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ORIGINAL RESEARCH

To Study Association Of Thyroid Dysfunction With Diabetes Mellitus In Antenatal Women

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ABSTRACT

Introduction: The two most prevalent endocrine conditions that can be seen during pregnancy are thyroid dysfunction and gestational diabetes (GDM). Changes in glucose metabolism and insulin resistance (IR) can both be linked to abnormalities in thyroid function. The study's objective was to ascertain whether pregnant women with gestational diabetes have aberrant thyroid hormone levels.

Material and methods: The medical files of 662 pregnant women who gave birth between 2020 and 2022, separated into two groups: 412 with GDM and 250 with normal glucose tolerance. Using the International Federation of Gynecology and Obstetrics (FIGO) and American Diabetes Association (ADA) standards, a 2-h, 75-g oral glucose tolerance test (OGTT) was used to determine the presence of gestational diabetes mellitus in the study group. TSH, free thyroxine, free triiodothyronine, the FT3:FT4 ratio, fasting plasma glucose, age, and body mass index were all examined in both groups' mean blood concentrations. The Mann-Whitney U-test was used to compare the two groups.

Results: Significantly greater TSH and FT3 concentrations (p 0.0001), lower FT4 concentrations (p 0.0001), and higher FT3:FT4 ratios (p 0.0001) were reported in patients who acquired GDM.

Conclusion: According to the findings of this pilot retrospective series, high-normal to high TSH levels, low-normal to low FT4 levels, and a high FT3:Ft4 ratio may all point to an increased risk of developing GDM.

Keywords: Thyroid dysfunction; pregnancy; insulin resistance; gestational diabetes mellitus

INTRODUCTION

Pathophysiologically speaking, diabetes mellitus (DM) and thyroid disease (TD) may be related [1-2]. Regarding insulin sensitivity and requirements, these interactions have significance and corresponding effects. Glycemic management may be hampered by thyroid disease that is undiagnosed. Thyroid hormones have been linked to the fundamental mechanisms regulating hunger and energy expenditure, which is ultimately connected to variations in insulin sensitivity. Patients with DM experience thyroid dysfunction

substantially more frequently [3-5]. The prevalence of thyroid abnormalities in diabetics is 13.4%, with type 1 diabetes mellitus in women accounting for the highest percentage (31%) and type 2 diabetes in men accounting for the lowest percentage (6.9%). [1]. According to information from the most recent IDF Diabetes Atlas [6], the prevalence of hyperglycemia in pregnancy was 15.8% worldwide in 2019, affecting 20.4 million live births. According to data [1, 3-5], gestational diabetes mellitus (GDM) caused 83.6% of cases.

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.

MATERIALS AND METHODS

In this case-control research, two groups of pregnant women were compared. The information was obtained retroactively from the medical files of 662 pregnant patients who had visited the clinic between 2020 and 2022. A GDM group (n = 412) and a control group (patients with normal glucose tolerance, n = 250) were created from the observed women. Using the International Federation of Gynecology and Obstetrics (FIGO) and American Diabetes Association (ADA) criteria, a 2-h, 75-g oral glucose tolerance test (OGTT) was used to diagnose GDM [11–13]. All patients had their TSH, FT4, FT3, and anti-TPO concentrations checked before the glucose challenge test was conducted. The American Thyroid Association [ATA], European Thyroid Association [ETA], and Endocrine Society were some of the major professional organisations that provided recommendations and standards, and these were utilised. ETA recommendations, which state that in the absence of a population-specific range, a fixed TSH trimester-specific range is used, such as the following: first trimester — 0.1-2.5 mIU/L; second trimester — 0.2-3.0 mIU/L; and third trimester — 0.3-3.0 mIU/L [15-16].

TSH, FT4, FT3, anti-TPO, FT3:FT4 ratio, fasting blood glucose (mmol/L), and body mass index (BMI) mean serum concentrations were compared. Based on the recognised weight: height2 ratio, the BMI of the patients was determined. The immunochemiluminescent method (Cobas 6000) was used to measure the TSH concentrations, and the laboratory TSH reference range for the non-pregnant population was 0.27-4.20 mUI/L. The immunochemiluminescent method (Cobas 6000) was used to measure the concentrations of FT4 and FT3, with the reference intervals for each being 12–22 pmol/L for FT4 in the non-pregnant population and 3.2–6.8 pmol/L for FT3. By using the electrochemiluminescent assay (ECLIA), antibodies were identified (Cobas 6000). By dividing plasma FT3 concentrations by FT4 concentrations, the FT3:FT4 ratio was calculated. The thyroid hormones' interassay coefficient of variability was 5%, while it was 13%.

