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# Psychiatric factors do not affect recurrence risk of hyperemesis gravidarum

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## Abstract

**Aim:** The aim of this study is to determine whether psychiatric symptoms affect recurrence risk of hyperemesis gravidarum (HG).

**Methods:** The study sample included 108 women with HG treated with i.v. fluids in their first pregnancy. Women were divided into two groups based on recurrence of HG in their second pregnancy. Participants submitted medical records and completed a survey regarding pregnancy characteristics and psychiatric symptoms. The  $\chi^2$ -test and Student's *t*-test were performed to compare the two groups.

**Results:** Eighty-four women (71%) had a recurrence of HG requiring i.v. fluid for dehydration, and were compared with 34 women (29%) who did not have a recurrence. There were no significant differences in obstetric history, although there was a trend toward greater time between first and second pregnancy in the recurrence group ( $P = 0.08$ ). There were no differences in pre-existing psychiatric diagnoses including anxiety, depression, bipolar disorder, panic or eating disorders. Following the first HG pregnancy, participants in both groups were well matched for all post-traumatic stress symptoms.

**Conclusion:** This study is the first to analyze the relationship of psychiatric factors to risk of recurrence of HG. No factors were identified that increase the risk of recurrence including stress symptoms following a HG pregnancy. Psychological sequelae associated with HG are probably a result of the physical symptoms of prolonged severe nausea and vomiting, medication and/or hospitalization, and likely play no role in disease etiology.

**Key words:** anxiety, depression, hyperemesis gravidarum, psychiatric, post-traumatic stress symptoms.

## Introduction

While most pregnant women experience considerable morning sickness, a rare condition called hyperemesis gravidarum (HG) involves nausea and vomiting so severe that sufferers of this disease can become dangerously dehydrated and malnourished. HG accounts for over 285 000 hospital discharges in the USA annually, with most authors reporting an incidence of 0.5–2%.<sup>1,2</sup> HG often results in dehydration,

electrolyte disturbance and nutritional deficiency in many cases, mandating i.v. hydration and, in severe cases, the use of parenteral nutrition. If left untreated, HG can result in Wernicke's encephalopathy,<sup>3</sup> central pontine myelinolysis,<sup>4</sup> hepatic dysfunction<sup>5</sup> and renal failure.<sup>6</sup> The diagnosis of HG is also associated with a fourfold increased risk of adverse outcome including low birthweights, intrauterine growth restriction, preterm delivery, and fetal and neonatal death.<sup>7–10</sup>

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Several lines of evidence support a genetic predisposition to nausea and vomiting in pregnancy (NVP). In the only study of NVP in twins, concordance rates were more than twice as high for monozygotic compared with dizygotic twins.<sup>11</sup> Approximately one-third of women affected by HG have an affected mother, and one out of five have an affected sister.<sup>12</sup> Such data suggest that a genetic predisposition may play a role in the development of HG and explains the high recurrence risk independent of change in partner.<sup>13</sup>

Based on a website survey sponsored by the Hyperemesis Education and Research Foundation, the risk for recurrence can be as high as 81%.<sup>14</sup> Understanding the recurrence risk has implications for counseling, treatment and disease etiology for women, especially because of the high percentage of women who change reproductive plans (37%) due to their experiences with HG.<sup>14</sup> Severe nausea and vomiting has been attributed historically to psychological conflicts, albeit with lack of supporting scientific evidence.<sup>2</sup> The theory that HG is psychological is due primarily to the fact that a biological cause for HG has yet to be identified. If HG is caused by psychological factors, we predict that psy-

chiatric symptoms will positively correlate with recurrence risk. Therefore, the aim of this study is to determine whether psychiatric symptoms are linked to risk of recurrence for HG patients. These results could potentially lead to better methods to predict recurrence and prepare for a HG pregnancy.

