Effect of Nausea and Vomiting on Anxiety and Depression Levels in Early Pregnancy

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ABSTRACT

Objective: Nausea and vomiting of pregnancy (NVP) have been reported to be associated with distinct physiological responses to psychosocial stress. In this study, we aimed to evaluate the impact of nausea and vomiting on anxiety and depression during pregnancy.

Materials and Methods: Eighty-three pregnant women with nausea and vomiting and 83 healthy pregnant women were included. All participants completed the demography- and pregnancy-related questionnaire, including Rhodes Index of Nausea and Vomiting, Beck Anxiety Inventory (BAI), and Edinburgh Postnatal Depression Scale (EPDS).

Results: The median BAI and EPDS levels were 13 (min-max: 0–43) and 7 (min-max: 0–20) for the study group and 4 (min-max: 0–26) and 4 (min-max: 0–16) for control group, respectively. A univariate analysis revealed a statistically significant increase in terms of BAI levels (p<0.001) between the groups, but no significant difference was observed in terms of EPDS. In a logistic regression analysis, both anxiety (p=0.018) and depression (p=0.022) were found to be affected by NVP. The BAI levels of the NVP group correlated with the severity of NVP.

Conclusion: According to the results of the present study, women with severe NVP experienced a higher level of anxiety and depression, which necessitates an extra awareness from healthcare professionals in order to be able to contribute effectively.

Keywords: Pregnancy, nausea and vomiting, rhodes index, anxiety, depression

Introduction

Nausea and vomiting during the early stages of pregnancy usually occur between the fifth and eighteenth weeks of pregnancy, and more than 70% of pregnant women have reported the presence of these symptoms extending until parturition [1-4]. Pregnant women with severe nausea and vomiting may have hyperemesis gravidarum (HG), a separate entity from nausea and vomiting of pregnancy (NVP), which if left untreated may lead to increased maternal and fetal morbidity. HG is infrequent when compared with NVP and occurs in 0.3%–2% of all pregnancies [1, 4, 5]. The severity of complaints might vary from one pregnant woman to another and even between pregnancies of the same woman, which suggest the contribution of genetic, biological, and psychological factors.

In addition to the physical condition of pregnancy, NVP and HG also negatively affect the mental health, quality of life, and functional capacity of women [6]. In severe cases, fetal development might also be affected. Although there are still questions regarding the exact cause of both conditions, it does appear to be associated with various metabolic and endocrine factors. In this context, the most implicated factor is suggested to be the production of the human chorionic gonadotropin hormone. Moreover, there is evidence that links this condition to alternation in a variety of hormones, including estrogen, progesterone, placental prostaglandin E2, and thyroid-stimulating hormone [1]. In addition, studies have shown that NVP may also be linked with psychological disturbances, including eating disorders, neurotic tendencies, hysteria, and rejection of pregnancy, as well as anxiety and depression with psychological stress related to poverty and marital conflicts [6, 7]. From these psychological disturbances, anxiety and depression exert a special importance, because apart from being a cause, it can also be a consequence of NVP. Therefore, assessing the

presence and severity of anxiety and depression in patients with NVP may be relatively more important from the general population.

The relationship between NVP, HG, anxiety, and depression has been studied in some trials. Most of the studies focused on NVP and HG found conflicting results with respect to the development of anxiety and depression disorders [7-9]. In addition to these conflicting results, some studies have been criticized for having limitations, including small sample size, lack of control group, lack of objective diagnostic criteria, and inappropriate study design [5, 8, 10, 11]. Hence, the objective of this prospective case-control study was to determine the prevalence and severity of anxiety and depression disorders in patients with NVP using specifically designed and validated tools.

Materials and Methods

Characteristics of the Patients
This prospective case-control study was designed at the Gynecology and Obstetrics clinic of Canakkale Onsekiz Mart University and was approved by the ethics board of the

same institution. The study was conducted with the guideline proposed by the World Medical Association of Helsinki, and written informed consent was obtained from all of the participating women.

