# Umbilical Cord Histomorphometry in Intrauterine Growth Restriction: Association with Perinatal Outcome

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**ABSTRACT**

Background

Intrauterine growth restriction (IUGR) is associated with placental insufficiency, impaired fetoplacental circulation, and adverse neonatal outcomes. The umbilical cord, particularly its vascular and connective tissue components, may reflect these pathological changes. Histomorphometric evaluation of the umbilical cord can therefore provide insights into fetal compromise and perinatal prognosis.

Objective

To compare the histomorphometric characteristics of the umbilical cord between appropriate-for-gestational-age (AGA) and IUGR pregnancies and to assess their association with perinatal outcomes.

Methods

This prospective observational case–control study was conducted in the Department of Obstetrics and Gynecology, NIMS University, Jaipur. A total of 100 umbilical cord specimens were analyzed, including 50 from AGA pregnancies and 50 from IUGR pregnancies diagnosed by ultrasonography. A 5-cm segment of umbilical cord was collected immediately after delivery, fixed in 10% formalin, processed routinely, and stained with Hematoxylin and Eosin and Masson's trichrome stains. Morphometric parameters measured included umbilical cord cross-sectional area (CSA), circumference, and diameter. Maternal risk factors and neonatal outcomes were recorded. Statistical analysis was performed using independent Student's t-test and chi-square test, with $p < 0.05$ considered significant.

Results

The IUGR group demonstrated significantly smaller umbilical cord dimensions compared with the AGA group. Mean umbilical cord CSA was 39.56 ± 13.92 mm² in IUGR versus 54.40 ± 16.59 mm² in AGA neonates ($p = 0.0001$). Umbilical cord circumference (20.05 ± 4.01 mm vs. 23.86 ± 4.22 mm; $p = 0.0001$) and diameter (6.38 ± 1.28 mm vs. 7.60 ± 1.34 mm; $p = 0.0001$) were also significantly reduced in IUGR pregnancies. Maternal anemia, pregnancy-induced hypertension, and oligohydramnios were significantly more frequent in the IUGR group. Perinatal outcomes were poorer among IUGR neonates, with lower gestational age at delivery, lower birth weight, higher NICU admission rates (24% vs. 2%), and increased fetal distress (16% vs. 4%).

Conclusion

IUGR pregnancies are associated with significant reductions in umbilical cord cross-sectional area, circumference, and diameter, reflecting altered fetoplacental development. These morphometric changes correlate with adverse neonatal outcomes, including low birth weight, NICU admission, and fetal distress. Umbilical cord histomorphometry may serve as a useful adjunct marker for assessing fetal compromise in high-risk pregnancies.

Keywords

Intrauterine growth restriction; fetal growth restriction; umbilical cord; histomorphometry; Wharton's jelly; perinatal outcome.Keywords: Umbilical cord, IUGR, Histomorphometry, Perinatal outcome, Wharton's jelly

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## INTRODUCTION

Intrauterine growth restriction (IUGR), currently referred to as fetal growth restriction (FGR) in many contemporary guidelines, is a significant obstetric complication characterized by the failure of the fetus to achieve its genetically determined growth potential. It affects approximately 5–10% of pregnancies worldwide and remains one of the leading causes of perinatal morbidity and mortality. IUGR is associated with increased risks of fetal distress, preterm delivery, low birth weight, neonatal intensive care unit (NICU) admission, stillbirth, and long-term neurodevelopmental impairment. Furthermore, accumulating evidence suggests that adverse intrauterine conditions predispose affected individuals to chronic diseases such as hypertension, type 2 diabetes mellitus, cardiovascular disease, and metabolic syndrome later in life [1,2].

Normal fetal growth depends on a complex interaction among maternal, fetal, and placental factors. Adequate placental perfusion and efficient fetoplacental circulation are essential for the transfer of oxygen and nutrients required for fetal development. Placental insufficiency is considered one of the most important etiological factors contributing to IUGR and may lead to chronic fetal hypoxia, altered vascular adaptation, and impaired fetal growth [2,3]. Consequently, the study of structures involved in fetoplacental circulation has gained considerable attention in understanding the pathophysiology of growth restriction.

