ORIGINAL ARTICLE

Accuracy of Fetal MCA Doppler Ultrasound Scan in Prediction of Neonatal Anemia in Iron Deficiency Anemic Patients

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Abstract

Background: ***Even in industrialized nations, iron deficiency anemia(IDA) is common during pregnancy. This is because, despite physiological adjustments, iron intake is typically inadequate to satisfy the increased requirements, and nutritional needs are generally not met.***

Aim and objectives: ***To determine whether foetal MCA doppler ultrasonography is effective in reducing newborn anemia in patients with iron-deficient anemia.***

Patients and methods: ***This prospective observational study, included 120-patients were selected from attendee of out-patient Obstetrics and Gynecology clinics of Al-Azhar University Hospitals from November 2023 till November 2024.***

Results: ***We observed a decreasing trend in MCA PI and RI with increasing anemia severity, with statistically significant differences(p=0.001). The sensitivity and specificity of MCA PI(57% and 86.8%) and MCA RI(66% and 86.9%) for predicting neonatal anemia were moderate to high. The positive predictive values(PPV) for MCA PI and RI were relatively low(48% and 51.4%, respectively), while the negative predictive values(NPV) were high(89.6% and 91.2%). This indicates that normal MCA PI and RI values are good indicators of the absence of fetal anemia, but abnormal values should be interpreted cautiously and in conjunction with other clinical findings.***

Conclusion: ***Fetal MCA Doppler parameters, particularly PI and RI, show promising potential as predictors of neonatal anemia in pregnancies complicated by maternal iron deficiency anemia. However, the moderate sensitivity and PPV suggest that these parameters should be used in combination with other clinical and laboratory findings for optimal management of these high-risk pregnancies.***

Keywords: Neonatal anemia; Fetal MCA

1. Introduction

A low red blood cell count or hemoglobin level below the normal range is the clinical definition of anemia. The normal range of hemoglobin in a population is used to define the disorder. A person with this disorder has hemoglobin levels that are two standard deviations below the median, which is the level that would be considered healthy for a population with the same age, gender, and pregnancy status.[1]

Even in industrialized nations, iron deficiency anemia(IDA) is common during pregnancy. This is likely due to inadequate physiologic adaptations to meet the increased iron requirements and to inadequate dietary iron intake. Fetal and maternal health can be severely compromised by IDA that goes untreated and undiagnosed. It is true that IDA is diagnosed using CBC and S. ferritin, and that chronic iron deficiency impacts the mother's overall health by causing weariness and diminished working capacity.[2]

The risks of prenatal morbidity, neurodevelopmental damage, and adult disorders, including diabetes and cardiovascular disease, are all raised in studies that found IUGR.[3]

IUGR is defined as "abdominal circumference>2SD below the mean for gestational age confirmed by serial assessment of the fetal growth parameters".[4]

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Color Doppler in ultrasound machines provides a chance for noninvasive hemodynamic monitoring as it can reliably predict adverse outcomes in SGA fetuses, so surveillance with Doppler is done when suspecting IUGR.[5]

The Cerebro-Umbilical ratio(C/U ratio) is a measure of the blood distribution between the placental and cerebral areas. Above 1 is the usual. Prior to 34 weeks of pregnancy, there is a strong correlation between fetal development, hypoxia, and behavior; however, this correlation weakens in cases of hypoxia due to increased placental resistance and cerebral vasodilation.[6]

The aim of this study is to evaluate the accuracy of fetal MCA doppler ultrasound scan in reduction of neonatal anemia in iron deficiency anemic patients.

2. Patients and methods

From November 2023 through November 2024, 120-patients were enrolled in this prospective observational cohort study. The patients were chosen from the out-patient obstetrics and gynecology clinics at Al-Hussein Hospitals, which are affiliated with Al-Azhar University. Data gathered using a randomized sampling procedure.

Both the study's protocol and the participants' written informed consents have been cleared by the local ethics committee.

Methods of randomization:

The randomization process involved selecting every nth patient fulfilling the inclusion criteria until the target sample size was achieved, ensuring unbiased selection.

