

Evaluation of Thyroid Dysfunction in Women with Gestational Diabetes Mellitus Compared to Healthy Pregnant Women Referred to Kowsar Hospital in Qazvin from 2017 to 2018

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Article Info

 10.30699/jogcr.5.1.6

Received: 2020/03/05;

Accepted: 2020/05/27;

Published Online: 12 Aug 2020;

Use your device to scan and read the article online



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ABSTRACT

Background & Objective: In this study, thyroid dysfunction in women with gestational diabetes mellitus was examined and compared to that in healthy pregnant women referred to Kowsar Hospital in Qazvin in 2017 and 2018.

Materials & Methods: In this case-control study, 100 women with gestational diabetes mellitus and 100 non diabetic healthy pregnant women who referred to Kowsar Hospital in Qazvin from 2017 to 2018 were selected using the convenience sampling method, and their serum thyroxine, anti-TPO, and TSH levels were determined and compared. Moreover, Apgar scores and anthropometric variables were compared between the two groups.

Results: In the present study, there were statistically significant differences between the groups in terms of the TSH level ($P=0.012$), assessed by the independent t-test, the thyroxine ($P=0.0001$) and anti-TPO ($P=0.008$) levels, both examined by the Mann-Whitney test, which associated with high levels of TSH and anti-TPO and low levels of thyroxine in the diabetic group. No differences were found regarding the Apgar scores and anthropometric variables between the groups ($P>0.05$).

Conclusion: Overall, according to the obtained results, it can be inferred that thyroid dysfunction, realized as hypothyroid with high anti-TPO levels, was more prevalent in women with gestational diabetes mellitus compared to healthy pregnant women.

Keywords: Diabetes, Pregnancy, Thyroid Function

Introduction

Gestational diabetes mellitus (GDM) and thyroid dysfunction in pregnancy are among the most prevalent diseases that influence pregnancy outcomes (1). Diabetes is one of the most common metabolic diseases associated with elevated blood glucose and metabolic alternations in lipids, sugars, and proteins, which has a prevalence of 3.5-5% during pregnancy (2). Its known complications during pregnancy include preeclampsia, preterm labor, miscarriage, congenital anomalies, shoulder dystocia, and stillbirth for the fetus. Accordingly, it is a strong risk factor for adverse pregnancy outcomes (3). The effects of diabetes will remain even after childbirth, and approximately 40% of women with GDM will develop overt diabetes within the next 20 years (4). Harmful effects of thyroid dysfunction during pregnancy have been proven to affect the course of pregnancy and fetal development (5). The fetus needs thyroxine for normal growth,

especially for brain development, and since the production and secretion of fetal thyroid hormones do not occur until the 20th week of pregnancy, fetal growth in the first trimester is completely dependent on the thyroxine transferred from the mother (6). There is a close correlation between maternal thyroid function and pregnancy outcomes; it has been observed that the presence of thyroid autoantibodies in the mother's blood associates with an increase in fetal loss in early pregnancy (7). Both untreated thyrotoxicosis and hypothyroidism relate to adverse pregnancy outcomes (8). Even in several studies, the presence of subclinical hypothyroidism associated with increased pregnancy complications, including placental abruption (increased three times), preterm labor (increased twice), and infants with low birth weight (increased twice). Furthermore, various conducted studies indicated that increased thyroid peroxidase antibodies

(TPO) in euthyroid pregnant women correlated with increased pregnancy complications, including prelabor rupture of membranes (PROM), miscarriage, and preterm labor (10). The prevalence of TPO antibodies in asymptomatic women has been reported to be 6-19% during pregnancy, and about 10% of pregnant women in the 16th week of pregnancy have TPO-Ab, which may be related to hyperthyroidism (11). The prevalence of thyroid dysfunction in pregnant women with type 1 diabetes is about three times more than the normal population. Even in some studies, 40% of pregnant women had concomitant type 1 diabetes and thyroid dysfunction. Among thyroid dysfunctions, subclinical hypothyroidism is more prevalent than other dysfunctions (12). Clinical and subclinical thyroid hyperthyroidism, like GDM, is an insulin resistance condition that can itself suggest a link between the two diseases. Several studies have proposed that maternal diabetes during pregnancy may affect T3 secretion or active T4 to T3 conversion in the fetus (13,14). This justifies the association of diabetes with thyroid dysfunction. The GDM prevalence in Iran was reported to be 4.7-7.4%. (15). Of pregnant women, 10-15%, suffer from thyroid dysfunction in the first half of their pregnancies (16). Some studies have reported the high prevalence of hypothyroxinaemia and high anti-TPO levels in women with GDM (17). According to what was mentioned earlier and given the possibility of a relationship between diabetes and thyroid dysfunction, despite various studies that examined the issue (10,18,19), the type of causal relationship between these diseases has not yet been proven in all the studies (20,21). Because many other causes, such as race, genetics, environmental factors, underlying diseases, diabetes identification criteria, and thyroid dysfunction, are involved in the study of this relationship (22), this study investigated the prevalence of thyroid dysfunction in pregnant women with GDM compared to healthy pregnant women who referred to Kowsar Hospital in Qazvin from 2017 to 2018.

