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Development and Validation of Composite Diagnostic Score for IUGR Using Morphometry and Oxidative Stress Parameters

Paras Thapa[1], Dr. Raindra Ved Pathak[2], Dr. Ranjit Ambad[3], Dr. Roshan Kumar Jha[4]Dr Shyambabu Prasad Rauniyar[5]

[1]PhD Scholar, Department of Anatomy, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi (Meghe), Wardha
[2]Associate Professor, Department of Anatomy, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi (Meghe), Wardha
[3]Professor, Department of Biochemistry, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi (Meghe), Wardha
[4] Assistant Professor, Department of Biochemistry, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi (Meghe), Wardha
[5] Tutor, Department of Anatomy, Datta Meghe Medical College, Wanadongri, Datta Meghe institute of Higher Education and Research, Sawangi (M), Wardha, Email:ID: shyambaburauniyar@gmail.com

Corresponding author:
Paras Thapa,
PhD Scholar, Department of Anatomy,
Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Sawangi (Meghe), Wardha
Email:***ID*** thaparas13@gmail.com

ABSTRACT

Intrauterine growth restriction (IUGR) is a major complication during childbirth leading to elevated perinatal morbidity and death rates. Heterogeneous etiologies and overlapping presentation complicate the early and accurate diagnosis of the disorder. The purpose of this study was to construct and test a composite diagnostic score with morphometric evaluation of the umbilical cord and oxidative stress indicators to enhance the ability to detect IUGR. 155 expectant women who were diagnosed with IUGR and 155 age-matched controls at gestational age were enrolled. Morphometric measurements of umbilical vessel wall thickness, lumen diameter and Wharton jelly area were taken. Malondialdehyde (MDA), superoxide dismutase (SOD) and total antioxidant capacity (TAC), were measured in the maternal serum. A composite score was calculated with multivariate logistic regression and tested with receiver operating characteristic (ROC). The composite score was highly diagnostic with an area under the curve (AUC) of 0.91, sensitivity of 88 and specificity of 85. The morphometric and oxidative markers had a moderate diagnostic value on their own, but when combined, the predictive value increased significantly. Composite diagnostic score could be effectively used as a clinical tool to diagnose IUGR pregnancies to help intervene in time and achieve better neonatal outcomes. Its clinical applicability should be confirmed by further large-scale prospective studies

KEYWORDS: Intrauterine growth restriction, Composite diagnostic score, Morphometry, Oxidative stress, Umbilical cord, Biomarkers.

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INTRODUCTION

Intrauterine growth restriction (IUGR) is defined as the failure of the fetus to achieve its genetically predetermined growth potential, often characterized by fetal weight below the 10th percentile for gestational age[1]. IUGR is associated with increased risks of perinatal morbidity, mortality, and long-term adverse outcomes such as neurodevelopmental delay and cardiovascular diseases [2]. Accurate and timely diagnosis of IUGR remains a clinical challenge due to its multifactorial etiology, including placental insufficiency, maternal factors, and fetal conditions[3]. Traditional methods of diagnosis relying on ultrasound biometry and Doppler studies have limitations in sensitivity and specificity, particularly in distinguishing constitutionally small fetuses from pathologically growth-restricted ones[4].

Recent research emphasizes the role of umbilical cord morphometry as a surrogate marker reflecting fetal well-being and placental function. Morphometric parameters such as vessel wall thickness, lumen diameter, and Wharton's jelly area may reflect vascular remodeling and connective tissue changes associated with impaired nutrient and oxygen delivery6. Studies have reported significant alterations in these parameters in IUGR pregnancies, indicating their potential diagnostic value [5].

Oxidative stress has also been implicated in the pathogenesis of IUGR through placental vascular dysfunction and increased

reactive oxygen species (ROS) production. Oxidative stress markers such as malondialdehyde (MDA), superoxide dismutase (SOD), and total antioxidant capacity (TAC) have been investigated as biochemical indicators of fetal and placental oxidative damage. While individually these parameters have demonstrated association with IUGR, their diagnostic accuracy is limited when used alone [6].

To enhance the diagnostic precision for IUGR, integrating multiple parameters into a composite score may offer superior clinical utility. Composite scoring systems combining morphometric and biochemical markers have not been extensively explored in this context. Developing a validated diagnostic score incorporating both structural and biochemical indicators of fetal compromise could facilitate earlier and more accurate identification of IUGR, guiding clinical management and improving outcomes[7].

This study aims to develop and validate a composite diagnostic score for IUGR by combining umbilical cord morphometry and oxidative stress parameters measured in maternal serum. We.

hypothesize that this integrative approach will yield higher sensitivity and specificity compared to individual markers, providing a novel tool for clinical application in obstetrics.

Aim and Objectives

Aim:

To develop and validate a composite diagnostic score combining umbilical cord morphometry and oxidative stress markers for accurate detection of IUGR.

