Assessment of anxiety and depression levels of pregnant women with hyperemesis gravidarum in a case-control study

Hiperemezis gravidarum'lu gebelerde anksiyete ve depresyon siklinin bir olgu-kontrol calismasi ile degilendirilmesi

Yavuz Şimşek1, Önder Çelik1, Ercan Yılmaz1, Abdullah Karaer1, Engin Yıldırım1, Saim Yoloğlu2

1Department of Obstetrics and Gynecology, Faculty of Medicine, İnönü University, Malatya, Turkey
2Department of Biostatistics, Faculty of Medicine, İnönü University, Malatya, Turkey

Abstract

Objective: The aim of this study was to determine the depression and anxiety levels of pregnant women with hyperemesis gravidarum by using the Beck depression and anxiety inventory scoring system in a Turkish population.

Material and Methods: To ascertain this relationship, a case-control study was conducted involving 86 pregnant women in their first trimester of pregnancy. Forty-one subjects had hyperemesis gravidarum, and 45 were healthy pregnant women who served as control subjects. The groups were adjusted for age, parity, and body mass index. All included women were subjected to baseline laboratory investigations including serum TSH and total hCG levels.

Results: There were no statistically significant differences between the groups with respect to the demographic and obstetric parameters and baseline laboratory investigations except the mean serum potassium level, which was significantly lower in patients with hyperemesis gravidarum than in the control group (p=0.039). Patients with hyperemesis gravidarum had significantly higher depression and anxiety scores than control cases (p=0.0001 and p=0.049, respectively).

Conclusion: Our results suggest that increased anxiety and depression levels may be involved in the pathogenesis of hyperemesis gravidarum and extra psychological support may be necessary during the treatment and follow-up of these patients.

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Introduction

Hyperemesis gravidarum (HG), a severe form of morning sickness, is one of the most common pregnancy-related complications. Considerable variations in the occurrence of HG, both between and within countries, have been reported. According to Eliakim, the prevalence of HG varies between 0.3% and 2% (1). HG is characterized by dehydration, electrolyte imbalance, nutritional depletion and the loss of at least 5% of body weight. HG is considered to be one of the most important pregnancy-related complications that begins in the first trimester and can last throughout pregnancy, although the symptoms usually resolve by week 20 (2). The condition generally requires frequent visits to the emergency room and sometimes repeated hospitalization for intravenous hydration.

Recently published studies have found that the point prevalence of depression ranges from 8.5% to 39.0% at different times during pregnancy and from 6.5% to 12.9% at different times during the first year postpartum, which are both
slightly higher than the depression frequency in non-pregnant women (3-5). HG is currently conceptualized as a biological illness with an unknown pathophysiological cause. Theories have suggested the influence of human chorionic gonadotropin, the pituitary axis, transient adrenal hyperthyroidism and psychogenic factors (6-8). It is well known that women of childbearing age are at an increased risk for depression and anxiety (9) and that pregnancy may increase the risk of depressive episodes (10). However, there is no data in the current literature to support the possibility that HG is a psychologically mediated process. On the basis of this background, the present study used the Beck inventory to determine a possible relationship between the HG and increased level of depression and anxiety in these women.

Material and Methods

A case-control study was conducted involving 86 pregnant women in their first trimester of pregnancy. The women were selected from the outpatient obstetrics clinic of our Department of Obstetrics and Gynaecology between September 2010 and April 2011. The patients were divided into two groups. The first group included patients with a diagnosis of HG (study group) and the second group was composed of healthy pregnant women who served as controls. The groups were adjusted for age, parity, and BMI. All participants were informed about the study and agreed to participate in the research. The study protocol was approved by the local ethics committee of the institution. The study was conducted in accordance with the basic principles of the Declaration of Helsinki.

Patient selection

The inclusion criteria for study group were as follows: (1) diagnosis of HG in a singleton pregnancy documented by the presence of severe vomiting (more than 3 times per day without any other obvious cause), an inability to maintain oral nutrition, weight loss of more than 3 kilograms and at least one positive ketonuria test (1, 2); (2) ability to speak Turkish and no physical or psychological disabilities that would prevent participating in the interventions; (3) no evidence of antenatal bleeding; (4) no pre-existing medical or psychiatric comorbid condition; (5) no antibiotic treatment, H2 blockers or proton pump inhibitors in the preceding month.

A comprehensive medical history was obtained from all pregnant women, including a history of medical disorders (e.g., peptic ulcer) and chronic medication intake (e.g., non-steroidal anti-inflammatory drugs) and exclusion of hyperthyroidism, psychological disorders, hepatic disorders, urinary tract infections or intracranial disorders. An ultrasound scan was performed for all cases, including foetal biometry, placental site, amount of amniotic fluid and exclusion of any relevant obstetric condition (e.g., twin pregnancy, molar pregnancy or missed abortion). In all patients, blood samples were taken for biochemical tests and hemogram during admission. Urine analysis for ketones was carried out for the detection of starvation ketosis.