Inclusion criteria:

Patients aged 20-35 years with a singleton living fetus≥36 weeks' gestation on admission(calculated by LMP and by 1st trimester ultrasound), and Patients with hemoglobin levels below 10gm/dl.

Exclusion criteria:

Patients with multifetal pregnancy, patients with other medical disorders, such as chronic hypertension, preeclampsia, D.M., and patients with hemoglobinopathies, or blood loss, such as placenta previa, congenital anomalies.

Sample size:

Amin et al.[7] provided the theoretical groundwork for this investigation, and the following assumptions were applied by Epi Info STATCALC to determine the sample size: With an 80% power, the two-sided confidence level is - 95%. I calculated an odds ratio of 1.115 with a 5% margin of error. Epi-Info yielded a maximum sample size of 113 in the end. Therefore, in order to account for potential cases of dropout during follow-up, the sample size was raised to 120 participants.

Methods:

The following were administered to all patients:

Each patient gave their informed consent after a thorough history was taken, including their current health status, any past medical conditions or surgeries, any complaints they may have had, and their family medical history. A thorough evaluation was carried out, which included taking vital signs(temperature, blood pressure, heart rate, and respiration rate) as well as looking for symptoms of paleness, cyanosis, jaundice, and enlarged lymph nodes.

Medical history, including any signs of frailty, the date and method of delivery, obstetric code, and last menstrual period(LMP).

Examination such as assessment for pallor, tachycardia, fundal height, ruptured membranes, and cervical dilation. Complete blood count(CBC) and serum ferritin were collected.

Ultrasonography:

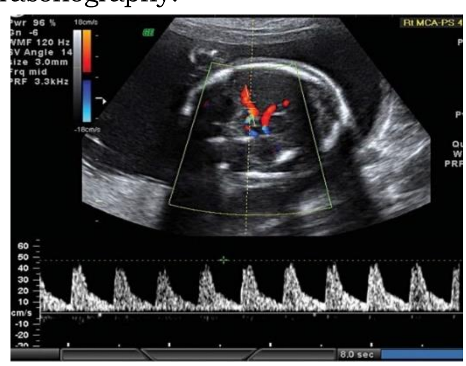

Figure 1. Insonation of the middle cerebral artery, with angle correction. Measurement of peak systolic velocity(cm/s).Brennand,[8]

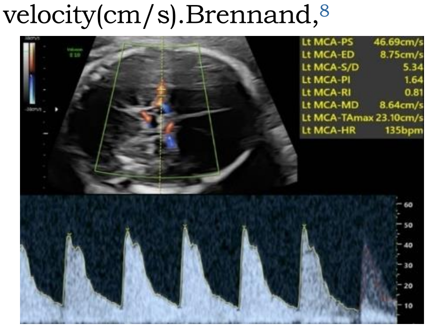

Figure 2. Acquisition of MCA Doppler flow. Note the use of the fetal suture as a window to capture MCA flow with minimal angle correction.Melber,[9]

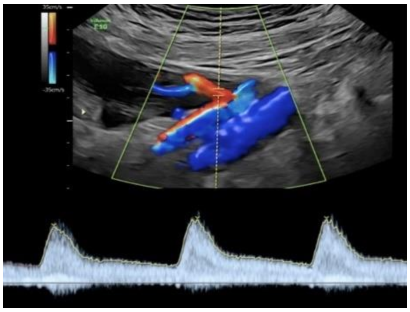

Figure 3. Normal uterine artery Doppler waveform obtained at the level where the uterine artery passes over the external iliac artery before it enters the uterine body.Melber,[9]

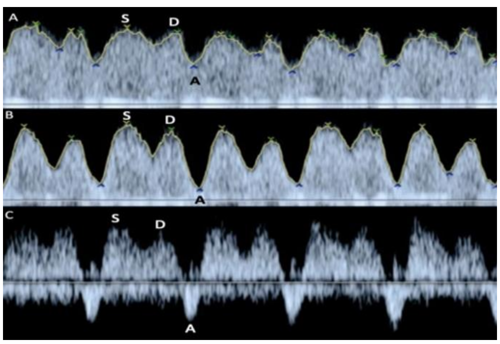

Figure 4. DV progression from normal to abnormal flow, producing the characteristic reversal in the A-wave. A: Normal ductus venosus Doppler flow waveform. B: Resistive A-wave, and C: reversed A-wave.Melber,[9]