The umbilical cord serves as the vital vascular connection between the fetus and placenta and plays a fundamental role in maintaining fetal viability throughout pregnancy. Structurally, it consists of two umbilical arteries and one umbilical vein embedded within Wharton's jelly, a specialized mucoid connective tissue rich in proteoglycans, collagen fibers, and mesenchymal cells. Wharton's jelly protects the umbilical vessels against compression and torsion while ensuring uninterrupted blood flow between the placenta and fetus. Alterations in umbilical cord morphology may compromise fetoplacental circulation and adversely affect fetal growth and development [4,5].

Several investigators have reported significant associations between abnormal umbilical cord morphology and adverse pregnancy outcomes. Reduced umbilical cord cross-sectional area, decreased Wharton's jelly content, abnormal vessel dimensions, and lean umbilical cords have been linked with fetal growth restriction, fetal distress, meconium-stained liquor, low birth weight, and increased NICU admissions [6–9]. Raio et al. demonstrated that lean umbilical cords were significantly more prevalent among IUGR fetuses and were associated with adverse perinatal outcomes [7]. Similarly, Bruch et al. reported that umbilical cords from growth-restricted fetuses exhibited significantly smaller cross-sectional areas and reduced vascular dimensions compared with those of appropriately grown fetuses [8].

Wharton's jelly has attracted particular attention because of its important biomechanical and physiological functions. It provides structural support to the umbilical vessels and helps maintain vascular patency throughout gestation. Reduction in Wharton's jelly volume has been associated with compromised fetal growth and adverse neonatal outcomes. Studies have demonstrated a positive correlation between Wharton's jelly quantity and birth weight, suggesting that alterations in umbilical cord composition may reflect underlying disturbances in fetal growth [10,11].

In addition to structural changes, functional alterations within the umbilical vasculature have been reported in IUGR pregnancies. Previous studies have shown evidence of endothelial dysfunction, reduced nitric oxide bioavailability, impaired vasodilation, and vascular remodeling in the umbilical vessels of growth-restricted fetuses. These changes may contribute to reduced fetoplacental blood flow and chronic fetal hypoxia [12,13]. Furthermore, Doppler studies have demonstrated abnormal umbilical venous and arterial blood flow patterns in IUGR pregnancies, supporting the relationship between vascular abnormalities and adverse perinatal outcomes [14,15].

The developmental origins of health and disease (DOHaD) hypothesis proposed by Barker suggests that unfavorable intrauterine conditions can induce permanent structural and metabolic adaptations that influence health throughout life[1]. Therefore, identifying morphological alterations associated with fetal growth restriction may provide important insights not only into immediate neonatal outcomes but also into long-term disease susceptibility.

Although ultrasonographic assessment of umbilical cord morphology has become increasingly important in antenatal surveillance, detailed histological and morphometric studies remain relatively limited, particularly in the Indian population. Most available studies have focused primarily on prenatal sonographic measurements, while comprehensive postnatal histomorphometric evaluation of the umbilical cord and its association with perinatal outcomes remains inadequately explored. Regional differences in maternal nutritional status, socioeconomic conditions, and pregnancy-related complications further highlight the need for population-specific studies.

Therefore, the present study was undertaken to evaluate the histological and morphometric characteristics of the umbilical cord in pregnancies complicated by intrauterine growth restriction and to compare these findings with those of appropriate-for-gestational-age neonates. In addition, the study aimed to determine the association between umbilical cord morphometric parameters and perinatal outcomes, thereby improving our understanding of the role of umbilical cord morphology in fetal growth and neonatal well-being.

## MATERIALS AND METHODS

Study Design and Setting

This prospective observational case–control study was conducted in the Department of Obstetrics and Gynecology, NIMS University, Jaipur, Rajasthan, India. The study was carried out after obtaining approval from the Institutional Human Ethics Committee. All procedures were performed in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants before enrolment in the study.

