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Prediction of Pregnancy Outcome in Preeclampsia by Using Umbilical Artery and Middle Cerebral Artery Doppler Indices in Third Trimester

Ehab Kamel Esmail Soliman*, Ali Abdelghany Bendary, Khaled Mohamed Salama, Mohamed Abd Elsalam Mohamed

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Abstract

Background: Pre-eclampsia is associated with uteroplacental circulatory dysfunction, which may have a detrimental impact on foetal growth and oxygenation during pregnancy. the
59 utilisation of colour Doppler investigations is a non-invasive, routine technique for
1 haemodynamically evaluation of fetal well-being. The study was intended to investigate the value of middle cerebral artery (MCA) and umbilical artery (UA) Doppler indices in the assessment of foetal wellbeing and the prediction of neonatal outcome in expectant women with preeclampsia.

Methods: This prospective cohort study was carried out on 100 pregnant women with
34 preeclampsia at Benha University Hospitals. Participants were allocated into a good neonatal outcome group (n = 62) and a bad outcome group (n = 38) based on the presence of at least one adverse neonatal outcome. All participants underwent detailed clinical assessment, laboratory
15 investigations, and ultrasonographic evaluation including fetal biometry and Doppler studies
45 of UA and MCA, with assessment of RI, PI, and cerebroplacental ratio (CPR). Neonatal outcomes were assessed using Apgar scores, cord blood gas analysis, NICU admission, and predefined criteria for adverse outcomes including perinatal death and fetal distress.

Results: The comparison among groups showed insignificant differences in UA PSV and EDV, while UA resistance indices were significantly elevated in the adverse outcome group
22 RI, S/D ratio, PI ($p < 0.001$, = 0.002 and 0.001). MCA indices also differed significantly, with
22 lower RI and PI and elevated S/D ratio ($p < 0.001$) in the adverse outcome group. Overall, UA

and MCA Doppler indices established a significant predictive ability ($p < 0.001$), with UA PI showing the best overall accuracy and MCA PI exhibiting the highest diagnostic performance (AUC = 0.975).

Conclusions: UA and MCA Doppler indices are useful for evaluating fetal well-being and predicting neonatal findings in preeclampsia. Increased UA resistance and decreased MCA resistance are associated with adverse outcomes, with UA PI and MCA PI showing strong predictive value for risk stratification.

Keywords: Pregnancy, Preeclampsia, Middle Cerebral Artery, Doppler Indices, Umbilical Artery

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Introduction:

Hypertensive conditions of pregnancy are among the leading causes of maternal and perinatal disease burden and fatality; it affects up to 10% of pregnancies globally. Pre-eclampsia is one such condition [1].

Pre-eclampsia is associated with uteroplacental circulatory dysfunction, which may have a detrimental impact on foetal growth and oxygenation during pregnancy. the utilisation of colour Doppler investigations is a non-invasive, routine technique for haemodynamically evaluation of fetal well-being. In pregnancies at high risk, these vascular Doppler analyses are applied primarily during the decision-making process. While uterine artery Doppler is primarily used for pre-eclampsia screening, this assessment was incorporated to improve understanding of materno-placental circulation and to explore its association with adverse perinatal outcomes [2].

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The use of Doppler measurement of placental circulation is a critical screening component for deficient placentation and its related complications, such as intrauterine growth restriction (IUGR) and pre-eclampsia [3]. Management of foetal growth restriction. The umbilical artery (UA) and the middle cerebral artery (MCA) in conjunction the equilibrium among declining placental perfusion and foetal hypoxia is demonstrated by Doppler [4].

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The UA Doppler indices are more effective in predicting IUGR or a poor perinatal finding in pre-eclamptic cases. The MCA pulsatility index (PI) does not accurately indicate the pathological changes severity during early gestation, as it frequently paradoxically displays normal values in certain severe instances. Consequently, the cerebralumbilical ratio should offer a higher degree of diagnostic accuracy compared with either vascular Doppler index when employed independently [5].

The study was intended to investigate the efficacy of MCA and UA Doppler indices in the assessment of foetal health and the prediction of neonatal outcomes in expectant women with preeclampsia.

