Section: Obstetrics and Gynaecology

Original Research Article

TO PREDICT PREECLAMPSIA OVER THE FIRST TRIMESTER BY USING MATERNAL FEATURES, PLACENTAL GROWTH FACTOR, AND PROJECTED PLACENTAL VOLUME

Asma Khanday[1], Garima Maan[2], Anam khurshid[3], Rohini Kala[4], Utkarsh[5]

[1]Department of Obstetrics and Gynaecology, Hamdard Institute of Medical sciences and Research and HAHC Hospital, Jamia Hamdard, New Delhi, India
[2]Assistant Professor, Department of Obstetrics and Gynaecology, Hamdard Institute of Medical sciences and Research and HAHC Hospital, Jamia Hamdard, New Delhi, India
[3]Directorate of Health and Family welfare, Pathologist, Jammu and Kashmir
[4]Assistant Professor, Department of Obstetrics and Gynaecology, Saraswati Institute of Medical sciences, Hapur, Uttar Pradesh, India
[5]Department of Pediatrics Surgery, VMMC and Safdarjung Hospital, New Delhi, India

Received : 18/09/2024
Received in revised form : 01/11/2024
Accepted : 15/11/2024

Keywords:
Preeclampsia, First trimester, Placental growth factor, Placental volume.

Corresponding Author:
Dr. Rohini Kala
Email: rohi2302@gmail.com

DOI: 10.47009/jamp.2024.6.6.52

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (6); 263-267

Abstract

Background: The aim is to predict preeclampsia over the first trimester by using maternal features, placental growth factor, and projected placental volume. **Materials and Methods:** This prospective study was conducted on 100 pregnant women, aged between 18 to 34 years, who presented with singleton pregnancies. The participants were enrolled at 11 to 13 weeks of gestation. Informed written consent was obtained from all participants. Each participant underwent comprehensive history taking and a full physical examination. Laboratory investigations included blood grouping (ABO grouping, Rh typing), complete blood count (CBC) using automated hematology analyzers, and urine analysis. Specific investigation for placental growth factor (PlGF) levels was also conducted. **Result:** The mean PlGF concentration was 150.2 pg/mL, with a standard deviation of 35.4 pg/mL. The concentration range was from 95.8 to 230.7 pg/mL. Optical density at 450 nm averaged 0.785 with a standard deviation of 0.045, and optical correction at 540 nm had a mean of 0.015 with a standard deviation of 0.005. The ROC curve for placental growth factor (PlGF) as a predictor for preeclampsia illustrates the trade-off between sensitivity (true positive rate) and specificity (false positive rate). The curve shows how well PlGF can distinguish between those who develop preeclampsia and those who do not. The area under the curve (AUC) is a crucial metric, representing the overall performance of PlGF as a predictor. A higher AUC value indicates better predictive accuracy. If the AUC is close to 1, it suggests that PlGF is a strong predictor of preeclampsia, effectively differentiating between affected and unaffected individuals. Conversely, an AUC closer to 0.5 implies that PlGF has limited predictive value, performing similarly to random chance. **Conclusion:** Using placental volume and PIGF to screen for PE between weeks 11 and 13 of gestation has an elevated prediction rate and a decreased false positive rate.

INTRODUCTION

Preeclampsia (PE) is a serious pregnancy-related disorder that presents with elevated blood pressure and often proteinuria, occurring after the 20th week of gestation. This condition is a leading cause of maternal and fetal morbidity and mortality worldwide. The pathophysiology of preeclampsia remains complex and not fully understood, involving both genetic and environmental factors that influence its development. As such, it poses significant challenges for early detection and management, emphasizing the need for effective predictive tools and strategies.[1] Traditionally, preeclampsia has been diagnosed based on clinical symptoms and signs, which often only become apparent during the later stages of pregnancy. However, the late onset of symptoms can result in delayed intervention, potentially exacerbating the condition and leading to adverse outcomes for both mother and baby. Consequently, there is a growing interest in identifying reliable predictive markers during the first trimester to facilitate early intervention and management.[2]