## Methods

Eligible patients were primarily recruited through advertising on the Hyperemesis Education and Research Foundation website at [www.HelpHer.org](http://www.HelpHer.org). The website receives over 80 000 unique visitors per month with the primary search term being 'hyperemesis gravidarum', making it one of the most visited sites on the disease and an excellent resource for recruitment. Participants were asked to submit their medical records and complete an online survey regarding information on a variety of demographic characteristics, pre-existing conditions, pregnancy symptoms and treatments, and maternal and fetal outcomes as reported in Tables 1–3. The majority of the subjects joined the study at the time they were pregnant and

**Table 1** Pregnancy history

Pregnancy history	Recurrence in second pregnancy	No recurrence in second pregnancy	<i>P</i>
Sample size	84	34	
No. of pregnancies	2.29	2.59	0.06
Miscarriage/fetal death in first pregnancy	<b>33.57% (3/84)</b>	<b>2.94% (1/34)</b>	1.00
Fertility treatment in first pregnancy	<b>3.61% (3/83)</b>	<b>2.94% (1/34)</b>	1.00
Vaginal delivery in first pregnancy	<b>93.67% (74/79)</b>	<b>84.85% (28/33)</b>	0.26
Spontaneous labor in first pregnancy	<b>53.57% (45/84)</b>	<b>50.00% (17/34)</b>	0.88
Labor (and not C-section no labor) in first pregnancy	<b>93.67% (74/79)</b>	<b>84.85% (28/33)</b>	0.26
	Average (SD)		
Age (years) at end of first pregnancy	27.11 (4.36)	26.88 (4.36)	0.82
Age (years) at end of second pregnancy	30.52 (4.38)	29.58 (4.38)	0.35
Time (years) between first and second pregnancy	3.42 (2.68)	2.71 (1.62)	0.08

All *P*-values were obtained through  $\chi^2$ -test except for age which was obtained through a Student's *t*-test. SD, standard deviation.

**Table 2** Psychiatric diagnoses prior to first pregnancy

Variable	Recurrence in second pregnancy	No recurrence in second pregnancy	<i>P</i>
Anxiety	14.29%	17.65%	0.86
Bipolar	1.19%	2.94%	1
Depression	13.10%	12.73%	1
Eating Disorder	7.14%	5.88%	1
Panic Disorder	5.95%	8.82%	0.87

All *P*-values were obtained through  $\chi^2$ -test.

**Table 3** Post-traumatic stress symptoms following first pregnancy

Variable	Recurrence in second pregnancy	No recurrence in second pregnancy	<i>P</i>
Had nightmares about it or think about it when you did not want to? (Y/N)	34.52%	50.00%	0.38
Tried hard not to think about it or went out of your way to avoid situations that reminded you of it? (Y/N)	33.33%	38.24%	0.09
Were constantly on guard, watchful or easily startled? (Y/N)	15.48%	20.59%	0.67
Felt numb or detached from others, activities or your surroundings? (Y/N)	14.29%	17.65%	0.46
How long did HG affect you emotionally? (number months, years, ongoing, describe)	No answer: 5 Months: 33 Ongoing: 36 Years: 10	No answer: 2 Months: 12 Ongoing: 15 Years: 5	0.88

All *P*-values were obtained through  $\chi^2$ -test. HG, hyperemesis gravidarum.

were sent a reminder to complete the survey pertaining to their respective pregnancy outcome following their due dates.

In order to focus on recurrence, only women between the age of 18 and 50 years who had at least two pregnancies that lasted beyond the second trimester were included in this analysis.

The clinical criteria were all participants who required i.v. fluid treatment for dehydration due to HG in their first pregnancy. Participants with recurrent pregnancies, defined as having i.v. fluid treatment for HG in the second pregnancy, were compared with participants who had no i.v. fluid treatment for HG and self-reported that they did not have HG in the second pregnancy.

