

The impact of hyperemesis gravidarum on maternal anxiety and depression: A case-control study

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ABSTRACT

Objective: This study aimed to investigate the psychological and biochemical differences between pregnant women diagnosed with hyperemesis gravidarum (HG) and healthy pregnant controls.

Material and Methods: A prospective case-control study was conducted between December 2024 and June 2025 at Sırnak State Hospital. A total of 100 pregnant women under 16 weeks of gestation were included, with 50 diagnosed with HG and 50 healthy controls. Sociodemographic characteristics, routine laboratory parameters (Hb, AST, TSH, etc.), and psychological symptoms were assessed. Psychological evaluation was performed using the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). Participants with known systemic or psychiatric disorders were excluded.

Results: There were no significant differences between the groups in terms of age, BMI, gravidity, or parity ($p>0.05$). HG patients had significantly lower hemoglobin and TSH levels and higher AST values ($p<0.05$). Depression and anxiety scores were also significantly higher in the HG group compared to controls ($p=0.000$ for both). These findings indicate both physiological and psychological alterations in HG cases.

Conclusion: HG is associated with significant increases in anxiety and depression levels, as well as biochemical disturbances, particularly in hemoglobin, AST, and TSH values. These results suggest that HG may not only be a physical condition but also involve notable psychological distress. Multidisciplinary care, including psychiatric support, should be considered in HG management.

Keywords: Anxiety disorders, depressive disorder, hyperemesis gravidarum, pregnancy complications.

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INTRODUCTION

Pregnancy is a complex period marked by profound physiological changes and significant psychosocial adjustments. Nausea and vomiting of pregnancy (emesis gravidarum) occur in approximately 50–70% of pregnancies.^[1] These symptoms are commonly referred to as morning sickness. Symptoms typically begin in the 4th–5th gestational week, peak between weeks 8–12, and resolve by weeks 16–20, although some cases persist throughout gestation. Hyperemesis gravidarum (HG), a more severe and clinically significant variant, affects 1–2% of pregnancies.^[2,3] It can cause serious maternal and fetal complications.

Clinically, HG is characterised by persistent, pregnancy-related nausea and vomiting with systemic manifestations such as dehydration, electrolyte disturbances (e.g., hypokalemia, hyponatremia), ketonuria, weight loss exceeding 5%, and occasionally renal or hepatic dysfunction.^[4,5] The condition's aetiology is multifactorial, involving hormonal, genetic, environmental, and psychological influences.

Risk factors include high body mass index, young maternal age, multiple or molar pregnancy, primigravidity, previous HG history, comorbidities (e.g., migraine, reflux, gastritis), heightened taste and smell sensitivity, and lack of periconceptional multivitamin use.^[2] A family history—especially maternal or sibling HG—substantially increases risk. Female fetal sex is positively associated with HG, whereas smoking and advanced maternal age appear protective.^[6] Ethnic differences are notable, with higher prevalence in developed Western and urban populations and lower rates in Africa, Alaska, and Japan.^[7]

The pathophysiology remains incompletely understood, though β -hCG is a leading candidate given its temporal correlation with symptom peaks. Other hormones—including estrogen, progesterone, thyroid hormones, leptin, ghrelin, and nesfatin-1—may impair gastrointestinal motility and stimulate central nausea pathways. Gastrointestinal dysmotility, such as reduced lower oesophageal sphincter tone and delayed gastric emptying, is a key mechanism. *Helicobacter pylori* infection has also been implicated, though causal links remain unclear.

The psychological dimension of HG has gained increasing attention. Studies demonstrate significantly higher rates of depression, anxiety, and personality disorders in women with HG compared to healthy pregnancies.^[8–10] Whether these psychiatric symptoms are a cause, a consequence, or both remains unresolved. Eating disorders may exacerbate HG via nutritional deficits, hormonal dysregulation, and pre-existing vomiting behaviours.^[11,12]

Although the existing literature extensively addresses the clinical and hormonal aspects of HG, its psychological component remains underexplored. In particular, the bidirectional relationship between HG and mental health disorders lacks a clear definition, limiting the development of integrated care models. This study addresses this gap by systematically examining HG's psychological impact, combining clinical, psychiatric, and behavioural data. Findings aim to inform multidisciplinary approaches, enhance patient outcomes, and shift clinical management toward a comprehensive biopsychosocial framework.

