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Prediction of Preeclampsia and Intrauterine Growth Restriction by Second Trimester Serum Beta HCG and Uterine Artery Colour Doppler Velocimetry in Primigravida

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Abstract

In this prospective cohort study, the effectiveness of combining second trimester maternal serum β-HCG levels with Colour Doppler ultrasound measurements is assessed. The study aims to predict pre-eclampsia and intrauterine growth restriction (IUGR) in 88 primigravidae women. Significant associations were found between elevated β-HCG levels and abnormal Doppler indices, including increased Pulsatility Index (PI) and Resistance Index (RI), with the development of pre-eclampsia and IUGR. The combined utilisation of these biomarkers greatly enhanced the accuracy of predictions, resulting in a high level of sensitivity and specificity. This indicates their potential value in regular prenatal screening. This approach has the potential to facilitate earlier interventions, which could lead to a decrease in the negative outcomes linked to these conditions.

Keywords: β-HCG, Colour Doppler Ultrasound, Pre-eclampsia, Intrauterine Growth Restriction (IUGR).

Introduction

Pre-eclampsia and intrauterine growth restriction (IUGR) pose significant health challenges in obstetrics, carrying risks for both mothers and neonates [1]. Pre-eclampsia is a complex multisystem disorder that involves hypertension and often proteinuria. It affects around 3-8% of pregnancies worldwide [2]. This condition has the potential to result in severe

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complications, such as eclampsia, HELLP syndrome, and the unfortunate outcome of maternal and fetal death. In developing countries, the high prevalence of pre-eclampsia, reaching up to 16.7%, emphasizes the pressing need for early and effective detection methods [3,4].

Identified in approximately 8% of pregnancies, IUGR is a major contributor to perinatal mortality and morbidity. It refers to a notable decrease in the potential growth of the foetus [5]. Infants born with IUGR face an increased likelihood of experiencing neonatal complications, including hypoxia, hypoglycemia, and long-term developmental challenges. Recognizing and effectively treating IUGR in its early stages can have a profound impact on patient outcomes, underscoring the importance of studying this crucial field [6,7].

It is thought that both conditions have a similar underlying cause that involves abnormal placentation. This can impact the flow of blood through the placenta and the transfer of nutrients from the mother to the foetus. Despite extensive research, there is still much to learn about the mechanisms behind these conditions and how they are connected [8,9]. Conventional approaches to anticipate and identify pre-eclampsia and IUGR involve assessing the mother's medical background, monitoring blood pressure, measuring urine protein levels, and conducting physical examinations to detect any discrepancies in uterine size relative to the gestational age [10,11]. Nevertheless, these approaches frequently detect the conditions only once clinical symptoms have become noticeable, potentially leading to suboptimal management [12].

There have been new developments in the field that involve the utilisation of biochemical markers like beta-human chorionic gonadotropin (β-HCG) and biophysical tools such as Colour Doppler ultrasound to evaluate the blood flow in the uterine artery. These methods have the potential to predict pre-eclampsia and IUGR earlier and with greater accuracy [13,14].

The objective of this study is to assess the efficacy of utilising second trimester maternal serum β-HCG levels in conjunction with Colour Doppler ultrasound measurements of the uterine artery to anticipate the likelihood of developing pre-eclampsia and IUGR. The objectives are as follows:

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1. The objective is to evaluate the significance of second trimester β-HCG levels in predicting pre-eclampsia and IUGR. The main aim is to determine specific threshold levels that are associated with a higher risk.
2. Assessing the effectiveness of Colour Doppler ultrasound in measuring uterine artery resistance indices, such as the Pulsatility Index and Resistance Index, as potential early indicators of abnormal placentation and associated complications.
3. The objective is to assess whether the combination of β-HCG and Colour Doppler measurements enhances the predictive accuracy, in comparison to using each method individually.

Methodology of the Study

Study Design

This prospective cohort study was undertaken at Jawaharlal Nehru medical hospital, Aligarh by the Departments of Obstetrics and Gynaecology and Radiodiagnosis and Pathology. The study covers September 2015–August 2017.

Study Population

The study included 88 primigravidae women in their first or early second trimesters recruited from the prenatal clinic. At enrollment, these women are 13–20 weeks pregnant.

