

Hyperemesis Gravidarum is Associated with Childhood Trauma, Depression, Trait Anxiety, and Somatization: a Case- Control Study

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ABSTRACT

Hyperemesis gravidarum is associated with childhood trauma, depression, trait anxiety, and somatization: a case-control study

Objective: Hyperemesis gravidarum (HG) is a disease characterized by severe nausea and vomiting; it is the most common cause of hospitalization in the first months of pregnancy. The effects of childhood trauma, anxiety types, and exaggeration of somatic sensations on HG have not been defined. In this study, it was aimed to investigate the relationship between HG and factors including depression, anxiety, childhood abuse, and exaggeration of physical sensations.

Method: Forty-five pregnant women diagnosed with HG and 45 healthy pregnant women were included in the study. Socio-demographic data form, Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), Somatosensory Amplification Scale (SSAS), Childhood Trauma Questionnaire (CTQ), and Pregnancy Unique Quantification of Emesis (PUQE) scales were administered to the participants in the study.

Results: No significant differences were observed between the groups in relation to socio-demographic data except income levels. The income level of the patient group was lower than that of the control group. Compared to the control group, scores for PUQE ($p<0.01$), BDI ($p<0.01$), Trait Anxiety Scale (TAI) ($p<0.05$), SSAS ($p<0.05$), and CTQ ($p<0.001$) were found to be significantly higher in the patient group. According to correlation analysis, while a relation was detected between PUQE scale results and CTQ, BDI, SSAS, and TAI results, no relation was found with the State Anxiety Inventory (SA).

Conclusion: In this study, a history of childhood trauma, depression, exaggeration of somatic sensations, and trait anxiety were found to be more common in individuals with HG. In addition, these factors were also found to be associated with the severity of nausea and vomiting.

Keywords: Anxiety, childhood trauma, depression, Hyperemesis Gravidarum, pregnancy

ÖZ

Hiperemezis gravidarum çocukluk travmaları, depresyon, sürekli kaygı ve somatizasyonla ilişkilidir: Vaka kontrol çalışması

Amaç: Hiperemezis gravidarum (HG) şiddetli bulantı-kusma ile seyreden bir hastalıktır, gebeliğin ilk aylarındaki hastane yatışlarının en sık nedenlerindendir. Çocukluktaki örselenmelerin, anksiyete türlerinin, bedensel duyuşları abartma özelliğinin HG üzerine etkisi bilinmemektedir. Bu çalışmada HG ile depresyon, anksiyete, çocukluk çağrı örselenmeleri ve bedensel duyuşlarını abartma ilişkisinin araştırılması amaçlanmıştır.

Yöntem: Çalışmaya HG tanısı konulmuş 45 gebe ile kontrol grubunu oluşturan 45 sağlıklı gebe alınmıştır. Çalışmaya alınan kişilere sosyodemografik veri formu, Beck Depresyon Ölçeği (BDÖ), Durumluksürekli kaygı ölçeği (DSKÖ), Bedensel Duyumları Abartma Ölçeği (BDAÖ), Çocukluk Çağı Travmaları Ölçeği (ÇÇTO), Gebelik Bulantı Kusma Ölçeği (GBKÖ) uygulanmıştır.

Bulgular: Gelir düzeyleri arasındaki sosyodemografik veriler karşılaştırıldığında gruplar arasında anlamlı farklılık görülmemiştir. Hasta grubunun gelir düzeyi kontrol grubuna göre daha düşüktür. Hasta grubunda kontrol grubuna göre GBKÖ ($p<0.01$); BDÖ ($p<0.01$); Sürekli Kaygı Ölçeği (SKÖ) ($p<0.05$); BDAÖ ($p<0.05$); ÇÇTO ($p<0.001$) anlamlı olarak yüksek bulunmuştur. Korelasyon analizine göre hasta grubu katılımcılarının GBKÖ skorları ile ÇÇTO, BDÖ, BDAÖ, SKÖ puanları arasında ilişkili tespit edilirken, DKÖ arasında ilişkili tespit edilememiştir.

