COMPARISON OF FETAL MIDDLE CEREBRAL ARTERY DOPPLER INDICES IN ANEMIC AND NON-ANEMIC PREGNANT FEMALES

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DOI: https://doi.org/10.5281/zenodo.15710115

Keywords
Fetal Hemodynamics, Maternal Anemia, Middle Cerebral Artery Doppler, Brain-Sparing Effect, Pregnancy Outcomes, Pulsatility Index (PI), Low- and Middle-Income Countries (LMICs), Resistive Index

Article History
Received on 13 May 2025
Accepted on 13 June 2025
Published on 21 June 2025

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Abstract
Maternal anemia remains a significant global health challenge, particularly in low- and middle-income countries like Pakistan, where its prevalence ranges from 38% to 60%. This condition has far-reaching implications for both maternal and fetal health, often leading to adverse pregnancy outcomes such as intrauterine growth restriction and perinatal mortality. ***Objective:*** *This study investigates the impact of maternal anemia on fetal cerebral hemodynamics, focusing on middle cerebral artery (MCA) Doppler indices, including pulsatility index (PI), resistive index, peak systolic velocity (PSV), and end-diastolic velocity (EDV).* ***Methods:*** *A cross-sectional design was employed to analyse data from 120 pregnant women, categorized into anemic and non-anemic groups based on hemoglobin levels. Doppler ultrasound was used to measure MCA indices, and statistical analyses were conducted to compare these parameters between the two groups.* ***Results:*** *Significant alterations in MCA Doppler indices were observed in anemic pregnancies, including reductions in PI (1.15 ± 0.15 vs. 1.32 ± 0.18) and RI (0.55 ± 0.05 vs. 0.61 ± 0.06), alongside increases in PSV (69.74 ± 8.65 cm/s vs. 57.83 ± 6.46 cm/s) and EDV (31.63 ± 6.79 cm/s vs. 23.08 ± 5.85 cm/s).* ***Conclusion:*** *The study highlights that early detection and effective management of maternal anemia is highly important to avoid adverse effects on fetal development. Timely interventions, including routine screening and supplementation of micronutrients, have a major impact on pregnancy outcomes.*

INTRODUCTION
Maternal anemia is a pervasive global health issue, affecting an estimated 40% of pregnancies worldwide, with prevalence rates varying significantly by region and socio-economic status [1]. Anemia in pregnancy is defined as hemoglobin levels less than 11 g/dL. It is categorized as mild (10.0–10.9 g/dL), moderate (7.0–9.9 g/dL), or severe (less than 7.0 g/dL) [2, 3]. This condition is still a critical challenge, especially in LMICs like Pakistan, where poor nutrition, added to inadequate health infrastructure and high fertility rates, is contributing to its widespread prevalence [4]. Recent global estimates indicate that about 36.5% of

pregnant women worldwide are anemic, with the highest prevalence recorded in sub-Saharan Africa (57.1%) and South Asia (52.5%) [5-7].

The effects of maternal anemia extend far beyond the health of the mother to include very strong effects on fetal development and pregnancy outcomes [8]. In pregnancy, a spectrum of adverse outcomes can be seen in association with maternal anemia, ranging from low birth weight to preterm birth, IUGR, and even perinatal mortality [9]. Researchers have also established associations with increased maternal morbidity and mortality in severe cases. In regions like South Asia, where maternal anemia results in more than half of all pregnant women, this is a huge burden on healthcare systems and families [10-12].

Fetal development is highly dependent on optimal maternal health, particularly adequate oxygen and nutrient transport facilitated by maternal hemoglobin [13]. Fifty percent of pregnancy anemia is explained by iron deficiency anemia; this subtype is the commonest form, in fact [14]. Consequently, oxygen transportation to the tissues of the fetus is impaired with resultant compensations in the aim of preserving fundamental organ functions. Of primary interest among them are changes involving fetal cerebral circulation. Therefore, noninvasive monitoring of such compensatory changes is feasible through Doppler ultrasound indices of the fetal middle cerebral artery [15].

