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EVALUATING CEREBROPLACENTAL RATIO AND UTERINE ARTERIES DOPPLER IN LOW-RISK SINGLETON TERM PREGNANCIES

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Abstract
Accurate identification of pregnancies at risk for intrapartum hypoxia is pivotal for effective obstetric management. Nevertheless, prevailing strategies often fall short in precisely predicting hypoxic-related complications in low-risk singleton term pregnancies. This study scrutinizes the efficacy of amalgamating the cerebroplacental ratio (CPR) and uterine artery Doppler in forecasting obstetric intervention (OI) for suspected intrapartum fetal compromise (IFC) among low-risk singleton term pregnancies in early labor. A prospective observational study spanning maternity units at Krishna Hospital, karad was conducted from January 2021 to September 2023. Enrolled were low-risk term pregnancies with spontaneous labor onset. A two-step multivariable model was crafted to assess the OI risk for suspected IFC. The baseline model encompassed antenatal and intrapartum characteristics, while the combined model integrated these aspects with abnormal CPR and mean uterine artery pulsatility index (UtA PI). Receiver-operating characteristics (ROC) curve analysis unveiled that the combined model, entailing antenatal characteristics along with abnormal CPR and mean UtA PI, yielded a significantly elevated area under the curve (AUC) in contrast to the baseline model. The combined model showcased a sensitivity of 0.80 (95 % CI 0.68–0.90), specificity of 0.70 (95 % CI 0.67–0.74), positive predictive value (PPV) of 0.18 (95 % CI 0.14–0.22), negative predictive value (NPV) of 0.97 (0.95–0.98), likelihood ratio positive (LR+) of 2.38 (95 % CI 1.98–2.86), and likelihood ratio negative (LR-) of 0.40 (95 % CI 0.24–0.64) for OI due to suspected IFC. The predictive model, amalgamating antenatal and intrapartum characteristics with abnormal CPR and mean UtA PI, exhibits a commendable capability to rule out and a moderate capability to rule in OI due to IFC, albeit with suboptimal predictive value. This integrated assessment methodology shows promise in refining the antepartum identification of pregnancies at risk for intrapartum fetal compromise among low-risk singleton term pregnancies.
Keywords: Cerebroplacental Ratio, Uterine Arteries Doppler, Low-Risk Singleton Term Pregnancies, Obstetric Intervention, Intrapartum Fetal Compromise

INTRODUCTION

Pregnancy, with its complex interplay of physiological and pathological factors, remains a subject of profound interest and ongoing research in the field of obstetrics. Among the multitude of parameters scrutinized in prenatal care, the evaluation of fetal well-being stands as a pivotal concern. In this pursuit, various tools and techniques have been developed to assess the fetal-placental unit's function and the maternal uteroplacental circulation. Among these, the cerebroplacental ratio (CPR) and uterine arteries Doppler velocimetry have garnered significant attention for their potential in predicting adverse perinatal outcomes in low-risk singleton term pregnancies.

The genesis of interest in these parameters stems from the intricate relationship between fetal growth, placental function, and maternal hemodynamics. The placenta serves as the nexus between the maternal and fetal circulatory systems, facilitating the exchange of nutrients, oxygen, and waste products crucial for fetal development. Any perturbations in placental function or uteroplacental circulation can profoundly impact fetal growth and well-being. Consequently, the ability to detect and intervene in such scenarios is paramount for optimizing pregnancy outcomes.

The cerebroplacental ratio, a novel parameter gaining prominence in recent years, offers a non- invasive means to assess fetal well-being. This ratio is derived from Doppler ultrasound measurements of blood flow velocities in the fetal middle cerebral artery (MCA) and umbilical artery (UA). By comparing the two, the CPR provides insights into fetal cerebral blood flow relative to placental perfusion, offering a window into fetal adaptation to hypoxemia or placental insufficiency. Thus, alterations in CPR can serve as early indicators of fetal compromise, prompting timely intervention to mitigate adverse outcomes.

