

## Study of the association of pregnancy unique quantification of emesis score with adverse feto-maternal outcomes in pregnancy: a prospective observational cohort study

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### ABSTRACT

**Background:** Nausea and vomiting of pregnancy (NVP) affect up to 80% of gestations, ranging from mild discomfort to severe hyperemesis gravidarum. While often dismissed as a benign condition, NVP may be linked to significant adverse feto-maternal outcomes. This prospective study evaluated the clinical utility of the pregnancy-unique quantification of emesis (PUQE-24) scoring system as a prognostic tool for predicting complications among 300 pregnant women at a tertiary care hospital in Eastern India.

**Methods:** This prospective observational study (April 2023–March 2025) categorized 300 first-trimester participants into mild ( $\leq 6$ ), moderate (7–12), and severe (13–15) NVP groups using the PUQE-24 scale. Demographic data, clinical markers (ketonuria, liver enzymes), and hospitalization metrics were documented. All participants were followed through delivery to record maternal outcomes (anemia, GDM, and hypertension) and fetal outcomes (birth weight and gestational age).

**Results:** NVP was classified as mild (46.3%), moderate (35.0%), and severe (18.7%). Severe cases showed significant correlations with maternal age  $\leq 30$  years. 100% of severe cases required hospitalization (mean 4.4 days) with an 83.9% readmission rate. Severe NVP also demonstrated significantly higher rates of anemia (78.6%), GDM (58.9%), preterm delivery (83.0%), and low birth weight (94.3%) compared to mild cases.

**Conclusions:** The PUQE-24 score is a vital prognostic tool. Strong associations between NVP severity and adverse outcomes like preterm birth and fetal growth restriction necessitate early standardized assessment and targeted intervention, especially in resource-limited settings.

**Keywords:** Hyperemesis gravidarum, Pregnancy-unique quantification of emesis, Nausea and vomiting of pregnancy

### INTRODUCTION

Nausea and vomiting of pregnancy (NVP) are the most common conditions experienced during gestation, affecting approximately 50–80% of pregnant women worldwide.<sup>1</sup> Symptomatology typically begins between the 4th and 6th week, peaks around 8–12 weeks and usually resolves by the 20th week.<sup>2</sup> While often considered a normal physiological aspect of pregnancy, NVP exists on

a spectrum ranging from mild discomfort to severe symptoms that can significantly impact maternal quality of life and lead to adverse outcomes.<sup>2,3</sup> At the extreme end lies hyperemesis gravidarum (HG), characterized by persistent vomiting, dehydration, ketosis, and weight loss exceeding 5% of pre-pregnancy weight.<sup>4,5</sup> HG affects 0.3–3.6% of pregnancies and frequently necessitates hospitalization for intravenous fluids and nutritional support.<sup>6</sup>

Management follows a stepwise approach, starting with dietary modifications and lifestyle changes.<sup>7</sup> Pharmacological interventions, such as vitamin B6 (pyridoxine) and doxylamine, are initiated if conservative measures fail.<sup>5,8</sup> For severe cases, various antiemetics or corticosteroids may be employed.<sup>5,9</sup>

PUQE score has emerged as a validated, reliable instrument for quantifying the severity of NVP. The original PUQE, developed by Koren et al, involved rating the daily number of vomiting episodes, the length of nausea in hours per day, and the number of retching episodes per 12 hours, and was validated in 2005.<sup>10,11</sup>

A modified-PUQE was proposed by Lacasse et al, which captured a wider period of pregnancy by covering symptoms that occurred from the very beginning of the gestation, while maintaining the same calculation and interpretation as the original index.<sup>12</sup>

Another significant modification, termed PUQE-24, was introduced by Ebrahimi et al.<sup>13</sup> This version is scored over a 24-hour period, evaluating three key dimensions: the duration of nausea in hours, the frequency of vomiting episodes, and the frequency of retching episodes. By adding the scores from the three categories, the severity of NVP can be categorized as mild (score  $\leq 6$ ), moderate (score 7-12), or severe (score  $\geq 13$ ).

This standardized system provides clinicians with objective criteria for diagnosis and treatment planning.<sup>13</sup> It moves beyond subjective patient reports, allowing for precise risk stratification. In research settings, the PUQE-24 is particularly valuable for identifying how specific gradients of symptoms rather than just the binary presence of hyperemesis gravidarum correlate with adverse feto-maternal outcomes such as preterm labor and fetal growth restriction.

