage, hypertensive disorders (gestational hypertension, preeclampsia), abruptio placentae, preterm delivery, caesarean section deliveries, and birth trauma [7–10]. Perinatal and neonatal morbidities associated with GDM and thyroid dysfunction include the following: macrosomia, shoulder dystocia, respiratory distress syndrome, neonatal hypoglycaemia, polycythaemia, hyperbilirubinaemia, impaired neurodevelopment of the child, and low birth weight [7–10].

The aim of the study was to determine whether there are abnormalities in thyroid hormone levels in pregnant women with gestational diabetes.

Vesselina Yanachkova, MD, PhD student, endocrinologist, Department of Endocrinology, Specialized Hospital for Active Treatment of Obstetrics and Gynaecology "Dr Shterev", Sofia, Bulgaria, 25–31 Hristo Blagoev St., Razsadnika quarter, 1330 Sofia, Bulgaria, tel: (+35) 9886436963; e-mail: v_ess@abv.bg

Material and methods

Study design and setting

This was a case-control study comparing two groups of pregnant women. For the purpose of the study the electronic database of "Dr Shterev Hospital" was used. We retrospectively reviewed the data from the electronic medical records of 662 pregnant women who had attended in the clinic in the period 2017–2019. Observed women were divided into two groups: a GDM group (n = 412) and a control group (patients with normal glucose tolerance, n = 250). The diagnosis of GDM was made with a 2-h, 75-g oral glucose tolerance test (OGTT) using the International Federation of Gynaecology and Obstetrics (FIGO) and American Diabetes Association (ADA) criteria [11–13]. TSH; FT4, FT3, and anti-TPO concentrations were evaluated in all patients at the time of performing the glucose challenge test. There is no established national reference range for TSH concentrations during pregnancy in Bulgaria. Therefore, the recommendations and criteria set out by some of the major professional organizations (American Thyroid Association [ATA], European Thyroid Association [ETA], Endocrine Society) were used. The Bulgarian Society of Endocrinology (BSE) have taken into account and borrowed the recommendations of ETA, according to which a fixed TSH trimester-specific range is used in the absence of a population-specific one, such as the following: first trimester — 0.1–2.5 mIU/L; second trimester: 0.2–3.0 mIU/L; third trimester: 0.3–3.0 mIU/L [15–16].

Mean serum concentrations of TSH, FT4, FT3, anti-TPO, FT3:FT4 ratio, fasting blood glucose (mmol/L), and body mass index (BMI) were compared. The BMI of the patients was calculated on the basis of the accepted weigh:height^2 ratio. The TSH concentrations were determined by the immunochemiluminescent method (Cobas 6000), and the laboratory TSH reference interval for the non-pregnant population was 0.27–4.20 mUI/L. FT4 and FT3 concentrations were determined by the immunochemiluminescent method (Cobas 6000), with the reference interval for the FT4, for the non-pregnant population — 12–22 pmol/L, and for FT3 — 3.2–6.8 pmol/L. Antibodies were determined by electrochemiluminescent method ECLIA (Cobas 6000). The FT3:FT4 ratio was derived by dividing plasma concentrations of FT3 by FT4. The interassay coefficient of variations were < 5% for the thyroid hormones and < 13% for the thyroid antibodies.

Due to the fact that Bulgaria is designated as an iodine-sufficient country, we conditionally assumed that the tested women were not iodine deficient.

In 210 of the women in the case group, the glucose challenge test was performed between the 10th and the 13th weeks of gestation due to a history of impaired glucose tolerance, obesity, or family history of diabetes mellitus. In the rest of the patients in the case group, as well as the patients in the control group, universal screening between 24–28 weeks of gestation was performed.

Study population

The inclusion criteria were:

— pregnant women aged between 18–40 years;
— diagnosis of GDM;
— history of normal thyroid function before conception;
— singleton pregnancy;
— The exclusion criteria were:
— age < 18 years or > 40 years;
— pre-existing diabetes (types 1 and 2);
— pre-existing thyroid dysfunction;
— multiple pregnancy.

