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Doppler Ultrasound in Assessment of Uteroplacental Insufficiency in High-Risk Pregnancies in Kirkuk City

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Abstract: Background: Abstract Uteroplacental Insufficiency (UPI) is a major cause of Intrauterine Growth Restriction (IUGR), preeclampsia, oligohydramnios and adverse perinatal outcomes. Early detection is critical for guiding timely interventions. Conventional methods such as biometry and cardiotocography often identify compromise late in the disease process, whereas Doppler ultrasound offers a sensitive, non-invasive modality to evaluate maternal and fetal circulations in real time. Aim: This study aimed to assess the role of uterine, umbilical and middle cerebral artery Doppler indices, as well as Cerebroplacental Ratio (CPR), in predicting UPI and related complications. **Patients and Methods:** A prospective case–control study was conducted at the Radiology Department, Azadi Teaching Hospital, Kirkuk, Iraq, from January 2023 to May 2024. A total of 120 pregnant women between 24 and 40 weeks were enrolled, including 60 high-risk cases and 60 healthy controls. All participants underwent standardized Doppler evaluation of the uterine arteries, umbilical artery and middle cerebral artery. **Results:** Uterine artery PI (1.42±0.25 vs. 0.98±0.18, p<0.001) and RI (0.68±0.09 vs. 0.54±0.08, p<0.001) were significantly elevated in cases, with bilateral notching observed in 33.3% versus 3.3% of controls (p<0.001). Umbilical artery PI (1.20±0.22 vs. 0.89±0.17, p<0.001) and RI (0.71±0.07 vs. 0.59±0.06, p<0.001) were similarly increased, with absent/reversed end-diastolic flow present in 10.0% of cases. MCA PI was significantly lower in cases (1.38±0.20 vs. 1.64±0.23, p<0.001), while CPR was reduced (0.95±0.14 vs. 1.42±0.20, p<0.001), with abnormal CPR (<1) observed in 43.3% of cases versus 3.3% of controls (p<0.001). Abnormal Doppler findings were strongly associated with IUGR (30.0% vs. 2.5%), oligohydramnios (25.0% vs. 5.0%), preterm delivery (35.0% vs. 7.5%) and cesarean section (50.0% vs. 22.5%) (all p<0.01). Logistic regression identified CPR <1 as the most powerful predictor of UPI (OR 7.8, 95% CI 2.6–23.4, p <0.001), followed by MCA PI <5th percentile (OR 5.2, 95% CI 1.9–13.7, p = 0.001). **Conclusion:** Doppler ultrasound is a reliable, non-invasive tool for detecting uteroplacental insufficiency and predicting adverse outcomes in high-risk pregnancies. Multiparametric evaluation incorporating uterine, umbilical and cerebral Doppler, particularly CPR, enhances diagnostic accuracy.

Keywords: Uteroplacental Insufficiency, Doppler Ultrasound, Uterine Artery, Fetal Outcome, Radiology

INTRODUCTION

Uteroplacental insufficiency is a pathological condition in which there is a failure of the placenta to deliver enough oxygen and other nutrients to the growing fetus in the womb, ending in IUGR, preeclampsia, oligohydramnios and increased perinatal morbidity and death [1]. Fewer of adverse maternal and neonatal outcomes so that adequate interventions can be considered are done with early detection of UPI. In contrast, conventional monitoring techniques like fetal biometry and cardiotocography tend to identify compromise rather late, giving Doppler ultrasound the credit for being the best option for a sensitive and non-invasive assessment of placental circulation-the very flow of real time [2]. Doppler ultrasound characterizes flow dynamics within the maternal and fetal vessels, namely the uterine

