



Relationship Between Gestational Diabetes and Thyroid Hormones in Pregnant Women

Gebelerde Gestasyonel Diyabet ve Tiroid Hormonları Arasındaki İlişki

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Abstract

Objective: Gestational diabetes and thyroid disorders are common disorders during pregnancy. This study investigated the relationship between gestational diabetes and thyroid hormone levels in pregnant women.

Method: This single-center study was conducted by analyzing retrospectively 190 pregnant women who admitted to the private internal medicine clinic between March 2019 and December 2022. Ninety pregnant women diagnosed with gestational diabetes mellitus (GDM) and one hundred pregnant women without GDM diagnosis were included in the study. The relationship between thyroid markers [thyroid-stimulating hormone (TSH) and free thyroxine hormone 4 (fT4)] and gestational diabetes was examined.

Results: Results did not show a statistically significant association between case and control regarding age and body mass index (p-value >0.05). There was a statistically significant difference between groups regarding TSH (p-value <0.05). Also, results did not find a statistically significant association between the case and healthy pregnant women regarding fT4 (p-value >0.05). There was a statistically meaningful association between healthy women and women with GDM in terms of subclinical hypothyroidism frequency (p-value <0.05).

Conclusion: TSH levels, fasting blood glucose and hypothyroidism are among the risk factors for the development of the gestational diabetes.

Keywords: Diabetes, hypothyroidism, gestational diabetes mellitus, pregnancy, thyroid disorders

Öz

Amaç: Gestasyonel diyabet ve tiroid bozuklukları gebelikte sık görülen bozukluklardır. Bu çalışma, gebe kadınlarda gestasyonel diyabet ile tiroid hormon düzeyleri arasındaki ilişkiyi araştırmak için yapıldı.

Yöntem: Bu tek merkezli çalışma, Mart 2019-Aralık 2022 tarihleri arasında özel dahiliye polikliniğine başvuran 190 gebenin retrospektif olarak incelenmesiyle yapılmıştır. Gestasyonel diyabet mellitus (GDM) tanısı alan 90 ve GDM tanısı almamış 100 gebe çalışmaya dahil edilmiştir. Çalışmada tiroid belirteçleri olan tiroid uyarıcı hormon (TSH) ve serbest tiroksin hormonu (fT4) ile gebelik diyabeti arasındaki ilişki incelenmiştir.

Bulgular: Yaş ve vücut kitle indeksi açısından olgu ve kontrol arasında istatistiksel olarak anlamlı bir ilişki saptanmadı (p-değeri >0,05). Gruplar arasında TSH açısından istatistiksel olarak anlamlı fark vardı (p-değeri <0,05). Ayrıca sonuçlarda, olgu ve sağlıklı gebeler arasında fT4 açısından istatistiksel olarak anlamlı bir ilişki bulunmadı (p-değeri >0,05). Sağlıklı gebe kadınlar ile GDM'li kadınlar arasında subklinik hipotiroidizm sıklığı açısından istatistiksel olarak anlamlı bir ilişki vardı (p-değeri <0,05).

Sonuç: TSH düzeyleri, açlık kan şekeri ve hipotiroidizm gestasyonel diyabet gelişimi için risk faktörleri arasındadır.

Anahtar kelimeler: Diyabet, gebelik, gestasyonel diyabet mellitus, hipotiroidizm, tiroid bozuklukları

Introduction

Thyroid disorders and diabetes are among the most common endocrine diseases worldwide (1). The prevalence of gestational diabetes mellitus (GDM) is increasing in parallel with the increase in the prevalence of obesity

and diabetes in the world (2). GDM is also increasing in Turkey; according to Turkish Statistical Institute data, in 2017, 16.2% of pregnant women suffered from GDM (3). Obesity, nutrition, and genetic factors play a vital role in the occurrence of GDM, which can be prevented by changing



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the dietary pattern and lifestyle (4). Gestational diabetes is a common disorder during pregnancy, called a degree of plasma glucose intolerance, caused by the inability of the pancreas to secrete insulin and a decrease in insulin sensitivity during pregnancy (5,6). Pregnant women whose pancreatic function during pregnancy is insufficient to overcome insulin resistance are diagnosed with gestational diabetes. Failure to control GDM increases the risk of premature birth, fetal macrosomia and hypocalcemia, and congenital abnormalities in the fetus (7-9).