Using the ETA's trimester-specific reference range for TSH during pregnancy, we divided patients in both groups as follows: euthyroid (TSH < 2.5 mIU/L); subclinical hypothyroidism (TSH > 2.5– < 4.2 mIU/L); hypothyroidism (TSH > 4.2 mIU/L), isolated maternal hypothyroxinaemia (IMH); and gestational thyrotoxicosis (Tab. 1). The main idea was to have different patient groups with different thyroid hormone concentrations for our analysis. This was done in order to assess the threshold of TSH concentrations at which changes in blood sugar levels could be observed. Regarding thyroid autoimmunity status, women were considered antibody positive if anti-TPO (thyroid peroxidase) antibodies concentrations were > 35 IU/mL. All patients underwent ultrasound of the thyroid gland with assessment of topography, size, structure, blood flow, and presence of nodules.

Levothyroxine therapy was initiated in all pregnant women with subclinical hypothyroidism and positive anti-TPO (n = 62) and in those with hypothyroidism (n = 63). Their thyroid hormones were monitored until the end of the pregnancy. In our study women with TSH levels > 2.5 mIU/L but < 4.2 mIU/L and without autoimmunity data were left without therapy. The aim was to evaluate the changes in their thyroid hormone concentrations. Their TSH and FT4 concentrations were monitored (at least once more before the end of the pregnancy). With this step we stopped using the ETA guidelines, instead following those of the ATA [14].

Patients with gestational thyrotoxicosis were excluded from the analysis.

Statistical analysis

Analysis was performed using Statistical Package for Social Sciences (SPSS) v.20.0. Data were expressed as percentages (numbers), means, or medians. Parametric and nonparametric tests for differences were used based on the normality of the distribution of Kolmogorov-Smirnov and Shapiro-Wilk, as well as for the uniformity of Fisher dispersions. The comparison between the two groups of patients (GDM group and control group) in terms of different indicators was made with the Mann-Whitney U-test. Non-metric variables were represented by relative frequencies (in percent). The chi-square test was used to compare the difference

Table 1. *Comparison of the thyroid status in both groups*

Thyroid hormone status	Antibodies presence (anti-TPO)	GDM group (n = 412)	Non-GDM group (n = 250)	p value
Euthyroid	Negative	165	172	< 0.0001
	Positive	68	2	
Subclinical hypothyroidism	Negative	58	11	0.302
	Positive	57	16	
Hypothyroidism	Negative	21	13	0.484
	Positive	32	14	
Isolated maternal hypothyroxinaemia	Yes	69	20	0.001
	No	343	230	

GDM — gestational diabetes mellitus; TPO — thyroid peroxidase

Table 2. *Characteristics of observed pregnant women*

Characteristics	GDM group (n = 412)	Control group (n = 250)	p value
Mean age [yrs]	33.3 (± 4.93)	32.8 (± 4.28)	0.251
BMI [kg/cm²]	26.078 (± 5.35)	22.9 (± 5.81)	0.422
Conception method			
Spontaneous	231 (56%)	192 (76.8%)	0.0006
ART	181 (44%)	58 (23.2%)	
Fasting plasma glucose [mmol/L]	5.47 (± 0.80)	4.80 (± 0.67)	< 0.001
TSH [mIU/L]	2.53 (± 1.36)	2.46 (± 0.80)	< 0.001
FT4 [pmol/L]	13.29 (± 2.62)	14.18 (± 3.12)	< 0.001
FT3 [pmol/L]	4.08 (± 0.78)	3.9 (± 0.68)	< 0.019
FT3:FT4 ratio — mean	0.350 (± 0.62)	0.27 (± 0.47)	< 0.001
Anti-TPO antibodies			
Positive (N)	157	32	
Negative (N)	255	218	
Gestational age at blood collection (weeks of gestation)	19 (± 2.5)	24 (± 2.5)	< 0.001