Sonuç: Bu çalışmada HG olanların çocukluk çağrı travmaları, depresyonları, bedensel duyuşlarını abartmaları, sürekli kaygıları kontrol grubuna göre daha fazladır ve ayrıca bulantı ve kusmanın şiddeti ile ilişkili bulunmuştur.

Anahtar kelimeler: Anksiyete, çocukluk çağrı travması, depresyon, gebelik, Hiperemezis Gravidarum

How to cite this article: Kivrak Y, Yagci I, Pasaoglu-Yagci H, Tasdelen Y, Asoglu M. Hyperemesis gravidarum is associated with childhood trauma, depression, trait anxiety, and somatization: a case-control study. Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2018;31:177-186.
<https://doi.org/10.5350/DAJPN2018310205>

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Date of receipt / Geliş tarihi:
November 3, 2017 / 3 Kasım 2017

Date of the first revision letter /
İlk düzeltme öneri tarihi:
December 12, 2017 / 12 Aralık 2017

Date of acceptance / Kabul tarihi:
February 5, 2018 / 5 Şubat 2018

The study was presented orally at the 52nd National Psychiatry Congress (November 16-20, 2016, Antalya, Turkey).

INTRODUCTION

Nausea and vomiting occur in about 50-80% of pregnant women in the first trimester (1). Hyperemesis gravidarum (HG), which is one of the most common causes of hospitalization in the first months of pregnancy is characterised by severe nausea and vomiting (1). The clinical picture in HG may be as severe as to cause weight loss accompanied by dehydration, ketosis, electrolyte and acid-base imbalance, and sometimes hepatic and renal insufficiency (1). The clinical manifestations of HG typically begin between the fourth and tenth week of gestation, usually ending before the 20th week of gestation (1). Its incidence is around 0.5% (1). The negative effects of nausea and vomiting manifest not only during pregnancy but may also continue after delivery. HG, which affects the quality of life of women significantly, has social as well as individual costs due to its effects on the health economy (2).

The etiopathogenesis of HG has not been clarified. Mostly, hormones associated with pregnancy are held responsible for the condition. In addition to these endocrinological hypotheses, infectious, immunological, psychological, metabolic, and anatomic factors have been indicated; however, the data obtained from all studies conducted to date are far from elucidating its etiopathogenesis (1). HG is regarded as a complex psychosomatic disease resulting from biological, psychological, and sociocultural factors (3). The question of whether HG causes psychiatric impairment or psychiatric disorders has attracted the attention of many researchers. The prevalence of HG was also found to be higher in patients with psychiatric disorders such as major depression, generalized anxiety disorder, avoidant personality disorder, or obsessive-compulsive personality disorder (4). Psychiatric disorders occur more frequently in pregnant women with HG than in healthy pregnant women (4,5). Although there are studies indicating that HG is associated with various mental problems, there are also studies that do not show any association (1). Therefore, this issue has not been explained completely.

It is known that traumatic events occurring during

childhood not only affect childhood itself, but also cause mental and physical problems in adulthood. Anxiety is generally accepted as a symptom that may coexist with many physical and mental diseases and affect their courses. Though there are studies on anxiety in pregnant women with HG, it is not known whether this is state or trait anxiety. Somatization is considered to be a somatic response emerging from mental and social problems (6). Although the importance of childhood traumas, type of anxiety, and somatosensory amplification were stated by numerous researchers, we have not been able to find any study investigating the association of state and trait persistent anxiety, somatosensory amplification, and childhood trauma in pregnant women with HG or the association of those factors with the severity of nausea and vomiting.

We planned to conduct this study in order to fill a gap in the literature as well as to find an answer to the question whether there is a relationship between nausea and vomiting in HG and anxiety, somatosensory amplification, or childhood traumas.

