



## Review

# Analysis of pre- and post-pregnancy issues in women with hyperemesis gravidarum



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## ABSTRACT

The purpose of this study is to determine the frequency of reporting of both pre-pregnancy and post-pregnancy psychosocial and physical issues in women with hyperemesis gravidarum (HG). Conditions in 449 women with HG were compared to 459 unaffected women (controls). Binary responses were analyzed using either Chi-squared or Fishers Exact test. Continuous responses were analyzed using a *t*-test.

Among 60 pre-pregnancy conditions surveyed, 10 common (>5%) maternal pre-pregnancy conditions were significantly more frequently reported by women with HG. Twenty rare (<5% controls) pre-pregnancy conditions with significantly increased reporting in the HG group were identified. Thirty (50%) pre-pregnancy conditions were similarly reported between cases and controls. Among 80 post-pregnancy factors surveyed, women with HG also showed significantly higher reporting for 7 common and 50 rare post-pregnancy outcomes. Women with HG are significantly more likely to self-report physical and psychosocial issues both before and after pregnancy.

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## 1. Introduction

Hyperemesis gravidarum (HG), severe nausea and vomiting of pregnancy, occurs in approximately 0.2–2% of pregnancies and leads to significant weight loss, dehydration, electrolyte imbalance, and ketonuria (Goodwin, 1998). Until 60 years ago, HG was an important cause of

maternal mortality with 10% of cases ending in death. Although maternal mortality has since decreased, significant maternal morbidity such as Wernicke's encephalopathy (Chiossi et al., 2006), acute renal failure (Hill et al., 2002), liver function abnormalities (Adams et al., 1968), splenic avulsion (Nguyen et al., 1995), esophageal rupture (Liang et al., 2002), pneumothorax (Schwartz and Rossoff, 1994), and post-traumatic stress continue to be reported (Fejzo et al., 2009). HG is also associated with poor fetal/child outcomes including a 4-fold increased risk of preterm birth and a 3-fold increased risk of neurodevelopmental delay in children (Fejzo et al., 2013; Fejzo et al., 2015).

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The cause and maternal consequences of HG are not well understood (Verberg et al., 2005). The objective of this study is to determine the self-reported frequency of both pre-pregnancy and post-pregnancy psychosocial and clinical conditions in women with hyperemesis gravidarum (HG) compared to controls.

## 2. Material and methods

### 2.1. Sample and settings

This case-control study is part of a larger investigation evaluating the genetics and epidemiology of hyperemesis gravidarum (HG). Eligible patients were primarily recruited through advertising on the Hyperemesis Education and Research Foundation Web site ([www.HelpHer.org](http://www.HelpHer.org)) between 2007 and 2014. The inclusion criteria for women with a history of HG were a diagnosis of HG in a singleton pregnancy and treatment with IV fluids and/or total parenteral nutrition/na-sogastric feeding tube. Participants with a history of HG were asked to submit their medical records. Minors (under 18 years) were not included in the study because few teens are expected to fit the study criteria for controls of having had two pregnancies.

Each woman with a history of at least one pregnancy affected with HG and treated with IV fluids was asked to recruit one acquaintance with at least 2 pregnancies lasting beyond 27 weeks to participate as a control. Because this study is part of a genetic and epidemiology study comparing women with a history of HG to controls, the requirement of 2 pregnancies for controls was to help ensure controls would not be misclassified. Albeit rare, some women may have normal nausea/vomiting in one pregnancy and HG in another, and therefore, selecting controls with a minimum of 2 pregnancies with normal or no nausea and vomiting of pregnancy (NVP) helps minimize enrollment of those types of controls. Controls were eligible if they experienced either no nausea/vomiting in pregnancy or normal nausea/vomiting that did not interfere with their daily routine, no weight loss due to nausea/vomiting and no medical attention in any pregnancy due to nausea. Controls were assessed for eligibility through self-reporting and medical records were not collected. Women with a history of HG and controls living outside the United States were excluded due to added time and costs to consent by phone and enroll participants. This study has been approved by the Institutional Review Board at UCLA, IRB # 09-08-122-01A.