For this study, 120 questionnaires were distributed to pregnant women with NVP in early pregnancy. However, 37 questionnaires were excluded because either they did not include enough details or were not eligible for inclusion (Figure 1). The final study group compromised 83 pregnant women with NVP followed up in the obstetrics and gynecology clinic of the same hospital. A control group consisted of 83 age, parity, and gestational age-matched healthy pregnant women without nausea and vomiting and admitted to the outpatient clinic for routine antenatal care. After inclusion, gestational age was determined according to the first day of last menstruation corrected by ultrasound finding when the discrepancy exceeded one week. A detailed sociodemographic data form was given to all subjects. Pregnancy characteristics, age, medication history, tobacco and alcohol use, and educational and familial status were recorded.

Inclusion criteria were a viable pregnancy of less than 14 weeks gestation, lack of fetal congenital malformations, lack of a systemic (gastrointestinal, renal, pulmonary, and cardiovascular system abnormalities) or hormonal disease that can cause nausea and vomiting, absence of diabetes mellitus, absence of previously known psychiatric disorders, and absence of multiple pregnancies and known obstetric complications. Pregnant women using medications (including antidepressant and antipsychotic drugs) that could alter the test results, history of current or past illegal drug abuse, and cognitive incompetence, which can make hard to score The Beck Anxiety Inventory (BAI) were excluded. render scoring challenging. The Beck Anxiety Inventory (BAI) were excluded.

Assessment
The Rhodes index of nausea and vomiting questionnaire was used to evaluate the presence and the severity of NVP. In order to evaluate NVP-associated psychological status two questionnaires, BAI and Edinburgh Postnatal Depression Scale (EPDS), were used.
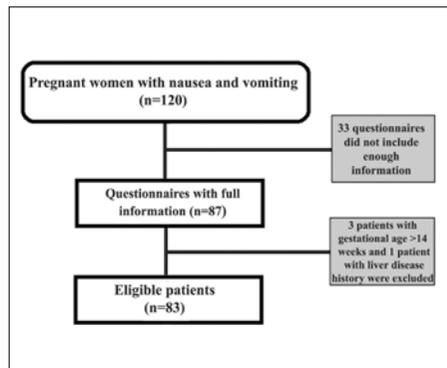

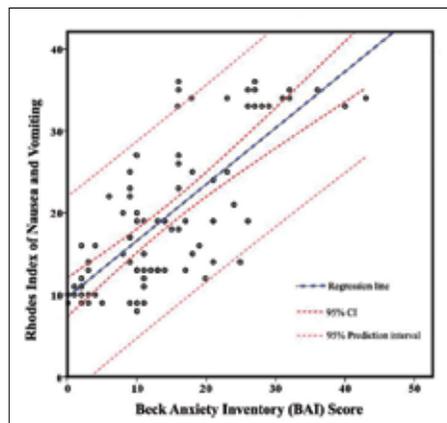**Figure 1.** Flow chart of the recruited participants

Figure 2. Correlation analysis between Rhodes Nausea and Vomiting index and Beck Anxiety Inventory (BAI) scores in NVP patients; lines representing the 95% confidence interval (CI) and the 95% prediction interval of the regression line

Table 1. Sociodemographic characteristics of study participants

	NVP patients (n=83)	Controls (n=83)	P
Age (years)	28.4±5.5	29.4±5.7	NS
Gestational age (weeks)	11.1±2.1	10.9±2.2	NS
BAI [median, (min-max)]	13 (0–43)	4 (0–26)	<0.001
EPDS [median, (min-max)]	7 (0–20)	4 (0–16)	NS
Gravida [median, (min-max)]	2 (1–7)	2 (1–5)	NS
Parity [median, (min-max)]	1 (0–4)	1 (0–3)	NS
Abortus [median, (min-max)]	0 (0–2)	0 (0–3)	NS
Occupation			NS
No (%)	65 (78.3)	59 (71.1)	
Yes (%)	18 (22.7)	24 (28.9)	
Education			NS
Illiterate (%)	5 (6.0)	4 (4.8)	
Primary (%)	22 (26.5)	13 (15.6)	
High (%)	32 (38.5)	36 (43.3)	
University (%)	24 (29.0)	30 (36.3)	
Housing			NS
Owned (%)	42 (50.6)	43 (51.8)	
Rented (%)	41 (49.4)	40 (48.2)	
Cigarette smoking			NS
No (%)	74 (89.1)	70 (84.3)	
Yes (%)	9 (10.9)	13 (15.7)	