METHOD

The study was a clinical observational study of case-control type. For our study, approval dated 09/10/2013 with decision number 2013/19 was obtained from the Ethics Committee of Kafkas University Faculty of Medicine.

Research was carried out in the units affiliated to the Department of Psychiatry and Department of Obstetrics and Gynecology of Kafkas University Faculty of Medicine. A preliminary study was conducted before enrolling the participants. The questionnaire prepared was administered to pregnant women who had been admitted to the gynecology and obstetrics outpatient clinic for examination. Afterwards, the final form was created. With a standard deviation of 5.4, the effect size of 3-point difference was determined to be 0.6. The smallest sample size was found to be 72, including 36 control and 36 subjects for $\alpha=0.05$ and a power of 80%. Considering that there may be missing and incorrect completions of the forms, the study was planned with

100 pregnant women, including 50 pregnant women with HG and 50 controls.

The patient group included 50 pregnant women, who were selected randomly from patients diagnosed with HG by the gynecology and obstetrics specialist as a result of physical examination and laboratory investigations (Beta hCG, free T3, free T4, thyroid stimulating hormone (TSH), estradiol, progesterone, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl-transferase (GGT), lactate dehydrogenase, alkaline phosphatase, total bilirubin, glucose levels, complete blood count, and complete urine analysis) and who volunteered to participate in the study. The control group included 50 randomly selected healthy pregnant women. Before beginning the study, aim and method were explained to the participants. Oral and written consent were obtained from the participants, who were then called to the psychiatric examination room. After we filled in the scales to be completed by the psychiatrist, the participants were asked to complete the scales that needed to be filled in by them.

For the patient group, inclusion criteria were determined as an HG diagnosis having been established and the absence of any other examination and laboratory findings that would explain this diagnosis. For the control group, inclusion criteria were determined as being in the same gestational week as the HG patients and no detection of any remarkable pathology in the examination and laboratory findings.

As exclusion criteria for the study, we determined the refusal to participate after being informed and the presence of clinically detected mental retardation and illiteracy.

Measures

Sociodemographic and Clinical Information Form:

The sociodemographic and clinical information form prepared by the researchers was used to assess the participants' sociodemographic and clinical characteristics. This form included multiple-choice and open-ended questions asking about the

participant's age, marital status, husband's age, place of birth, place of residence, occupation, monthly income, family monthly income, educational status, parents' educational status, the family type in which she was born and had grown up, any history of psychiatric disease, smoking and alcohol consumption, history of comorbid diseases, number of children, family type, gestational week, and history of HG.

Beck Depression Inventory (BDI): This is a self-rating scale developed by Beck used to measure emotional, somatic, cognitive, and motivational symptoms occurring in depression (7). A validity and reliability study for the Turkish version of the scale was conducted (8).

State and Trait Anxiety Inventory (STAI): This was developed by Spielberger et al. (9) in 1970 with the aim of determining state and trait anxiety levels separately. The State Anxiety Inventory (SAI) is a relatively sensitive tool for assessing suddenly changing emotional reactions. The Trait Anxiety Scale (TAI), which is composed of 20 items in the second part of the instrument, aims to measure the continuity of anxiety that the person has a tendency to experience in general. The total score obtained from both scales varies between 20-80. A high score indicates a high anxiety level, low score low anxiety level (10). The validity and reliability of the Turkish version of the scale was tested by Oner and LeCompte (10).

Somatosensory Amplification Scale (SSAS): This is a scale investigating somatosensory amplification. It was developed by Barsky et al. (11) in order to explain somatization. Its Turkish reliability study was conducted by Gulec et al. (12).

Childhood Trauma Questionnaire (CTQ): In the present study, the Childhood Trauma Questionnaire (CTQ) was used to assess abuse and neglect experiences before the age of 20 years retrospectively and quantitatively. This scale, which was developed by Bernstein et al. (13), is composed of 28 questions. The Turkish validity and reliability study

of the scale was conducted by Sar et al. (14). The scale in respect to childhood abuse encompasses five sub-domains including sexual, physical, emotional abuse and emotional and physical neglect (13).

