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ORIGINAL ARTICLE

Maternal Anemia and Fetal Doppler Indices in the Third Trimester of Pregnancy

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Abstract

Background: **Complications for the mother and fetus are usually linked to maternal anemia. It may also cause a shift in fetal blood flow by decreasing the oxygen supply to the developing baby.**

Aim: **The aim of this study is to assess the impact of maternal anemia on the umbilical artery and middle cerebral artery Doppler indices in the third trimester of pregnancy.**

Patients and methods: **This was a prospective case-control study on 200 pregnant women separated into two groups at El-Hussein University Hospital: 100 pregnant women with varying degrees of anemia (Mild, Moderate, and Severe) were involved in group I (the study group), whereas 100 pregnant women without anemia (group II) served as the control group from January to June of 2021.**

Result: **There was a high statistically significant decrease in middle cerebral artery (MCA) resistance index (RI), pulsatility index (PI), S/D ratio and an increase in uterine artery (UA) RI, PI, S/D ratio with the increase in severity of anemia in the studied groups. There was a high statistically significant difference in the C/U ratio between the studied groups (*P* value < 0.001), it was lower than normal in moderate and severe anemic groups (1.08 ± 0.14 and 0.99 ± 0.12, respectively).**

Conclusion: **Maternal anemia had a considerable impact on the fetal UA and MCA Doppler indices, and this impact grew as the anemia's severity rose.**

Keywords: Anemia, Cerebral/umbilical artery, Hemoglobin

1. Introduction

One of the most important global public health issues is anemia, which ranks as the second most common cause of disability worldwide. One of the typical medical issues during pregnancy is it. There is a physiological drop in hemoglobin during pregnancy due to the increased plasma volume to decrease blood viscosity to aid in better circulation in the placenta. This drop is considered normal to a limited level.[1]

Maternal anemia is defined by the World Health Organization (WHO) as a low blood hemoglobin level below 11.0 g/dl. The degree of anemia was classified as light if the hemoglobin level was between 9.0 and 10.9 g/dl, moderate if it was between 7.0 and 8.9 g/dl, and severe if it was below 7.0 g/dl.[2] According to the 2011 report of WHO, it was estimated that 32.4 million pregnant women (38.2%) were anemic. Africa and Asia showed the highest prevalence of anemia with pregnancy compared with other regions (44.6% and 39.3%, respectively). 30% of pregnant ladies in Egypt were anemic and the percentage of severe anemia among pregnant women reached 0.3%.[3]

Iron deficiency is regarded to be the main cause of anemia in underdeveloped countries, despite the fact that there are other potential causes as well. Another factor contributing to the high frequency of anemia in Africa is the presence of contagious illnesses including HIV, helminths infestations, and malaria.[4] Health for the mother and the fetus or kid may be at risk from anemia during pregnancy. The mother's bad health outcomes include weariness, reduced productivity, immune system impairment, higher risk of cardiac decompensation, and a rise in

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postpartum hemorrhage incidence. 23% of maternal mortality in underdeveloped nations are indirectly caused by anemia during pregnancy.[5]

Preterm birth, low birth weight, intrauterine growth restriction, intrauterine and neonatal death, and infant mortality are among risks that are increased by anemia during pregnancy. The negative consequences are inversely correlated with the degree of anemia.[6] Abdel-Megeed and colleagues[7] conducted a study in Egypt in 2018 to detect the effect of maternal anemia on fetal Doppler parameters and reported the presence of a significant difference regarding uterine artery (UA) resistance index (RI), pulsatility index (PI), and C/U ratio between anemic pregnant patients and the control group, but their research was conducted on little number of control group.

This research is going to use Doppler velocimetry –which is a simple and noninvasive method-to show whether maternal anemia has a significant effect on the fetal health or not and if so, the relation between severity of maternal anemia and fetal affection.

2. Patients and methods

In this prospective case-control research, 200 pregnant women were separated into two groups and studied at El-Hussein University Hospital. 100 pregnant women with varying degrees of anemia (Mild, Moderate, and Severe) were enrolled in group I (the study group), whereas 100 pregnant women without anemia (group II) served as the control group from January 2021 to June 2022.

