

Evaluation of the Cerebro-Placental Ratio and Doppler Indices of the Umbilical and Middle Cerebral Arteries at 27-40 Weeks of Normal Gestation

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ABSTRACT

Objective: To measure the Pulsatility Index (PI) and Resistive Index (RI) in the Umbilical Artery (UA) and the Middle Cerebral Artery (MCA) between 27-40 weeks of a normal intrauterine pregnancy, and to calculate the Cerebro-Placental (CP) ratio for all patients.

Study Design: Cross-sectional study.

Place and Duration of Study: Tertiary Care Hospital of Rawalpindi, Pakistan, from Jun 22 to Mar 23.

Methodology: This study included the females with normal third-trimester pregnancies from 27 weeks, excluding anomalies, multiple pregnancies, maternal smoking, documented complications, and pre-existing medical conditions. Duplex Doppler measured middle cerebral artery (MCA) and umbilical artery (UA) indices, and the CP ratio. SPSS Version 23:00 was used for data analysis.

Results: In this study, 183 pregnant females were considered, with a predominant age range of 26-30 years (40.4%). The mean age was 28.60 ± 5.01 years, and the mean gestational age was 34.21 ± 2.91 weeks. Maximum patient frequency occurred in the 34th week of gestation (13.6%). Strong, negative correlation between CP ratio and UA pulsatility index was observed for nearly every gestation week ($p < 0.05$).

Conclusion: The study identifies distinct gestational age-related patterns in foetal middle cerebral artery (MCA) and umbilical artery (UA) Doppler indices. The CP ratio emerges as a valuable parameter, showcasing potential application, particularly in intrauterine growth restriction (IUGR) cases.

Keywords: Doppler Velocimetry, Foetal Monitoring, Middle Cerebral Artery.

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INTRODUCTION

Doppler ultrasonography (DU) velocimetry is a widely recognized method for monitoring fetal and uterine blood vessels during pregnancy. Doppler waveforms, which indicate changes in circulation, can be used to predict adverse perinatal outcomes.¹ It has been used for antenatal monitoring for a considerable time. In 1977, DU was successfully introduced in obstetric imaging and fetal monitoring.² In a groundbreaking development, Fitzgerald and colleagues were the first to noninvasively demonstrate the blood flow pattern in the umbilical cord (UC) and proposed that abnormalities in the waveforms of the umbilical artery (UA) could serve as indicators of intrauterine growth restriction (IUGR). This innovative approach to waveform analysis also led to various essential clinical applications.³

Doppler evaluation of the umbilical artery (UA) has now become a routine procedure for monitoring

fetal well-being during the antenatal period. This technique allows assessment of blood flow and can help identify potential issues with placental function and fetal oxygenation.⁴ Additionally, Doppler assessment of the fetal middle cerebral artery (MCA) has been extensively employed for diagnosing fetal anemia. By measuring the blood flow velocity in the MCA, healthcare providers can detect fetal anemia, which is crucial for timely and appropriate management to ensure optimal outcomes for both mother and baby.⁵

Waveforms of DU (Doppler ultrasound) not only indicate blood velocity but also furnish valuable insights into diverse dimensions of blood flow, encompassing the detection and direction of flow, flow volume, velocity profile, and impedance. To minimize inter- and intra-observer variability, angle-independent Doppler indices have been developed for flow velocimetry and are currently extensively utilized.⁶

In the context of Doppler ultrasonography, certain blood vessels are easier to examine and yield

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consistent results. Specifically, the middle cerebral artery (MCA) and the umbilical artery (UA) are more accessible for evaluation and provide reliable measurements. The MCA has been extensively studied, especially for its role in assessing problems with the placenta and diagnosing anaemia in the foetus.⁷

Combining Doppler measurements from both the middle cerebral artery (MCA) and the Umbilical Artery (UA) to calculate the Cerebro-Placental ratio (CP ratio) is an effective method for assessing foetal well-being.⁸ A reduced CP ratio indicates increased blood flow to the brain, enhancing the accuracy in predicting adverse outcomes and complications compared to relying solely on Doppler measurements from either the MCA or UA.⁹ This ratio's use has been increasing in the surveillance of at-risk foetuses through regular intervals of Doppler studies.¹⁰

In this study, we aimed to establish normal values for the resistive index (RI) & pulsatility index (PI) of MCA and UA during the 27-40 weeks of a normal intrauterine pregnancy. We also sought to calculate the CP ratio in a group of pregnant individuals with normal gestation. This was done to create a foundation for Doppler measurements in the Pakistani context, which is important for monitoring and managing high-risk pregnancies. While Doppler index reference ranges are present in the literature of western countries, there is a lack of similar research focusing on the Pakistani population.