Pregnancy-Unique Quantification of Emesis (PUQE): Scoring tests have been developed to perform an objective clinical assessment in patients with nausea and vomiting. Of these tests, the Rhodes

Table 1: Sociodemographic characteristics of the hyperemesis gravidarum and the control groups

	HG (n=45)		Control (n=45)		χ^2	p
	Mean	SD	Mean	SD	0.409	0.68
Age	27.530	4.727	27.930	4.550	0.409	0.68
	n		n			
Occupation status						
Employed	11		16		1.323	0.25
Unemployed	34		39			
Spouse's occupation						
Employed	43		44		0.345	0.55
Unemployed	2		1			
Monthly income						
Less than 1500TL	28		17		5.378	0.02
More than 1500TL	17		28			
Education status						
Less than secondary school	10		6		1.216	0.27
More than secondary school	35		39			
Birth place						
City	13		17		1.252	0.53
Town	11		12			
Village	21		16			
Residence						
City	28		34		3.924	0.14
Town	11		4			
Village	6		7			
Premarital family type						
Nuclear family	34		38		1.111	0.29
Extended family	11		7			
Paternal education						
Secondary school and less	28		23		1.131	0.28
More than secondary school	17		22			
Maternal education						
Secondary school and less	36		34		0.257	0.61
More than secondary school	9		11			
Family income						
Less than 1500TL	19		16		0.421	0.51
More than 1500TL	26		29			
Family type						
Nuclear family	38		38		0	1
Extended family	7		7			
Intended pregnancy						
Yes	40		43		1.394	0.23
No	5		2			
HG history						
Yes	8		2		4.050	0.04
No	37		3			

p<0.05, SD: Standard deviation, χ^2 : Chi-square; HG: Hyperemesis gravidarum

test, which was originally developed for the assessment of nausea and vomiting associated with chemotherapy, has subsequently also been used for the assessment of nausea and vomiting associated with pregnancy (15). Although this test was considered as the gold standard, it was regarded as not very useful since it included too many questions. PUQE, which is one of the tests with more simple questions, using the Rhodes scoring system, was found to be as valuable and sensitive as the Rhodes test (16). The PUQE asks about the number of nausea episodes, vomiting, and retching. There was consistency between the results of the PUQE and Rhodes tests (16).

Statistical Analysis

Statistical Package for the Social Sciences version (SPSS) 20 was used for the assessment of the data obtained from the participants. Following the descriptive statistical analysis (frequency, percentage distribution, mean±standard deviation), independent groups t-test was used for assessing the difference between each two groups in the case of continuous variables, while the chi-square test was used for categorical variables. Since the number of samples was sufficient, the coefficient of variation was not high, the sample met the criteria for normal distribution, and the homogeneity condition was provided by the Levene Test, independent groups t-test was used for comparison of the means between the groups, and Pearson correlation test was used for investigating the relationship between the variables. When the homogeneity was not met, the differences between groups were examined by the

Mann-Whitney U test. Regression analysis was performed to evaluate prediction of the dependent variable by the independent variable. Stepwise input method was selected for regression analysis. The statistical significance level for the results was accepted as $p<0.05$.

RESULTS

Since six people did not accept to participate in the study and four people filled in the form incompletely, the data of 90 people including 45 patients and 45 controls were included in the evaluation. The age range of the patient group varied between 21-38 years, while the age range of the control group was between 20-39 years. The mean age of the HG group was found to be 27.530 ± 4.727 years while the mean age of the control group was 27.930 ± 4.550 years ($p>0.05$) (Table 1). All women in the patient as well as the control group were married. Comparing the HG group with the control group, no difference was detected in terms of employment status, level of education, place of birth, place of residence, the family type in which she had grown up, education of father, education of mother, income of the family in which she lived, family type, desiring pregnancy, or SAI (43.26 ± 7.40 , 43.40 ± 5.16 , $p>0.05$), whereas a difference was noted in terms of income status, presence of HG in the previous pregnancies, and BDI (17.130 ± 8.628 , 7.640 ± 4.440 , $p<0.01$), TAI (45.40 ± 5.16 , 41.73 ± 4.95 , $p=0.011$), SSAS (36.57 ± 7.67 , 30.31 ± 6.35 , $p=0.04$), CTQ (41.80 ± 10.77 , 34.86 ± 4.00 , $p=0.028$), PUQE (12.380 ± 1.319 , 5.020 ± 1.740 , $p<0.01$) (Table 2).

