

Frequency of Hyperemesis Gravidarum and associated risk factors among pregnant women

Mehwish Nawaz, Rishma, Sahib Gul Afridi, Asifullah Khan, Sulaiman Shams

Abstract

Objectives: To determine the frequency of hyperemesis gravidarum (HG) and associated factors among pregnant women.

Method: The hospital-based cross-sectional study was conducted from October 2016 to March 2017 at Lady Reading Hospital (LRH), Peshawar, District Headquarter Hospital (DHQ), Mardan, and District Headquarter Hospital, Nowshera, Khyber Pakhtunkhwa, Pakistan, and comprised data of 146 pregnant women with hyperemesis gravidarum. Data was compiled using pre-designed proforma. Frequency data of HG was also collected from the two hospitals of Peshawar and Mardan presenting in 2015 and 2016. Blood samples of all patients were analysed for serum electrolytes and complete blood count. Data was analyzed using Microsoft Excel 2010.

Results: Mean frequency of HG in LRH Peshawar and DHQ Mardan during 2015 and 2016 was 14.5% and 8.34% respectively. Of the 146 women, 103(70.5%) belonged to Nowshera, 24(16.4%) to Peshawar and 19(13%) to Mardan. The overall mean age was 27 ± 4.9 years, and maximum number of patients 67(45.89%) were aged 26-30 years. Major risk factor was urinary tract infection in Nowshera 30(29%) and Mardan 5(26.3%), while no major factor was identified in Peshawar. Patients in the first trimester were 59(57.28%) in Nowshera, 19(100%) in Mardan and 19(83.3%) in Peshawar, and primigravidas were 19(18.4%), 6(25%) and 8(42%) respectively. Overall, 119(81.5%) patients had no history of abortion.

Conclusion: The prevalence of hyperemesis gravidarum was high in Nowshera, Mardan and Peshawar, predominantly during the first trimester of pregnancy.

Keywords: Hyperemesis gravidarum, Frequency, Risk factors, Nausea, Vomiting. (JPMA 70: 613; 2020)
<https://doi.org/10.5455/JPMA.656>

Introduction

Hyperemesis gravidarum (HG) is a severe complication of pregnancy characterised by severe nausea and vomiting. It occurs in 0.3-2% of all pregnancies.¹ It usually results in dehydration, starvation, loss of >5% of pre-pregnancy body-weight and electrolyte imbalance. It is the commonest indication of hospitalisation in the first half of pregnancy, and is also a cause of pre-term delivery. Human chorionic gonadotropin (HCG) hormone is the most often stated likely cause of HG. The mechanism by which HCG causes HG remains unclear, but proposed mechanisms include a stimulating effect on the secretory processes in the upper gastrointestinal tract (GIT) or by stimulation of thyroid function because of its structural similarity to thyroid stimulating hormone (TSH).² Although most women with nausea and vomiting have symptoms limited to the first trimester, some patients have symptoms in their second trimester and a small percentage of women have prolonged course with symptoms extending until delivery. It is estimated that 70-80% of pregnant women experience nausea and vomiting. Nausea and vomiting in pregnancy

(NVP) is more common in younger women with education level <12 years, non-smokers and obese women.³ NVP has been associated with low income level and part-time employment status.⁴ Due to HG, career problems, difficulties in taking sick leave and loss of job during hospitalisation have been frequently reported by working women.⁵ Another cause of HG is high levels of thyroxine, oestrogen and progesterone. It is the most common cause of hospitalisation and is potentially lethal if not treated. States of high oestrogen concentration, such as low parity and high maternal body mass index (BMI), have been associated with higher incidence of HG.³ It is a common pregnancy complication and is a multifactorial condition that has been associated with many risk factors, including multiple gestations, trophoblastic disease, HG with prior pregnancy, foetal abnormalities, such as triploidy, trisomy 21 and hydrops foetalis, and nulliparity.⁶ More recently, it had been noted that mothers carrying fetuses with Down's Syndrome (DS), a condition associated with elevated HCG, are more likely to have NVP. Family history of HG is also a risk, with approximately 28% women reporting a history of HG in their mothers and 19% reporting their sisters had similar symptoms.⁷ HG is common in patients with low socioeconomic status and is most common in women carrying a female foetus.⁸ Studies on patients suffering from

.....
 Department of Biochemistry Abdul Wali Khan University, Mardan Pakistan.

