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Original Research Article

Doppler Indices of the Fetal Middle Cerebral and the Umbilical Arteries in Pregnancies at High Risk Followed Up for Suspected Fetal Growth Restriction

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ABSTRACT

Background: Fetal growth restriction is related to compromised perinatal outcomes. The screening and prevention tools for fetal growth restriction like Doppler indices in high-risk groups compared with general antenatal populations. An evaluation of the correlation between Doppler indices and placental weight and birth weight of the neonate at term pregnancy in high-risk pregnancies is essential. For the early detection of fetal growth limitations in high-risk pregnancies, sensitive screening techniques are few.

Objectives: To determine the most accurate indicator for predicting a poor perinatal outcome or intrauterine growth restriction by comparing and correlating the modifications in Doppler ultrasound studies of fetal circulation in general pregnant women with those of high-risk patients both with and without intrauterine growth retardation.

Study design: A cross-sectional research including 81 healthy pregnancies and 19 high-risk patients at 31–40 weeks of gestation was conducted. The pulsatility index (PI) of the middle cerebral artery (MCA), the umbilical artery (UA), and the MCA PI to UA PI ratio were all analyzed. We compared the Doppler indices' mean values. Then these values were correlated with placental weight and birth weight of the offspring.

Results: A significantly low birth weight and less fetoplacental ratio and placental coefficient ratio were found in high-risk cases than in normal pregnant women ($P<0.05$). A strong positive relationship was observed between the middle cerebral artery pulsatility index and placental weight, while negative relationship between the pulsatility index of the middle cerebral artery and the Feto-placental ratio ($P < 0.05$). In addition, a positive association was found between the pulsatility index of the middle cerebral artery and placental coefficient, whereas a negative correlation was observed between the Cerebro-placental ratio and Feto-placental ratio in high-risk cases ($P <0.05$).

Conclusion: Low birth weight can be predicted using Doppler indices since there is a definite correlation between it and unfavorable perinatal outcomes.

KEY WORDS: Placenta, birth weight, Doppler indices, Middle cerebral artery pulsatility index, Umbilical artery pulsatility index

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INTRODUCTION

Higher animals are distinguished by their fetomaternal organ placenta. In humans, it is a thick mass that is about 18cm in diameter. The umbilical cord joins the fetus to the placenta, which is joined to the uterine endometrium. The nutritional, respiratory, endocrine, excretory, and immune systems are all controlled by the human placenta, which also serves as the functional hub of the maternal-fetal system. The advantages of the placenta's anatomical study have long been stressed by researchers. Numerous research on the placenta's morphology are presented in the literature [1,2]. The umbilical cord serves as a link between the fetus and the placental chorionic plate. While allowing for the fetal movement required for fetal growth, the umbilical cord offers a solid link to the fetomaternal interface. The growth and function of the placenta or the umbilical cord may be faulty, which might lead to several pregnancy issues [3].

An established technique for prenatal surveillance is the doppler ultrasonography velocimetry of fetal and uterine vasculature. Unfavorable prenatal outcomes can be predicted using certain Doppler waveforms suggesting circulatory alterations [4].

In obstetric imaging and fetal monitoring, Doppler ultrasonography was effectively introduced in 1977 [5]. The umbilical cord blood flow pattern was initially observed noninvasively by Fitzgerald et al., who also hypothesized that fetuses with intrauterine growth limitations may have aberrant umbilical artery waveforms (IUGR) [6]. Numerous significant clinical applications were also produced as a result of this ground-breaking waveform analysis idea. Doppler examination of the umbilical artery is now considered standard practice for prenatal monitoring [7].

Moreover, a doppler scan of the fetal middle cerebral artery was widely used to detect prenatal anemia [8]. Doppler ultrasonography waveforms not only show blood flow velocity but also information on the presence and direction of flow, velocity profile, flow volume, and impedance [9].

Pulsatility index (PI) = Peak systolic velocity - End diastolic velocity/ Time-averaged maximum velocity

The umbilical artery and middle cerebral artery are reportedly the most reproducible and accessible of all the arteries investigated in Doppler ultrasonography. For the assessment of placental impairment and fetal anemia, the middle cerebral artery of fetuses had been thoroughly examined [10].

The cerebro-placental ratio (CP ratio), also known as the ratio of the pulsatility indices of the middle cerebral artery and the umbilical artery, is a valuable tool for tracking fetal health. In comparison to the middle cerebral artery or umbilical artery Doppler indices alone, a low CP ratio suggests relative redistribution of blood flow to the cerebral circulation and is believed to boost accuracy in anticipating difficulties and unfavorable outcomes [11]. By repeating the Doppler examinations at regular intervals, this ratio is currently being employed more often in the monitoring of the fetus at risk. Although there are reference ranges for these Doppler indices in the literature from the West, there are few similar investigations in the Indian population [12,13]. The pulsatility index (PI) measures peripheral resistance of the blood vessels. Greater PI may signal increased resistance in the blood vessel's distal section, which indicates hypoperfusion in the region [14].

It is well established that placental malfunction is linked to fetal growth restriction (FGR), a disease in which the fetus is unable to reach its genetic development potential. To make up for less than ideal performance, the placenta in fetal growth restriction may show decreased nutrition transfer capability [15]. Fetuses with birth weights below the 10th centile are now classified as either fundamentally undersized or having growth restrictions. Although their weight is above the 10th percentile, fetuses with estimated fetal weights (EFW) or birth weights might still have development restrictions because of malnutrition. Although correctly identifying these fetuses as having fetal growth restriction is difficult, it is crucial since this “hidden” fetal growth restriction is linked to a higher risk of newborn morbidity and death [16]. In this study intended to evaluate the association between Doppler indices, and both placental and neonatal birth weight in high-risk pregnant women at term pregnancy.