*Data presented as mean ± SD or N (%); SD — standard deviation; GDM — gestational diabetes mellitus; BMI — body mass index; ART — artificial conception; TSH — thyroid-stimulating hormone; FT4 — free thyroxine; FT3 — free triiodothyronine; TPO — thyroid peroxidase

between two percentages. In all tests, $p < 0.05$ was considered statistically significant. We used receiver operating characteristic (ROC) curve analysis, giving a level of sensitivity and specificity, to evaluate the TSH indicator as a predictor for GDM. It was estimated as the area under the curve (AUC) with 95% confidence interval (CI). The AUC ranged from 0.5 (no predictive ability) to 1 (predictive value).

Results

The main characteristics of observed pregnant women are presented in Table 2. The data of 662 women who met the inclusion and exclusion criteria were included in the study. The mean age of women in the GDM group was 33.3 (± 4.93) and 32.8 (± 4.28) for the control group. The mean BMI in GDM group was 26.078 (± 5.35), while for the control group it was 22.9 (± 5.81) ($p = 0.422$). Regarding the method of conception, spontaneous pregnancies predominated ($p = 0.0006$) in both groups. In the comparative analysis of the mean concentrations of TSH, patients with GDM, regardless of the time of its establishment (I, II, or III trimester of pregnancy) showed higher concentrations of TSH (2.53 ± 1.36) compared with those in the control group (2.46 ± 0.80) mIU/L ($p < 0.0001$). The mean FT4 concentrations in the diabetes group were lower — 13.29 (± 2.62) *vs*. 14.18 (± 3.12) pmol/L for the control group. Regarding the mean concentrations of FT3, patients with gestational diabetes mellitus had higher mean concentrations of FT3 (4.08 ± 0.78) compared with patients in the control group (3.9 ± 0.68) pmol/L. In patients with gestational diabetes mellitus there was a higher ratio of FT3:FT4 (0.35 ± 0.62 *vs*. 0.27 ± 0.47) for the control group.

Thyroid hormone concentrations were monitored in patients with GDM, who had normal TSH and did not require thyroxin therapy. It was found that with the progress of pregnancy in a large proportion of patients (42 women) there was an increase of the TSH concentrations above 3 mIU/L, which was a prerequisite for the addition of levothyroxine therapy. There was a tendency for a decrease in the FT4 concentrations and maternal hypothyroxinaemia was observed in almost all patients (n = 87). FT3 concentrations in the same patient group were higher.

Using ROC curve analysis, the sensitivity and specificity of TSH, FT4, and FT3 as indicators and diagnostic predictors for GDM were evaluated (Fig. 1–3).

The area under the curve (AUC) of TSH for prediction of GDM was 0.71 (AUC = 0.71, SE = 0.02, 95% CI: 0.671–0.75). A threshold concentration of TSH ≥ 2.58 mUI/L could predict GDM with a sensitivity of 43.6% and a specificity of 92.4% (Fig. 1). The AUC of FT4 was 0.60 (SE = 0.02, 95% CI: 0.55–0.65) (Fig. 2) and of FT3 was 0.56 (SE = 0.02, 95% CI: 0.51–0.60) (Fig. 3).

The cut-off concentration of FT3 ≥ 4.99 pmol/L could exclude GDM with a sensitivity of 14.4% and a specificity of 96.40%. The cut-off concentration of FT4 ≥ 13.2 pmol/L could exclude GDM with a sensitivity of 55.4 % and a specificity of 61.80%.

