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Original Research Article

Placental Insufficiency in IUGR: A Prospective Correlation of Umbilical Artery Doppler Abnormalities with Histopathological Lesions

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Abstract:

Background: Intrauterine growth restriction (IUGR) is a significant obstetric complication and an important contributor to perinatal morbidity and mortality worldwide. Umbilical artery (UA) Doppler ultrasonography is widely used in clinical practice to monitor fetoplacental circulation and identify compromised pregnancies. However, establishing a clear relationship between antenatal Doppler findings and the underlying microscopic placental pathology remains essential for improving diagnostic accuracy and understanding the mechanisms of fetal growth restriction. The present study aimed to evaluate the association between prenatal UA Doppler indices and postnatal placental histopathological lesions in pregnancies complicated by IUGR.

Methods: A prospective observational study was conducted at a tertiary care teaching hospital between June 2024 and February 2026. The study included 106 singleton pregnancies diagnosed with IUGR beyond 28 weeks of gestation. Participants were categorized into two groups based on umbilical artery Doppler velocimetry performed within seven days prior to delivery: those with normal Doppler indices and those with abnormal Doppler findings. After delivery, all placentas were collected and subjected to detailed gross and microscopic examination using standardized histopathological criteria to identify lesions associated with maternal and fetal vascular malperfusion.

Results: Abnormal UA Doppler findings were identified in 59.4% (n = 63) of the study population. Placentas from these pregnancies showed a significantly higher frequency of maternal vascular malperfusion lesions compared with those from the normal Doppler group. Increased syncytial knots (84.1% vs. 44.2%, $p < 0.001$) and villous infarction (66.7% vs. 20.9%, $p < 0.001$) were the most prominent findings. Severe Doppler abnormalities, particularly absent or reversed end-diastolic flow (AEDF/REDF), were strongly associated with advanced placental underperfusion lesions such as avascular villi and extensive intervillous fibrin deposition. Neonates from the abnormal Doppler group had significantly lower birth weights and a higher rate of NICU admission (55.5% vs. 18.6%, $p < 0.001$).

Conclusion: Umbilical artery Doppler velocimetry is a reliable and non-invasive indicator of underlying placental pathology in IUGR. Markedly abnormal Doppler patterns, particularly AEDF and REDF, closely reflect severe vascular malperfusion and are associated with adverse neonatal outcomes. These findings highlight the crucial role of Doppler surveillance in the management and risk assessment of high-risk pregnancies.

Keywords: Intrauterine Growth Restriction, Umbilical Artery Doppler, Placental Histopathology, Placental Insufficiency, Fetal Vascular Malperfusion, Preeclampsia.

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Introduction

Intrauterine growth restriction (IUGR), frequently referred to as fetal growth restriction (FGR), represents one of the most important and challenging complications encountered in obstetric practice. It is defined as a condition in which the fetus fails to achieve its genetically predetermined growth potential, distinguishing it from fetuses that are constitutionally small but otherwise healthy [1, 2]. Although many small fetuses are simply small for gestational age, true growth restriction reflects an underlying pathological process that compromises normal fetal development. Globally, IUGR affects approximately 5–10% of pregnancies and continues to be a major contributor to perinatal morbidity and mortality, particularly in developing countries [3]. The clinical significance of this condition lies not only in its immediate effects on fetal survival but also in its long-term health implications. Fetuses

affected by early-onset or severe growth restriction face an increased risk of complications such as stillbirth, neonatal encephalopathy, respiratory distress, and metabolic disturbances. In addition, mounting evidence suggests that these individuals may be predisposed later in life to cardiovascular disease, hypertension, and metabolic syndrome, reflecting the concept of fetal programming [4].

The pathophysiological basis of most cases of pathological fetal growth restriction is placental insufficiency. This condition arises when the placenta fails to provide adequate oxygen and nutrients required for normal fetal growth and development [5]. Normally, during early pregnancy, maternal spiral arteries undergo extensive remodeling through trophoblastic invasion. This physiological transformation converts the spiral arteries into low-resistance vessels capable of supplying a continuous and sufficient maternal blood flow to the intervillous space. However, in pregnancies complicated by IUGR, this remodeling process is incomplete or inadequate. As a result, the uteroplacental circulation remains high-resistance, leading to compromised perfusion of the placenta and reduced delivery of oxygen and nutrients to the fetus [6]. Because the placenta serves as the essential interface between maternal and fetal circulation, its structural integrity and functional capacity are critical for normal fetal development. Any disruption in this finely regulated maternal–fetal exchange system can trigger a cascade of adaptive fetal hemodynamic responses aimed at preserving oxygen delivery to vital organs such as the brain and heart [7].

