

A Prospective Case Control Study of Maternal-Fetal Outcomes in Pregnant Women with Hyperemesis Gravidarum at Tertiary Care Hospital Tirupati

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Abstract

Background: One of the most common symptoms seen in pregnant women before the 20th week of pregnancy is nausea and vomiting; an exaggeration of these symptoms, known as hyperemesis gravidarum (HG), can lead to maternal and foetal catastrophes, as well as death.

Aim: To investigate certain risk factors and maternal and foetal outcomes of Hyperemesis Gravidarum at Tirupati Tertiary Care Hospital.

Methods: A prospective hospital-based case control observational study was conducted on 60 pregnant women with diagnosed HG and 60 pregnant women without HG as a control group.

The prevalence of HG was found to be 2.8% among pregnant women in our study. The majority of these women (53.3%) were between the ages of 21 and 25. There is a strong association between hyperemesis gravidarum and preterm labour. There is an association between hyperemesis gravidarum and birth weight. There is a significant association between hyperemesis gravidarum and birth weight. Upper Lower & Lower socioeconomic status (66.6%), primigravida (71.7%), and BMI:18.5 (58.3%) were identified as important risk factors for developing HG. However, gestational age of less than 10 weeks (51.7%) was found to be less likely to be a risk for HG. Low birth weight (p=0.002), small for gestational age (p=0.02), IUGR (p=0.05), anaemia (p=0.04), maternal weight loss (p=0.002), ketonuria (p=0.01), and electrolyte imbalance (p=0.001) were all significantly associated with hyperemesis gravidarum.

Conclusion: Hyperemesis gravidarum has a significant impact on maternal health. Multiparity and a history of HG are risk factors for developing the condition, which should be monitored in at-risk pregnant women so that early intervention can be implemented to avoid any negative outcomes.

Keywords: Hyperemesis Gravidarum, Fetal Outcomes, Maternal Outcomes.

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Introduction

During pregnancy, 70% to 80% of pregnant women experience nausea and vomiting, with varying degrees of severity [1]. Hyperemesis gravidarum causes emotional and psychological disturbances and can significantly impair pregnant women's quality of life [2,3]. Hyperemesis gravidarum is associated with maternal weight loss, nutritional deficiencies, and fluid and electrolyte abnormalities, all of which can result in negative foetal and maternal outcomes [4,5].

Hyperemesis gravidarum is an extreme form of nausea and vomiting defined as Persistent Excessive Vomiting before 22 weeks of gestation, affecting approximately 0.3% to 3% of pregnancies [6] and characterised by protracted excessive vomiting, belching, retching, severe dehydration, and weight loss, necessitating hospitalisation [7]. India had the highest prevalence of 3.2%. It is most common between the fourth and tenth weeks of gestation and usually resolves by the twentieth week [8].

Hyperemesis gravidarum occurs at a high rate in multiple births, nulliparity, previous history of unsuccessful pregnancy, obesity, and similar history in previous pregnancy. A low rate of hyperemesis gravidarum is associated with advanced maternal age and a history of cigarette smoking [7]. Excessive vomiting in pregnancy causes weight loss, dehydration, acidosis due to starvation, alkalosis due to loss of hydrochloric acid in vomitus, and other electrolyte imbalances such as hypokalemia. Malnutrition and other serious complications may result. Some cases may develop hyperpyrexia, albuminuria, peripheral neuritis, and, in severe cases, ophthalmoplegia, ataxia, confusions (Wernickes encephalopathy), and hepatic changes [8,9]. According to some studies, hyperemesis gravidarum is associated with an increased risk of gestational diabetes mellitus, pregnancy-induced hypertension as

maternal outcomes, and small for gestational age (SGA) and preterm delivery as foetal outcomes [10]. Previous studies yielded contradictory results, necessitating further research into the potential effect of hyperemesis gravidarum on pregnancy outcome.

Despite the fact that this health problem is massive and has serious consequences, there is a scarcity of studies demonstrating the magnitude of the problem and the factors that contribute to it in our region. Hence, the primary goal of this study is to determine the prevalence of hyperemesis gravidarum and associated factors among women attending our teaching hospital's antenatal clinic.

The study could help all women affected by this health problem, as well as health care providers, find a long-term solution.

Materials and Methods

Study design: A prospective observational case-control study.

The sample size was calculated using Epi Info, a programme developed by the Centers for Disease Control and Prevention that can be accessed at <https://www.cdc.gov/epiinfo/index.html>.

First, the "STATCALC" option was chosen for sample size calculation, followed by "unmatched case-control studies." The sample size was estimated using a 95% confidence level, an 80% power of study, a 1:1 control-to-case ratio, a 5% alpha error, 2 as the expected odds ratio, and a 35% proportion of control exposed.

