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RESEARCH ARTICLE
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INCIDENCE OF PREECLAMPSIA IN PATIENTS PRESENTING WITH HYPEREMESIS GRAVIDARUM IN SECOND TRIMESTER OF PREGNANCY: A STUDY AT KHYBER TEACHING HOSPITAL, MTI, PESHAWAR

Dr Sumbal Afridi[1], Dr Laila Hussain[2], Dr Farrukh Gul[3], Dr Reema Fateh[4*], Dr Rahat Bibi[5]

[1]Consultant Obstetrician and Gynaecologist, Gulshan Maternity Hospital, Kohat, Pakistan
[2]FCPS, Trainee Medical Officer, Gynae & Obs Department, MTI Khyber Teaching Hospital Peshawar, Pakistan
[3]Consultant, Gynae & Obs Department, Ismail Medical Complex Matta Swat, Pakistan
[4*]Consultant, Gynae & Obs Department, Luqman International Hospital Saidu Sharif Swat, Pakistan
[5]Trainee Medical Officer, Obstetrics & Gynae Department, Khyber Teaching Hospital Peshawar, Pakistan

***Corresponding author:** Dr Reema Fateh
*Email: reemafateh88@icloud.com

ABSTRACT

Background: Hyperemesis gravidarum is a severe form of nausea and vomiting during pregnancy, typically beginning between 4 and 6 weeks of gestation, affecting approximately 0.3 to 3% of pregnancies, and is a leading cause of early pregnancy hospitalization. There is some evidence that HG is associated with placental dysfunction and hypertensive disorders, including preeclampsia, which is the major cause of maternal morbidity.

Objective: To establish the incidence of preeclampsia in women with second-trimester HG in a tertiary care hospital in Peshawar.

Methods: The study was a descriptive cross-sectional study at Gynae & Obs Department, MTI Khyber Teaching Hospital Peshawar, Pakistan from 1st July, 2024 to 31st December, 2024. Women between 14 and 28 weeks of gestation during pregnancy and whose HG was confirmed were recruited, and those women who had a history of chronic hypertension, thyroid, kidney, and hepatic problems were excluded. Blood pressure, proteinuria, and clinical information were obtained.

Results: In 200 participants (100 HG and 100 controls), the incidence of preeclampsia was 25% in patients with HG and 10% in controls. HG patients presented with high blood pressure, proteinuria, severe weight loss, and increased hospitalization requirements.

Conclusion: Second trimester HG is closely linked with the risk of preeclampsia and close monitoring, early screening, and multidisciplinary care are considered to improve the outcome of second trimester HG.

INTRODUCTION

Hyperemesis gravidarum (HG) is excessive nausea and vomiting in pregnancy that may lead to severe maternal and fetal morbidity, including nutritional deficiency, dehydration, and weight loss. Diagnosis involves clinical evaluation, lab tests, and imaging, and treatment depends on symptom severity, including fluid replacement, medications, nutritional support, and hospitalization if

necessary.In recent studies, HG, particularly in the second trimester, can be a predictor of hypertensive pregnancy-related disorders, including preeclampsia, which has emerged as a leading cause of maternal and neonatal morbidity and mortality in most regions globally (1). The pathophysiology of HG is difficult and involves hormonal, genetic, and metabolic factors, and increasing data points to the potential involvement of placental dysfunction, which also plays a central role in the pathogenesis of preeclampsia (2,3). There are similarities in the etiological processes of the two conditions (such as abnormal placentation, endothelial maladaptation, and immune maladaptation), and this is why the exploration of the relationship between the conditions is given priority (4). Adequate and timely monitoring and processing of maternal outcomes can be enhanced by HG screening of women at risk of preeclampsia as a part of clinical practice.