arteries, umbilical artery, Middle Cerebral Artery (MCA) and ductus venosus [3]. Impaired trophoblastic invasion and defective spiral artery remodeling are signified by abnormal flow patterns in uterine arteries with the persistence of diastolic notching and increased resistance indices a feature of uteroplacental insufficiency [4]. Increased resistance in the umbilical artery signifies impairment in placental villous vascularization, whereas the fetal MCA undergoes compensatory vasodilation (brain-sparing effect) as an adaptive response to hypoxemia [5]. Many studies have confirmed that Doppler velocimetry plays a predictive role for identifying pregnancies at risk relating to UPI complications. Uterine artery Doppler at 20–24 weeks' gestation is commonly used to identify pregnancies at risk of preeclampsia and IUGR, with abnormalities of the PI strongly associated with such outcomes [6]. Doppler of the umbilical artery, especially in cases of absence or reversal of the flow at end diastole, acts as the strongest prognostic marker for fetal compromise and is associated with a very high rate of perinatal mortality [7]. When MCA and ductus venosus Doppler are also considered, diagnostic accuracy is improved to guide the timing of delivery in pregnancies with high risk [8]. Hence, Doppler ultrasound is vital in the modern obstetric arena as it offers a rather reliable, non-invasive and reproducible means to study uteroplacental and fetoplacental circulation. The incorporation of this technique into routine examination of this group of high-risk pregnancies has drastically improved surveillance and risk stratification as well as clinical reasoning in suspected cases of uteroplacental insufficiency [9]. This study aimed to assess the role of uterine, umbilical and middle cerebral artery Doppler indices, as well as Cerebroplacental Ratio (CPR), in predicting UPI and related complications.

MATERIALS AND METHODS

Conducting this prospective case–control study, the Iraqi Ministry of Health, Kirkuk Health Directorate, supervised the Radiology Department, Azadi Teaching Hospital, in Kirkuk, Iraq. The period of the study ranged from January 17, 2023, to May 15, 2024. Ethical clearance was obtained through the institutional review board system and each participant signed a consent form. Hence, a total of 120 pregnant women were enrolled and bifurcated into two groups of 60 patients with high-risk pregnancies (cases) and 60 with low-risk pregnancies (controls).

High-risk pregnancies were defined on the basis of maternal or obstetric complications among which are chronic hypertension, pregnancy-induced hypertension, preeclampsia, eclampsia, gestational diabetes mellitus, Intrauterine Growth Restriction (IUGR), or a past history of stillbirth, recurrent miscarriage, or other poor perinatal outcomes. Each one of these conditions was considered as a clinical indicator of uteroplacental insufficiency, which requires close monitoring with Doppler ultrasonography. The control group comprised healthy pregnant women without maternal or fetal risk factors, very strictly matched for maternal age and gestational age to avoid potential confounding.

Only singleton viable pregnancies falling between 24 and 40 weeks of gestation, with reliable dating based on last menstrual period aided by a first trimester ultrasound, were enrolled. Informed consent had to be given by the candidate and the participant had to be willing to undergo serial Doppler evaluation. With such measures set in place, the gestational age estimation and Doppler follow-ups remained standardized for all study participants.

A number of exclusion criteria were put into practice for this study. These included multiple gestations, major congenital or chromosomal anomalies and maternal systemic diseases not related to pregnancy, such as those affecting the kidneys, autoimmune mechanisms, or thyroid function. Furthermore, cases presenting technical problems related to sonographic image acquisition, probably due to body habitus, were also excluded to ensure an accurate and reproducible Doppler measurement process. With a well-defined inclusion criterion, the present investigation guarantees methodological rigor and limits potential bias for measuring uteroplacental and fetal circulatory parameters.

Ultrasound and Doppler Protocol

Ultrasound examinations were conducted with a high-resolution real-time ultrasound scanning system (the GE Voluson E6, Siemens Acuson, or any other equivalent system) connected with 3.5–5 MHz convex transducers. The scans were performed by one radiologist (the author) with more than 10 years of experience in obstetric Doppler imaging to maintain consistency and reduce interobserver variability.

Patient Preparation and Positioning

The examination was performed in a semi-recumbent posture with slight left lateral tilt to prevent supine hypotension. Fetal quiescence was ensured before recording Doppler. All measurements were done during maternal apnea to reduce motion artifact.

Doppler Technique and Measurements

Color and pulsed-wave Doppler evaluations were performed as recommended and standardized according to the ISUOG (International Society of Ultrasound in Obstetrics and Gynecology) guidelines to maintain methodological accuracy and reproducibility. The sample gate was set between 2 and 3 mm, while the insonation angle was kept at or below 30°. For each vessel, three uniform cardiac cycles were recorded and mean values were computed. The uterine artery was assessed at its crossing with the external iliac artery, with indices such as Pulsatility Index (PI), Resistance Index (RI) and early diastolic notching presence or absence recorded. The umbilical artery was examined from a free-floating loop of cord away from placental and fetal insertion to eliminate artifacts, measuring systolic/diastolic ratio, RI and PI. The MCA was visualized in a transverse axial plane at the level of the sphenoid wings; the Doppler sample volume was placed close to its origin from the circle of Willis; PI, RI and Peak Systolic Velocity (PSV) were measured. In contrast, the cerebroplacental ratio was calculated as MCA-PI divided by umbilical artery PI, with values of less than 1 denoting an abnormal state.