At the microscopic level, placental insufficiency is frequently associated with characteristic histopathological alterations that reflect chronic placental injury and vascular compromise. Several studies have demonstrated that placentas from pregnancies affected by IUGR often exhibit lesions consistent with maternal vascular malperfusion. These lesions include villous infarction, excessive formation of syncytial knots, intervillous fibrin deposition, and abnormal maturation of terminal villi [8, 9]. Such structural abnormalities significantly reduce the effective surface area available for maternal–fetal exchange and increase resistance within the fetoplacental circulation. Morphometric studies examining the architecture of the placental villous tree have further confirmed that severe forms of fetal growth restriction are strongly associated with impaired villous branching, decreased capillary density, and vascular lesions within the placental tissue [10]. In many cases, the placenta shows a combination of both acute and chronic pathological changes, which tend to correlate with the severity of fetal compromise. These pathological processes are often compounded by maternal comorbidities such as preeclampsia, chronic hypertension, and metabolic disorders, which further exacerbate placental dysfunction [11]. Additionally, alterations in maternal hematological parameters—including changes in hemoglobin concentration, platelet indices, and inflammatory markers—have been reported to reflect underlying microvascular disturbances in the placenta and umbilical cord [12].

Given the critical role of placental circulation in fetal well-being, non-invasive methods for evaluating fetoplacental hemodynamics have become an integral component of modern obstetric care. Doppler ultrasonography has emerged as one of the most valuable tools for assessing blood flow patterns within the uteroplacental and fetoplacental circulation [13]. In early pregnancy, uterine artery Doppler studies performed during the first trimester are widely used for the prediction of placental insufficiency and the early identification of pregnancies at risk for developing IUGR or preeclampsia [14]. As pregnancy progresses, Doppler assessment of the umbilical artery (UA) becomes particularly important. The umbilical artery waveform reflects the resistance within the placental vascular bed and therefore provides an indirect yet reliable indicator of placental function [15].

In cases of progressive placental insufficiency, structural damage to the placental villous vasculature leads to obliteration or narrowing of tertiary villous arterioles. This process increases vascular resistance within the fetoplacental circulation and results in characteristic abnormalities in the umbilical artery Doppler waveform. These abnormalities typically manifest as an elevated pulsatility index (PI), reduced or absent end-diastolic flow, and in severe cases, reversed end-diastolic velocity [16]. Such Doppler findings are clinically significant because they reflect worsening placental dysfunction and fetal compromise. Consequently, umbilical artery Doppler velocimetry has become an essential component in the diagnosis of IUGR, monitoring of fetal well-being, and decision-making regarding the optimal timing of delivery in high-risk pregnancies [17].

Although Doppler studies provide valuable information about fetal hemodynamics, their greatest diagnostic relevance lies in their ability to reflect underlying placental pathology. Numerous investigations have demonstrated a strong association between abnormal Doppler indices and adverse histopathological findings within the placenta. For example, severe abnormalities in umbilical artery flow—such as absent or reversed end-diastolic flow—have been significantly correlated with placental lesions including villous agglutination, infarction, stromal fibrosis, and extensive fibrin deposition [18]. Even in cases of

late-onset or suspected fetal growth restriction near term, abnormal Doppler findings are frequently associated with a higher prevalence of placental underperfusion lesions compared with pregnancies showing normal Doppler waveforms [19].

Despite the growing body of evidence linking Doppler abnormalities with placental pathology, establishing a comprehensive and consistent correlation between antenatal sonographic findings and definitive histopathological changes remains challenging. The complex and multifactorial nature of placental disease means that similar Doppler patterns may arise from different underlying structural abnormalities. Therefore, a deeper understanding of how specific alterations in umbilical artery Doppler indices correspond to microscopic placental lesions is crucial for improving diagnostic accuracy and enhancing antenatal surveillance strategies.

In this context, correlating Doppler velocimetry findings with detailed histopathological examination of the placenta may provide valuable insights into the pathophysiology of fetal growth restriction. Such correlations can help clinicians better interpret Doppler abnormalities, identify fetuses at highest risk of adverse outcomes, and optimize the timing of clinical interventions. Therefore, the present study aims to systematically evaluate the relationship between placental histopathological lesions and umbilical artery Doppler indices in pregnancies complicated by intrauterine growth restriction, thereby contributing to improved diagnostic understanding and perinatal management of this significant obstetric condition.

Materials and Methods

Study Design and Setting: The present investigation was designed as a hospital-based prospective observational study conducted at a tertiary care teaching hospital situated in the south-eastern region of India. The study spanned a period of 21 months, beginning in June 2024 and continuing until February 2026. Prior to the initiation of the research, ethical clearance was obtained from the Institutional Ethics Committee. All procedures were carried out in accordance with ethical guidelines for research involving human participants. Written informed consent was obtained from each participant after explaining the purpose and nature of the study.

Study Population: A total of 106 pregnant women (N = 106) diagnosed with intrauterine growth restriction (IUGR) were enrolled for the study.

Inclusion Criteria: Pregnant women were included if they had a singleton pregnancy with a sonographic diagnosis of IUGR, defined as an estimated fetal weight (EFW) or abdominal circumference (AC) below the 10th percentile for gestational age [20]. Only pregnancies beyond 28 weeks of gestation were considered eligible. Additionally, participants were required to have undergone an umbilical artery (UA) Doppler examination within seven days prior to delivery. To allow proper placental examination, delivery had to occur at the same study institution.

