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Hyperemesis Gravidarum in the Second Trimester as a Risk Indicator for Preterm Birth

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ABSTRACT

A severe type of nausea and vomiting during the early stages of pregnancy is called hyperemesis gravidarum. Preterm delivery has been reported to be significantly associated with hyperemesis gravidarum. **Objectives:** To determine the association between preterm birth and hyperemesis gravidarum in female attending an antenatal care clinic in the second trimester. **Methods:** This Cohort1study was carried out at the Department of Obstetrics and Gynaecology, Sahiwal Teaching Hospital, Sahiwal. A total of 200 female were enrolled and divided into two groups with and without hyperemesis gravidarum. Then female were followed up in OPD until delivery. If female had a delivery before 37 weeks of gestation, then preterm birth was labelled. Data were analyzed in SPSS version 23.0. **Results:** The mean age of the female was 31.25 ± 5.98 years. In our study, 40 (40%) female were primigravida. The mean gestational age at presentation was 17.47 ± 3.51 weeks, while at delivery it was 37.27 ± 1.94 weeks. In the exposed group, preterm birth was noted in 45 (45%) cases, while in the unexposed group, preterm birth was noted in 15% cases. Thus, there was 1.909 times more risk of preterm birth in females with hyperemesis gravidarum as compared with female without hyperemesis gravidarum, i.e., RR=1.909 (95% CI; 1.483, 2.457, p<0.001). **Conclusions:** There is more than about two times greater risk of preterm birth in female with hyperemesis gravidarum during the second trimester of their pregnancy.

INTRODUCTION

During the first 20 weeks of pregnancy, morning sickness affects the majority of pregnant women [1, 2]. A severe type of nausea and vomiting that is common in the early stages of pregnancy is called hyperemesis gravidarum. It can cause dehydration, ketonuria, weight loss, and necessitate hospitalization [3, 4]. In the early stages of pregnancy, around half of women have both nausea and vomiting, while another quarter experience just nausea. Hyperemesis gravidarum has a reported incidence of 0.3% to 1.0%. Preterm delivery and low birth weight are adverse obstetric outcomes associated with hyperemesis gravidarum. The cause is not known. According to reports, more than 16% of babies could be delivered at a preterm stage [5, 6]. The risk of unfavorable perinatal outcomes might be increased by undernutrition and inadequate maternal weight gain throughout pregnancy, according to prior epidemiologic and animal research [7] involving preterm delivery and low birth weight [8]. The relationship between hyperemesis gravidarum and premature delivery might be explained by several processes. A well-known cause of malnourishment, dehydration, inadequate weight growth, and even weight loss is hyperemesis gravidarum. According to studies, women who suffer from hyperemesis gravidarum frequently consume inadequate amounts of calories and nutrients, sometimes falling short of 50% of the necessary diet [9, 10]. Due to a lack of evidence, often

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hyperemesis gravidarum remains neglected, which may lead to more severe outcomes, as preterm birth is associated with many other complications. So want to conduct this study to confirm the association of preterm birth with hyperemesis gravidarum. This study guides us to improve local guidelines and help to adopt a new strategy for management and prevention of hyperemesis gravidarum so that hazardous outcomes can be prevented. Despite the known association of hyperemesis gravidarum with adverse pregnancy outcomes, limited research has specifically focused on its occurrence during the second trimester and its direct impact on preterm birth. Most studies emphasize early pregnancy nausea and vomiting without differentiating gestational timing, creating a knowledge gap regarding second-trimester cases. This lack of localized evidence underscores the need to assess the risk of preterm birth in women presenting with hyperemesis gravidarum during this critical period. This study aims to find out the association of hyperemesis gravidarum in women who manifest in the second trimester of pregnancy is linked to an early birth.

