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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) 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/nasogastric 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 women 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 comorbities 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
		Avg. (range)			
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					
(Average year born)	2003	2002	$P < 0.01$		

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Table 2
Significant reporting of common pre-pregnancy conditions (HG vs controls).

Factor	HG group (%) $n = 449$	Control group (%) $n = 459$	Significance (HG vs. control)	Odds ratio	95% CI
Allergies	188 (41.87%)	142 (30.94%)	$P = 0.0006$	1.608	1.2243 to 2.1120
Anxiety disorder	86 (19.2%)	25 (5.45%)	$P < 0.0001$	4.1128	2.5791 to 6.5586
Dental cavities	163 (36.3%)	132 (28.8%)	$P = 0.0154$	1.4119	1.0681 to 1.8663
Depression	79 (17.6%)	38 (8.28%)	$P < 0.0001$	2.3655	1.5677 to 3.5693
Gynecologic disorder	56 (12.5%)	23 (5.01%)	$P = 0.0001$	2.7012	1.6315 to 4.4722
Immune disorder	57 (12.7%)	26 (5.66%)	$P = 0.0003$	2.4216	1.4931 to 3.9274
Migraine	104 (23.2%)	60 (13.1%)	$P = 0.0001$	2.0046	1.4142 to 2.8416
Motion sickness	146 (32.5%)	53 (11.6%)	$P < 0.0001$	3.6911	2.6069 to 5.2262
Premenstrual syndrome	120 (26.7%)	58 (12.6%)	$P < 0.0001$	2.5217	1.7847 to 3.5632
TMJ*	76 (16.9%)	29 (6.32%)	$P < 0.0001$	3.0212	1.9269 to 4.7368

* Temporomandibular joint disorder.

3.3. Post-pregnancy characteristics

Among 70 post-pregnancy items surveyed, women with HG were significantly more likely to report 7 common (Table 5) and 50 rare (Table 6) conditions and characteristics. Twenty-three items were reported at similar frequencies in cases and controls (Table 7). Among the 10 significantly increased pre-pregnancy conditions, anxiety disorder, dental cavities, depression, migraine, and premenstrual syndrome continued to be reported at a significantly higher rate after an HG pregnancy. Reports of depression and anxiety disorder increased to 25% and 28% respectively following a pregnancy affected by HG. Reports of allergies were significantly different prior to pregnancy, but similar after pregnancy. Among psychosocial issues, 68% of women who experienced an HG pregnancy reported missing work compared to 13% of controls. The physical and psychosocial issues that were rarely reported by controls, but commonly reported by cases are shown in Table 6. In cases, the highest reporting of rare physical post-pregnancy conditions include motion sickness (23%), irritable bowel (10%), temporomandibular joint disorder (TMJ, 10%), debilitating muscle weakness (8%), and gastroesophageal reflux (8%). The highest reporting of rare psychosocial issues after an HG pregnancy included future pregnancy attitude change (78%), negative mental experience (67%), inability of self-care (58%), negative feelings toward others (56%), and psychiatric problems (52%).

4. Discussion

Women with HG are significantly more likely to report physical and psychosocial conditions both before and after pregnancy. Among common pre-pregnancy conditions, motion sickness was reported prior to pregnancy in a-third of women with HG, and thus, may predict a pregnancy with more severe nausea. A link between motion sickness and susceptibility to NVP has been hypothesized (Black, 2002), but this is the first evidence showing a link between pre-existing motion sickness and HG. An increase in reporting of TMJ and dental cavities prior to pregnancy are also novel findings. Due to the large number of factors surveyed, some of the conditions reported may be increased by chance alone. However, it is conceivable that oral health can have an impact on nausea and vomiting.

Other potential predictors identified in this study have been linked to HG previously, including migraine and immune dysfunction/allergies (Heinrichs, 2002; Leylek et al., 1999). Increased reporting of pre-existing gynecologic disorders and premenstrual syndrome are consistent with theories of a reproductive etiology. Reports of depression and anxiety were also found in this study to be significantly increased prior to pregnancy. Depression and anxiety are often increased during an HG pregnancy, but usually resolve when symptoms subside (Tan et al., 2014). Approximately one quarter of the women in this study self-

Table 3
Significant reporting of rare pre-pregnancy conditions (HG vs controls).