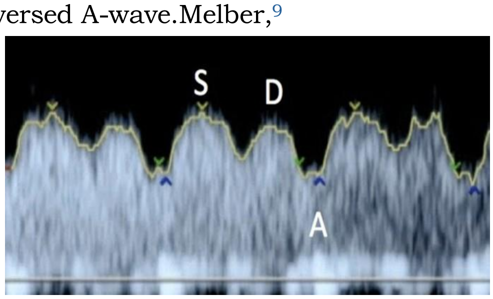

Figure 5. Normal ductus venosus Doppler waveform. S: peak systolic velocity during ventricular systole; D: passive ventricular filling during the first half of diastole; A(A-wave): atrial contraction during the second half of diastole or"atrial kick".Melber,[9]

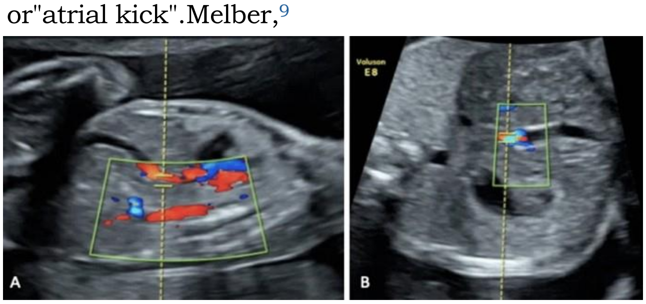

Figure 6. Ductus venosus Doppler flow acquisition in sagittal (a)and axial (b)planes.Melber,[9]

The ultrasound was performed to evaluate viability, placental site, estimated fetal weight(EFW), and amniotic fluid index using a 3.5MHz curvilinear transducer on a Voluson 58-GE ultrasound machine(Seoul, South Korea), equipped with color-flow mapping and a 50-Hz high-pass filter. Measurements were performed in a semi-recumbent position. Color-flow imaging was used to visualize the middle cerebral artery(MCA). Pulsed Doppler was performed with a sample volume of 5mm.

MCA-PSV Evaluation:

The foetal head's transverse segment was used for ultrasonographic identification of the circle of Willis and the MCA. At an angle of approximately twenty degrees, pulsed-wave Doppler was applied to the front one-third of the MCA. Without any indication of fetal movement or respiration, three consecutive waveforms were captured. We used the maximum value, expressed in cm/s, as the peak systolic velocity(PSV). The PSV was recalculated using the MoM as a multiplier, and this result was then utilized for additional analysis.

Group-A (Mild Anemia):

Patients with hemoglobin concentrations between 9,000-10,900mg/dL received oral ferrous fumarate at a therapeutic dose of 100-200mg/day. Iron therapy continued for three months to replenish stores, with adequate replacement confirmed when ferritin levels reached 50ng/mL to maintain maternal and neonatal iron stores.

Group-B(Moderate Anemia):

Patients with hemoglobin concentrations between 7,000 and 8,900 mg/dL received iron sucrose parenterally. The dose was calculated using the following formula: IV iron dose(mg)=blood volume(dL)×hemoglobin deficit×3.3, which reflects the amount of iron (in milligrams) in each gram of hemoglobin. Blood volume(mL)=65mL×weight in kg(blood volume/kg=65mL/kg). Blood volume(dL)=blood volume(mL)/100. Hemoglobin deficit=difference between observed and desired hemoglobin(desired hemoglobin: 11g%).

Group-C(Severe Anemia):

Patients with hemoglobin concentrations<7,000 mg/dL received blood transfusions in the form of packed red blood cells(RBCs). Each unit contained 200mL RBCs, equivalent to 200mg iron.