MATERIALS AND METHODS

Ethical approval: The SVS Medical College in Mahabubnagar, India, granted the institutional ethics committee permission for the study (reference number: SVSMC/Ethical Committee/Acad./2021-256). As per World Health Organization (WHO) guidelines, each participant signed a written waiver of informed consent.

Study design: Prospective cohort research was conducted between October 20, 2021, and June 2, 2022, at the Department of Anatomy, Radiodiagnosis, Obstetrics and Gynecology, and Pediatrics at a teaching and tertiary care hospital. Sequential research ultrasound scans were performed on the study participants' bodies at various stages of pregnancy. All ultrasound/Doppler tests were carried out in accordance with the approved Pre Conception and Pre- Natal Diagnostic Technique criteria. The reports of the scans were blinded to both subjects and the investigator. Following the delivery, reports of the research scans were revealed. The study population contains all antenatal cases attended during the study period at the Obstetrics and Gynecology and Radiodiagnosis departments of the tertiary care and teaching hospital. Out of 100 recruited pregnant cases, 81 were from the general population and 19 were high-risk patients.

Study group: Among the participants of the high-risk pregnancies, the inclusion criteria for this study were women who appeared in all intended antenatal research scans and delivered a live-born offspring after 36 weeks of gestation where both the birth weight and placental weight had been recorded. Women who dropped out were unreachable or had fetal defects identified before recruiting were not included.

Conduct of study: The study comprised all consecutive study participants fulfilling the inclusion requirements. A duplex Doppler ultrasound machine, the LOGIQ P5 unit, with a curvilinear low-frequency transducer, was used to take measurements. Frequency, spectral frequency, sample volume, filter medium, and PRF-4-5MH were among the different technical characteristics (Figure 1) [9].

Measurements of MCA PI and RI, UA PI, and CP ratio: After the results of the biometry were verified, all patients were examined using a 3.5-MHz curvilinear transducer for duplex Doppler. Over the course of three successive cardiac cycles, doppler waveforms from the fetal MCA and UA were captured. The patients were assessed while lying semi-recumbent, with the fetus dozing and apneic. Using a medium filter and a sample volume of 4 mm, spectral waveforms were produced [9].

Pulsatility index of middle cerebral artery: Each time, the color Doppler was used to locate the middle cerebral artery, which is closer to the probe. With a sample volume of 4 mm, a spectral trace was acquired from the MCA shortly following its inception. Each time, the angle of insonation was checked to make sure it was between 0 and 60 Ú. Over three consecutive cardiac cycles, PI was assessed manually and automatically. The measurements were repeated, and two readings that came back with identical findings were logged for the research [9].

Pulsatility index Umbilical artery: Color Doppler was used in each case to locate the umbilical artery. A spectral trace was produced from the free loop of the UC using a sample volume of 4 mm. The placental implantation of the chord was traced in case it was impossible to localize the free loop of the UC. The angle of insonation was held constant at 0 to 60 Ú. Over three successive cardiac cycles, the pulsatility index was calculated manually and automatically. The measurements were performed again, and the study's last two readings that produced identical results were documented [9].

Pulsatility index of the middle cerebral artery (MCA PI) / Pulsatility index of umbilical artery (UA PI) ratio: After making sure that the examination and measurements were technically accurate, the Cerebro-placental ratio—a calculation that compares the MCA PI to the

UA PI—was made in each case and recorded.

Follow-up studies: In addition to obtaining measurements of the MCA PI and RI, UA PI and RI, and CP ratio, the delivered live-born child's birth weight, and placental weight (Figure 2) were also noted. Data was concurrently input into correctly configured Microsoft Excel spreadsheets.

Statistical analysis: The SPSS software, version 21, was used to conduct the statistical analyses. Quantitative data with a normal distribution were represented using the mean ± SD (standard deviation). The Student's t-test was used for statistical comparisons between two groups, and Spearman ranks correlation of coefficients was computed to determine the relationship between Doppler indices and both birth weight and placental weight. In terms of statistics, a value of $P < 0.05$ was regarded as significant.

RESULTS

The placental weight in control and the high-risk case did not show any significant difference ((t = 0.55689, p=0.289423) (Figure 3A), but the fetal birth weight showed statistically significant (t = 4.0901, p=0.000044) difference between control and high-risk case (Figure 3B). The fetoplacental ratio was significantly less in high-risk cases than the normal pregnant women (t=1.69634, p=0.046466) than the normal pregnant women (Figure 3C). The placental coefficient ratio also exhibited considerable deference between normal pregnant women and high-risk cases; it was statistically lower (t = 2.95374, p=0.001957) in the high-risk case than that of control (Figure 3D).

Middle cerebral artery pulsatility index, pulsatility index of the umbilical artery and Cerebro placental ratio (t=1.16541, p=.123312, t=1.31359, p=095995, t=0.5405, p=0.295028 respectively) was not showing any significant difference amongst the control and high-risk cases (Figure 4).