Previous research has established associations between HG and adverse outcomes such as preeclampsia, placental abruption, and low birth weight.<sup>14-17</sup> However, most studies focus on the binary presence of HG rather than the gradient of NVP severity.<sup>18-21</sup> Clinical observations suggest that increasing NVP severity aligns with higher incidences of IUGR, preterm labor, PPROM, and oligohydramnios. Despite this, there is a notable dearth of literature from the Indian subcontinent evaluating these specific relationships. This prospective observational study aims to investigate the association between PUQE-24 scores and adverse feto-maternal outcomes in a tertiary care hospital in Eastern India. Understanding these relationships would enable risk stratification, targeted surveillance, and timely interventions for high-risk pregnancies.

## METHODS

This prospective, hospital-based cohort study was conducted within the Department of Gynaecology and

Obstetrics at Tata Main Hospital from April 2023 to March 2025. A total of 300 pregnant women with singleton pregnancy, attending the OPD in the first trimester (gestational age  $< 12$  weeks) were enrolled upon presenting with symptoms of nausea and vomiting.

Women unwilling to participate, those with multiple or molar pregnancies, pre-existing medical conditions such as diabetes or hypothyroidism, known hemoglobinopathies, elevated beta HCG during screening or with non-obstetric surgical or medical causes of emesis were excluded from the study. Informed written consent was obtained. Upon enrolment, detailed demographic, obstetric, and medical history was collected. Based on self-reported experiences of NVP, the severity of NVP was assessed using the PUQE-24 score (Table 1).

Based on the scores, participants were categorized into mild ( $\leq 6$ ), moderate (7-12), and severe (13-15) NVP groups. Signs of dehydration was clinically assessed. Apart from routine antenatal investigations, blood for LFT, serum electrolytes, and urine sample for estimation of urinary ketones were sent for women with moderate and severe NVP and for those requiring admission. The length of stay was documented for patients requiring hospitalization.

Patients were treated following standard protocols and guidelines. All participants were followed up throughout their pregnancy and readmission rates were also recorded. All participants were followed up till delivery and pregnancy outcomes (maternal and neonatal outcomes) were noted.

Maternal outcomes assessed included incidence of anemia, GDM, blood pressure changes, pregnancy loss, and gestational age at delivery. Fetal outcomes evaluated included growth parameters on fetal growth scan, amniotic fluid index, Doppler studies, birth weight, and perinatal asphyxia. All details were recorded in a predesigned, pretested proforma.

## Statistical analysis

The collected data was organized and tabulated in Microsoft Excel 2016 (Microsoft Office 2016 package) and statistical analysis was done using statistical package for social sciences (SPSS) version 23.0 (IBM Corp., Illinois, Chicago). The data was analyzed by appropriate statistical tools and represented by various tables, graphs, and diagrams. Continuous variables were expressed as mean  $\pm$  standard deviation (SD), and categorical variables were expressed as relative frequency and percentage. Mean PUQE scores were compared across different maternal and fetal outcomes by Mann Whitney U test. Comparison of various parameters across mild, moderate and severe NVP was conducted using Kruskal-Wallis test for continuous variables and Chi-square or Fisher's exact test for categorical variables. A  $p < 0.05$  was considered statistically significant.

**Table 1: The PUQE-24 scoring system.**

Questions (in the last 24 hours)	1 Point	2 Points	3 Points	4 Points	5 Points
How long have you felt nauseated or sick to your stomach?	Not at all	1 hour or less	2-3 hours	4-6 hours	More than 6 hours
Have you vomited or thrown up?	I did not throw up	1-2 times	3-4 times	5-6 times	7 or more times
How many times have you had retching or dry heaves?	No time	1-2 times	3-4 times	5-6 times	7 or more times
<b>Additional questions</b>					
<b>How many hours have you slept out of 24 hours? Why?</b>					
<b>On a scale of 0 to 10, how would you rate your well-being? (0=worst possible; 10=the best you felt before pregnancy)</b>					
<b>Can you tell me what causes you to feel that way?</b>					

Scoring interpretation: mild≤6; moderate=7-12; severe=13-15

## RESULTS

Most participants were primigravidae aged ≤30 years (Table 2).

