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Original Article

PREDICTIVE MARKERS FOR ADVERSE PREGNANCY OUTCOMES: INSIGHTS FROM A PROSPECTIVE COHORT STUDY ON MATERNAL FACTORS, BIOMARKERS, AND UTERINE ARTERY DOPPLER RESULTS

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ABSTRACT

Objective: Effective prediction tools are necessary for better outcomes when it comes to pregnancy-related complications such as intrauterine growth restriction (IUGR), pregnancy-induced hypertension (PIH), and premature birth. In order to improve early risk diagnosis and treatment, this study investigates relationships between maternal variables, first-trimester biomarkers, and second-trimester uterine artery Doppler findings.

Methods: Correlations between demographic characteristics, maternal dual test indicators (serum beta-HCG, serum PAPPA), and uterine artery Doppler tests were examined in a prospective cohort study including 500 pregnant women. Statistical studies evaluated correlations with IUGR, PIH, and premature birth.

Results: Serum beta-HCG levels below the 5th percentile correlated significantly with preterm birth (RR 2.3131, p = 0.0288). Low serum PAPP-A levels (<5th percentile) associated with PIH (RR 2.1447, p = 0.0204) and IUGR (RR 2.0953, p = 0.0002). Uterine artery Doppler indices (>0.58 RI) demonstrated associations with PIH (RR 2.2448) and IUGR (RR 1.6293).

Diastolic notching correlated with preterm birth, PIH, and IUGR.

Conclusion: The potential of serum beta-HCG, PAPP-A, and uterine artery Doppler indices as useful predictors of unfavorable pregnancy outcomes is highlighted by this study, which also highlights their use in early risk detection.

Keywords: Pregnancy complications, Predictive markers, Uterine artery doppler, Maternal biomarkers, Preterm birth, Pregnancy-induced hypertension, Intrauterine growth restriction

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INTRODUCTION

Pregnancy, labor, and delivery, together with natural biological processes, often result in favorable outcomes for women and kids. Deviations from the norm, on the other hand, might lead to serious morbidity or even death for the mother and baby. It can be challenging to predict disorders like as preeclampsia, preterm birth, early rupture of membranes, and fetal growth restriction, particularly in nulliparous women for whom maternal history and conventional risk factors may not be sufficient [1].

A risk-based approach is becoming the norm in modern prenatal care since it is imperative to predict adverse obstetric outcomes early in pregnancy. It is now necessary to identify risk factors, such as decreased fertility, older mothers, and higher body mass index, in order to begin preventative treatment programs and minimize potential issues. Understanding the intricate relationships between biochemical outcomes, biophysical parameters, and less-than-ideal pregnancy outcomes is crucial given the changing face of society, the effects of late marriages and lifestyle adjustments on reproductive patterns, and the implications for reproductive patterns [2].

Unquestionably, the placenta plays a crucial role during pregnancy. Intrauterine growth restriction (IUGR) and pregnancy-induced hypertension (PIH) are two conditions associated with early interruption of placental function, particularly in the first trimester. Understanding the molecular pathways involving insulin and insulin-like growth factors, as well as PAPPA's role in regulating free IGF levels, further emphasizes the complexity of fetal growth regulation [3].

Recent retrospective investigations have linked low levels of maternal serum PAPPA and free β-HCG to pregnancy difficulties. This highlights the need for accurate and sensitive prediction testing to identify at-risk groups and provide timely intervention. The intricate relationship between inadequate placentation and adverse outcomes, including pre-eclampsia, fetal growth restriction, fetal mortality, and abruptio placenta, emphasizes the importance of early detection [4].

Impaired placentation is characterized by insufficient trophoblastic invasion of spiral arteries, which leads to increased blood flow impedance in uterine arteries. Doppler ultrasonography studies that include waveform indices or notching present one potentially helpful strategy for identifying women who are at risk throughout the first and second trimesters. Prompt interventions that are guided by these assessments have the potential to lower maternal and fetal morbidity and mortality [5].