METHODS

After taking approval from the hospital ethical review committee (158/IRB/SLMC/SWL), this cohort study was conducted at the Department of Obstetrics and Gynaecology, Sahiwal Teaching Hospital, Sahiwal, from November 2024 to April 2025. A sample size of 200 female; 100 female for both groups, was estimated by fixing the power of the study at 80%, significance level at 5% and percentage of preterm birth, i.e. 31.1% in exposed and 4.9% in unexposed cases in the second trimester of pregnancy [11]. The non-probability purposive sampling technique was used to include female, who fulfilled the following criteria. Female aged 20-40 years of parity <5 presenting during the second trimester of pregnancy (gestational age 12-24 weeks on USG) were included. Exposed Group: Female with Hyperemesis gravidarum, i.e. nausea and vomiting in the 2nd trimester. Female with a PUQE-24 (Pregnancy-Unique Quantification of Emesis) score of 13 or higher will be enrolled in the study. Unexposed Group: Female without Hyperemesis Gravidarum. At the same time, female with gestational or chronic Hypertension, diabetes, cardiac problems, asthma, multiple pregnancy or congenital abnormalities in the fetus after 23 weeks of gestation were not included. Informed written consent was taken to accomplish the research. A demographic profile with contact details was also obtained. Then female were separated into two groups with or without hyperemesis gravidarum. Then female were followed up in OPD every month until delivery of the fetus. At the time of delivery, an ultrasound was performed by the researcher to confirm the gestational age. If a female had a delivery before 37 weeks of gestation, then preterm birth was labelled. Female, who did not present for delivery and were lost to follow-up were replaced by new cases. All this procedure was recorded on a proforma and analyzed by SPSS version 23.0. Relative Risk was measured to assess the association between preterm birth and hyperemesis gravidarum. RR>1 was kept as significant (Figure 1).

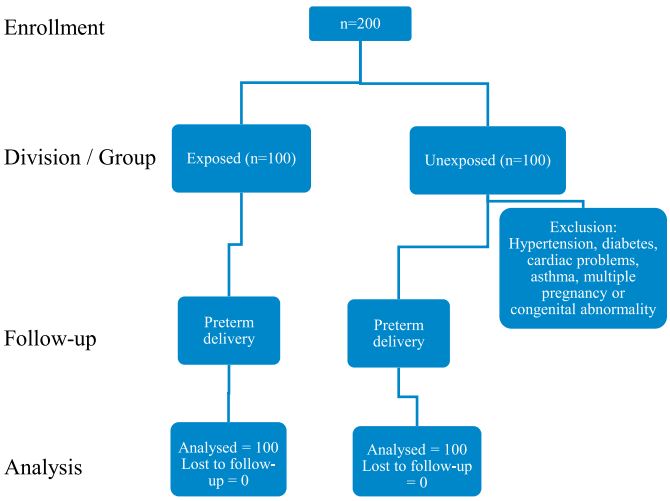

Figure 1: Patient Flow Diagram (n=200)

RESULTS

In the exposed group, the mean age of females was 26.25 ± 4.21 years, while in the unexposed group, the mean age was 36.25 ± 1.96 years. In the exposed group, the mean BMI of female was 26.88 ± 4.93 kg/m2, while in the unexposed group, the mean BMI was 26.59 ± 5.14 kg/m2. In the exposed group, 40 (40%) female were primigravida, 35 (35%) female were primiparous, and 25 (25%) were multiparous. In the unexposed group, 0 (%) female were primigravida, 15 (15%) female were primiparous, and 85 (85%) were multiparous. In the exposed group, 73 (73%) females were housewives, while 27 (27%) were working women. In the exposed group, 16 (16%) female had active lifestyle, 69 (69%) had a sedentary lifestyle, while 15 (15%) were doing gym/exercise. In the unexposed group, 17 (17%) female had an active lifestyle, 53 (53%) had a sedentary lifestyle, while 30 (30%) were doing gym/exercise. In the exposed group, 58 (58%) female were taking home-made food, 13 (13%) were taking fast food >3 times a week, 23 (23%) were taking street food >3 times a week, while 6 (6%) were following a diet plan. In the unexposed group, 58 (58%) female were taking home-made food, 19 (19%) were taking fast food >3 times a week, 18 (18%) were taking street food >3 times a week, while 5 (5%) were following a diet plan. In the exposed group, 30 (30%) were living in urban areas, 37 (37%) were coming from rural areas, while 33 (33%) were living in semi-urban areas. In the unexposed group, 31 (31%) were living in urban areas, 37 (37%) were coming from rural areas, while 32 (32%) were living in semi-urban areas. In the exposed group, 43 (43%)

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female had low socioeconomic class, 41 (41%) were from middle-class families, and 16 (16%) were from high socioeconomic class. In the unexposed group, 34 (34%) female had low socioeconomic class, 37 (37%) were from middle-class families, and 29 (29%) were from high socioeconomic class. The mean gestational age at enrolment was 17.85 ± 3.57 weeks in the exposed group, while 17.10 ± 3.42 weeks in the unexposed group. The mean gestational age at delivery was 36.60 ± 1.99 weeks in the exposed group, while 37.95 ± 1.64 weeks in the unexposed group (Table 1).