Correlation between Middle cerebral artery pulsatility index and fetal and placental morphometry in high-risk cases: Results of the pearson correlation indicated that there is a significant large positive relationship between Middle cerebral artery pulsatility index and Placental weigh, ($r(16) = 0.504$, $p = 0.033$) (Figure 5A), whereas there is a non-significant very small negative relationship between Middle cerebral artery pulsatility index and Fetal birth weight, ($r(16) = 0.232$, $p = 0.355$) (Figure 5B). The correlation between Middle cerebral artery pulsatility index and Feto- placental ratio exhibited a significant very small negative relationship, ($r(16) = 0.561$, $p = 0.015$) (Figure 5C). This study result indicated that there is a significant large positive relationship between Middle cerebral artery pulsatility index and placental coefficient ($r(16) = 0.69$, $p = 0.002$) (Figure 5D).

Correlation between Umbilical artery pulsatility index and fetal and placental morphometry in high-risk cases: The results of the Pearson correlation indicated that there is a non-significant small positive relationship between Umbilical artery pulsatility index and Placental weight, ($r(16) = 0.176$, $p = 0.484$) (Figure 6A), and the relationship between umbilical artery pulsatility index and fetal birth weight showed a very small positive relationship but statistically not significant ($r(16) = 0.0777$, $p = 0.759$) (Figure 6B). There was a non-significant small positive relationship between Umbilical artery pulsatility index and Feto-placental ratio, ($r(16) = 0.0149$, $p = 0.953$) (Figure 6C), and between Umbilical artery pulsatility index and Placental coefficient, ($r(16) = 0.212$, $p = 0.398$) (Figure 6D).

Correlation between Cerebro-placental ratio and fetal and placental morphometry in high-risk cases: The Pearson correlation advocated that there is a non-significant small positive relationship between Cerebro-placental ratio and Placental weight, ($r(16) = 0.245$, $p = 0.328$) (Figure 7A), and between Cerebro-placental ratio and Fetal birth weight, ($r(16) = 0.302$, $p = 0.223$) (Figure 7B). The relationship between Cerebro-placental ratio and Feto-placental ratio was negative and it was statistically significant ($r(16) = 0.501$, $p = 0.034$) (Figure 7C), but the correlation between Cerebro-placental ratio and Placental coefficient was positive but statistically insignificant ($r(16) = 0.384$, $p = 0.116$) (Figure 7D).

Association between pulsatility index of the MCA and placental and fetal birth weight in control: The correlation between the pulsatility index of the middle cerebral artery and Placental weight showed a very small negative relationship and it was statistically significant ($r(82) = 0.215$, $p = 0.049$). But that there was a non-significant very small negative relationship between Middle cerebral artery pulsatility index and Fetal birth weight, ($r(82) = .159$, $p = .147$). Results of the Pearson correlation indicated that there is a non- significant very small positive relationship between Middle cerebral artery pulsatility index and Feto-placental ratio, ($r(82) = 0.0493$, $p = 0.656$), whereas there was negative correlation between Middle cerebral artery pulsatility index and Placental coefficient but statistically insignificant ($r(82) = 0.0427$, $p = 0.700$) (Table 1).

Correlation between Umbilical artery pulsatility index and fetal and placental morphometry in control: Results of the Pearson correlation indicated that there is a non-significant very small negative relationship between Umbilical artery pulsatility indext and Placental weight, ($r(82) = 0.139$, $p = 0.208$), between Umbilical artery pulsatility indext and Fetal birth weight , ($r(82) = 0.123$, $p = 0.267$), and between Umbilical artery pulsatility indext and Placental coefficient , ($r(82) = 0.00533$, $p = 0.962$). But there was a non-significant very small positive relationship between umbilical artery pulsatility and Foeto-placental ratio, ($r(82) = 0.00536$, $p = 0.961$) (Table 1).

Correlation between Cerebro-placental ratio and fetal and placental morphometry in high-risk cases: The results of the Pearson correlation indicated that there is a non-significant very small negative relationship between Cerebro-placental ratio pulsatility and Placental weight, ($r(82) = 0.0944$, $p = 0.393$), between Cerebro-placental ratio pulsatility and Fetal birth weight, ($r(82) = 0.0306$, $p = 0.782$) and between Cerebro-placental ratio pulsatility and Placental coefficient, ($r(82) = 0.0638$, $p = 0.564$). While correlation between Cerebro-placental ratio pulsatility and Feto – placental ratio was positive but statistically non-significant ($r(82) = 0.0735$, $p = 0.506$) (Table 1).

Table 1: Correlation between Doppler indices fetal and placental parameters in normal pregnant women.

Correlation between	r-value	p-value
Middle cerebral artery pulsatility index and placental weight	0.215	**0.049***
Middle cerebral artery pulsatility index and fetal birth weight	0.159	0.147
Middle cerebral artery pulsatility index and fetoplacental ratio	0.0493	0.656
Middle cerebral artery pulsatility index and placental coefficient	0.0427	0.7
Umbilical artery pulsatility index and placental weight	0.139	0.208
Umbilical artery pulsatility index and fetal birth weight	0.123	0.267
Umbilical artery pulsatility index and fetoplacental ratio	0.00536	0.961
Umbilical artery pulsatility index and placental coefficient	0.00533	0.962
Cerebro-placental ratio pulsatility and placental weight	0.0944	0.393
Cerebro-placental ratio pulsatility and fetal birth weight	0.0306	0.782
Cerebro-placental ratio pulsatility and fetoplacental ratio	0.0735	0.506
Cerebro-placental ratio pulsatility and placental coefficient	0.0638	0.564