Inclusion Criteria

- Primigravidae.
- Gestational age between 13 and 20 weeks at the time of first screening.
- Normotensive and non-proteinuric at the time of enrollment.
- Aged between 18 and 40 years.

Exclusion Criteria

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- Multiple pregnancies.

- Known congenital fetal malformations.

- Pre-existing hypertension or renal diseases.

- Diabetes mellitus.

- Molar pregnancy.

- History of chromosomal disorders like Down syndrome.

- Existing cardiovascular disease.

Data Collection Methods

Participants undergo a detailed initial assessment including medical history, physical examination, and baseline laboratory tests.

Ultrasound and Doppler Studies:

- First Ultrasound (13-20 weeks): Transabdominal Doppler ultrasound to measure the Pulsatility Index (PI) and Resistance Index (RI) of the uterine arteries. The presence of early diastolic notches is recorded.

- Second Ultrasound (26-30 weeks): A follow-up Doppler ultrasound to reassess the PI, RI, and the persistence of diastolic notches.

Biochemical Analysis:

- β-HCG Measurement: Maternal serum β-HCG levels are measured during the second trimester using a chemiluminescence immunoassay. The assay is calibrated to detect and quantify the concentration of β-HCG, providing a high-throughput and sensitive measurement.

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Statistical Analysis

Data will be analysed with SPSS. Pre-eclampsia and IUGR are the main consequences. Descriptive statistics: Mean, median, standard deviation, frequencies, and percentages for continuous and categorical variables.

- Logistic regression models will assess the predictive power of β-HCG levels and Doppler indices (PI and RI) for pre-eclampsia and IUGR. ROC curves will establish the best cutoff values for outcome prediction.

To evaluate predictive models, sensitivity and specificity will be calculated.

Follow-up

Participants are followed through their pregnancy and delivery. The perinatal outcomes, including the birth weight, Apgar scores, and any neonatal intensive care unit admissions, are recorded. Post-delivery, the final diagnosis of pre-eclampsia or IUGR is confirmed based on clinical and laboratory criteria.

Results of the Study

A group of 88 first-time pregnant women were observed from the second trimester until delivery. The objective of the study was to make predictions about pre-eclampsia and IUGR by analysing β-HCG levels and conducting Colour Doppler ultrasound.

Demographic and Baseline Characteristics

-Age Range: The participants' ages ranged from 18 to 40 years, with an average age of 25.3 years.

- The average gestational age at the time of first screening was 16 weeks upon enrollment.

High β-HCG Levels: The study discovered a significant association between high β-HCG levels in the second trimester and the development of pre-eclampsia and IUGR.

Findings from Doppler Ultrasound - Unusual Doppler Indices: Elevated Pulsatility Index (PI > 1.45) and Resistance Index (RI > 0.58) at 20 weeks gestation were linked to increased risks of developing pre-eclampsia (P = 0.01) and IUGR (P = 0.03).

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- The presence of early diastolic notches observed during the first ultrasound showed a correlation with the later development of pre-eclampsia (P = 0.05) and IUGR (P = 0.05).

Achieving a sensitivity of 82% and specificity of 88%, the predictive accuracy for pre-eclampsia was significantly improved by combining β-HCG levels with Doppler indices in the model. In the case of IUGR, the combined model demonstrated a sensitivity of 78% and a specificity of 85%.

- Analysing the ROC Curve: The combined model demonstrated exceptional predictive value, with an area under the ROC curve (AUC) of 0.91 for pre-eclampsia and 0.89 for IUGR.

Pregnancy Outcomes - Pre-eclampsia: Among the 88 participants, pre-eclampsia was observed in 18 individuals, accounting for 20.5% of the cases.

- Out of the 88 participants, a total of 16 individuals (18.2%) were found to have been diagnosed with IUGR.
- Delivery Outcomes: For individuals diagnosed with pre-eclampsia, half experienced preterm deliveries before 37 weeks. Similarly, among those with IUGR, more than half had newborns with birth weights below the 10th percentile for their gestational age.

Statistical Analysis

The results of the combined predictive model showed statistical significance ($P < 0.05$), which supports the hypothesis that the integration of β-HCG levels with Colour Doppler indices improves the early prediction of pre-eclampsia and IUGR.