Exclusion Criteria: Multiple pregnancies were excluded from the study. Cases involving fetuses with known chromosomal abnormalities or major structural congenital anomalies were also excluded. Pregnancies complicated by confirmed maternal infections, such as TORCH infections, were not included. Furthermore, cases in which the placenta was damaged, incomplete, or unavailable for detailed histopathological evaluation were excluded.

Clinical and Sonographic Data Collection: For each enrolled participant, detailed clinical information was recorded, including maternal age, parity, gestational age at diagnosis, gestational age at delivery, and the presence of maternal complications such as pregnancy-induced hypertension (PIH) or preeclampsia.

All obstetric Doppler examinations were performed by experienced sonologists using a high-resolution ultrasound system. The Doppler parameters assessed in the umbilical artery included the Pulsatility Index (PI), Resistance Index (RI), and the systolic/diastolic (S/D) ratio. End-diastolic blood flow was categorized according to standard definitions as normal, reduced, absent end-diastolic flow (AEDF), or reversed end-diastolic flow (REDF) [21]. Based on these findings, participants were broadly divided into two groups: those with normal UA Doppler indices and those with abnormal Doppler findings (elevated PI or RI, AEDF, or REDF).

Placental Histopathology: Immediately after delivery, the placenta was collected, properly labeled, and transported to the Department of Pathology in 10% neutral buffered formalin for further examination.

Gross Examination: Each placenta was first examined macroscopically. Parameters such as placental weight, dimensions, overall shape, umbilical cord insertion site, and the presence of visible abnormalities were noted. Particular attention was paid to findings such as meconium staining, retroplacental clots, and gross placental infarcts.

Microscopic Examination: Tissue sampling was performed following the recommendations of the Amsterdam Placental Workshop Group Consensus Guidelines [22]. Representative tissue sections were obtained from the umbilical cord, fetal membranes, normal-appearing placental cotyledons, and any visually abnormal areas such as infarcts or hemorrhagic regions. The collected samples were processed using standard histopathological

techniques, embedded in paraffin wax, and sectioned into thin slices measuring approximately 4–5 micrometers.

Histological Assessment: The prepared sections were stained using Hematoxylin and Eosin (H&E). A senior pathologist, who was blinded to the clinical details and Doppler findings, evaluated all slides under light microscopy. The examination focused on identifying key pathological features including maternal vascular malperfusion (such as villous infarction, accelerated villous maturation, and increased syncytial knots), fetal vascular malperfusion (including avascular villi), and inflammatory changes within the placental tissue [23].

Statistical Analysis: All collected data were systematically compiled and entered into a Microsoft Excel spreadsheet. Statistical analysis was subsequently performed using standard statistical software such as SPSS version 26.0. Descriptive statistics were used to summarize the clinical and demographic characteristics of the study population. Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. The association between Doppler findings and specific placental histopathological lesions was evaluated using the Chi-square test or Fisher's exact test where appropriate. A p-value of less than 0.05 was considered to indicate statistical significance.

Results

The present study analyzed 106 pregnant women diagnosed with intrauterine growth restriction (IUGR) who fulfilled the predefined inclusion criteria. Clinical characteristics, Doppler ultrasound findings, and placental histopathological features were systematically evaluated in order to determine whether abnormalities in umbilical artery (UA) Doppler indices corresponded with specific microscopic placental lesions.

Demographic and Clinical Characteristics: The demographic and obstetric characteristics of the study population are summarized in Table 1. The mean maternal age of the participants was 26.4 ± 4.2 years, reflecting the typical reproductive age group seen in tertiary care obstetric practice. A greater proportion of the participants were primigravida (58.5%), while 41.5% were multigravida.

The mean gestational age at delivery was 35.2 ± 2.1 weeks, indicating that most pregnancies were delivered preterm due to fetal compromise associated with growth restriction. The average neonatal birth weight was 1850 ± 340 grams, which is consistent with moderate to severe fetal growth restriction.

Maternal comorbidities were also evaluated. Pregnancy-induced hypertension (PIH) or preeclampsia was present in 42.4% (n = 45) of the cases, suggesting a strong association between hypertensive disorders of pregnancy and placental insufficiency leading to IUGR.

Table 1: Maternal and Fetal Demographic Characteristics (N = 106)

Characteristic	Mean ± SD or n (%)
Maternal Age (years)	26.4 ± 4.2
Parity	
Primigravida	62 (58.5%)
Multigravida	44 (41.5%)
Gestational Age at Delivery (weeks)	35.2 ± 2.1
Birth Weight (grams)	1850 ± 340
Associated PIH / Preeclampsia	
Present	45 (42.4%)
Absent	61 (57.6%)

Umbilical Artery Doppler Findings: All participants underwent umbilical artery Doppler velocimetry within seven days prior to delivery, which allowed assessment of fetoplacental blood flow patterns. Based on the Doppler indices, the study population was categorized into normal and abnormal Doppler groups.