Patients with gestational ages between 28 and 40 weeks, single pregnancies (determined by their last period or an earlier ultrasound), and a living fetus with appropriate fetal ultrasound characteristics were required for inclusion. While the following criteria were used to exclude people: any significant fetal abnormalities, hemoglobinopathies of any kind, hemolytic anemia, persistent infection-related anemia, Obstetrical conditions such as oligohydramnios or polyhydramnios, Diabetes, preeclampsia, bronchial asthma, and other maternal illnesses.

In exchange for their involvement in the research, all study participants underwent the following: written permission for this participation and record-keeping, the patient's age personal background, Last Menstrual Period (LMP) is a measure of cycle regularity and menstrual history, Previous surgical and medical histories. Additionally, the examination included a general one that included checking the patient's pulse, blood pressure, temperature, and breathing rate as well as a chest and heart exam, an abdominal exam, and an obstetric examination.

Maternal venous samples: Samples were withdrawn for hemoglobin concentration. Trans-abdominal Doppler ultrasound examinations were performed to eligible pregnant ladies at third trimester with special concern about fetal biometry, major congenital anomalies, and amniotic fluid index, Doppler study of the umbilical, fetal middle cerebral arteries was done. Approval of the concerned administrative Ethical authority was obtained, written informed consent after explaining the aim of the study was obtained from all studied pregnant ladies and Confidentiality was obtained in data collection, examination and investigation results.

Preparatory phase included Review of literature and Construction of questionnaire. While in the second phase (collection of data), the researcher introduced himself to all participants. Nature and aim of study were explained to eligible pregnant females, the data was collected, examination was carried out by the researcher, and investigations were carried out under his supervision, controls matched cases in age, gestational age, and in having neither chronic diseases nor diseases related to pregnancy.

2.1. Statistical analysis

The IBM SPSS software program version 20.0 was used to analyze data entered into the computer (Armonk, NY: IBM Corp) number and percentage were used to describe qualitative data. The normality of the distribution was examined using the Kolmogorov–Smirnov test. Range, mean, standard deviation, median, and interquartile range were used to describe quantitative data (IQR). After that, the proper statistical analyses were used. The significance of the findings was assessed at the 5% level.

3. Results

Regarding demographic information, Table 1 demonstrated that there was no statistically significant difference between the analyzed groups and anthropometrics except parity. 60% of cases were multiparous while more than half (57%) of controls were nulliparous. (Table 2) showed that there was high statistically significant difference between the studied groups as regard hemoglobin. In cases, according to severity of anemia there was 44 pregnant women in mild cases (hemoglobin 9.0–10.9 g/dl), 30 pregnant women in moderate cases (hemoglobin 7.0–8.9 g/dl) and 26 pregnant women in severe cases (hemoglobin <7.0 g/dl).

Table 3 showed that there was a high statistically significant difference between degree of anemia severity and middle cerebral artery (MCA) Doppler

Table 1. Comparison between the studied groups as regard demographic data and anthropometrics.

	Cases ($n = 100$)	Controls ($n = 100$)	Test	P
Maternal age				
Range	22–40	22–40	$t = 0.675$	0.501
Mean ± SD	31.24 ± 5.14	30.75 ± 5.13		
Residence	Number (%)	Number (%)		
Rural	23 (23.0)	22 (22.0)	$\chi^2 = 0.029$	0.866
Urban	77 (77.0)	78 (78.0)		
Occupation				
Not working	69 (69.0)	75 (75.0)	$\chi^2 = 0.893$	0.345
Working	31 (31.0)	25 (25.0)		
Parity				
Nulliparous	40 (40.0)	57 (57.0)	$\chi^2 = 5.785$	0.016*
Multiparous	60 (60.0)	43 (43.0)		
Gestational age				
Range	31–40	31–40	$t = 0.277$	0.782
Mean ± SD	35.47 ± 2.87	35.58 ± 2.74		
Weight				
Range	60.5–92.5	63–91	$t = 0.221$	0.825
Mean ± SD	76.08 ± 6.91	76.29 ± 6.85		
Height				
Range	158–173	158–173	$t = 0.996$	0.320
Mean ± SD	165.04 ± 4.89	165.7 ± 4.47		
BMI				
Range	24.2–31.4	24.6–30.9	$t = 0.528$	0.598
Mean ± SD	27.9 ± 1.95	27.76 ± 1.88		

t stands for the student *t*-test; χ^2 for the chi square test; P for the P value when comparing two categories; and *for statistical significance at P 0.05.

indices RI, PI and S/D ratio. These indices decrease as the severity of anemia increases. For example, MCA PI is 1.39 in women with severe anemia, 1.41 in women with moderate anemia, 1.49 in those with mild anemia and 1.51 in control group.

