



Depression Associated with Hyperemesis Gravidarum among Pregnant Females Attending Zagazig University Hospitals: A Case Control Study

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ABSTRACT

Background: Hyperemesis gravidarum (HG) is characterized by intractable nausea and vomiting, dehydration, large ketonuria, and loss of more than 5% of pre-pregnancy weight. HG adversely affect maternal wellbeing, significantly leads to physical, psychological, social consequences and hospitalization. The psychological component of HG remains unclear; and the relationship between HG and psychological problems such as depression is not completely understood. **Aim:** To assess the relationship between HG and psychological problems mainly depression; and to assess its presence and severity in pregnant women with and without HG. **Methods:** A case-control study on 26 cases of pregnant women hospitalized with the diagnosis of HG and 26 pregnant women with nausea and vomiting of pregnancy were evaluated as the control group. All patients in the study completed the 24-hour Pregnancy Unique Quantification of Emesis and Nausea (PUQE) , Beck depression inventory (BDI). **Results:** There was a high statistical significant difference between HG cases and controls regarding frequency of emesis ,retching and self-evaluation of well-being. Mean of BDI was 30.69±5.4 in HG cases while it was 16.69 ±6.62 in control group (p <0.05) with high statistical significant difference. **Conclusion:** Depression was more common and severe in cases with HG compared with controls.

Key words: Hyperemesis gravidarum, Depression, Nausea, Vomiting.

INTRODUCTION

Nausea and vomiting in pregnancy (NVP) is one of the most common symptoms of pregnancy affecting 50–85% of all women during the first half of pregnancy [17]. NVP range from mild to moderate symptoms up to severe ,the severest form of NVP is called hyperemesis gravidarum (HG) [6]. Unlike NVP, hyperemesis gravidarum (HG) is characterized by very severe and debilitating symptoms [12].

Hyperemesis gravidarum (HG) is defined as “persistent and excessive vomiting starting before the end of the 22nd week of gestation and further subdivides the condition into mild and severe, with severe being associated with metabolic disturbances such as carbohydrate depletion, dehydration, or electrolyte imbalance .HG is a diagnosis of exclusion, characterized by

prolonged and severe nausea and vomiting, dehydration, large ketonuria, and more than 5% body weight loss” [19]. Hyperemesis gravidarum affects nearly 0.3%–3.6% of all pregnancies worldwide [3]. HG is considered a disease of unknown pathophysiological origin [9]. But it is widely acknowledged that it has a multifactorial theories including genetic, endocrine, and gastrointestinal factors are involved in its pathogenesis [6]. Hyperemesis gravidarum (HG) has a great impact on maternal quality of life and wellbeing [10]. HG can also affect the psychological state of pregnant women [18]. As it significantly leads to physical, psychological, social consequences and causes financial problems [16]. It is also a major reason for hospital admission throughout pregnancy [12]. Psychological illness has been reported as both a

complication, and predisposing factor for HG even though there remains a debate regarding the direction of association and despite recognition of the severity of symptoms, the negative effects on women's lives can sometimes be underappreciated by health professionals, social workers and the general public [7]. There is a significantly higher rate of depression in women with HG compared to healthy pregnant women [15]. Unfortunately depression causes a negative impact on employment, household responsibilities, parenting and family relationships [6]. So an urgent shift in care and treatment to holistically approach that appreciates, addresses and manages the psychological symptoms caused by HG [15]. Although many recent studies demonstrated higher rates of depression in pregnant women with HG, few studies have evaluated the cause-and-effect relationship of that psychological disorder and pregnancy [18].

So the aim of this case-control study is to assess presence and severity of depression in pregnant women with and without hyperemesis gravidarum and to assess the relationship between hyperemesis gravidarum and depression.

PATIENTS AND METHODS

Setting and sample

The patients were selected from women with HG hospitalized in the Obstetric Inpatient ward of Zagazig University Hospital. The study was approved by the Zagazig University faculty of medicine ethics committee. The study's objectives and procedures were explained, they were reassured about the strict confidentiality of any obtained information, and written informed consent was given. A letter obtained from faculty of medicine of Zagazig University to the Obstetrics and Gynecology hospital in the same university.