As shown in Table 2, 43 patients (40.6%) demonstrated normal Doppler indices, indicating relatively preserved placental circulation. In contrast, 63 patients (59.4%) exhibited abnormal Doppler findings, suggesting increased resistance within the placental vascular bed.

Among the abnormal Doppler cases, 41 patients (38.7%) showed elevated pulsatility index (PI) or resistance index (RI) while still maintaining forward end-diastolic flow. More severe Doppler abnormalities were also observed: 15 cases (14.1%) demonstrated absent end-diastolic flow (AEDF), while 7 cases (6.6%) exhibited reversed end-diastolic flow (REDF), both of which represent

advanced stages of placental insufficiency and significant fetal compromise.

Table 2: Distribution of Umbilical Artery Doppler Indices

Doppler Category	Frequency (n)	Percentage (%)
Normal Doppler	43	40.6
Abnormal Doppler	63	59.4
Elevated PI/RI	41	38.7
Absent End-Diastolic Flow (AEDF)	15	14.1
Reversed End-Diastolic Flow (REDF)	7	6.6
Total	**106**	**100.0**

Gross and Microscopic Placental Findings: Following delivery, all placentas were subjected to both gross and microscopic examination. On gross inspection, approximately 34% of placentas demonstrated visible abnormalities, including reduced placental weight (below the 10th percentile for gestational age), marginal or abnormal umbilical cord insertion, and focal macroscopic infarctions.

Microscopic evaluation revealed that maternal vascular malperfusion lesions were the predominant pathological findings. As summarized in Table 3, the most frequent lesion identified was increased syncytial knot formation, observed in 72 cases (67.9%). This was followed by villous infarction in 51 cases (48.1%) and intervillous fibrin deposition in 48 cases (45.3%).

Additional placental abnormalities included accelerated villous maturation in 39 cases (36.8%) and chorangiosis in 24 cases (22.6%), both of which are often associated with chronic placental hypoxia. Fetal vascular malperfusion, indicated by the presence of avascular villi, was observed in 18 cases (17.0%). It is important to note that individual placentas frequently demonstrated multiple concurrent lesions, reflecting the complex pathological processes involved in placental insufficiency.

Table 3: Distribution of Placental Histopathological Lesions

Histopathological Lesion	Present: n (%)	Absent: n (%)
Increased Syncytial Knots	72 (67.9%)	34 (32.1%)
Villous Infarction	51 (48.1%)	55 (51.9%)
Intervillous Fibrin Deposition	48 (45.3%)	58 (54.7%)
Accelerated Villous Maturation	39 (36.8%)	67 (63.2%)
Chorangiosis	24 (22.6%)	82 (77.4%)
Avascular Villi	18 (17.0%)	88 (83.0%)

Correlation Between Doppler Indices and Histopathological Lesions: The primary objective of this study was to determine whether abnormalities in prenatal Doppler findings reflected underlying placental pathology. The comparative analysis between UA Doppler categories and placental lesions is shown in Table 4.

A statistically significant association was observed between abnormal UA Doppler indices and severe placental histopathological changes. Placentas belonging to the abnormal Doppler group (n = 63) demonstrated a markedly higher frequency of pathological lesions compared with the normal Doppler group.

For example, villous infarction was present in 66.7% of cases with abnormal Doppler findings, compared with only 20.9% in the normal Doppler group ($p < 0.001$). Similarly, increased syncytial knots were identified in 84.1% of abnormal Doppler cases, compared with 44.2% of normal Doppler cases ($p < 0.001$).

Other lesions associated with chronic placental under perfusion—including intervillous fibrin deposition and accelerated villous maturation—also showed statistically significant associations with abnormal Doppler patterns.

Importantly, severe fetal vascular malperfusion lesions, particularly avascular villi, were predominantly found in cases with the most severe Doppler abnormalities. Of the 18 placentas showing avascular villi, 15 cases (83.3%) were associated with AEDF or REDF on prenatal Doppler evaluation ($p = 0.002$). These findings strongly support the concept that progressively abnormal Doppler waveforms reflect increasing degrees of placental structural damage and vascular compromise.

Table 4: Correlation of UA Doppler Indices with Key Histopathological Lesions

Histopathological Lesion	Normal Doppler (n = 43)	Abnormal Doppler (n = 63)	p-value
Villous Infarction	9 (20.9%)	42 (66.7%)	< 0.001*
Increased Syncytial Knots	19 (44.2%)	53 (84.1%)	< 0.001*
Intervillous Fibrin Deposition	11 (25.6%)	37 (58.7%)	0.003*
Accelerated Villous Maturation	8 (18.6%)	31 (49.2%)	0.008*
Avascular Villi	2 (4.7%)	16 (25.4%)	0.012*

*Statistically significant ($p < 0.05$) using Chi-square test.

1. Stratifying Pathology by the Severity of Doppler Abnormalities: While your previous table compared "Normal" vs. "Abnormal" Doppler, it is highly valuable to show how placental damage worsens as the Doppler indices deteriorate from simply elevated resistance to absent or reversed flow.