Factor	HG group (%) $n = 449$	Control group (%) $n = 459$	Significance (HG vs. control)	Odds ratio	95% CI
Chronic constipation	32 (7.13%)	8 (1.74%)	$P = 0.0003$	4.3261	1.9710 to 9.4953
Chronic diarrhea	19 (4.23%)	4 (0.87%)	$P = 0.0036$	5.0262	1.6962 to 14.8934
Chronic dizziness	21 (4.68%)	6 (1.31%)	$P = 0.0051$	3.7044	1.4809 to 9.2665
Chronic fatigue	22 (4.9%)	6 (1.31%)	$P = 0.0035$	3.8899	1.5621 to 9.6865
Chronic infection	18 (4.01%)	1 (0.22%)	$P = 0.0042$	19.1276	2.5425 to 143.9020
Chronic nausea	18 (4.01%)	1 (0.22%)	$P = 0.0042$	19.1276	2.5425 to 143.9020
Debilitating muscle weakness/fatigue	8 (1.78%)	0 (0.0%)	$P = 0.0486$	17.6931	1.0181 to 307.4716
Eating disorder	24 (5.35%)	12 (2.61%)	$P = 0.0389$	2.1035	1.0388 to 4.2597
Fibromyalgia	9 (2.0%)	2 (0.44%)	$P = 0.0494$	4.6739	1.0042 to 21.7534
GERD*	37 (8.24%)	9 (1.96%)	$P = 0.0001$	4.4903	2.1410 to 9.4173
Hearing loss	8 (1.78%)	1 (0.22%)	$P = 0.0463$	8.3084	1.0349 to 66.7042
Hypoglycemia	43 (9.58%)	6 (1.31%)	$P < 0.0001$	7.9963	3.3682 to 18.9838
Inner ear disorder	11 (2.45%)	2 (0.44%)	$P = 0.0236$	5.7386	1.2647 to 26.0382
Irritable bowel	59 (13.1%)	16 (3.49%)	$P < 0.0001$	4.1886	2.3712 to 7.3990
Joint abnormality	16 (3.56%)	5 (1.09%)	$P = 0.0191$	3.3552	1.2186 to 9.2378
Panic disorder	51 (11.4%)	14 (3.05%)	$P < 0.0001$	4.073	2.2205 to 7.4710
Special diet	47 (10.5%)	19 (4.14%)	$P = 0.0004$	2.7075	1.5625 to 4.6916
Stomach ulcer	19 (4.23%)	3 (0.65%)	$P = 0.0023$	6.7163	1.9734 to 22.8583
Thyroid disorder	31 (6.9%)	15 (3.27%)	$P = 0.0146$	2.1952	1.1683 to 4.1249
Vertigo	15 (3.34%)	3 (0.65%)	$P = 0.0091$	5.2535	1.5103 to 18.2734

* Gastroesophageal reflux disease

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Table 4
Non-significant reporting of pre-pregnancy conditions (HG vs controls).