NVP severity was classified using PUQE scores (Table 3).

**Table 2: Distribution according to baseline characteristics (n=300).**

Characteristics	Frequency (N)	Percentage
<b>Age (years)*</b>		
≤25	99	33.0
26-30	98	32.7
31-35	81	27.0
>35	22	7.3
<b>Gravida</b>		
Primigravida	154	51.3
Multigravida	146	48.7
<b>Gestational age at presentation (weeks)</b>		
5-6 <sup>+</sup> 6	72	24.0
7-8 <sup>+</sup> 6	110	36.7
9-10 <sup>+</sup> 6	88	29.3
11-12 <sup>+</sup> 6	30	10.0

\*Mean ( $\pm$ SD) – 28.4 ( $\pm$ 5.1); median (IQR) – 29 (24-33); minimum, maximum – 19,36

Maternal age significantly correlated with NVP severity, with women over 30 years more likely to experience severe symptoms (53.6%). Clinical complications increased dramatically with NVP severity. No women with mild NVP experienced dehydration, weight loss, raised

liver enzymes, or ketonuria, while these were affected in most of the severe cases (Table 4).

**Table 3: Distribution according to severity of NVP (according to PUQE score) at first presentation (n=300).**

Severity of NVP at first presentation	Frequency (N)	Percentage
<b>Mild (≤6)</b>	139	46.3
<b>Moderate (7-12)</b>	105	35.0
<b>Severe (13-15)</b>	56	18.7

All severe NVP cases required hospitalization (average 4.4 days) compared to none in the mild group. Readmission rates were similarly stratified: 83.9% for severe, 50.5% for moderate, and none for mild cases. Maternal outcomes demonstrated strong correlations with NVP severity (Figure 1).

All pregnancy losses (5.4%) occurred exclusively in the severe NVP group. Preterm delivery showed a clear gradient: 83.0% in severe cases, 62.9% in moderate, and only 16.6% in mild cases.

Among adverse fetal outcomes, small-for-gestational-age fetuses were identified in 58.9% of severe NVP cases compared to 15.8% in mild cases; and low birth weight (<2.5 kg) affected 94.3% of infants born to women with severe NVP versus 38.1% in the mild group. While reduced amniotic fluid and perinatal asphyxia were more common with increasing NVP severity, these associations did not reach statistical significance.

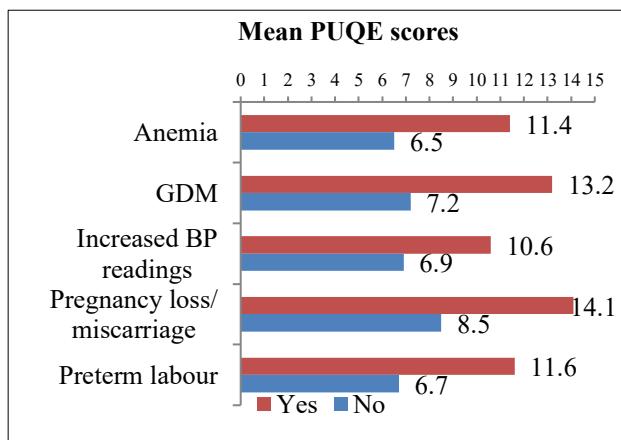
**Table 4: Association of baseline characteristics with severity of NVP at first presentation (n=300).**

Characteristics	Mild NVP (n=139) N (%)	Moderate NVP (n=105) N (%)	Severe NVP (n=56) N (%)	P value
<b>Dehydration</b>				
Present	0 (0.0)	20 (19.1)	48 (85.7)	<0.001*
Absent	139 (100.0)	85 (80.9)	8 (14.3)	
<b>Weight loss</b>				
Yes	0 (0.0)	10 (9.5)	31 (55.4)	<0.001*

Continued.