Primary Outcome:

Evaluation of the accuracy of fetal MCA Doppler ultrasound scan in predicting neonatal anemia in iron-deficient anemic patients.

Secondary Outcomes:

Prenatal Outcomes:

Fetal growth restriction(estimated fetal weight<2.5kg). Assessment of amniotic fluid index abnormalities (oligohydramnios or polyhydramnios) . Evidence of intrauterine hypoxia(based on Doppler studies).

Natal Outcomes:

Low Apgar score(<7 at 1 and/or 5minutes). Mode of delivery(vaginal delivery, assisted delivery, or cesarean section). Signs of fetal distress during labor(abnormal heart rate patterns).

Postnatal Outcomes:

Incidence of neonatal respiratory distress syndrome(RDS); neonatal intensive care unit(NICU) admission rates; neonatal weight at birth(<2.5kg); and Evidence of neonatal hypoxia(cord blood pH<7.2).

Statistical analysis:

I used SPSS for all analyses. P-value<0.05 indicated statistical significance. If data were not normally distributed, means and standard deviations or medians with interquartile ranges were used to describe continuous variables such as maternal age, gestational age, hemoglobin levels, and serum ferritin. Categories like parity, anemia severity, and delivery style were summarized as frequencies and percentages.

The primary and secondary outcomes were newborn anemia rates (hemoglobin<7g/dL and/or hematocrit<30%) given as percentages. Frequencies and percentages were used to characterize fetal growth restriction, amniotic fluid abnormalities, and neonatal outcomes(RDS, NICU admission, low Apgar scores).

To assess categorical factors, including anemia severity, neonatal anemia status, mode of delivery, and NICU admission, chi-square or Fisher's exact tests were used. Anemia severity groups were compared using independent t-tests or Mann-Whitney U-tests based on normality testing for continuous variables such as MCA-PSV levels and birth weight.

The sensitivity, specificity, PPV, and NPV of MCA-PSV in predicting newborn anemia were assessed using a ROC curve. Diagnostic accuracy was assessed using AUC.

Maternal hemoglobin, MCA-PSV, and fetal weight were used in logistic regression to predict neonatal anemia. Significant predictors have aORs with 95% confidence intervals. Multiple imputation was used for continuous variables like hemoglobin and MCA-PSV if the missing rate was above 5%. Imputing missing categorical variables via mode substitution. To ensure robustness of findings with and without imputed data, sensitivity analyses were performed.

3. Results

Table 1. Demographic data of the studied women.

Demographic data		N	Mean	SD	p-value
Age	mild	47	27.19	4.735	0.470
	mod	62	26.19	3.883	
	severe	11	26.73	3.228	
	Total	120	26.63	4.183	
GA	mild	47	37.72	0.452	0.559
	mod	62	37.81	0.398	
	severe	11	37.82	0.405	
	Total	120	37.78	0.419	
BMI	mild	47	32.3	1.43	0.43
	mod	62	31.4	2.43	
	severe	11	29.9	2.54	
	Total	120	32.4	1.483	
Parity	mild	47	1.2	0.5	0.43
	mod	62	1.3	0.9	
	severe	11	2.4	0.8	
	Total	120	1.9	0.23	

GA=Gestational age, SD=standard deviation.

There was no statistically significant difference regarding age and gestational age,p=0.470 and 0.559. The mean age for the whole population was 26.6±4.1 years, while the mean GA was 37.7±0.41 weeks.

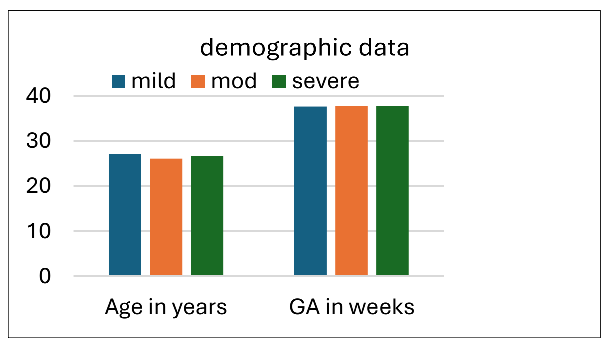

Figure 7. Demographic data of the pregnant women.