Inclusion criteria

Age (18-35y), viable intrauterine pregnancy confirmed by precise date of the last menstrual period and an ultrasound scan and during the first trimester of pregnancy.

Exclusion criteria

Pregnant women with previous diagnosis of psychiatric disorders (e.g. depression, anxiety, eating disorders, bipolar disorder), History of any medical problem (e.g. endocrine abnormalities, gastrointestinal, cardiovascular and pulmonary system disease), Medication (including: anti-depressants, Anti psychotics. or other psychiatric drugs during the last 6 months and multiple pregnancies. Twenty-six patients with HG who required hospitalization due to dehydration, ketonuria, weight loss, and severe nausea and vomiting during their first trimester were included in the study. Gestational week was detected with ultrasound screening on the basis of the last menstruation date. After recording the participants' sociodemographic characteristics in the obstetric clinic, after receiving medical treatment, patients with HG completed the modified 24-hour pregnancy unique quantification of emesis and nausea (PUQE) then Beck depression inventory (BDI).

A control group of 26 pregnant women with normal nausea and vomiting during the first trimester was recruited from the obstetric outpatient clinic. The control group also completed the same questionnaires. Each questionnaire took about 5-10 minutes to be filled and all the questionnaires were filled in one session in both groups.

Measures

1-Sociodemographic characteristics of the women included seven domains:

- Education and cultural domain (for both husband & wife)
- Occupation domain (for both husband & wife)
- Family possessions domain
- Family domain
- Home sanitation domain
- Economic domain
- Health care domain

Social class was classified into low, middle, and high level depending on the score calculated (84).

-Low (2nd quartile ≤ 42)

-Middle (3rd quartile ≤ 63)

-High level (4th quartile ≤ 84)

2-Modified 24-hour PUQE (Pregnancy unique quantification of emesis and nausea):

developed in order to assess the severity of emesis (nausea and vomiting) in pregnancy [13]. The three PUQE questions each have a rating from 1–5, thus the composite sum (PUQE-score) ranged from 3–15. A score between 3–6 points was defined as mild NVP, 7–12 points as moderate NVP and scores ≥ 13 points was classified as severe NVP/HG [15]. The QOL question was a rating scale of the woman's wellbeing at present with a range between zero (the worst possibly imaginable) and ten (equaled as good as she felt before the start of this pregnancy [15]).

3-Beck depression inventory (BDI): The BDI is a 21-item self-report questionnaire that assesses severity of depression. Individuals are asked to rate themselves on a 0–3 spectrum (0 = least, 3 = most) with a score range of 0–63. The cut-offs used are: 0–8, no depression; 9–13, minimal depression; 14–19, mild depression; 20–28, moderate depression; and 29–63, severe depression. The total score is the sum of all items [1].

Data analysis

• The collected data were analyzed by computer using Statistical Package of Social Services version 24 (SPSS), Data were represented in tables and graphs.

• Continuous Quantitative variables e.g. age were expressed as the mean \pm SD & median (range), and categorical qualitative variables were expressed as absolute frequencies (number) & relative frequencies (percentage).

• Suitable statistical tests of significance e.g.: TEST: 31.636, Mann Whitney U test and Chi-square test were used after checked for normality.

• The results were considered statistically significant when the significant probability was less than 0.05 ($P < 0.05$). P -value < 0.001 was considered highly statistically significant (HS), and P -value ≥ 0.05 was considered statistically insignificant (NS).

RESULTS

The mean age of the studied Hyperemesis gravidarum cases was 24 ± 2.46 years old, with a range from 20 to 28 years old, while mean age of nausea and vomiting of pregnancy (NVP) group was (25.04 ± 5.02 yrs. old) with no statistical significant difference between both groups in age and occupation as most of HG cases and nausea and vomiting of pregnancy (NVP) were house wives (92.3% and 73.1%) respectively (Table 1).