HG has been documented in up to 3 percent of pregnancies, but with varying degrees of severity, which may sometimes result in emergency care, hospitalization, or intravenous fluids (5). The time of HG and the degree of the condition significantly influence the outcome of pregnancy, and the incidences of severe incidents and those identified late in pregnancy are linked with an increased number of adverse events, including hypertensive disorders, intrauterine growth restriction, and preterm birth (6). B-type natriuretic peptide has been found to be higher in patients with HG, possibly reflecting systemic or extra-gastrointestinal actions, providing clues about the cardiac stress, and again, its systemic implications (7). Saudi Arabia and South Asian literature illustrate how regional epidemiological trends of pregnancy-related diseases, including molar pregnancy, reflect a changing maternal health environment and its interplay with complications, including HG (8). These tendencies explain the need for region-specific studies, including the current research in one of the tertiary care hospitals in Peshawar, Pakistan, to determine the region-specific risk factors and subsequently, devise prevention strategies.

Recent research indicates that HG, during the second trimester, may be a predisposing factor to other pregnancy complications that include intrahepatic cholestasis of pregnancy and placental insufficiency (9). Nutritional deficiencies that occur alongside chronic vomiting, which involves low protein content, have been observed to be correlated with poor placental growth and, consequently, poor pregnancy outcomes (10). New biomarkers such as ADAMTS-1 levels have been explored to explain the molecular mechanisms of HG and how these mechanisms can be applied to forecast the severity of the disease, as well as comorbidity (11). The increasing prescription of psychotropic medications such as mirtazapine and olanzapine to treat non-response cases is also a good trend because it indicates a trend towards considering HG as a multidisciplinary disorder, which also needs psychiatric-level treatment (12). These clinical developments are justified by the new research that dispels the outdated conception of the etiology of HG that contributes to the bio-foundation of the disorder and shapes more specific interventions (13).
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High levels of HbA1c in early pregnancy are linked to poor ultrasound outcome and birth outcomes, and interplay with metabolic malfunction and pregnancy-related complications, which may be overlapping with HG (14). There have been a few studies suggesting a neuropsychiatric element, and a few researchers have also attributed HG to changes in the central nervous system pathway, which might be why it is chronic and does not respond to a traditional antiemetic intervention (15). In addition, pregnancy-specific liver dysfunction, such as acute fatty liver of pregnancy and intrahepatic cholestasis, has also been associated with HG in other studies, suggesting that hepatic monitoring should be carefully monitored in patients with this condition (16). Likewise, acute kidney injury in pregnancy is a rare occurrence that has also been observed in severe presentations of HG, suggesting multi-organ involvement in extreme cases (17).

HG is still a clinical issue with diagnostic and therapeutic limitations. Despite the improvement of the pathophysiology of different forms of tuberculosis, its unpredictable course complicates its

treatment, particularly in low-resource settings where evidence-based treatment is not necessarily available. The recent literature suggests that such a complex is driven by genetic predisposition, hormonal levels, and placental factors (18). The COVID-19 pandemic has also influenced the diagnosis and treatment of pregnancy complications, where there is a risk of overdiagnosing pregnancy complications like fetal growth restriction, which has a similar clinical appearance to HG (19,20). Furthermore, the complication of gestational transient thyrotoxicosis, which frequently appears in HG, also complicates the situation, as its presence may exacerbate the symptoms of a woman, as well as influence the outcome of her pregnancy, which only reinforces the validity of a detailed study of this patient group (21).

The current body of research on the subject suggests the existence of a strong association between HG and poor pregnancy outcomes, particularly preeclampsia. The underlying pathophysiology of the conditions is similar or slightly different, and this explains the need to distinguish between the diagnosis of the conditions and their stratification in the first trimester in pregnant women who have been continuously vomiting until the second trimester.

Objective: To establish the prevalence of preeclampsia in pregnant women who present with second-trimester hyperemesis gravidarum within a tertiary care hospital in Peshawar, with the goal of enhancing early diagnosis, treatment, and maternal-fetal outcomes.

MATERIALS AND METHODS

Study Design: Cross-sectional study.

Study Setting: The research was carried out at Gynae & Obs Department, MTI Khyber Teaching Hospital Peshawar, Pakistan.