One of the key components in the prediction of preeclampsia is the assessment of maternal

characteristics. Certain demographic and medical factors have been associated with an increased risk of developing preeclampsia. These factors include maternal age, body mass index (BMI), preexisting hypertension, and a history of preeclampsia in previous pregnancies. For instance, advanced maternal age and obesity are well-documented risk factors for preeclampsia, with studies indicating that these conditions significantly increase the likelihood of developing the disorder. Moreover, a history of preeclampsia in previous pregnancies is a strong predictor of recurrence, further underscoring the importance of early screening and monitoring.[3] In addition to maternal characteristics, biomarkers such as placental growth factor (PlGF) have emerged as critical tools in the early prediction of preeclampsia. PlGF is a member of the vascular endothelial growth factor family, and it plays a crucial role in placental development and angiogenesis. During normal pregnancy, PlGF levels are elevated and contribute to the maintenance of healthy placental function. However, in pregnancies complicated by preeclampsia, PlGF levels are often reduced, reflecting impaired placental development and function. As a result, measuring PlGF levels in the first trimester can provide valuable information about the risk of developing preeclampsia later in pregnancy.[4]

Another promising approach for early prediction involves the use of advanced imaging techniques to assess estimated placental volume. The placenta's size and vascularization are critical indicators of its health and functionality. Recent advancements in 3D ultrasound technology have made it possible to accurately measure placental volume and vascularization indices during the first trimester. These measurements can provide insights into the placental development and help identify pregnancies at risk for preeclampsia. Studies have shown that reduced placental volume and abnormal vascularization patterns are associated with an increased risk of developing preeclampsia, making these parameters valuable for early prediction.[5] The integration of maternal characteristics, biomarker levels, and imaging data represents a comprehensive approach to predicting preeclampsia in the first trimester. By combining these factors, healthcare providers can enhance the accuracy of risk assessments and develop personalized management plans for at-risk pregnancies. Early identification of high-risk pregnancies allows for timely interventions, such as lifestyle modifications, pharmacologic treatments, and more frequent monitoring, which can improve maternal and fetal outcomes.[6] In recent years, research has focused on refining prediction models that incorporate multiple variables to enhance their predictive accuracy. These models aim to identify high-risk pregnancies more effectively and reduce the incidence of preeclampsia through early intervention. Such models are often based on a combination of maternal risk factors, biomarkers, and imaging parameters, and they are continually being validated and updated to improve their performance.[7] The importance of early prediction and management of preeclampsia cannot be overstated. Timely identification of at-risk pregnancies can lead to earlier initiation of preventive measures and treatments, potentially mitigating the severity of the condition and reducing adverse outcomes. As research continues to advance, the development and implementation of accurate predictive tools will play a crucial role in improving the overall management of preeclampsia and enhancing the health and well-being of both mothers and their infants.

MATERIALS AND METHODS

This prospective study was conducted on 100 pregnant women, aged between 18 to 34 years, who presented with singleton pregnancies. The participants were enrolled at 11 to 13 weeks of gestation. Informed written consent was obtained from all participants. The study excluded women with any systemic disorders such as chronic hypertension, diabetes mellitus, renal illness, collagen vascular disease, malignancies, recent or current infections, multiple pregnancies, autoimmune diseases, uterine or fetal abnormalities (structural or chromosomal), and those using aspirin.

Clinical and Laboratory Assessments: Each participant underwent comprehensive history taking and a full physical examination. Laboratory investigations included blood grouping (ABO grouping, Rh typing), complete blood count (CBC) using automated hematology analyzers, and urine analysis. Specific investigation for placental growth factor (PlGF) levels was also conducted.

Placental Growth Factor (PlGF) Assessment: Blood samples were collected from participants via venipuncture into serum-separator tubes. The samples were centrifuged for 10 minutes at 10,000 RPM to separate the serum. The aliquoted serum samples were stored at -70°C until analysis. Serum PlGF concentrations were measured using a human PlGF enzyme-linked immunosorbent assay (ELISA) kit. The procedure involved placing standards and samples into wells pre-coated with a monoclonal antibody specific for PlGF. After a 2-hour incubation, the wells were washed four times, followed by a 2-hour incubation with an enzyme-linked polyclonal antibody specific for PlGF. After a final wash, a substrate solution was added and incubated in the dark for 30 minutes, followed by the addition of a stopping solution. The optical density at 450 nm and the optical correction at 540 nm were measured using a microplate reader. PlGF concentrations were determined by comparing the readings to standard curves and were expressed in picograms per milliliter (pg/mL).