All pregnant women with excessive vomiting in the first trimester who attended the OPD or were admitted to the OBG department at the government maternity hospital, SVMC, Tirupati, were studied.

The study will take place between November 2020 and November 2021 at the Government Maternity Hospital at Sri Venkateswara

Medical College in Tirupati.

Data were gathered from all pregnant women who had been diagnosed with or had a history of hyperemesis gravidarum. Pregnant women who did not have hyperemesis gravidarum served as the control group.

All pregnant women with Molar pregnancy, Pregestational Diabetes Mellitus, Pregestational Hypertension, and all pregnant women with medical disorders that cause nausea and vomiting, such as pyelonephritis and appendicitis, were excluded.

All pregnant women with a singleton pregnancy who have been hospitalised and treated for hyperemesis gravidarum are included in the study. The control group consists of the same number of pregnant women with singletons who do not have hyperemesis graviduum.

All pregnant women with hyperemesis gravidarum are admitted and examined for signs of dehydration. Laboratory investigations such as complete blood picture, liver functional tests, renal functional tests, thyroid profile, serum electrolytes, and urine ketone bodies are performed, and other causes of vomiting such as acute gastroenteritis, intestinal obstruction, and others are ruled out. These women are treated with intravenous fluids and antiemetics and are discharged after tolerating oral foods and symptom improvement. These women are followed throughout their pregnancy, and their maternal and foetal outcomes are evaluated and compared to the control group. To avoid bias in selecting the control group, similar parameters are used as in cases. The following information is collected for each pregnant woman: age, obstetric score, gestational age at HG admission, number of episodes, hydration status, presence of ketonuria, any electrolyte imbalance, number of kgs lost by patient due to HG, antenatal complications if any, gestational age at delivery, mode of delivery, birth weight,

APGAR at 1st and 5th minute. The severity of HG was determined by the number of vomiting episodes and the gestational age at which the pregnant woman was hospitalised with hyperemesis gravidarum. The maternal outcomes studied were weight gain during pregnancy, abortions, gestational hypertension, gestational diabetes mellitus, anaemia, oligohydramnios, intrauterine growth restriction, gestational age of delivery, and mode of delivery. Neonatal outcomes assessed include the first- and fifth-minute APGAR scores, birth weight, and perinatal death.

Operational definitions

Cases are defined as women in their antenatal period who have been clinically diagnosed with HG by their doctor.

Controls: Pregnant women who had not been diagnosed with HG.

Hyperemesis gravidarum is defined as severe nausea and vomiting during pregnancy that prevents oral intake of food and leads to dehydration and ketonuria.

Statistical analysis: The Student's t test (independent, two-tailed) was used to determine the significance of the parameters in the study on a continuous scale between both groups (inter group analysis) on metric parameters. Fisher's exact test/chi-square test were used to determine the significance of the parameters in this study on a categorical scale between both groups. In all statistical tests, p value 0.05 was used to indicate a significant difference. Statistical analysis was performed with SPSS (IBM Corp. Version 20.0. Armonk, NY, USA).

Results

Hyperemesis gravidarum is more common in primigravida, or women between the ages of 21 and 25. Hyperemesis gravidarum is more common in people with low socioeconomic status. There is a strong association between

socioeconomic status and hyperemesis gravidarum (P value -0.001).

In the current study, 58.3% are underweight, 33.3% have a normal BMI, and 5% are overweight. There is an association between hyperemesis gravidarum and preconception BMI. Pregnant women who are underweight are more likely to develop Hyperemesis gravidarum.

The onset of hyperemesis gravidarum occurred in 51.7% of cases between 6- 10 gestational weeks, 31.7% between 11-15 weeks, 10% between 16-20 weeks, and 6.7% had HG >20 weeks.

35 Pregnant women who had 6 episodes per day gained 9-11kgs more than those who had more than 6 episodes per day, who gained 6-8 kgs. There were a total of 25 patients with more than six episodes of vomiting per day, with 14 of them gaining 6-8 kg throughout the pregnancy.

The electrolyte imbalance in the test group was 20 (33.3%), while there was no electrolyte imbalance in the control group. The distribution of ketonuria in the test group was 28.3%, with no ketonuria seen in the control group.

The prevalence of Oligohydramnios was nearly the same in cases and controls. Women who had more episodes of vomiting were significantly more likely to have a low birth weight.

There is an association between hyperemesis gravidarum and preterm labour. There is no association between Hyperemesis gravidarum and gestational diabetes or hypertension.