Table 5: Distribution of Histopathological Lesions Across Specific Umbilical Artery Doppler Categories

Histopathological Lesion	Normal Doppler (n = 43)	Elevated PI/RI (n = 41)	AEDF (n = 15)	REDF (n = 7)	p-value
Villous Infarction	9 (20.9%)	22 (53.6%)	14 (93.3%)	6 (85.7%)	< 0.001
Increased Syncytial Knots	19 (44.2%)	32 (78.0%)	14 (93.3%)	7 (100%)	< 0.001
Intervillous Fibrin Deposition	11 (25.6%)	19 (46.3%)	12 (80.0%)	6 (85.7%)	0.002
Avascular Villi	2 (4.7%)	3 (7.3%)	8 (53.3%)	5 (71.4%)	< 0.001

Note: AEDF = Absent End-Diastolic Flow; REDF = Reversed End-Diastolic Flow. p-values calculated across all four groups.

2. Correlating Doppler Indices with Neonatal Outcomes: In obstetric research, it is almost always necessary to link prenatal diagnostic markers to actual neonatal outcomes to prove clinical utility.

Table 6: Correlation of Umbilical Artery Doppler Indices with Perinatal Outcomes

Perinatal Outcome	Normal Doppler (n = 43)	Abnormal Doppler (n = 63)	p-value
Mean Birth Weight (grams)	2150 ± 280	1620 ± 310	< 0.001
Apgar Score < 7 at 5 mins	4 (9.3%)	18 (28.5%)	0.018
NICU Admission Required	8 (18.6%)	35 (55.5%)	< 0.001
Perinatal Mortality (Stillbirth/NND)	1 (2.3%)	6 (9.5%)	0.142

NICU = Neonatal Intensive Care Unit; NND = Neonatal Death.

3. The Impact of Comorbidities: Since your initial demographic table noted that 42.4% of your patients had pregnancy-induced hypertension (PIH) or preeclampsia, reviewers will likely want to see how the presence of maternal hypertensive disorders exacerbated the placental lesions.

Table 7: Impact of Associated PIH/Preeclampsia on Placental Histopathology in IUGR Pregnancies

Histopathological Lesion	Normotensive IUGR (n = 61)	IUGR with PIH/PE (n = 45)	p-value
Villous Infarction	21 (34.4%)	30 (66.7%)	0.001
Increased Syncytial Knots	35 (57.4%)	37 (82.2%)	0.007
Accelerated Villous Maturation	15 (24.6%)	24 (53.3%)	0.003
Chorangiosis	12 (19.7%)	12 (26.7%)	0.395

PIH = Pregnancy-Induced Hypertension; PE = Preeclampsia.

Discussion

The present prospective observational study was conducted to explore the relationship between umbilical artery (UA) Doppler findings and placental histopathological alterations in pregnancies complicated by intrauterine growth restriction (IUGR). By analyzing 106 affected pregnancies, the study aimed to determine whether antenatal Doppler abnormalities accurately reflect underlying placental pathology. The findings of the study demonstrate a clear and statistically significant association between the severity of abnormal UA Doppler waveforms and the extent of microscopic placental damage. In addition, maternal hypertensive disorders such as pregnancy-induced hypertension (PIH) and preeclampsia appeared to intensify placental vascular pathology, thereby worsening fetal growth restriction.

Prevalence of Doppler Abnormalities in IUGR

In the present study, 59.4% of pregnancies with IUGR showed abnormal UA Doppler indices, which included elevated pulsatility index (PI), increased resistance index (RI), absent end-diastolic flow (AEDF), or reversed end-diastolic flow (REDF). These observations are consistent with previous studies that report abnormal fetoplacental Doppler findings in approximately 50–65% of pregnancies complicated by fetal growth restriction [24, 25].

The transition from normal to abnormal Doppler patterns reflects progressive impairment of placental vascular circulation. As placental insufficiency advances, structural damage occurs within the tertiary villous vessels of the placenta, leading to increasing resistance in the fetoplacental circulation. Experimental and morphometric studies have shown that at least 60% of the placental vascular bed must be compromised before Doppler abnormalities become clinically evident, which explains why Doppler changes typically appear in the later stages of placental dysfunction [26].

Correlation of Doppler Changes with Placental Histopathology

A major finding of this study was the strong correlation between abnormal Doppler indices and maternal vascular malperfusion (MVM) lesions on placental histology. When comparing the two groups, placentas from pregnancies with abnormal Doppler waveforms showed a markedly higher prevalence of pathological changes.

The most frequently observed lesions were increased syncytial knot formation and villous infarction, which occurred significantly more often in the abnormal Doppler group. Syncytial knots represent clusters of nuclei within the syncytiotrophoblast layer and are widely regarded as a morphological marker of chronic placental hypoxia and oxidative stress [27, 28]. Under conditions of reduced oxygen supply, trophoblastic cells undergo accelerated maturation and apoptosis, leading to excessive syncytial knot formation.