This study aims to explore the relationships between maternal variables, first-trimester blood biomarkers, and second-trimester uterine artery Doppler results, with a focus on their predictive utility for third-trimester obstetric complications. By navigating the intricate web of pregnancy and contributing to the advancement of more effective techniques for early risk diagnosis and treatment, our aim is to enhance overall pregnancy outcomes [6].

MATERIALS AND METHODS

Study setting and design

This prospective cohort study was conducted at the Department of Obstetrics and Gynecology from November 2022 to June 2024. The study included 500 first-trimester antenatal patients attending the outpatient department, irrespective of their parity status.

Participants

Inclusion criteria were limited to pregnant women in their first trimester with singleton pregnancies. Exclusion criteria encompassed

multiple pregnancies, essential hypertension, pregestational diabetes, severe anemia, systemic lupus erythematosus (SLE), renal and heart diseases, and fetal congenital malformations.

Data collection

After obtaining written informed consent, participants were briefed during their first antenatal visit. Data collected included age, parity, educational level, race, socioeconomic status, obstetric history, family and past medical history, smoking habits, and physical activity levels. Clinical assessments included measuring mean arterial pressure (MAP) and body mass index (BMI). Routine antenatal investigations encompassed general and systemic examinations.

Laboratory tests and ultrasonography

Maternal serum pregnancy-associated plasma protein-A (PAPP-A) and free β-hCG levels were measured between 11 to 14 w using the ELISA method. Results were normalized to multiples of the median (M. O. M) for normal pregnancies. Value below the 5th percentile or above the 95th percentile were considered abnormal. Doppler ultrasound assessments of the uterine artery velocity waveform were performed at 20-22 w, with a resistance index (RI) greater than 0.58 or persistent early diastolic notching deemed abnormal.

Definitions of study outcomes

Pregnancy-induced hypertension (PIH) was defined as hypertension diagnosed after 20 w of gestation with accompanying proteinuria. Intrauterine fetal growth restriction (IUGR) or fetal growth restriction (FGR) was identified by estimated fetal weight or abdominal circumference less than the 10th percentile. Preterm delivery was defined as delivery before 37 completed weeks of gestation.

Statistical analysis

Data presentation included categorical variables as numbers and percentages and continuous variables as mean±SD and median. The normality of the data was assessed using the Kolmogorov-Smirnov test. Statistical tests applied included the unpaired t-test or Mann-Whitney test for continuous variables and the Chi-Square test or Fisher's exact test for categorical data. Diagnostic tests calculated sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). Relative risk was also determined. Statistical significance was established at $p<0.05$. Data management was conducted using an MS EXCEL spreadsheet, with analysis performed via Statistical Package for the Social Sciences (SPSS) version 21.0.

RESULTS

The results reveal significant associations between maternal serum markers, uterine artery Doppler indices, and adverse pregnancy outcomes. Table 1 indicates a notable relationship between serum β-HCG levels below the 5th percentile and preterm birth (RR 2.3131, p = 0.0288). Conversely, higher levels (>95th percentile) show no association. Table 2 demonstrates a significant correlation between low serum PAPP-A levels (<5th percentile) and the development of PIH (RR 2.1447, p = 0.0204), while table 3 shows a similar association with IUGR (RR 2.0953, p = 0.0002). Uterine artery Doppler findings in table 4 reveal a significant association between resistance index (RI)>0.58 and both PIH (RR 2.2448) and IUGR (RR 1.6293). Diastolic notching in table 5 is associated with preterm birth, PIH, and IUGR, emphasizing its potential as a comprehensive predictive marker. These findings underscore the utility of these markers in anticipating adverse pregnancy outcomes.