This study has been approved by the institutional review board of the University of California (#09-08-122-01A). Using the data gathered from the participants' medical records and online survey results, 118 respondents were included in the recurrence study and categorized according to the binary response variable of recurrence as defined previously. Self-reported medically diagnosed emotional/behavioral disorders were collected via online survey and answers were compared between the recurrence group and the non-recurrence group. Post-HG-pregnancy stress symptoms were drawn from questions (shown in Table 3) assessing the three post-traumatic stress disorder symptom categories and compared between the recurrence and non-recurrence group: (i) re-experiencing; (ii) avoidance/numbing; and (iii) hyperarousal. The  $\chi^2$ -test was performed to compare groups according to these binary responses, and Student's *t*-test was used to compare respondents according to continuous explanatory variables. All the variables used in the regression had a 0% missing response rate.

## Results

### Pregnancy characteristics

Eighty-four women (71%) had a recurrence of HG requiring i.v. fluid treatment for dehydration, and were compared with 34 women (29%) who did not have severe nausea and vomiting in their second pregnancy. Table 1 compares the pregnancy characteristics of the two groups. All participants were from the USA. Cases who recurred and those who did not recur were well matched for obstetric history (Table 1); there were no significant differences in obstetric history, although there was a trend toward greater time between first and second pregnancy in the group that recurred (*P* = 0.08) and a trend toward more pregnancies in the group that did not recur (*P* = 0.06).

### Psychiatric health prior to first pregnancy

Table 2 shows psychiatric health conditions (prior to the first pregnancy) that were compared. There were no differences in pre-existing psychiatric diagnoses including anxiety, depression, bipolar disorder, panic or eating disorders. Pre-existing psychiatric conditions do not play a role in risk of recurrence of HG.

### Post-traumatic stress symptoms (PTSS) following a HG pregnancy

Table 3 shows post-traumatic stress symptoms following HG pregnancies. Participants in both groups were well matched for all PTSS. There is no increased risk of recurrence in patients with PTSS following HG pregnancies.

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## Discussion

This study focuses on examining psychological factors that could possibly affect one's chance of a HG recurrence. Our findings show pre-existing psychological conditions and post-pregnancy stress symptoms have no impact on the risk of a recurrence of HG. Most observed factors were closely matched between the group reporting recurrence of HG and the group not reporting recurrence. There is a trend toward a longer duration (3.2 vs 2.7 years) between pregnancies and increased recurrence risk, which is similar to findings from a previous study,<sup>15</sup> but this trend was not statistically significant in either study.

This study has limitations, particularly that sample sizes are small and the subjects are not randomly sampled from the overall population of HG sufferers. Nevertheless, the results of this study have implications for counseling. One should expect a recurrence risk of over 70% independent of pre-pregnancy psychiatric diagnoses. As many as 18% of women with HG experience full criteria stress symptoms following a HG pregnancy,<sup>16</sup> but it should provide some comfort to these women that PTSS are unlikely to increase the risk of recurrence.

The cause of HG is unknown. Studies continue to focus on a psychiatric etiology despite the fact that no cause and effect have ever been scientifically proven and more and more studies refute this hypothesis.<sup>17</sup> Studies in support of a psychological etiology are primarily based on the fact that women with HG have increased risk of depression and anxiety while suffering from HG. However, this is more likely the result of prolonged physical symptoms, dehydration, malnutrition, medication and hospitalization, rather than causal. Control groups never include women who are currently suffering from similar physical symptoms and thus are not comparable. One would not compare the emotional/behavioral symptoms of cancer patients to a control group of healthy patients and presume an increase in depression and anxiety in the cancer group is evidence that depression and anxiety cause cancer, but this is done over and over in publications on HG.<sup>18</sup>

Herein, for the first time, both our cases and controls have suffered from HG in their first pregnancy, and we show that there is no correlation between either pre- or post-pregnancy psychiatric conditions and recurrence of HG. This study provides strong scientific evidence against a psychogenic etiology by showing that psychological factors do not play a role in risk of recurrence. Avoiding a recurrence is a critical topic to

women who have experienced a HG pregnancy. Future studies are imperative to decipher the etiology of HG and should focus on analyzing genetic and environmental factors associated with the disease, and identify factors that minimize the risk of recurrence.

## Disclosure

The authors confirm that the results of this manuscript have not been distorted by research funding or conflicts of interest.

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