

Posttraumatic stress symptoms following pregnancy complicated by hyperemesis gravidarum

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Abstract

Objective. Hyperemesis gravidarum (HG) can be accompanied by severe physical and emotional distress. Most studies have focused on the physical and psychological stress associated with this condition during the affected pregnancy. This study explores posttraumatic stress symptoms (PTSS) and negative life outcomes following HG pregnancies.

Methods. A total of 610 women (HG = 377 and control = 233) were recruited and completed an online survey. χ^2 -square analyses were used to compare the HG and control groups on various life outcome variables.

Results. Eighteen percent of women with HG reported full criteria PTSS ($n = 68$). Negative life outcomes regarding financial and marital status, career, as well as psychological and physical well-being differed significantly for the HG groups compared to the control group ($0.001 < p < 0.05$).

Conclusions. PTSS is common following HG pregnancies and is associated with negative life outcomes including inability to breastfeed, marital problems, financial problems, and inability of self care.

Keywords: Nausea, pregnancy, posttraumatic stress disorder

Introduction

Hyperemesis gravidarum (HG), severe nausea and vomiting of pregnancy, accounts for over 285,000 hospital discharges in the US annually, with most authors reporting an incidence of 0.5%–2% [1,2]. HG can often result in dehydration, electrolyte disturbance, and nutritional deficiency mandating intravenous hydration. In severe cases, patients may require the use of parenteral nutrition. If left untreated, HG is associated with maternal complications including Wernicke's encephalopathy [3], central pontine myelinolysis [4], hepatic dysfunction [5], renal failure [6], and preterm delivery. Fetal and neonatal complications include low birth weight, intrauterine growth restriction, and fetal and neonatal death [7–9].

The most common treatment modalities include intravenous (IV) hydration and serotonin inhibitors [10]. However, treatment is not always effective, resulting in therapeutic termination in as many as 15.2% of cases [11], extreme weight loss of more than 15% of prepregnancy weight in more than a quarter of cases, and symptoms lasting throughout the entire pregnancy in as many as 22% of cases [12]. Investigation into the psychosocial burden of HG showed that 80% of women

reported a negative psychosocial impact, with posttraumatic stress self-reported in 10% of cases without extreme weight loss and more than 20% of pregnancies with extreme weight loss [12,13].

Several studies have shown that HG is associated with severe emotional distress during pregnancy. Pirimoglu et al. [14] concluded that cases with HG had significantly higher distress scores than controls, and Tan et al. [15] showed that 37.3% of participants fulfilled the criteria for both anxiety and depression during their HG pregnancy. Meighan and Wood [16] described HG as so debilitating that patients had little concern for anything else, including the fetus. Munch [17] showed that perceived delays in diagnosing and/or instituting treatment were viewed as contributing to unnecessary exacerbations of the illness and hospitalizations, increased emotional strain, and psychological stress.

While prior studies have demonstrated evidence of physical and emotional symptoms during HG pregnancies [18], studies of physical and emotional symptoms following pregnancy remain limited. In this study, we investigate whether a pregnancy complicated by HG is associated with postpartum stress symptoms and negative life outcomes.

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Methods

Sample and settings

This study is part of a larger investigation evaluating the genetics and epidemiology of HG. A total of 610 women have been recruited. Eligible patients were primarily recruited through advertising on the hyperemesis education and research foundation website at www.HelpHer.org. The inclusion criteria for cases were a diagnosis of HG and treatment with IV fluids and/or total parenteral nutrition/nasogastric feeding tube, independent of hospitalization because some treatments were given to patients in an outpatient setting. 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 and it would be difficult to justify the risks/benefits to normal control minors. Women over the age of 50 years were not included because the duration since the incident pregnancies raises the possibility of recall bias. Because multiple or abnormal gestations may be associated with HG due to unique physiological pathways, women with these types of pregnancies were also excluded.

Each case was asked to recruit a friend with at least two pregnancies that went beyond 27 weeks to participate as a control. Controls were eligible if they experienced normal (did not interfere with their daily routine) or no nausea/vomiting in their pregnancy, no weight loss due to nausea/vomiting, and no medical attention in their pregnancy due to nausea. Relatives of participants in the study were not included in the study as the case-control study depends on nonrelatedness of individuals in the study. There was a 3:2 ratio of HG patients ($n = 377$) to controls ($n = 233$). This study has been approved

by Institutional Review Boards, USC IRB # HS-06-00056 and UCLA IRB # 09-08-122-01A.