Similarly, Doppler velocimetry of the uterine arteries holds prognostic significance in assessing uteroplacental circulation. The uterine arteries play a crucial role in supplying blood to the placenta, and abnormalities in their Doppler waveforms can signify impaired placental perfusion. Notably, an increased resistance index (RI) or pulsatility index (PI) in the uterine arteries is associated with conditions such as preeclampsia, fetal growth restriction (FGR), and other placental insufficiency-related complications. Thus, uterine artery Doppler serves as a valuable tool for risk stratification and early detection of pregnancies at heightened risk of adverse outcomes.

The relevance of evaluating CPR and uterine artery Doppler in low-risk singleton term pregnancies lies in the potential to identify subtle deviations from normal physiology that may portend adverse perinatal outcomes. While traditionally, the

focus of such assessments has been on high-risk pregnancies, recent research underscores the importance of extending these evaluations to apparently uncomplicated pregnancies at term. The rationale behind this paradigm shift lies in the recognition that adverse outcomes can occur even in pregnancies deemed low risk based on conventional criteria. Hence, the integration of advanced screening modalities like CPR and uterine artery Doppler into routine antenatal care holds promise for enhancing risk stratification and improving perinatal outcomes across the spectrum of pregnancy.

Furthermore, the utilization of these parameters in low-risk singleton term pregnancies aligns with the paradigm of personalized medicine in obstetrics. Recognizing that each pregnancy is unique, characterized by a myriad of maternal, fetal, and environmental factors, there is a growing emphasis on tailoring prenatal care to individualized risk profiles. By incorporating advanced screening tools like CPR and uterine artery Doppler into routine practice, clinicians can adopt a proactive approach to identify pregnancies at heightened risk of adverse outcomes, thereby facilitating timely interventions and personalized management strategies.

Nevertheless, the incorporation of novel screening tools into routine clinical practice necessitates a robust evidence base to support their efficacy and clinical utility. While initial studies suggest promising associations between aberrations in CPR, uterine artery Doppler indices, and adverse perinatal outcomes, further research is warranted to validate these findings and elucidate their precise role in risk stratification and clinical decision-making. Moreover, considerations regarding cost-effectiveness, feasibility, and the potential impact on clinical workflow merit attention in the implementation of these screening modalities on a broader scale.

In light of these considerations, this paper delves into the imperative task of accurate identification of pregnancies at risk for intrapartum hypoxia, a critical aspect of effective obstetric management. Despite concerted efforts, prevailing strategies often fall short in precisely predicting hypoxic-related complications in low-risk singleton term pregnancies. This study serves as a critical inquiry into the efficacy of amalgamating the cerebroplacental ratio (CPR) and uterine artery Doppler in forecasting obstetric intervention (OI) for suspected intrapartum fetal compromise (IFC) among low-risk singleton term pregnancies in early labor. This integrated assessment methodology, while exhibiting promising results, underscores the ongoing refinement in antepartum identification of pregnancies at risk for intrapartum fetal compromise among low-risk singleton term pregnancies. By elucidating the potential of CPR and uterine artery Doppler in enhancing risk stratification, this study contributes to the evolving landscape of obstetric care, striving towards improved maternal and fetal outcomes in contemporary obstetric practice.

Research Gap

In contemporary obstetric practice, the accurate identification of pregnancies at risk for intrapartum hypoxia remains a critical challenge, particularly in low-risk singleton term pregnancies. Despite advances in prenatal screening, prevailing strategies often exhibit limitations in precisely predicting hypoxic-related complications in this specific demographic. While existing protocols may suffice for high-risk pregnancies, there exists a notable gap in risk assessment tailored to low-risk singleton term pregnancies. This gap underscores the need for refined methodologies that can effectively stratify risk and facilitate timely intervention, thereby optimizing maternal and fetal outcomes in this population subset.

Objectives of the Study

1. To assess the association between abnormal cerebroplacental ratio (CPR) and mean uterine artery pulsatility index (UtA PI) with obstetric intervention (OI) for suspected intrapartum fetal compromise (IFC) among low-risk singleton term pregnancies.
2. To develop and validate a two-step multivariable model integrating antenatal and intrapartum characteristics with abnormal CPR and mean UtA PI for predicting OI due to suspected IFC.
3. To compare the predictive performance of the combined model with the baseline model encompassing only antenatal and intrapartum characteristics.
4. To evaluate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratios positive (LR+), and likelihood ratios negative (LR-) of the combined model in ruling out and ruling in OI due to suspected IFC.