METHODOLOGY

This is a cross-sectional study which was conducted prospectively at a tertiary care hospital in Rawalpindi, following approval from the institutional ethical review board (IERB letter # 0060). The sample size, determined as $n=81$ using the WHO calculator, by using a variance of 0.0529 for the Umbilical Artery Pulsatility Index,⁹ 95% confidence level, and an estimated margin of error of 5%. However, in the present study, data were collected from 183 pregnant females between June 2022 and March 2023 using a non-probability consecutive sampling technique, ensuring they met the inclusion criteria for Doppler ultrasonography.

Inclusion Criteria: All pregnant patients aged 18 to 45 years with normal third-trimester pregnancies from 27 to 40 weeks of gestation were included.

Exclusion Criteria: Patients with foetal anomalies before recruitment, pregnancies involving multiple

foetuses, a maternal smoking history, recorded complications during the ongoing pregnancy before enrolment, any prior medical conditions in mother (e.g., chronic kidney disease, diabetes, hypertension) that may impact the baby, instances where complications emerge in the current pregnancy within the study duration, all constitute exclusion criteria.

The qualified participants from the study cohort who met the inclusion criteria were enrolled. Measurements were obtained utilizing a Doppler duplex ultrasound apparatus, specifically the Toshiba Xario 200, was equipped with a curvilinear probe having low-frequency. All cases underwent duplex Doppler examination. Doppler waveforms were recorded from both the UA and MCA of foetus across three continuous cardiac cycles.

For MCA RI and PI assessment, the MCA closer to the probe was recognised using colour Doppler in every patient. A spectral trace was acquired from the MCA right after its origin. Angle correction was performed for each case, ensuring that the angle of insonation fell between 59 and 60 degrees. Both manual and auto mode measurements of PI and RI were taken over three continuous cardiac cycles. The measurements were done again, and two consecutive readings displaying consistent results were documented for study purpose. Similar method was applied for UA PI and RI assessment.

After confirming technically acceptable examinations and measurements, the CP ratio was calculated as; the ratio of the pulsatility index (PI) for the middle cerebral artery (MCA PI) to the pulsatility index for the umbilical artery (UA PI), for each case. The gathered data underwent entry and analysis through Statistical Package for Social Sciences (SPSS) version 23.00. A scatter plot was generated to visually represent the compiled data. Frequencies and percentages and mean & standard deviations were assessed for categorical and quantitative data respectively. By applying Pearson correlation, the relationship of UA RI & PI, MCA RI & PI, CP Ratio & UA PI, and CP Ratio & MCA PI for each gestational period from 27-40 weeks, was determined. Results were taken as significant at p -value ≤ 0.05 .

RESULTS

The current study enrolled a total of $n=183$ pregnant women; out of which, bulk of the cases had an age in range of 26-30 years, and frequency was 74(40.4%); followed by 31-35 years [44(24.0%)] and 21-25 years [43(23.5%)]. The mean age of the cases was

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28.60±5.01 years, and mean gestational age was 34.21±2.91 weeks. Mean values of Doppler indices have also been shown in Table-I.

Table-I: Descriptive Statistics of age, Gestational age and Doppler indices (n=183)

Variables	Mean±SD
Age (years)	28.60±5.01
Gestational Age (weeks)	34.21±2.91
Doppler Indices	
Resistive Index of UA	0.57±0.08
Pulsatility Index of UA	0.89±0.17
Umbilical artery Systolic Diastolic ratio	2.57±0.28
Resistive Index of MCA	0.75±0.08
Pulsatility Index of MCA	1.61±0.31
Cerebro-placental Ratio	1.85±0.41

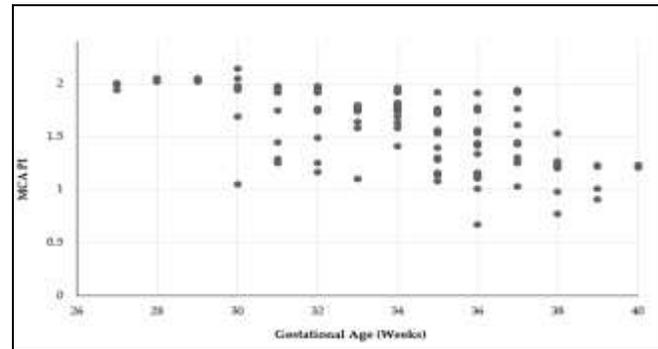
UA=Umbilical Artery; MCA=Middle Cerebral Artery