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Table 1: Demographic and Baseline Characteristics of Participants

Characteristic	Detail
Total Participants	88
Age Range	18 - 40 years
Mean Age	25.3 years
Average Gestational Age at Enrollment	16 weeks

Table 2: β-HCG Levels and Associations with Outcomes

β-HCG Level Percentile	Association with Pre-eclampsia	Association with IUGR
Above 75th Percentile	P = 0.02	P = 0.04

Table 3: Doppler Ultrasound Findings

Doppler Index	Critical Value	Associated with Pre-eclampsia (P-value)	Associated with IUGR (P-value)
Pulsatility Index (PI)	> 1.45	0.01	0.03
Resistance Index (RI)	> 0.58	0.01	0.03
Early Diastolic Notches	Present	0.05	0.05

Table 4: Combined Predictive Model Performance

Model Components	Sensitivity	Specificity	Area Under ROC Curve (AUC)
Pre-eclampsia Prediction	82%	88%	0.91
IUGR Prediction	78%	85%	0.89

Table 5: Pregnancy Outcomes

Outcome	Number of Participants	Percentage
Total Pre-eclampsia Cases	18	20.5%
Total IUGR Cases	16	18.2%
Preterm Deliveries in Pre-eclampsia	9 (of 18)	50%
Neonates Below 10th Percentile for IUGR	9 (of 16)	56%

These tables provide a concise and organized overview of the results from the study, making it easier to understand and interpret the key findings and their statistical significance.

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Discussion

This prospective cohort study offers valuable insights into the early prediction of pre-eclampsia and intrauterine growth restriction (IUGR) through the use of a combination of β-HCG levels and Colour Doppler ultrasound measurements [15]. The study emphasised that higher levels of β-HCG in the second trimester, especially those above the 75th percentile, have a strong correlation with the occurrence of both pre-eclampsia and IUGR. It appears that β-HCG, a substance produced by the placenta, may serve as a marker for assessing placental function and any associated disorders [16].

In addition, the utilization of Colour Doppler ultrasound for assessing the Pulsatility Index (PI) and Resistance Index (RI) of the uterine artery has demonstrated its effectiveness in identifying pregnancies that may be at risk [17]. Higher incidences of pre-eclampsia and IUGR were found to be associated with elevated PI and RI values, as well as the presence of early diastolic notches. These findings suggest that abnormal placental implantation and insufficient uteroplacental blood flow are important factors in the development of these conditions [18].

The predictive model, which combines β-HCG levels and Doppler ultrasound findings, demonstrates enhanced sensitivity and specificity when compared to using each method separately. The integrated approach yielded impressive results, with an area under the ROC curve (AUC) of 0.91 for pre-eclampsia and 0.89 for IUGR. These values demonstrate the high predictive accuracy of the model. The biomarkers' impressive sensitivity and specificity highlight their potential to be included in regular prenatal screening programs. This could lead to earlier intervention and potentially decrease the negative health outcomes associated with these conditions [19].

Nevertheless, despite these encouraging outcomes, the study does have some limitations. These include the relatively small number of participants and the fact that it was conducted at a single center. These factors may impact the ability to apply the findings to a broader population. Future studies need to replicate these findings in larger and more diverse populations to validate the efficacy of the combined predictive model. In addition, conducting longitudinal studies could offer valuable insights into the long-term outcomes of pregnancies

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impacted by pre-eclampsia and IUGR. This would help to strengthen the clinical usefulness of early predictive markers [18,20].

Conclusion

The study provides strong evidence that the combination of second trimester maternal serum β-HCG levels and Colour Doppler ultrasound measurements of uterine artery indices greatly improve the ability to predict pre-eclampsia and intrauterine growth restriction (IUGR). Utilizing these biomarkers in combination not only enhances the precision of diagnosis but also enables prompt intervention, potentially reducing the negative consequences linked to these ailments. These findings strongly support the use of these screening tools in routine prenatal care protocols, given their high sensitivity and specificity, which indicate excellent predictive value. Further research should prioritise conducting larger, multi-center studies to confirm these findings and investigate how to effectively implement these predictive tools across different populations, with the aim of enhancing maternal and neonatal health outcomes on a universal scale.

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