Table 2. Hb level among neonates according to severity of anemia.

Hb level	Severity of anemia	N	Mean	SD	95%CI LB	95%CI UB	p-value
	mild	47	9.7957	0.08329	9.7713	9.8202	0.001
	mod	62	8.0694	0.48775	7.9455	8.1932	
	severe	11	6.4909	0.20226	6.3550	6.6268	
	Total	120	8.6008	1.11833	8.3987	8.8030	

The mean Hb level for neonates with mild anemia was 9.7±0.08g/dl, mod anemia 8.06±0.4g/dl while for neonates with severe anemia was 6.4±0.2g/dl,p=0.001.

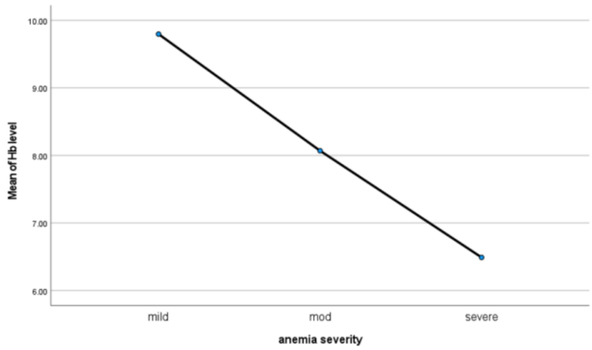

Figure 8. PLOT curve of HB level.

Table 3. Vital signs among women according to the severity of anemia.

Vital signs		N	Mean	SD	95% CI LB	95% CI UB	P-value
HR	mild	47	122.38	12.760	121.64	129.13	0.589
	mod	62	126.73	13.912	119.19	126.26	
	severe	11	128.64	12.266	115.40	131.88	
	Total	120	123.85	13.281	121.45	126.25	
SBP	mild	47	114.23	13.549	110.26	118.21	0.611
	mod	62	114.94	13.023	111.63	118.24	
	severe	11	110.64	12.738	102.08	119.19	
	Total	120	114.27	13.152	111.89	116.64	
DBP	mild	47	72.72	9.019	70.08	75.37	0.412
	mod	62	73.03	8.832	70.79	75.28	
	severe	11	69.09	10.747	61.87	76.31	
	Total	120	72.55	9.076	70.91	74.19	

The mean Heart rate for mild anemia was 122.3±12.7, for mod anemia 126.7±13.9, and for severe anemia 128.6±12.2b/m, p=0.589. On the other hand, the mean SBP and DBP for mild anemia was 114.2±13.5, 72.7±9.019, for mod anemia 114.9±13.07, 73.03±8.8, and 110.6±12.7 and 69.09±10.7mmHg, p=611, p=0.412.

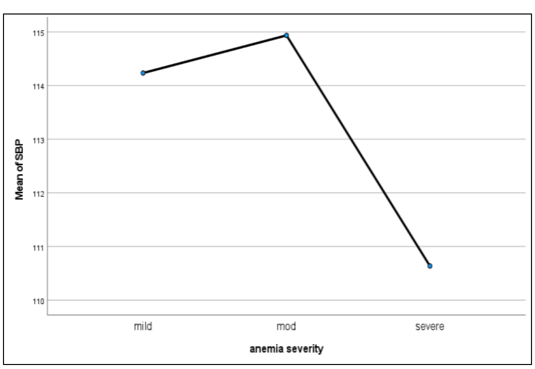

Figure 9. PLOT curve of mean SBP.

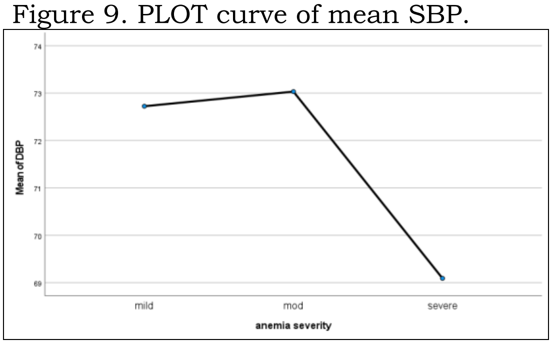

Figure 10. PLOT curve of mean DBP.