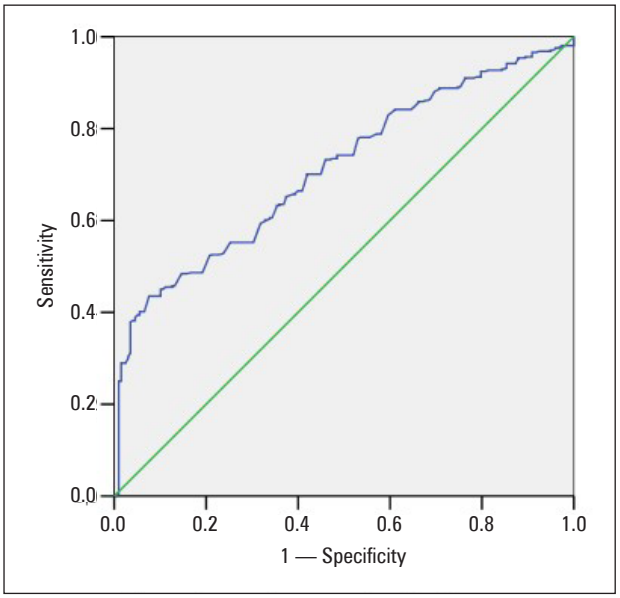

Figure 1. *The receiver operating characteristic (ROC) curve analysis — thyroid-stimulating hormone (TSH). Diagonal segments are produced by ties*

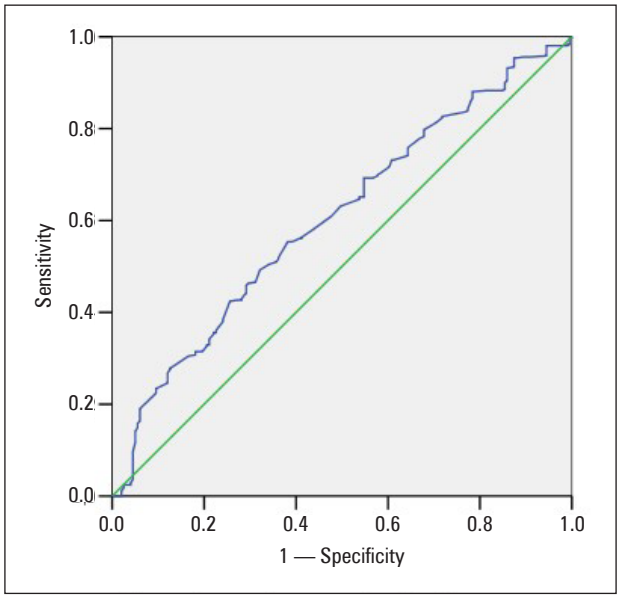

Figure 3. *The receiver operating characteristic (ROC) curve analysis — free triiodothyronine (FT3). Diagonal segments are produced by ties*

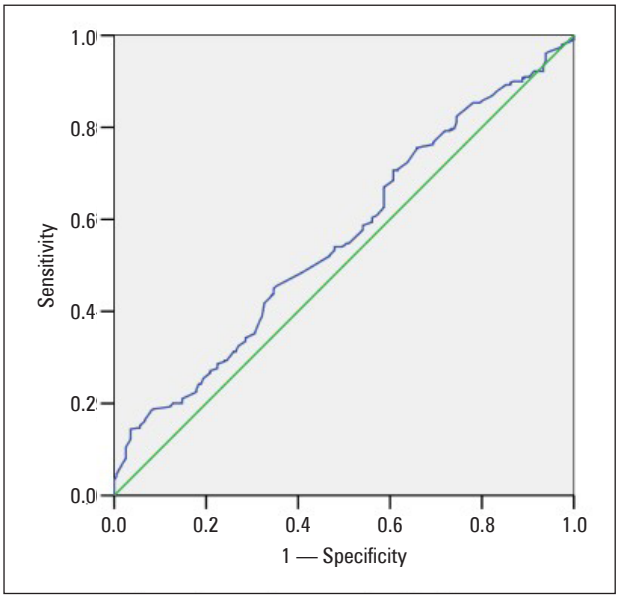

Figure 2. *The receiver operating characteristic (ROC) curve analysis — free thyroxine (FT4). Diagonal segments are produced by ties*

Discussion

The present study will allow the relationship between thyroid function and carbohydrate metabolism to be understood. Our results confirm that early parallel screening for GDM and thyroid dysfunction is crucial in order to avoid complications in the course of pregnancy.