Patients and Methods:

This prospective cohort study was conducted on 100 pregnant women at the Department of Obstetrics and Gynecology, Benha University Hospitals.

The cases provided written consent that was informed. The investigation was conducted with the sanction of the Ethical Committee of Benha University Hospitals.

Participants were allocated into two groups regarding the incidence of adverse outcomes into: Good outcomes group: 62 pregnant females who didn't have any adverse outcomes after delivery and Bad outcomes group: 38 pregnant females who had at least one adverse outcome after delivery.

The inclusion criteria for this study were as follows: singleton pregnancies with a gestational age between 34 and 40 weeks that were diagnosed with preeclampsia according to the criteria of the International Society for the Study of Hypertension in Pregnancy. This is defined as new-onset hypertension after 20 weeks of gestation, with diastolic blood pressure ≥90 mmHg on at least two occasions 4 hours apart or ≥110 mmHg on a single reading, in addition to proteinuria ≥300 mg/24 hours or ≥2+ on dipstick testing from two separate urine samples collected at least 4 hours apart [6]. The study also encompassed pregnancies with suspected foetal growth restriction, which is presented as an estimated foetal weight that is below the 10th percentile for gestational age. This condition may be detected through ultrasonography or clinical examination.

Exclusion criteria comprised multiple pregnancies, congenital fetal anomalies, type 1 IUGR, maternal comorbidities as diabetes mellitus, renal or cardiac disease, history of rupture of membranes, as well as patient refusal or loss to follow-up.

All women underwent complete history taking, clinical assessment (general and obstetric), and laboratory tests.

At the time of delivery serial ultrasonographic biometry and Doppler velocimetry of the MCA and UA were conducted, as indicated by aberrant BPP (<6/10), cessation of foetal growth, gestational age ≥37 weeks, or worsening of maternal condition.

In a supine position with slight left lateral tilt ultrasonography was done using a transabdominal convex probe (3.5–7 MHz). Fetal biometry (BPD, HC, AC, FL) was obtained following standard protocol [7].

16 16 Doppler studies of the UA and MCA were conducted by color Doppler with an insonation angle close to 0° (not exceeding 60°) and a 4 mm sample volume. The MCA was assessed near 36 its origin with angle correction, while the UA was evaluated at the free loop of the cord. PI and RI were calculated over three cardiac cycles, and CPR was derived as MCA PI divided by UA PI [8].

Neonatal assessment included adverse outcomes defined as fetal distress, perinatal death, 42 meconium-stained amniotic fluid, 5-minute Apgar score <7, and NICU admission >24 hours. Umbilical cord blood gases were analyzed for pH, PaO_2, $PaCO_2$, base excess, and bicarbonate, 52 with fetal hypoxia and acidosis (pH <7.20) and base excess ≤ −12 mmol/L [9]. Apgar scores were recorded at 1 and 5 minutes based on standard criteria [10].

35 The primary outcome variables included MCA resistance index (RI) and peak systolic velocity (PSV), UARI and PI, and the MCA/UARI ratio. Additional neonatal outcome variables included cord blood gas parameters, specifically umbilical arterial pH, PaO_2, $PaCO_2$, base excess (BE), and bicarbonate (HCO_3^-), which were used as objective indicators of fetal acid–base status and hypoxia. Secondary outcomes included the 5-minute Apgar score, risk factors associated with IUGR and preeclampsia, cord blood pH and other cord blood gas parameters

and fetal hypoxia and metabolic acidosis and/or base excess were also considered as adverse neonatal outcomes.

Sample Size Calculation:

The sample size was assessed by G power software version 3.1.9.4 at Odds ratio 1.22, power 80% and α error .05. This yielded a total sample size of 100 women [11].

Statistical analysis

SPSS version 28 (IBM©, Armonk, NY, USA) was employed to evaluate the statistical analysis. The Shapiro–Wilk test and histograms were performed to assess the normality of the data distribution. The unpaired Student t-test was performed to compare the two groups, and the quantitative data were expressed as mean and standard deviation (SD). The standard deviation quantifies the range of values around the mean, whereas the mean denotes the average of observations. The Chi-square test or Fisher's exact test was employed to analyse qualitative variables, which were presented as frequencies and percentages, as appropriate. The Chi-square test was employed to compare categorical variables among groups, while Fisher's exact test was implemented when sample sizes were diminutive. Statistical significance was defined as P value < 0.05.