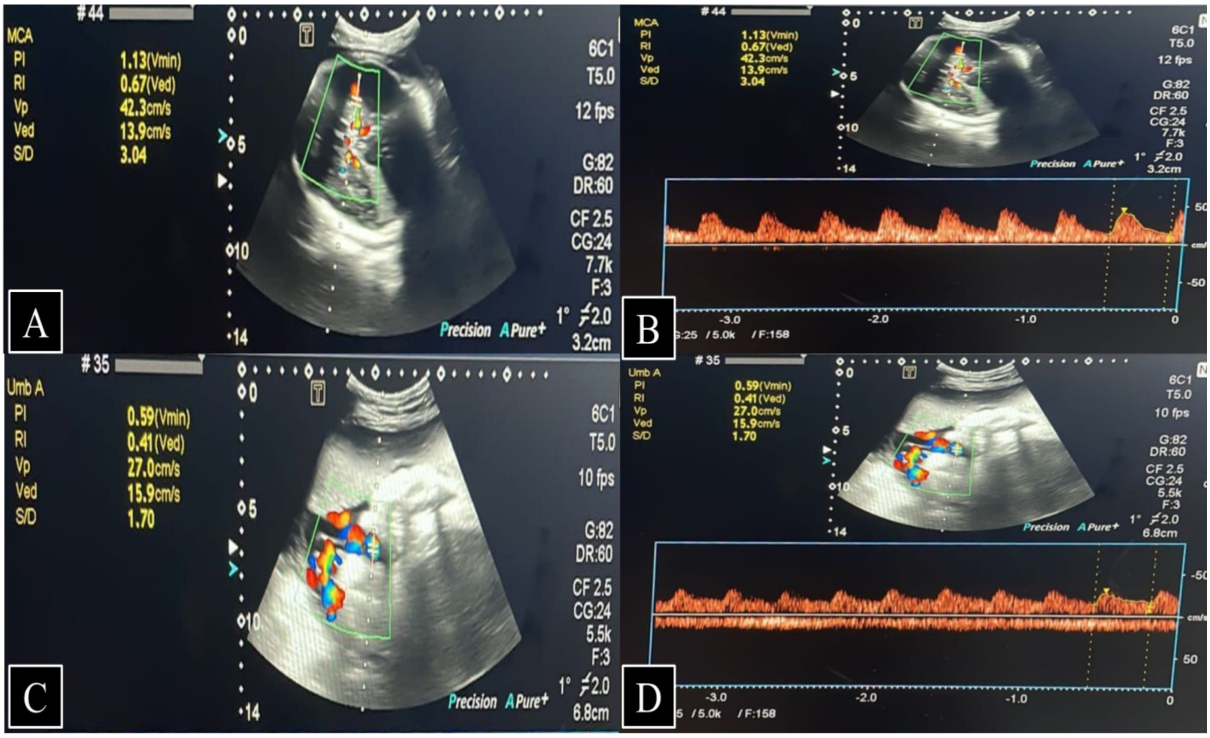

Fig. 1: Representative scan copies of Doppler velocimetry procedures for the middle cerebral artery and Umbilical artery. (a) Identification of middle cerebral artery, (b) correction of beam angle and calculation of middle cerebral artery Doppler indices by auto method, (c) identification of free-floating segment of the umbilical cord, (d) correction of beam angle and calculation of Umbilical artery Doppler indices by the auto method.

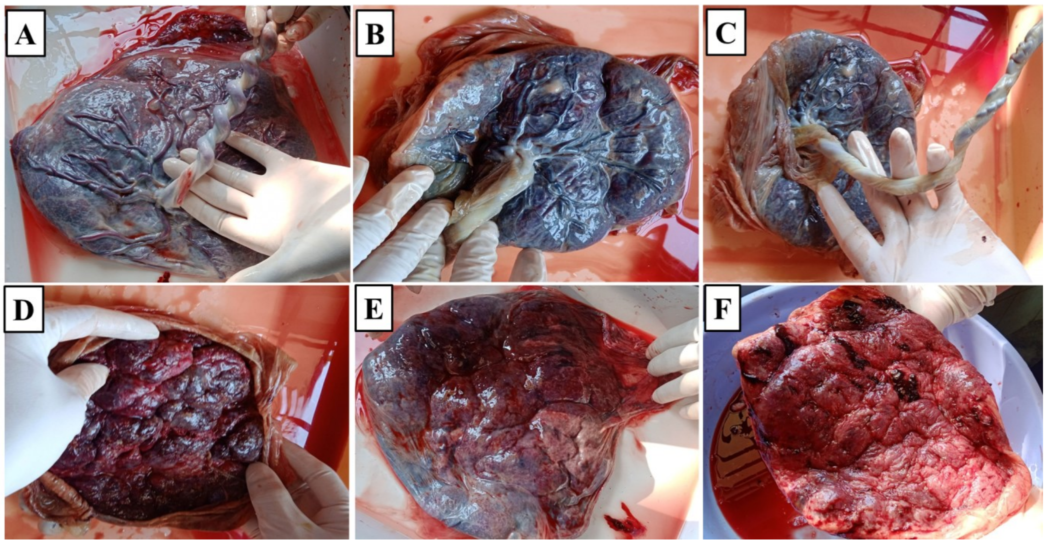

Fig. 2: Representative photographs of at term placenta depicting A, B, C – Amniotic membrane covered smooth and shiny fetal surface attached by the umbilical cord, D, E, F, - rough reddish maternal surface with 15 -20 cotyledons.