Characteristics	Mild NVP (n=139) N (%)	Moderate NVP (n=105) N (%)	Severe NVP (n=56) N (%)	P value
No	139 (100.0)	95 (90.5)	25 (44.6)	
<b>LFT</b>				
Normal	139 (100.0)	14 (13.3)	3 (5.4)	<0.001*
Raised	0 (0.0)	91 (86.7)	53 (94.6)	
<b>Urinary ketones</b>				
Present	0 (0.0)	86 (81.9)	54 (96.4)	<0.001*
Absent	139 (100.0)	19 (18.1)	2 (3.6)	
<b>Serum electrolytes</b>				
Normal	139 (100.0)	105 (100.0)	51 (91.1)	0.002*
Abnormal	0 (0.0)	0 (0.0)	5 (8.9)	

\*P value was calculated using Chi square test or Fisher exact test (for categorical variables) and p<0.05 was considered to be statistically significant



**Figure 1: Comparison of mean PUQE scores according to maternal outcomes (n=300).**

## DISCUSSION

Our analysis showed that the severity of NVP significantly increased with maternal age ( $30.6 \pm 4.0$  years in women with severe NVP compared to  $27.1 \pm 5.5$  years in women with mild NVP,  $p<0.001$ ). This finding contradicts some earlier reports suggesting that younger women experience more severe symptoms but aligns with studies by Louik et al who found an association between increased maternal age NVP severity.<sup>22</sup> Contrary to previous studies reporting higher rates of NVP in primigravida with an 80% chance of recurrence in subsequent pregnancies, our study did not find a statistically significant association between gravidity and NVP severity ( $p=0.213$ ) suggesting that the severity of NVP may be influenced by factors other than gravidity alone.<sup>23</sup> This is consistent with research by Vikanes et al, who reported that parity alone was not a strong predictor of NVP severity.<sup>24</sup> Prior research by Lacroix et al reported that NVP symptoms typically peak around 9-10 weeks of gestation.<sup>23</sup> Our data revealed a similar and significant association between gestational age at presentation and NVP severity ( $p=0.014$ ), with severe NVP more common in later first-trimester presentations.

Dehydration was observed in 22.7% of cases, with a striking prevalence of 85.7% among those with severe

NVP ( $p<0.001$ ). This prominent association between severe NVP and dehydration underscores the physiological impact of persistent vomiting on fluid balance, as also highlighted by Simanjuntak et al.<sup>25</sup> Weight loss was significantly more prevalent in women with severe NVP (55.4%,  $p<0.001$ ) similarly documented by Fejzo et al.<sup>26</sup> Elevated liver function tests were observed in 94.6% cases in the severe NVP group ( $p<0.001$ ). This high occurrence of hepatic dysfunction in severe cases is consistent with previous studies and suggests a systemic impact of severe NVP beyond gastrointestinal symptoms.<sup>27</sup> Similarly, the presence of urinary ketones in 96.4% cases with severe NVP indicate the metabolic consequences of reduced caloric intake and dehydration, as also reported by Birkeland et al.<sup>28</sup>

Electrolyte disturbances, though less common (1.7% overall), were exclusively found in the severe NVP group (8.9%), highlighting the potential for significant metabolic derangement in severe cases. This pattern of electrolyte imbalance aligns with case reports of severe complications in hyperemesis gravidarum by Chiossi et al and systematic review by Popa et al.<sup>27,29</sup>

Women with severe NVP experienced symptoms for significantly longer periods ( $4.1 \pm 0.6$  months) compared to those with mild symptoms ( $2.2 \pm 1.0$  months,  $p<0.001$ ) similar to the study by Lacroix et al.<sup>23</sup> All women with severe NVP required hospital admission compared to 78.1% with moderate NVP and none with mild symptoms ( $p<0.001$ ). This finding is consistent with studies by Trovik and Vikanes, who identified hyperemesis gravidarum as a leading cause of hospitalization during early pregnancy.<sup>30</sup> Furthermore, the duration of hospital stay was significantly longer in severe cases ( $4.4 \pm 0.6$  days) compared to moderate cases ( $1.6 \pm 1.4$  days,  $p<0.001$ ), indicating the increased healthcare burden associated with severe NVP. Readmission rates were 83.9% in severe cases compared to 50.5% in moderate cases ( $p<0.001$ ). Gazmararian et al also reported NVP as the most common reasons for hospitalization during pregnancy.<sup>31</sup>