Study procedures

Participants were asked to submit their medical records and complete an online survey regarding family history, treatment, and outcomes. The majority of participants, both cases and controls, joined the study and began the survey during their pregnancies and were automatically prompted to complete the survey on outcome following their due date.

Online survey

An online survey was used to obtain information on a variety of demographic characteristics (e.g., age, gender, and ethnicity), preexisting conditions, pregnancy symptoms and treatments, and maternal and fetal outcomes. Full stress criteria was used as a proxy for posttraumatic stress symptoms (PTSS). The classification of full stress criteria was drawn from seven questions assessing the three posttraumatic stress disorder (PTSD) symptom categories: (1) reexperiencing, (2) avoidance/numbing, and (3) hyperarousal. The survey instrument is included in Appendix 1.

Statistical analyses

Data were analyzed using Statistical Program for Social Sciences (SPSS) version 15.0 software for Windows (SPSS, Chicago, IL). Descriptive statistics were generated for all demographic, pregnancy-related clinical and pregnancy-related outcome variables. χ -square analyses were performed to evaluate for differences in demographic and pregnancy-related clinical and outcome variables among three HG groups (HG, full stress symptom HG, and no HG). Participants were

Table I. Demographic information.

	<i>f</i> (%)			<i>p</i>		
	No HG (A, $n = 233$)	HG (B, $n = 309$)	Full criteria (C, $n = 68$)	A-B	B-C	A-C
Ethnicity						
Afro-American	1 (0.4)	5 (1.6)	2 (2.9)			
American- Indian - White	3 (1.3)	4 (1.1)	0 (0)			
Asian	2 (0.8)	2 (0.5)	0 (0)			
Hispanic	4 (1.7)	13 (4.2)	2 (2.9)			
Other	1 (0.4)	9 (2.9)	1 (1.5)			
White	224 (96.1)	276 (89.3)	63 (92.6)	0.26	0.66	0.66
Country of origin						
AUS	1 (0.4)	1 (0.3)	0 (0)			
CAN	3 (1.3)	2 (0.5)	0 (0)			
DEU	1 (0.4)	4 (1.0)	0 (0)			
GBR	3 (1.3)	1 (0.3)	0 (0)			
ISR	1 (0.4)	1 (0.3)	0 (0)			
NLD	0 (0)	1 (0.3)	0 (0)			
NZL	0 (0)	1 (0.3)	0 (0)			
UKR	0 (0)	1 (0.3)	0 (0)			
USA	222 (95.3)	295 (95.5)	68 (100)	0.91	0.99	0.99
Age (years)						
Range	25-53	23-55	23-47			
Mean	37	35	34			
SD	5	6	6	0.28	0.13	0.13

Table II. PTSS symptoms.

	f (%)		p
	HG (B, n = 309)	Full criteria (C, n = 68)	
Nightmares of HG	38 (12.3)	52 (76.5)	<0.001
Nightmares for more than a year after delivery/loss	78 (25.2)	63 (92.6)	<0.001
Reexperiencing			
Partial criteria	70 (22.7)	21 (30.9)	<0.001
Full criteria	23 (7.4)	47 (69.1)	
Avoided being reminded for more than a year after loss/delivery	10 (3.2)	44 (64.7)	<0.001
Detached	7 (2.3)	31 (45.6)	<0.001
Avoid situations that remind you of HG	29 (9.4)	46 (67.6)	<0.001
Avoidance/Numbing			
Partial criteria one	37 (12.0)	29 (42.6)	<0.001
Partial criteria two	4 (1.3)	25 (36.8)	
Full criteria	0 (0)	14 (20.6)	
Watchful	2 (0.6)	27 (36.7)	<0.001
Watchful for more than a year after loss/delivery	30 (9.7)	58 (85.3)	<0.001
Hyperarousal			
Partial criteria one	32 (10.4)	51 (75)	<0.001
Full criteria two	0 (0)	17 (25)	

categorized as exhibiting full criteria for full stress criteria symptoms if they exhibited at least one symptom from each of the three PTSD categories. All calculations used actual values. Less than 1% of the participants had missing data and so adjustments were not made for missing data.