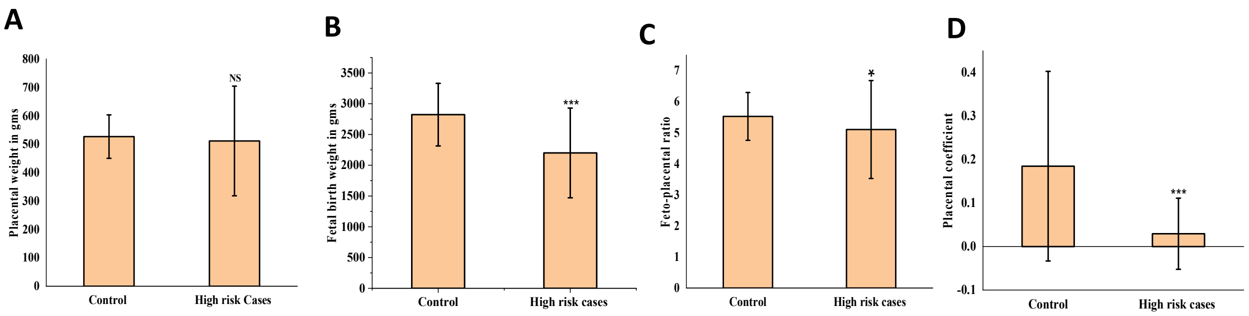

Fig. 3: A] Placental weight B] Fetal weight C] Feto-placental ratio D] placental coefficient of the high-risk group compared with control. All values were expressed as mean ± standard deviation (S.D). The superscripted stars (*) indicate statistical significance. ***p<0.001, **p<0.01, *p<0.05, NS-Non-significant.

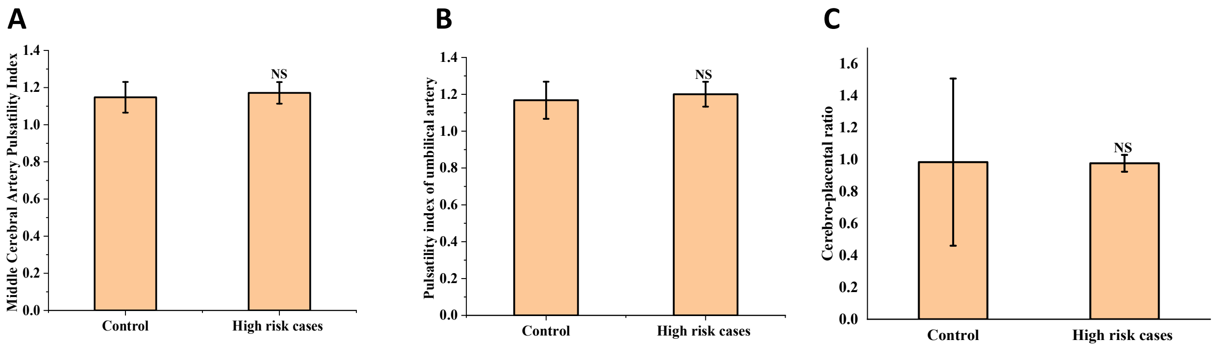

Fig. 4: A] Middle cerebral artery pulsatility index, B] Umbilical artery pulsatility index and C] Cerebro-placental ratio of the high-risk group compared with control. All values are expressed as mean ± standard deviation (S.D). The superscripted stars (*) indicate statistical significance. ***p<0.001, **p<0.01, *p<0.05, NS-Non-significant.