Results:

The baseline characteristics of the cohort participants are illustrated in Table 1.

Table 1: Baseline characteristics of the study participants

		N =100
Age (year)		35.4 ± 4.1
BMI (kg/m^2)		32.2 ± 5.8
Residence	**Urban**	38 (38%)
	Rural	62 (62%)
Parity		3 (2 - 4)
Abortion		1 (0 - 1)

Data reported as mean ± SD, median (interquartile range, IQR), BMI: Body mass index.

The UA and MCA Doppler indices among the studied preeclamptic pregnancies showed variability in both umbilical and fetal cerebral vascular impedance, with mean UA PSV and

EDV of 96.6 ± 10.2 cm/s and 26.7 ± 2.5 cm/s, and corresponding RI, S/D ratio, and PI of 0.74 ± 0.12, 3.03 ± 0.44, and 1.25 ± 0.32; MCA indices were 0.80 ± 0.27 for RI, 3.45 ± 0.35 for S/D ratio, and 1.22 ± 0.27 for PI. Neonatal outcomes exhibited a mean birth weight of 2.86 ± 0.54 kg and a mean 5-minute Apgar score of 7.2 ± 1.7, with adverse outcomes occurring in 38% of cases, most commonly NICU admission >24 hours, followed by low Apgar score and low birth weight, indicating a considerable burden of neonatal morbidity. **Table 2**

Table 2: UA Doppler and MCA indices in the participants

		n =100
PSV (cm/s)		96.6 ± 10.2
EDV (cm/s)		26.7 ± 2.5
RI		0.74 ± 0.12
S/D ratio		3.03 ± 0.44
PI		1.25 ± 0.32
RI		0.8 ± 0.27
S/D ratio		3.45 ± 0.35
PI		1.22 ± 0.27
Neonatal outcomes		
Birth weight (kg)		2.86 ± 0.54
5 min Apgar score		7.2 ± 1.7
Adverse outcome		38 (38%)
Types of adverse outcomes	**NICU admission for > 24hrs**	28 (28%)
	5 min Apgar score <7	20 (20%)
	Low birth weight	16 (16%)
	Neonatal death	5 (5%)

Data reported as mean ± SD. EDV: End-diastolic velocity, PSV: Peak systolic velocity, S/D: systolic/diastolic, PI: Pulsatility index, RI: Resistance index, NICU: Neonatal intensive care unit.

The comparison between good and adverse neonatal outcome groups demonstrated insignificant differences in UA PSV (p = 0.324) and EDV (p = 0.670). However, UA RI were significantly elevated in the adverse outcome cases, including RI (p < 0.001), S/D ratio (p = 0.002), and PI (p < 0.001), indicating increased placental resistance. In contrast, MCA Doppler indices demonstrated significant differences, with lower RI (p = 0.001) and PI (p < 0.001), and an elevated S/D ratio (p < 0.001) in the adverse outcome group, reflecting reduced cerebral vascular resistance. **Table 3**

Table 3: UA and MCA indices in the studied populations

	Good outcomes group (n =62)	Bad outcomes group (n =38)	P value
PSV (cm/s)	97.42 ± 8.56	95.16 ± 12.32	0.324
EDV (cm/s)	26.6 ± 2.39	26.82 ± 2.64	0.670
RI	0.7 ± 0.14	0.8 ± 0.05	**<0.001***
S/D ratio	2.93 ± 0.51	3.18 ± 0.26	**0.002***
PI	1.1 ± 0.2	1.5 ± 0.33	**<0.001***
RI	0.86 ± 0.3	0.71 ± 0.16	**0001***
S/D ratio	3.29 ± 0.33	3.7 ± 0.22	**<0.001***
PI	1.39 ± 0.18	0.94 ± 0.1	**<0.001***

