



Araştırma

2022; 31 (3):301-306

COMPARISON OF EMOTIONAL STATE IN HYPEREMESIS GRAVIDARUM PATIENTS WITH AND WITHOUT
NORMAL THYROID FUNCTION TESTS
HİPEREMEZİS GRAVİDARUM HASTALARINDA TİROİD FONKSİYON TESTLERİ NORMAL OLANLAR VE TİROİD
FONKSİYON TESTLERİ NORMAL OLMAYANLAR ARASINDAKİ DUYGU DURUM KARŞILAŞTIRILMASI

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This study, it was aimed to evaluate the mood differences between those with normal thyroid function test (TFT) and those with abnormal TFT in patients with hyperemesis gravidarum. Therefore, thyroid function tests of pregnant women who were diagnosed with hyperemesis gravidarum during the three-month study period were evaluated. Patients were divided into two groups according to normal and abnormal thyroid function tests. Each group consisted of 50 patients. The demographic characteristics of both groups were recorded and Beck depression and anxiety scales were applied to the groups. Although the Beck depression inventory score was 58% in pregnant women with normal TFT and 56% in non-normal patients, this difference was not statistically significant ($p>0.05$). According to Beck Anxiety Inventory scores, there was a statistically significant difference between patients with abnormal TFT and patients with normal TFT ($p<0.05$). Also, patients with abnormal TFT tended to be more anxious than those with normal TFT ($p<0.1$). A moderately strong negative correlation was found between Beck depression and Beck anxiety inventory scores in the patient group with abnormal TFT (Spearman's rho = -0.403; $p=0.004$). In addition, there was a weak negative correlation between Beck depression inventory score and social security status (Spearman's rho = -0.287; $p=0.043$), while a weak positive correlation was found between Beck depression inventory score and history of miscarriage (Spearman's rho = 0.287; $p=0.043$). In this study, although there was no significant difference in depression between patients with hyperemesis gravidarum with and without normal TFT, it was determined that anxiety levels were higher in patients with abnormal TFT compared to those with normal TFT.

Keywords: Anxiety, depression, hyperemesis gravidarum, thyroid function test

ÖZ

Bu çalışmada hiperemesis gravidarum hastalarında tiroid fonksiyon testi (TFT) normal olanlar ve TFT'si normal olmayanlar arasındaki duygu durum farklılıklarının değerlendirilmesi amaçlanmıştır. Bu nedenle üç aylık çalışma döneminde hiperemesis gravidarum tanısı alan gebelerin tiroid fonksiyon testleri değerlendirildi. Hastalar normal ve anormal tiroid fonksiyon testlerine göre iki gruba ayrıldı. Her grup 50 hastadan oluşuyordu. Her iki grubunda demografik özellikleri kayıt edilerek gruplara Beck depresyon ve anksiyete ölçekleri uygulandı. Beck depresyon envanteri puanı TFT'si normal olan gebelerde %58, normal olmayanlarda %56 olmasına rağmen bu fark istatistiksel olarak anlamlı değildi ($p>0.05$). Beck anksiyete envanteri puanlarına göre anormal TFT'si olan hastalar ile normal TFT'si olan hastalar arasında istatistiksel olarak anlamlı fark vardı ($p<0.05$). Ayrıca anormal TFT'si olan hastalar, normal TFT'si olanlara göre daha endişeli olma eğilimindeydi ($p<0.1$). Anormal TFT'si olan hasta grubunda Beck depresyon ile Beck anksiyete envanteri puanları arasında orta kuvvette negatif korelasyon tespit edildi (Spearman's rho = -0.403; $p=0.004$). İlave olarak Beck depresyon envanteri puanı ile sosyal güvenlik durumu arasında zayıf bir negatif ilişki bulunurken (Spearman's rho = -0.287; $p=0.043$), Beck depresyon envanteri puanı ile düşük öyküsü arasında zayıf bir pozitif korelasyon tespit edilmiştir (Spearman's rho = 0.287; $p=0.043$). Bu çalışmada TFT'si normal olan ve olmayan hiperemesis gravidarumlu hastalar arasında depresyon açısından anlamlı bir fark olmadığı halde, TFT'si normal olmayanlarda, normal olanlara kıyasla kaygı düzeylerinin daha yüksek olduğu belirlenmiştir.