Maximum frequency of patients was in 34th week of gestation 25(13.6%) followed by 35th and 36th gestational week, 24(13.1%) and 23(12.5%) respectively. The scatter plot shown in Figure-1 (a, b) depicted little bit rising curve and a plateau in the beginning for MCA RI and PI values for gestational age 27th to 30th week, and thereafter a negative trend was noted from 30th to 40th week, which stated a negative relationship with the age of gestation. Correlation analysis was done between MCA RI and MCA PI for each week of gestation, which showed positive correlation ($p<0.05$) for each gestation week except 27th, 28th, 29th, and 40th week (Table-II). The UA RI and UA PI values, scatter plotted against gestational age in Figure-2 (a, b) showed a linear and negative correlation of UA PI as well as UA RI with gestational age throughout from 27 weeks to 40 weeks. There was a strongly positive relation between UA RI and UA PI from 30th to 37th gestation week ($p<0.01$) (Table-II). Correlation of Cerebro-placental ratio was analysed with UA PI and MCA PI as presented in table-II, which showed statistically negative and strong correlation of CP ratio with UA PI for almost each gestation week ($p<0.01$). A scatter plot diagram of CP ratio for gestational age revealed a negative and linear correlation as shown in Figure-3.

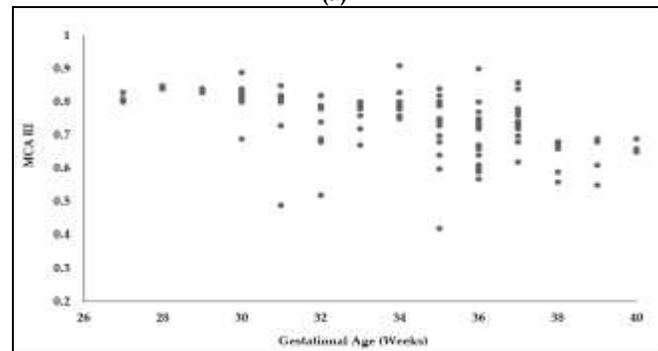
DISCUSSION

The study findings demonstrated that fetal umbilical artery (UA) and middle cerebral artery (MCA) Doppler indices vary significantly with advancing gestational age. The MCA Resistance Index (RI) and Pulsatility Index (PI) followed a parabolic trend, suggesting dynamic changes in cerebral

perfusion corresponding to evolving fetal brain demands during early and late gestation.

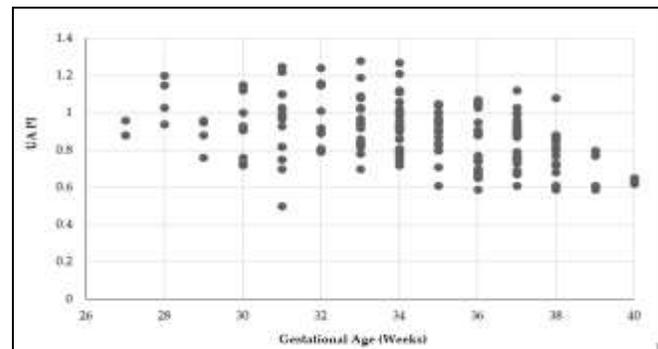


(a)

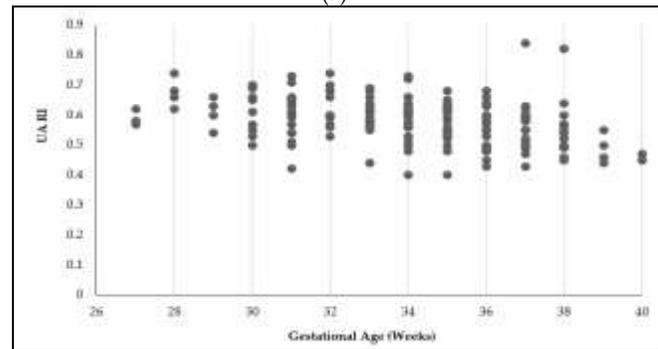


(b)

Figure-1: Scatter plot Diagram of MCA PI (a) and MCA RI (b)



(a)



(b)

Figure-2: Scatter plot diagram of UA PI (a) and UA RI (b)