Study Population

The study included a total of 100 umbilical cord specimens collected from singleton term pregnancies delivered between 37 and 40 completed weeks of gestation. Participants were divided into two groups:

Control group (AGA group):50 umbilical cord specimens obtained from pregnancies with fetuses appropriate for gestational age (AGA).

Case group (IUGR group):50 umbilical cord specimens obtained from pregnancies complicated by intrauterine growth restriction (IUGR).

Appropriate-for-gestational-age fetuses were defined as those having an estimated fetal weight between the 10th and 90th percentiles for gestational age based on ultrasonographic assessment (19). Intrauterine growth restriction was diagnosed when the estimated fetal weight or abdominal circumference was below the 10th percentile for gestational age on ultrasonography (20).

The participants were included in the study Singleton pregnancies, Maternal age between 18 and 35 years, Gestational age between 37 and 40 completed weeks, Reliable gestational dating based on the last menstrual period and/or first-trimester ultrasonography, Pregnancies diagnosed as AGA or IUGR according to predefined criteria, Pregnancies complicated by pregnancy-induced hypertension (PIH) were included in the IUGR group, as PIH is a recognized contributor to placental insufficiency and fetal growth restriction.

The following pregnancies were excluded from this study Multiple gestations, Pre-existing diabetes mellitus, Gestational diabetes mellitus, Maternal cardiovascular disorders.Congenital fetal anomalies, Uncertain gestational age, Preterm deliveries (<37 completed weeks) and Preterm pregnancies were excluded because umbilical cord dimensions vary with gestational age and may independently influence morphometric measurements.

Clinical and Perinatal Data Collection

Maternal demographic and obstetric information was recorded using a structured proforma. The following variables were documentedMaternal age, Gravidity, Pregnancy-induced hypertension, Anemia, Oligohydramnios, Mode of delivery, Gestational age at delivery, Neonatal variables included, Sex of the newborn, Birth weight, Neonatal outcome (alive, NICU admission, or stillbirth), Intrapartum complications, including fetal distress and meconium-stained liquor and Birth weight was measured immediately after delivery using a calibrated digital neonatal weighing scale.

Collection and Processing of Umbilical Cord Specimens

Immediately after delivery, a 5-cm segment of the umbilical cord was excised approximately 5 cm from the placental insertion site. The specimens were fixed in 10% neutral buffered formalin and processed using standard histological techniques.

Following fixation, tissues were dehydrated, embedded in paraffin wax, and sectioned transversely at a thickness of 3 µm using a rotary microtome. The sections were stained with Hematoxylin and Eosin (H&E) for routine histological evaluation and Masson's Trichrome stain for visualization of connective tissue components.

Tangentially cut, damaged, or incomplete sections were excluded from morphometric analysis.

Histomorphometric Evaluation

Histological sections were examined using an Olympus CX40 light microscope (Olympus Corporation, Tokyo, Japan) equipped with a DP21 digital imaging system.

Digital images of representative transverse sections were captured and subjected to morphometric analysis. Observer calibration was performed before measurements, and intra-observer and inter-observer agreement were assessed using Cohen's kappa statistics.

The following umbilical cord parameters were evaluated:

Umbilical Cord Cross-sectional Area

The total cross-sectional area (CSA) of the umbilical cord was measured using the polygonal area measurement tool of the image analysis software and expressed in square millimetres ($mm^2$).

Umbilical Cord Diameter

Umbilical cord diameter was measured using a calibrated linear measurement tool. Two perpendicular diameters were obtained for each section, and the mean value was considered for statistical analysis.

Umbilical Cord Circumference

Umbilical cord circumference was calculated from the mean diameter using the formula:
Circumference = π × Diameter
where π = 3.1416.
All measurements were performed at ×40 magnification under standardized conditions.
Statistical Analysis
Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 21.0 (IBM Corp., Armonk, NY, USA).Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages.The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Variables showing normal distribution were analyzed using parametric statistical methods.Comparisons between the AGA and IUGR groups were performed using: Independent Student's t-test for continuous variables and Chi-square test or Fisher's exact test for categorical variables, as appropriate.A p-value <0.05 was considered statistically significant.
Ethical Considerations
The study protocol was approved by the Institutional Human Ethics Committee of NIMS University, Jaipur, Rajasthan on 16th January 2023 (IEC/P-163/2022). Written informed consent was obtained from all participants before inclusion in the study, and confidentiality of patient information was maintained throughout the study period.