	HG group (%)	Control group (%)	Significance		
Factor	$n = 449$	$n = 459$	(HG vs. control)	Odds ratio	95% CI
Amenorrhea	*19 (4.23%)*	27 (5.88%)	$P = 0.2588$	0.707	0.3873 to 1.2907
Arterial/intestinal/uterine rupture	*1 (0.22%)*	2 (0.44%)	$P = 0.5831$	0.51	0.0461 to 5.6450
Arthritis	*8 (1.78%)*	4 (0.87%)	$P = 0.2396$	2.0635	0.6169 to 6.9017
Attention deficit disorder	9 (2.00%)	5 (1.09%)	$P = 0.2704$	1.8573	0.6176 to 5.5855
Autism	*1 (0.22%)*	0 (0.00%)	$P = 0.4921$	3.0736	0.1249 to 75.6526
Balance disorder	*2 (0.45%)*	2 (0.44%)	$P = 0.9824$	1.0224	0.1434 to 7.2897
Bipolar	*6 (1.34%)*	0 (0.00%)	$P = 0.0767$	13.469	0.7565 to 239.8087
Birth defect	*5 (1.11%)*	6 (1.31%)	$P = 0.79$	0.8502	0.2576 to 2.8061
Blood clot	4 (0.89%)	3 (0.65%)	$P = 0.6839$	1.3663	0.3041 to 6.1396
Delayed gastric emptying	1 (0.22%)	1 (0.22%)	$P = 0.9876$	1.0223	0.0637 to 16.3953
Fainting spells	23 (5.12%)	13 (2.83%)	$P = 0.0812$	1.8523	0.9263 to 3.7038
Gum disease	12 (2.67%)	7 (1.53%)	$P = 0.2331$	1.7731	0.6917 to 4.5455
High blood pressure	8 (1.78%)	3 (0.65%)	$P = 0.1360$	2.7574	0.7268 to 10.4609
Hip dysplasia	3 (0.67%)	4 (0.87%)	$P = 0.727$	0.7651	0.1703 to 3.4382
Infertility	31 (6.90%)	25 (5.45%)	$P = 0.3624$	1.2875	0.7475 to 2.2175
Irregular periods	74 (16.5%)	63 (13.7%)	$P = 0.2467$	1.2404	0.8615 to 1.7858
Learning disability	10 (2.22%)	9 (1.96%)	$P = 0.7793$	1.139	0.4584 to 2.8298
Mitral valve prolapse	13 (2.90%)	11 (2.40%)	$P = 0.6399$	1.2143	0.5382 to 2.7399
Muscle or skeletal pain	14 (3.12%)	7 (1.53%)	$P = 0.1179$	2.0782	0.8308 to 5.1981
Other dental/gum diagnoses	6 (1.34%)	14 (3.05%)	$P = 0.0871$	0.4305	0.1640 to 1.1304
Ovarian hyperstimulation	0 (0.00%)	0 (0.00%)	$P = 0.9912$	1.0222	0.0202 to 51.6329
Pancreatitis	0 (0.00%)	1 (0.22%)	$P = 0.5092$	0.34	0.0138 to 8.3689
Polycystic ovaries	18 (4.01%)	11 (2.40%)	$P = 0.1717$	1.7009	0.7941 to 3.6431
Postural orthostatic tachycardia	4 (0.89%)	0 (0.00%)	$P = 0.1354$	9.2828	0.4983 to 172.9265
Raynaud's syndrome	14 (3.12%)	7 (1.53%)	$P = 0.1179$	2.0782	0.8308 to 5.1981
Schizophrenia	0 (0.00%	0 (0.00%)	$P = 0.9912$	1.0222	0.0202 to 51.6329
Scoliosis	29 (6.46%)	24 (5.23%)	$P = 0.4301$	1.2515	0.7168 to 2.1849
Seizures	5 (1.11%)	7 (1.53%)	$P = 0.5888$	0.7272	0.2291 to 2.3083
Skin disorder	13 (2.90%)	9 (1.96%)	$P = 0.3628$	1.4908	0.6308 to 3.5233
Tachycardia	11 (2.45%)	4 (0.87%)	$P = 0.0741$	2.8567	0.9028 to 9.0392

reported depression and anxiety following their HG pregnancies. However both conditions are not associated with recurrence risk (Magtira et al., 2015). Therefore, a possible explanation is that controls without a history of anxiety and/or depression were more likely to volunteer to participate in this study, biasing the findings.

Among the 20 pre-existing factors that were rarely reported by controls, 4 novel items (hypoglycemia, irritable bowel, panic disorder, and special diet) were reported in 10% or more women with HG. In the future, it may be of interest to determine whether pre-pregnancy treatment of hypoglycemia, irritable bowel, panic disorder, and/or changes to a restricted diet has an impact on severity of nausea and vomiting in pregnancy. Pre-pregnancy factors that have been linked to an increased risk of HG and were not addressed in this study include ethnicity (Vikanes et al., 2008), low or high body mass index (Vikanes et al., 2010b), younger age (Bailit, 2005), saturated fat intake (Signorello et al., 1998), and family history (Vikanes et al., 2010a, Zhang et al., 2011).

While five of seven common post-pregnancy items were also reported at an increased rate prior to HG, the remaining two items, missed work (reported by 68% cases vs 13% controls) and stretchmarks (38% cases vs 25% controls) may be increased due to the physical and psychological demands and the rapid weight loss and weight gain that can occur in HG pregnancies.