Duration of the Study: The research was conducted in the period of 6 months, from 1st July, 2024 to 31st December, 2024**.**

Inclusion Criteria: They included pregnant women 14-28 gestation weeks who presented with severe nausea and vomiting to the point of dehydration, weight loss greater than 5% of pre-pregnancy weight, or electrolyte imbalance, and who were willing to participate.

Exclusion Criteria: Women with more than one pregnancy, pre-existing chronic hypertension, diabetes mellitus, thyroid conditions, renal or hepatic conditions, or other major medical conditions that might confound the diagnosis of preeclampsia or hyperemesis gravidarum were ruled out.

Methods

The study population consisted of all the eligible participants recruited in the antenatal outpatient and inpatient units of Gynae & Obs Department, MTI Khyber Teaching Hospital Peshawar. Maternal age, parity, gestational age, and pregnancy complications of previous pregnancies were documented after obtaining informed consent, followed by a detailed demographic and obstetric history. Vital signs, weight measurement, and physical examination were performed as a clinical assessment. The presence of hyperemesis gravidarum was proven by continuous vomiting, loss of more than 5% of the pre-pregnancy weight, dehydration, and lab results that showed electrolyte imbalances. The ultrasonography was used to determine gestational age. Blood pressure measurements were performed during each visit with standard procedures, and urine samples were analyzed for proteinuria. The diagnosis of preeclampsia was made based on international criteria, including systolic blood pressure of 140 mmHg or higher, diastolic blood pressure of 90 mmHg or higher after 20 weeks of gestation, proteinuria (≥300mg/24 hours), or organ dysfunction. The data were captured in a pre-designed proforma. SPSS version 25 was used to perform statistical analysis. The association statistic was tested by descriptive statistics and chi-square tests at a significance cutoff of $p<0.05$.

Results

The research population was 200 pregnant women, who were separated into 100 pregnant women developing hyperemesis gravidarum (HG) during their second trimester and 100 pregnant women

who did not develop HG (as a control group). The majority of the cohort were aged 25 to 29 years (30 percent) and 20 to 24 years (25 percent). The 35 years and above age group comprised 15 percent of the sample, and maternal age is clearly distributed.

Table 1: Age distribution of participants

Age Group	Patients
<20	10
20–24	25
25–29	30
30–34	20
35+	15

Preeclampsia was also a more prevalent disease in patients with HG, and preeclampsia was found in 25% of patients compared to 10% of patients in the control group. This is significant ($p<0.05$) to show that a relationship exists between second-trimester HG and the occurrence of preeclampsia.

Table 2: Preeclampsia incidence by HG status

Group	Total Patients	Preeclampsia Cases	Incidence (%)
With HG	100	25	25
Without HG	100	10	10

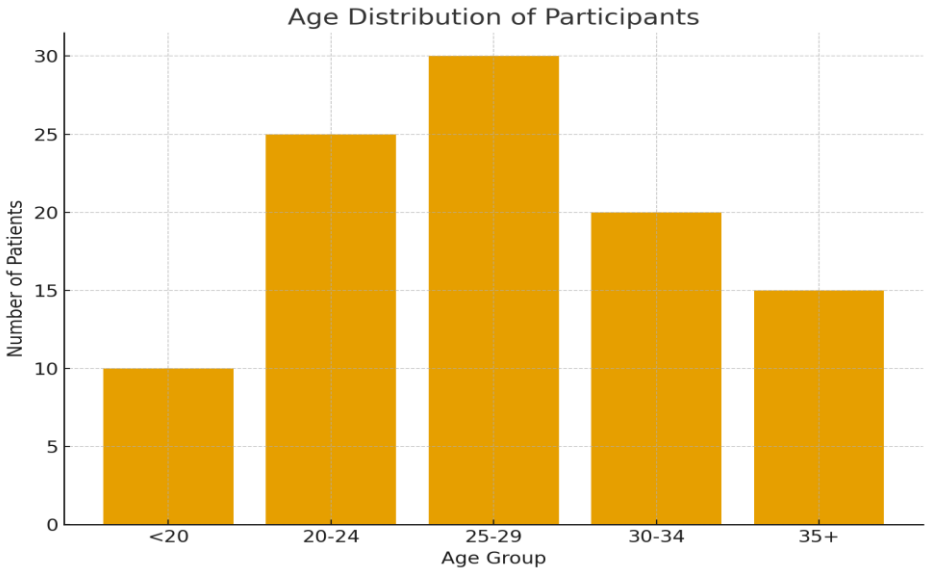
Clinical examination showed that the patients of HG were characterized by an increase in mean systolic and diastolic blood pressure and a significant loss of weight, accompanied by proteinuria. The mean systolic blood pressure was 142mmHg and the mean diastolic pressure was 92mmHg. Proteinuria was 350 mg/24 hours on average, and weight loss was 7.5 percent of pre-pregnancy body weight.