Anemia (hemoglobin  $<11$  g/dl at 28 weeks) was seen in 78.6% cases in the severe NVP group compared to 31.7%

in mild cases ( $p<0.001$ ). This may be attributed to nutritional deficiencies resulting from prolonged reduced intake and malabsorption, as also suggested by Maslin et al.<sup>32</sup> Gestational diabetes mellitus (GDM) also showed a strong association with NVP severity, affecting 58.9% of women with severe symptoms compared to only 6.5% in the mild group ( $p<0.001$ ). This unexpectedly high prevalence of GDM in severe NVP cases contrasts with some previous studies that reported no significant association.<sup>33</sup> Elevated blood pressure had a significantly higher prevalence in the severe NVP group (80.4%,  $p<0.001$ ). This association between severe NVP and hypertensive disorders aligns with findings by Fiaschi et al, who reported an increased risk of pre-eclampsia in women with hyperemesis gravidarum.<sup>34</sup>

Notably, all pregnancy losses (1.0% overall) occurred exclusively in the severe NVP group (5.4%,  $p=0.023$ ) similar to the study by Hinkle et al, who found associations between severe NVP and increased risk of pregnancy loss.<sup>33</sup> A high rate of preterm birth was reported among women with moderate (62.9%) and severe (83.0%) NVP compared to only 16.6% in the mild group ( $p<0.001$ ) similar to a systematic review by Jansen et al.<sup>35</sup> Small for gestational age (SGA) was observed in 58.9% in the severe NVP group compared to 15.8% in the mild group ( $p<0.001$ ). This finding is consistent with research by Koudijs et al, who proposed that placental dysfunction related to maternal nutritional deficiencies might contribute to growth restriction in pregnancies complicated by hyperemesis gravidarum.<sup>36</sup> Low birth weight (<2.5 kg) showed the strongest association with NVP severity among all fetal outcomes, affecting 94.3% of infants born to mothers with severe NVP compared to 38.1% in the mild group ( $p=0.001$ ). This dramatic increase in low birth weight with increasing NVP severity supports findings from a meta-analysis by Veenendaal et al, which reported a 42% increased risk of low birth weight in pregnancies complicated by hyperemesis gravidarum.<sup>17</sup>

Women who developed anemia had significantly higher mean PUQE scores ( $11.4\pm2.9$ ) compared to those without anemia ( $6.5\pm2.3$ ,  $p<0.001$ ). Similarly, participants who developed GDM had markedly elevated scores ( $13.2\pm1.7$  versus  $7.2\pm2.9$ ,  $p<0.001$ ), as did those with elevated blood pressure readings ( $10.6\pm2.6$  versus  $6.9\pm2.4$ ,  $p<0.001$ ). The highest PUQE scores were observed in women who experienced pregnancy loss, preterm delivery and in fetuses showing growth restriction ( $p<0.001$ ) had significantly higher mean PUQE scores ( $11.6\pm1.4$ ) compared to those with normal growth ( $7.2\pm1.2$ ,  $p<0.001$ ), and women who delivered low birth weight infants had elevated scores ( $10.7\pm1.7$  versus  $7.0\pm1.4$ ,  $p<0.001$ ). These findings suggest that the PUQE score may serve as a valuable predictor of adverse maternal and fetal outcomes, supporting its use not only as a diagnostic tool for NVP severity but also as a prognostic indicator for pregnancy complications. This application of the PUQE score aligns with research by Koren and Cohen, who advocated for its

broader use in clinical decision-making and risk assessment.<sup>37</sup>

Despite its prospective design, this study has several limitations that should be considered when interpreting the results. The single-center nature of the study may reduce the generalizability of findings to more diverse populations with different demographic profiles or healthcare access. Furthermore, there may also be confounding factors not fully accounted for in the analysis, such as pre-existing maternal conditions, development of pregnancy complications or socioeconomic factors that could influence pregnancy outcomes. Addressing these limitations in future research through multi-center studies with larger sample sizes and diverse demographic profiles would strengthen the external validity of these results.

## CONCLUSION

The findings of the present study highlight the clinical utility of the PUQE score as both a diagnostic and prognostic tool in the management of NVP. The strong associations observed between NVP severity and adverse feto-maternal outcomes—particularly pregnancy loss, preterm birth, small for gestational age (SGA), and low birth weight—emphasize the need to recognize NVP not merely as a benign and transient feature of pregnancy, but as a potential risk factor for serious complications that warrants appropriate clinical attention. Early identification of women with more severe symptoms, as indicated by higher PUQE scores, along with timely intervention, may help mitigate these adverse outcomes, especially in resource-limited settings, where advanced fetal surveillance tools may not be readily available.

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