Pregnant patients with HG were given a standard initial treatment of intravenous fluids with saline (with the addition of potassium chloride as required if patient was hypokalemic), oral thiamine (10 mg daily) and an intravenous antiemetic.

Data collection

Data were collected at the time of admission using a series of forms completed during face-to-face interviews by trained interviewers to determine the psychological status of the patients. After obtaining written informed consent, one of the co-authors (who was blinded to the study groups) carried out the interviews. The first form consisted of questions regarding the demographic characteristics of the patients. The second form included the Turkish versions of the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). The BDI and BAI are 21-item self-report instruments used to assess the severity of symptoms of depression and anxiety, respectively (11, 12). Each response is assigned a score, ranging from 0 (not at all bothered) to 3 (severely bothered), indicating the severity of the symptoms.

Individual questions of the BDI assess mood, pessimism, sense of failure, self-dissatisfaction, guilt, punishment, self-dislike, self-accusation, suicidal ideas, crying, irritability, social withdrawal, body image, work difficulties, insomnia, fatigue, appetite, weight loss, bodily preoccupation and loss of libido. It was translated into Turkish, and its reliability was recalculated by Hisli (13). For the Turkish population, a score of 17 or above represents depression, according to Hisli (13). We used these cut-off scores to determine the levels of depression. The BAI is designed to measure anxiety levels. It is scored by summing the responses, with higher total scores indicating higher levels of anxiety. The validity and reliability of the BAI in the Turkish population have been shown by Ulusoy et al. (14).

Sample size

The sample size of 41 patients per arm provides approximately 80% power at the two-sided significance level of 5% to detect at least a twofold increase in the frequency of anxiety and depression in patients with HG, assuming that the incidence of anxiety and depression is 10% in uncomplicated pregnancies (10).

Statistical analysis

Statistical analyses were performed using the SPSS for the Windows version 13.0 program. Continuous variables were reported as mean±standard deviation (SD). Categorical variables were reported as number and percent. Normality for continuous variables in groups was determined by the Shapiro Wilk test. The variables showed a normal distribution (p>0.05), so an unpaired t test and a Pearson’s chi-square test were used to compare the continuous and categorical variables between the groups. A value of p<0.05 was considered statistically significant.

Results

Obstetric characteristics of the groups in terms of age, parity, gestational age and weight at admission were similar and are
shown in Table 1 (p>0.05). The distribution of educational level and monthly income in the study and control groups is given in Table 2.

There were no statistically significant differences between the groups with respect to the baseline laboratory investigations (Table 3) except the mean serum potassium level, which was significantly lower in patients with HG than in the control group (p=0.039).

Mean BDI and BAI scores for the two groups are given in Table 4. Patients with HG had significantly higher BDI and BAI scores than control cases (p=0.0001 and p=0.049, respectively). Furthermore, 63.4% (n=26) of the patients in the HG group and 28.8% (n=13) of the control cases had a BDI score higher than 17. The difference was statistically significant (p=0.0001). The mean number of vomiting attacks in the HG group was 5.7, ranging from 1-10 per day. All patients in the study group were

Table 1. Demographic data of the HG and control groups

| Parameter                  | HG (n=41) (mean±SD) | Control (n=45) (mean±SD) | p   |
|----------------------------|---------------------|--------------------------|-----|
| Maternal age (years)       | 27.5±6.0            | 29.6±6.5                 | 0.141 |
| Parity                     | 1.14±1.20           | 1.10±1.17                | 0.815 |
| Gestational age (weeks)    | 9.5±2.3             | 10.5±2.8                 | 0.07 |
| Pre-preg. weight           | 64.5±9.0            | 62.4±10.2                | 0.336 |
| Pre-preg. BMI              | 24.0±2.4            | 23.5±3.4                 | 0.24 |
| Weight at admission        | 62.6±8.3            | 64.3±9.3                 | 0.518 |
| BMI at admission           | 23.1±2.4            | 24.1±3.2                 | 0.09 |

Table 2. Distribution of educational level and monthly income of the HG and control groups

| Parameter              | HG (n=41) | Control (n=45) | p  |
|------------------------|-----------|----------------|----|
| Education              |           |                |    |
| Primary-Middle school  | 26        | 64%            | 22 | 48.9 | 0.127 |
| High school            | 9         | 22%            | 19 | 42.2 |
| College                | 6         | 14.6%          | 4  | 8.9  |
| Monthly income         |           |                |    |
| *TL <500               | 13        | 31.7%          | 18 | 40   | 0.844 |
| *TL 500-1000           | 15        | 36.6%          | 13 | 28.9 |
| *TL 1000-2000          | 8         | 19.5%          | 9  | 20   |
| *TL >2000              | 5         | 12.2%          | 5  | 11.1 |