The middle cerebral artery is an important vessel in fetal circulation, and its main function is to carry oxygenated blood to the developing brain. The pulsatility index, resistive index, peak systolic velocity, end-diastolic velocity, and systolic-to-diastolic ratio are all critical indices of cerebral hemodynamics [16]. All these indices are altered by changes in maternal hemoglobin levels and may reflect an adaptation mechanism due to maternal anemia. There are, in particular, reduced maternal oxygenations, leading to low PI and RI due to the vasodilation of cerebral arteries that then compensate in such a manner as to make oxygen supply the main one for the head-that very well is considered to be "the brain-sparing effect" [17].

Studies highlight the significance of these Doppler indices in evaluating fetal well-being [18-20]. The MCA PI and RI were significantly lower in pregnant women with anemia compared to controls without anemia, indicating increased cerebral blood flow [21]. Similarly, the sensitivity and specificity of MCA-PSV for diagnosing fetal anemia were 90.2% and 92.9%, respectively [22]. Recent progress in the field of AI-assisted Doppler analysis has further improved the accuracy of such measurements, with suggesting accuracy of over 95% for the diagnosis of fetal anemia in resource-poor settings [23].

In Pakistan, maternal anemia is a widespread and persistent health issue, with prevalence rates estimated to range from 38% to 60%, varying by region and population demographics [24]. Contributory factors include low dietary iron intake, high parity, a lack of good prenatal care, and vast socio-economic inequalities [25]. These predisposing factors all too often cause poor fetal outcome in the form of stillbirths, neonatal mortality, and long-term neurodevelopmental disability. Given the high prevalence and grave consequences of maternal anemia, there is an urgent requirement for region-specific studies to provide the necessary evidence for clinical and public health guidelines. This study attempts to fill this significant gap by investigating the association of maternal anemia with fetal MCA Doppler indices in a Pakistani population and provides important insights into fetal cerebral circulation adaptations in resource-limited settings.

This study has following objectives, 1) To compare the fetal middle cerebral artery Doppler indices (PI, RI, PSV, EDV, and S/D ratio) between anemic and non-anemic pregnant women. 2) To evaluate the impact of varying degrees of maternal anemia on fetal cerebral hemodynamics and identify patterns of adaptation. 3) To provide region-specific data that can inform clinical guidelines and public health strategies for managing maternal anemia in LMIC settings like Pakistan.

1. Methodology

This cross-sectional analytical study was conducted at Umer Lab & Diagnostics, Abbas Plaza, GT Road, Kot Addu, over a 12-month period following institutional ethical approval from University of Lahore . A total of 120 pregnant women were recruited using convenience sampling. Participants were divided equally into two groups: 60 anemic (hemoglobin <11.0 g/dL) and 60 non-anemic (hemoglobin ≥11.0 g/dL) pregnant women. Inclusion criteria included maternal age between 18 and 45 years, second or third trimester of pregnancy, and documented hemoglobin levels. Exclusion criteria were multiple pregnancies, intrauterine growth restriction (IUGR), and fetal anomalies. Fetal middle cerebral artery (MCA) Doppler indices, including pulsatility index (PI), resistive index [1], peak systolic velocity (PSV), end-diastolic velocity (EDV), and systolic-to-diastolic (S/D) ratio, were assessed using a Canon Aplio 500 ultrasound machine equipped with color Doppler. Scans were performed with participants in a supine position, ensuring optimal visualization of the MCA using axial imaging of the fetal head. Measurements were recorded during fetal apnea to minimize variability. Maternal hemoglobin levels were analyzed using the Merk Microlab 300 system on the same day as the Doppler examination. Data were analyzed using SPSS version 26. Descriptive statistics summarized demographic and clinical variables. Independent samples t-tests compared Doppler indices between groups, with a p-value <0.05 considered statistically significant. Scatterplots evaluated relationships between maternal hemoglobin levels and Doppler indices. Ethical considerations included informed consent, confidentiality, and participants' right to withdraw without penalty.