Table 4. Low APGAR score, NICU admission and EFW.

		Low APGAR score at 5min		NICU		EFW<2500g	
		Frequency	%	Frequency	%	Frequency	%
anemia	mild	4	3%	3	2%	9	7%
severit	mod	8	6%	7	5%	14	11%
y	severe	9	7.5%	10	8%	11	9%

Neonates with severe anemia constituted(7.5%) of low APGAR score, while mod and mild anemic neonates constituted 8(6%) and 4(3%) with low APGAR score. On the other hand, neonates with severe anemia were admitted 10(8%) at NICU, while 11(9%) neoantes with EFW<2500g.

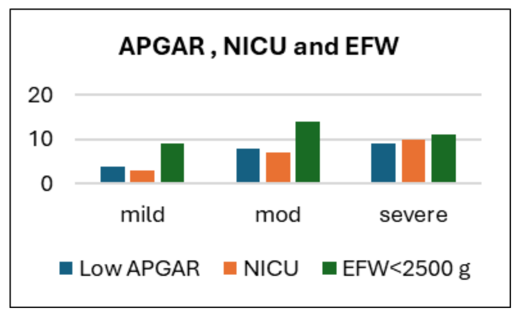

Figure 11. APGAR, NICU and EFW.

Table 5. Measurement of doppler among pregnant women.

	MILD ANEMIA	MOD ANEMIA	SEVERE ANEMIA	P-VALUE
MCA PSV	1.9±0.4	1.83±0.43	1.6±0.35	0.4
MCA PI	1.59±0.17	1.6±0.27	1.32±0.21	0.001
MCA RI	0.76±0.06	0.74±0.05	0.67±0.08	0.001

MCA PI and RI showed a decreasing trend with the increasing severity of anemia with the mean value of 1.59±0.17 and 0.76±0.06 in mild anemia group, 1.6±0.27 and 0.74±0.05 in moderate anemia group, and 1.32±0.21 and 0.67±0.08 in severe anemia group.

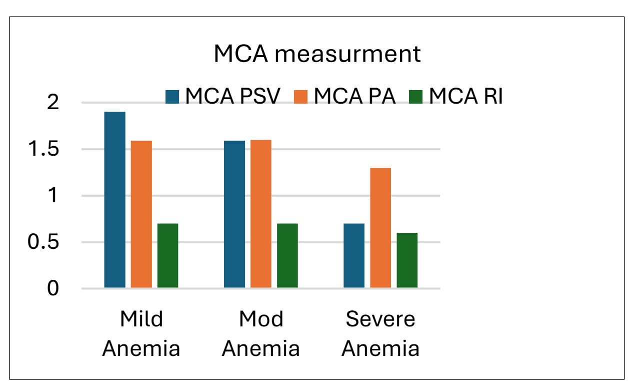

Figure 6. MCA measurement.

Table 12. Measurement of doppler among newborn(N=120)

	ANEMIC NEWBORN=12			NON-ANEMIC NEW BORN=112	P-VALUE
	Mild Anemia	Mod Anemia	Severe Anemia		
MCA PSV	1.9±0.4	1.83±0.43	1.6±0.35	1.1±0.12	0.023
MCA PI	1.59±0.17	1.6±0.27	1.32±0.21	1.7±0.430	0.001
MCA RI	0.76±0.06	0.74±0.05	0.67±0.08	0.87±0.034	0.001

Assessment of newborn anemic status revealed that 112-newborn were delivered without anemia, while 8-newborn were delivered and diagnosed with anemia. There was statistically significant difference between anemic and non-anemic newborn regarding MCA-PSV, MCA-PI and MCA-RI.