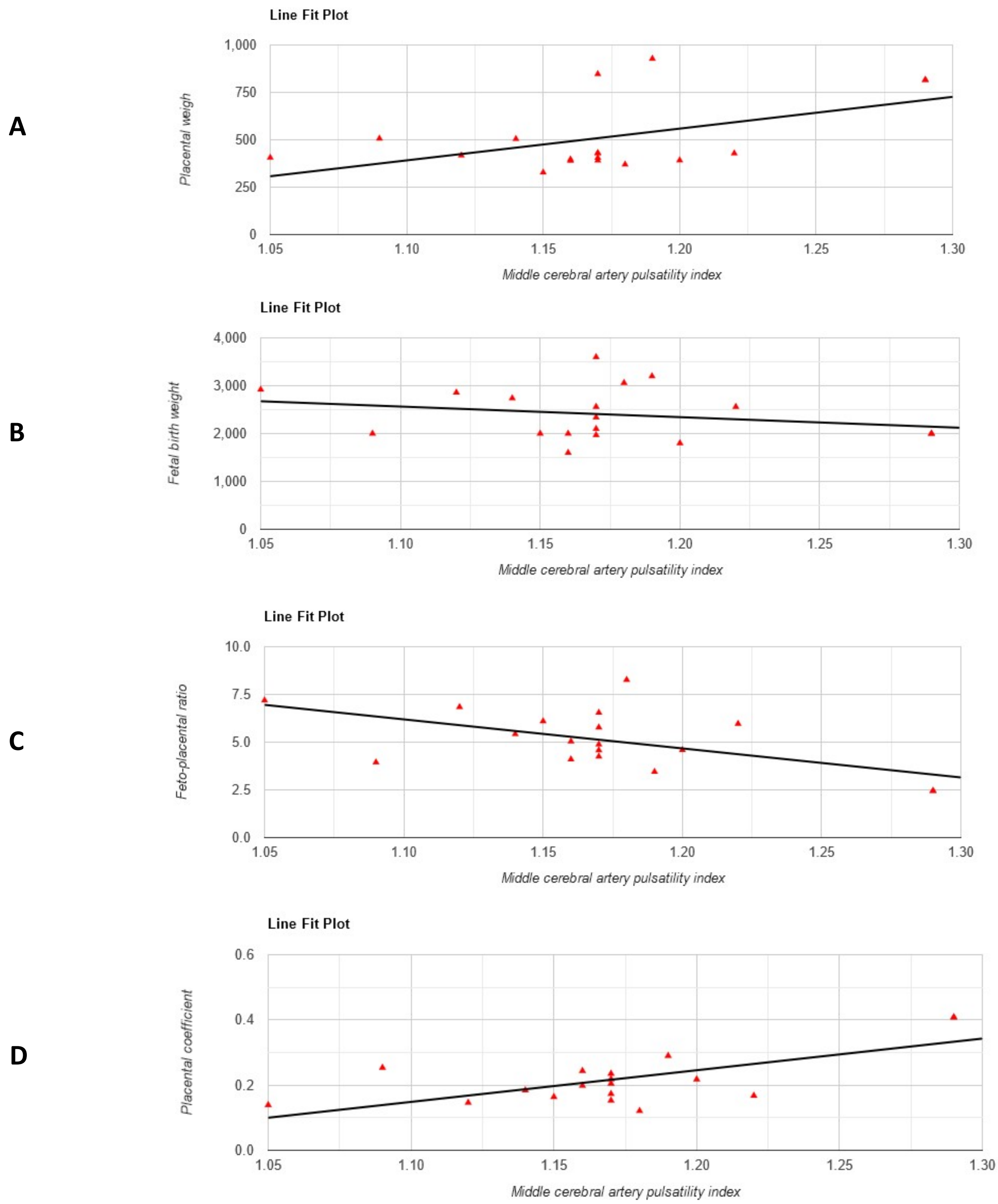

Fig. 5: Correlation between A] Middle cerebral artery pulsatility index and placental weight, B] Middle cerebral artery pulsatility index and fetal birth weight C] Middle cerebral artery pulsatility index and fetoplacental ratio D] Middle cerebral artery pulsatility index and placental coefficient of high-risk group pregnant women.