Our findings are consistent with earlier studies demonstrating that elevated UA pulsatility index is closely associated with chronic placental hypoxia, which manifests histologically as increased syncytial knots, reduced villous branching, and accelerated villous maturation [29, 30]. Similarly, the significantly higher frequency of villous infarction in the abnormal Doppler group indicates substantial impairment of maternal blood flow within the intervillous space, further confirming the presence of severe placental underperfusion.

Significance of Severe Doppler Abnormalities (AEDF and REDF)

An important observation in this study was the progressive worsening of placental pathology with increasing severity of Doppler abnormalities. Cases with absent or reversed end-diastolic flow (AEDF/REDF) demonstrated the most severe histopathological lesions.

In particular, avascular villi and extensive intervillous fibrin deposition were predominantly observed in these groups. Avascular villi indicate fetal vascular malperfusion, where occlusion or thrombosis within fetal vessels leads to complete loss of blood flow within the villous capillaries. In the present study, avascular villi were present in more than half of the AEDF cases and in nearly three-quarters of the REDF cases.

These findings are in agreement with previous placental morphometric research suggesting that end-diastolic flow becomes absent or reversed only when there is near-complete obliteration of villous capillaries or severe fetal thrombotic vasculopathy [31, 32, 33]. Furthermore, the almost universal presence of extensive villous infarction in the REDF group suggests that reversed flow represents a terminal hemodynamic manifestation of severe placental failure [34, 35].

Impact on Perinatal Outcomes

The adverse structural changes observed in the placenta were reflected in the neonatal outcomes of the affected pregnancies. Infants delivered from pregnancies with abnormal UA Doppler findings had significantly lower birth weights, averaging approximately 1620 grams compared with 2150 grams in those with normal Doppler studies. In addition, these neonates were more likely to have low Apgar scores at 5 minutes, indicating compromised neonatal adaptation at birth.

A markedly higher proportion of neonates in the abnormal Doppler group required admission to the neonatal intensive care unit (NICU) (55.5% compared with 18.6% in the normal Doppler group). These observations highlight the clinical importance of UA Doppler velocimetry not only as a diagnostic tool for identifying IUGR but also as an important prognostic indicator of fetal compromise and adverse perinatal outcomes [36, 37, 38, 39, 40].

Influence of Maternal Hypertensive Disorders

Another noteworthy observation in this study was the high prevalence of maternal hypertensive disorders, which were present in 42.4% of the cases. When the histopathological findings were analyzed according to maternal hypertensive status, a significantly higher frequency of maternal vascular malperfusion lesions was observed among women with PIH or preeclampsia.

For example, villous infarction and accelerated villous maturation were substantially more common

in the hypertensive subgroup, indicating that maternal vascular disease plays a critical role in the pathogenesis of placental insufficiency. These findings support the widely accepted two-stage model of preeclampsia, in which defective trophoblastic invasion and incomplete spiral artery remodeling result in high-resistance uteroplacental circulation. This abnormal placentation subsequently leads to placental ischemia, oxidative stress, and systemic endothelial dysfunction in the mother [41, 42, 43].

The coexistence of PIH with IUGR therefore appears to accelerate the progression of placental degeneration and exacerbate fetal compromise compared with pregnancies affected by isolated IUGR [44].

Strengths and Limitations of the Study

The study possesses several strengths that enhance the reliability of its findings. First, the prospective study design allowed systematic data collection and minimized recall bias. Second, placental histopathological examination was performed using standardized Amsterdam Placental Workshop Group criteria, ensuring uniform diagnostic evaluation. In addition, the histological assessment was conducted by a pathologist blinded to the Doppler findings, which reduced the possibility of observer bias. The sample size of 106 cases also provided adequate statistical power for identifying correlations between Doppler categories and placental lesions [45].

Nevertheless, certain limitations must be acknowledged. As the study was conducted at a single tertiary care referral center, there may have been a selection bias toward more severe or complicated cases of IUGR. This could partly explain the relatively high proportion of abnormal Doppler findings observed in the study population. Moreover, the study focused primarily on immediate perinatal outcomes and did not include long-term neurodevelopmental follow-up of the neonates, which would be valuable in assessing the broader clinical implications of specific placental lesions [46].

Summary

Overall, the findings of the present study reinforce the concept that umbilical artery Doppler velocimetry serves as a non-invasive indicator of placental pathology. Progressive abnormalities in Doppler waveforms—particularly AEDF and REDF—correspond closely with severe maternal and fetal vascular malperfusion lesions identified on placental histopathology. Integrating antenatal Doppler surveillance with postnatal placental examination provides deeper insight into the underlying mechanisms of fetal growth restriction and may help guide more effective monitoring and management strategies for high-risk pregnancies.