Materials and Methods

In this analytical epidemiological case-control study, 100 healthy pregnant women and 100 pregnant women with GDM were selected among all women referred to Kowsar Hospital in Qazvin in 2017 and 2018 and were willing to participate in the study, using the convenience sampling method. The required information was recorded in a prepared checklist, containing maternal age, gestational age, gravity, BMI, serum levels of TSH, FT4, anti-TPO-GTT, and the

neonate's height, weight, head circumference, and Apgar score. Inclusion criteria were gestational age ≥ 24 weeks, maternal age from 18 to 40 years old, single pregnancy, and disruptions to glucose tolerance test (GTT) (FBS > 92 , BS 1h > 180 , BS 2h > 153). Exclusion criteria were multiple pregnancies and maternal age < 18 years old and > 40 years old and other metabolic diseases. After signing a written consent, 5 cc of blood was taken from all patients by phlebotomy, and the serum TSH, FT4, and anti-TPO levels were measured and compared between the two groups. Both groups studied the same gestational age. After collecting the required information from all 200 patients, the collected data were analyzed using SPSS 22 (SPSS Inc., Chicago, IL., USA). For the qualitative variables, frequencies and frequency percentages were used, and means and standard deviations were applied for the quantitative variables. Moreover, the Fisher and Chi-squared tests were used, and a P-value less than 0.05 was considered significant for interpreting the relationships between the variables. At all stages of the study, the patients' personal information was not disclosed and was only revealed to them. Besides, written consents were obtained from all the patients, and no fee was imposed on the patients. Moreover, no changes were made in the process of examining and treating these patients.

Results

In the current study, 200 pregnant women, including 100 women with GDM and 100 women without GDM, were examined. The most important variables compared between the two groups were thyroid indicators, the TSH, FT4, and anti-TPO levels, and were assessed by carrying out serum evaluations. The patients' mean age was 28 years, and their mean gestational age was 27 weeks. The mean height, weight, and head circumference of the neonates were 49 cm, 3384 g, and 33 cm, respectively.

According to the independent t-test, other than the maternal BMI ($P=0.0001$), there were no significant differences between the two groups regarding the other quantitative background variables ($P>0.05$) (Table 1).

As can be seen in Table 2, based on the Chi-squared test, there were no differences between the two groups in terms of preeclampsia, preterm labor, and C-section ($P>0.05$).

Table 1. A frequency distribution of quantitative background variables in the two groups of case and control

	Group	M	SD	P-value
Age	Diabetes	28.4	4.7	$>0/05$
	Control	27.8	4.8	
Gestational age	Diabetes	27	1.5	>0.05
	Control	26.8	1.6	

	Group	M	SD	P-value
Height	Diabetes	48.7	1.5	0.62
	Control	48.8	1.5	
Weight	Diabetes	3406	327	0.322
	Control	3362	303	
Head circumference	Diabetes	33.3	0.9	0.858
	Control	33.2	1	
Apgar score	Diabetes	9.10	0	1
	Control	9.10	0	
Maternal BMI	Diabetes	25.1	2	0.0001
	Control	23	2.3	

Table 2. A frequency distribution of maternal outcomes in the two groups

	Diabetes (N=100)	Control (N=100)	Sig
	Percent	Percent	
Preeclampsia	5	4	1
Preterm labor	4	4	1
C-section	22	19	0.726

Based on the independent t-test, there were significant differences between the two groups in terms of all the four laboratory variables, including TSH

($P=0.012$), anti-TPO ($P=0.008$), and 2-hour FT4 ($P=0.0001$) (Table 3). Both groups studied the same gestational age.

Table 3. A frequency distribution of the FT4, anti-TPO, and TSH levels in the two groups

	Diabetes (N=100)	Control (N=100)	Sig
	M±SD	M±SD	
FT4	4.9±9.1	3.4±12.3	0.0001
Anti-TPO	16.9±9.3	14.3±9.5	0.008
TSH	2.9±1.1	1.8±0.8	0.012