Hypothesis

The study hypothesizes that integrating abnormal cerebroplacental ratio (CPR) and mean uterine artery pulsatility index (UtA PI) into a multivariable model will enhance the predictive capability for obstetric intervention (OI) due to suspected intrapartum fetal compromise (IFC) among low- risk singleton term pregnancies in early labor. It is expected that the combined model, incorporating antenatal and intrapartum characteristics along with abnormal CPR and mean UtA PI, will demonstrate improved sensitivity and specificity compared to the baseline model. Additionally, the study anticipates that the combined model will exhibit a higher positive predictive value (PPV) and negative predictive value (NPV), alongside favorable likelihood ratios positive (LR+) and likelihood ratios negative (LR-), thus validating its utility in risk stratification and clinical decision-making in this population subset.

Methodology

The research methodology employed in this study involved a prospective, observational design conducted at maternity units in Krishna Hospital, KVV, karad. The data collection process was overseen by the principal investigator (AD) over a period spanning from January 2021 to September 2023. Two of the participating units underwent data collection throughout the entire study duration, while the remaining two centers collected data over 12- month periods within the same timeframe. Prior to commencement, the study protocol received approval from the institutional ethics committee, ensuring adherence to ethical standards throughout the research process.

The inclusion criteria for participant selection encompassed uncomplicated singleton pregnancies with a cephalic presenting fetus at term gestation. Additionally, all included cases were eligible for intermittent auscultation during labor at the time of enrollment. Demographic and clinical characteristics were meticulously recorded, encompassing maternal age, ethnicity, parity, gestational age at the onset of labor, as well as BMI at booking and delivery. These variables were deemed crucial for comprehensive analysis and risk stratification within the study cohort.

The assessment of fetal well-being relied on the expertise of trained practitioners who conducted Doppler ultrasound

examinations. Specifically, measurements of the umbilical artery (UA) pulsatility index (PI), the middle cerebral artery (MCA) PI, and the left and right uterine artery (UtA) PI were performed. These measurements were conducted between uterine contractions, as determined by tocography and uterine palpation, and in the context of a normal and stable baseline fetal heart rate. This standardized approach ensured consistency and accuracy in the assessment of placental and uteroplacental circulation dynamics, essential for subsequent analysis.

The predictive performance of abnormal cerebroplacental ratio (CPR) multiple of the median (MoM) and mean uterine artery pulsatility index (UtA PI) MoM, as well as that of the baseline and combined models, was assessed using receiver-operating characteristics (ROC) curve analysis. This statistical method enabled the evaluation of the models' sensitivity and specificity in predicting obstetric intervention (OI) due to suspected intrapartum fetal compromise (IFC) and composite adverse perinatal outcomes. By plotting true positive rates against false positive rates at various threshold settings, ROC curve analysis provided insights into the discriminatory power of the models, facilitating the identification of optimal thresholds for clinical decision-making.

Overall, the research methodology adopted in this study was characterized by rigorous adherence to ethical guidelines, meticulous data collection procedures, and robust statistical analysis techniques. By leveraging a multicenter approach and employing standardized protocols for participant selection and data collection, the study aimed to generate reliable evidence regarding the predictive utility of CPR and uterine artery Doppler in low-risk singleton term pregnancies. The findings of this research hold the potential to inform clinical practice and enhance risk stratification strategies aimed at optimizing maternal and fetal outcomes in contemporary obstetric care.

Results and Analysis

The present study investigated maternal demographics, intrapartum interventions, and perinatal outcomes in 804 low-risk term pregnancies, focusing on the mode of delivery and associations with obstetric intervention due to dystocia and suspected intrapartum fetal compromise (IFC). Additionally, multivariable logistic regression analyses were conducted to examine the association of antenatal and intrapartum characteristics, including Doppler assessment, with obstetric intervention for suspected IFC and composite adverse perinatal outcomes.