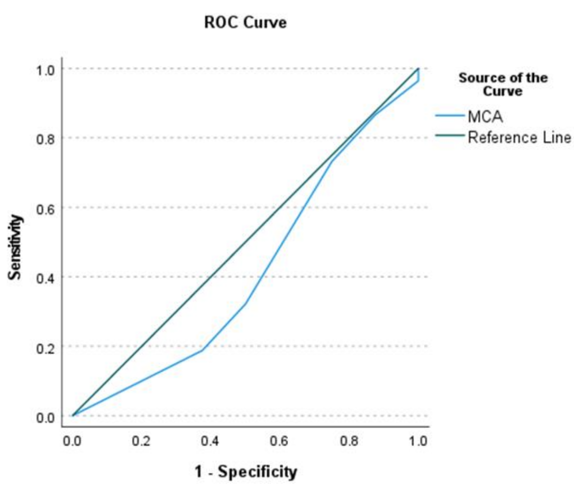

Figure 13. ROC curve of MCA-PSV.

4. Discussion

The findings of this study underscore the role of maternal anemia in shaping fetal hemodynamics and neonatal outcomes. One of the most critical observations is the significant variation in neonatal hemoglobin levels across anemia severity groups. The lower hemoglobin levels observed in neonates of severely anemic mothers can be attributed to the reduced iron transfer to the fetus, a hallmark of maternal iron-deficiency anemia.

This aligns with Evidence that maternal anemia limits placental iron availability, directly impacting fetal hemoglobin synthesis.[10]

The poorer neonatal outcomes observed in the severe anemia group further highlight the adverse impact of maternal anemia. Low APGAR scores, higher NICU admissions, and increased rates of low birth weight are consistent with the deleterious effects of fetal hypoxia and growth restriction. These outcomes can be attributed to impaired placental function, which reduces nutrient and oxygen delivery to the fetus, exacerbating the risks of neonatal complications. This is supported by findings from Rani et al.,[11] who reported similar trends in anemic pregnancies.

The absence of significant differences in maternal vital signs(HR, SBP, and DBP) across anemia severity groups is noteworthy. This stability can be attributed to compensatory mechanisms in chronic anemia, such as increased cardiac output and reduced systemic vascular resistance, which help maintain maternal hemodynamic stability despite varying degrees of anemia. These findings are consistent with observations by Abdel-Megeed et al.,[10] who noted that maternal vitals may not always correlate with anemia severity.

Doppler ultrasound emerged as a valuable non-invasive tool in this study, particularly for assessing MCA PI and RI. The high specificity of these indices(86.8% and 86.9%) underscores their reliability in ruling out severe fetal anemia, although their moderate sensitivity highlights the need for complementary diagnostic approaches. This aligns with research by Srikumar et al.,[12] who emphasized the importance of using Doppler parameters in conjunction with clinical and laboratory findings to improve diagnostic accuracy.

The significant differences in neonatal hemoglobin levels across anemia severity groups in this study(mild:9.7±0.08g/dL; moderate:8.06±0.4g/dL; severe:6.4±0.2g/dL; p= 0.001) emphasize the critical relationship between maternal anemia and neonatal hematological health. These findings are supported by Abdel-Megeed et al.,[10] who similarly reported that neonates born to anemic mothers exhibited hemoglobin levels ranging between 5.0-10.9g/dL, compared to 11.0-13.8g/dL in non-anemic pregnancies.

Contrary to expectations, MCA PSV in this study did not show statistically significant differences across anemia severity groups(severe:1.6±0.35, moderate:1.83±0.43, mild:1.9±0.4;p=0.4). This result diverges from studies such as Maisonneuve et al.,[13] where PSV was identified as a sensitive marker of fetal anemia in cases of Rh isoimmunization, with PSV values exceeding 1.5 times the median in anemic fetuses.

Low APGAR scores(<7 at five minutes) were significantly more common in neonates of severely anemic mothers(7.5%) compared to those with moderate(6%) and mild(3%) anemia. These findings align with Rani et al.,[11] who reported even higher rates of poor APGAR scores(15% in severe anemia, 8% in moderate anemia, and 2% in mild anemia). The reduced APGAR scores can be attributed to fetal hypoxia, impaired placental function, and poor intrauterine growth, all of which are exacerbated by maternal anemia. A low APGAR score is a strong indicator of neonatal distress, requiring immediate medical intervention. This study's findings underscore the need for routine maternal anemia screening, as early intervention could prevent neonatal asphyxia and improve immediate postnatal outcomes.