Table (1): Frequency distribution of sociodemographic characteristics of the Studied groups (No=52)

Item	Hyperemesis gravidarum (N=26)		Nausea and vomiting of pregnancy (NVP) (N=26)		Test	P-value
	No.	%	No.	%		
Age (years)						
• Mean \pm SD	24 \pm 2.46		25.04 \pm 5.02		*338.00	1.000
• Median (Range)	24 (20-28)		23.5(20-41)			(NS)
Education						
Illiterate	6	23.1	3	11.5	#13.520	0.035 (S)
Read and write	8	30.8	0	0.0		
Primary/Preparatory education	2	7.7	4	15.4		
Secondary	4	15.4	9	34.6		
Intermediate/institute	2	7.7	5	19.2		
University	4	15.4	5	19.2		
Occupation						

Item	Hyperemesis gravidarum (N=26)		Nausea and vomiting of pregnancy (NVP) (N=26)		Test	P-value
	No.	%	No.	%		
Non-working /house wife	24	92.3	19	73.1	#4.248	0.373 (NS)
Unskilled manual worker	0	0.0	1	3.8		
Skilled manual worker	0	0.0	1	3.8		
Semiprofessional / clerk	2	7.7	4	15.4		
Professional	0	0.0	1	3.8		

* Mann Whitney U test.

Chi-square test.

P < 0.05 is significant.

NS: Not significant.

Table (2): Socioeconomic level of the Studied groups (No=52)

Item	Hyperemesis gravidarum (N=26)		Nausea and vomiting of pregnancy (NVP) (N=26)		Test	P-value
	No.	%	No.	%		
Residence						
• Rural	12	46.2	13	50.0	0.077	0.782 (NS)
• Urban	14	53.8	13	50.0		
Socioeconomic level						
Low (2 nd quartile ≤42)	22	84.6	8	30.8	15.581	0.000* (HS)
Middle (3 rd quartile ≤ 63)	4	15.4	17	65.4		
High level (4 th quartile ≤84)	0	0.0	1	3.8		

Chi-square test.**P < 0.05 is significant.****NS: Not significant.**

There was no significant difference between both groups regarding residence as less than half of HG cases are residents of rural areas (46.2%). As regard social class, most of HG cases had low socioeconomic status 84.6 % while about 2/3 of nausea and vomiting of pregnancy (NVP) were middle socioeconomic status with high statistical significance (Table 2).

Table (3): According to modified 24-hour pregnancy unique quantification of emesis and nausea (PUQE): Nausea and self –evaluation by rating of well-being among the Studied groups (No=52)

Item	Hyperemesis gravidarum (N=26)		Nausea and vomiting of pregnancy (NVP) (N=26)		Test	P-value
	No.	%	No.	%		
On average in a day, for how long have the woman feel nauseated or sick to stomach						
• Not at all	0	0.0	2	7.7		
• 1 hour or less	0	0.0	8	30.8		

Item	Hyperemesis gravidarum (N=26)		Nausea and vomiting of pregnancy (NVP) (N=26)		Test	P-value
	No.	%	No.	%		
• 2-3 hours	0	0.0	4	15.4	#19.333	0.000* (HS)
• 4-6 hours	6	23.1	2	7.7		
• > 6 hours	20	76.9	10	38.5		
On average in a day, have the woman vomited or thrown up						
• Did not throw up	0	0.0	4	15.4	#37.746	0.000* (HS)
• 1-2 times	2	7.7	13	50.0		
• 3-4 times	0	0.0	7	26.9		
• 5-6 times	16	61.5	1	3.8		
• ≥7 times	8	30.8	1	3.8		
On average in a day, how many times have the woman had retching or dry heaves without bringing anything up						
• Did not throw up	0	0.0	5	19.2	#27.649	0.000* (HS)
• 1-2 times	2	7.7	10	38.5		
• 3-4 times	0	0.0	4	15.4		
• 5-6 times	12	46.2	0	0.0		
• ≥7 times	12	46.2	7	26.9		
Self-evaluation by rating of well-being						
Mean ± SD	4.07±1.72		6.38±2.29		##135.00	0.000* (HS)
Median (Range)	4(2-7)		7(0-10)			

Chi-square test.

Mann Whitney U test.

P < 0.05 is significant.

NS: Not significant.

There was a high statistical significant difference between both groups regarding frequency of emesis, retching and self-evaluation of well-being (p=0.000) (Table 3).