In the control group, only one patient had intrauterine growth restriction (IUGR) out of 60 patients with hyperemesis gravidarum. Hyperemesis gravidarum is associated with IUGR/SGA (P=0.05).

When compared to the control group, only 4 members had preterm delivery (P= 0.02).

There is an association between hyperemesis gravidarum and preterm labour. In the current study, women with HG have pregnancies that last no longer than 40 weeks.

The study group had 86.7% normal deliveries, 11.7% Caesarean deliveries, and 1.7% instrumental deliveries. In the control group, 88.3% of deliveries were normal, 10% were Cesarean, and 1.7% were instrumental.

In the study group, 26.7% of babies had a low birth weight of 2.1-2.5kgs, 56.7% of babies had a birth weight of 2.6-3kgs, and 11.7% of babies had a birth weight of 3.1-3.5kgs. In the control group, 5% of babies had a low birth weight of 2.1-2.5kgs, 40% of babies had a birth weight of 2.6-3kgs, and 38.3% of babies had a birth weight of 3.1-3.5kgs. There is association between hyperemesis gravidarum and birth weight.

There is an association between hyperemesis gravidarum and birth weight. Pregnant women who experience frequent vomiting and gain less weight are more likely to have a low birth weight.

Out of 60 cases of Hyperemesis gravidarum, 25 members had more than six episodes per day, and 12 women delivered babies weighing 2.1-2.5kg. This means that patients who have severe vomiting are more likely to have low birth weight babies. Whereas in women who had 6 episodes of vomiting per day, the majority of the women gave birth to babies weighing more than 2.5kg.

There is no significant difference in the APGAR score at the first and fifth minutes of NICU admission. The aetiology of HG is multifactorial. The severity of the symptoms, the impact of the symptoms on a woman's quality of life, and the safety of the foetus all influence how these symptoms are managed. In our study, the presence of hyperemesis gravidarum requiring admission had no negative pregnancy outcomes. However, if the symptoms are severe with increased

vomiting, those who gained less weight had adverse pregnancy outcomes such as poor maternal weight gain, IUGR, and low birth weight. A large group study involving

multiple centres is still required to further analyse the actual impact of HG on pregnancy outcome.

Table 1: Socio-demographic characteristics, maternal, and Obstetrics risk of pregnant women with and without HG

Characteristics	Categories	Cases		Controls		P value
		N	%	N	%	
Age (yrs)	≤ 20	12	20.0%	10	16.7%	0.485
	21 - 25	32	53.3%	29	48.3%	
	26 - 30	13	21.7%	19	31.7%	
	31 - 35	3	5.0%	1	1.7%	
	> 35	0	0.0%	1	1.7%	
Socioeconomic status	Upper	2	3.3%	15	25.0%	0.04
	Upper Middle	8	13.3%	22	36.6%	
	Lower Middle	10	16.6%	21	35.0%	
	Upper Lower	25	41.6%	2	3.3%	
	Lower	15	25.0%	0	0.0%	
BMI	< 18.5	35	58.3%	-	-	-
	18.5 - 24.9	20	33.3%	-	-	
	25 - 29.9	5	8.3%	-	-	
Parity	Primi	43	71.7%	43	71.7%	-
	Multi	17	28.3%	17	28.3%	
Onset of HG in Wks. of Gestation	6 - 10	31	51.7%	-	-	-
	11 - 15	19	31.7%	-	-	
	16 - 20	6	10.0%	-	-	
	> 20	4	6.7%	-	-	
Severity of HG(episodes/day)	<6	35	58.3%	-	-	-
	>6	25	41.7%	-	-	
Weight loss(kg)	No loss	0	0.0%	60	100.0%	0.002
	3 - 5	12	20.0%	0	0.0%	
	6 - 8	48	80.0%	0	0.0%	
Electrolyte imbalance	Yes	20	33.3%	0	0.0%	0.001
	No	40	66.7%	1	100.0%	
Ketonuria	Yes	17	28.3%	0	0.0%	0.01
	No	43	71.7%	1	100.0%	
Weight Gain	6 - 8	26	43.33%	8	13.33%	0.0012
	9 - 11	30	50%	46	76.67%	
	12 - 14	4	12.5%	6	10%	
Oligohydramnios	Yes	7	11.7%	3	5.0%	0.186
	No	53	88.3%	57	95.0%	
Anaemia	Yes	10	16.7%	4	6.7%	0.04
	No	50	83.3%	56	93.3%	
Gestational diabetes	Yes	3	5.0%	2	3.3%	0.309