* Turkish liras

Table 3. Laboratory values of the HG and control groups

| Parameter                  | HG (n=41) (mean±SD) | Control (n=45) (mean±SD) | p   |
|----------------------------|---------------------|--------------------------|-----|
| Hb (g/dl)                  | 12.8±1.03           | 15.1±17.3                | 0.398 |
| White blood cell (10³/ml)  | 8.8±2.4             | 9.3±1.9                  | 0.276 |
| Platelet (10³/ml)          | 241±49.9            | 248±59.2                 | 0.532 |
| Na (mmol/l)                | 135.2±2.36          | 133.9±18.9               | 0.661 |
| K (mmol/l)                 | 3.8±0.39            | 4.01±0.48                | 0.039 |
| ALT (U/l)                  | 17.4±13.6           | 16.2±10.9                | 0.644 |
| AST (U/l)                  | 15.9±8.6            | 14.2±4.20                | 0.254 |
| Urea (mg/dl)               | 8.4±2.2             | 8.07±2.79                | 0.533 |
| Creatinine (mg/dl)         | 0.67±0.71           | 0.54±0.10                | 0.228 |
| TSH (µIU/ml)               | 1.02±0.83           | 1.22±0.93                | 0.336 |
| Total hCG (10³ IU/ml)      | 105±47.14           | 89±42.11                 | 0.107 |
Admitted to the inpatient department for the treatment of hyperemesis. The mean length of hospital stay was 1.4 days, ranging from 1-7 days. None of the patients required parenteral nutrition.

**Discussion**

This study has shown that women with severe vomiting during their pregnancy had considerably more anxiety and depression than a well-matched control group of healthy antenatal women. Hisli defined the depression limit point in the Beck depression scale as 17 and above for the Turkish population (13). According to this cut-off value, it was determined that more than half of our patients were depressive. This considerably higher level of depression in pregnant patients with HG may be due to inadequate food intake, lack of energy and severe fatigue, lack of socialization, loss of hope that nausea and vomiting will cease before birth and fear of not being able to feed the developing baby.

It is unquestionable that pregnancy itself is a major life stressor that can precipitate or exacerbate depressive tendencies. In a Swedish population-based study, Andersson et al. reported a 14-percent point prevalence of psychiatric disorders during pregnancy (15, 16).

Increased stress, depression or anxiety related with pregnancy may be more marked in women suffering from hyperemesis. However, these women are often excluded from studies of the emotions of women during pregnancy, and not enough is known about their psychological state. It is important to recognise and treat maternal anxiety and depression in pregnant patients with hyperemesis, both for the sake of the women themselves and their foetuses. It has been shown that women with prenatal anxiety or stress have higher rates of spontaneous abortion (17, 18) and are more likely to deliver premature infants (19). There is also evidence that if a mother is significantly stressed while pregnant, her child is substantially more likely to have emotional or cognitive problems, including an increased risk of attention deficit/hyperactivity disorder, anxiety and language delay (20).

A few previous studies have examined the relationship between anxiety and/or depression and HG, and the results have been inconclusive. Swallow et al. showed that nausea and vomiting in early pregnancy was associated with psychiatric morbidity (21). They reported that the severity of nausea and vomiting correlated independently with the level of anxiety/insomnia and depression. Similarly, Poursharif et al. showed that in a large cohort of women with HG, over 80% reported a negative psychosocial impact, including anxiety and depression, some of which continued after the pregnancy (22). In their review, Kim et al. suggested that the quality of life of women with HG is severely disrupted and normalizing the patient’s sense of demoralization should always be considered during the treatment of these cases (23). Other studies, however, contradict these findings and found no increase in psychiatric illness in women with HG during pregnancy (24, 25). In the present investigation, we also found that mean BDI and BAI scores were significantly higher in hyperemetic pregnant patients than in the control antenatal women (p<0.05). In the HG group, 26 women (63.4%) had a BDI score of higher than 17, signifying depression for the Turkish population (13), compared with only 13 (28.8%) of the controls.

It is unclear whether the psychological or psychiatric morbidity is a cause or consequence of HG. In the past, severe vomiting during pregnancy was often perceived as an expression of maternal resentment towards her unwanted pregnancy. Various psychological stresses have been linked with hyperemesis, including emotional immaturity, strong mother dependence and anxiety and tension related to the pregnancy. More recently, however, investigators have argued that the psychological symptoms are a result of stress arising from the physical burden of HG rather than a cause (21). All the patients in the present study knew they had hyperemesis of pregnancy. Interestingly, Sikkema et al. found anxiety levels to be lower in women with preeclampsia who were unaware of their condition (26).

The present study has clear limitations. The major limitation to this study design was the fact that only a small number of hyperemetic pregnant patients were surveyed and that the results were obtained from a single institution. Other limitations of our study included its subjective nature and data collection method, which created difficulties in ascertaining a ‘cause and effect’ relationship between the higher anxiety and depression and HG.

In conclusion, this study adds to the evidence that those suffering with HG during pregnancy may be more anxious and depressed than women with uncomplicated pregnancies. Depression and anxiety during pregnancy are treatable but can be devastating for maternal and foetal health. Therefore, health professionals need to be aware that extra psychological support may be necessary during the treatment and follow-up of hyperemetic pregnant women.

**Conflict of interest**

No conflict of interest was declared by the authors.

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