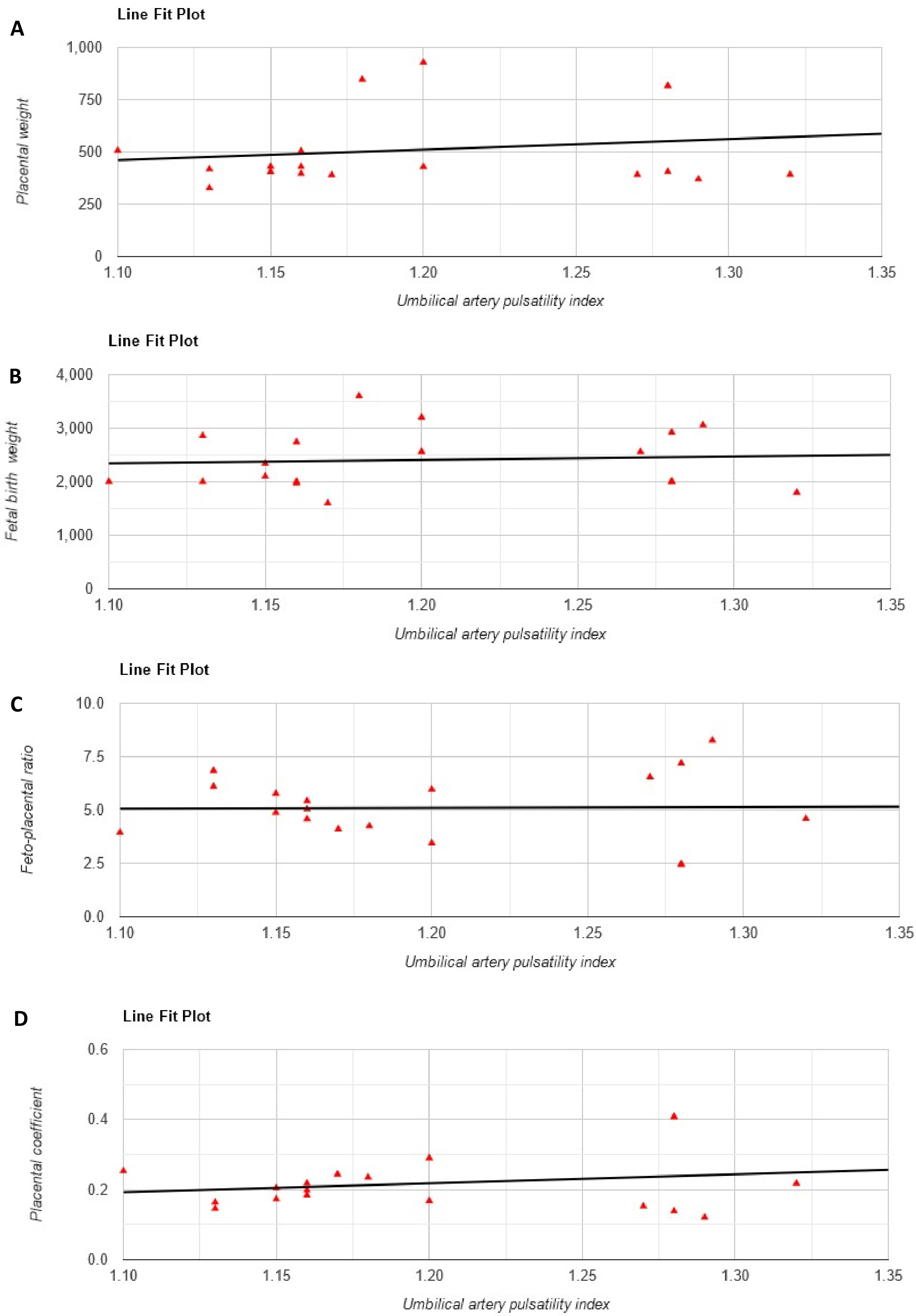

Fig 6: Correlation between A] Umbilical artery pulsatility index and placental weight, B] Umbilical artery pulsatility index and fetal birth weight C] Umbilical artery pulsatility index and fetoplacental ratio D] Umbilical artery pulsatility index and placental coefficient of high-risk group pregnant women.

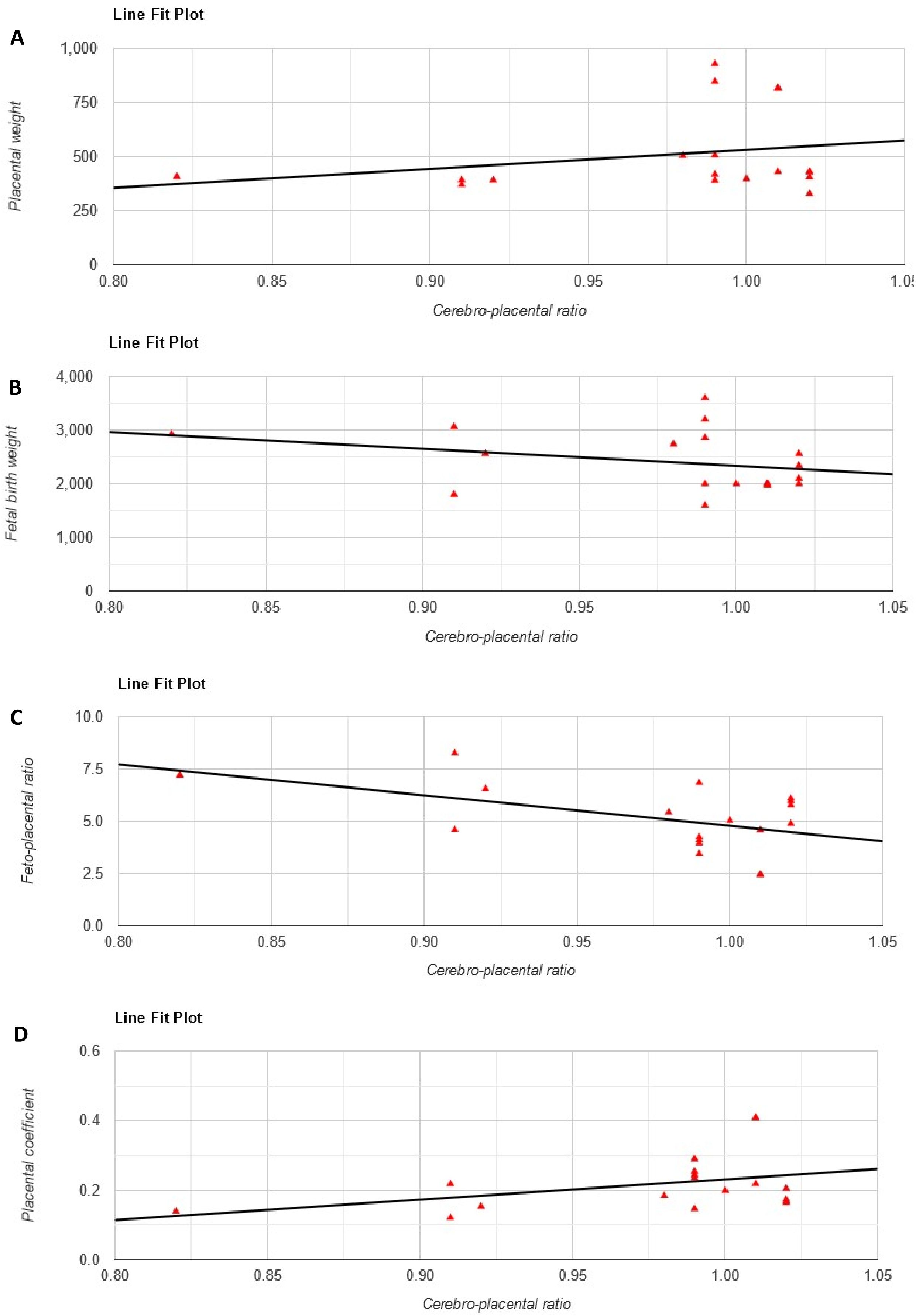

Fig. 7: Correlation between A] Cerebro-placental ratio and placental weight, B] Cerebro-placental ratio and fetal birth weight C] Cerebro-placental ratio and fetoplacental ratio D] Cerebro-placental ratio and placental coefficient of high-risk group pregnant women.

DISCUSSION

Results of this study demonstrated no difference in the placental weight between normal high-risk cases, whereas there is low birth weight and less fetoplacental ratio and placental coefficient ratio in high-risk cases than in normal pregnant women. But Doppler indices of Middle cerebral artery pulsatility index, pulsatility index of the umbilical artery and cerebro-placental ratio was not showed any significant difference between the control and high-risk cases.