The Statistical Package for Social Sciences (SPSS) version 20.0 was used for the analysis. Data were presented as means, medians, or percentages (numbers). The Mann-Whitney U-test was used to compare the two patient groups (GDM group and control group) in terms of several markers. Relative frequencies were used to express non-metric variables (in percent). The difference between two percentages was compared using the chi-square test. p 0.05 was regarded as statistically significant in each test. We assessed the TSH indicator as a predictor for GDM using receiver operating characteristic (ROC) curve analysis, which provides a level of sensitivity and specificity.

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 3mIU/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.

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	

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
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
Gestational age at blood collection (weeks of gestation)	19 (± 2.5)	24 (± 2.5)	< 0.001

Anti-TPO antibodies Positive Negative	 157 255	 32 218	
Conception Method Spontaneous ART	 231 181	 192 58	0.0006

DISCUSSION

Understanding the connection between thyroid function and glucose metabolism is made possible by the current work. Our findings support the need for early parallel screening for thyroid dysfunction and GDM in order to prevent pregnancy-related problems. It is common knowledge that thyroid hormones are crucial for the metabolism of glucose. As a result, it has been proposed that thyroid dysfunction contributes to the pathogenesis of GDM. Maternal glucose homeostasis during pregnancy may be impacted by abnormal thyroid function. The half-life of insulin is shortened, and the concentration of GLUT-2 on the hepatocyte membrane is increased by endogenous thyroid hormone synthesis, among other causes.

The half-life of insulin is halved in hyperthyroidism. By lowering the C-peptide/pro-insulin ratio, pro-insulin levels rise. Impairment in carbohydrate tolerance and insulin resistance are the results of increased intestinal glucose absorption, endogenous glucose synthesis, lipolysis, catecholamines, glucagon, and growth hormone levels [17, 18]. Delays in peripheral glucose assimilation and delayed absorption as well as decreased hepatic glucose synthesis are all symptoms of hypothyroidism. Insulin resistance and decreased peripheral glucose consumption follow [17]. The degree of extra-thyroid T4 to T3 conversion activity may be indicated by the ratio of serum free T3 (FT3) to free T4 (FT4) (FT3/FT4 ratio).

In healthy people, the ratio of FT3/FT4 remains stable. The peripheral activity of thyroid hormones may be impacted by high or low FT3/FT4 ratios [17, 19]. Increased FT3: FT4 ratios are linked to metabolic process problems, including high blood pressure, insulin resistance, and lipid profile. Greater peripheral deiodinase activity and increased peripheral conversion of FT4 to physiologically active FT3 are what cause the drop in FT4 levels. As a result, the ratio of FT3 to FT4 has increased [17, 19].

It has been demonstrated that maternal weight influences peripheral deiodinase activity; the higher the weight, the higher the activity. This is connected to an increase in the conversion of FT4 to active FT3, and fT3 triggers the synthesis of endogenous glucose. Peripheral deiodinase activity rises throughout pregnancies when there is weight gain or obesity. Due to this, FT3 now dominates FT4 in the ratio of free thyroid hormones. Due to their impact on endogenous glucose production and insulin resistance, changes in thyroid hormone levels are the underlying cause of anomalies in glucose homeostasis [17, 18]. According to the current case-control study, women with GDM have greater TSH, FT3 concentrations, and a larger FT3:FT4 ratio.

CONCLUSION

The current study unequivocally demonstrates that patients with GDM frequently have thyroid hormone status abnormalities. This calls into question whether all pregnant women need to undergo early, universal screening for GDM and thyroid dysfunction. In the first trimester of pregnancy, early parallel screening for thyroid and carbohydrate abnormalities would aid in the early detection of GDM and/or thyroid dysfunction. It is appropriate to seek for abnormalities in carbohydrate metabolism in patients with thyroid dysfunction as well as to look for abnormalities in thyroid hormone levels in patients with dysglycemia, but further research and analysis are required to identify which of the two problems is major. These pilot

retrospective series' findings suggest that high-normal to high TSH and FT3 concentrations as well as a high FT3:FT4 ratio may be signs of a higher risk of developing GDM.

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