### 2.2. Study procedures

Participants were asked to complete an online survey regarding detailed information including pre-pregnancy conditions and maternal outcomes. The majority of participants, both women with a history of HG and controls, joined the study and began the survey during their pregnancies and were automatically prompted to complete the survey on fetal outcome following their due date. Participants were prompted every six months to update the survey. Participants were asked to fill out the survey for all past, current, and “future” pregnancies

(pregnancies that occurred when participants were prompted to update the survey). Survey questions can be found in the Supplementary material.

### 2.3. Statistical analyses

Psychosocial and physical conditions from 449 women with HG were compared to psychosocial and physical conditions from 459 unaffected women, both before and after their first pregnancy. The sample size was determined by the enrollment period (2007–2014) rather than using power calculations to predict sample size because this is an exploratory study and there was no way to estimate the frequencies of many of the conditions surveyed. Conditions were categorized into common and rare, with rarity established as having <5% of subjects in the control group presenting the condition. Binary responses were analyzed using either a Chi-square or Fisher Exact test, and continuous responses were analyzed using a *t*-test. There were no exclusion criteria for comorbidities in cases or controls. The threshold for significance was  $P < 0.05$ .

## 3. Results

### 3.1. Demographic characteristics

Participants were of similar height and equally likely to report a vaginal delivery (Table 1). Women with HG were significantly more likely to be white and weigh more on average than controls. Cases were also significantly more likely to be younger and have a later (average) year of birth of first child (due to the study design where controls were required to have at least 2 pregnancies).

### 3.2. Pre-pregnancy characteristics

Among 60 pre-pregnancy conditions and characteristics surveyed, women with HG were significantly more likely to report 10 common (Table 2) and 20 rare (Table 3) pre-existing conditions. Half (30) of the 60 surveyed conditions and characteristics were self-reported at similar frequencies in cases and controls (Table 4). Physical issues including motion sickness, migraines, chronic gastrointestinal conditions, dental issues, and immune conditions were more commonly reported by cases. Cases were also significantly more likely to report emotional diagnoses including anxiety and depression. Gynecological issues that were significantly more frequently reported by cases included premenstrual syndrome and diagnosis of a gynecologic disorder, while amenorrhea, infertility, irregular periods, ovarian hyperstimulation, and polycystic ovaries were reported at similar frequencies in cases and controls. Rare reporting (<5%) of several pre-pregnancy characteristics and conditions in controls, were commonly reported (>5%) in cases. These include chronic constipation (7%), gastroesophageal reflux disease (8%), hypoglycemia (10%), irritable bowel (13%), panic disorder (11%), special diet (11%), and thyroid disorders (7%).

**Table 1**  
Demographic characteristics.

| Demographics                       | HG (%)          | Control group (%) | Significance | Odds ratio | 95% CI                |
|------------------------------------|-----------------|-------------------|--------------|------------|-----------------------|
| Sample size                        | 449             | 459               |              |            |                       |
| Race (White)                       | 394 (88)        | 423 (92)          | $P = 0.0282$ | 0.6097     | 0.3919 to 0.9486      |
| Vaginal delivery                   | 327 (73)        | 354 (77)          | $P = 0.1354$ | 0.795      | 0.5883 to 1.0744      |
| Average weight of group (pounds)   | 150.56 (95–330) | 138.96 (95–300)   | $P < 0.0001$ |            | –15.88529 to –7.30567 |
| Average year born                  | 39 (17–71)      | 41 (27–61)        | $P < 0.0001$ |            | –2.90172 to –1.21202  |
| Average height of group (inches)   | 65.15 (49–78)   | 64.81 (45–80)     | $P = 0.1159$ |            | –0.762637 to 0.081838 |
| First child<br>(Average year born) | 2003            | 2002              | $P < 0.01$   |            |                       |

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