Table 4 illustrated that all UA Doppler indices (RI, PI, SD ratio) except PSV increase as the severity of anemia increases, and this increase had a high statistic indication (P values < 0.001). UA RI is 0.71 among pregnant ladies having severe anemia compared with 0.69 among those with moderate anemia compared with 0.62 among those with mild anemia compared with 0.59 among those with normal hemoglobin level. According to (Table 5), there is a substantial statistical difference between

Table 2. Comparison between the studied groups as regard hemoglobin.

	Cases ($n = 100$)	Controls ($n = 100$)	Test	P
Hemoglobin				
Range	5.3–10.8	11–13.9	$t = 20.888$	<0.001*
Mean ± SD	8.4 ± 1.66	12.35 ± 0.9		
Severity of anemia	Number (%)	Number (%)		
Normal	0 (0.0)	100 (100.0)	$\chi^2 = 200.0$	<0.001*
Mild	44 (44.0)	0 (0.0)		
Moderate	30 (30.0)	0 (0.0)		
Severe	26 (26.0)	0 (0.0)		

mild, moderate, and severe anemia severity when it comes to fetal weight, heart rate, and AFI.

4. Discussion

In the current study, we hypothesized that the fetus of the anemic mother could be adversely affected, and would exhibit abnormalities in their parameters during antenatal care. To test this hypothesis, using a prospective design, we studied 100 pregnant anemic ladies and the same number of ladies was studied as control as regard socio-demographic data, general maternal and abdominal examination, fetal ultrasound assessment with more concern on UA and MCA Doppler indices.

The age of the patients in the case and control groups was matched to exclude the effect of age on the results. Multiparous women were more prone to be anemic versus nulliparous. Parity is a risk factor for maternal anemia due to frequent pregnancies, inadequate spacing, and poor nutritional replacement.

In same line with our results, Amin and colleagues[8] conducted a prospective comparative study on 512 pregnant women attended Kasralainy Maternity Hospital with IDA and classified them into three groups of mild, moderate, and severe anemia, they reported that the percentage of multiparous women was the highest among severe anemic group (90.24%), also they formed 80% of moderately anemic and 39.1% of mild anemic groups.

The study between our hands showed no significant difference between cases and controls in BMI. The reverse was mentioned by Amin and colleagues[8] who showed that more than half (56.1%) of the studied patients with severe anemia were underweight compared with 10% in patients with mild or moderate anemia. The different results may be accused to the different methodology as no control group was studied. Also, BMI can be affected by many factors like genetic factors, dietary, and physical lifestyles, and muscle mass.

Regarding MCA Doppler indices, our results showed that the more the severity of anemia, the lower MCA RI, PI and S/D ratio numbers. The means of MCA RI were 0.83 ± 0.04, 0.79 ± 0.07, 0.74 ± 0.08, and 0.7 ± 0.07 in the control, mild anemic, moderate anemic, and severe anemic groups, respectively with a high significant difference. No significant difference was noticed between the different groups as regard MCA PSV. This is supported by results of Abdel-Megeed and colleagues[7] who reported similar results.

The fetal blood flow is redistributed to maintain cerebral oxygenation as a result of maternal anemia, known as the brain-sparing reflex, which is thought

Table 3. Relation between anemia severity and MCA Doppler indices.