Table 1: Socio-demographic Characteristics of the Participants (n=200)

Characteristics	Groups	
	Exposed (n=100)	Unexposed (n=100)
Age		
Years	26.25 ± 4.21	36.25 ± 1.96
BMI		
Kg/m^2	26.88 ± 4.93	26.59 ± 5.14
Primigravida		
Parity=nil	40 (40%)	0 (%)
Primiparous		
Parity=1	35 (35%)	15 (15%)
Multiparous	-	-
Parity=2-4	25 (25%)	85 (85%)
Occupation		
Housewife	73 (73%)	68 (68%)
Working women	27 (27%)	32 (32%)
Life Style		
Active	16 (16%)	17 (17%)
Sedentary	69 (69%)	53 (53%)
Gym / Exercise	15 (15%)	30 (30%)
Dietary Habits		
Homemade Food	58 (58%)	58 (58%)
Fast Food	13 (13%)	19 (19%)
Street Food	23 (23%)	18 (18%)
Following A Diet Plan	6 (6%)	5 (5%)
Residence		
Urban	30 (30%)	31 (31%)
Rural	37 (37%)	37 (37%)
Semi-Urban	33 (33%)	32 (32%)
Socioeconomic Status		
Low	43 (43%)	34 (34%)
Middle	41 (41%)	37 (37%)
High	16 (16%)	29 (29%)
Gestational Age		
At Presentation	17.85 ± 3.57	17.10 ± 3.42
At Delivery	36.60 ± 1.99	37.95 ± 1.64*

*Significance (p-value)<0.001 (Independent samples t-test)

In our study, preterm birth was noted in 60 (30%) cases, out of which 45 (45%) cases were exposed to hyperemesis gravidarum and 15 (15%) were unexposed. There was about two times more risk of preterm birth in exposed females compared to unexposed females, i.e. OR=1.909 (Table 2).

Table 2: Association of Preterm Birth with Hyperemesis Gravidarum (n=200)

Characteristics		Groups		Total
		Unexposed	Exposed	
Preterm Birth	Yes	45 (45%)	15 (15%)	60 (30%)
	No	55 (55%)	85 (85%)	140 (70%)
Total		100	100	200

RR = 1.909 (95% CI; 1.483, 2.457, p<0.001)

The data were stratified for the age of female, and it was observed that younger female, less than 30 years of age, all presented with hyperemesis gravidarum, and most of them had preterm births (56.3%). But in advanced age (above 30 years), there was no preterm birth in female exposed to hyperemesis gravidarum. While in the unexposed female, preterm birth occurred in 15% cases only. Among primigravida exposed to hyperemesis gravidarum, 40 (100%) female had preterm birth, while none in the unexposed primigravida female. In primiparous exposed female, preterm birth was noticed in 5 (14.3%) cases, while in 15 (100%) cases in unexposed primiparous female. Although the risk was insignificant (RR: 0.250 (95% CI: 0.117, 0.534)). Among multigravida, there was no preterm birth, whether the female had hyperemesis gravidarum or not. In female with an active lifestyle, preterm birth occurred in 5 (31.3%) exposed female, while in 2 (11.8%) unexposed female, depicting the relative risk of 1.688. In female with a sedentary lifestyle, preterm birth occurred in 35 (50.7%) exposed female, while in 9 (17.0%) unexposed female, depicting the relative risk of 1.825. This showed that if female had hyperemesis gravidarum and having a sedentary lifestyle, the risk is also doubled for preterm birth. While female doing exercise during pregnancy or going gym are also at doubled risk of preterm birth (RR: 2.00 (95% CI: 0.911, 4.392) (Table 3).

Table 3: Association of Preterm Birth with Hyperemesis Gravidarum When Controlled for Effect Modifiers (n=200)

Variables	Preterm Birth	Groups		RR (95% CI)
		Exposed	Unexposed	
Age 20-30 Years	Yes	45 (56.3%)	0 (0%)	NA
	No	35 (43.8%)	0 (0%)	
Age 31-40 Years	Yes	0 (0%)	15 (15%)	1.235 (1.126, 1.355)
	No	20 (100%)	85 (85%)	
Primigravida	Yes	40 (100%)	0 (0%)	NA
	No	0 (0%)	0 (0%)	
Primiparous	Yes	5 (14.3%)	15 (100%)	0.250 (0.117, 0.534)
	No	30 (85.7%)	0 (0%)	
Multigravida	Yes	0 (0%)	0 (0%)	NA
	No	25 (100%)	85 (100%)	
Active Lifestyle	Yes	5 (31.3%)	2 (11.8%)	1.688 (0.882, 3.230)
	No	11 (68.8%)	15 (86.2%)	