Correspondence: Sahib Gul Afridi. Email: drafridi@awkum.edu.pk

HG show conflicting results, with some reporting effects on neonatal outcome and others reporting a rather beneficial association with pregnancy outcome.⁹ Hyperthyroidism has been associated with HG severity. Transient hyperthyroidism may be responsible for 40-70% of thyroid function abnormalities in pregnancy, and it usually resolves by 18 weeks without treatment.¹⁰ Several other mechanisms that have been proposed for HG include changes in GIT motility, thyroid dysfunction, hypofunction of the anterior pituitary and adrenal cortex, and abnormalities of corpus luteum.¹¹ Women who had HG were found to be more likely to consider termination.¹² HG incidence was higher in women with unplanned pregnancies compared to those with planned pregnancies.¹³ Genetic predisposition suggested that genetic component is essential in discovering an HG aetiology.¹⁴ RYR2 has two variants; L3277R is novel and G1886S is common. The common variant is segregated with HG in two families. By replication of G1886S, a study found that common variants rs790899 and rs1891246 were significantly associated with HG and weight-loss. A number of studies have been reported on HG prevalence and its association worldwide.^{13,15-20} To our knowledge, no such study has been conducted in the Khyber Pakhtunkhwa (KP) province of Pakistan. The current study was planned to fill that gap in literature by ascertaining HG incidence and its associated risk factors among the pregnant women hospitalized in selected regions of the province.

Subjects and Methods

The hospital-based cross-sectional study was conducted

from October 2016 to March 2017 at Lady Reading Hospital (LRH), Peshawar, District Headquarter Hospital (DHQ), Mardan, and DHQ Nowshera, KP, Pakistan, and comprised data of pregnant women, including primigravidas, aged 15-45 years with HG presenting with NVP and morning sickness, and admitted to hospital. Frequency data of HG for previous two years i.e. 2015 and 2016 was also obtained from LRH Peshawar and DHQ Mardan while no such data was available from Nowshera. Approval was taken from the Institute. For the purpose of the study, severe NVP was defined as having the feeling and vomiting at least three times a day. Those who vomited due to normal NVP were excluded. During the study period only 146 HG confirmed patients were recruited from all the three hospitals included in the study.

After taking informed consent from each subject, data was obtained using a pre-designed proforma which was filled by the patients themselves. Data collected included age, literacy, socio-demographic parameters, obstetric history and current antenatal risk factors. Blood samples were taken from the HG patients and were tested for serum electrolyte and complete blood count (CBC).

Data was analysed using Microsoft Excel 2010, and was expressed as frequencies and percentages as well as means and standard deviation (SD), as applicable.

Results

In 2015, the frequency of HG at LRH Peshawar and DHQ Mardan was 4680/32500 (14.4%) and 66/1065 (6.19%),

Table-1: Socio-demographic data of hyperemesis gravidarum (HG) patients (N=146).

Parameters	Nowshera	Means± SD	Mardan	Means± SD	Peshawar	Means±SD	Total	Means±SD
Age								
16-20	5(4.85%)		5(26.31%)		6(25%)		16(10.95%)	
21-25	18(17.47%)		6(31.57%)		9(37.5%)		33(22.60%)	
26-30	61(59.22%)		3(15.7%)		3(12.5%)		67(45.89%)	
31-35	15(14.56%)	27.8± 4.2	5(26.3%)	25.1±5.7	5(20.43%)	25±5.94	25(17.12%)	27±4.9
36-40	3(2.91%)		-		1(4.16%)		4(2.73%)	
41-45	1(0.97%)		-		-		1(0.68%)	
Total	103		19		24		146(99.97%)	
Education								
Illiterate	73(70.87%)		9(47.3%)		11(45.83%)		93(63.69%)	
Middle	4(3.88%)		2(10.52%)		1(4.16%)		7(4.79%)	
Matric	14(13.59%)		5(26.3%)		3(12.5%)		22(15.0%)	
Intermediate	2 (1.94%)		1(5.26%)		3(12.5%)		6(4.10%)	
Graduate	7 (6.79%)		2(10.5%)		5(20.83%)		14(9.58%)	
University	3(2.91%)		-		1(4.16%)		4(2.73%)	
Total	103		19		24		146(99.95%)	
Status								
Housewives	100 (97 %)		17(89.47%)		20(83.33%)		137(93%)	
Working women	3(2.91%)		2(10.52%)		4(16.66%)		9(6.16%)	
Total	103		19		24		146(99.96%)	

SD: standard deviation.

Table-2: Obstetric history of hyperemesis gravidarum (HG) patients (N=146).