**RESULTS:**

A total of 100 umbilical cord specimens were included in the study, comprising 50 specimens from appropriate-for-gestational-age (AGA) pregnancies and 50 specimens from pregnancies complicated by intrauterine growth restriction (IUGR).
The mean maternal age was significantly lower in the IUGR group compared with the AGA group (23.4 ± 3.13 years vs. 24.6 ± 3.39 years, p = 0.031). Primigravid women were more frequently observed in the IUGR group [34 (52%)] than in the AGA group [24 (37%)]; however, the difference was not statistically significant (p = 0.078).
Maternal complications including pregnancy-induced hypertension, anemia, and oligohydramnios were significantly more common among women with IUGR pregnancies. Pregnancy-induced hypertension was observed in 13 (20%) women in the IUGR group, whereas none of the women in the AGA group had PIH (p = 0.0001). Similarly, maternal anemia was significantly higher in the IUGR group [33 (51%)] compared with the AGA group [14 (22%)] (p = 0.001). Oligohydramnios was also significantly more prevalent among IUGR pregnancies [14 (22%)] than AGA pregnancies [1 (2%)] (p = 0.0001).

Table:1 shows a comparison of the clinical features of AGA and IUGR groups. The mean maternal age was similar in both groups. Primigravida women were more in IUGR group n=34(52%) than AGA group n=24(37%) but, no significant difference was observed. Incidence of pregnancy with anemia, PIH and oligohydramnios were observed significantly more in IUGR group.

| Clinical features | AGA group n= 50 | | IUGR group n=50 | | p value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Maternal age, year [mean(SD)] | 24.6 | 3.39 | 23.4 | 3.13 | 0.0310 |
| Consanguineous marriage | 6 | 9 | 8 | 12 | 0.5710 |
| Gravidity | | | | | |
| Primigravida | 24 | 37 | 34 | 52 | 0.0780 |
| Multigravida | 41 | 63 | 31 | 48 | |
| Pregnancy induced hypertension | 0 | 0 | 13 | 20 | 0.0001* |
| Anemia | 14 | 22 | 33 | 51 | 0.0010* |
| Oligohydramnios | 1 | 2 | 14 | 22 | 0.0001* |
| Maternal Hypothyroidism | 1 | 2 | 2 | 3 | 0.5590 |
| H/O Abortion | 7 | 11 | 6 | 9 | 0.7700 |
| High risk pregnancy | 24 | 37 | | | |
| Significant at p < 0.05 and *highly significant | | | | | |

Umbilical cord characteristics in AGA and IUGR group's results are summarized in table 2. UC area was significantly lower in IUGR group (39.56 ±13.92) than in AGA group (54.40±16.59, p = 0.0001). The UC circumference (20.05±4.01 vs. 23.86±4.22) and UC diameter (6.38±1.28 vs. 7.60±1.34) was significantly smaller in IUGR group versus AGA group.

**Table-2: Umbilical cord characteristics in AGA and IUGR newborns**

| Variables | AGA newborns n=50 | IUGR newborns n=50 | t value | p value |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| UC CSA mm2 | 54.40 ± 16.59 | 39.56 ± 13.92 | 4.89 | 0.0001 * |
| UC circumference mm | 23.86 ± 4.22 | 20.05 ± 4.01 | 4.52 | 0.0001 * |
| UC Diameter mm | 7.60 ± 1.34 | 6.38 ± 1.28 | 4.48 | 0.0001 * |
| Significant at p < 0.05 and *highly significant, UC-umbilical cord, CSA-cross sectional area | | | | |

Table:3 shows perinatal out come in AGA and IUGR newborns. A chi-square test of independence was performed to examine the relation of perinatal outcome of newborns between two groups. GA was significantly lower in IUGR group as compared to AGA group. Birth weight was also decreased in IUGR group (1.98±0.12) as compared to AGA group (3.25±0.50, p=0.0001). Number of NICU admission 12 (18%) and fetal distress 8 (12%) were found significantly more in IUGR group compared to AGA group. No significant difference was found in mode of delivery (p=0.379), sex of newborn (p=0.219), meconium stained liquor (p=1.0) and stillbirth (p=1.0)