Anahtar kelimeler: Anksiyete, depresyon, hiperemesis gravidarum, tiroid fonksiyon testi

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Makale Geliş Tarihi : 18.08.2021

Makale Kabul Tarihi: 20.07.2022

INTRODUCTION

Nausea and vomiting seen in pregnancy may sometimes be severe enough to prevent oral intake, in which dehydration symptoms such as thirst, hollowing of the eyes, and dry skin may reach disturbing levels. This condition may severely impact the quality of life and comfort of pregnant women, becoming a psychologically abrasive and difficult process. The state of severe nausea and vomiting during pregnancy is known as hyperemesis gravidarum. Significant changes in the thyroid gland and thyroid functions are observed in pregnancy. These changes begin with increased production of thyroxine-binding globulin. Subsequently, secondary to this increase, integral and bound maternal thyroid hormone levels increase, resulting in decrease in thyroid-stimulating hormone (TSH). Human chorionic gonadotropin (hCG) hormone, which increases in the first trimester of pregnancy and weakly stimulates TSH receptors, also has an effect on the decrease in TSH levels. As hCG increases, it binds to TSH receptors, causing the thyroid gland to produce more hormones, and increased thyroid hormone levels lead to decreased TSH. This decrease is observed in the early weeks of pregnancy, afterwards, TSH levels return to basal levels. In the final weeks of pregnancy, increase in TSH may occur due to deiodinase enzyme secreted from the placenta. All of these mechanisms occur in the background of the physiological process related to thyroid gland during pregnancy (1). Thyroid hormones play a vital role in the completion of neuronal development in the fetus. This role is especially important in the first six months of pregnancy, in which the fetal thyroid gland has not completed maturity and necessary thyroid hormones are attained from the mother (2-4). During pregnancy, thyroid gland activation and vascularization increases, and its iodine uptake mechanism changes, resulting in hyperplasia and increased weight (5-7). It is known that psychological symptoms play a role in the underlying mechanism of hyperemesis gravidarum (8). At the same time, it has been observed in hyperemesis gravidarum patients that thyroid hormones may increase and regress to basal levels with treatment and persist at normal levels as pregnancy progresses (9,10). Elevated thyroid hormone levels increase stress, insomnia, irritability, and uneasiness in pregnant women, causing changes in emotional state. This emotional state may affect or interfere with the changes in emotional state that play a role in the underlying basis of hyperemesis gravidarum. From this standpoint, distinguishing this difference is important in order to plan treatment and manage illness. Therefore, in this study, it was aimed to compare the emotional states of hyperemesis gravidarum patients with and without normal thyroid function tests (TFT).

MATERIAL AND METHODS

Within the 3-month study period, took place between July 2018 and October 2018, total of 100 pregnant patients diagnosed with hyperemesis gravidarum were included in the study. Using stratified random sampling method, patients were divided into two groups of consecutive 50 individuals according to thyroid function tests; the control group consisted of patients with normal thyroid function tests, and the other

group consisted of patients with abnormal thyroid function tests. The sample size was calculated as 100 by power analysis. In addition to severe nausea and vomiting, impaired oral intake, ketone positivity in urine, and dehydration symptoms were also taken into consideration for hyperemesis gravidarum diagnosis. Patients with conditions that may have contributed to impaired thyroid function or those taking medications that could cause changed emotional state were excluded from the study. Number of gravidae, parity, miscarriages, and abortions along with comorbidities, nicotine and alcohol use as well as demographic characteristics of the patients were documented. Venous blood was taken for thyroid function tests after diagnosis and hospitalization of the patients. To assess thyroid function tests as within normal limits, TSH values were evaluated using 0.1-2.5 mIU/L in the first trimester and 0.2-3 mIU/L in the second trimester as reference intervals. Since the normal intervals for triiodothyronine (T3) and free thyroxine (T4) are undefined in pregnancy, they were not used for evaluation.