Results

Demographic characteristics

As shown in Table I, the sample was mostly Caucasian (92%) and from USA (96%). The average age was 35.3 years (SD = 6.0). No significant differences were found among the groups for any demographic characteristic.

Percentage of patients with HG and HG with full criteria of stress symptoms

Among 377 participants with HG, 18% (n = 68) of those patients met the qualifications for full stress criteria. As shown in Table II, there was a significant difference between the proportions of participants with HG and of the women with full stress symptom criteria HG in the PTSD-related stress symptom categories of reexperiencing (p < 0.001), avoidance/numbing (p < 0.001), and hyperarousal (p < 0.001). Among controls, a significantly lower percentage of women reported psychiatric problems after pregnancy than both the HG group (p < 0.001) and the full stress criteria HG group (p < 0.001).

Associated outcomes

As shown in Table III, there was a significant difference in the proportion of women who did not breastfeed (p < 0.001), who missed time from work or school (p < 0.001), who lost or quit their jobs (p < 0.001), who had marital and financial problems (p < 0.001), and who were unable to provide child

Table III. Outcomes associated with PTSS following pregnancy.

	f (%)			p		
	No HG (A, n = 233)	HG (B, n = 309)	Full criteria (C, n = 68)	A-B	B-C	A-C
Baby did not receive breast milk	25 (10.7)	109 (35.3)	22 (32.4)	<0.001	0.38	0.65
Difficulty producing breast milk	36 (15.5)	44 (14.2)	20 (29.4)	0.14	<0.05	<0.05
Persistent negative feelings toward child due to pregnancy experience	0 (0)	7 (2.3)	5 (7.4)	0.58	<0.05	<0.05
Missed time from work/school postpartum	11 (4.7)	146 (47.2)	47 (69.1)	<0.001	0.001	0.001
Lost job/quit school postpartum	1 (0.4)	53 (17.2)	18 (26.5)	<0.001	0.057	0.08
Marital problems postpartum	1 (0.4)	57 (18.4)	34 (50)	<0.001	<0.001	<0.001
Divorce postpartum	1 (0.4)	12 (4)	2 (2.9)	0.13	0.52	0.71
Financial problems postpartum	0 (0)	64 (20.7)	38 (55.9)	<0.001	<0.001	<0.001
Lost house/residence postpartum	0 (0)	10 (3.2)	3 (4.4)	0.057	0.43	0.63
Inability of child care postpartum	0 (0)	20 (6.5)	10 (14.7)	<0.05	<0.05	<0.05
Inability of self-care postpartum	2 (0.8)	96 (31.0)	37 (54.4)	<0.001	<0.001	<0.001
Psychiatric problems postpartum	2 (0.8)	87 (28.2)	57 (83.8)	<0.001	<0.001	<0.001

care ($p < 0.05$) or self-care ($p < 0.001$) postpartum between the HG and control groups. As shown in Table III, there was a significant difference in the percentages of women with no HG to women with full stress symptom criteria HG in producing breast milk ($p < 0.05$), in having persistent negative feelings toward their child after birth due to their pregnancy experience ($p < 0.05$), missed time from work and school ($p = 0.001$), marital and financial problems ($p < 0.001$), and in inabilities of child care ($p < 0.05$) and self-care ($p < 0.001$) postpartum.

Discussion

This is the first cross-sectional examination of stress symptoms and maternal outcomes in participants with HG and confirms the hypothesis that women with HG are more likely to experience stress symptoms and negative life outcomes after pregnancy compared to women without HG. Full criteria PTSS are common (18%) following pregnancies complicated by HG. These findings are consistent with a previous study by Poursharif et al. [13] that examined the psychosocial burden of HG patients. Poursharif et al. [13] found that 80% of a cohort of HG patients ($n = 626$) reported negative socioeconomic changes (job loss or difficulties), attitude changes toward pregnancy (including fear of future pregnancies), and psychiatric issues (including depression and anxiety). Furthermore, 10% of the cohort of women with HG self-reported posttraumatic stress [13].