It is well known that thyroid hormones play an important role in glucose metabolism. Therefore, thyroid dysfunction has been suggested to play a role in the aetiology of GDM. Abnormal thyroid function during pregnancy may affect maternal glucose homeostasis. Several mechanisms are involved in this process: reduction of the half-life of insulin; and endogenous production of thyroid hormones increases the concentration of GLUT-2 on the hepatocyte membrane.

In hyperthyroid state, the half-life of insulin is halved. Pro-insulin levels increase by decreasing the C-peptide/pro-insulin ratio. Intestinal glucose absorption, endogenous glucose production, and lipolysis are also increased as well as the levels of catecholamines, glucagon, and growth hormone, which leads to impaired carbohydrate tolerance and insulin resistance [21, 22].

Hypothyroidism is associated with delayed glucose absorption and peripheral glucose assimilation, and reduced hepatic glucose production. This results in reduced peripheral glucose utilization and insulin resistance [21].

The ratio of serum free T3 (FT3) to free T4 (FT4) (FT3/ / FT4 ratio) may reflect the degree of extra-thyroid T4 to T3 conversion activity. The FT3/FT4 ratio is constant in healthy adults. High or low FT3 / FT4 ratios may affect the peripheral activity of thyroid hormones [20, 21].

The increased ratio of FT3: FT4 is associated with disorders of metabolic processes: lipid profile, blood pressure, insulin resistance. The decrease in FT4 levels is determined by increased peripheral deiodinase activity and increased peripheral conversion of FT4 to biologically active FT3. As a result, there is an increased ratio of FT3: FT4 [20, 21].

Peripheral deiodinase activity has been shown to be dependent on maternal weight - the higher the maternal weight, the greater the activity. This is associated with increased conversion of FT4 to active FT3, and fT3 induces endogenous glucose production. Weight gain or obesity during pregnancy leads to increased peripheral deiodinase activity. This changes the ratio of free thyroid hormones FT3:FT4 in favour of FT3. Changes in thyroid hormone levels underlie abnormalities in glucose homeostasis due to their effects associated with endogenous glucose production and insulin resistance [21, 22].

The present case-control study shows that women with GDM have higher TSH and higher FT3 concentrations and FT3:FT4 ratio.

Isolated maternal hypothyroxinaemia was also seen with higher frequency (21.12%). It is well known that isolated that IMH is characterized by normal TSH and low FT4 concentrations. The causes of IMH include iodine deficiency, changes in metabolism of the thyroid hormones during pregnancy, obesity, and environmental and angiogenic factors. Studies show that IMH could be associated with increased risk of preterm delivery, placental abruption, gestational diabetes, and impaired neurocognitive development of the child [18].

The percentage of anti-TPO-positive patients was higher in the GDM group — 38.1% *vs*. control group — 12.8%. The percentage of women in need of substitution therapy with thyroxin was higher in the GDM group — 26.6% compared with the control group — 17.2%. Our findings confirmed the results from previous prospective studies, which reported increased incidence of GDM in women with overt or subclinical hypothyroidism as well as isolated maternal hypothyroxinaemia [23–29]. It can be argued that there is a link between TSH, FT4, and FT3 concentrations and carbohydrate metabolism, although none of the conducted studies can ascertain whether changes in thyroid hormone levels lead to carbohydrate disorders [23–29].

Conclusion

The present study clearly shows that patients with GDM often have abnormalities in thyroid hormone status. This raises the question of the need for early universal screening for GDM and thyroid dysfunction in all pregnant women. Early parallel screening for carbohydrate and thyroid disorders in the first trimester of pregnancy would help to obtain an early diagnosis of GDM and/or thyroid dysfunction. Additional studies and analyses are needed to determine which of the two disorders is major, but it is appropriate to look for abnormalities in carbohydrate metabolism in patients with thyroid dysfunction as well as to look for abnormalities in thyroid hormone levels in patients with dysglycaemia. The results of these pilot retrospective series reveal that high-normal to high concentrations of TSH and FT3 as well as high FT3:FT4 ratio could indicate increased risk of development of GDM.