Fifty rare post-pregnancy conditions were reported at a significantly increased percentage in cases. Among these rare maternal outcomes, 23 were reported in 10% or more of women with HG, which can be divided into physical and psychosocial outcomes. The physical post-pregnancy conditions that were not reportedly significantly increased prior to pregnancy included irregular periods and permanent physical condition. The negative psychosocial post-pregnancy outcomes include increased reporting of change in eating habits, financial problems, change in attitude toward future pregnancy, inability of child care, inability of self care, intervention to prevent pregnancy, lost job, marital problems, moved, negative feelings toward baby, negative feelings toward others, negative mental experience, post-traumatic stress disorder, psychiatric problems, and relative required for care. Negative psychosocial issues following HG pregnancies have been noted previously (Poursharif et al., 2008) and suggest that even though nausea and vomiting may subside after birth, there is a lasting impact.

Table 5
Significant reporting of common post-pregnancy conditions (HG vs controls).

	HG group (%)	Control group (%)	Significance		
Factor	$n = 449$	$n = 459$	(HG vs. control)	Odds ratio	95% CI
Anxiety disorder	125 (27.8%)	24 (5.23%)	$P < 0.0001$	6.9927	4.4149 to 11.0756
Dental cavities	117 (26.1%)	60 (13.1%)	$P < 0.0001$	2.3435	1.6621 to 3.3044
Depression	112 (24.9%)	37 (8.06%)	$P < 0.0001$	3.7905	2.5452 to 5.6451
Migraine	72 (16.0%)	31 (6.75%)	$P < 0.0001$	2.6368	1.6927 to 4.1073
Missed work	304 (67.7%)	58 (12.6%)	$P < 0.0001$	14.4951	10.3272 to 20.3453
Premenstrual syndrome	76 (16.9%)	30 (6.54%)	$P < 0.0001$	2.9137	1.8675 to 4.5459
Stretchmarks	170 (37.9%)	114 (24.8%)	$P < 0.0001$	1.844	1.3868 to 2.4520

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Table 6
Significant reporting of rare post-pregnancy conditions (HG vs controls).