To assess emotional state of the study participants, Beck Depression Inventory and Beck Anxiety Inventory scales were administered separately. Beck Depression Inventory was developed in 1961 by Aaron T. Beck and consists of 21 parameters evaluating behavior and depressive state of mind. The inventory takes about 10 minutes to complete. The scale was adapted in Turkish in 1988 (11). The scale's validity and reliability study was conducted by Aktürk (12). According to scores they received from the scale, depression levels of the patients were recorded as normal, mild, moderate. Beck's Anxiety Inventory also consists of 21 parameters and patients were classified as none, mild, moderate in terms of anxiety symptoms based on their test results. This test's validity and reliability study was conducted in 1988 (13).

Statistical Analysis

SPSS 22.0 for Windows software program was used for statistical analysis. Descriptive statistics were given as mean, standard deviation, minimum and maximum for numerical variables. Spearman Correlation Analysis analyzed the relationships between numerical variables since the parametric test condition was not met. Pearson's chi-square test is used to discover if there is a relationship between two categorical variables. Comparisons of numerical variables in two independent groups were made using the Mann Whitney U test since the normal distribution condition was not met. Statistical alpha significance was accepted as $p < 0.05$. The study was conducted in accordance to the principles of the Helsinki Declaration. The study received ethics approval from the Zonguldak Bülent Ecevit University Ethics Committee and informed written consent was obtained from all study participants.

RESULTS

Participants with impaired thyroid function tests all had TSH values below the normal reference intervals for the first and second trimesters. Mean age was 27.88 in participants with normal TFT and 28.80 in patients with abnormal TFT. Mean gravidae was 1.80 ± 0.78 in those with normal TFT and 1.68 ± 0.74 in patients with abnormal TFT. Mean parity was 0.62 ± 0.53 in those with nor-

mal TFT and 0.50 ± 0.614 in patients with abnormal TFT. There was no statistically significant difference between the groups according to mean age, and gravidae and parity numbers (Table I).

groups. According to Beck Anxiety Inventory scores, patients with abnormal TFT tended to be more anxious compared to those with normal TFT, and this finding was statistically significant ($p < 0.1$), (Table III).

Table I. General Characteristics of the Pregnant Women

	Normal Thyroid Function Tests		Abnormal Thyroid Function Tests		P value
	Mean \pm sd	Min-Max	Mean \pm sd	Min-Max	
Age	27.88 \pm 3.98	19-38	28.80 \pm 3.82	19-38	0.241
Parity	0.62 \pm 0.53	0-2	0.50 \pm 0.614	0-2	0.195
Gravida	1.80 \pm 0.78	1-4	1.68 \pm 0.74	1-3	0.451
	Number	%	Number	%	P value
Smoking	Yes	6	12	3	0.295
	No	44	88	47	
Comorbidity	Yes	3	6	5	0.461
	No	47	94	45	
Educational Status	Elementary	3	6	2	0.211
	Middle School	6	12	2	
	High School	26	52	21	
	Graduate	7	14	15	
Miscarriage History	Bachelor	8	16	10	-
	No	46	92	46	
Abortion History	One	4	8	4	-
	No	45	90	45	
Social Security	One Social security institution	5	10	5	0.372
	Green Card	42	84	45	
		8	16	5	

A total of 58% of participants with normal TFT and 56% with abnormal TFT had normal Beck Depression Inventory scores and this difference was not statistically significant ($p > 0.05$). Similarly, there was no difference between the groups according to patients with mild and moderate depression scores.