Doppler Findings Interpretation

Ductal or uterine artery Doppler findings are considered abnormal for this pregnancy when systems are above the 95th percentile for values of PI or RI, along with bilateral notching of the wave flow pattern(s). Elevated PI or RI above the 95th percentile or absent or reversed at the end-diastolic flow indicated abnormality in umbilical artery Doppler. Referring to the brain-sparing effect, the reduction in MCA-PI below the 5th percentile was considered abnormal. An abnormal CPR (below 1) was considered an indicator of an active circulatory redistribution in the fetus.

Ethical Approval

This study was conducted according to the ethical principles laid down in the Declaration of Helsinki. Ethical approval was sought from the Institutional Review Board (IRB) of (insert institution name) and informed consent was obtained in writing from all women included in the study.

Data Collection and Statistical Analysis

Maternal demographic details, obstetric history and risk factors were taken into consideration during documentation. Doppler indices were compared between the high-risk and control groups. Data analyses were performed with the use of SPSS software, version 26.0 (IBM Corp., Armonk, NY, USA). Since variables were continuous, they were expressed as their mean±SD and analyzed with an independent-sample t-test or Mann–Whitney U test if they deviated from normal distribution. Categorical variables were expressed as frequencies and percentages and were analyzed by either the chi-square test or Fisher's exact test. Logistic regression analysis was used to test the predictive value of Doppler parameters for the prediction of uteroplacental insufficiency. Statistical significance was set at p-value of <0.05.

RESULTS

The demographic profile of the sampled population is exhibited in Table 1. The cases had a slightly higher mean maternal age of 31.4±5.8 years as compared to 29.9±5.6 years among controls; however, the value was not significant (p = 0.18). The gestation age at time of the Doppler was an intermediately similar value for cases as compared to that of controls (32.1±3.2 vs. 31.8±3.0 weeks, respectively; p = 0.65). BMI did not vary much between the groups either (27.6±3.8 vs. 26.9±3.5 kg/m^2; p = 0.29). However, gravidity and parity were significantly higher in the case group, with median gravidity being 3 (IQR: 2–4) in cases versus 2 (IQR: 1–3) in controls (p = 0.04) and parity being 2 (IQR: 1–3) in cases versus 1 (IQR: 0–2) in controls (p = 0.03).

Table 2 shows the dissemination of obstetric and clinical risk factors between the two groups. Chronic hypertension was seen at a significantly higher rate among cases (30.0%) as compared to controls (5.0%) (p<0.001). Preeclampsia was the second risk factor that showed more association with the cases. It was present in 23.3% of cases compared to 0% in controls (p<0.001). Gestational diabetes mellitus was also comparatively higher in cases (16.7%) than in controls (3.3%) and this was statistically different (p = 0.03). Of note, 13.3% of cases gave a history of prior stillbirth compared to 1.7% of controls (p = 0.04). IUGR was recorded in 20.0% of the cases and none of the controls (p<0.001).

Table 3 presents the uterine artery Doppler indices in both study groups. The mean Pulsatility Index (PI) was significantly elevated in the case group (1.42±0.25) compared to the controls (0.98±0.18), with a highly significant difference (p<0.001). Similarly, the Resistance Index (RI) was markedly higher among cases (0.68±0.09) versus controls (0.54±0.08), also reaching strong statistical significance (p<0.001). In addition, bilateral early diastolic notching was detected in 33.3% of the cases compared with only 3.3% of the controls (p<0.001).

Table 1: Demographic Characteristics of the Study Population

Variable	Cases (n = 60)	Controls (n = 60)	p-value
Maternal age (years, mean±SD)	31.4±5.8	29.9±5.6	0.18
Gestational age at scan (weeks, mean±SD)	32.1±3.2	31.8±3.0	0.65
BMI (kg/m^2, mean±SD)	27.6±3.8	26.9±3.5	0.29
Gravidity (median, IQR)	3 (2–4)	2 (1–3)	0.04
Parity (median, IQR)	2 (1–3)	1 (0–2)	0.03