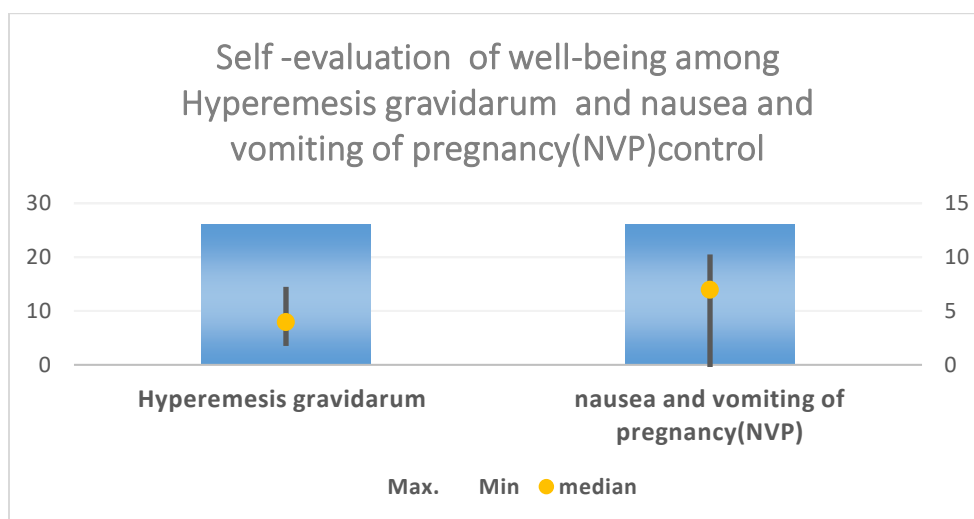


Figure (1): Self -evaluation among Hyperemesis gravidarum and nausea and vomiting of pregnancy (NVP)

Figure (1) demonstrates that nausea and vomiting of pregnancy (NVP) estimating that they were doing well, more than HG cases. The mean in hyperemesis cases was (4.07±1.72) while it was (6.38±2.29) in nausea and vomiting of pregnancy (NVP).

Table (4): The Beck depression inventory among the Studied groups (No=52)

Item	Hyperemesis gravidarum (N=26)		Nausea and vomiting of pregnancy (NVP) (N=26)		Test	P-value
	No.	%	No.	%		
Levels of Depression						
▪ Normal ups and downs	0	0.0	5	19.2	Fisher's	0.018*
▪ Mild mood disturbance	0	0.0	8	30.8	Fisher's	0.002*
▪ Borderline clinical depression	0	0.0	5	19.2	Fisher's	0.018*
▪ Moderate depression	14	53.8	8	30.8	#2.836	0.092
▪ Severe depression	12	46.2	0	0.0	#15.6	0.000*
The beck depression inventory						
Mean ± SD	30.69±5.4		16.69±6.62		##27.000	0.000* (HS)
Median (Range)	29(22-40)		16.5(5-29)			

TEST: 31.636 P- VALUE =0.000*

Chi-square test. ## Mann Whitney U test.

P < 0.05 is significant.

NS: Not significant.

Hyperemesis gravidarum cases suffered from moderate and severe depression (53.8% and 46.2%) respectively, while nausea and vomiting of pregnancy (NVP) ranged from normal ups and downs, mild mood disturbances, borderline clinical depression and moderate depression,

mean of the beck depression inventory was 30.69±5.4 in Hyperemesis gravidarum cases while it was 16.69 ±6.62 in nausea and vomiting of pregnancy (NVP), with high statistical significant difference (Table 4).

DISCUSSION

Nausea and vomiting in pregnancy (NVP) is common and affect up to 80% of all pregnancies. Unlike NVP, hyperemesis gravidarum (HG) is characterized by severe, debilitating symptoms, Besides its physical symptoms such as dehydration and electrolyte imbalance, HG can also affect quality of life and the psychological state of pregnant women^[18] Despite the common psychosomatic symptoms observed in patients with HG, the psychological components of the disease have not been fully understood^[2]. The psychological theory for describing the pathogenesis of HG suggests that either the presence of conversion or somatization disorder or the exaggerated response of a patient to stress may cause HG. Although nausea and vomiting during pregnancy were more commonly seen in dependent, hysterical, depressive, and anxious women, severe and persistent vomiting itself might also cause the psychological problems in patients^[18]. Our results are consistent with Topalahmetoğlu et al, who found that depression was significantly more common and more severe in the HG group than in the controls^[18].