Results and Discussion

The following section presents the findings of this study, including descriptive statistics, group comparisons, correlations, and regression analyses.

1.1. Descriptive Statistics and Group Comparisons

Table 1 summarizes the descriptive statistics and group-wise comparisons of key variables. Significant differences were observed between anemic and non-anemic participants. Hemoglobin levels were markedly lower in the anemic group (9.63 ± 0.95 g/dL) compared to the non-anemic group (11.67 ± 0.72 g/dL, $p < 0.001$). Doppler indices also exhibited notable variations. The pulsatility index (PI) was significantly reduced in the anemic group (1.15 ± 0.15) compared to the non-anemic group (1.32 ± 0.18, $p < 0.001$). Similarly, the resistance index [1] was lower in anemic participants (0.55 ± 0.05 vs. 0.61 ± 0.06, $p < 0.001$). Conversely, peak systolic velocity (PSV) and end-diastolic velocity (EDV) were elevated in the anemic group (PSV: 69.74 ± 8.65 cm/s, EDV: 31.64 ± 6.79 cm/s) compared to the non-anemic group (PSV: 57.83 ± 6.46 cm/s, EDV: 23.08 ± 5.85 cm/s, both $p < 0.001$). The mean S/D ratio was lower in anemic participants (2.26 ± 0.26) compared to non-anemic participants (2.62 ± 0.42). The overall mean was 2.44 ± 0.39, with a statistically significant difference ($p < 0.001$). These findings highlight significant hemodynamic adaptations in response to maternal anemia.

Table 1: Descriptive Statistics and Group Comparisons for Key Variables

Parameter	N	Anemic (Mean ± SD)	Non-Anemic (Mean ± SD)	Total (Mean ± SD)	Range	p-value
Age (years)	120	-	-	25.63 ± 4.60	17–40	-
Gestational Age (weeks)	120	-	-	34.56 ± 3.32	19–40	-
Hemoglobin (Hb, g/dL)	120	9.63 ± 0.95	11.67 ± 0.72	10.58 ± 1.30	7–14	<0.001
Pulsatility Index (PI)	120	1.15 ± 0.15	1.32 ± 0.18	1.23 ± 0.19	0.73–1.77	<0.001
Resistance Index	120	0.55 ± 0.05	0.61 ± 0.06	0.58 ± 0.06	0.39–0.74	<0.001
Peak Systolic Velocity (PSV, cm/s)	120	69.74 ± 8.65	57.83 ± 6.46	63.79 ± 9.67	44.3–95.0	<0.001
End-Diastolic Velocity (EDV, cm/s)	120	31.63 ± 6.79	23.08 ± 5.85	27.36 ± 7.64	12.3–45.2	<0.001
Systole/Diastole Ratio (S/D)	120	2.26 ± 0.26	2.61 ± 0.42	2.44 ± 0.39	1.64–3.90	<0.001

1.2. Correlations Between Hemoglobin and Doppler Indices

Table 2A presents the correlations between hemoglobin levels and Doppler indices. Hemoglobin levels were positively correlated with pulsatility index (PI: r = 0.591, p < 0.01) and resistance index (RI: r = 0.594, p < 0.01) also shown in fig 1. In contrast, hemoglobin levels were negatively correlated with peak systolic velocity (PSV: r = -0.732, p < 0.01) and end-diastolic velocity (EDV: r = -0.705, p < 0.01). These findings underscore the significant relationship between maternal anemia and fetal hemodynamic adaptations.

1.3. Regression Analysis

The regression analysis (Table 2B) identified hemoglobin levels as a significant predictor of pulsatility index (PI). Hemoglobin levels were strongly positively associated with PI (\u03B2 = 0.591, p < 0.001) also shown in fig 2, emphasizing the role of maternal anemia in influencing fetal vascular resistance.