Thyroid disorders are more common in women than in men and are divided into hyperthyroidism and hypothyroidism based on thyroid stimulating hormone (TSH) and free thyroxine (fT4) and free triiodothyronine (fT3) serum levels (10). The thyroid gland's impaired functionality causes a decline in the production of thyroid hormones, leading to hypothyroidism, an endocrine condition. The categorization of hypothyroidism into overt and subclinical types is based on the specific biochemical abnormalities observed (11). The effect of diabetes on thyroid function is known, and thyroid hormones also have a reciprocal effect on carbohydrate metabolism and pancreas function (12). Some researchers have reported a higher prevalence of thyroid disorders in diabetic patients (13).

Pregnancy has a significant impact on thyroid function. An increase in protein binding to thyroxine, an increase in the production of thyroid hormones, and stimulation of the thyroid by gonadotropin occur in pregnancy (14). The role of thyroid dysfunction in the occurrence of GDM can be investigated according to the role of thyroid hormones in glucose metabolism and homeostasis (12).

The primary goal of this research is to examine the association between thyroid disorders and gestational diabetes. In previous studies, conflicting results have been reported by scholars. Some studies have reported a relationship between hypothyroidism and the risk of GDM (15). On the other hand, no significant relationship has been reported in some studies (16). Identifying the relationship between thyroid disorders and GDM is crucial in timely diagnosis and providing more effective treatments. Considering the adverse effects of thyroid disorders on the health of the fetus and the prevalence of these disorders in Turkish women, in this study, comprehensive research was conducted to investigate the relationship between gestational diabetes and thyroid hormone.

Materials and Methods

This retrospective case-control study includes 190 pregnant women referred to the clinic of Centermed Plus between March 2019- December 2022. In this case-control study, 190 pregnant women aged 20 to 35 years, who underwent 75 g the orale glucose tolerantie test (OGTT) between 24 and 28 weeks of gestation and were diagnosed with gestational diabetes, were randomly selected from archive scanning. Ethics Committee Approval of the research was obtained from University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Hospital (date: 07.08.2023, decision no: 2023-15) and written inform consent were taken from all patients.

In this study, the total number of participants were divided in two groups including case (women with gestational diabetes; n=90) and control (healthy women; n=100) groups. Gestational diabetes was diagnosed by performing a fasting blood sugar test in the 24th to 28th week of pregnancy. If blood sugar was less than or equal to 92 mg/dL was considered healthy, 92-125 mg/dL was considered prediabetes, and more than 126 mg/dL was considered diabetic. The OGTT test was performed for pregnant women in prediabetes and diabetic groups. In this test, after consuming 75 grams of glucose, plasma glucose level was measured in three stages: before the drink, "1-hour post-prandial blood sugar (mg/dL)" and "2-hour post-prandial blood sugar (mg/dL)". If the fasting plasma glucose level was more than 92 mg/dL, one hour later more than 180 mg/dL, and two hours later more than 153 mg/dL, it was identified as gestational diabetes. With the retrospective screening method of the pregnant women's files, the blood results of the patients in the first trimester (between the first 6 and 20 weeks), TSH, free T4, fasting blood glucose values recorded in our dataset. Diagnosis of hypothyroidism was made by the TSH value. The subclinical hypothyroidism was defined as having a high TSH level (> 4.0 µIU/mL) and a low or normal fT4.

Statistical Analysis

The Kolmogorov-Smirnov test was performed to test the normality of variables. Mean and standard deviations (SD) were measured to check each continuous variable, including age, body mass index (BMI), fasting blood sugar (FBS), TSH, and fT4. The Mann-Whitney U test was accomplished to investigate the difference between healthy women and women with gestational diabetes in all variables. For categorical data, the number of data (n) and percentage (%) was used to describe the data. The chi-square tests were employed to compare groups with categorical variables.

For statistically significant, it is considered not significant as $p > 0.05$. SPSS v.26 was utilized for statistical analyses.

G-Power v.3.1 was used to calculate the sample size, and two groups' total mean and standard deviations were measured based on the non-parametric test with a power of 95%, 0.05 type 1 error, and effect size of 50% for at least 176 (88 patients for each group) (17).