According to Beck Anxiety Inventory scores, there is a statistically significant difference between patients with abnormal TFT and those with normal TFT ($p < 0.05$), (Table II). If we combine Normal and Mild in one category, and compare these groups as "Normal / Mild and Moderate" we find a statistically significant difference. Because, according to the BECK scale, there is no significant difference between few and absent, but the main difference is between moderate and the other two

According to the correlation between data of the patient group with abnormal TFT, there was a statistically negative correlation of moderate strength between Beck depression inventory and Beck anxiety inventory scores (Spearman's $\rho = -0.403$; $p = 0.004$). There was a weak negative correlation between Beck depression inventory score and social security status (Spearman's $\rho = -0.287$; $p = 0.043$). In other words, not having social security increases depression. In addition, there was a weak positive correlation between Beck depression inventory score and miscarriage history (Spearman's $\rho = 0.287$; $p = 0.043$). That is to say, in patients with high depression scores, there is increased rate of previous miscarriage. The positive correlations between comorbidity and history of miscarriage and abortion was also statis-

tically significant ($\rho=0.333$, $p=0.018$; $\rho=0.639$, $p=0.00$, respectively), (Table III).

Table II. Number and Percentage According to Beck Inventory in Patients with Normal and Abnormal Thyroid Function Tests

		Normal Thyroid Function Tests		Abnormal Thyroid Function Tests		P value
		Number	%	Number	%	
Beck Depression Inventory	Normal	29	58	28	56	0.761
	Mild	18	36	17	34	
	Moderate	3	6	5	10	
Beck Anxiety Inventory	None	14	28	29	58	<0.001
	Mild	32	64	11	22	
	Moderate	4	8	10	20	

Table III. Number and Percentage of Normal/Mild, Moderate groups according to Beck Inventory in Patients with Normal and Abnormal Thyroid Function Tests

		Normal Thyroid Function Tests		Abnormal Thyroid Function Tests		P value
		Number	%	Number	%	
Beck Depression Inventory	Normal / Mild	47	94	45	90	0.461
	Moderate	3	6	5	10	
Beck Anxiety Inventory	Normal / Mild	46	92	40	80	<0.084*
	Moderate	4	8	10	20	

Table IV. Correlation of Data in Patients with Altered TFT

Spearman's rho		Beck depression inventory	Beck anxiety inventory	Smoking	Comorbidity	Educational status	Social security	Miscarriage history	Abortion history	Age
Beck depression inventory	Rho	1.000	-.403**	-.003	.170	.168	-.287*	.287*	-.069	-.151
	P		.004	.982	.239	.243	.043	.043	.633	.295
Beck anxiety inventory	Rho	-.403**	1.000	.076	-.203	-.173	.094	-.044	-.225	.094
	P	.004		.601	.157	.230	.517	.760	.117	.516
Smoking	Rho	-.003	.076	1.000	-.084	.155	.084	-.0084	.236	.404**
	P	.982	.601		.561	.284	.561	.561	.099	.004
Comorbidity	Rho	.170	-.203	-.084	1.000	0.256	.111	.333*	.639**	-.487**
	P	.239	.157	.561		.072	.442	.018	.000	.000
Education	Rho	.168	-.173	.155	0.256	1.000	-.389**	.020	.290*	0.104
	P	.243	.230	.284	.072		.005	.893	.041	.469
Social security	Rho	-.287*	.094	.084	.111	-.389**	1.000	.111	.098	-.204
	P	.043	.517	.561	.442	.005		.442	.497	.155
Miscarriage history	Rho	.287*	-.044	0.084	.333*	.020	.111	1.000	.147	-.378**
	P	.043	.760	.561	.018	.893	.442		.307	.007
Abortion history	Rho	-.069	-.225	.236	.639**	.290*	.098	.147	1.000	-0.194
	P	.633	.117	.099	.000	.041	.497	.307		.175
Age	Rho	-.151	.094	.404*	-.487**	0.104	-.204	-.378**	-0.194	1.000
	P	.295	.516	.004	.000	.469	.155	.007	.175	