Middle cerebral artery	Normal ($n = 100$)	Mild ($n = 44$)	Moderate ($n = 30$)	severe ($n = 29$)	Test	*P*
RI						
Range	0.76–0.97	0.70–0.92	0.62–0.90	0.60–0.85	F = 42.86	<0.001*
Mean ± SD	0.83 ± 0.04	0.79 ± 0.07	0.74 ± 0.08	0.70 ± 0.07		
PI						
Range	1.35–1.79	1.34–1.77	1.22–1.71	1.12–1.69	F = 7.576	<0.001*
Mean ± SD	1.51 ± 0.11	1.49 ± 0.13	1.41 ± 0.15	1.39 ± 0.19		
S/D ratio						
Range	2.99–4.64	2.86–4.78	2.64–4.61	2.55–4.08	F = 6.379	<0.001*
Mean ± SD	3.85 ± 0.45	3.89 ± 0.61	3.62 ± 0.58	3.42 ± 0.49		
Peak systolic						
Range	31.4–53	31.3–52.3	33.2–52.1	32–52	F = 0.7	0.553
Mean ± SD	42.49 ± 6.49	40.85 ± 6.85	41.59 ± 4.74	42.22 ± 7.32		

F stands for one-way ANOVA; *P* for the *P* value when comparing two categories; and * for statistical significance at *P* 0.05.

to limit the oxygen supply to the fetus (particularly in severe instances). This response is a key player in how fetuses adapt to oxygen deprivation.[9] End diastolic flow rises in the presence of substantial maternal anemia, which lowers MCA-RI values.[10]

In the contrary to MCA indices, this study clarified that most of umbilical artery indices increased as the severity of anemia increased. Means of UA RI were 0.59 ± 0.08, 0.62 ± 0.08, 0.69 ± 0.06, and 0.71 ± 0.06, means of UA PI were 0.79 ± 0.01, 0.81 ± 0.1, 0.89 ± 0.21, and 1.03 ± 0.28, means of UA S/D ratio were 2.17 ± 0.08, 2.2 ± 0.06, 3.08 ± 0.62, and 3.32 ± 0.62 in the control, mild anemic, moderate anemic, and severe anemic groups, respectively. There was no significant difference between groups regarding UA PSV.

This is in agreement with Jain and colleagues[9] who revealed that the mean UA RI was 0.6 ± 0.09, 0.63 ± 0.05, 0.66 ± 0.05, and 0.7 ± 0.04 among controls, mild, moderate, and severely anemic groups, respectively (*P* value 0.001). In the control group, the mean of UA PI was 0.79 ± 0.03 compared with 0.78 ± 0.08 in mild anemic group, 0.78 ± 0.08 in the moderate anemic group and, 1.35 ± 0.3 in the severely anemic group (*P* value 0.000). Regarding UA S/D ratio, means were 2.11 ± 0.04, 2.19 ± 0.03, 2.85 ± 0.36, and 3.21 ± 0.81 in the control, mild anemic, moderate anemic, and severely anemic groups, respectively (*P* value 0.000).

As the gestation advances, the high vascular resistance seen in the first trimester progressively reduces because of the increased volume of the umbilical artery. Because of this reduction in vascular resistance, blood flow in the umbilical artery remains unimpeded in the forward direction during the whole cardiac cycle. The normal UA waveform resembles a sawtooth, with the flow direction constantly going forward. In a healthy pregnancy, the UA impedance, as measured by the RI, drops from 0.756 to 0.609. Abnormal waveforms indicate that diastolic flow is either missing or reversed. Maternal anemia causes a rise in RI values due to a decrease in end diastolic flow, which is succeeded by an absence of end diastolic flow (RI = 1), and lastly, a reversal of end diastolic flow Kuber and colleagues.[11]

Table 4. Relation between anemia severity and UA Doppler indices and C/U ratio.