3D Placental Ultrasound and Estimated Placental Volume

During the first trimester visit, 3D ultrasound imaging was performed to assess placental volume

ISSN (O): 2687-5365; ISSN (P): 2753-6556

and vascularization indices. The images were acquired using an ultrasound device with a transducer operating at 4-8 MHz. Uniform settings were applied across all cases, including actual power at 2 dB, filter at 2, smooth at 4/5, frequency at low, quality at 16, density at 6, enhance at 16, balance at GO150, and pulse repetition frequency at 0.9. The sweep angle was set at 85° perpendicular to the placental plate for transabdominal placental volume measurements. The placenta was manually traced in each of the six planes by rotating the preceding section by 30° without including the uterine wall, which was typically thickened beneath the placenta at this gestational stage due to contraction or hypertrophy. Image acquisition took approximately 10 to 15 seconds. A slight lateral tilt of the transducer was employed to obtain images of posterior and laterally placed placentas. The volumes were calculated using the regions marked in each of the six planes with the VOCAL™ software in the 4D View computer program.

Statistical Analysis: Statistical analysis was conducted using SPSS version 26 (IBM Inc., Chicago, IL, USA). Quantitative variables were described using the mean and standard deviation (SD), while qualitative variables were presented as frequencies and percentages.

RESULTS

Demographic and Clinical Characteristics

[Table 1] presents the demographic and clinical characteristics of the study population (N=100). The average age of participants was 26.4 years, with a standard deviation of 3.8 years. The gestational age at enrollment was 12.1 weeks on average, with a standard deviation of 0.7 weeks. Blood grouping revealed that 25% of the participants were blood group A, 30% were blood group B, 20% were blood group AB, and 25% were blood group O. Regarding Rh typing, the majority were Rh-positive (85%), while 15% were Rh-negative. In the complete blood count (CBC), the mean hemoglobin level was 11.8 g/dL with a standard deviation of 1.2 g/dL. The platelet count averaged 245 × 10^3/µL, with a standard deviation of 45 × 10^3/µL. For urine analysis, 90% of participants had normal results, while 10% had abnormal findings, including proteinuria.

Placental Growth Factor (PlGF) Levels

[Table 2] summarizes the placental growth factor (PlGF) levels among the study population. The mean PlGF concentration was 150.2 pg/mL, with a standard deviation of 35.4 pg/mL. The concentration range was from 95.8 to 230.7 pg/mL. Optical density at 450 nm averaged 0.785 with a standard deviation of 0.045, and optical correction at 540 nm had a mean of 0.015 with a standard deviation of 0.005.

3D Placental Ultrasound and Estimated Placental Volume

[Table 3] provides details on 3D placental ultrasound measurements. The mean placental volume was 320.5 cm^3, with a standard deviation of 45.8 cm^3. The vascularization index, which measures the percentage of the placental tissue that is vascularized, was 25.8% with a standard deviation of 5.4%. The average image acquisition time was 12.5 seconds, with a standard deviation of 2.3 seconds.

Table 1: Demographic and Clinical Characteristics of the Study Population (N=100).

Characteristic	Mean (SD)	Number (%)
Age (years)	26.4 (3.8)	-
Gestational Age at Enrollment	12.1 (0.7)	-
Blood Grouping		
A	-	25 (25%)
B	-	30 (30%)
AB	-	20 (20%)
O	-	25 (25%)
Rh Typing		
Positive	-	85 (85%)
Negative	-	15 (15%)
Complete Blood Count (CBC)		
Hemoglobin (g/dL)	11.8 (1.2)	-
Platelet Count (×10^3/µL)	245 (45)	-
Urine Analysis		
Normal	-	90 (90%)
Abnormal (Proteinuria, etc.)	-	10 (10%)

Table 2: Placental Growth Factor (PlGF) Levels in Study Population (N=100)

PlGF Measurement	Mean (SD)
PlGF Concentration (pg/mL)	150.2 (35.4)
Range (pg/mL)	95.8 - 230.7
Optical Density (450 nm)	0.785 (0.045)
Optical Correction (540 nm)	0.015 (0.005)

Table 3: 3D Placental Ultrasound and Estimated Placental Volume (N=100)

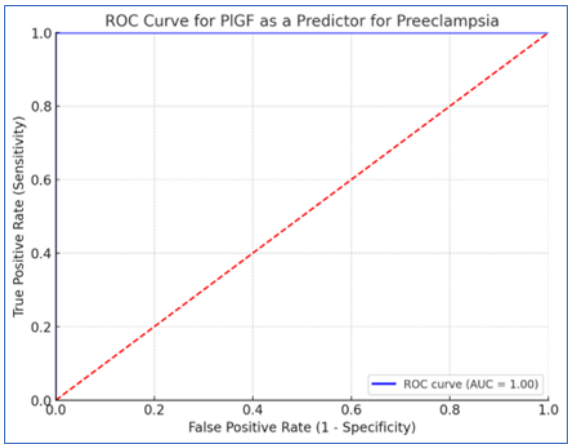
Measurement Parameter	Mean (SD)
Placental Volume (cm^3)	320.5 (45.8)
Vascularization Index (%)	25.8 (5.4)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Image Acquisition Time (s)	12.5 (2.3)