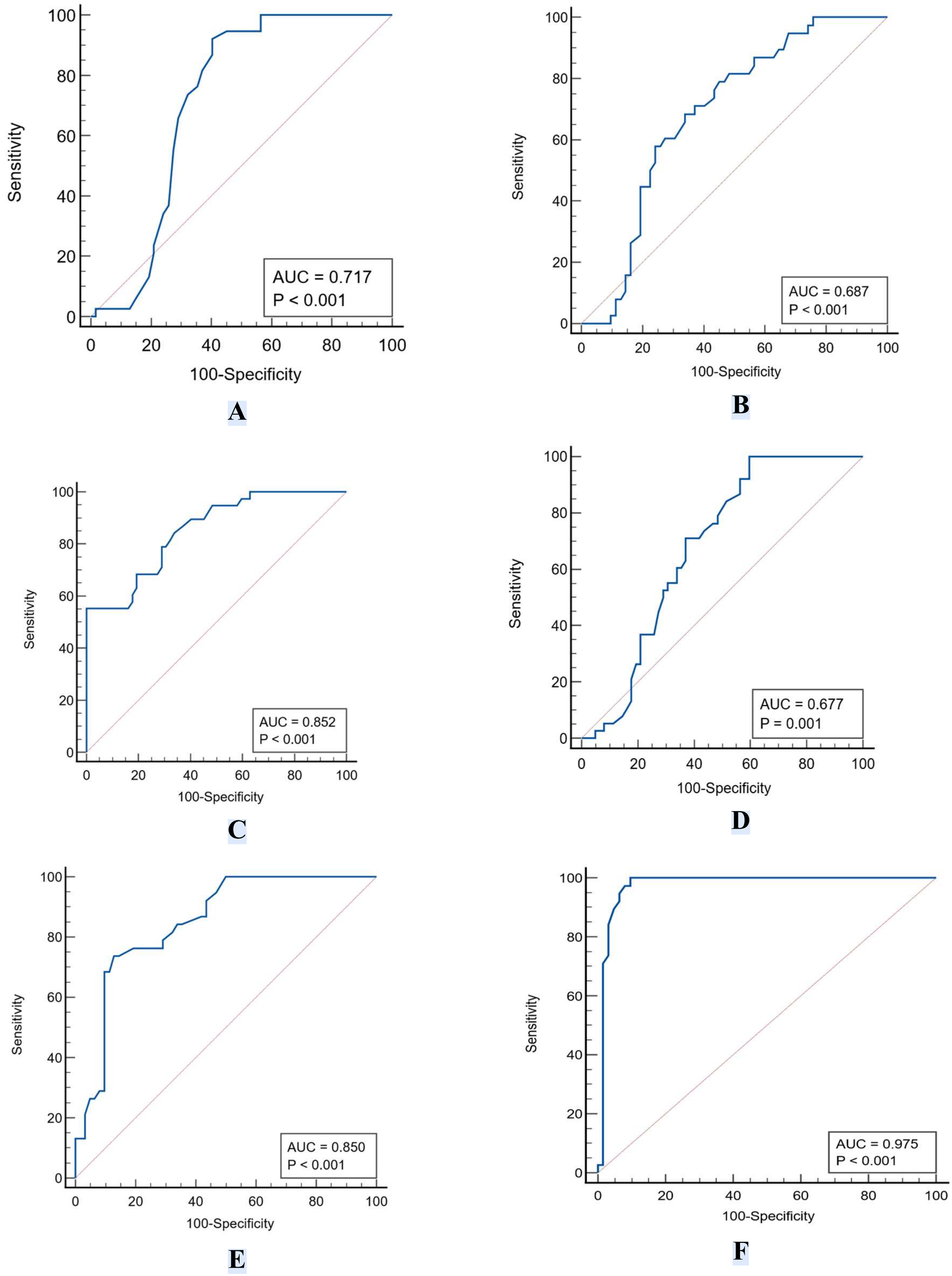
Data reported as mean ± SD. S/D: systolic/diastolic, PI: Pulsatility index, PSV: Peak systolic velocity, EDV: End-diastolic velocity, RI: Resistance index, *Statistically significant as p value <0.05.