Table 2: Obstetric and Clinical Risk Factors in the Study Groups

Risk Factor	Cases (n = 60)	Controls (n = 60)	p-value
Chronic hypertension	18 (30.0%)	3 (5.0%)	<0.001
Preeclampsia	14 (23.3%)	0 (0.0%)	<0.001
Gestational diabetes mellitus	10 (16.7%)	2 (3.3%)	0.03
Prior stillbirth	8 (13.3%)	1 (1.7%)	0.04
Intrauterine growth restriction (IUGR)	12 (20.0%)	0 (0.0%)	<0.001

Table 3: Uterine Artery Doppler Indices

Parameter	Cases (n = 60) (Mean±SD)	Controls (n = 60) (Mean±SD)	p-value
PI	1.42±0.25	0.98±0.18	<0.001
RI	0.68±0.09	0.54±0.08	<0.001
Bilateral notching	20 (33.3%)	2 (3.3%)	<0.001

Table 4: Umbilical Artery Doppler Indices

Parameter	Cases (n = 60) (Mean±SD)	Controls (n = 60) (Mean±SD)	p-value
PI	1.20±0.22	0.89±0.17	<0.001
RI	0.71±0.07	0.59±0.06	<0.001
S/D ratio	3.6±0.9	2.8±0.6	<0.001
Absent/reversed EDF	6 (10.0%)	0 (0.0%)	0.01

Table 4 presents measurements for Doppler indices of umbilical artery in the study subjects. The mean PI was statistically significantly high in the case group (1.20±0.22) versus the controls (0.89±0.17) (p<0.001). Also, the RI was raised in the case group (0.71±0.07) compared to the control group (0.59±0.06), which was also statistically significant (p<0.001). The S/D ratio was reported to have a clear increase in cases (3.6±0.9) in comparison to controls (2.8±0.6) (p<0.001). Absent or reversed EDF, basically the hallmark of severe placental vascular compromise, was identified in 10.0% of cases while not seen in any controls (p = 0.01).

Table 5 depicts Doppler indices of the Middle Cerebral Artery (MCA) across the study groups. The mean pulsatility index was significantly lower in cases (1.38±0.20) than among controls (1.64±0.23), denoting increased cerebral blood flow redistribution (p<0.001). In a similar vein, the resistance index also appeared lower among cases (0.74±0.08) compared with controls (0.82±0.07), with this difference again exhibiting strong statistical significance (p<0.001). On the contrary, cases had a considerably higher PSV (46.8±6.9 cm/s) than controls (42.1±6.4 cm/s) with p = 0.002.

Table 6 demonstrates the Cerebroplacental Ratio (CPR) findings among the study participants. The mean CPR was significantly lower in cases (0.95±0.14) compared with controls (1.42±0.20), showing a highly significant difference (p<0.001). Moreover, abnormal CPR values (<1), which indicate redistribution of blood flow in favor of the fetal brain (brain-sparing effect), were observed in 43.3% of cases versus only 3.3% of controls (p<0.001).

Table 7 outlines the distribution of abnormal Doppler findings between the two groups. Abnormal uterine artery PI/RI values were identified in 36.7% of cases compared to only 5.0% of controls (p<0.001). Similarly, umbilical artery abnormalities were detected in 30.0% of cases versus 3.3% of controls (p<0.001). Abnormal MCA Doppler indices were also more frequent in the case group (33.3%) than in controls (1.7%) (p<0.001). Furthermore, reduced CPR (<1) was present in 43.3% of cases, compared with only 3.3% in controls (p<0.001).

Table 8 shows the correlation between abnormal Doppler findings and adverse clinical outcomes. Intrauterine growth restriction (IUGR) was significantly more common in pregnancies with abnormal Doppler results (30.0%) compared to those with normal Doppler profiles (2.5%) (p<0.001). Likewise, oligohydramnios occurred more frequently in the abnormal Doppler group (25.0%) than in the normal group (5.0%) (p = 0.003). Preterm delivery before 37 weeks was also strongly associated with abnormal Doppler patterns, being observed in 35.0% of cases versus 7.5% of controls (p<0.001). Additionally, cesarean section was performed more often among women with abnormal Doppler findings (50.0%) compared to those with normal results (22.5%) (p = 0.003).