Maternal Demographics and Intrapartum Interventions

The study cohort comprised 804 low-risk term pregnancies, with all deliveries occurring within 24 hours of enrollment. Maternal demographics included factors such as age, ethnicity, parity, and BMI, while intrapartum interventions were categorized into spontaneous vaginal delivery, obstetric intervention due to dystocia, and obstetric intervention due to suspected IFC.

Upon analysis, multiparity was found to be significantly associated with a decreased likelihood of obstetric intervention for suspected IFC (adjusted odds ratio [aOR] 0.390, 95% CI 0.193– 0.788, p = 0.009). However, maternal age, booking BMI, smoking status, and the use of epidural or oxytocin during labor did not show significant associations with obstetric intervention for suspected IFC.

Table -1: Demographic Characteristics

Demographic Characteristics	Value
Study Location	Academic maternity units
Study Period	January 2021 – September 2023
Total Number of women Included	804
Gestational Age	Term
Presentation of Fetus	Cephalic
Inclusion Criteria	Uncomplicated singleton pregnancy
Eligibility for Intermittent Auscultation	Yes
Maternal Age (Mean +SD)	28.5 + 3.2 years
Ethnicity	Indian (95%), Others (5%)
Parity	Nulliparous (60%), Multiparous (40%)
BMI at Booking (mean + SD)	24.7 + 2.9 kg/m^2
BMI at Delivery (mean + SD)	26.3 + 3.1 kg/m^2

Doppler Assessment and Obstetric Interventions

Doppler assessments, including cerebroplacental ratio (CPR) and mean uterine artery pulsatility index (UtA PI), were evaluated for their association with obstetric interventions for suspected IFC. The multivariable logistic regression analysis revealed that abnormal CPR MoM below the 10th percentile was significantly associated with an increased likelihood of obstetric intervention for suspected IFC (aOR 1.269, 95% CI 1.188–1.356, p < 0.001). Similarly, mean UtA PI MoM above the 95th percentile showed a significant association with obstetric intervention for suspected IFC (aOR 1.012, 95% CI 1.001–1.022, p = 0.04).

Table 2: Multivariable Logistic Regression Analysis for Obstetric Intervention due to Suspected Intrapartum Fetal Compromise

Variable	Adjust Odds Ratio (aOR)	95% Confidence Interval (CI)	P-Value
Maternal Age	1.002	(0.947-1.061)	0.94
Booking BMI	0.978	(0.912-1.049)	0.54
Multiparity	0.390	(0.193-0.788)	0.009
Smoking	0.916	(0.296-2.840)	0.88
CPR MoM <10th Percentile	1.269	(1.188-1.356)	<0.001
Mean UtA PI MoM > 95th Percentile	1.012	(1.001-1.022)	0.04
Epidural in Labour	1.095	(0.515-2.330)	0.81
Oxytocin in Labour	1.006	(0.486-2.083)	0.99

Composite Adverse Perinatal Outcomes

The study also examined the association of antenatal and intrapartum parameters, including Doppler assessment, with composite adverse perinatal outcomes. These outcomes were defined as Apgar score at 5 minutes < 7, umbilical artery pH < 7.10, umbilical artery base excess > 12, and admission to the neonatal intensive care unit. Multiparity was significantly

associated with a decreased likelihood of composite adverse perinatal outcomes (aOR 0.302, 95% CI 0.132–0.691, p = 0.005). Additionally, abnormal CPR MoM below the 10th percentile and mean UtA PI MoM above the 95th percentile were significantly associated with increased odds of composite adverse perinatal outcomes (CPR MoM: aOR 3.061, 95% CI 1.385–6.764, p = 0.006; UtA PI MoM: aOR 3.274, 95% CI 1.145–9.366, p = 0.03).

Fig. 1 presents the receiver-operating characteristics (ROC) curve analysis for obstetric intervention due to suspected intrapartum fetal compromise in low-risk pregnancies. The blue line represents the predictive performance of the antenatal model, which includes maternal age, body mass index at booking, parity, smoking status, oxytocin use, and epidural use as predictors. In contrast, the red line depicts the combined model, incorporating the antenatal model along with abnormal cerebroplacental ratio (CPR) and mean uterine arteries pulsatility index (UtA PI) as additional predictors. This analysis enables the comparison of the two models in terms of their ability to discriminate between pregnancies requiring obstetric intervention and those that do not. The ROC curve provides insight into the sensitivity and specificity of each model, aiding clinicians in selecting the most effective risk stratification approach for low-risk pregnancies.