	No	57	95.0%	58	96.7%	
Gestational hypertension	Yes	6	10.0%	4	6.7%	0.5
	No	54	90.0%	56	93.3%	
IUGR	Yes	10	16.7%	1	1.7%	0.0044
	No	50	83.3%	59	98.3%	
Gestational Age at Delivery (weeks)	< 34	4	6.7%	1	1.7%	0.02
	34 - 36	5	8.3%	3	5.0%	
	37 - 39	51	85.0%	49	81.7%	
	≥ 40	0	0.0%	7	11.7%	
Mode of delivery	Vaginal	52	86.7%	53	88.3%	0.958
	C-section	7	11.7%	6	10.0%	
	Instrumental	1	1.7%	1	1.7%	

Table 2: Correlation between Severity of Hyperemesis Gravidarum and Pregnancy Weight Gain and Anemia.

		No of Episodes/day		P value
		< 6kg	> 6kg	
Weight Gain (kg)	3 - 5	1	4	0.01
	6 - 8	8	14	
	9 - 11	23	6	
	12 - 14	3	1	
	19 - 21	0	0	
Anemia	N	4	6	-

Table 3: Neonatal risk factors/Characteristics from the pregnant with and without HG

Characteristics	Categories	Cases		Controls		P value
		N	%	N	%	
Birth Weight(kgs)	1.5 - 2	2	3.3%	0	0.0%	0.001
	2.1 - 2.5	16	26.7%	3	5.0%	
	2.6 - 3	34	56.7%	24	40.0%	
	3.1 - 3.5	7	11.7%	23	38.3%	
	3.6 - 4	1	1.7%	10	16.7%	
APGAR at 1 min	4 - 6	5	8.3%	3	5.0%	0.464
	7 - 10	55	91.7%	57	95.0%	
APGAR at 5 min	4 - 6	1	1.7%	1	1.7%	0.9
	7 - 10	59	98.3%	59	98.3%	
NICU admissions	No	55	91.7%	56	93.3%	0.729
	Yes	5	8.3%	4	6.7%	

Table 4: Association between Severity of Hyperemesis Gravidarum and neonatal birth weight

No of Episodes/ day	Birth weight (kg)					Total	P value
	1.5 - 2	2.1 - 2.5	2.6 - 3	3.3 - 3.5	3.6 - 4		
<6	0	4	24	6	1	35	0.002
>6	2	12	10	1	0	25	
Total	2	16	34	7	1	60	

Discussion

We made an effort to investigate the impact of hyperemesis on maternal and foetal outcomes at the government maternity hospital Tripathi between November 2020 and 2021. The current study identified the risk factors associated to HG. Risk identification may reduce adverse perinatal outcomes, hospitalisation, time lost from paid employment, and emotional and psychological problems.

During the study period, a total of 2100 pregnant women were screened, and 60 of them had Hyperemesis gravidarum, making the prevalence of Hyperemesis gravidarum 2.8%. According to other studies, the prevalence of hyperemesis gravidarum is approximately 0.3-3% of pregnancies based on different diagnostic criteria and ethnic variation in study populations. Several large population studies indicate ethnic variation in the incidence of HG [11-13]. A Malaysian study and an Eastern Asian population study found prevalence rates of 3.9% and 3.6%, respectively [14,15].

Pregnant women in India and Sri Lanka had the highest prevalence, while those in Western Europe had the lowest [16].

In our study, the most commonly affected age group with hyperemesis gravidarum was 21-25 years old, accounting for 53.3% of all cases. In another study, mothers between the ages of 20 and 24 were more likely to develop HG [16].

The prevalence of HG decreases with age. This could be due to a higher prevalence of pregnancy in this age group, particularly

among Indians [17]. The current study found that pregnant women who lived in cities were more likely to have HG than those who lived in rural areas. Pregnant women with HG are more sensitive to certain smells in their environment. As a result, the urban environment may cause hyperemesis as a conditioned response to a specific environmental agent such as taking the underground, being around cosmetics, eating away from home, or noise (television). Furthermore, urban women may be more sensitive psychologically than rural counterparts.

In our study, the majority of pregnant women with hyperemesis gravidarum were primipara, accounting for 71.7%. In the current study, a significant relationship between parity and HG was observed. Another study, by Parihar S *et al.*, supports this finding. This difference may be due to the fact that multiparous women who had hyperemesis in their first pregnancy cope with the symptoms much better than a nulliparous mother who is very anxious about her pregnancy. It is extremely rare for a multiparous woman to have hyperemesis without having had hyperemesis in her first pregnancy [18].