The incidence of NICU admissions in this study was highest among neonates born to severely anemic mothers(8%), compared to those with moderate(5%) and mild anemia(2%). These findings mirror those of Bakhtiar et al.,[14] who reported NICU admission rates of 18% in severe anemia cases. NICU admissions are often necessitated by complications such as respiratory distress, low birth weight, or neonatal anemia requiring transfusions. The current study's lower NICU admission rates may reflect advancements in antenatal care, including improved anemia management and closer fetal monitoring. Nevertheless, the consistent association between anemia severity and NICU admissions highlights the long-term burden of maternal anemia on healthcare systems and neonatal morbidity.

Low birth weight(<2500g) was observed in 9% of neonates in the severe anemia group, compared to 11% in the moderate group and 7% in the mild group. Kidanto et al.,[15] found similar trends, with 20% of neonates born to severely anemic mothers classified as low birth weight, compared to 12% in moderate anemia and 5% in mild anemia. Low birth weight is a consequence of intrauterine growth restriction(IUGR), which results from placental insufficiency and reduced nutrient transfer caused by maternal anemia. The findings of this study reinforce the need for nutritional interventions during pregnancy to address anemia and mitigate its effects on fetal growth.

Maternal heart rate(HR), systolic blood pressure(SBP), and diastolic blood pressure(DBP) showed no significant differences across anemia severity groups in this study (HR:severe=128.6±12.2 bpm, moderate= 126.7± 13.9 bpm, mild=122.3±12.7 bpm; p=0.589). These findings are consistent with Abdel-Megeed et al.,[10] who also reported stable maternal vital signs in anemic pregnancies. Chronic anemia often triggers compensatory mechanisms, such as increased cardiac output and reduced systemic vascular resistance, which help maintain hemodynamic stability. The absence of significant changes in maternal vitals underscores the importance of Doppler studies, as they reveal fetal hypoxia and hemodynamic changes that might not be evident in maternal parameters.

MCA PI and RI demonstrated moderate sensitivity(57% and 66%) but high specificity(86.8% and 86.9%) in predicting neonatal anemia. These findings align with Srikumar et al.,[12] who reported similar diagnostic accuracy for MCA Doppler indices in detecting fetal anemia. The high negative predictive value(89.6% for PI and 91.2% for RI) observed in this study confirms that normal MCA Doppler values can reliably rule out severe fetal anemia. However, the moderate sensitivity highlights the need for complementary diagnostic tools, such as maternal hemoglobin levels and neonatal hematological parameters.

Comparing the present study to international studies, the findings of this study align with regional research conducted in Egypt, such as Abdel-Megeed et al.,[10] which reported similar trends in MCA Doppler indices and neonatal outcomes among anemic pregnancies. Both studies observed a progressive decrease in MCA PI and RI values with increasing anemia severity, consistent with the brain-sparing effect.

The relationship between maternal anemia and neonatal outcomes such as low birth weight, low APGAR scores, and NICU admissions was particularly notable in this study. Similar studies, such as Bakhtiar et al.,[14] found comparable associations, with a higher incidence of NICU admissions among severely anemic mothers. This trend is likely related to the decreased oxygen delivery to the fetus, leading to complications such as respiratory distress syndrome and the need for intensive care after birth.

Regarding low birth weight, this study found that 9% of neonates born to severely anemic mothers had a birth weight less than 2500grams. These results mirror those observed by Kidanto et al.,[15] who documented similar rates of low birth weight in pregnancies complicated by anemia.

4. Conclusion

Embryonic MCA In cases where the mother has iron deficiency anemia, the Doppler parameters PI and RI may be useful in predicting the risk of newborn anemia. However, the moderate sensitivity and PPV suggest that these parameters should be used in combination with other clinical and laboratory findings for optimal management of these high-risk pregnancies.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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