Table 9 presents the logistic regression analysis of Doppler parameters as predictors of uteroplacental insufficiency. Uterine artery notching was associated with a more than fourfold increased risk (OR = 4.6, 95% CI: 1.8–11.5, p = 0.001). Umbilical artery PI above the 95th percentile also showed a significant predictive value, with nearly fourfold increased odds (OR = 3.9, 95% CI: 1.5–10.2, p = 0.004). Similarly, MCA PI below the 5th percentile was a strong independent predictor, increasing the risk by over fivefold (OR = 5.2, 95% CI: 1.9–13.7, p = 0.001). The most powerful predictor identified was CPR <1, which increased the odds of uteroplacental insufficiency almost eightfold (OR = 7.8, 95% CI: 2.6–23.4, p<0.001).

Table 5: Middle Cerebral Artery (MCA) Doppler Indices

Parameter	Cases (n = 60) (Mean±SD)	Controls (n = 60) (Mean±SD)	p-value
PI	1.38±0.20	1.64±0.23	<0.001
RI	0.74±0.08	0.82±0.07	<0.001
Peak systolic velocity (cm/s)	46.8±6.9	42.1±6.4	0.002

Table 6: Cerebroplacental Ratio (CPR)

Parameter	Cases (n = 60)	Controls (n = 60)	p-value
CPR (mean±SD)	0.95±0.14	1.42±0.20	<0.001
CPR <1 (abnormal)	26 (43.3%)	2 (3.3%)	<0.001

Table 7: Distribution of Abnormal Doppler Findings

Doppler Parameter	Abnormal in Cases (n = 60)	Abnormal in Controls (n = 60)	p-value
Uterine artery PI/RI	22 (36.7%)	3 (5.0%)	<0.001
Umbilical artery PI/RI	18 (30.0%)	2 (3.3%)	<0.001
MCA PI/RI	20 (33.3%)	1 (1.7%)	<0.001
CPR <1	26 (43.3%)	2 (3.3%)	<0.001

Table 8: Correlation Between Abnormal Doppler and Clinical Outcomes

Outcome	Abnormal Doppler (n = 40)	Normal Doppler (n = 80)	p-value
Intrauterine growth restriction	12 (30.0%)	2 (2.5%)	<0.001
Oligohydramnios	10 (25.0%)	4 (5.0%)	0.003
Preterm delivery (<37 weeks)	14 (35.0%)	6 (7.5%)	<0.001
Cesarean section	20 (50.0%)	18 (22.5%)	0.003

Table 9: Logistic Regression Analysis of Doppler Parameters as Predictors of Uteroplacental Insufficiency

Doppler Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Uterine artery notching	4.6	1.8 – 11.5	0.001
Umbilical artery PI >95th	3.9	1.5 – 10.2	0.004
MCA PI <5th percentile	5.2	1.9 – 13.7	0.001
CPR <1	7.8	2.6 – 23.4	<0.001