Gravidity	Nowshera (%age)	Mardan	Peshawar (%age)	Total (%age)
1-2	30 (29.12%)	8 (42.10%)	13 (54.16%)	51 (34.93%)
3-4	35 (33.98%)	10 (52.63%)	8 (33.33%)	53 (36.30%)
5-6	38 (36.89%)	1 (5.26%)	3 (12.5%)	42 (28.76%)
Total	103	19	24	146 (99.99%)
Parity				
None	19 (18.44%)	7 (36.84%)	8 (33.33%)	34 (23.28%)
1-2	37 (35.92%)	10 (52.63%)	10 (41.66%)	57 (39.72%)
3-4	28 (27.18%)	2 (10.5%)	5 (20.83%)	35 (22.60%)
≥5	19 (18.44%)	-	1 (4.16%)	20 (14.38%)
Total	103	19	24	146 (99.98%)
Abortions				
None	85 (82.5%)	14 (73.68%)	20 (83.33%)	119 (81.5%)
1-2	10 (9.70%)	5 (26.31%)	4 (16.66%)	19 (10.95%)
≥3	8 (7.76%)	-	-	8 (5.47%)
Total	103	19	24	146
Outcomes of previous pregnancy				
None	17 (16.50%)	7 (36.84%)	8 (33.33%)	32 (21.91%)
NVD	82 (79.6%)	11 (57.89%)	13 (54.16%)	106 (72.60%)
CS	4 (3.88%)	1 (5.26%)	3 (12.5%)	8 (5.47%)
Total	103	19	24	146 (99.98%)

NVD: Normal vaginal delivery; CS- Caesarean section.

Table-3: Distribution of hyperemesis gravidarum (HG) patients on the basis of current antenatal risk factors (N=146).

Risk factors	Nowshera (%age)	Mardan (%age)	Peshawar (%age)	Total (%age)
None	27 (26.21%)	9 (47.36%)	21 (87.5%)	57 (39.04%)
Anorexia	2 (1.94%)	-	-	2 (1.36%)
Multiple pregnancy	-	1 (5.26%)	-	1 (0.68%)
Gastro-Intestinal (GIT) diseases	25 (24.27%)	-	-	25 (17.80%)
Urinary Tract Infection (UTI)	30 (29.12%)	5 (26.31%)	-	35 (23.97%)
Anaemia	12 (11.65%)	1 (5.26%)	1 (4.16%)	14 (9.64%)
Anaemia & UTI	3 (2.91%)	-	1 (4.16%)	4 (2.73%)
Hypertension	3 (2.91%)	1 (5.26%)	-	4 (2.73%)
Diabetic	-	-	1 (4.16%)	1 (0.68%)
GIT & High blood pressure	-	1 (5.26%)	-	1 (0.68%)
Anaemia & GIT diseases	-	1 (5.26%)	-	1 (0.68%)
UTI and hypertension	1 (0.97%)	-	-	1 (0.68%)
Total	103	19	24	146 (99.94%)

and the corresponding numbers in 2016 were 5040/34315(14.68%) and 101/883(11.43%).

Of the 146 women in the study, 103(70.5%) belonged to Nowshera, 24(16.4%) to Peshawar and 19(13%) to Mardan. The overall mean age was 27±4.9 years and maximum number of patients 67(45.89%) were aged 26-30 years (Table-1).

Obstetric history noted the gestational age and gravidity of the subjects as well as previous abortions, if any, and

outcome of previous pregnancies (Table-2; Figures-1, 2).

Major risk factor was urinary tract infection in Nowshera 30(29%) and Mardan 5(26.3%), while no major factor was identified in Peshawar (Table-3).

Serum electrolytes and CBC results of confirmed HG patients showed normal values for all parameters (data not shown) and revealed no potential association with the prevalence of HG in study samples ($p>0.05$).