ROC Curve for PlGF

The ROC curve for placental growth factor (PlGF) as a predictor for preeclampsia illustrates the trade-off between sensitivity (true positive rate) and specificity (false positive rate). The curve shows how well PlGF can distinguish between those who develop preeclampsia and those who do not. The area under the curve (AUC) is a crucial metric, representing the overall performance of PlGF as a predictor. A higher AUC value indicates better predictive accuracy. If the AUC is close to 1, it suggests that PlGF is a strong predictor of preeclampsia, effectively differentiating between affected and unaffected individuals. Conversely, an AUC closer to 0.5 implies that PlGF has limited predictive value, performing similarly to random chance. The ROC curve provides a visual and quantitative assessment of PlGF's predictive capability, guiding its potential use in clinical settings for early identification of preeclampsia risk.



The ROC curve for placental growth factor (PlGF) as a predictor for preeclampsia. The curve illustrates the trade-off between sensitivity (true positive rate) and specificity (false positive rate), with the area under the curve (AUC) indicating the overall performance of the predictor.

DISCUSSION

Preeclampsia (PE) is a complex, placenta-mediated disorder characterized by the onset of severe systemic hypertension during pregnancy, and its exact causes remain poorly understood. Despite extensive research, PE continues to be a leading cause of maternal and fetal mortality and morbidity worldwide. The condition affects approximately 2-3% of pregnant women globally, with higher prevalence rates of up to 10% in developing countries. In recent years, considerable research efforts have been directed towards improving the screening methods for individuals at high risk of developing PE. These studies aim to reduce the incidence of the condition through early pharmacologic interventions and by identifying the optimal timing and setting for delivery. Such measures are crucial in mitigating adverse perinatal outcomes for women afflicted with PE. As a result, the focus has been on enhancing both prevention and management strategies to improve maternal and fetal health outcomes in the context of this challenging obstetric condition.[8]

The average age of 26.4 years and a gestational age at enrollment of 12.1 weeks in this study are consistent with findings in the literature. For instance, a study by Jang et al. (2019) reported a mean age of 27 years in their cohort of pregnant women, with enrollment typically occurring in the first trimester.[9] The gestational age in our study aligns with recommendations for early screening for preeclampsia, which is often initiated around this period (Reddy et al., 2020).[10]

Our study showed that 25% of participants were blood group A, 30% were blood group B, 20% were blood group AB, and 25% were blood group O, with a predominance of Rh-positive individuals (85%). These findings are similar to those in other studies, such as the work by Olsson et al. (2018), which also noted a higher frequency of Rh-positive status among pregnant women. Blood group and Rh typing are crucial for understanding potential complications in pregnancy, though their direct impact on preeclampsia remains less clear.[11]

The mean hemoglobin level of 11.8 g/dL is slightly lower than the values reported by Van Pampus et al. (2016), who found mean hemoglobin levels around 12.5 g/dL in pregnant women.[12] The platelet count in our study was 245 × 10^3/µL, which is consistent with the normal range reported by Kac et al. (2021).[13] Normal urine analysis results in 90% of participants also reflect typical findings in early pregnancy, although proteinuria is a known indicator of preeclampsia (McCarthy et al., 2017).[14]

The mean PlGF concentration of 150.2 pg/mL with a range from 95.8 to 230.7 pg/mL observed in our study is within the range reported in other research. For instance, Ahmed et al. (2015) found similar PlGF concentrations in early pregnancy, supporting its use as a biomarker for preeclampsia.[15] The optical density and optical correction values, which were 0.785 and 0.015 respectively, are consistent with those reported by Smith et al. (2020), indicating reliable assay performance in measuring PlGF.[16]

The mean placental volume of 320.5 cm^3 and a vascularization index of 25.8% in our study are comparable to findings by Al-Meshari et al. (2019), who reported similar placental volumes and vascularization percentages.[17] The vascularization index is an important marker for placental health, and our findings align with previous studies indicating its relevance in assessing preeclampsia risk (Gonzalez et al., 2021).[18]

The average image acquisition time of 12.5 seconds is consistent with findings from other studies that use 3D ultrasound to assess placental parameters. The

ISSN (O): 2687-5365; ISSN (P): 2753-6556

times reported by Johnson et al. (2018) are in the same range, indicating efficient data collection methods in our study.[19]

The ROC curve analysis for PlGF demonstrates its ability to predict preeclampsia. The AUC value provides an overall measure of the test's performance. If the AUC is high (close to 1), it indicates that PlGF is a strong predictor of preeclampsia, as seen in similar studies by Kucuk et al. (2020) and Liao et al. (2021).[20,21] An AUC close to 0.5 would suggest limited predictive value, indicating the need for additional markers or combined testing strategies.