The diagnostic performance of UA and MCA Doppler indices demonstrates statistically significant ability to predict adverse neonatal outcomes. Among UA parameters, RI showed the highest sensitivity (92.1%) and NPV (92.5%), while PI demonstrated the best overall accuracy (AUC = 0.852) compared to S/D ratio and RI. For MCA indices, PI exhibited the strongest predictive value with the highest sensitivity (92.1%), specificity (93.6%), and AUC (0.975), followed by S/D ratio. Overall, MCA PI showed superior diagnostic performance compared to other indices, indicating its strong predictive value for adverse neonatal outcomes in preeclamptic pregnancies. **Table 4**

Table 4: Receiver operator characteristic curve analysis of the ability of UA Doppler and MCA Doppler indices to predict bad pregnancy outcomes in pregnant women with preeclampsia in third trimester

	UA RI	UA S/D ratio	UA PI
Cut-off value	>0.73	>3.09	>1.19
Sensetivity	92.1%	68.4%	78.9%
Specificity	59.7%	66.1%	70.9%
PPV	58.3%	55.3%	62.5%
NPV	92.5%	77.4%	84.6%
AUC	0.717	0.687	0.852
P value	**<0.001***	**<0.001***	**<0.001***
	MCA RI	**MCA S/D ratio**	**MCA PI**
Cut-off value	≤0.8	>3.57	≤1.09
Sensetivity	71.1%	73.7%	92.1%
Specificity	62.9%	87.1%	93.6%
PPV	54%	77.8%	90%
NPV	78%	84.4%	96.7%
AUC	0.677	0.850	0.975
P value	**0.001***	**<0.001***	**<0.001***

39 UA: Umbilical Artery; RI: Resistive Index; S/D ratio: Systolic/Diastolic ratio; PI: Pulsatility Index; PPV: Positive
31 Predictive Value; MCA: Middle Cerebral Artery; NPV: Negative Predictive Value; AUC: Area Under the Curve.
*Statistically significant.

26 

3 **Figure 1: ROC curve analysis of the ability of (A) UA RI, (B) UA S/D ratio, (C) UA PI, (D) MCA RI, (E) MCA S/D ratio, and (F) MCA PI to predict bad pregnancy outcomes in third trimester women with preeclampsia.**

Discussion

Preeclampsia is a severe global health issue that results in maternal and adverse fetal outcomes, affecting 2% to 8% of pregnancies [12].

In the present study, we found that UA Doppler indices between women with good neonatal outcomes and those with at least one adverse neonatal outcome. PSV and EDV did not differ significantly among the two groups. In contrast, indices reflecting downstream placental resistance were worse in the adverse outcome group. UA RI was elevated in the bad outcome cases compared with the good outcome cases, with a marked significant difference ($p<0.001$). Similarly, the S/D ratio was elevated among cases with adverse outcomes ($p=0.002$), and the PI was also significantly elevated ($p<0.001$).

These observations align with prior evidence that elevated UA resistance indices correlate with compromised fetoplacental circulation and adverse perinatal findings associated with hypertensive disorders. Studies have demonstrated that abnormal UA PI, RI, and S/D ratio are significantly related to poor fetal outcomes, as low Apgar scores, reduced birth weight, and elevated want for NICU, supporting the relevance of UA Doppler assessment in risk stratification of high-risk pregnancies. UA RI and UA PI were significantly related to adverse findings as low Apgar scores and low birth weight, with RI cut-offs showing high sensitivity and specificity, though exact thresholds varied by study design [13].

Adedo et al.[13] highlighted that in terms of RI, the study group had an elevated mean of 0.74 ± 0.17 with a range of 0.5–1.26, comparing with the controls, which had a mean of 0.68 ± 0.11 and a range of 0.4–0.8, with a substantial difference ($p < 0.001$). For PI, the study cases also had an elevated mean of 1.27 ± 0.64 (range 0.7–4.7), compared to 1.02 ± 0.29 (range 0.5–1.5) in controls ($p <0.001$). The S/D was raised in the study cases (3.49 ± 1.08, range 2.66–4.88) compared to the control group (3.11 ± 0.71, range 2.30–3.4), with a substantial variation ($p < 0.001$).