Table 2: Correlations and Regression Analysis for Doppler Indices and Hemoglobin

A. Correlations Between Hemoglobin and Doppler Indices

Variable	PI	RI	PSV	EDV
Hemoglobin (Hb, g/dL)	0.591**	0.594**	-0.732**	-0.705**

Note: p < 0.01

B. Regression Analysis (Dependent Variable: Pulsatility Index)

Predictor	B	Std. Error	\u03B2	p-value
Hemoglobin (Hb, g/dL)	0.084	0.011	0.591	<0.001
Constant	0.340	0.113	-	0.003

1.4. Independent Sample T-Test for Doppler Indices

Table 3 highlights the independent sample t-test results. Significant mean differences were observed between anemic and non-anemic groups for all Doppler indices. For example, the mean difference in pulsatility index (PI) was -0.196 (95% CI: -0.256 to -0.135, p < 0.001). Similarly, significant differences were noted for resistance index (RI: -0.065, 95% CI: -0.084 to -0.046), peak systolic velocity (PSV: 11.949, 95% CI: 9.182 to 14.716), and end-diastolic velocity (EDV: 8.913, 95% CI: 6.660 to 11.167). These results further confirm that maternal anemia leads to substantial changes in fetal cerebral hemodynamics.

Table 3: Independent Sample T-Test Results for Doppler Indices

Parameter	Mean Difference	95% CI (Lower)	95% CI (Upper)	p-value
Pulsatility Index (PI)	-0.175	-0.235	-0.115	<0.001
Resistance Index	-0.058	-0.078	-0.038	<0.001
Peak Systolic Velocity (PSV, cm/s)	11.91	9.149	14.671	<0.001
End-Diastolic Velocity (EDV, cm/s)	8.56	6.265	11.848	<0.001