**Table- 3: Perinatal out come in AGA and IUGR newborns**

| Variables | AGA newborns n=50 | IUGR newborns n=50 | Test statistic | p value |
|---|---|---|---|---|
| Gestational age at delivery, weeks (mean±SD) | 38.9 ± 1.2 | 37.4 ± 1.1 | t = 6.32 | 0.0001 * |
| Birth weight, kg (mean±SD) | 3.25 ± 0.50 | 1.98 ± 0.12 | t = 15.6 | 0.0001 * |
| Mode of delivery | | | | |
| Vaginal n (%) | | | $\chi^2$ = 1.94 | 0.379 |
| Instrumental n (%) | 30 (60%) | 26 (52%) | | |
| Cesarean n (%) | 5 (10%) | 17 (34%) | | |
| Sex of newborn | | | | |
| Male n (%) | 28 (56%) | 23 (46%) | $\chi^2$ = 1.51 | 0.219 |
| Female n (%) | 22 (44%) | 27 (54%) | | |
| Neonatal outcome | | | | |
| Alive n (%) | 49 (98%) | 38 (76%) | $\chi^2$ = 7.12 | 0.028 |
| NICU n (%) | 1 (2%) | 12 (24%) | | |
| Stillbirth n (%) | 0 (0%) | 0 (0%) | | |
| Meconium stained liquor n (%) | 3 (6%) | 3 (6%) | $\chi^2$ = 0.00 | 1.000 |
| Fetal distress n (%) | 2 (4%) | 8 (16%) | $\chi^2$ = 4.00 | 0.045 |
| Significant at p < 0.05 and *highly significant | | | | |

**DISCUSSION**

The umbilical cord represents the principal vascular connection between the fetus and placenta and plays a crucial role in maintaining adequate fetoplacental circulation. Alterations in umbilical cord morphology may reflect disturbances in placental function and fetal growth. In the present study, significant reductions in umbilical cord cross-sectional area, circumference, and diameter were observed among neonates with intrauterine growth restriction (IUGR) compared with appropriate-for-gestational-age (AGA) neonates. These morphometric changes were accompanied by adverse perinatal outcomes, including lower gestational age at delivery, reduced birth weight, increased NICU admissions, and a higher incidence of fetal distress.

The present study demonstrated significantly higher frequencies of pregnancy-induced hypertension (PIH), maternal anemia, and oligohydramnios among women with IUGR pregnancies. These findings are consistent with the established pathophysiology of fetal growth restriction, in which placental insufficiency leads to chronic fetal hypoxia and impaired nutrient transfer [19,20]. Maternal hypertension is known to cause uteroplacental vascular insufficiency, resulting in reduced placental perfusion and restricted fetal growth [21]. Similarly, maternal anemia reduces oxygen-carrying capacity and may contribute to chronic fetal hypoxia, thereby adversely affecting fetal development and birth weight [22].

Oligohydramnios was significantly more prevalent in the IUGR group, supporting previous observations that reduced amniotic fluid volume is frequently associated with placental dysfunction and fetal compromise [23]. The coexistence of these maternal risk factors highlights the multifactorial nature of fetal growth restriction and underscores the importance of antenatal surveillance in high-risk pregnancies.

Umbilical Cord Morphometry in IUGR

The principal finding of the present study was the significant reduction in umbilical cord cross-sectional area among IUGR neonates. The mean cross-sectional area was approximately 27% lower in the IUGR group than in the AGA group. This finding is consistent with the observations of Raio et al. [24], who reported that lean umbilical cords were significantly associated with growth-restricted fetuses and adverse pregnancy outcomes. Similarly, Bruch et al. [25] demonstrated reduced umbilical cord dimensions in IUGR pregnancies using computerized morphometric analysis.