We observed that adverse outcome group demonstrated a significantly lower MCA RI compared with the good outcome cases (p=0.001), indicating reduced cerebral vascular resistance in fetuses with poor outcomes. In addition, the MCA S/D was elevated in the adverse cases in comparison to the good outcome cases (p<0.001). The MCA PI was also significantly decreased among cases with adverse outcomes (0.94 ± 0.10 vs 1.39 ± 0.18; p<0.001).

Adedo et al. [13] demonstrated that foetuses with aberrant UADI had an elevated incidence of
55 preterm deliveries at <37 weeks of gestation, a higher rate of neonatal admission, and a lower APGAR score comparing with controls. Additionally, it was observed that AEDF and REDF led to perinatal mortality, whereas decreased diastolic flow did not, but it was associated with a reduced APGAR score and reduced birth weight. Suggesting that the severity of uteroplacental insufficiency is a determining factor in the perinatal outcomes in pregnancies complicated by FGR. AEDF/REDF are associated with more severe adverse outcomes than decreased diastolic flow.

Eight participants of AEDF and two participants of REDF were reported by Afroze and Begum [14] 3/8 of AEDF infants perished of IUFD, two of them of neonatal death, and 3 survived. One of the REDF neonates was stillborn, while the other passed away on the seventh day of life. Netam *et al.* [15] found a total mortality for foetuses with AEDF or REDF. Madazli *et al.* [17] reported a perinatal death rate of 40%, although Brodszki *et al.* [18] documented 59% perinatal death in 44 foetuses with REDF.

We found that at a cut-off value of >0.73, UA RI showed the highest sensitivity (92.1%) and a high NPV (92.5%), indicating strong ability to rule out adverse outcomes when the test is negative; however, its specificity was modest (59.7%), reflecting a relatively higher false-positive rate. At a cut-off of >3.09, the UA S/D ratio demonstrated moderate
48 discriminative ability with sensitivity of 68.4% and specificity of 66.1%, along with lower predictive values (PPV 55.3%, NPV 77.4%). At a cut-off >1.19, UA PI achieved the best

overall diagnostic performance, with the highest AUC=0.852, and a more balanced sensitivity (78.9%) and specificity (70.9%).

Similarly, other cohorts focused on preeclamptic or growth-restricted pregnancies found that abnormal UA Doppler indices were related to adverse neonatal outcomes, as well as reduced birth weight and NICU admission, affirming the correlation among elevated UA impedance and perinatal complications [19].

In the present study, we found that all MCA Doppler indices were statistically significant predictors of adverse pregnancy findings in preeclamptic women in the third trimester (p <0.001). MCA PI showed the strongest diagnostic performance: at a cut-off value of ≤1.09, it achieved the highest sensitivity (92.1%) and specificity (93.6%), with excellent predictive values (PPV 90% and NPV 96.7%) and an AUC of 0.975. MCA S/D ratio also demonstrated good predictive ability, with a cut-off of >3.57 yielding sensitivity of 73.7% and high specificity of 87.1% (AUC=0.850), suggesting that an elevated S/D ratio is a fairly reliable marker of adverse outcome. In comparison, at a cut-off of ≤0.8, MCA RI had a moderate sensitivity (71.1%) and specificity (62.9%) (AUC=0.677).

These results align well with trends reported previously in the obstetric Doppler literature, though there are nuances in cut-offs and performance metrics. For example, Lin et al. [20] found that MCA RI exhibited reasonable predictive value for fetal compromise, reporting sensitivities and specificities in comparable ranges, though not as high as MCA PI in your cohort, supporting the notion that MCA PI is often more reliable than RI alone for adverse outcome prediction.

Orabona et al. [21] documented that 46.4% of patients experience adverse perinatal outcomes.
12 The MCA PI/UmA PI and MCA PI/Uterine A PI ratio was both more valid, in terms of an
30 unfavourable perinatal outcome, than each of their components individually.