Results

A total of 190 age-matched (27.01 ± 3.54) and BMI-matched (26.95 ± 4.55) pregnant women participated in this study.

Table 1 shows explanatory details of investigation variables. The mean and median age of the pregnant women was 27.01 and 28 years ($SD = 3.54$). The mean and median BMI of the pregnant women was 26.95 and 27.3 kg/m^2 ($SD = 4.55$). The mean and median FT4 of the women was 1.24 and 1.12 ng/dL ($SD = 0.38$). The mean and median TSH of the participants was 2.27 and 2.01 $\mu IU/mL$ ($SD = 1.2$). The mean and median FBS of the participants were 9.94 and 90 mg/dL ($SD = 1.2$).

Table 2 shows study parameters of healthy women and women with gestational diabetes included in the research.

Table 1. Explanatory details of investigation variables in pregnant women (n=190)

Investigation variables	Median (range)	mean \pm SD
Age (years)	28 (20-35)	27.01 ± 3.54
BMI (kg/m^2)	27.3 (18.7-35)	26.95 ± 4.55
fT4 (ng/dL)	1.12 (0.95-4.01)	1.24 ± 0.38
TSH ($\mu IU/mL$)	2.01 (0.46-7.98)	2.27 ± 1.2
FBS (mg/dL)	90 (62-142)	93.49 ± 15.65

SD: Standard deviation. BMI: Body mass index, fT4: Free thyroxine 4, TSH: Thyroid stimulating hormone, FBS: Fasting blood sugar

Table 2. The comparison of healthy women and women with gestational diabetes in study parameters

Study parameters	Case (women with gestational diabetes) (n=90) M \pm SD	Control (healthy women) (n=100) M \pm SD	p-value
Age (years)	27.01 ± 3.6	27.1 ± 3.51	0.874*
BMI (kg/m^2)	26.84 ± 4.73	27.06 ± 4.40	0.846*
fT4 (ng/dL)	1.23 ± 0.33	1.25 ± 0.42	0.947*
TSH ($\mu IU/mL$)	2.81 ± 1.48	1.77 ± 0.51	<0.001*
FBS (mg/dL)	103.17 ± 16.55	84.78 ± 7.72	<0.001*

M: Mean, N: Number of subjects, BMI: Body mass index, FBS: Fasting blood sugar, TSH: Thyroid-stimulating hormone, FT4: Free thyroxine, *Mann-Whitney U test, SD: Standard deviation

A Mann-Whitney U test did not find statistically meaningful difference between women with gestational diabetes and control in terms of fT4 (p -value > 0.05).

As can be seen from the Table 2, there was a statistically significant association between women with GDM and controls regarding TSH and FBS (p -value < 0.001). The TSH values in case group (2.81 ± 1.48) was higher than controls (1.77 ± 0.51). The FBS values in case group (103.17 ± 16.55) was higher than controls (84.78 ± 7.72).

There was a statistically meaningful association between healthy women and women with GDM in terms of subclinical hypothyroidism frequency (p -value < 0.05). As stated in Table 3, the women with gestational diabetes had 26.6% (n=24) hypothyroidism. The healthy women had a 11% (n=11).

Figure 1 shows the comparison of healthy women and GDM in TSH. As can be seen from the Figure 1, the frequency of hypothyroidism in female cases is twice as high as in the control group.

Discussion

In this study, thyroids hormone values and the subclinical hypothyroidism frequency of women with GDM were compared with the control group. According to the results,

Table 3. The significant relationship between case and control groups and hypothyroidism frequency

Variable	Case (n=90) n (%)	Control (n=100) n (%)	p-value
Hypothyroidism	24 (26.6)	11 (11)	0.006*
	66 (57.4)	89 (89)	

*chi-square test

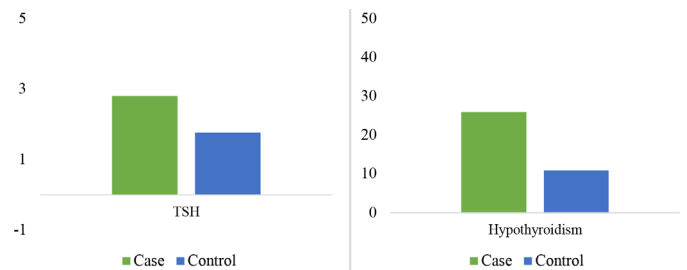


Figure 1. The comparison of healthy women and women with gestational diabetes in TSH and FBS