In this study, the mean age of the studied Hyperemesis gravidarum cases was 24 ± 2.46 years old, with a range from 20 to 28 years old, while mean age of nausea and vomiting of pregnancy (NVP) group was (25.04 ± 5.02 yrs. old) with no statistical significant difference between both groups in age and occupation (**Table 1**) and this is consistent with a case-control study over 83 women with nausea and vomiting of pregnancy and 83 pregnant women without symptoms of nausea and vomiting as controls in Çanakkale, Turkey where the mean maternal age of study and control groups were 28.4 ± 5.5 and 29.4 ± 5.7 years, respectively^[4].

In the same table most of Hyperemesis gravidarum cases and nausea and vomiting of pregnancy (NVP) were house wives (92.3% and 73.1%) respectively and this is in agreement with the case-control study done in Selçuk University hospital in Turkey over 48 women with HG and 44 healthy pregnant

women where most of the participants were unemployed (92.4%)^[1].

In this study: The educational level in the nausea and vomiting of pregnancy (NVP) was significantly higher than in HG cases (34.6% secondary school vs 30.8% read and write) respectively ($p=0.035$) (**Table 1**). This is inconsistent with the case-control study over 100 pregnant women with HG and 100 healthy pregnant women as controls in Rize, Turkey and found that The educational level in HG patients was significantly higher than that of the control group ($p = 0.009$). This may be due to different locality of the study and near half of our both groups lived in rural areas where no enough attention paid for education of females.^[8]

In this study, regarding modified 24-hour pregnancy unique quantification of emesis and nausea (PUQE): Nausea and well-being scoring (**Table 3**) there was high statistical significant difference between both groups regarding rate of nausea, rate of vomiting ,rate of retching and well-being score ,and this is consistent with the findings of a prospective cohort study on 38 women hospitalized due to HG and 31 healthy pregnant controls attending routine antenatal Check-up at health centers in Norway and found that compared to controls, hyperemesis patients had significant higher PUQE-score (median 13 vs. 7) respectively (95% CI). And lower self- evaluation of well-being (median score 3 vs. 6) respectively (95% CI)^[5].

Regarding the well-being question, was a rating scale of the woman's wellbeing at present with a range between zero (the worst possibly imaginable) and ten (equaled as good as she felt before the start of this pregnancy). Well-being score was compared between patients and controls and found that vomiting of pregnancy (NVP) were doing well, more than HG cases mean(4.07 ± 1.72);(6.38 ± 2.29) and range from (2-7) median4 ;(0-10) median7 for hyperemesis cases and NVP respectively with high statistical significant difference (**Table 3**) . This is consistent with the cohort study that found the well-being score was significantly lower in

patients compared to control group (median score 3 vs. 6) (95% CI) among hyperemesis cases and NVP respectively [5].

In this study (Table 4) according to the beck depression inventory found that HG cases suffered from moderate and severe depression (53.8% and 46.2%) respectively, this is consistent with a prospective case-control study in Turkey over 78 pregnant women with HG and the control group consisted of 82 healthy pregnant women who never had experienced any nausea and vomiting and found that among the HG cases; 42 (53.9%) had moderate or severe depression disorder [2].

The current study also showed that the Mean of beck depression inventory (BDI) was 30.69 ± 5.4 in HG cases while it was 16.69 ± 6.62 in nausea and vomiting of pregnancy (NVP), ($p < 0.05$) with high statistical significant difference (Table 4) and this is in agreement with the case control study done over 5 HG cases and 41 healthy pregnant women as controls in Istanbul, Turkey and found that mean of BDI score for HG cases was 21.16 ± 11.77 and for NVP was 9.63 ± 6.09 ($p < 0.001$) with high statistical significant difference [11].

CONCLUSION

This study concluded that depression was more common and severe in patients with hyperemesis gravidarum compared with nausea and vomiting of pregnancy. The more severe symptoms of nausea and vomiting the more severe depression. The findings of this study indicated that psychological distress associated with hyperemesis gravidarum was a direct consequence. The psychological aspect of hyperemesis gravidarum is very important and the psychological burden of hyperemesis shouldn't be neglected.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgements

We are grateful to all women for participating in this case-control study.

Financial Disclosure

The authors declared that this study received no financial support.

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