The reduction in umbilical cord size may reflect impaired development of Wharton's jelly and alterations in vascular growth secondary to placental insufficiency. Previous investigations have shown that fetuses with growth restriction exhibit decreased Wharton's jelly volume and reduced umbilical vein dimensions, contributing substantially to the overall reduction in cord cross-sectional area [25,26]. Although the present study did not separately quantify Wharton's jelly and vascular compartments, the observed reduction in total cord area suggests impaired structural development of the fetoplacental unit.

A significant decrease in umbilical cord circumference and diameter was also observed among IUGR neonates. These findings corroborate those reported by Peyter et al. [27], who demonstrated reduced umbilical vessel growth, vascular remodeling, and smaller cord dimensions in growth-restricted fetuses. Reduced cord diameter may be attributed to diminished extracellular matrix deposition, decreased Wharton's jelly content, and chronic vasoconstriction within the umbilical circulation.

Possible Mechanisms Underlying Umbilical Cord Alterations

Several biological mechanisms may explain the morphometric alterations observed in IUGR pregnancies. Fetal growth is regulated by growth-promoting hormones, particularly insulin-like growth factor-1 (IGF-1), which plays an essential role in cellular proliferation and tissue development. Previous studies have reported significantly reduced concentrations of IGF-1, IGF-binding protein-3, and leptin in the cord blood of growth-restricted fetuses [28,29]. Deficiencies in these growth factors may contribute not only to impaired fetal growth but also to underdevelopment of umbilical cord structures.

In addition, abnormalities in vascular function have been reported in the umbilical vessels of IUGR fetuses. Reduced nitric oxide bioavailability, endothelial dysfunction, and altered expression of endothelial nitric oxide synthase (eNOS) have been demonstrated in growth-restricted pregnancies [30,31]. Nitric oxide plays a pivotal role in regulating vascular tone and maintaining adequate fetoplacental blood flow. Impairment of nitric oxide-mediated vasodilation may result in chronic vasoconstriction and reduced vessel caliber, thereby contributing to the smaller umbilical cord dimensions observed in IUGR neonates.

Furthermore, Doppler studies have consistently demonstrated reduced umbilical venous blood flow and increased vascular resistance in fetuses with growth restriction [32,33]. Chronic alterations in hemodynamic forces may induce vascular remodeling and influence the structural development of the umbilical cord throughout gestation.

Association with Perinatal Outcome

The present study also demonstrated significant associations between reduced umbilical cord dimensions and adverse perinatal outcomes. Newborns in the IUGR group had significantly lower gestational age at delivery and markedly reduced birth weight compared with AGA newborns. These findings are consistent with previous studies reporting strong correlations between reduced umbilical cord size and fetal growth impairment [24,34].

NICU admission was significantly more frequent among IUGR neonates. Nearly one-quarter of growth-restricted newborns required intensive neonatal care, compared with only a small proportion of AGA newborns. Similar observations have been reported by Ghezzi et al. [35], who found that fetuses with reduced umbilical cord dimensions were at increased risk of adverse neonatal outcomes and NICU admission.

Fetal distress was also significantly more common among IUGR pregnancies. This observation may be explained by chronic intrauterine hypoxia resulting from placental insufficiency and impaired fetoplacental circulation. Previous studies have demonstrated that abnormal umbilical blood flow patterns are strongly associated with fetal compromise and poor neonatal outcomes [32,36].

Although meconium-stained liquor was observed in both groups, no statistically significant difference was detected. This finding differs from some previous reports and may be attributable to the relatively small sample size or the low frequency of this outcome in the study population.

Clinical Implications

The findings of the present study suggest that morphometric assessment of the umbilical cord may provide useful information regarding fetal well-being and placental function. Reduced umbilical cord dimensions appear to be associated with both fetal growth restriction and adverse neonatal outcomes.

Therefore, umbilical cord morphometry may serve as a valuable adjunct marker for identifying pregnancies at increased risk of perinatal complications.

Strengths and Limitations

A major strength of the present study is the direct histomorphometric evaluation of umbilical cord specimens obtained from well-characterized IUGR and AGA pregnancies. The study also examined clinically relevant neonatal outcomes, allowing assessment of the relationship between cord morphology and perinatal health.