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Sedentary Lifestyle	Yes	35 (50.7%)	9 (17.0%)	1.825 (1.361, 2.448)
	No	34 (49.3%)	44 (83.0%)	
Gym / Exercise	Yes	5 (33.3%)	4 (13.3%)	2.00 (0.911, 4.392)
	No	10 (66.7%)	26 (86.7%)	

DISCUSSION

In our study, we observed preterm births in 60 (30%) female. The female in the exposed group had 1.909 times more risk of preterm births (45% cases) as compared to unexposed female (15% cases). Thus, this study observed RR=1.909 (95% confidence interval: 1.483, 2.457). In many studies, hyperemesis gravidarum has been linked to a higher risk of unfavorable obstetric outcomes, like preterm birth, low birthweight, and small-for-gestational-age babies [12, 13]. According to prospective cohort study by McCarthy and fellows, women with severe hyperemesis gravidarum were more likely than those without the condition to give birth spontaneously before their due date (adjusted OR, 2.6; 95% CI: 1.2–5.7) [14]. These findings are almost similar to our study, confirming that the risk of preterm birth doubled in the presence of hyperemesis gravidarum. Placental abruption and undersized for gestational age newborns are among the linked placental dysfunction diseases that are much more likely to occur in pregnancies complicated by hyperemesis gravidarum in the second trimester of pregnancy [15]. During the research period, the overall prevalence of hyperemesis gravidarum among primiparous women in Norway was 0.89% (95% CI: 0.88–0.92). Hyperemesis gravidarum was most common in women born in India and Sri Lanka (3.2%), whereas it was least common in women born in Western Europe (0.8%). The odds of developing hyperemesis gravidarum were 3.4 (95% CI: 2.7-3.5) and 3.3 (95% CI: 2.6-3.4) times higher for women born in Africa (excluding North Africa) and India or Sri Lanka, respectively [16, 17]. These studies also showed a significant association of hyperemesis gravidarum with preterm birth, as we observed in our study. One study reported that the frequency of preterm birth was 3.0% in females with hyperemesis gravidarum, while 2.8% in female without hyperemesis gravidarum [18]. Other studies supported this evidence and reported that preterm birth was found to be 7.4-7.6% among hyperemesis gravidarum female, while 5.7-5.8% among controls [19, 20]. Paauw *et al.* observed a very high risk of preterm birth in the presence of hyperemesis gravidarum. They observed that the frequency of preterm birth was very high among females with hyperemesis gravidarum (31.1%) as compared to controls (4.8%) [21]. In a study by Vandraas *et al.* reported that reduced risk of very preterm birth (OR=0.66; 95% CI: 0.5-0.9) and large-for-gestational-age (OR=0.9; 95% CI: 0.8-0.9) in female having hyperemesis gravidarum [22]. Other studies supported this evidence and reported that preterm birth was found to be 7.4-7.6% among hyperemesis gravidarum female, while 5.7-5.8% among controls [19, 21]."A study by Bolin et al. showed that the risk of preterm (<37 weeks) pre-eclampsia was more than doubled, the risk of placental abruption was three times higher, and the risk of a small for gestational age birth was 39% higher for women with hyperemesis gravidarum who were admitted for the first time in the second trimester (adjusted OR; (95% CI) were: 2.09 (1.38-3.16), 3.07 (1.88-5.00), and 1.39 (1.06-1.83), respectively) [18]. Reduced gestational age and longer hospital stays are more common among infants born to mothers who experienced hyperemesis gravidarum. The most frequent cause of hospitalization during the first trimester of pregnancy is hyperemesis gravidarum, which is surpassed only by premature labor for the whole pregnancy [11].

This study was limited by its single-center design and relatively small sample size, which may affect the generalizability of the findings. Additionally, lifestyle and dietary habits were self-reported, potentially introducing recall bias. Future research should include multicenter studies with larger cohorts and consider biochemical markers to better understand the pathophysiological mechanisms linking hyperemesis gravidarum with preterm birth, ultimately guiding more effective prevention and management strategies.

CONCLUSIONS

It was concluded that there is about a two times greater risk of preterm birth in females having hyperemesis gravidarum in the second trimester. Consequently, hyperemesis gravidarum can lead to adverse pregnancy outcomes and can cause complications to the neonate in the neonatal period and beyond. So in future, keeping in mind the risk of preterm birth, we will plan and implement strategies to manage female with hyperemesis gravidarum to prevent preterm labor and delivery and reduce life-threatening risks to neonates.

Authors' Contribution

Conceptualization: SA
Methodology: MS, QJ
Formal analysis: QJ
Writing and Drafting: QJ
Review and Editing: QJ, MS, SA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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