Table 3: Clinical characteristics of patients with HG

Variable	Value
Mean SBP (mmHg)	142
Mean DBP (mmHg)	92
Mean Proteinuria (mg/24h)	350
Mean Weight Loss (%)	7.5

The age distribution of the participants in a bar graph also indicates that the highest percentage of HG cases was among women aged 25-29 years, and subsequently, women aged 20-24 years. The minimal prevalence was observed in younger women below the age of 20 years, suggesting that HG prevalence is age-specific.

The hospitalization history showed that the patients with HG required further inpatient treatment due to complications associated with it, which were dehydration and electrolyte disorders. This group of women was twice as likely to develop preeclampsia, a fact which confirmed the value of HG as a risk factor that predisposes women to hypertensive pregnancy disorders. The results underline the significance of a close observation of the blood pressure rate and the levels of urine protein in women who still experience continuous vomiting throughout the second trimester.



Discussion

Hyperemesis gravidarum (HG) is a severely morbid pregnancy-related disease of nausea and vomiting with high maternal and fetal morbidity. The prevalence of preeclampsia in the population of women with HG during the second trimester was found to be significantly higher than that of women without HG, which confirms the earlier literature, which links HG to poor maternal health, including hypertensive pregnancy disease (1). The group shows the feasibility of considering HG as not only a gastrointestinal disease but a multifactorial disease with systemic consequences that can be applied to detect complications such as preeclampsia as a clinical manifestation. In line with the study by Cécile et al., the common pathophysiology of HG and preeclampsia, the placenta and endothelial stress damage, responds to the role that close antenatal care plays in the targeted women (2). The higher rates of preeclampsia found in the study are in line with the previous findings that have attributed the HG to the diseases associated with placental dysfunction by incorporating the preeclampsia, intrauterine growth retardation, and preterm birth (3,4).

The etiology of the two diseases depends on abnormalities of the placenta, and studies show that abnormal trophoblastic invasion and increased concentrations of antiangiogenic factors are central to the two diseases (4). The high level of hospitalization and medical intervention that was witnessed in this study among HG patients is similar to other jurisdictions, where HG has been defined as a dominant cause of maternal morbidity and a contributing factor to pregnancy-related hospital admissions (5). Moreover, HG presentation during the second trimester is of a specific concern because severity and persistence after the first trimester are excellent predictors of poor maternal and fetal outcomes, demonstrated in large retrospective studies (6). The systemic character of HG is also represented through the occurrence of biochemical markers. Indicatively, high levels of B-type natriuretic peptide have been reported in patients with HG, indicating the presence of cardiovascular stress and justifying the linkage with hypertensive diseases (7).