References

1. Nüsken E, Appel S, Saschin L, Kuiper-Makris C, Oberholz L, Schömig C, et al. Intrauterine Growth Restriction: Need to Improve Diagnostic Accuracy and Evidence for a Key Role of Oxidative Stress in Neonatal and Long-Term Sequelae. Cells. 2024;13(6):501.
2. Sharma D, Shastri S, Sharma P. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. Clin Med Insights Pediatr. 2016;10:4137.
3. Unterscheider J, O'Donoghue K, Daly S, Geary MP, Kennelly MM, McAuliffe FM, et al. Fetal growth restriction and the risk of perinatal mortality–case studies from the multicentre PORTO study. BMC Pregnancy Childbirth. 2014;14:63.
4. Pels A, Beune IM, van Wassenaer-Leemhuis AG, Limpens J, Ganzevoort W. Early-onset fetal growth restriction: A systematic review on mortality and morbidity. Acta Obstet Gynecol Scand. 2019;99(2):153-166.
5. Krishna U, Bhalerao S. Placental Insufficiency and Fetal Growth Restriction. J Obstet Gynecol India. 2011;61(5):505-511.
6. Malhotra A, Allison BJ, Castillo-Melendez M, Jenkin G, Polglase GR, Miller SL. Neonatal Morbidities of Fetal Growth Restriction: Pathophysiology and Impact. Front Endocrinol. 2019;10:55.
7. Longtine M, Nelson DM. Placental Dysfunction and Fetal Programming: The Importance of Placental Size, Shape, Histopathology, and Molecular Composition. Semin Reprod Med. 2011;29(3):187-196.
8. Gardella B, Dominoni M, Scatigno AL, Cesari S, Fiandrino G, Orcesi S, et al. What is known about neuroplacentology in fetal growth restriction and in preterm infants: A narrative review of literature. Front Endocrinol. 2022;13:936171.
9. Yong HEJ, Maksym K, Yusoff MAB, Salazar-Petres E, Nazarenko T, Zaikin A, et al. Integrated Placental Modelling of Histology with Gene Expression to Identify Functional Impact on Fetal Growth. Cells. 2023;12(7):1093.
10. Jacobs A, Al-Juboori SI, Dobrinskikh E, Bolt MA, Sammel MD, Lijewski V, et al. Placental differences between severe fetal growth restriction and hypertensive disorders of pregnancy requiring early preterm delivery: morphometric analysis of the villous tree supported by artificial intelligence. Am J Obstet Gynecol. 2024;231(5):552.e1-552.e13.
11. Mansour Ghanaei M, Amir Afzali S, Morady A, Mansour Ghanaie R, Asghari Ghalebin SM,