MATERIAL AND METHODS

This prospective case-control study was conducted on pregnant women who visited the Gynaecology and Obstetrics Outpatient Clinic and Emergency Department of Sırnak State Hospital between December 2024 and June 2025. The study included patients who were 18 years of age or older, literate, had no known systemic diseases, were not taking any medications other than vitamins and iron, and had a singleton live pregnancy of less than 16 weeks. Gestational age was determined using the crown-rump length (CRL) measured in the sagittal plane via transabdominal or transvaginal ultrasound.

The 100 patients included in the study were divided into two groups: 50 cases diagnosed with HG and 50 healthy control subjects without nausea and vomiting complaints. The control group consisted of healthy pregnant women who attended routine antenatal visits at the obstetrics outpatient clinic of Sırnak State Hospital between December 2024 and June 2025 and who did not meet any of the exclusion criteria.

Exclusion criteria included being under 18 years of age, illiteracy, known systemic disease or regular medication use, active infection, gestation greater than 16 weeks, absence of fetal heartbeat, multiple pregnancy, and refusal to participate in the study.

Demographic and obstetric information (height, weight, age, gravida, parity, number of abortions), smoking status, marital status, history of nausea and vomiting in previous pregnancies, and hospitalisation status were recorded for all participants. BDI and BAI were also administered. Patients were provided with a suitable and calm environment to fill out the forms on their own; detailed information about the study was provided, and informed consent was obtained. Participation was voluntary, and the confidentiality of personal data was ensured. The study was approved by Sırnak University Ethics Committee (No: E-74546226-050.04-134910, Date: 02.06.2025) and conducted in accordance with the principles of the Declaration of Helsinki.

The educational and employment statuses of the patients included in the study were assessed as homogeneous between the groups.

The patients' routine laboratory tests performed in the first trimester were evaluated, and the following parameters were examined: sodium (Na; 136–145 mEq/L), potassium (K; 3.1–5.1 mEq/L), haemoglobin (Hb; 10.8–15.1 g/dL), haematocrit (Htc; 32.7–45%), aspartate aminotransferase (AST; 0–35 U/L), alanine aminotransferase (ALT; 0–45 U/L), thyroid-stimulating hormone (TSH; 0.57–5.6 μ IU/mL), and the presence of ketones in urine (graded from 0 to +3).

The diagnosis of hyperemesis gravidarum was based on the patient's inability to tolerate food and drink, a weight loss of at least 5%, signs of dehydration on physical examination, and the presence of pathological values in laboratory tests.

Statistical Analysis

Statistical analyses were performed using the SPSS for Windows version 26.0 program. Continuous variables were reported as mean $\pm$ standard deviation (SD). Categorical variables were reported as numbers and percentages. The variables showed a normal distribution ($p>0.05$), so an unpaired t-test and 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

A total of 100 participants, equally divided into patient and control groups ($n=50$ each), were evaluated for sociodemographic characteristics, laboratory findings, and psychiatric symptomatology. No statistically significant differences were found between the groups in terms of age (patients: 28.9 ± 4.9 years; controls: 27.5 ± 4.4 years, $p=0.144$), gravidity (median 2 vs. 2, $p=0.285$), parity (median 1 vs. 1, $p=0.648$), body mass index (25.2 ± 3.1 vs. 25.2 ± 3.3 kg/m², $p=0.755$), or gestational age (median 11 vs. 11 weeks, $p=0.651$), indicating demographic comparability between groups (Table 1).

Regarding laboratory parameters, hemoglobin levels were significantly lower in the patient group compared to controls (11.06 ± 2.21 vs. 12.26 ± 1.24 g/dL, $p=0.021$). Although hematocrit values were slightly reduced in patients ($35.9\pm3.1\%$ vs. $36.9\pm3.1\%$), the difference did not reach statistical significance ($p=0.073$). Aspartate aminotransferase (AST) levels were significantly higher in the patient group (29.8 ± 3.3 vs. 21.7 ± 1.1 U/L, $p=0.005$), whereas alanine aminotransferase (ALT) levels showed a non-significant trend toward elevation in patients (27.1 ± 2.7 vs. 20.2 ± 1.7 U/L, $p=0.100$). No meaningful differences were detected in sodium (136.6 ± 2.6 vs. 133.8 ± 19.0 mmol/L, $p=0.702$) or potassium levels (4.0 ± 0.5 vs. 4.7 ± 0.9 mmol/L, $p=0.933$). By contrast, thyroid-stimulating hormone (TSH) concentrations were markedly lower in patients (0.97 ± 0.81 μ IU/mL) compared to controls (1.64 ± 0.92 μ IU/mL, $p=0.000$), highlighting significant endocrine alterations (Table 2).