	HG group (%)	Control group (%)	Significance		
Factor	$n = 449$	$n = 459$	(HG vs. control)	Odds ratio	95% CI
Attention deficit disorder	9 (2.0%)	1 (0.22%)	$P = 0.0342$	9.3682	1.1819 to 74.2531
Blood clot	8 (1.78%)	1 (0.22%)	$P = 0.0463$	8.3084	1.0349 to 66.7042
Chronic constipation	26 (5.79%)	8 (1.74%)	$P = 0.0024$	3.4651	1.5516 to 7.7385
Chronic diarrhea	18 (4.01%)	3 (0.65%)	$P = 0.0032$	6.348	1.8567 to 21.7039
Chronic dizziness	56 (12.5%)	5 (1.09%)	$P < 0.0001$	12.9384	5.1318 to 32.6207
Chronic fatigue	23 (5.12%)	1 (0.22%)	$P = 0.0017$	24.7277	3.3249 to 183.9054
Chronic infection	17 (3.79%)	2 (0.44%)	$P = 0.0034$	8.9919	2.0652 to 39.1501
Chronic nausea	19 (4.23%)	0 (0.0%)	$P = 0.0093$	41.6272	2.5055 to 691.5949
Debilitating muscle weakness	36 (8.02%)	2 (0.44%)	$P < 0.0001$	19.9177	4.7659 to 83.2393
Delayed gastric emptying	12 (2.67%)	2 (0.44%)	$P = 0.0166$	6.2746	1.3963 to 28.1970
Divorce or separation	13 (2.9%)	1 (0.22%)	$P = 0.0119$	13.656	1.7788 to 104.8350
Eating habits changed	221 (49.2%)	10 (2.18%)	$P < 0.0001$	43.5215	22.6428 to 83.6522
Fainting spells	13 (2.9%)	1 (0.22%)	$P = 0.0119$	13.656	1.7788 to 104.8350
Fibromyalgia	12 (2.67%)	1 (0.22%)	$P = 0.0152$	12.5767	1.6284 to 97.1330
Financial problems	164 (36.5%)	2 (0.44%)	$P < 0.0001$	131.4877	32.3539 to 534.3729
Future pregnancy attitude change	350 (78.0%)	14 (3.05%)	$P < 0.0001$	112.1212	62.9704 to 199.6362
Gastroesophogeal reflux	35 (7.8%)	7 (1.53%)	$P = 0.0001$	5.4589	2.3985 to 12.4243
Gum disease	20 (4.45%)	6 (1.31%)	$P = 0.0075$	3.5198	1.4001 to 8.8485
Gynecologic disorder	32 (7.13%)	5 (1.09%)	$P = 0.0001$	6.9679	2.6897 to 18.0505
High blood pressure	15 (3.34%)	5 (1.09%)	$P = 0.0281$	3.1382	1.1309 to 8.7087
Husband strain (i.e. lost his job)	184 (41.0%)	2 (0.44%)	$P < 0.0001$	158.6566	39.0603 to 644.4371
Hypoglycemia	27 (6.01%)	2 (0.44%)	$P = 0.0003$	14.6197	3.4554 to 61.8550
Immune problems	35 (7.8%)	17 (3.7%)	$P = 0.0094$	2.1981	1.2127 to 3.9841
Inability of child care	45 (10.0%)	1 (0.22%)	$P = 0.0001$	51.0149	7.0003 to 371.7737
Inability of self care	261 (58.1%)	4 (0.87%)	$P < 0.0001$	157.9189	57.9793 to 430.1257
Inner ear disorder	9 (2.0%)	1 (0.22%)	$P = 0.0342$	9.3682	1.1819 to 74.2531
Intervention preventing pregnancy	68 (15.1%)	4 (0.87%)	$P < 0.0001$	20.3018	7.3387 to 56.1635
Irregular periods	48 (10.7%)	19 (4.14%)	$P = 0.0003$	2.772	1.6022 to 4.7960
Irritable bowel syndrome	45 (10.0%)	9 (1.96%)	$P < 0.0001$	5.5693	2.6888 to 11.5358
Joint abnormalities	16 (3.56%)	1 (0.22%)	$P = 0.0062$	16.9238	2.2348 to 128.1638
Lost job	135 (30.1%)	11 (2.4%)	$P < 0.0001$	17.5101	9.3139 to 32.919
Lost residence	16 (3.56%)	2 (0.44%)	$P = 0.0046$	8.4434	1.9300 to 36.9384
Marital problems	142 (31.6%)	5 (1.09%)	$P < 0.0001$	42.2762	17.1284 to 104.3462
Motion sickness	104 (23.2%)	21 (4.58%)	$P < 0.0001$	6.2874	3.8531 to 10.2596
Moved	81 (18.0%)	17 (3.7%)	$P < 0.0001$	5.7228	3.3321 to 9.8289
Muscle or skeletal pain	29 (6.46%)	5 (1.09%)	$P = 0.0002$	6.2695	2.4046 to 16.3468
Negative feelings toward baby	56 (12.5%)	8 (1.74%)	$P < 0.0001$	8.0331	3.7830 to 17.0581
Negative feelings toward others	252 (56.1%)	9 (1.96%)	$P < 0.0001$	63.9594	32.2201 to 126.9643
Negative mental experience	301 (67.0%)	1 (0.22%)	$P < 0.0001$	931.473	129.6433 to 6692.5332
Panic attacks	59 (13.1%)	7 (1.53%)	$P < 0.0001$	9.7685	4.4106 to 21.6350
Permanent physical condition	62 (13.8%)	0 (0.0%)	$P = 0.0004$	148.2258	9.1388 to 2404.1269
Positive mental change	227 (50.6%)	3 (0.65%)	$P < 0.0001$	155.4234	49.1981 to 491.0035
Post-traumatic stress disorder	59 (13.1%)	3 (0.65%)	$P < 0.0001$	22.9949	7.1521 to 73.9317
Psychiatric problems	231 (51.5%)	14 (3.05%)	$P < 0.0001$	33.6812	19.1760 to 59.1585
Relative required for care	107 (23.8%)	1 (0.22%)	$P < 0.0001$	143.2924	19.9011 to 1031.7386
Special diet	33 (7.35%)	10 (2.18%)	$P = 0.0005$	3.5618	1.7337 to 7.3172
Tachycardia	13 (2.9%)	3 (0.65%)	$P = 0.0189$	4.5321	1.2827 to 16.0136
Thyroid disorder	32 (7.13%)	15 (3.27%)	$P = 0.0104$	2.2715	1.2125 to 4.2552
TMJ (jaw joint dysfunction)	45 (10.0%)	11 (2.4%)	$P < 0.0001$	4.5365	2.3148 to 8.8904
Vertigo	12 (2.67%)	1 (0.22%)	$P = 0.0152$	12.5767	1.6284 to 97.1330

A major limitation of the study is that for the control population, the average year of the first pregnancy was 2002, a full year earlier than cases (2003), suggesting that the control group had on average an extra year between the pregnancy and the time of completing the survey. Therefore, the control population was significantly more likely to rely on memory for their survey compared to the cases. It is widely thought that a person's perception of negative aspects of an experience decrease over time (particularly with pregnancy), suggesting that the control population is more likely to report decreased prevalence or severity of negative conditions and characteristics based on the duration between pregnancy and the survey.