TSH: Thyroid-stimulating hormone, FBS: Fasting blood sugar

women with gestational diabetes show a significant difference in thyroid disorders compared to healthy pregnant women, consistent with previous studies (15,18-22). Elevated first-trimester TSH levels in pregnant women with normal fT4 levels are associated with an increased risk of GDM. Also, the presence of hypothyroidism in women with GDM is associated with an approximately two times greater likelihood in healthy pregnant women.

In a similar study, Fernández Alba et al. (15), identified the higher first trimester TSH level as a risk factor for GDM by examining the data of 6775 Spanish pregnant women. Demiral Sezer and Topaloglu (21), tested the relationship between thyroid hormones and GDM on 160 Turkish women with multicenter data. High TSH levels had a significant relationship with gestational diabetes. Kent et al. (22), showed that TSH in women with GDM was significantly higher than control group in a meta-analysis. Chen et al. (16), reported no significant relationship between higher TSH level and risk of GDM by investigating the data of 2.849 Chinese pregnant women. Although conflicting results have been reported regarding the significant relationship between higher TSH levels and GDM, it can be concluded that a level of TSH higher than ($>4.0 \mu\text{IU/mL}$) can be considered a risk factor in pregnant women for GDM.

The prevalence of subclinical hypothyroidism in this study was 26.6% in women with GDM. Which was significantly higher than healthy pregnant women, consistent with previous studies (18-20). Imdad and Shylaja (18) reported 27 cases of hypothyroidism in 100 women with gestational diabetes. The frequency of hypothyroidism was higher in diabetic women. Latifah et al. (19), reported 12-15% for prevalence of hypothyroidism in women with GDM. Reviewing every study in this field is impossible, and meta-analyses and survey articles can be used to compare the results. In a comprehensive review, Dincgez et al. (20), studied hundreds of articles on the relationship between maternal subclinical hypothyroidism and GDM. In their conclusion, they emphasized the effectiveness of maternal subclinical hypothyroidism in increasing the risk of GDM. No significant relationship between two was reported in others meta-analyses, which examined a much smaller number of articles (23,24). The finding of the current studies shows that hypothyroidism in pregnant women has a more increased risk for GDM than healthy pregnant women overall. Hypothyroidism has an adverse impact on glucose homeostasis by causing insulin resistance. Pregnant women with hypothyroidism increase insulin resistance and in this condition the risk of GDM increases (25,26).

In this study, age-matched and BMI-matched pregnant women participated so that age and obesity did not affect the results. Previous studies have shown that the risk of gestational diabetes increases with increasing BMI and maternal age (21,27). The frequency of this disease is higher in women older than 25 and $\text{BMI} \geq 25.0 \text{ kg/m}^2$ (28).

Study Limitations

The number of participants in the paper is relatively small, and it is suggested to conduct research with a higher number of participants. Gestational diabetes and thyroid disorders may be affected by geographical and racial factors. One of the limitations of this study is that the patients' data from a single center, and it is suggested to use patients' data in several centers in future studies. Examining the effect of demographic information such as education, income level, and hereditary history of diabetes and thyroid failure in mothers can add to the positive aspects of the study.

Conclusion

In overview, fasting blood glucose, higher TSH levels, and subclinical hypothyroidism was among the factors leading to GDM and can be considered important risk factors. The benefits of regular screening for thyroid function during pregnancy are controversial. Based on the findings of this study, regular screening for thyroid function in pregnant women is beneficial and safe for timely prevention and providing more effective treatments. Nevertheless, there is a requirement for more randomized-prospective studies to be conducted.

Ethics

Ethics Committee Approval: Ethics Committee Approval of the research was obtained from University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Hospital (date: 07.08.2023, decision no: 2023-15).

Informed Consent: The need for informed consent was waived under the approval of the local ethics committee due to the retrospective design.

Peer-review: Internally and externally peer-reviewed.

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