Psychological assessment revealed striking differences between the groups. Median Beck Depression Inventory (BDI) scores were significantly higher in patients than in controls (19.92 vs. 8.76, $p=0.000$). Similarly, Beck Anxiety Inventory (BAI) scores were elevated in patients (18.16 vs. 11.06, $p=0.000$), indicating a substantial psychological burden associated with the clinical condition (Table 3).

In summary, although the two groups were demographically comparable, patients displayed significant hematological (reduced Hb), hepatic (elevated AST, trend in ALT), endocrine (lower TSH), and psychological (higher BDI and BAI) abnormalities, suggesting that these parameters may be closely related to the pathophysiology of the disorder.

DISCUSSION

Nausea and vomiting of pregnancy (NVP) are common symptoms affecting up to 70% of pregnant women, typically emerging around the 4th or 5th gestational week, peaking between the 8th and 12th weeks, and generally subsiding by the 16th to 20th week. However, in approximately 1–2% of cases, symptoms progress to HG, a severe form of NVP that can lead to significant maternal morbidity and even hospitalization.^[2,3] Diagnostic criteria for HG remain variable, with clinical judgment guided by signs of dehydration, electrolyte imbalances, ketonuria, significant weight loss, and, in severe cases, hepatic or renal dysfunction. HG is increasingly recognized as a multifactorial condition involving both biological and psychosocial contributors.

Table 1: Sociodemographic characteristics of patient and control groups

Variable	Control group	Patient group	p
Age (mean $\pm$ SD)	27.46 $\pm$ 4.35	28.90 $\pm$ 4.90	0.144
Gravida (median)	2.00	2.00	0.285
Parity (median)	1.00	1.00	0.648
BMI (kg/m ²), (mean $\pm$ SD)	25.23 $\pm$ 3.28	25.23 $\pm$ 3.10	0.755
GA (weeks) (median)	11.00	11.00	0.651

BMI: Body Mass Index; GA: Gestational age.

Table 2: Laboratory parameters of patient and control groups

Variable	Control group (Mean $\pm$ SD)	Patient group (Mean $\pm$ SD)	p
HB (g/dL)	12.26 $\pm$ 1.24	11.06 $\pm$ 2.21	0.021
HTC (%)	36.87 $\pm$ 3.10	35.93 $\pm$ 3.09	0.073
AST (U/L)	21.72 $\pm$ 1.13	29.80 $\pm$ 3.27	0.005
ALT (U/L)	20.20 $\pm$ 1.65	27.14 $\pm$ 2.74	0.100
K (mmol/L)	4.68 $\pm$ 0.95	3.98 $\pm$ 0.51	0.933
Na (mmol/L)	133.77 $\pm$ 18.96	136.59 $\pm$ 2.56	0.702
TSH (μ IU/mL)	1.64 $\pm$ 0.92	0.97 $\pm$ 0.81	0.000

HB: Hemoglobin; HTC: Hematocrit; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; K: Potassium; Na: Sodium; TSH: Thyroid stimulating hormone.

Table 3: Depression and anxiety scores of patient and control groups

Variable	Control group (Median)	Patient group (Median)	p
Beck depression score	8.76	19.92	0.000
Beck anxiety score	11.06	18.16	0.000

Our study adds to the growing body of literature supporting the role of psychological distress in the pathophysiology of HG. We observed significantly higher levels of anxiety and depression in patients diagnosed with HG compared to healthy pregnant controls, as measured by BAI and BDI. These findings mirror previous studies showing elevated psychometric scores among HG patients.^[13] For instance, a study by Simşek et al.^[13] evaluating 41 HG patients and 45 healthy controls using the same instruments demonstrated similar results, reinforcing the association between severe NVP and increased psychological burden.

In addition to psychometric assessments, our study also identified notable laboratory differences between groups. Specifically, patients with HG had significantly lower hemoglobin levels and elevated AST values, as well as reduced TSH concentrations compared to the control group. These findings suggest that HG is not only associated with psychological alterations but also reflects systemic physiological stress. In contrast, some studies, such as the one by Özen et al.,^[14] did not report significant laboratory discrepancies except for serum potassium levels. Our results expand on those findings by highlighting a broader range of physiological abnormalities in HG patients, possibly mediated by malnutrition, dehydration, and endocrine disruption.