Likewise, the shift in epidemiological patterns of pregnancy complications such as molar pregnancy has redirected the clinical emphasis on the early detection and management of disorders such as HG in various groups of the population, especially in South Asian states (8). The role of HG in predicting other pregnancy-related complications, like intrahepatic cholestasis, has also been reported and has shown that HG may be an early warning factor of multisystem involvement (9). Protein malnutrition and other nutritional problems can also augment the incidence of defects in placental development, and this factor is one of the reasons why preeclampsia is more likely in this study (10). Potential biomarkers, including concentrations of ADAMTS-1, which are associated with the severity of HG and associated risks, and can be utilized in early predictive models, have also been identified by recent studies (11). Moreover, pharmacological treatment of refractory HG is not limited to standard

antiemetic medications, and psychotropic drugs of mirtazapine and olanzapine are under discussion as an option of pharmacotherapy in severe cases (12).

The evidence that has come up and resulted in these developments has assisted in laying down the biological aspect of the condition and in the need to treat and manage the condition as a biological condition (13). The research is compatible with the evidence that suggests that metabolic factors interact with adverse pregnancy outcomes. The level of HbA1c has been identified to be high in the cases of abnormal ultrasound images, which are normally attributed to gestational carbohydrate intolerance, and in situations where fetal outcome is poor, indicating that metabolic dysfunction may also be contributing to the risks that HG patients are experiencing (14). The neuropsychiatric aspect of HG that Nicholson refers to also provides a general description of the multifactorial etiology of the disorder and its chronicity and relatedness with psychiatric comorbidity (15). Moreover, it has been previously demonstrated that liver-specific diseases that occur during pregnancy, including acute fatty liver and cholestasis, are likely to co-occur with HG, which strengthens the association between the latter and the dysfunction of the system on a general basis (16). Likewise, acute kidney illness has also been associated with severe HG, especially within susceptible groups (e.g., kidney transplant survivors), which, in turn, demonstrates that in the most extreme cases, it can impact more than just a single organ (17).

According to the recent literature, some of the diagnostic and therapeutic issues of HG are especially problematic in resource-limited environments. Although the genetic, hormonal, and placental basis of HG has improved, the condition remains underdiagnosed and undertreated, which, in turn, leads to high maternal morbidity (18). COVID-19 has also affected the pattern of diagnostics, and some studies have described possible overdiagnosis of fetal growth restriction during lockdowns, which can confound the presentation of clinical manifestations of HG, and which can provide false information needed to accurately classify risk (19). The correlation of HG with the transient gestational thyrotoxicosis also gives a new dimension to maternal health risks. Women with HG are likely to have thyroid dysfunction caused by hCG-mediated thyroid stimulation, which has been associated with worse disease and higher pregnancy complications (21). This endocrine interaction can also explain the increased rates of preeclampsia among HG patients in this study, and may justify the importance of thyroid testing in the treatment of such women.

The low and middle-income countries, such as Pakistan, are especially applicable in this study, where the first and third-world countries are not well-off yet, and the antenatal care coverage is limited. This classification of HG as a risk factor of preeclampsia allows clinicians to administer earlier interventions, including enhanced blood pressure levels, proteinuria screening, and nutrition. The risk should be minimized by the development of maternal health and early pregnancy education programs. In this connection, interventions such as obstetricians, nutritionists, and mental health workers also help to improve the prognosis of HG women.

Conclusion

It is demonstrated in this study that the incidence of preeclampsia and hyperemesis gravidarum (HG) during the second trimester of pregnancy is strongly correlated and that HG is a potential early clinical indicator of risky pregnancies. The risk of preeclampsia was two times higher in women who reported an episode of persistent vomiting after the first trimester as compared to women who did not have HG, which emphasises the need to detect it early and pay close attention. The findings are consistent with current literature suggesting that HG has pathophysiological pathways in common with hypertensive diseases of pregnancy, such as placental dysfunction, endothelial stress, and metabolic derangements. Blood pressure assessment, protein urine examination, and nutritional screening of women with HG as routine could benefit maternal and fetal care, particularly in low-resource settings like Pakistan. The next step of research should be the development of predictive models and assessment of biomarkers to optimize risk stratification and interventions in time to ensure better perinatal care.

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