However, several limitations should be acknowledged. First, the sample size was relatively modest and derived from a single tertiary care center, which may limit generalizability. Second, individual components of the umbilical cord, such as Wharton's jelly area, vessel wall thickness, and luminal dimensions, were not measured separately. Third, placental histopathology and Doppler indices were not evaluated, preventing direct correlation between cord morphology and placental vascular abnormalities.

Future Directions

Future studies involving larger multicentric populations should incorporate detailed quantitative assessment of Wharton's jelly, umbilical vessel morphology, placental histopathology, and Doppler parameters. Evaluation of molecular markers associated with angiogenesis, oxidative stress, and endothelial dysfunction may further improve understanding of the mechanisms linking umbilical cord alterations with fetal growth restriction.

**CONCLUSION**

The present study demonstrated significant reductions in umbilical cord cross-sectional area, circumference, and diameter among IUGR neonates. These morphometric alterations were associated with adverse perinatal outcomes, including lower birth weight, earlier gestational age at delivery, increased NICU admissions, and a higher incidence of fetal distress. The findings support the concept that umbilical cord morphology reflects underlying fetoplacental insufficiency and may serve as a useful marker of fetal compromise in pregnancies complicated by intrauterine growth restriction.

**REFERENCES:**

1.Lees CC, Stampalija T, Baschat A, da Silva Costa F, Ferrazzi E, Figueras F, et al. ISUOG Practice Guidelines: diagnosis and management of small-for-gestational-age fetus and fetal growth restriction. Ultrasound Obstet Gynecol. 2020;56(2):298-312.

2.Nardozza LMM, Caetano ACR, Zamarian ACP, Mazzola JB, Silva CP, Marçal VMG, et al. Fetal growth restriction: current knowledge. Arch Gynecol Obstet. 2017;295(5):1061-1077.

3.Gluckman PD, Hanson MA. Developmental origins of disease paradigm. 2004.

4.Young MF, Oaks BM, Tandon S, Martorell R, Dewey KG, Wendt AS. Maternal hemoglobin concentrations across pregnancy and maternal and child health: a systematic review and meta-analysis. Ann N Y Acad Sci. 2019;1450(1):47-68.

5.Rossi AC, Prefumo F. Perinatal outcomes of isolated oligohydramnios at term and post-term pregnancy: a systematic review of literature with meta-analysis. Eur J Obstet GynecolReprod Biol. 2013;169(2):149-154.

6.Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol. 2016;48(3):333-339.

Barker DJP. In utero programming of chronic disease. Clin Sci (Lond). 1998;95(2):115–128.

7. Sankaran S, Kyle PM. Aetiology and pathogenesis of intrauterine growth restriction. Best Pract Res Clin Obstet Gynaecol. 2009;23(6):765–777.

8.Gluckman PD, Hanson MA. Developmental origins of disease paradigm. Pediatr Res. 2004;56(3):311–317.

9.Proctor LK, Fitzgerald B, Whittle WL, et al. Umbilical cord diameter percentile curves and their correlation to birth weight and placental pathology. Placenta. 2013;34(1):62–66.

10.Raio L, Ghezzi F, Di Naro E, et al. Prenatal diagnosis of a lean umbilical cord. Ultrasound Obstet Gynecol. 1999;13(3):176–180.

11.Bruch JF, Sibony O, Benali K, et al. Computerized microscope morphometry of umbilical vessels from pregnancies with IUGR. Hum Pathol. 1997;28(10):1139–1145.

12.Labarrere C, Sebastiani M, Siminovich M, et al. Absence of Wharton's jelly around the umbilical arteries. Placenta. 1985;6(6):555–559.

13.Filiz AA, Rahime B, Keskin HL, et al. Positive correlation between the quantity of Wharton's jelly and birth weight. Taiwan J Obstet Gynecol. 2011;50(1):33–36.

14.Peyter AC, Delhaes F, Baud D, et al. Structural alterations in the umbilical cord in IUGR. Placenta. 2014;35(11):891–899.