The results of this study show that a significantly greater percentage of women with HG experienced stress symptoms of PTSD and negative psychosocial outcomes after pregnancy than the control group of women with unaffected pregnancies. As one might predict, this study also found that a significantly larger percentage of women with HG and full criteria for PTSS, reported negative psychosocial outcomes than both the no HG group and the general HG group. It appears that women reporting PTSS criteria from all three symptom groups of reexperiencing, avoidance/numbing, and hyperarousal may be at a greater risk for lasting negative psychosocial outcomes following a pregnancy complicated by HG. It is possible that some of the factors analyzed may have been present prior to or during pregnancy, independent of HG. Indeed, women with full PTSS criteria reported more anxiety and depression prior to pregnancy than those with HG who did not experience full PTSS criteria. However, this difference was not statistically significant and participants were asked to report only on stressors that were 'a direct result of this pregnancy,' not, for example, on preexisting anxiety, depression, nor marital conflict. In addition, the control group reported significantly less postpartum psychiatric problems (0.8%, compared to 83.8% in the full criteria PTSS group), so the 'background' level of 'normal' anxiety and postpartum depression are not likely to significantly affect the results of this study, and the findings are likely due primarily to HG.

A major strength of this study stems from the collaboration with the HER Foundation, which allowed collection of outcome data on a large sample of women affected by HG. To date, most studies of HG have been small case series or population studies relying on hospital databases with no information on maternal outcome. Thus, this study is the first case-control report of its kind. However, additional investigations are needed because only part of the PTSD spectrum was explored in this study.

Admittedly, this study has some methodological concerns. One potential limitation arises from the use of an internet-based survey. While internet-based research is quickly becoming scientifically recognized as a reliable recruiting tool, the study population consists only of cases with internet access, and thus may represent women of higher education and income. We feel, however, our study remains generalizable since we have no reason to suspect that education level and income would affect the likelihood of having PTSS and other associated findings. We cannot rule out the possibility that women more severely affected physically and/or emotionally may have been more willing to search for information and continue their participation in the study than the general population. However, since most women were enrolled in the study during their pregnancy, the severity of their postpartum symptoms should not have influenced their participation.

Another limitation is that the study is based on self-reports, which can lead to misclassification of PTSS symptoms and outcomes. However, we believe it would be highly unlikely for women to misrepresent themselves, as the affected individuals are required to have been treated with IV therapy for severe nausea and vomiting and asked to send in medical records to confirm treatment.

Finally, the use of self-selection of friend controls may introduce some bias. However, this study is a part of a larger study on the genetics and epidemiology of HG that covers 27 pages of survey questions (approximately 30 questions on the participant's background, 18 questions relating to each pregnancy, and 24 relating to pregnancy outcomes), of which only a subset were analyzed herein. Therefore, it is unlikely that friend controls of participants, who primarily joined the study while pregnant, were selected with a bias related to PTSS. Additionally, analysis of survey data using the same participants and methods has been published previously [19].

The cause of HG remains unknown. While previous studies have noted a possible psychogenic origin, other researchers have indicated less of a psychiatric influence. For example, Seng et al. [20] found that less than 10% of patients have a psychiatric disorder preceding HG and Simpson et al. [21] found no evidence for a psychosomatic etiology. More recent studies suggest a genetic component [19,22].

The findings of this study indicate that HG can often result in PTSS and is significantly associated with complications including difficulty producing breast milk, marital difficulties, financial problems, and inability of self-care postpartum. This suggests that HG can lead to a prolonged impact on both maternal, child, and family well being. Future research should focus on (1) how to identify at-risk subjects through genetic and epidemiologic analyses, (2) long-term follow-up studies on duration of PTSS symptoms and outcomes, and (3) analysis of the impact on infant and child. Additionally, the influence of interventions such as more effective treatment of HG and supportive postpartum care to lessen PTSS needs to be evaluated.

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References

1. Wier LM, Levit K, Stranges E, Ryan K, Pfunter A, Vandivort R, Santora P, Owens P, Stocks C, Elixhauser A. HCUP facts and figures: statistics on hospital-based care in the United States,