Discussion

In this case-control study, statistically significant differences were found between the two groups in terms of the TSH level ($P=0.012$), examined by the independent test, and the thyroxine ($P=0.0001$) and anti-TPO ($P=0.008$) levels, assessed by the Mann-Whitney test, which associated with low levels of TSH and high levels of thyroxine and anti-TPO in the diabetic group. In a study done by Hui, aimed at investigating the effects of hypothyroidism on GDM in 98 pregnant women with GDM in 2012 in South Korea, it was found that hypothyroidism exacerbated metabolic disorders and adverse pregnancy outcomes in women with GDM. It was also recommended that women with GDM should be monitored for thyroid dysfunction and treated if they suffer from it (9). This finding can also be deduced from the results of the current study. In a study conducted by Rahimi *et al.* in 2000, which examined thyroid dysfunction in pregnant women with GDM and overt DM, 61 patients with GDM and 35 healthy women were screened, and the levels of anti-TPO, TSH, T3RU, T3,

and T4 were evaluated in the two groups. According to their conclusion, thyroid dysfunction in the GDM group was similar to that of the control group (10). This finding is not in line with the results of the present study. In 2013, a cohort study carried out by Tirosh *et al.*, which studied the prevalence of maternal and neonatal morbidity and outcomes in women with concomitant hypothyroidism and diabetes, 87,213 women were examined. The results of this study indicated that the prevalence of diabetes and hypothyroidism in the study population was 0.17%. Comparing the groups under study demonstrated that the infertility ratio ($P=0.001$), preeclampsia ($P=0.001$), chronic hypertension ($P=0.001$), preterm labor ($P=0.001$), and C-section ($P<0.001$) were higher in women with DM and hypothyroidism compared to the normal population (11). This is while no statistically significant relationship was observed in the current study, which may be due to the smaller number of samples studied in the present study. Shuai Yang performed a study in

China and evaluated the low serum level of thyroid hormone in pregnancy and its association with an increased risk of GDM. In the mentioned study, 27,513 pregnant women were checked in terms of serum thyroid and GDM levels. The GDM prevalence significantly correlated with increased age, increased BMI, and having a family history of diabetes, and the serum FT4 levels significantly reduced in pregnant women with DM (12). The findings of the current study were in contrast with these findings. In a retrospective study conducted by Zoo TI *et al.* in 2003 in Italy, 112 patients with GDM were examined. This study aimed to evaluate the relationship between GDM and thyroid dysfunction and concluded that there was a relationship between GDM and thyroid dysfunction. The patients with GDM were at a higher risk for clinical and subclinical hypothyroidism compared to others (13). However, in this study, an increase in FT4 and a decrease in TSH were observed, which was contrary to the mentioned study. In a case-control study conducted by Rawal *et al.* in 12 hospitals in the United States, the results of which were published in 2018, 107 women with GDM were examined and compared to 214 healthy pregnant women. Statistically significant relationships were found between GDM and FT3 and the ratio to FT4. However, in the case of TSH and FT4 alone, there were no differences between the two groups with and without GDM (23). These findings are inconsistent with the results of the current study. This difference could be due to the lack of uniformity in the number of people studied in the study groups. In an analytical study done by Huang *et al.* in China, the results of which were published in 2019, 2,023 pregnant women were studied and it was found that people with high anti-TPO levels, regardless of their TSH and FT4 levels, were at a higher risk for GDM compared to others. This is while TSH and FT4 alone did not associate with GDM (24). In the present study, not only anti-TPO but also two factors of TSH and FT4 had significant relationships. In a study performed by Shahbazian *et al.* in Iran, the results of which were published in 2013, 61 women with GDM and 35 pregnant women, as a control group, were examined. It was found that the frequency of thyroid dysfunction was similar in both groups. Besides, the frequency of anti-TPO levels in the GDM group was higher than the control group; however, the observed difference was not significant (25). The reason for the difference between this study and the results of the current study was the sample that was much smaller than the sample studied in the mentioned study.

Recommendations: Finally, it is recommended that more studies be performed with a bigger sample size considering other possible diseases during pregnancy so that the relationships in the spectrum of endocrine diseases be assessed. It is also possible to achieve more reliable results by controlling confounding factors. Furthermore, conducting studies in several centers can increase the generalizability of results.

Conclusion

In general, considering all the aspects of the issue, it is suggested that thyroid dysfunction is more common in women with GDM than in non-diabetic pregnant women. This dysfunction is realized by hypothyroidism associated with high levels of anti-TPO, which has no major clinical significance and does not have a definite effect on fetal and maternal complications.

Acknowledgments

This study was the result of a doctoral dissertation approved by Qazvin University of Medical Sciences, which was implemented with the financial support of this university. The authors would like to express their sincere appreciation to all the staff working at the women's department and all the people who helped them in conducting this study.

Conflict of Interest

Authors declared no conflict of interests.

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How to Cite This Article:

Hasani F, Movahed F, Lalooha F, Noori E. Evaluation of Thyroid Dysfunction in Women with Gestational Diabetes Mellitus Compared to Healthy Pregnant Women Referred to Kowsar Hospital in Qazvin from 2017 to 2018. *J Obstet Gynecol Cancer Res*. 2020; 5(1) :6-10

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