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Table-II: Correlation Between UA PI and RI, MCA PI and RI, CP Ratio and UA PI, CP Ratio and MCA PI for Gestational Period 27-40 weeks (n=183)

Gestational Age in Weeks (n)	MCA PI and MCA RI r(p-value)	UA PI and UA RI r(p-value)	CP Ratio and MCA PI r(p-value)	CP Ratio and UA PI r(p-value)
27(3)	0.908(0.275)	0.928(0.121)	0.92(0.246)	-0.143(0.909)
28(4)	0.556(0.444)	0.942(0.058)	-0.982(0.018)	-0.999(0.001)
29(4)	0.192(0.808)	0.980(0.020)	0.353(0.647)	-0.994(0.006)
30(11)	0.683(0.020)	0.919(<0.001)	0.579(0.062)	-0.511(0.108)
31(18)	0.719(0.001)	0.823(<0.001)	0.218(0.384)	-0.783(<0.001)
32(11)	0.717(0.013)	0.978(<0.001)	0.580(0.062)	-0.498(0.119)
33(16)	0.901(<0.001)	0.843(<0.001)	0.581(0.018)	-0.839(<0.001)
34(25)	0.408(0.043)	0.840(<0.001)	0.359(0.078)	-0.828(<0.001)
35(24)	0.730(<0.001)	0.600(0.002)	0.746(<0.001)	-0.714(<0.001)
36(23)	0.760(<0.001)	0.781(<0.001)	0.508(0.013)	-0.659(<0.001)
37(21)	0.940(<0.001)	0.916(<0.001)	0.249(0.276)	-0.595(0.004)
38(16)	0.870(<0.001)	0.195(0.470)	0.611(0.012)	-0.627(0.009)
39(4)	0.989(0.011)	0.848(0.152)	0.993(0.007)	-0.999(0.001)
40(3)	0.982(0.122)	0.982(0.121)	-0.999(0.021)	-0.965(0.169)

MCA=Middle Cerebral Artery; UA=Umbilical Artery; PI=Pulsatility Index; RI=Resistive Index; CP ratio=Cerebro-Placental Ratio

Doppler velocimetry is essential in prenatal care, providing insights into foetal well-being by examining utero-placental, umbilical, and foetal vessels to guide clinical decisions.¹¹ Doppler ultrasonography (DU) analyses foetal blood flow patterns, predicts adverse outcomes, and helps monitor health by detecting issues like intrauterine growth restriction and foetal anaemia. Its non-invasive nature enhances decision-making and improves outcomes for both mother and baby in modern obstetric practice.¹² Doppler examinations of the middle cerebral artery (MCA) are essential for understanding how the foetus responds to placental dysfunction. This response is seen as cerebral vasodilation and a shift in blood flow from the foetus's periphery to the brain, known as the 'brain-sparing effect.' This adaptation occurs initially for a specific period. It's important to note that the PI and RI values of the MCA change throughout a standard pregnancy.¹²

Research conducted by Perkovic *et al.*, has revealed a consistent parabolic pattern in RI and PI of the MCA. Notably, this pattern exhibits a plateau between 28 and 30 weeks, suggesting an elevated demand for the foetal brain during both early and late stages of pregnancy.¹³ This plateau phase between 28 and 30 weeks advocates increased demand for blood supply to the foetal brain during both early and late stages of gestation. In alignment with prior investigations, current study has likewise demonstrated a parabolic curve, reaching its apex at 30th gestation week, followed by a gradual decline. Current findings also revealed a positive correlation between the PI and RI of the MCA for each gestation week except 27th, 28th, 29th, and 40th week. On the contrary, Wang *et al.*, showed a negative correlation after 30th week. Differences in results are indicative of variations in blood flow dynamics and vascular resistance in the MCA during different stages of pregnancy.¹⁴

Karabay *et al.*, also demonstrated a moderately positive correlation till 30th week and a negative correlation thereafter, further indicating the complex nature of blood flow regulation in the foetal brain during late pregnancy.¹⁵ Another study by Srikumar *et al.*, identified a similar parabolic pattern in the reference curve for the RI. Their findings indicated a gradual increase from 0.68 at 18 weeks to a peak of 0.8 at 28 weeks, followed by a decline to 0.61 at 42 weeks.¹⁶ Although the gestational period reported was considerably wider than in our study, the observed trend was significantly comparable.