BAI: Beck Anxiety Inventory; EPDS: Edinburgh Postnatal Depression Scale; NVP: nausea and vomiting of pregnancy; NS: not significant

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Rhodes index of nausea and vomiting

The Rhodes index of nausea and vomiting questionnaire is a validated and objective form used to grade the presence and severity of nausea and vomiting and to follow the clinical progression of the disorder [12]. Historically, it was proposed by Rhodes and his colleagues in 1984 to evaluate nausea and vomiting in patients with tumoural disease receiving chemotherapy. This scoring system is based on a five-point scale and has a total of eight items capturing nausea, vomiting, and the components (duration, severity, and distress) of each symptom in the preceding 12 hours. A minimum score of eight and a maximum of 40 can be obtained with this scale. Scores below eight are recorded as no nausea and vomiting in the previous 12 hours, scores of 9–18 are recorded as mild, scores of 19–32 are recorded as medium, and scores 33–40 are recorded as severe NVP.

Beck Anxiety Inventory

The BAI is a 21-item self-report questionnaire that lists anxiety symptoms, such as "shakiness in legs," "scared," and "worry of losing control." Patients were asked to rate how much each of these symptoms concerned them in the previous week on a scale ranging from zero (not at all) to three. The total score can range from zero with a maximum of 63 [13]. Based on the total score, 8-15 points represent a mild level of anxiety, 16-25 indicates a medium level, and 26-63 points are an indication of severe anxiety level. The Turkish validity and reliability trial of BAI was performed by Ulusoy and colleagues. [14].

Edinburgh Postnatal Depression Scale

EPDS is a 10-item questionnaire developed to assist in identifying possible symptoms of depression in the postpartum period [15]. Moreover, it has adequate sensitivity and specificity to identify depression symptoms in the antenatal period and is useful in identifying symptoms of anxiety [16]. Although EPDS is not a diagnostic scoring tool, items of the scale refer to distinct clinical depression complaints, such as sleep disorders and weakness. The total evaluation was performed by adding the scores for each of the 10 items. A total score of 13 or more is considered a cut-off point for the possible depression diagnosis.

Statistical Analysis

The Statistical Package for Social Sciences (Version 19, SPSS Inc., Chicago, IL, USA) for Windows software was used to analyze data. Continuous variables were tested for normality using the Kolmogorov–Smirnov test. Student's t-test was used to compare the data that was normally distributed. Data non-normally distributed were compared using the Mann–Whitney U test. Comparison of more than two independent groups was performed by the Kruskal–Wallis test. A Spearman correlation analysis was used to analyze the correlation between the NVP and BAI scores of patients. A p value of<0.005 was used to indicate statistical significance. The factors that affect anxiety and depression status were evaluated using a logistic regression analysis. In both of the analysis, depression and anxiety were considered as dependent variables and age, occupation status, education level, gravidity, and emesis were considered as independent variables. Backward conditional logistic regression was performed for analysis.

Results

In total, 83 women with NVP and 83 pregnant women without symptoms of nausea and vomiting were included in the study. The mean maternal age of study and control groups were 28.4±5.5 and 29.4±5.7 years, respectively. Median gestational age of study participants was 11.1±2.1 weeks and 10.9±2.2 weeks for controls. No statistically significant difference was observed between the study and control groups in terms of maternal and gestational age, gravidity, parity, abortus, occupation, housing, and education levels. Only nine women in the NVP group reported a history of cigarette smoking before pregnancy, which was statistically insignificant between groups. Median BAI and EPDS levels were 13 (0–43) and 7 (0–20) for the study group and 4 (0–26) and 4 (0–16) for the control group, respectively. Although a statistically significant increase in terms of BAI levels (p=<0.001) was observed between the two groups, no significant difference was observed between the groups in terms of EPDS (p=0.654). Table 1 shows sociodemographic characteristics of study participants.