In our study, 66.6% of the cases had a low socioeconomic status, whereas previous research has shown that a low socioeconomic status is a risk factor for hyperemesis gravidarum [19-21]. Low socioeconomic status is also a major risk factor for H.pylori infection, as crowded populations are associated with an increased risk of H.pylori

infection transmission [21].

In the current study, the majority of women (51.7%) had hyperemesis gravidarum between 8 and 12 weeks of gestation, followed by 11-15 weeks (31.7%), 16-20 weeks (10%), and >20 weeks (6.7%). Gabra A stated that the onset of Hyperemesis gravidarum typically begins between 6 and 8 weeks of gestation and peaks by 12 weeks [22].

The severity of Hyperemesis gravidarum is measured by the number of vomiting episodes per day, which is 6 in 58.3% of women and >6 in 41.7% of cases. All of the women lost between 3 and 8 kg, were dehydrated, and the appearance of 40 (75%) of the women was unappealing. All of the women had normal blood urea and serum creatinine levels, as well as liver function tests [23].

Bezircioglu I *et al.*, study stated that prevalence of *Helicobacter pylori* infection is more among the women with Hyperemesis gravidarum and anemia [24].

Eight hyperemesis gravidarum women (22.2%) and one control woman (2.8%) tested positive for *Helicobacter pylori* stool antigen (HpSA) and the difference is statistically significant ($p=0.037$). Anemia is found in five women with Hyperemesis gravidarum, four of whom are HpSA positive.

The prevalence of gestational diabetes mellitus is the same in both the study and control groups ($p=0.309$), indicating that there is no significant relationship between Hyperemesis and gestational diabetes, which is consistent with previous findings.

Sangeeth Parihar [18] investigated the effects of hyperemesis gravidarum on pregnancy outcomes. Only 36 of the 1100 pregnant women screened in their study had Hyperemesis gravidarum. Only three of the 36 participants developed gestational

diabetes, indicating that there is no association between Hyperemesis and gestational diabetes.

In our study, the prevalence of intrauterine growth restriction (IUGR) / SGA differs significantly between the two groups. SGA babies were born to 10/60 women who had hyperemesis, but only 2/60 mothers in the control group who did not have hyperemesis had SGA babies. The majority of studies have identified association between hyperemesis and premature babies [23,24].

Huang W *et al* concluded that HG was significantly associated with multiple risk factors, implying that HG indirectly increased the risk of foetal growth restriction. (FGR) [25].

In the Dodds L *et al* [26] study, 1,270 of the 156,091 singleton pregnancies had hyperemesis. Infants born to Hyperemesis women are more likely to be low birth weight, small for gestational age (SGA), and born before 37 weeks of gestation. However, some studies have found no association between Hyperemesis gravidarum and IUGR. Still, a larger group study involving many centers is warranted to assess the actual impact of hyperemesis on foetal outcome.

The majority of studies were observed a significant positive association between hyperemesis and preterm birth [23,24]. According to some studies, the association between hyperemesis gravidarum and preterm births is insignificant.

Vikanes *et al* study found low birthweight in women with Hyperemesis gravidarum. In a study involving 819 women with hyperemesis gravidarum, Fejzo *et al* observed that 8% of the women had low birth weight infants [27]. Hyperemesis gravidarum has been associated to an increased risk of adverse foetal outcomes such as low birth weight, preterm birth, and small for gestational age infants.

In our study, pregnant women who had a higher frequency of vomiting episodes had IUGR babies. Patients who had more than 6 episodes of vomiting in a day had a higher proportion of IUGR/ SGA babies ($P=0.002$), which is consistent with the findings of a few studies [28,29].

A recent study identified association between pregnancy weight gain and the number of vomiting episodes. Mothers who had more vomiting episodes gained less weight overall ($p=0.01$).

In both groups, the rate of sex distribution, mode of delivery, APGAR at 1min and 5min, and NICU admissions are the same.

Mc Carthy and colleagues [28] conducted a prospective cohort study on 3,423 nulliparous women. Those with Severe HG had a higher risk of spontaneous preterm birth than women without HG. Preeclampsia, small for gestational age, low birth weight, and infant sex ratio had no significant association. The study by Vikanes *et al* found no significant association between HG and poor perinatal outcomes. According to the Hastoy *et al* study, women with Hyperemesis gravidarum have an increased risk of having a low birth weight [29].

Conclusion

Pregnant women with Hyperemesis gravidarum are more likely to be younger and primigravida. Women who have more than six episodes of vomiting per day are more likely to have less weight gain during pregnancy, as well as anaemia and IUGR as maternal outcomes. The foetal outcomes are low birth weight and SGA. The majority of women with less severe vomiting (6 episodes/day) do not have an adverse pregnancy outcome.

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