*. Correlation is significant at 0.05

**.. Correlation is significant at 0.01

DISCUSSION

Hyperemesis gravidarum is a condition more commonly seen in early weeks of pregnancy and affects about 2% of pregnant women (14). Hyperthyroidism may be observed in 66% of these women (15). Transient hyperthyroidism is caused by increased hCG hormone in the early weeks of pregnancy and binding of hCG to TSH receptors due to similarity of hCG to the alpha subunits of TSH. As a result, transient increase in thyroid hormones may lead to irritability, insomnia, restlessness, and continuous anxiety and the patient's affect may differ depending on the disease. Hyperthyroidism seen in hyperemesis gravidarum patients is separated from autoimmune hyperthyroidism by lack of antithyroid antibodies (16). Until now, many studies have investigated the relationship between thyroid function and disease in pregnant women with hyperemesis gravidarum and have found elevated thyroid hormones at various levels (17). Psychological conditions are also known to be among the causes of hyperemesis gravidarum. Knowing how psychological factors in etiology change with different thyroid dysfunction is important for disease management, treatment planning, and care services. When studies on the subject are examined, it is seen that they have mostly studied hyperemesis gravidarum in pregnant women as a whole. In other words, there is no study that has evaluated emotional states of hyperemesis gravidarum patients according to groups depending on thyroid functions. We believe our study is the first to implement this grouping, in a national sense. In this context, Şimşek et al. compared emotional states of pregnant women with and without diagnosis of hyperemesis gravidarum and found that pregnant women diagnosed with hyperemesis gravidarum had greater tendency towards depression and anxiety (18). In another study without grouping, Hızlı et al. reported that pregnant women with hyperemesis gravidarum were more prone to depression compared to pregnant women without nausea and vomiting (19). Similarly, Swallow et al. indicated that emotional states and potential psychological factors could show various fluctuation according to nausea and vomiting in pregnant women and that the condition was important in terms of depression and anxiety disorders (20).

Öz et al. emphasized the benefit of knowing emotional states and psychological symptoms of hyperemesis gravidarum patients and its importance for treatment of disease, and that pregnant women diagnosed with hyperemesis gravidarum were more irritable, obsessive, and depressive compared to healthy pregnant women. They used SCL-90 test to determine emotional symptoms (21). In our study, we used the Beck depression and Beck anxiety inventories. As the aforementioned study also screened emotional states other than depression and anxiety, it may have been more detailed in terms of psychological factor screening, however, it also did not group patients according to thyroid function tests.

Uğuz et al. also investigated hyperemesis gravidarum diagnosed patients, also without grouping, and found that they were more anxious compared to the control group consisting of pregnant women without nausea and vomiting (22). Simpson et al. determined that pregnant women diagnosed with hyperemesis gravidarum

were more prone to hypochondriasis (23).

Annagüret al. attributed the onset of most psychological symptoms that could be considered pathological to the pregestational period. They also demonstrated that pregnant women diagnosed with hyperemesis gravidarum may have more psychiatric pathologies compared to healthy people (24).

CONCLUSION

While there was no difference between hyperemesis gravidarum patients with and without normal thyroid function tests in terms of depression, hyperemesis gravidarum patients with abnormal thyroid function test results had more anxiety compared to those with normal thyroid function test results. Knowing how psychological factors change in thyroid dysfunctions will be useful for the management of the disease and treatment planning in patients with hyperemesis gravidarum. In such cases, patients with hyperemesis gravidarum with abnormal thyroid function tests may be asked for a psychiatric opinion to reduce anxiety.

Limitations of the study: Although the sample size of the study was sufficient, the fact that this study was conducted from a single center created a limitation in the study.

Conflict of Interest

The authors declare that they have no conflict of interest

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