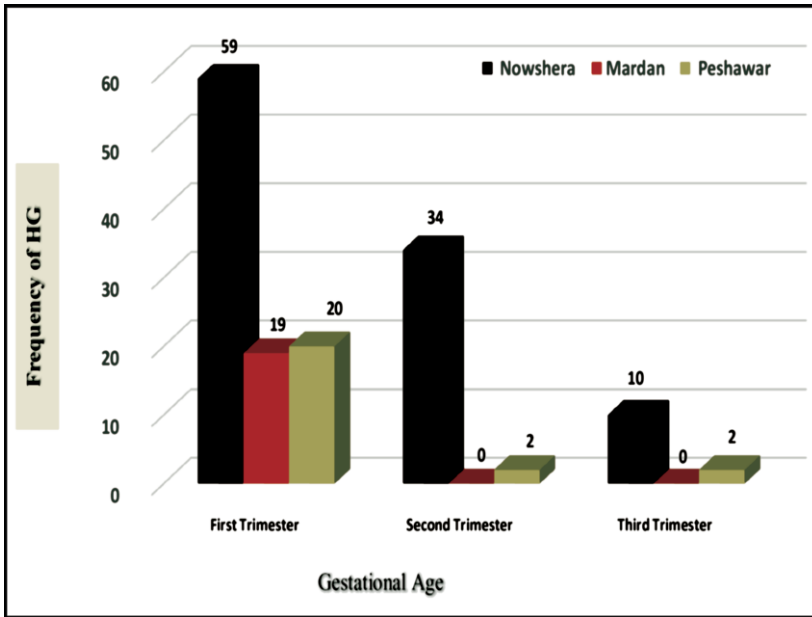


Figure-1: Distribution of hyperemesis gravidarum (HG) patients with respect to three stages of pregnancy (N=146).

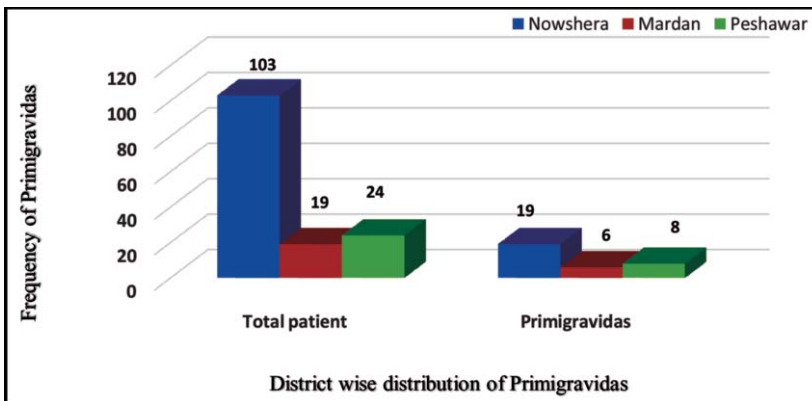


Figure-2: Frequency of hyperemesis gravidarum (HG) patients in primigravidas (N=146).

Discussion

HG, a severe complication in pregnancy, is defined by many as severe NVP.²¹ The HG prevalence in the current study is in agreement with some studies,¹⁵ and in contrast with others.^{16,17,20}

The current study noted the highest HG prevalence in the 26-30 years age group, which was in line with a study which reported 30.55% at age 25-29 years,²² and in contradiction with another study which reported the highest percentage at age 21-25 years.¹⁷

In the current study, majority of the women were admitted in their first trimester which was consistent with

earlier results.^{17,20} Of all the HG patients, 18.49% were primigravida in the current study and the finding was contradictory to 34.7% reported earlier.¹⁸ The present study revealed risk factors like UTI, GTI diseases and multiple pregnancy, which were somewhat consistent with one study¹⁷ and was in contrast to another which found hyperthyroidism, diabetes and previous molar pregnancy as HG risk factors.²⁰ In the current study, 69% women were illiterate, 93.8% were housewives and were unaware of the lethal aspects of HG. Similar results have been reported earlier.¹⁸ The current study also reported that there were no previous history of abortion in 81.5% subjects. An earlier study reported much higher percentage of abortions in HG patients.¹⁹

In terms of limitations, the current study has a much smaller sample size than what is necessary for better analysis. Also, genetic analysis of HG is required to find out the exact causes. Large-scale studies are recommended that may systematically review the risk factors and causal pathways of HG and evaluate the association between HG and its association with socio-economic status, geographic variation and other understudied parameters.

Conclusion

HG frequency was found to be high in Nowshera, Mardan and Peshawar, predominantly during the first trimester of pregnancy, with UTI being the major risk factor.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Kuru O, Sen S, Akbayir O, Goksedef BP, Özürmeli M, Attar E, et al. Outcome of pregnancies complicated by Hyperemesis Gravidarum. Arch Gynecol Obstet. 2012; 285:1517-21.
2. Poursharif B, Korst LM, MacgibbonKW, Fejzo MS, Romero R, Goodwin TM. Elective pregnancy termination in a large cohort of women with hyperemesis gravidarum. Contraception. 2007; 76:451-5.
3. Vikanes ÅV, Støer NC, Magnus P, Grjibovski AM. Hyperemesis gravidarum and pregnancy outcomes in the Norwegian mother and child cohort—a cohort study. BMC Pregnancy Childbirth. 2013;