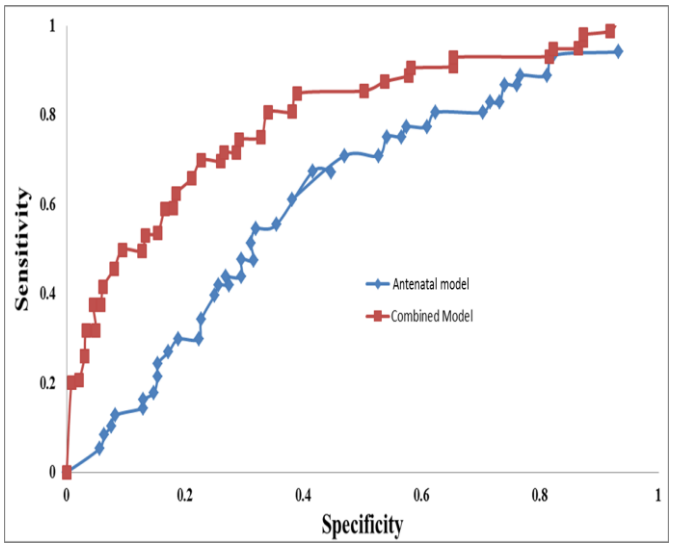

Fig. 1 Receiver-operating characteristics (ROC) curve analysis for obstetric intervention due to suspected intrapartum fetal compromise in low-risk pregnancies.

Fig. 2 illustrates the receiver-operating characteristics (ROC) curve analysis for composite adverse perinatal outcomes associated with obstetric intervention due to suspected intrapartum fetal compromise in low-risk pregnancies. This analysis evaluates the performance of the predictive models in distinguishing between pregnancies with and without adverse perinatal outcomes. The ROC curve provides a visual representation of the trade-off between sensitivity and specificity at various thresholds. A curve that closely approaches the upper left corner of the plot indicates higher discriminatory ability, with the area under the curve (AUC) serving as a measure of the model's predictive accuracy. This figure enables clinicians to assess the effectiveness of the combined predictive model, incorporating maternal and fetal Doppler parameters, in identifying pregnancies at risk of adverse perinatal outcomes.

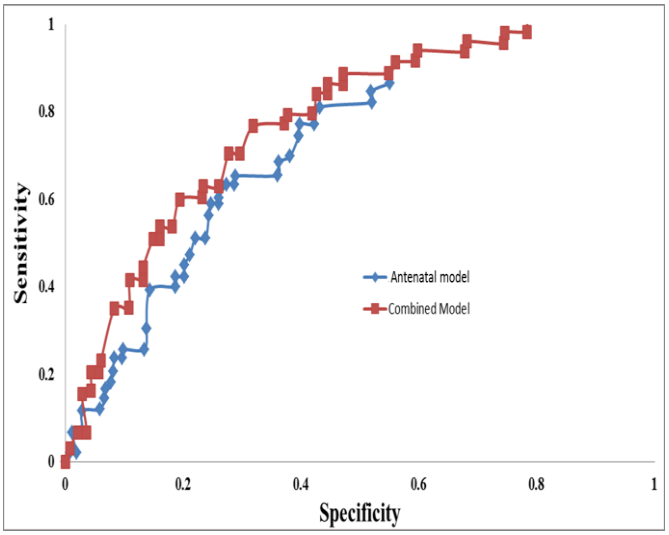

Fig. 2: Receiver-operating characteristics (ROC) curve analysis for composite adverse perinatal outcomes associated with obstetric intervention due to suspected intrapartum fetal compromisein low-risk pregnancies.