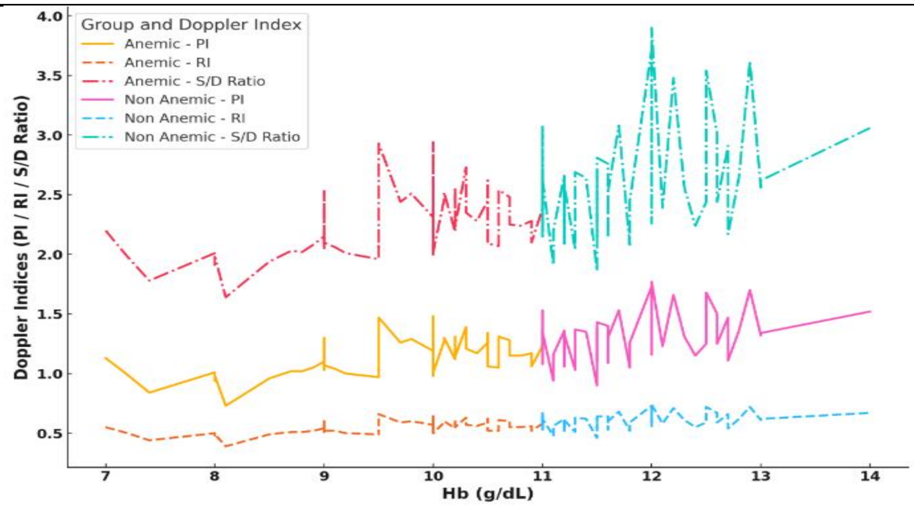

Figure1: Relationships Between Hb Levels and Doppler Indices

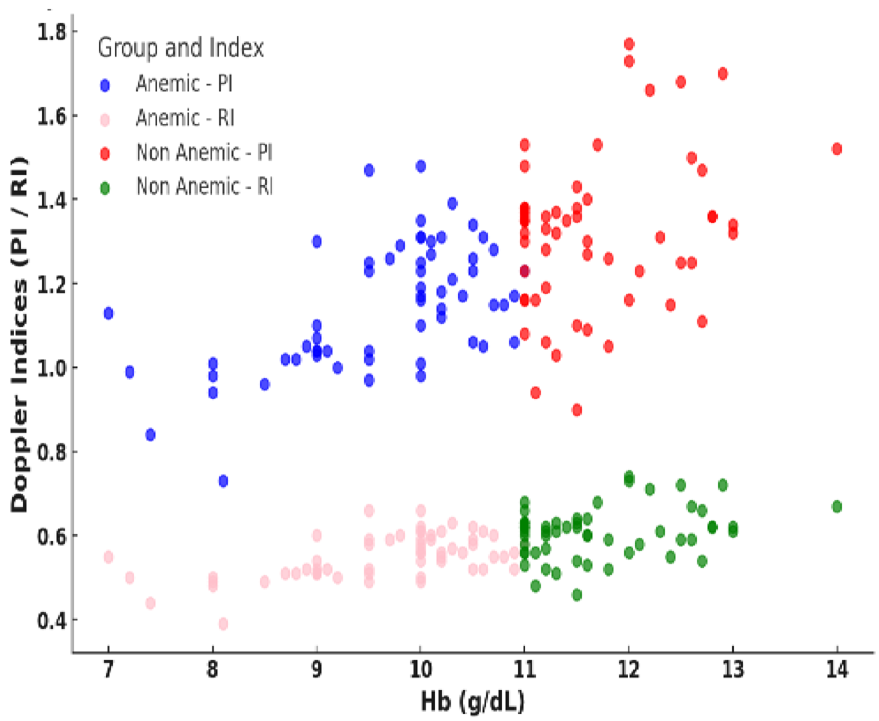

Figure.1: Comparison of Hb Levels with PI and RI in Anemic and Non-Anemic Groups

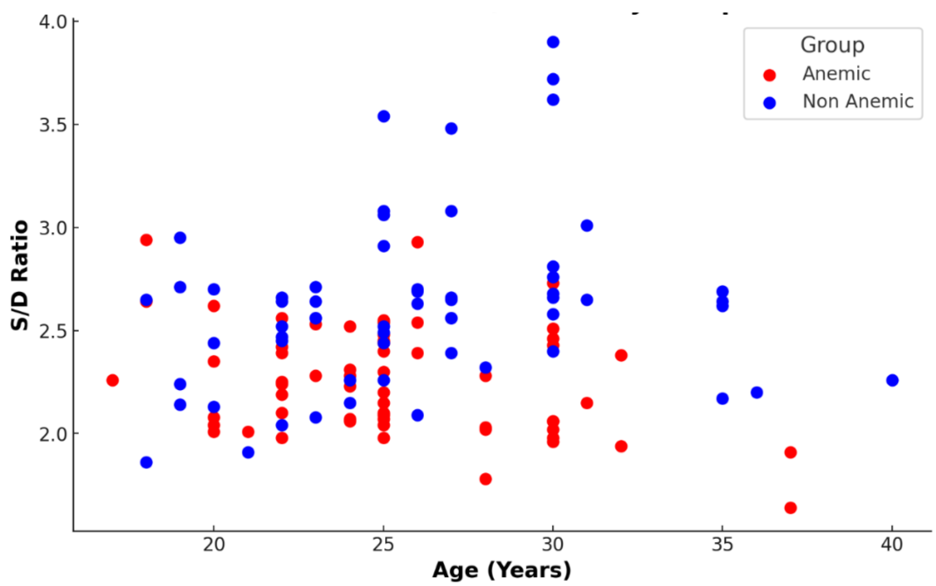

Figure 2: Relationship between Age and S/D Ratio (Systole-Diastole Ratio) for Anaemic and Non-Anaemic groups

2. Discussion

The findings in this study show that maternal anemia significantly impacts the fetal cerebral circulation, as reflected in significantly altered MCA Doppler parameters. These changes, including lower pulsatility index and resistive index, and higher peak systolic velocity and end-diastolic velocity, point out the "brain-sparing effect" as a compensatory mechanism. This effect reflects the fetus's adaptive response to hypoxic conditions caused by reduced maternal hemoglobin levels [26].