- 13:169.
 4. Noel M, Lee MD, SumonaSaha, MD. Nausea and Vomiting of Pregnancy. *Gastroenterol Clin North Am.* 2011; 40: 309-334.
 5. Poursharif B, Korst LM, Fejzo MS, MacGibbon KW, Romero R, Goodwin TM. The psychosocial burden of hyperemesis gravidarum. *J Perinatology.* 2007; 1–6.
 6. EinarsonTR , Piwko C, Koren G . Quantifying the global rates of nausea and vomiting of pregnancy: a meta-analysis. *J Popul Ther Clin Pharmacol.* 2013; 20: e171-83.
 7. Roseboom TJ, Ravelli AC, Van der post JA, Painter RC. Maternal characteristics largely explain poor pregnancy outcome after Hyperemesis Gravidarum. *Eur J Obstet Gynecol Reprod Biol.* 2011; 156: 56-9.
 8. Fejzo MS, Ingles SA, Wilson M, Wang W, MacGibbon K, Romero R, et al. High prevalence of severe nausea and vomiting of pregnancy and Hyperemesis Gravidarum among relatives of affected individuals. *Eur J Obstet Gynecol Reprod Biol.* 2008; 141:13-7.
 9. Goodwin TM. Hyperemesis Gravidarum. *Clinical Obstetrics and Gynecology.* 1998; 41: 597-605.
 10. Verberg MF, Gillott DJ, Al-Fardan N, Grudzinskas JG. Hyperemesis gravidarum, a literature review. *Hum Reprod Update.* 2005; 5: 527-39.
 11. Hershman JM. Physiological and pathological aspects of the effect of human chorionic gonadotropin on the thyroid. *Best Pract Res Clin Endocrinol Metab.* 2004; 18:249-65.
 12. Poursharif B, Korst LM, Macgibbon KW, Fejzo MS, Romero R, Goodwin TM. Elective pregnancy termination in a large cohort of women with hyperemesis gravidarum. *Contraception.* 2007;76: 451-5.
 13. Aksoy AN. Hyperemesis Incidence in Planned versus Unplanned Pregnancy. *Eurasian J Med.* 2008; 40: 72-4.
 14. Fejzo MS, Myhre R, Conde LC, Macgibbon KW, Sinsheimer JS, Prasad MV, et al. Genetic analysis of Hyperemesis Gravidarum reveals association with intracellular calcium release channel (RYR2) *Mol Cell Endocrinol.* 2017; Elsevier. 2016; 439: 308-16.
 15. Chin RKH, Lao TTH, Kong AMY. Hyperemesis Gravidarum in Chinese women. *Obstet Gynaecol Res.* 1987; 13: 261-4.
 16. Tan PC, Jacob R, Quek KF, Omar SZ. The fetal sex ratio and the metabolic, biochemical, hematological and clinical indicators of severity of Hyperemesis Gravidarum. *BJOG.* 2006;113: 733-7.
 17. Mahmoud GA. Prevalence and risk factors of Hyperemesis Gravidarum among Egyptian pregnant women at the women's health center. *Med J Cairo.* 2012; 2: 161-8.
 18. Vikanes A, Gribrovski MA, Vangens S, Magnus P. Length of residence and risk of Hyperemesis Gravidarum among first generation immigrants to Norway. *Eur J Public Health.* 2008; 18: 460-5.
 19. Kamalak, Köşüş N, Köşüş A, Hizli C, Ayrim A, Kurt G. Is there any effect of demographic features on development of Hyperemesis Gravidarum in Turkish population? *Turk J Med Sci.* 2013; 43: 995-9.
 20. Kuru O, Sen S, Akbayır O, Goksedef BP, Özürmeli M, Attar E, et al. Outcome of pregnancies complicated by Hyperemesis Gravidarum. *Arch Gynecol Obstet.* 2012; 285:1517.
 21. McCarthy FP, Lutowski JE, Greene RA. Hyperemesis Gravidarum current perspective. *Int J Women's Health.* 2014; 6:719-25.
 22. Fiaschi L, Nelson-Piercy C, Tat LJ. Hospital admission for hyperemesis gravidarum: A nationwide study of occurrence reoccurrence and risk factors among 8.2 million pregnancies. *Hum Reprod.* 2016; 31:1675-84.
-