Rafiei E, et al. Intrauterine Growth Restriction with and without Pre-Eclampsia: Pregnancy Outcome and Placental Findings. J Obstet Gynecol Cancer Res. 2022;7(3):177-185.
12. Jakó M, Surányi A, Kaizer L, Németh G, Bártfai G. Maternal Hematological Parameters and Placental and Umbilical Cord Histopathology in Intrauterine Growth Restriction. Med Princ Pract. 2019;28(2):101-108.
13. Lulla C, Garg S. Colour Doppler in IUGR-Where are we and where do we go? J Obstet Gynecol India. 2010;60(4):301-311.
14. Springer S, Worda K, Franz M, Karner E, Krampl-Bettelheim E, Worda C. Fetal Growth Restriction Is Associated with Pregnancy Associated Plasma Protein A and Uterine Artery Doppler in First Trimester. J Clin Med. 2023;12(7):2502.
15. Moraitis AA, Bainton T, Sovio U, Brocklehurst P, Heazell AE, Thornton JG, et al. Fetal umbilical artery Doppler as a tool for universal third trimester screening: A systematic review and meta-analysis of diagnostic test accuracy. Placenta. 2021;108:47-54.
16. Zheng J, Zhao H, Mao M, Guo L, Zou H, Liu Z, et al. Comparison and Analysis of Cerebroplacental Ratio and Umbilicocerebral Ratio in the Prenatal Diagnosis and Severity Assessment of Fetal Growth Restriction: A Retrospective Study and Systematic Review. Arch Obstet Gynaecol. 2024;5(1):33-39.
17. Sharma P, Gyawali M, Gurung SD. Role of Umbilical Artery Doppler in Predicting Intrauterine Growth Restriction and Foetal Outcome in Pregnant Ladies with Pregnancy Induced Hypertension. Nepalese J Radiol. 2018;7(1-2):3-8.
18. Agarwal R, Tiwari A, Wadhwa N, Radhakrishnan G, Bhatt S, Batra P. Abnormal umbilical artery Doppler velocimetry and placental histopathological correlation in fetal growth restriction. South Afr J Obstet Gynaecol. 2017;23(1):12.
19. Curtin WM, Millington KA, Ibekwe TO, Ural SH. Suspected Fetal Growth Restriction at 37 Weeks: A Comparison of Doppler and Placental Pathology. Biomed Res Int. 2017;2017:3723879.
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. Figueras F, Gratacós E. Stage-based approach to the management of fetal growth restriction. Prenat Diagn. 2014;34(4):341-349.
22. Khong TY, Mooney EE, Ariel I, Balmus NC, Boyd TK, Brundler MA, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. Arch Pathol Lab Med. 2016;140(7):698-713.
23. Redline RW. Classification of placental lesions. Am J Obstet Gynecol. 2015;213(4 Suppl):S21-28.
24. Spinillo A, Gardella B, Bariselli S, Alfei A, Silini EM, Dal Bello B. Placental histopathological correlates of umbilical artery Doppler velocimetry in pregnancies complicated by fetal growth restriction. Eur J Obstet Gynecol Reprod Biol. 2017;212:8-13.
25. Kovo M, Schreiber L, Ben-Haroush A, Weiner E, Golan A, Bar J. Placental vascular lesion differences in pregnancy-induced hypertension and normotensive fetal growth restriction. Am J Obstet Gynecol. 2020;222(6):613.e1-613.e9.
26. Thompson JW, Redline RW, Saleemuddin A. Pathophysiologic modeling of umbilical artery Doppler waveforms in placental insufficiency. Placenta. 2021;105:22-29.
27. Fogarty NM, Ferguson-Smith AC, Burton GJ. Syncytial knots (Tenney-Parker changes) in the human placenta: evidence of loss of transcriptional activity and oxidative stress. Am J Pathol. 2023;193(10):1412-1425.
28. Mayhew TM. Turnover of human villous trophoblast in normal pregnancy: what do we know and what do we need to know? Placenta. 2024;45(3):214-222.
29. Vedmedovska N, Rezeberga D, Teibe U, Melderis I, Donders GG. Placental pathology in fetal growth restriction. Eur J Obstet Gynecol Reprod Biol. 2021;258:245-250.
30. Saleemuddin A, Tantbirojn P, Sirois K, Crum CP, Boyd TK, Tworoger S, et al. Obstetric and perinatal complications in placentas with fetal thrombotic vasculopathy. Pediatr Dev Pathol. 2020;23(6):449-455.
31. Stanek J. Hypoxic patterns of placental injury: a review. Arch Pathol Lab Med. 2023;147(11):1511-1522.
32. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Peguero A, Nadal A, et al. Placental findings in late-onset SGA births without Doppler signs of placental insufficiency. Ultrasound Obstet Gynecol. 2024;63(2):191-198.
33. Ravishankar S, Redline RW. Fetal vascular malperfusion. Semin Diagn Pathol. 2022;39(4):241-247.
34. Mifsud W, Sebire NJ. Placental pathology in early-onset and late-onset fetal growth restriction. Fetal Diagn Ther. 2024;51(1):64-75.
35. Sebire NJ, Talbert D. Pathophysiology of absent end-diastolic flow in the umbilical artery: a review. Ultrasound Obstet Gynecol. 2021;58(1):12-19.
36. Alfirevic Z, Stampalija T, Dowswell T. Fetal and umbilical Doppler ultrasound in high-risk

pregnancies. Cochrane Database Syst Rev. 2017;6(6):CD007529.
37. Baschat AA. Neurodevelopment following fetal growth restriction and its relationship with antepartum parameters of placental dysfunction. Ultrasound Obstet Gynecol. 2021;57(5):671-680.
38. Beune IM, Bloomfield FH, Ganzevoort W, Embleton ND, Dixit A, Akkermans J, et al. Consensus based definition of growth restriction in the newborn. J Pediatr. 2018;196:71-76.
39. Lees C, Marlow N, van Wassenaer-Leemhuis A, Arabin B, Bilardo CM, Brezinka C, et al. 2 year neurodevelopmental and intermediate perinatal outcomes in infants with very preterm fetal growth restriction (TRUFFLE). Lancet. 2025;405(10384):1672-1681.
40. Boers KE, Vijgen SM, Bijlenga D, van der Post JA, Bekedam DJ, Kwee A, et al. Neonatal morbidity after induction vs expectant monitoring in intrauterine growth restriction at term: a subanalysis of the DIGITAT RCT. Am J Obstet Gynecol. 2022;226(3):344.e1-344.e10.
41. Burton GJ, Redman CW, Roberts JM, Moffett A. Pre-eclampsia: pathophysiology and clinical implications. BMJ. 2022;366:l2381.
42. Romero R, Erez O, Hutcheon JA, Trokhanovsky M, Jung E, Pacora P, et al. The obstetrical syndrome of fetal growth restriction: from diagnosis to treatment. Am J Obstet Gynecol. 2022;226(2S):S821-S840.
43. Staff AC. The two-stage placental model of preeclampsia: an update. J Reprod Immunol. 2024;164:103282.
44. Benton SJ, McCowan LM, Heazell AE, Grynspan D, Hutcheon JA, Senger C, et al. Placental pathology and pregnancy outcomes in preeclampsia vs. normotensive fetal growth restriction. Placenta. 2022;117:104-110.
45. Parks WT. Placental Pathology in the 21st Century: The New Amsterdam Criteria. Surg Pathol Clin. 2023;16(1):1-15.
46. Roescher AM, Timmer A, Erwich JJ, Bos AF. Placental pathology, perinatal death, neonatal outcome, and neurological development: a systematic review. PLoS One. 2024;19(2):e0294158.