DISCUSSION

Our findings demonstrated significantly elevated uterine artery PI and RI, with a higher frequency of bilateral notching among high-risk pregnancies, reflecting impaired trophoblastic invasion and increased placental resistance. These results match the performed studies that noted similar relationships between abnormal Doppler indices of the uterine artery and adverse pregnancy events, mainly preeclampsia and FGR, according to the studies of Meler *et al*. [1] and Ashoor *et al*. [2]. Similar results were obtained by Karpagam *et al*. [3] and Liu *et al*. [4] and they stressed that the uterine artery patterns have prognostic importance in distinguishing placental insufficiency. Conversely, some meta-analyses have indicated that uterine artery Doppler alone presents limited predictive capability when used in isolation and argued that it is better combined with maternal risk factors or other Doppler parameters for enhanced performance, as is discussed by Heidweiller-Schreurs *et al*. [5]. Following the umbilical artery results in our study yielded higher PI and RI values, with absent or reversed end-diastolic flow in 10% of the cases-a situation consistent with severe fetoplacental compromise. Moraitis *et al*. [6] and Vannevel *et al*. [7] had also supported these findings by confirming the strong predictive value of abnormal umbilical artery indices for adverse perinatal outcomes. Moreover, Cochrane reviews have solidly established that using umbilical artery Doppler surveillance in pregnancies at risk lowers the rates of perinatal morbidity and mortality [8]. Thus, our data further conform with current international recommendations, including those by ISUOG and SMFM, which recommend umbilical artery Doppler as a first-line test for fetal surveillance in pregnancies at risk [9,10]. Concerning the meno cerebral artery, in our study, PI and RI were significantly lower and PSV was higher in the case group to full effect of brain sparing. Our results find harmony with those obtained by Chen *et al*. [11] and Paranavitana *et al*. [12], who stated that such reduced MCA impedance represents the fetal adaptive redistribution in chronic hypoxemia. Similar evidence was injected by Ochoa *et al*. [13], who corroborated the use of MCA Doppler for determining fetal hemodynamic adaptation in placental insufficiency. However, Sun *et al*. [14], questioned the value of the MCA Doppler indices in predicting long-term neurodevelopmental outcomes and stated that although these indices may well be used in predicting perinatal compromise, it remains uncertain whether their relevance still remains linked to long-term neurological sequelae. In our study, the CPR appeared to be significantly decreased in cases, with 43.3% of cases showing abnormal values. This finding reinforced the stand of CPR as a strong marker for adverse outcomes, a fact that finds parallelism in the systematic reviews of Novillo-Del Álamo *et al*. [15] and Dall'Asta *et al*. [16]. In the same vein, Bhardwaj *et al*. [17], found CPR to be a significant predictor of emergency cesarean and neonatal intensive care admission. Furthermore, however, some analyses, including the one by Heidweiller-Schreurs *et al*. [5], performed on aggregated individual participant data, show very limited added value of CPR above umbilical artery PI-an observation contrasting with our regression analyses where CPR was the strongest competitor. This difference could be attributed to different study designs, population risk profiles and CPR cut-off thresholds. The close associations in our study have been labeled Doppler abnormalities and clinical outcomes such as IUGR, oligohydramnios, preterm delivery and cesarean section by Chavan *et al*. [18], Kale *et al*. [19] and Buca *et al*. [20], all stress the importance of abnormal Doppler indices to adverse obstetric and neonatal outcomes. Our logistic regression further supports the CPR <1, MCA PI below the 5th percentile and uterine artery notching as the strongest independent variables-distinguishing uteroplacental insufficiency, as also highlighted by Raj *et al*. [21], Bunyan *et al*. [22] and Chen *et al*. [23]. Consistent with modern surveillance strategies, such as those developed in the TRUFFLE study, this ranking uses UA, MCA, CPR and ductus venosus Doppler to direct timing of delivery [24,25].

CONCLUSION

data This study demonstrated that Doppler ultrasound is one of the excellent tools that non-invasively evaluate uteroplacental insufficiency in high-risk pregnancies. Significantly elevated resistance indices of uterine and umbilical arteries, increased frequency of bilateral notching and abnormal cerebroplacental ratio were strongly related to clinical adverse outcomes like intrauterine growth restriction, oligohydramnios, preterm delivery and higher cesarean section rates. From among Doppler parameters, CPR <1 was found to be the best predictor of uteroplacental compromise. These findings recommend incorporating multiparametric Doppler evaluation combining uterine, umbilical and cerebral indices in routine surveillance of high-risk pregnancy for the betterment of perinatal outcomes.

Recommendations

Doppler ultrasound can be recommended for incorporation into the antenatal care of pregnant women at increased risk for placental dysfunction, given the present findings. Regular assessment of uterine artery and umbilical artery waveforms with MCA and CPR measurements enhances the early detection of fetal hemodynamic compromise and serves as a basis for determining the appropriate intervention to be taken. Evidence-based protocols should be implemented so that the use of Doppler is standardized for its application in high-risk pregnancy situations, such as those put forth by ISUOG, SMFM and RCOG. Further, radiologists and obstetricians need training in the appropriate acquisition and interpretation of Doppler to ensure the best diagnostic yield possible. A synthesis of Doppler findings with maternal risk factors and biochemical markers in the context of sound clinical judgment will provide the best predictive accuracy and pave the way for accurate and individualized management of pregnancies.

Limitations

This study is afflicted with certain limitations. The setting of the study in a single tertiary center in Kirkuk may

render the findings non-applicable in populations of different demography and healthcare settings. The sample size, relatively adequate for an initial assessment of pairwise comparison, is small enough not to elucidate the complete variability of Doppler indices with certain gestational ages and risk categories. Evaluation of long term neonatal outcomes, particularly neurodevelopmental follow-up, was not undertaken; thus, this study is limited in scope to perinatal end points. In addition, without a doubt, intra- and inter-observer variability is a limiting factor that could not be entirely abolished, although the Doppler measurements were standardized as much as possible. Future multicenter studies with larger cohorts, longitudinal follow-up and biomarker integration are necessary for the validation and further augmentation of these findings.

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