Table 2: Comparison of BDI, SAI, SSAS, CTQ, TAI results between HG and control groups

	HG		Control		t	p
	Mean	SD	Mean	SD		
BDI	17.13	8.62	7.64	4.44	6.558	<0.001
SAI	43.26	7.40	43.40	5.16	2.614	0.921
TAI	45.40	5.16	41.73	4.95	-0.99	0.011
SSAS	36.57	7.67	30.31	6.35	2.873	0.04
CTQ	41.80	10.77	34.86	4.01	4.058	0.028

SD: Standard deviation, HG: Hyperemesis gravidarum, BDI: Beck Depression Inventory, SAI: State Anxiety Inventory, TAI: Trait Anxiety Inventory, SSAS: Somatosensory Amplification Scale, CTQ: Childhood Trauma Questionnaire

Table 3: Correlation between PUQE and BDI, SAI, TAI, SSAS, CTQ in the patient group

	PUQE	
	r	p
BDI	0.58	<0.001
SSAS	0.34	0.001
TAI	-0.27	0.798
SAI	0.27	0.008
CTQ	-0.30	0.004

r value of p<0.01 significance, PUQE: Pregnancy-Unique Quantification of Emesis and Nausea Scale, BDI: Beck Depression Inventory, SAI: State Anxiety Inventory, TAI: Trait Anxiety Inventory, SSAS: Somatosensory Amplification Scale, CTQ: Childhood Trauma Questionnaire

In the correlation analysis, the score of PUQE did not show a correlation with the score of CTQ ($r=-0.27$, $p>0.05$), but it showed a correlation with CTQ ($r=-0.30$, $p<0.01$), TAI ($r=0.27$, $p<0.01$), SSAS ($r=0.34$, $p<0.01$), and BDI ($r=0.58$, $p<0.01$) (Table 3).

Linear regression analysis was performed to evaluate the variables predicting nausea and vomiting. SAI, TAI, BDI, SSAS, CTQ, and gestational age were taken as independent variables. In the first stage of the stepwise multiple regression model, at first the BDI scores were entered and explained 34% of the variance $F(1.88)=45.87$, $p<0.001$. In the second stage, when the gestational age was entered $F(1.87)=6.43$, $p=0.013$, it explained 39% of the variance, and in the third stage, when the CTQ scale score was entered, it was observed to explain 42% of the variance $F(1.86)=4.33$, $p=0.04$. According to the standardized regression coefficients, the significance order of the predictive values on gestational vomiting was as follows: depression, gestational age, childhood traumas. According to the

multiple regression analysis performed, the equation $Y = 5.8 + ([0.25 \times BDI] + [-0.36 \times \text{gestational age}] + [0.08 \times CTQ])$ resulted (Table 4).

DISCUSSION

The results of our study showed that the scores of depression, somatosensory amplification, childhood trauma, and trait anxiety of pregnant women with HG were both higher and were associated with the severity of nausea and vomiting compared to those without this disease. Also, depression, gestational age, and childhood traumas are predictors of hyperemesis gravidarum.

It was demonstrated that there may be a relationship between the severity of HG and the severity of anxiety and depression symptoms (17,18). However, while anxiety was reported to be higher in these studies, the type of anxiety was not stated. In our study, the difference was found to arise from state anxiety rather than trait anxiety. Also, our study showed that the severity of HG was associated not only with depression and anxiety but also with somatosensory amplification and childhood trauma.