Morris et al. [22] conducted a 35 studies to predict foetal well-being using MCA Doppler. MCA Doppler had likelihood ratio for a positive test result of 2.77 and 1.36 for predicting adverse perinatal outcomes and perinatal mortality, and negative likelihood ratios of 0.58 and 0.51 for predicting perinatal mortality.

Another body of work shows that cerebral blood flow changes, particularly reduced resistance and PI in the MCA, reflect *'brain-sparing'* responses to hypoxia and placental insufficiency. Belfort demonstrated that lower MCA RI and PI are predictive of compromise in cases who develop preeclampsia, reinforcing your finding that fetuses with adverse outcomes had lower resistance indices consistent with altered cerebral hemodynamics [23].

While some older studies suggest MCA PI alone may be less reliable than combined ratios (such as CPR or MCA/UA ratio) for adverse outcome prediction, our results strongly support MCA PI as a standalone marker with robust predictive ability. For example, Ozeren et al. [24] found the highest predictive accuracy for composite ratios rather than MCA PI alone, highlighting variability across settings and echoing the importance of context in interpreting Doppler performance.

Although some studies have reported variability in the predictive value of individual MCA measures, the overarching consensus is that abnormal MCA Doppler parameters, particularly in combination with other indices such as the CPR, correlate with adverse perinatal results in preeclamptic and growth-restricted pregnancies [25].

Contrasting findings do exist in the literature. Some studies have reported that umbilical artery Doppler findings may outperform MCA indices in certain populations. For example, earlier work suggested that umbilical artery Doppler parameters, particularly when used in combination with maternal and fetal clinical data, may be slightly better predictors of adverse perinatal outcomes than isolated MCA measures [11].

The current research has determined that the UAD S/D is the highly sensitive recorded 62.0% among the three indices in predicting low birth weight. However, this finding is inconsistent with Adedo et al [13] which documented that the UAD PI is more sensitive comparing with the RI and S/D ratio. This discrepancy may be attributable to the population's disparities, as this index study exclusively includes preeclamptic cases.

Irowa O, 2023 [26] showed that Both PI and RI show similar sensitivity (74.2%) for predicting preterm delivery, with RI demonstrating a higher specificity of 57.4% compared to PI's 50.7%.
4 The S/D ratio, however, has the maximum specificity (68.5%) and 52.1% as PPV. Among the indices, RI also shows the highest NPV of 79.5%, indicating its better ability to predict the absence of preterm delivery. The UA PI emerges as the most sensitive index for expecting a low Apgar score, with a sensitivity of 80%. On the other hand, the S/D ratio has the greatest PPV (38.0%) and specificity (66.2%). The PI once again outperforms the other indices in terms of PPV, with an impressive value of 88.7%. This suggests that PI is a more accurate predictor of adverse neonatal outcomes, while the S/D ratio provides better specificity, especially in
4 excluding non-adverse outcomes. In addition, comparing the UA PI, RI, and S/D ratio as a marker for low birth weight. RI had the highest specificity (74.4%) among the three indices, while the more sensitive (62.0%) was S/D ratio. The UA PI and S/D ratio have the largest NPV (72.9%), and PPV (73.2%).

The findings of this analysis are similar to Chanprapaph *et al.* [27] (66.7%, 78.85%, 74.42%, and 68.02%) and Gyawali *et al.* [28] (76%, 76.9%, 79.2%, and 73.5%, in the same order). Fleischer *et al.* [29] found that a S/D ratio of over 3 in predicting FGR had a sensitivity of 78%, which is similar to the sensitivity of 75% for S/D ratios of over 3.11.

Limitations included limited sample size and single-center design. Its cross-sectional design precludes long-term follow-up and assessment of temporal relationships. In addition, potential confounding factors such as maternal comorbidities, lifestyle, and genetic influences were not fully addressed.

Conclusions:

58 Doppler indices of the UA and MCA are useful for assessing fetal wellbeing and predicting neonatal outcomes in preeclampsia. Increased UA resistance and decreased MCA resistance are associated with adverse outcomes, with UA PI and MCA PI showing strong predictive value for risk stratification.

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