Table 1: Relation of abnormal serum B-HCG levels with preterm birth

Percentile	MOM	Preter m	Normal	Sensitivity	Specificity	PPV	NPV	Relative risk	P value
<5th percentile	<0.47	7(16.67%)	35(83.33%)	17.50%	92.39%	16.6 7%	92.7 9%	2.3131	0.0288
>95th percentile	>2.38	0(0.00%)	4(100.00%)	0.00%	99.13%	0.00%	91.9 4%	1.2272	0.8795

Table 2: Relation of serum papp-a with PIH

Percentile	MOM	PIH	Normal	Sensitivity	Specificity	PPV	NPV	Relative risk	P value
<5th percentile	<0.46	11(15.07%)	62(84.93%)	26.83%	86.49%	15.0 7%	92.9 7%	2.1447	0.0204
>95th percentile	>2.83	0(0.00%)	3(100.00%)	0.00%	99.35%	0.00%	91.7 5%	1.5000	0.7607

Table 3: Relation of serum pappa-a with IUGR

Percentile	MOM	IUGR	Normal	Sensitivity	Specificity	PPV	NPV	RR	P value
<5th percentile	<0.46	24(32.88%)	49(67.12%)	26.37%	88.02%	32.88%	84.31%	2.0953	0.0002
>95th percentile	>2.83	0(0.00%)	3(100.00%)	0.00%	99.27%	0.00%	81.69%	0.6803	0.7715

Table 4: Relation of RI with preterm

Relation of RI		Preterm birth		Total
		N	Y	
RI	<0.58	196(93.33%)	14(6.67%)	210 (100.00%)
	>0.58	264(91.03%)	26(8.97%)	290 (100.00%)
T	Total	460(92.00%)	40 (8.00%)	500 (100.00%)

Table 5: Distribution of patients according to diastolic notch

Distribution of patients	Frequency	Percentage
A	475	95.00%
P	25	5.00%
Total	500	100.00%

DISCUSSION

This research examines the complex realm of third-trimester pregnancy complications, a period especially prone to negative health outcomes. As lifestyles evolve, obstetricians globally face increasing challenges, including preterm birth, pregnancy-induced hypertension (PIH), and intrauterine growth restriction (IUGR). This study aims to evaluate the effectiveness of maternal dual test markers, uterine artery Doppler studies, and demographic factors in predicting these complications to enhance pregnancy outcomes [7, 8].

The research analyzed 500 pregnant women in their antenatal phase to determine the relationship between various factors and the incidence of preterm birth, PIH, and IUGR during the third trimester. Factors studied included age, parity, body mass index (BMI), and mean arterial pressure (MAP), along with maternal dual test markers such as serum betaHCG and serum PAPP-A, and uterine artery Doppler parameters like resistance index and diastolic notching [9, 10].

Findings indicate that 8.00% of the women experienced preterm delivery, 8.20% developed PIH, and 18.20% had infants with IUGR. A significant link was found between low beta-HCG levels and preterm births, with a relative risk of 2.3131 in women with levels below the 5th percentile. This connection was not observed with PIH or IUGR. Conversely, low first-trimester serum PAPP-A levels were significantly correlated with the development of PIH and IUGR, with relative risks of 2.1447 and 2.0953, respectively. However, these levels did not correlate with preterm birth, contradicting some earlier studies [11, 12].

Furthermore, the uterine artery Doppler studies revealed a significant association between a resistance index greater than 0.58 and the development of PIH and IUGR, with corresponding relative risks of 2.2448 and 1.6293. Diastolic notching was also notably associated with preterm birth, PIH, and IUGR, highlighting its potential as a comprehensive predictor [13].

While the study considered demographic variables such as age, parity, BMI, and MAP, it found no significant links between maternal age or parity and complication development. BMI showed a notable association with PIH, which aligns with some studies but not others, pointing to the complex dynamics involved in predicting outcomes.

The research acknowledges limitations, including the limited duration of the study, its relatively small sample size, and possible demographic disparities within the population. Additionally, potential errors in interpreting uterine artery Doppler studies add another layer of complexity to the findings.

CONCLUSION

In conclusion, this study delves into third-trimester complications in 500 pregnant women, unveiling serum beta-HCG and PAPP-A as predictive markers for preterm birth, PIH, and IUGR. Uterine artery Doppler, particularly resistance index and diastolic notching, emerges as a valuable screening tool. Despite limitations, the study lays the groundwork for refined predictive models.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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