American Journal of Medicine and Medical Sciences 2026, 16(2): 581-582
DOI: 10.5923/j.ajmms.20261602.41

Serum GDF-15 as a Predictor of Hyperemesis Gravidarum Severity in Early Pregnancy

Mamadieva M. G.[1], Shokirova S. M.[2], Zufarova Sh. A.[2]

[1]Andijan State Medical Institute, Andijan, Uzbekistan
[2]Tashkent State Medical University, Tashkent, Uzbekistan

Abstract Hyperemesis gravidarum represents the most severe form of nausea and vomiting in early pregnancy and is associated with dehydration, metabolic disturbances, and adverse maternal outcomes. Identification of reliable biochemical predictors of disease severity remains an important clinical challenge.

Keywords Hyperemesis gravidarum, Early pregnancy, GDF-15, Nausea and vomiting of pregnancy, Biomarker, Disease severity

1. Introduction

Nausea and vomiting of pregnancy (NVP) affects more than half of pregnant women and typically develops during the first trimester [11]. While symptoms are mild in most cases, approximately 10–15% of women experience moderate or severe manifestations, with hyperemesis gravidarum representing the extreme form of the condition [5,6]. Despite extensive research, the underlying mechanisms of hyperemesis gravidarum remain incompletely understood [6]. Recent evidence suggests a central role of placental-derived factors influencing appetite regulation and emetic pathways [1,3]. Growth Differentiation Factor-15 (GDF-15) is a stress-responsive cytokine belonging to the transforming growth factor-β family and is actively secreted by trophoblastic tissue during early pregnancy [1]. Experimental and clinical studies have demonstrated that GDF-15 acts on the brainstem via the GFRAL receptor, leading to appetite suppression and induction of nausea and vomiting [2]. Elevated maternal circulating levels of GDF-15 have been associated with increased severity of NVP and hyperemesis gravidarum [3,10].

2. Materials and Methods

Serum GDF-15 levels were measured using enzyme-linked immunosorbent assay (ELISA), as described in previous studies evaluating GDF-15 in pregnancy-related nausea and vomiting [3,10].

Disease severity classification was based on commonly accepted clinical criteria, including frequency of vomiting, weight loss, and signs of dehydration [5,12].

This observational study included 120 pregnant women between 6 and 12 weeks of gestation.

- Study group: 80 women with clinical symptoms of nausea and vomiting
- Control group: 40 asymptomatic healthy pregnant women

The groups were comparable in terms of age, gestational age, parity, and pre-pregnancy body mass index.

Assessment of Disease Severity

Severity was classified as mild, moderate, or severe (hyperemesis gravidarum) based on:

- Frequency of vomiting episodes per day
- Percentage of weight loss
- Clinical signs of dehydration and ketonuria

Laboratory Analysis

Venous blood samples were collected after overnight fasting. Serum GDF-15 levels were measured using a commercially available ELISA kit. Results were expressed in pg/mL.

Statistical Analysis

Data were analyzed using SPSS software.

Quantitative variables were expressed as mean ± standard deviation. Group comparisons were performed using Student's t-test. ROC curve analysis was used to determine predictive thresholds, sensitivity, specificity, and area under the curve (AUC). A p-value <0.05 was considered statistically significant.

3. Results

The observed progressive increase in serum GDF-15 levels with increasing disease severity is consistent with

Received: Jan. 3, 2026; Accepted: Jan. 29, 2026; Published: Feb. 7, 2026
Published online at http://journal.sapub.org/ajmms

findings reported in previous cohort and case-control studies [3,10]. Women with hyperemesis gravidarum demonstrated significantly higher GDF-15 concentrations compared with asymptomatic pregnant controls ($p < 0.001$), which aligns with earlier reports [1]. Serum GDF-15 levels increased significantly with disease severity: 3180 ± 760 pg/mL in mild cases, 4620 ±910 pg/mL in moderate cases, and 6720 ± 1250 pg/mL in hyperemesis gravidarum, compared to 2170 ± 640 pg/mL in controls ($p < 0.001$). ROC analysis demonstrated high predictive accuracy of GDF-15 for moderate-to-severe disease (AUC = 0.89). A threshold value >4000 pg/mL showed 82% sensitivity and 78% specificity for predicting severe clinical progression.

Mild symptoms were observed in 56.3% of women, moderate in 31.2%, and severe hyperemesis gravidarum in 12.5%.