2008. Rockville, MD: Agency for Healthcare Research and Quality; 2010 (<http://www.hcup-us.ahrq.gov/reports.jsp>).
2. Verberg MF, Gillott DJ, Al-Fardan N, Grudzinskas JG. Hyperemesis gravidarum, a literature review. *Hum Reprod Update* 2005;11(5):527–539.
 3. Wood P, Murray A, Sinha B, Godley M, Goldsmith HJ. Wernicke's encephalopathy induced by hyperemesis gravidarum. *Br J Obstet Gynaecol* 1983;90(6):583–586.
 4. Peeters A, Van de Wyngaert F, Van Lierde M, Sindic CJM, Laterre EC. Wernicke's encephalopathy and central pontine myelinolysis induced by hyperemesis gravidarum. *Acta Neurol Belg* 1993;93:276–282.
 5. Adams RH, Gordon J, Combes B. Hyperemesis gravidarum. I. Evidence of hepatic dysfunction. *Obstet Gynecol* 1968;31:659–664.
 6. Hill JB, Yost NP, Wendel Jr GD. Acute renal failure in association with severe hyperemesis gravidarum. *Obstet Gynecol* 2002;100(5 pt 2):1119–1121.
 7. Dodds L, Fell DB, Joseph KS, Allen VM, Butler B. Outcomes of pregnancies complicated by hyperemesis gravidarum. *Obstet Gynecol* 2006;107(2 Pt 1):285–292.
 8. Bailit JL. Hyperemesis gravidarum: epidemiologic findings from a large cohort. *Am J Obstet Gynecol* 2005;193(3 pt 1):811–814.
 9. Kallen B. Hyperemesis during pregnancy and delivery outcome: a registry study. *Eur J Obstet Gynecol Reprod Biol* 1987;26:291–302.
 10. Goodwin TM, Poursharif B, Korst LM, MacGibbon K, Fejzo MS. Secular trends in the treatment of hyperemesis gravidarum. *Am J Perinatol* 2008;25(3):141–147.
 11. Poursharif B, Korst L, MacGibbon KW, Fejzo MS, Romero R, Goodwin TM. Voluntary termination in a large cohort of women with hyperemesis gravidarum. *Contraception* 2007;76(6):451–455.
 12. Fejzo MS, Poursharif B, Korst LM, Munch S, Romero R, Goodwin TM. Symptoms and pregnancy outcomes associated with extreme weight loss among women with hyperemesis gravidarum. *J Womens Health* 2009;18(12):1981–1987.
 13. Poursharif B, Fejzo MS, MacGibbon KW, Korst LM, Romero R, Goodwin TM. The Psychosocial burden of hyperemesis gravidarum. *J Perinatol* 2008;28(3):176–181.
 14. Pirimoglu ZM, Guzelmeric K, Alpay B, Balcik O, Unal O, Turan MC. Psychological factors of hyperemesis gravidarum by using the SCL-90-R questionnaire. *Clin Exp Obstet Gynecol* 2010;37(1):56–59.
 15. Tan PC, Vani S, Lim BK, Omar SZ. Anxiety and depression in hyperemesis gravidarum: prevalence, risk factors and correlation with clinical severity. *Eur J Obstet Gynecol Reprod Biol* 2010;149(2):153–158.
 16. Meighan M, Wood AF. The impact of hyperemesis gravidarum on maternal role assumption. *J Obstet Gynecol Neonatal Nurs* 2005;34(2):172–179.
 17. Munch S. A qualitative analysis of physician humanism: women's experiences with hyperemesis gravidarum. *J Perinatol* 2000;20:540–547.
 18. Munch S, Korst LM, Hernandez GD, Romero R, Goodwin TM. Health-related quality of life in women with nausea and vomiting of pregnancy: the importance of psychosocial context. *J Perinatol* 2011;31(1):10–20.
 19. Zhang Y, Cantor RM, Macgibbon K, Romero R, Goodwin TM, Mullin PM, Fejzo MS. Familial aggregation of hyperemesis gravidarum. *Am J Obstet Gynecol* 2011;204(3):230e1–7.
 20. Seng JS, Schrot JA, van De Ven C, Liberzon I. Service use data analysis of pre-pregnancy psychiatric and somatic diagnoses in women with hyperemesis gravidarum. *J Psychosom Obstet Gynaecol* 2007;28(4):209–217.
 21. Simpson SW, Goodwin TM, Robins SB, Rizzo AA, Howes RA, Buckwalter DK, Buckwalter JG. Psychological factors and hyperemesis gravidarum. *J Womens Health Gend Based Med* 2001;10(5):471–477.
 22. Vikanes A, Skjaerven R, Grjibovski AM, Gunnes N, Vangen S, Magnus P. Recurrence of hyperemesis gravidarum across generations: population based cohort study. *BMJ* 2010;29:340.