The factors described in the univariate analysis were further examined using a logistic regression analysis, and our results indicated that the only emesis was an independent risk factor for anxiety (p=0.018) and depression (p=0.22; Table 2, 3).

According to the Rhodes scoring system, the study group was divided into three groups. Overall, 41 (49.3%) women were classified as mild, 24 (28.9%) as moderate, and 18 (21.8%) as severe NVP. The median BAI levels of mild, moderate, and severe NVP patients were 9 (0–25), 16 (6–26), and 27 (16–43) respectively. Median EPDS levels of mild, moderate, and severe NVP patients were 4 (0–20), 5 (2–20), and 11 (5–18) respectively. The BAI levels were significantly higher in severe NVP patients compared to mild (p<0.001) and moderate (p<0.001) NVP. Although a trend for increasing EPDS levels was found in moderate and severe NVP, this was not statistically significant (Table 4).

According to the BAI levels, pregnant women (study group and control group) were divided into four groups. In total, 77 women had no anxiety, 48 had mild, 29 had medium, and 12 (10.8%) had severe anxiety. Out of 18 women

Table 2. Logistic regression analysis of factors that effects anxiety levels

	B	OR	95% CI	p
Constant	−1.917	0.147		0.0001
Emesis (0)		1.0		
Emesis (1)	0.851	2.341	1.022–5361	0.018

OR: odds ratio; CI: confidence interval
Note: Backward conditional Logistic Regression analysis (step 5)
Dependent variable: Anxiety (No: 0; Yes: 1)
Independent variables: Age, Education (University: 0, high: 1, illiterate/primary: 2), Occupation (No: 0, Yes: 1), gravidity (>5:0, 3–4:1, 1-2:2); Emesis (No: 0, Yes: 1)

Table 3. Logistic regression analysis of factors that effects depression levels

	B	OR	95% CI	p
Constant	−2.317	0.099		0.0001
Emesis (0)		1.0		
Emesis (1)	1.096	2.993	1.172–7.644	0.022

OR: odds ratio; CI: confidence interval
Note: Backward conditional Logistic Regression analysis (step 5)
Dependent variable: Depression (No: 0; Yes: 1)
Independent variables: Age, Education (University: 0, high: 1, illiterate/primary: 2), Occupation (No: 0, Yes: 1), gravidity (>5:0, 3–4:1, 1-2:2); Emesis (No: 0, Yes: 1)

with severe NVP, 11 (61.1%) had severe anxiety, 5 (27.8%) had medium, and 2 (11.1%) had mild levels of anxiety (Table 5). The correlation analysis revealed a significant correlation between NVP severity and BAI levels (r=0.699; p<0.001; Figure 2).

Discussion

In this study, we demonstrated that women experiencing NVP have elevated anxiety levels, which are correlated with the severity of NVP. Moreover, in the logistic regression analysis, emesis was observed to be an independent variable for anxiety and depression. No correlation was observed between depression scores and NVP grades according to the Rhodes scoring system.

Nausea and vomiting are common medical conditions seen in pregnancy, affecting 70%-80% of all pregnant women [17]. Although women who experience NVP have symptoms usually limited to the first trimester, some women experience these symptoms throughout the pregnancy. HG is a severe form of NVP and an important cause of maternal morbidity during pregnancy affecting 0.4%-3% of pregnancies [18]. HG may result in weight loss; nutritional deficiencies; ketosis; and abnormalities in fluids, electrolyte levels, and acid-base balance. We did not categorize our severe NVP patients as HG because of the lack of some referral criteria, which renders a definitive HG diagnosis difficult.