Conflict of interest

All authors have contributed sufficiently to the project to be included as authors, and all those who are qualified to be authors are listed in the author by line. To the best of our knowledge, no conflict of interest, financial or other, exists.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Hage M, Zantout MS, Azar ST. Thyroid disorders and diabetes mellitus. J Thyroid Res. 2011; 2011: 439463, doi: 10.4061/2011/439463, indexed in Pubmed: 21785689.
2. Stohl HE, Ouzounian J, Rick AM, et al. Thyroid disease and gestational diabetes mellitus (GDM): is there a connection? J Matern Fetal Neonatal Med. 2013; 26(11): 1139–1142, doi: 10.3109/14767058.2013.773309, indexed in Pubmed: 23461673.
3. Perros P, McCrimmon RJ, Shaw G, et al. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. Diabet Med. 1995; 12(7): 622–627, doi: 10.1111/j.1464-5491.1995.tb00553.x, indexed in Pubmed: 7554786.
4. Gray RS, Borsey DQ, Seth J, et al. Prevalence of subclinical thyroid failure in insulin-dependent diabetes. J Clin Endocrinol Metab. 1980; 50(6): 1034–1037, doi: 10.1210/jcem-50-6-1034, indexed in Pubmed: 7372784.
5. Chubb SAP, Davis WA, Inman Z, et al. Prevalence and progression of subclinical hypothyroidism in women with type 2 diabetes: the Fremantle Diabetes Study. Clin Endocrinol (Oxf). 2005; 62(4): 480–486, doi: 10.1111/j.1365-2265.2005.02246.x, indexed in Pubmed: 15807880.
6. International Diabetes Federation. IDF Diabetes Atlas. 9th ed. International Diabetes Federation, Brussels 2019.
7. Bodmer-Roy S, Morin L, Cousineau J, et al. Pregnancy outcomes in women with and without gestational diabetes mellitus according to the International Association of the Diabetes and Pregnancy Study Groups criteria. Obstet Gynecol. 2012; 120(4): 746–752, doi: 10.1097/AOG.0b013e31826994ec, indexed in Pubmed: 22996090.
8. Lee KW, Ching SM, Ramachandran V, et al. Prevalence and risk factors of gestational diabetes mellitus in Asia: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2018; 18(1): 494, doi: 10.1186/s12884-018-2131-4, indexed in Pubmed: 30547769.
9. Svare JA, Hansen BB, Mølsted-Pedersen L. Perinatal complications in women with gestational diabetes mellitus. Acta Obstet Gynecol Scand. 2001; 80(10): 899–904, doi: 10.1034/j.1600-0412.2001.801006.x, indexed in Pubmed: 11580734.
10. Rosario PW, Carvalho M, Calsolari MR. TSH reference values in the first trimester of gestation and correlation between maternal TSH and obstetric and neonatal outcomes: a prospective Brazilian study. Arch Endocrinol Metab. 2016; 60(4): 314–318, doi: 10.1590/2359-3997000000132, indexed in Pubmed: 26886091.
11. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. Diab Care. 2019; 43(Suppl 1): S14–S31, doi: 10.2337/dc20-s002.
12. Bulgarian Society of Endocrinology. Recommendations for good clinical practice for Diabetes Mellitus [In Bulgarian]. Bulgarian Society of Endocrinology, Sofia 2019.
13. Hod M, Kapur A, Sacks D, et al. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care#. Int J Gynaecol Obstet. 2015; 131: S173–S211, doi: 10.1016/s0020-7292(15)30033-3, indexed in Pubmed: 26433807.
14. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management