Childhood traumas are not only associated with the severity of the disease in patients with HG, but also with certain somatic disorders such as chronic pain and post-traumatic stress disorder, eating disorders, somatization disorder, depression-anxiety disorders, cardiovascular diseases, and substance dependence (19). Childhood traumas affect women's quality of life negatively as well (20). Suicidal-depressive symptoms and somatic complaints in pregnancy have been associated with

Table 4: Regression results on the prediction of pregnancy nausea vomiting

	B Coefficient	SE	B	p	F	R ²
Model 1						
BDI	0.28	0.042	0.59	<0.001	45.83	0.34
Model 2						
BDI	0.28	0.04	0.59	<0.001	27.54	0.39
Gestational age	-0.39	0.15	-0.21	0.013*		
Model 3						
BDI	0.25	0.04	0.53	<0.001	20.50	0.42
Gestational age	-0.36	0.15	-0.20	0.017*		
CTQ	0.08	0.04	0.18	0.040*		

SE: Standard error, B: Beta, BDI: Beck Depression Inventory, CTQ: Childhood Trauma Questionnaire, *p<0.05

childhood traumas (21), but this relationship has not been determined clearly. It is thought that there may be various underlying mechanisms. Regarding the assumed first mechanism, it is argued that demographic factors such as nicotine/substance addictions, marital status, education levels, and working conditions may be associated with gestational health problems in individuals who experienced these adverse life events (22). For the assumed second mechanism, it is argued that exposure to adverse experiences early in life, such as being abused as a child, may cause early stimulation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to hyperactivity of the corticotropin-releasing hormone (CRH), facilitating the development of the disease (23). The HPA axis coordinates many basic physiological functions and the stress response of the body (24). In addition, animal and human studies demonstrate that early traumas lead to epigenetic changes in genes that regulate the stress response (25). Although epigenetic changes often occur during fertilization and fetal development, DNA methylation can develop associated with several factors including toxins, environmental conditions, stress in life, and with the nutritional status of infants, children, and adults (25). Eventually, these changes can be passed on to future generations. Investigators conducting studies on postmortem brain tissues of suicide victims have observed that individuals reporting abuse in their childhood periods have higher rates of DNA methylation in their glucocorticoid receptor promoter regions. In addition, they observed reduced glucocorticoid receptor gene activity in the hippocampus of individuals without any history of childhood abuse (25). These studies demonstrate that stressor factors can be detrimental to the development of the central nervous system and can affect the structures, biochemistry, and function of the brain, leading to adverse consequences. We could not find any study evaluating childhood traumas in patients with HG in our search. Considering that psychopathologies in adulthood are more common in individuals with childhood traumas, it can be suggested that HG can be more common in these individuals.

When the rate of desiring pregnancy was taken into consideration, 88.9% of pregnant women with HG and 95.6% of those in the control group had desired the pregnancy. No statistically significant difference was found between the two groups in terms of desiring pregnancy. It has been shown that women who experienced severe nausea-vomiting during pregnancy had less-desired pregnancy than those who did not experience severe nausea-vomiting (26). This finding is inconsistent with the literature. According to the findings of this study, reluctance towards pregnancy may not be an important factor in the development of HG, or the role of pregnancy in HG may vary according to the culture. Special attention is given to being fertile in the culture of our region, while, again according to regional culture, women who do not have children are stigmatized as "infertile," and every woman who does not have any children considers herself as being defective. Furthermore, studies conducted in Turkey demonstrated that women who did not have children tended to have more psychiatric diseases compared to those with children (27). Conducting further studies may be beneficial for elucidating this issue.