Psychosocial factors may play a significant role in the progression of psychiatric disorders and NVP progression. Although numerous studies have shown that psychiatric disorder diagnosis is elevated in NVP and HG, some contrary reports suggest that in the course of NVP and/or HG, no elevation exists in terms of psychiatric disorders. In a recent prospective case-control study by Aksoy et al. [19], the mean Beck depression inventory scores were found to be elevated compared with the control group. Authors speculated that psychological disturbances linked with HG were a direct effect rather than a cause of HG. Similarly, in a study by Kender et al. [20], the sociodemographic data showed no difference between HG and control groups, but depression and anxiety levels were found to be elevated in the HG patients. Contrary to these findings, Bozzo et al. [7] reported that there was no significant association between depressive symptoms and NVP probably due to the small size of their study population. Although in the present study, the univariate analysis did not demonstrate any relation between depression and severe NVP, anxiety levels of severe NVP patients were significantly elevated. Moreover, the logistic regression analysis showed that apart from multiple sociodemographic variables, the only independent variable that affected anxiety and depression levels was NVP.

Elevated stress levels, anxiety, or depression linked with pregnancy may be more marked in women suffering from NVP. In this study, we found that according to the Rhodes scoring system, symptoms of anxiety were more prominent among medium and severe NVP cases. Studies from Turkey have also suggested a significant correlation between HG and depression and anxiety. Şimşek et al. [21] demonstrated that women complicated with serious vomiting during their pregnancies had noticeably more anxiety and depression than a well-matched control group of healthy antenatal women. In an elegant article by Annagür and colleagues [22], it was reported that depression and anxiety scores were significantly higher in women with HG and HG appears to be associated with depression and anxiety symptoms rather than deterioration of eating attitudes and body image. In this context, no difference was noted in the present study between NVP grades and sociodemographic factors, including pregnancy characteristics, gestational age, patient age, educational status, smoking, and employment status. Moreover, these factors were not associated with psychiatric symptoms. In a recent article by Kamalak et al. [23], only education level of the pregnant women, monthly income, HG in the previous pregnancy, and short time intervals between pregnancies were found to be related to HG development. In a study by Roseboom et al. [24], it was reported that women with HG were slightly younger, had a lower income, and had more often conceived through assisted reproduction techniques. Contrary to these findings, Tsang et al. [25] reported results similar to the present study, demonstrating that women with HG had demographic characteristics that were comparable to the general obstetric population in terms of age, gravidity, race, and marital status.

This study has some limitations, and the recognition of these should help improve future research efforts. The major limitation of this study is the research design. Because our study was cross-sectional, we failed to display a clear causal relationship between NVP and psychiatric symptoms. Secondly, despite our findings, relatively moderate sample size limits the power of the present study. A significant difference in terms of sociodemographic variables could have been determined, if our study group had included larger numbers of subjects. Thirdly, it would be noteworthy if we had also used objective structured clinical evaluation tools as a method to assess anxiety and depression in early pregnancy.

In conclusion, the findings of our study demonstrated that anxiety levels of pregnant cases with NVP were more than those of healthy pregnant cases. No significant difference between the NVP group and healthy control group in terms of sociodemographic and gestational characteristics were found. It is important for clinicians to appropriately and promptly diagnose and follow-up pregnant women with NVP and NVP-associated anxiety and depression to reduce pregnancy-related complications.

Table 4. BAI and EPDS of the study group

	Nausea and vomiting of pregnancy			
	Mild (n=41)	Moderate (n=24)	Severe (n=18)	p
BAI [median, (min-max)]	9 (0–25)	16 (6–26)	27 (16–43)	<0.001*
EPDS [median, (min-max)]	6 (0–20)	7 (2–20)	9 (5–18)	NS

*mild vs. moderate p=0.002; mild vs. severe p<0.001; moderate vs. severe p=<0.001
NS: Not significant; BAI: Beck Anxiety Inventory; EPDS: Edinburgh Postnatal Depression Scale

Table 5. Anxiety levels of study participants according to Rhodes index of nausea and vomiting

	Anxiety levels				
	No anxiety	Mild	Medium	Severe	Total
Controls n (%)	59 (71.1)	17 (20.4)	7 (8.5)	0 (0)	83 (100)
Study Group n (%)					
Mild NVP	17 (41.5)	18 (43.9)	6 (14.6)	0 (0)	41 (100)
Moderate NVP	1 (4.2)	11 (45.8)	11 (45.8)	1 (4.2)	24 (100)
Severe NVP	0 (0)	2 (11.1)	5 (27.8)	11 (61.1)	18 (100)

NVP: nausea and vomiting of pregnancy

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