of Thyroid Disease During Pregnancy and the Postpartum. Thyroid. 2017; 27(3): 315–389, doi: 10.1089/thy.2016.0457, indexed in Pubmed: 28056690.
15. Bulgarian Society of Endocrinology. Recommendations for good clinical practice for thyroid disease [in Bulgarian]. Bulgarian Society of Endocrinology, Sofia 2019.
16. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012; 97(8): 2543–2565, doi: 10.1210/jc.2011-2803, indexed in Pubmed: 22869843.
17. Lazarus J, Brown R, Daumerie C, et al. 2014 European Thyroid Association Guidelines for the Management of Subclinical Hypothyroidism in Pregnancy and in Children. Eur Thyroid J . 2014; 3(2): 76–94, doi: 10.1159/000362597, indexed in Pubmed: 25114871.
18. Korevaar TIM, Medici M, Visser TJ, et al. Thyroid disease in pregnancy: new insights in diagnosis and clinical management. Nat Rev Endocrinol. 2017; 13(10): 610–622, doi: 10.1038/nrendo.2017.93, indexed in Pubmed: 28776582.
19. Ray S, Gosh S. Thyroid Disorders and Diabetes Mellitus: Double Trouble. J Diab Res Ther. 2016; 2(1), doi: 10.16966/2380-5544.113.
20. Männistö T, Vääräsmäki M, Pouta A, et al. Thyroid dysfunction and autoantibodies during pregnancy as predictive factors of pregnancy complications and maternal morbidity in later life. J Clin Endocrinol Metab. 2010; 95(3): 1084–1094, doi: 10.1210/jc.2009-1904, indexed in Pubmed: 20080846.
21. Rawal S, Tsai MY, Hinkle SN, et al. A Longitudinal Study of Thyroid Markers Across Pregnancy and the Risk of Gestational Diabetes. J Clin Endocrinol Metab. 2018; 103(7): 2447–2456, doi: 10.1210/jc.2017-02442, indexed in Pubmed: 29889229.
22. Oguz A, Tuzun D, Sahin M, et al. Frequency of isolated maternal hypothyroxinemia in women with gestational diabetes mellitus in a moderately iodine-deficient area. Gynecol Endocrinol. 2015; 31(10): 792–795, doi: 10.3109/09513590.2015.1054801, indexed in Pubmed: 26190538.
23. Yang Y, Li Q, Wang Q, et al. Thyroid antibodies and gestational diabetes mellitus: a meta-analysis. Fertil Steril. 2015; 104(3): 665–71. e3, doi: 10.1016/j.fertnstert.2015.06.003, indexed in Pubmed: 26151621.
24. Agarwal MM, Dhatt GS, Punnose J, et al. Thyroid function abnormalities and antithyroid antibody prevalence in pregnant women at high risk for gestational diabetes mellitus. Gynecol Endocrinol. 2006; 22(5): 261–266, doi: 10.1080/09513590600630470, indexed in Pubmed: 16785147.
25. Gong LL, Liu He, Liu LH. Relationship between hypothyroidism and the incidence of gestational diabetes: A meta-analysis. Taiwan J Obstet Gynecol. 2016; 55(2): 171–175, doi: 10.1016/j.tjog.2016.02.004, indexed in Pubmed: 27125397.
26. Maleki N, Tavosi Z. Evaluation of thyroid dysfunction and autoimmunity in gestational diabetes mellitus and its relationship with postpartum thyroiditis. Diabet Med. 2015; 32(2): 206–212, doi: 10.1111/dme.12580, indexed in Pubmed: 25186500.
27. Iranparvar M, Ghorbani H, Azami A, et al. Thyroid dysfunction and autoimmunity in pregnant women with gestational diabetes mellitus: a cross-sectional study. Int J Adv Med. 2015: 350–353, doi: 10.18203/2349-3933.ijam20151007.
28. Velkoska Nakova V, Krstevska B, Dimitrovski Ch, et al. Prevalence of thyroid dysfunction and autoimmunity in pregnant women with gestational diabetes and diabetes type 1. Prilozi. 2010; 31(2): 51–59, indexed in Pubmed: 21258277.
29. Vafaeimanesh J, Asgarani F, Bagherzadeh M, et al. Thyroid function in pregnant women with gestational diabetes: Is screening necessary? Thyroid Res Pract. 2015; 12(1): 3, doi: 10.4103/0973-0354.147271.