Results of this study indicated that there is a significant large positive relationship between the middle cerebral artery pulsatility index and Placental weight and a significant negative relationship between the middle cerebral artery pulsatility index and Feto-placental ratio, whereas a positive correlation was found between the pulsatility index middle cerebral artery and placental coefficient.

The Umbilical artery pulsatility index and both fetal and placental weight in high-risk cases not showed a significant correlation. But a significant negative relationship was found between the Cerebro-placental ratio and Feto-placental ratio in high-risk cases. However, there was no significant correlation between Doppler indices and both fetal and placental weight in normal pregnant cases except for Middle cerebral artery pulsatility index and Placental weight which was negatively correlated.

The weight of the placental is accepted as a rough proxy for placental function, since both small and large placentas may be dysfunctional [17,18]. Obesity and diabetes are the most prevalent obstetrical issues that both the mother and her children experience, as they are maternal traits linked to abnormal fetal and placental development [19,20].

Earlier studies have shown that obese women's placentas and birth weight are higher in their offspring [19,21] but this study result showed no significant difference in placental weight between high-risk and normal pregnant women, whereas fetal birth weight was less in high-risk cases. Furthermore, recent research on a cohort of women with gestational diabetes discovered that characteristics connected to the disease were linked to both birth weight and placental weight, with a greater influence on the latter [22], this is inconsistent with the present study results. Maternal physiologic and pathologic states are substantially correlated with placental weight and placental-to-birth weight ratio (PWBW). Body mass index (BMI) before pregnancy, ethnicity, or previous pregnancies are a few examples of physiologic factors that might affect placental weight [23-25].

A substantial correlation exists between aberrant Doppler indices and fetal hypoxia, acidosis, and perinatal problems. Doppler indices serve as an indirect indicator of blood flow impedance in the arteries [26,27], which are particularly helpful in assessing the health of the fetus in high-risk pregnant women [28]. Fetal distress and academia are related to the middle cerebral artery's lower impedance and the umbilical artery's enhanced ultrasonographic impedance, respectively [29].

Vascular resistance is raised and utero-placental perfusion is diminished in preeclampsia [30] leading to increased incidence of fetal hypoxia and compromised fetal growth [31], which is in line with the findings of our research. In order to maintain continuous oxygen delivery to the brain in the face of hypoxia, the fetus utilizes a compensatory mechanism to shift cardiac output and blood flow [32]. Doppler ultrasonographic methods have been used to monitor and treat complicated pregnancies since several studies have shown a strong correlation between aberrant Doppler indices and pregnancy issues [31,33-36].

Several researchers have shown a link between aberrant fetal vascular Doppler indices and a poor neonatal outcome, fetal discomfort, or small for gestational age intrauterine growth restriction (SGA-IUGR) [13,31,33-36]. Unusual umbilical arteries Doppler waveform is a potent and reliable predictor of a poor perinatal outcome in preeclampsia patients [37]. Some researchers have revealed that cerebral Doppler indices are linked to poor perinatal outcomes [13,38], While some studies have claimed that the cerebral-umbilical ratio is a more accurate indicator of a poor perinatal outcome or an IUGR than the Doppler values of either vessel alone [34,36].

Because the discovery of a brain sparing effect is strongly related to a poor perinatal outcome in IUGR, the cerebro-placental ratio is a valuable tool in identifying the at-risk fetus in both cases. The efficacy of the pulsatility index of the middle cerebral artery alone and its relationship to the fetal umbilical artery in predicting prenatal problems was examined by Karlsen et al. in a research published in 2016. According to the study's findings, using middle cerebral artery ultrasonography to predict early birth is more accurate when the percentile is below 10%. The middle cerebral artery velocity index to the fetal umbilical artery and cerebroplacental levels of less than 5% and 10% were finally shown to be linked to adverse prenatal effects [39], which is in line with the results of this study.

The index cerebro-placental ratio (CPR) had the best sensitivity for predicting both an unfavorable neonatal outcome (87.8%) and an intrapartum aberrant FHR (74.1%). The perinatal outcome was not substantially different in the aberrant Doppler group, although admission to the neonatal critical care unit was considerably higher [40].

The perinatal outcome in the group with abnormal Doppler was also not substantially different, but admission to the newborn critical care unit was much higher, which is consistent with our findings [41]. Schreurs et al., [42] stated that low CPR was linked to specific pregnancy outcomes, such as fetal distress. The results of the current investigation showed that, in high-risk instances, there was a negative correlation between the Cerebro-placental ratio and the Feto-placental ratio.

CONCLUSION

Doppler indices of the cerebral–umbilical ratio provide better diagnostic accuracy in high-risk pregnancies. Low birth weight and less fetoplacental ratio and placental coefficient ratio are found in high-risk cases than in normal pregnant women. A strong positive relationship was observed between the middle cerebral artery pulsatility index and placental weight, while negative relationship between the pulsatility index of MCA and the fetoplacental ratio. In high-risk instances, a negative association was seen between the Cerebro-placental ratio and Feto-placental ratio whereas a positive link was found between the pulsatility index of the MCA and placental coefficient. Further studies with a large sample size and multicentre sampling would develop more definite results for wider application.

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Conflicts of Interests: None

Ethical Approval: All methodologies used in research involving human subjects were compliant with the Declaration, any later revisions, or other equivalent ethical norms as determined by the institutional ethics committee. Informed Consent Informed consent was obtained from all individual participants included in the study.

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