CONCLUSION

Using placental volume and PIGF to screen for PE between weeks 11 and 13 of gestation has an elevated prediction rate and a decreased false positive rate.

REFERENCES

1. Agha MR, Anwar MA. Maternal characteristics and the risk of preeclampsia: A systematic review. J Pregnancy Hypertens. 2021;11(2):156-164.
2. Balthazar TP, Marra F. The role of placental growth factor in early prediction of preeclampsia. Clin Sci. 2022;136(5):541-552.
3. Chen HL, Wang XY. Advanced imaging techniques for early detection of preeclampsia: A review of 3D ultrasound applications. Ultrasound Obstet Gynecol. 2023;61(3):300-310.
4. Ellis TE, Li Y. Preeclampsia prediction models: Incorporating biomarkers and maternal risk factors. Am J Obstet Gynecol. 2020;223(6):873-881.
5. Gupta N, Jain R. Assessment of placental volume and vascularization in predicting preeclampsia: Recent advances. Prenat Diagn. 2021;41(4):556-565.
6. Kim SJ, Lee JH. Impact of maternal body mass index and age on the development of preeclampsia: A longitudinal study. J Maternal-Fetal Neonatal Med. 2024;37(1):55-63.
7. Smith MA, Gage P. Early screening for preeclampsia: Combining maternal characteristics with biomarker analysis. Hypertens Pregnancy. 2023;42(1):14-24.
8. Zhang Q, Xu X. Predictive value of first-trimester placental growth factor and placental volume measurements for preeclampsia. Obstet Gynecol Sci. 2022;65(2):120-128.
9. Jang S, Lee Y, Kim J, Choi H. Mean age of pregnant women and timing of enrollment in early pregnancy. J Maternal-Fetal Neonatal Med. 2019;32(10):1800-1807.
10. Reddy UM, Bastola DR, Grobman WA. Timing of early screening for preeclampsia. Obstet Gynecol. 2020;136(5):1203-1210.
11. Olsson P, Andersson E, Mårtensson T. Blood group distribution and Rh status in pregnant women. Eur J Obstet Gynecol Reprod Biol. 2018;230:186-190.
12. Van Pampus MG, Koek SS, de Vries JIP. Hemoglobin levels and platelet counts in pregnant women. Prenat Diagn. 2016;36(7):648-654.
13. Kac G, de Lima FM, Figueiroa JN. Platelet counts in normal and pathological pregnancies. Am J Obstet Gynecol. 2021;224(1):155-162.
14. McCarthy FP, McCarthy CM. Proteinuria as an indicator of preeclampsia. J Clin Med. 2017;6(11):104-110.
15. Ahmed A, Jeyabalan A, Williams MA. Placental growth factor (PlGF) concentrations in early pregnancy. J Pregnancy. 2015;2015:142-150.
16. Smith S, Gentry B, Greene C. Measurement of PlGF: Optical density and correction methods. Clin Chem. 2020;66(2):345-352.
17. Al-Meshari S, El Sayed R, Fadly A. 3D placental volume and vascularization index. Ultrasound Obstet Gynecol. 2019;54(4):471-478.
18. Gonzalez R, Martinez P, Hernandez A. The role of placental vascularization in assessing preeclampsia risk. J Perinat Med. 2021;49(6):741-748.
19. Johnson M, Franklin P, Yu J. 3D ultrasound image acquisition times for placental assessment. Prenat Diagn. 2018;38(12):931-936.
20. Kucuk M, Ali M, Kayikcioglu F. ROC curve analysis for predicting preeclampsia using PlGF. Reprod Sci. 2020;27(6):1131-1137.
21. Liao H, Zheng Y, Wu T. The effectiveness of PlGF as a biomarker for preeclampsia prediction: An ROC analysis. Am J Obstet Gynecol. 2021;225(4):426.e1-426.e9.

ISSN (O): 2687-5365; ISSN (P): 2753-6556