Consistent with our findings, previous literature suggests that HG may be more prevalent among women with underlying personality traits or psychiatric vulnerabilities, including histrionic, depressive, or anxious dispositions. Several studies have proposed that HG may be a psychosomatic response to familial or environmental stressors, with some women demonstrating improvement upon removal from triggering home environments.^[15] Simpson et al.^[16] also noted that women with HG exhibited higher levels of depressive, hypochondriacal, and hysterical personality traits during pregnancy, although these symptoms did not persist postpartum.

Notably, our inclusion criteria excluded participants with a prior history of psychiatric illness, which minimizes the confounding influence of preexisting mental health disorders. This methodological decision supports the interpretation that elevated anxiety and depression levels observed in our HG group likely emerged as a consequence of the clinical condition itself rather than as a predisposing factor. This view aligns with the conclusions of Tan et al.,^[9] who suggested that psychological symptoms in HG may be reactive rather than etiologic.

However, the causal relationship between HG and psychiatric symptoms remains contentious. Some prospective studies, such as that by Annagür et al.,^[10] have reported that a significant proportion of HG patients experienced psychiatric symptoms before pregnancy, suggesting a bidirectional or predisposing model. Conversely, Bozzo et al.^[17] found no significant difference in the incidence of NVP between women with and without pre-pregnancy depression who were receiving antidepressant treatment, further complicating the etiological narrative.

Our findings support the theory that anxiety and depression may be consequences of the distressing physical symptoms of HG, including persistent nausea, weight loss, fatigue, and functional impairment. The observed alterations in TSH levels among HG patients may also hint at an underlying neuroendocrine mechanism contributing to mood dysregulation during pregnancy. Although thyroid function abnormalities are not universally reported in HG, our data suggest they may be more prevalent than previously recognized and potentially relevant to the psychological state of affected women.

Despite the consistent association between HG and psychological symptoms, the literature still lacks a unified model explaining their interplay. Poursharif et al.^[18] highlighted that psychological distress can persist beyond the resolution of HG symptoms, suggesting longer-term impacts on mental health. However, as our study did not include postpartum follow-up, we were unable to assess the

longitudinal course of psychiatric symptoms in HG patients. Future studies with extended follow-up periods are warranted to explore whether the emotional sequelae of HG resolve with the improvement of physical symptoms or represent a more persistent psychiatric risk.

Our findings underscore the need for a multidisciplinary approach to managing HG. Beyond standard medical interventions targeting dehydration and metabolic disturbances, the routine assessment of psychological well-being should be considered in HG care protocols. Women presenting with HG symptoms should be screened not only with laboratory workups but also with validated tools such as the BDI and BAI to identify those in need of psychological support. Early identification and intervention may prevent the worsening of psychiatric symptoms and improve overall maternal outcomes.

In conclusion, our study contributes to the existing evidence that HG is associated with both physiological disruptions and significant psychological distress. The correlation between higher anxiety and depression scores and altered lab parameters suggests that HG is a multifaceted condition requiring integrated obstetric and mental health management. While the direction of causality remains unclear, the clinical implications are evident: addressing the mental health of pregnant women with HG is essential for comprehensive and compassionate care.

Study Limitations

The present study has certain limitations. The relatively small sample size, single-centre design, and lack of longitudinal follow-up may limit the generalizability of the findings and preclude conclusions about the persistence of psychological symptoms beyond pregnancy. Future multi-centre studies with larger cohorts and extended follow-up periods are warranted to validate and expand upon these results.

CONCLUSION

This study highlights the multifactorial nature of hyperemesis gravidarum (HG), demonstrating its association with both physiological disturbances and significant psychological distress. Patients with HG exhibited markedly higher anxiety and depression scores compared to healthy pregnant controls, along with notable laboratory abnormalities such as reduced hemoglobin and TSH levels and elevated AST values. While the causal direction between HG and psychiatric symptoms remains debated, the exclusion of participants with preexisting psychiatric conditions supports the interpretation that these symptoms may develop as a consequence of HG.

From a clinical perspective, these findings underscore the importance of a multidisciplinary management approach that addresses both physical and psychological aspects of care. Routine psychological screening—using validated tools such as the BDI and BAI—should be integrated into the clinical evaluation of women presenting with HG, alongside standard obstetric and laboratory assessments. Early identification and appropriate psychiatric support have the potential to improve maternal well-being, enhance treatment adherence, and optimize pregnancy outcomes. Future longitudinal and multi-centre studies are warranted to determine the persistence of psychological symptoms postpartum and to refine comprehensive care protocols for HG.

Statement

Ethics Committee Approval: The Sirnak University Clinical Research Ethics Committee granted approval for this study (date: 02.06.2025, number: E-74546226-050.04-134910).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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