These reductions in the PI and RI of anemic pregnancy can only confirm the unequivocal evidence for fetal cerebral vasodilation. This adaptive change has important implications for the proper delivery of oxygen and substrates to the fetal brain during periods of maternal hypoxia [27]. The PI was significantly lower in the anemic group (1.15 ± 0.15) compared to the non-anemic group (1.32 ± 0.18, $p < 0.001$), while the RI also showed a marked reduction (0.55 ± 0.05 in anemic versus 0.61 ± 0.06 in non-anemic pregnancies, $p < 0.001$). These findings align with the available literature on the validity of MCA Doppler indices as predictors of fetal status during hypoxic stress [20]. On the other hand, increased PSV and EDV in anemic pregnancies support the brain-sparing effect. The PSV was significantly higher in the anemic group (69.74 ± 8.65 cm/s) compared to the non-anemic group (57.83 ± 6.46 cm/s, $p < 0.001$), with an increased EDV (31.64 ± 6.79 cm/s in anemic versus 23.08 ± 5.85 cm/s, $p < 0.001$). These changes reflect increased cerebral blood flow, a compensatory response that favors the brain for oxygen supply over other organs [28].

The brain-sparing effect in this study is based on the physiological response to maternal anemia, especially iron deficiency anemia, which impairs oxygen transport capacity due to reduced levels of hemoglobin. This hypoxemic state induces fetal adaptations aimed at optimizing oxygen delivery to vital organs. The reduced vascular resistance in cerebral arteries, evidenced by lower PI and RI, thus facilitates this process [29]. Furthermore, inversely correlated statistical values between maternal hemoglobin level versus PSV-EDV are represented with $r = -0.745$, $p < 0.01$; $r = -0.726$, $p < 0.01$, respectively; this indeed reveals that maternal anemia does directly influence changes in fetal hemodynamics [30].

The MCA Doppler indices hold a promise of being able to noninvasively monitor fetal well-being as an inexpensive modality for prenatal care in resource-limited settings [31]. Regular screening for maternal anemia, coupled with the addition of Doppler studies in the standard prenatal protocol, provide the opportunity to identify fetal compromise well in advance and intervene on time. The results presented herein agree with the earlier literature regarding maternal anemia impacts on fetal cerebral hemodynamics [32]. For instance, reports have constantly shown that the MCA PI and RI were reduced in pregnant women with anemia; thus, such adaptive mechanisms might be universal. The higher values of PSV and EDV in this study further agree with a number of evidences in this regard considering increased cerebral perfusion as a hallmark for brain-sparing effect [33].

Concomitant advances in the technology of Doppler ultrasound have, in turn, further enhanced such measurements in respect of their accuracy and reliability. The sensitivity and specificity reported for MCA Doppler indices when detecting fetal anemia are often more than 90%, underlining their clinical utility [34]. Maternal anemia is still the leading health problem in LMICs, and in areas of Pakistan, the prevalence rate is as high as 60%. The study has clearly pointed out that interventions regarding this condition are urgently needed, which must be region-specific Moreover, given the strong associations of maternal hemoglobin levels with Doppler indices in this study, there's a distinct possibility of using these Doppler indices as early markers of fetal compromise [35].

3. Conclusion

This study provides compelling evidence of the significant impact of maternal anemia on fetal cerebral hemodynamics, with alterations in MCA Doppler indices serving as key markers of fetal adaptation to hypoxic conditions. These findings are characterized by reduced pulsatility and resistive indices, with increased peak systolic and end-diastolic velocities, emphasizing the physiological brain-sparing effect that prioritizes oxygen delivery to the fetal brain in conditions of compromised maternal hemoglobin levels. These findings also provide support not only for the role of MCA Doppler indices as a useful diagnostic tool but also for its potential in early identification of fetal compromise. Maternal anemia is a vital factor in fetal health, especially in the developing world where health care facilities are usually very poor, hence demands an enhanced state of clinical vigilance and appropriate prenatal monitoring systems.

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