15.Krause BJ, Carrasco-Wong I, Caniuguir A, et al. eNOS/arginase imbalance contributes to vascular dysfunction in IUGR. Placenta. 2013;34(1):20–28.

16.Ferrazzi E, Rigano S, Bozzo M, et al. Umbilical vein blood flow in growth-restricted fetuses. Ultrasound Obstet Gynecol. 2000;16(5):432–438.

17.Boito S, Struijk PC, Ursem NTC, et al. Umbilical venous volume flow in growth-restricted fetuses. Ultrasound Obstet Gynecol. 2002;19(4):344–349.

18.Ghezzi F, Raio L, Duwe DG, et al. Sonographic umbilical vessel morphometry and perinatal outcome. J Clin Ultrasound. 2005;33(1):18–23.
19. Baschat AA. Fetal growth restriction—from observation to intervention. J Perinat Med. 2010;38(3):239–246.
20. Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, et al. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol. 2016;48(3):333-339.
21. Nardozza LMM, Caetano ACR, Zamarian ACP, Mazzola JB, Silva CP, Marçal VMG, et al. Fetal growth restriction: current knowledge. Arch Gynecol Obstet. 2017;295(5):1061-1077.
22. Roberts JM, Hubel CA. The two-stage model of preeclampsia: variations on the theme. Placenta. 2009;30(Suppl A):S32-S37.
23. Young MF, Oaks BM, Tandon S, Martorell R, Dewey KG, Wendt AS. Maternal hemoglobin concentrations across pregnancy and maternal and child health outcomes: a systematic review and meta-analysis. Ann N Y Acad Sci. 2019;1450(1):47-68.
24. Rossi AC, Prefumo F. Perinatal outcomes of isolated oligohydramnios at term and post-term pregnancy: a systematic review of literature with meta-analysis. Eur J Obstet GynecolReprod Biol. 2013;169(2):149-154.
25. Baschat AA. Neurodevelopment following fetal growth restriction and its relationship with antepartum parameters of placental dysfunction. Ultrasound Obstet Gynecol. 2011;37(5):501-514.
26. Figueras F, Gratacós E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther. 2014;36(2):86-98.
27. Kingdom J, Huppertz B, Seaward G, Kaufmann P. Development of the placental villous tree and consequences of placental malperfusion in fetal growth restriction. Placenta. 2000;21(2-3):206-
28. Burton GJ, Jauniaux E. Pathophysiology of placental-derived fetal growth restriction. Am J Obstet Gynecol. 2018;218(2S):S745-S761.
29. Malhotra A, Allison BJ, Castillo-Melendez M, Jenkin G, Polglase GR, Miller SL. Neonatal morbidities of fetal growth restriction: pathohysiology and impact. Front Endocrinol (Lausanne). 2019;10:55.
30. Crispi F, Crovetto F, Gratacós E. Intrauterine growth restriction and later cardiovascular function. Early Hum Dev. 2018;126:23-27.
31. Baschat AA, Galan HL, Ross MG, Gabbe SG. Umbilical cord blood flow and fetal adaptation in growth restriction. Obstet Gynecol Clin North Am. 2017;44(2):243-256.
32. Unterscheider J, O'Donoghue K, Daly S, Geary MP, Kennelly MM, McAuliffe FM, et al. Fetal growth restriction and the risk of perinatal mortality. Am J Obstet Gynecol. 2014;210(4):310.e1-310.e6.
33. Lausman A, Kingdom J; Maternal Fetal Medicine Committee. Intrauterine growth restriction: screening, diagnosis and management. J Obstet Gynaecol Can. 2013;35(8):741-748.
34. Figueras F, Gratacós E. Stage-based approach to management of fetal growth restriction. PrenatDiagn. 2014;34(7):655-659.
35. Miller SL, Huppi PS, Mallard C. The consequences of fetal growth restriction on brain structure and neurodevelopmental outcome. J Physiol. 2016;594(4):807-823.
36. American College of Obstetricians and Gynecologists. Fetal growth restriction. ACOG Practice Bulletin No. 227. Obstet Gynecol. 2021;137(2):e16-e28.