Umbilical artery	Normal ($n = 100$)	Mild ($n = 44$)	Moderate ($n = 30$)	severe ($n = 29$)	Test	*P*
RI						
Range	0.48–0.72	0.50–0.74	0.56–0.76	0.60–0.78	F = 25.828	<0.001*
Mean ± SD	0.59 ± 0.08	0.62 ± 0.08	0.69 ± 0.06	0.71 ± 0.06		
PI						
Range	0.65–0.99	0.62–1.09	0.64–1.5	0.75–1.8	F = 18.963	<0.001*
Mean ± SD	0.79 ± 0.1	0.81 ± 0.1	0.89 ± 0.21	1.03 ± 0.28		
S/D ratio						
Range	2.08–2.71	2.11–2.29	2.13–3.91	2.18–4.62	F = 130.254	<0.001*
Mean ± SD	2.17 ± 0.08	2.2 ± 0.06	3.08 ± 0.62	3.32 ± 0.62		
Peak systolic						
Range	26.2–49.8	25.8–47.3	26.6–44	27.8–52.3	F = 1.201	0.311
Mean ± SD	35.5 ± 6.4	34.9 ± 5.34	36.64 ± 4.25	37.38 ± 7.27		
MCA/UA RI ratio						
Range	1.1–2.02	0.97–1.84	0.82–1.36	0.8–1.27	F = 48.06	<0.001*
Mean ± SD	1.43 ± 0.21	1.32 ± 0.24	1.08 ± 0.14	0.99 ± 0.12		

F stands for one-way ANOVA; *P* for the *P* value when comparing two categories; and * for statistical significance at *P* 0.05.

Table 5. Relation between anemia severity and other fetal parameters.

Obstetrics outcome	Normal ($n = 100$)	Mild ($n = 44$)	Moderate ($n = 30$)	Severe ($n = 29$)	Test	*P*
Fetal weight						
Range	2.2–4.1	1.7–3.1	1.8–3.1	1.8–3.1	F = 36.819	<0.001*
Mean ± SD	3.16 ± 0.57	2.41 ± 0.47	2.42 ± 0.39	2.39 ± 0.43		
Fetal heart rate						
Range	121–158	103–146	102–147	102–145	F = 27.293	<0.001*
Mean ± SD	140.36 ± 10.73	125.11 ± 12.43	123.43 ± 13.1	128.5 ± 13.16		
Amniotic fluid index						
Range	6.6–16.9	3.2–14.2	3.1–13.9	4.2–13.2	F = 11.164	<0.001*
Mean ± SD	11.37 ± 2.8	9.13 ± 3.44	8.41 ± 3.31	9.24 ± 2.79		

The distribution of fetal blood flow (between the cerebral and placental areas) depends on the C/U resistance ratio, which is determined as the ratio of MCA RI to UA RI. This figure is usually more than 1.1 during a typical pregnancy. Pregnancy age has no bearing on its accuracy as a predictor of fetal growth restriction or hypoxia Abdel and colleagues.[12] By calculating C/U ratio and comparing between the four groups in this item we found that, the mean C/U ratio was 1.43 ± 0.21 in the non-anemic group, 1.32 ± 0.24 in the mildly anemic group, 1.08 ± 0.14 in the moderately anemic group, and 0.99 ± 0.12 in the severely anemic group with a highly significant difference (*P* value < 0.001).

In case of hypoxia, the increase in UA RI (due to increase in placental resistance) and at the same time, vasodilatation of the fetal MCA leads to decrease in the C/U ratio Abdel and colleagues.[12] Amin and colleagues[8] reported supportive results. They found that C/U values were within normal among group of mild anemia (2.24 ± 0.25). While, C/U values were below normal range in moderate and severe anemia groups (1.11 ± 0.14 and 0.95 ± 0.07, respectively) which were corrected after 10-day treatment (10 days later 1.89 ± 0.38 and 2.08 ± 0.2 in moderate and severe anemic groups, respectively).

4.1. Conclusion

In conclusion, it was discovered that maternal anemia significantly affected the fetal Doppler indices in both the middle cerebral artery and the umbilical artery in the third trimester of pregnancy. The severity of the anemia has a direct correlation with this consequence.

Limitations of our investigation involve the nature of the study design. Because it was a prospective case-control study, no results on the temporal association were revealed (i.e. risk factors responsible for developing anemia). Furthermore, the study was conducted at a single tertiary care facility (El-Hussein University Hospital), with the vast bulk of study cases coming from urban areas. As a result, the study's findings could not be generalized to Egypt's pregnant population because the majority of these women live in rural areas with limited access to antenatal care, and the prevalence of anemia would have been even higher if the study had been conducted in the general population.

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There are no conflicts of interest.

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