The findings of this study highlight the importance of Doppler assessment, specifically CPR and mean UtA PI, in predicting obstetric interventions for suspected IFC and composite adverse perinatal outcomes in low-risk term pregnancies. The multivariable logistic regression analyses revealed significant associations between abnormal Doppler parameters and increased likelihood of obstetric interventions and adverse perinatal outcomes.

Table 3: Multivariable Logistic Regression Analysis for Composite Adverse Perinatal Outcomes

Variable	Adjust Odds Ratio (aOR)	95% Confidence Interval (CI)	P-Value
Maternal Age	1.026	(0.966-1.089)	0.40
Booking BMI	0.959	(0.889-1.035)	0.29
Multiparity	0.302	(0.132-0.691)	0.005
Smoking	0.205	(0.027-1.536)	0.12
CPR MoM $<10^{th}$ Percentile	3.061	(1.385-6.764)	0.006
Mean UtA PI MoM > 95^{th} Percentile	3.274	(1.145-9.366)	0.03
Epidural in Labour	1.585	(0.662-3.796)	0.30
Oxytocin in Labour	1.916	(0.849-4.323)	0.12

The receiver-operating characteristics (ROC) curve analysis demonstrated that the combined model, integrating antenatal characteristics with abnormal CPR and mean UtA PI, exhibitedgood capacity to rule out and moderate capacity to rule in obstetric interventions for suspected IFC and adverse perinatal outcomes. However, it is crucial to acknowledge the limitations of these predictive models, particularly the poor positive predictive value (PPV), which suggests suboptimal accuracy in predicting outcomes.

Conclusion

In conclusion, this study underscores the significance of integrating maternal and fetal Doppler parameters into predictive models for the assessment of obstetric interventions due to suspected intrapartum fetal compromise and composite adverse perinatal outcomes in low-risk term pregnancies. The findings highlight the association between abnormal Doppler parameters, such as CPR and mean UtA PI, and increased likelihood of obstetric interventions and adverse perinatal outcomes. Despite limitations, including suboptimal positive predictive value, the combined model demonstrates promising capacity to rule out and moderate capacity to rule in obstetric interventions and adverse perinatal outcomes. This study contributes valuable insights into risk stratification and management strategies for low-risk term pregnancies, ultimately aiming to improve maternal and fetal outcomes in contemporary obstetric care.

Limitations of the Study

While this study provides valuable insights, several limitations must be acknowledged. Firstly, the retrospective nature of the data collection may introduce inherent biases and limit the generalizability of the findings. Additionally, the reliance on Doppler assessment for risk stratification may be influenced by factors such as operator variability and equipment calibration. Furthermore, the sample size of the study cohort may impact the statistical power and precision of the results. Future research endeavors should address these limitations through prospective, multicenter studies with larger sample sizes and standardized protocols to enhance the robustness and reliability of the findings.

Clinical Implications of the Study

The findings of this study have significant clinical implications for obstetric practice. By identifying associations between abnormal Doppler parameters and obstetric interventions for suspected intrapartum fetal compromise, clinicians can enhance risk assessment and facilitate timely interventions to optimize maternal and fetal outcomes. Incorporating maternal and fetal Doppler assessments into routine antenatal care protocols may aid in early identification of pregnancies at heightened risk of adverse outcomes, enabling targeted surveillance and intervention strategies. Additionally, the implementation of combined predictive models may enhance risk stratification and decision-making processes in clinical practice, ultimately improving perinatal outcomes for low-risk term pregnancies.

Future Recommendations

Moving forward, several avenues for future research and clinical practice refinement emerge from this study. Firstly, prospective, multicenter studies with larger sample sizes are warranted to validate the findings and enhance the generalizability of the results. Standardized protocols for Doppler assessment and risk stratification should be established to minimize variability and ensure consistency across different healthcare settings. Moreover, longitudinal studies tracking maternal and fetal outcomes beyond the intrapartum period are needed to assess the long-term implications of abnormal Doppler parameters on neonatal health and development. Additionally, advancements in technology and methodology may offer opportunities to refine predictive models and enhance their clinical utility in risk assessment and management of low-risk term pregnancies. By addressing these recommendations, future research endeavors can further contribute to the optimization of maternal and fetal outcomes in contemporary obstetric care.

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