Another major limitation is that this is a case-control study with self-selected cases and controls picked out by the cases. Thus, we are looking at a study in which it is difficult to know whether the cases are representative of all cases of HG. The controls are clearly not a sample of the general population. This type of selection leads to an unknown degree of bias. One must consider the findings of this descriptive study as a hypothesis-generating endeavor. Future research should focus on determining whether the increase in reporting of specific pre- and post-pregnancy physical and psychosocial factors is generalizable to all women with HG.

Conflict of interest

The authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.autneu.2016.07.005.

Table 7
Non-significant reporting of post-pregnancy conditions (HG vs controls).

Factor	HG group (%) $n = 449$	Control group (%) $n = 459$	Significance (HG vs control)	Odds ratio	95% CI
Allergies	115 (25.6%)	106 (23.1%)	$P = 0.3767$	1.1466	0.8466 to 1.5530
Amenorrhea	27 (6.01%)	25 (5.45%)	$P = 0.7134$	1.1107	0.6343 to 1.9450
Arterial/intestinal/uterine rupture	0 (0.0%)	1 (0.22%)	$P = 0.5092$	0.34	0.0138 to 8.3689
Arthritis	12 (2.67%)	6 (1.31%)	$P = 0.1484$	2.0732	0.7713 to 5.5727
Balance disorder	3 (0.67%)	0 (0.0%)	$P = 0.1920$	7.2038	0.3710 to 139.8698
Barretts esophagus	1 (0.22%)	0 (0.0%)	$P = 0.4921$	3.0736	0.1249 to 75.6526
Bipolar disorder	7 (1.56%)	0 (0.0%)	$P = 0.0604$	15.5763	0.8869 to 273.5507
Custody issues	2 (0.45%)	0 (0.0%)	$P = 0.2914$	5.1341	0.2458 to 107.2442
Eating disorder	7 (1.56%)	1 (0.22%)	$P = 0.0643$	7.2534	0.8888 to 59.1969
Hearing loss	2 (0.45%)	0 (0.0%)	$P = 0.2914$	5.1341	0.2458 to 107.2442
Hip dysplasia	2 (0.45%)	1 (0.22%)	$P = 0.5586$	2.0492	0.1852 to 22.6802
Infertility	19 (4.23%)	11 (2.4%)	$P = 0.1268$	1.7996	0.8464 to 3.8260
Liver abnormality	3 (0.67%)	1 (0.22%)	$P = 0.3306$	3.0807	0.3192 to 29.7292
Mitral valve prolapse	8 (1.78%)	5 (1.09%)	$P = 0.3846$	1.6472	0.5347 to 5.0738
Myalgic encephalitis	1 (0.22%)	0 (0.0%)	$P = 0.4921$	3.0736	0.1249 to 75.6526
Pancreatitis	4 (0.89%)	0 (0.0%)	$P = 0.1354$	9.2828	0.4983 to 172.9265
Polycystic ovaries	10 (2.23%)	5 (1.09%)	$P = 0.1878$	2.0683	0.7013 to 6.0999
Raynauds	6 (1.34%)	6 (1.31%)	$P = 0.9694$	1.0226	0.3273 to 3.1947
Schizophrenia	0 (0.0%)	0 (0.0%)	$P = 0.9912$	1.0222	0.0202 to 51.6329
Scoliosis	15 (3.34%)	7 (1.53%)	$P = 0.0827$	2.2317	0.9012 to 5.5265
Seizures	1 (0.22%)	1 (0.22%)	$P = 0.9876$	1.0223	0.0637 to 16.3953
Skin abnormalities	14 (3.12%)	7 (1.53%)	$P = 0.1179$	2.0782	0.8308 to 5.1981
Stomach ulcer	6 (1.34%)	1 (0.22%)	$P = 0.0917$	6.2032	0.7438 to 51.7346

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