Another aspect that attracts the attention of researchers is the relationship between employment of women and HG. Weigel et al. (28) showed an increased risk in housewives, and similarly, Kallen et al. (29) detected lower rates of nausea and vomiting in women who worked outside the home compared to those working at home. We did not find any significant difference in terms of employment status between the two groups. The inconsistency with the literature might be a result of the insufficiently developed industry in our region. The share of agriculture and livestock production is great in the economy of our region. Women working in the fields and with livestock in rural areas might have considered themselves as non-employed since they did not work for a salary.

The mean score of SSAS for patients was found to be higher than that of the control group. Studies on somatization in HG patients are limited. Pirimoglu et al. (3) found the somatization scores higher in the HG group compared to healthy pregnant women. However, Swallow et al. (30) detected that

nausea and vomiting in the early pregnancy period were associated with psychiatric problems and the severity of nausea and vomiting was associated with somatic symptoms. Somatization is defined as the expression of underlying psychiatric, psychological, or social complaints through somatic complaints that cannot be explained medically (31). Even though the exact cause of somatization is not known, there are some ideas suggesting that somatosensory amplification plays a role in its process (11). In this study, in line with previous work, it was found that somatosensory amplification might also have played a role in HG.

No difference was detected in terms of mean SAI score between the HG and control group, whereas the mean TAI score was found to be higher in the HG group. It is known that anxiety scores are higher in patients with HG (5). The cause of high trait anxiety levels in the patient group might be related to the fact that the symptoms are continuous, that they lead to dysfunction in social and work life and as a result of these, anxiety about the future for herself and her baby emerges.

Our study had certain limitations. One of these was that the sample group included only cases that had been admitted to a University Hospital. However, a university is a tertiary health care institution that also receives patients from many surrounding cities, which might decrease the significance of this limitation. Although there have been studies conducted with a lower number of cases, the low number of cases in the patient and control group in our study may be regarded as another limitation. Considering that α was 0.05 and the power was 80%, our sample size may be regarded as adequate. Still, larger samples may be considered to increase the power of the study. It is difficult to establish the cause-and-effect relationship since our study was cross-sectional. Conducting prospective controlled trials including pre-pregnancy, pregnancy, and postpartum period may reveal the role of psychiatric causes in HG more clearly. Although the validity and reliability of the scales that we used had been shown both for the original and the Turkish versions, the fact that they were not specific for HG may be considered as a limitation. However, the scales that we used have been used frequently for HG patients as well as in other physical and mental diseases.

In conclusion, this is the first study indicating that depression, gestational age, and childhood traumas are predictor variables of HG. It is also the first study that demonstrate demonstrate childhood traumas, somatosensory amplification, and depression might be associated with the severity of HG. The results of this study may be beneficial in two fields. First of all, they may help clinicians while following a patient with HG. HG is usually followed up by primary care physicians and gynecology and obstetrics specialists. Knowing the predictor variables of hyperemesis may contribute to an appreciation of the severity of HG and the importance of a psychiatric approach in the treatment by clinicians. Secondly, our study may help researchers working in the fields of psychiatry and obstetrics and gynecology. Knowing the predictors of hyperemesis may open the way for researchers investigating the common biochemistry and neuroimaging findings related to this issue. In our study, we could not identify the causal relationship and could not clarify whether the results of our study are valid for every culture. Studies conducted prospectively in many different regions and cultures may contribute to elucidating the etiology of HG.

Contribution Categories		Author Initials
Category 1	Concept/Design	I.Y., Y.K., H.P.Y.
	Data acquisition	I.Y., H.P.Y.
	Data analysis/Interpretation	I.Y., Y.K., M.A., Y.T.
Category 2	Drafting manuscript	I.Y.
	Critical revision of manuscript	I.Y., Y.K., Y.T., M.A., H.P.Y.
Category 3	Final approval and accountability	I.Y., Y.K., H.P.Y., M.A., Y.T.
Other	Technical or material support	N/A
	Supervision	N/A
	Securing funding (if applicable)	N/A

Informed Consent: Written consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: This study was supported by the Kafkas University Directorate of Scientific Research Projects (project no: 2015-TS-43).

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