Objectives:

To measure and compare umbilical cord morphometric parameters and oxidative stress markers between IUGR and normal pregnancies.

To develop a composite diagnostic score integrating these parameters and validate its predictive accuracy for IUGR.

Materials and Methods

This cross-sectional analytical study was conducted at a tertiary care hospital. 155 pregnant women diagnosed with IUGR based on fetal weight below the 10th percentile on ultrasound and abnormal Doppler studies were recruited along with 155 gestational age-matched healthy controls. Inclusion criteria were singleton pregnancies between 32- and 40-weeks' gestation, absence of maternal systemic illnesses (hypertension, diabetes), no fetal congenital anomalies, and informed consent. Exclusion criteria included multiple gestations, maternal infections, chromosomal abnormalities, and antioxidant supplementation during pregnancy.

At delivery, segments of umbilical cord 2 cm distal to placental insertion were collected and fixed in 10% formalin. Paraffin-embedded sections were stained with hematoxylin and eosin. Morphometric analysis was performed using digital image software to measure vessel wall thickness, lumen diameter, and Wharton's jelly cross-sectional area.

Simultaneously, maternal venous blood was collected at delivery to assess oxidative stress markers. MDA levels were measured using thiobarbituric acid reactive substances (TBARS) assay, SOD activity by inhibition of nitroblue tetrazolium reduction, and TAC by colorimetric assay with Trolox equivalents.

Statistical analysis involved comparing mean values between groups using independent t-tests. Multivariate logistic regression was used to develop a composite diagnostic score incorporating significant morphometric and oxidative stress variables. Receiver operating characteristic (ROC) curve analysis evaluated the diagnostic accuracy of the score. Statistical significance was set at $p < 0.05$.

Results

Table 1: Comparison of Umbilical Cord Morphometric and Oxidative Stress Parameters Between IUGR and Controls

Parameter	IUGR (mean ± SD)	Control (mean ± SD)	p-value
Vessel wall thickness (µm)	130.4 ± 15.2	95.1 ± 13.6	<0.001
Lumen diameter (µm)	140.7 ± 18.7	180.3 ± 20.1	<0.001
Wharton's jelly area (mm²)	7.5 ± 1.2	10.3 ± 1.6	<0.001

Malondialdehyde (MDA, nmol/mL)	5.9 ± 0.8	3.3 ± 0.6	<0.001
Superoxide dismutase (SOD, U/mL)	43.2 ± 6.1	60.2 ± 5.7	<0.001
Total antioxidant capacity (TAC, mmol Trolox equiv.)	0.82 ± 0.10	1.22 ± 0.15	<0.001

Table 2: Composite Diagnostic Score and ROC Curve Analysis

Diagnostic Tool	Area Under Curve (AUC)	Sensitivity (%)	Specificity (%)
Morphometry alone	0.84	80	78
Oxidative stress markers alone	0.81	75	72
Composite score (morphometry + oxidative stress)	0.91	88	85

IUGR cases were characterized by much higher vessel wall thickness and MDA levels and a smaller lumen, Wharton jelly area, SOD activity, and TAC than controls ($p < 0.001$). When morphometric and oxidative parameters were combined to form composite score, the diagnostic accuracy (AUC=0.91) was better than the parameters.

Discussion

We have demonstrated in our study the usefulness of incorporating umbilical cord morphometry and oxidative stress indicators in a composite diagnostic score of IUGR. The measured large changes in vessel wall thickness, lumen diameter, and Wharton jelly area support the structural remodelling pattern of IUGR 8. Hypoxia and defective placental perfusion may be compensated by increased vessel wall thickness. Loss in the jelly of Wharton might impair cord elasticity and strength, and additional affect fetal blood flow 9.

High malondialdehyde (MDA) levels and reduced superoxide dismutase (SOD) activity and total antioxidant capacity (TAC) are evidence of an increase in the burden of oxidative stress in IUGR pregnancies10. It has been demonstrated that oxidative stress plays a role in endothelial dysfunction and derailing placental angiogenesis, which leads to fetal developmental retardation.Although morphometric and oxidative stress parameters individually demonstrate moderate diagnostic value, their combination into a composite score significantly improves sensitivity and specificity for IUGR diagnosis. The composite score's AUC of 0.91 suggests excellent discriminative ability, supporting the hypothesis that combining structural and biochemical indicators captures multiple facets of fetal compromise [11].

Previous studies have separately evaluated morphometry or oxidative stress markers in IUGR but lacked integrated approaches. Our findings underscore the importance of multifactorial assessment in complex obstetric conditions, aligning with recent trends favoring combined biomarker panels [12].

Conclusion

The development of a composite diagnostic score combining umbilical cord morphometry and oxidative stress markers provides a promising tool for accurate detection of IUGR. This integrative approach improves diagnostic performance beyond individual parameters, potentially enabling earlier identification and intervention in affected pregnancies. Further validation in larger, prospective cohorts is essential before routine clinical implementation

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