A significant progressive increase in serum GDF-15 concentration was observed with increasing disease severity. Women with hyperemesis gravidarum exhibited more than a threefold elevation in GDF-15 levels compared with controls ($p < 0.001$).

ROC analysis demonstrated that serum GDF-15 effectively discriminated women with moderate-to-severe disease from those with mild or no symptoms. A cut-off value >4000 pg/mL showed optimal diagnostic performance (AUC = 0.89).

4. Discussion

Our findings support the hypothesis that excessive placental secretion of GDF-15 plays a key role in the pathogenesis of hyperemesis gravidarum [1,2]. Activation of appetite-regulating pathways in the brainstem by elevated GDF-15 may exacerbate nausea, vomiting, and weight loss during early pregnancy [2,3]. Early identification of women at high risk using biochemical markers such as GDF-15 may improve clinical management, reduce hospitalization rates, and prevent severe maternal complications [4,8,12]. Previous cohort and case-control studies have reported significantly higher circulating GDF-15 levels in women with HG compared with asymptomatic pregnant controls [3,10]. From a clinical perspective, identification of reliable biomarkers such as GDF-15 may improve early risk stratification and management of HG [4,12]. Psychological and quality-of-life impairment associated with severe HG further highlights the importance of early diagnosis and intervention [7].

5. Conclusions

Serum GDF-15 is a strong predictor of disease severity in nausea and vomiting of pregnancy, confirming its potential clinical utility as an early biomarker for hyperemesis gravidarum [1,3,10]. Measurement of serum GDF-15 in early pregnancy may assist in identifying women at increased risk of moderate-to-severe NVP and hyperemesis gravidarum.

REFERENCES

[1] Fejzo MS, Sazonova OV, Sathirapongsasuti JF, et al. Placental gene GDF15 is associated with hyperemesis gravidarum. Nature Communications. 2018; 9: 1178. doi: 10.1038/s41467-018-03258-0.

[2] Hsu JY, Crawford TD, Chang JY, et al. Non-homeostatic body weight regulation through a brainstem-restricted receptor for GDF15. Nature. 2017; 550(7675): 255–259. doi: 10.1038/nature24042.

[3] Petry CJ, Lewis RM, Osmond C, et al. Associations of maternal circulating GDF15 with nausea and vomiting in pregnancy and birth outcomes: A prospective cohort study. Scientific Reports. 2020; 10: 9807. doi: 10.1038/s41598-020-66638-3.

[4] Fejzo MS, MacGibbon KW, Mullin PM. Why are women still dying from nausea and vomiting of pregnancy? Gynecologic and Obstetric Investigation. 2019; 84(1): 1–4. doi: 10.1159/000494927.

[5] London V, Grube S, Sherer DM, Abulafia O. Hyperemesis gravidarum: A review of recent literature. Pharmacology. 2017; 100(3–4): 161–171. doi: 10.1159/000477853.

[6] Verberg MF, Gillott DJ, Al-Fardan N, Grudzinskas JG. Hyperemesis gravidarum, a literature review. Human Reproduction Update. 2005; 11(5): 527–539. doi: 10.1093/humupd/dmi021.

[7] Mitchell-Jones N, Gallos I, Farren J, Tobias A, Bottomley C, Bourne T. Psychological morbidity associated with hyperemesis gravidarum: A systematic review and meta-analysis. BJOG. 2017; 124(1): 20–30. doi: 10.1111/1471-0528.14180.

[8] Koot MH, Grooten IJ, Van der Post JAM, et al. Risk factors for hyperemesis gravidarum: A systematic review and meta-analysis. American Journal of Obstetrics and Gynecology. 2020; 223(5): e1–e18. doi: 10.1016/j.ajog.2020.03.009.

[9] Kim E, Lee Y, Park J. Maternal metabolic factors associated with nausea and vomiting in early pregnancy. Journal of Obstetrics and Gynaecology Research. 2021; 47(6): 1982–1990. doi: 10.1111/jog.14740.

[10] Olsen HG, Lomo J, Jacobsen MB, et al. Increased plasma levels of GDF15 in hyperemesis gravidarum. PLoS ONE. 2021; 16(3): e0249124. doi: 10.1371/journal.pone.0249124.

[11] Gadsby R, Barnie-Adshead AM, Jagger C. A prospective study of nausea and vomiting during pregnancy. British Journal of General Practice. 1993; 43(371): 245–248.

[12] American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin No. 189: Nausea and vomiting of pregnancy. Obstetrics & Gynecology. 2018; 131(1): e15–e30. doi: 10.1097/AOG.0000000000002456.