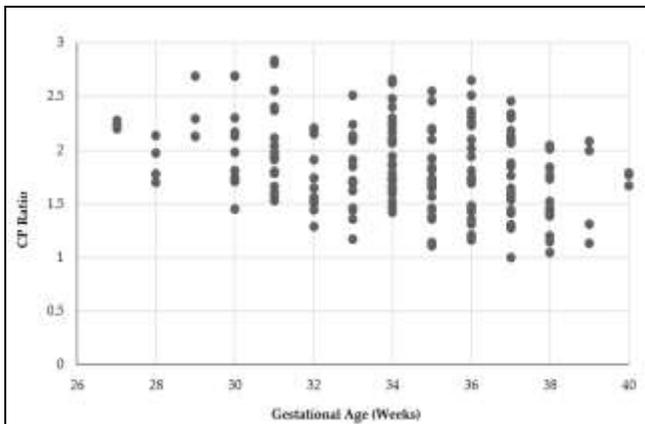


Figure-3: Scatter plot Diagram of CP Ratio

The decline in foetal MCA PI observed after the 28th week of gestation is likely indicative of diminishing vascular resistance as gestational age increases as reported by Kale *et al.*, The UA plays a critical role in the development and health of the foetus, and deviations in foeto-placental circulation can lead to complications such as IUGR, cord accidents, and stillbirths.¹⁷

Hussein *et al.*, established clear associations between deviated values from normal, of UA PI & RI, and systolic/diastolic (S/D) ratio with conditions like hypertensive pregnancy disorders, IUGR, and intraventricular haemorrhage.¹⁸ He also reported a gradual decrease in UA PI and RI in both male and female foetuses from 28th to 36th week of gestation period. Our study aligns with this trend, illustrating a linear graph for UA RI and PI with a consistent decline over gestation, illustrating a negative and strong correlation between UA RI and PI as gestation progresses. This correlation strengthens the notion that as gestation progresses, there is a consistent reduction in vascular resistance and pulsatility in the umbilical artery, which is crucial for adequate blood flow and nutrient exchange between the mother and the foetus. While Leavitt *et al.*, and their co-workers have defined normal reference ranges for UA Doppler indices, the applicability of these values across diverse populations remains uncertain.¹⁹

In current investigation, the trend for UA PI across different gestational periods closely resembles that elaborated by Lv *et al.*,²⁰ Similarly, the existing study's decreasing trend for UA RI and PI is also in line with those in a parallel study by Bhide *et al.*, attributed to biological consistency in UA PI changes across gestational periods.²¹

The CP has become an important parameter for assessing antenatal and perinatal complications in higher-risk pregnancies.²² Our correlation analysis shows a strong negative relationship between the CP ratio and UA PI throughout most gestation weeks, indicating changing blood volume needs for the fetal brain. There is limited literature on CP ratio reference ranges in normal pregnancies, with Bonnevier *et al.*,²³ Notably, no prior studies have examined the correlation between MCA PI, UA PI, and the CP ratio. Our research uniquely addresses the lack of established reference values for MCA and UA Doppler velocimetry in normal gestation within the Pakistani population, highlighting its significance.

This study has certain limitations that warrant consideration. Firstly, the relatively lower number of cases within the 27–29 weeks gestation range hinders the meaningful calculation of Doppler indices tailored to these specific timeframes. Additionally, the single-centre nature of the study may introduce a potential source of bias that could impact the generalizability of the results. Furthermore, being an observational study conducted by a single investigator, the research is susceptible to inherent limitations associated with this study design. These constraints should be taken into account when interpreting and applying the findings. Future researches are recommended to relate the Doppler indices findings with clinical outcomes to explore the practical relevance of the findings.

CONCLUSION

The foetal UA and MCA Doppler indices exhibit distinct patterns based on the age of gestation. The MCA RI and PI demonstrate a parabolic curve, possibly linked to the proportional rise in blood supply to the foetal brain requirements during both the early and late stages of pregnancy. Conversely, UA RI and PI show a gradual drop over the course of gestation, likely reflecting a reduction in the resistance of the placenta as the pregnancy advances. The CP ratio, which is derived from both the indices of UA and MCA, emerges as a more comprehensive physiological parameter, displaying a negative correlation with UA PI. This suggests the potential utility of CP ratio as an additional parameter, particularly in cases of IUGR. However, broader application of these findings necessitates further exploration through larger-scale, multicentre studies to validate and enhance their relevance.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

QM & NA: Data acquisition, data analysis, critical review, approval of the final version to be published.

MZA & SA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AZB & MHJ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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