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Original Research Article

Effect of maternal anaemia on foetal Doppler indices during third trimester of pregnancy

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ABSTRACT

Background: Anaemia is amongst the most common medical disorders encountered during pregnancy all over the world. India has a high rate of anaemia in pregnant women. Anaemia has a recognizable effect on both maternal and foetal health during pregnancy and on perinatal outcome, contributing remarkably to maternal morbidity and mortality. Routine foetal monitoring is an essential investigation for such females with special emphasis on obstetrics Doppler ultrasonography. Various changes due to foetal hypoxia due to maternal anaemia can be remarkably appreciated on Doppler helping in timely management. The objective of this study was to evaluate the effect of maternal anaemia on foetal Doppler indices.
Methods: 400 pregnant women were assessed in a cross-section observational study done in the department of Radiodiagnosis in MYH, Indore, India. These women were divided into three groups of mild, moderate and severe anaemia based on the level of haemoglobin.
Results: Umbilical artery resistive and pulsatility indices were found to be increased with the increasing severity of anaemia while middle cerebral artery indices and CPR showed a decreasing trend with the increasing severity of anaemia.
Conclusions: We found that severe maternal anaemia is associated with marked adaption in foetal haemodynamics. Obstetrics Doppler can be used as an accurate measure of surveillance for foetal monitoring and will help in appropriate management.

Keywords: Anaemia, Pregnant women, Doppler ultrasonography

INTRODUCTION

Globally, anaemia has been recognized as the most common form of nutritional deficiency worldwide, specifically in developing countries. It is considered a serious global public health problem that particularly affects young children and pregnant women. Pregnancy is a physiological state with altered hormonal and biochemical state. Increased demand which is increased even more in multigravida females especially in less spaced pregnancies, along with the background characteristics like low socioeconomic status, early age of marriage associated with increase in susceptibility to infectious diseases like hookworm infestations may serve to be the underlying factors associated with prevalence of anaemia during pregnancy.

In pregnancy, iron deficiency is found to be the most common cause as the demand of iron increases during late pregnancy by six to seven times.[2] The WHO defines anaemia as a haemoglobin less than 13 g/dl in adult men and less than 12 g/dl in non-pregnant adult women while in pregnant women anaemia is said to occur when haemoglobin is less than 11 g/dl.[1] It is more prevalent in developing countries than developed countries with prevalence of approx. 53.9% is seen in pregnant women of

Madhya Pradesh, India.[3] Varying degrees of maternal anaemia results in different types of compensatory mechanisms in foetus which may or may not result in adverse perinatal outcome. Increased risk of IUGR, premature delivery and perinatal mortality are found to be associated with maternal anaemia. Routine foetal monitoring is an important aspect in these pregnant women and has become an essential tool in the past decade. Ultrasound with its non-invasive, non-ionising radiation features has become the most widely acceptable investigation in pregnancy. Any placental and foetal dysfunction in such foetuses can be assessed using Doppler sonography since the haemodynamic changes will be demonstrated well before the clinical manifestation of obstetric complications. Timely detection of foetal hypoxia due to anaemia is possible with Doppler ultrasonography which in turn will help in appropriate management. Thus, chance of perinatal complications and in turn perinatal morbidity and mortality can be reduced.

Aim and objectives

The aim of this study was to study the effect of maternal anaemia on foetal Doppler indices- pulsatility index (PI) and resistive index (RI) of the umbilical artery and middle cerebral artery, cerebroplacental ratio (CP ratio) in 3rd trimester.

METHODS

This study was conducted in department of radio diagnosis M. G. M. Medical College and M. Y. Hospital, Indore from Apr-2021 to Aug-2022. in close association with department of obstetrics and gynaecology. A total of 400 patients who attended the obstetrics outpatient and inpatient ward during their third trimester, were included in the study. They were randomized into three sub groups according to degree of anaemia namely mild, moderate and severe. The pregnant women in active labour, with any haemoglobinopathies, any diagnosed maternal morbidity or with congenital foetal anomaly were excluded from this study.

The study was performed using real time grey scale and colour Doppler ultrasonography using convex probes of frequency ranging from 3 to 5 MHZ. The scan was performed with the patients in supine position on an exam table. For umbilical arterial (UmA) Doppler, free loop along the longitudinal axis of the vessels was focussed and then with adequate sample gate and scaling Doppler pattern was measured. UmA Doppler indices will be considered abnormal if values are above 95th percentile. For middle cerebral arterial (MCA) Doppler, circle of Willis and then proximal MCA was identified. The pulsed-wave Doppler gate should then be placed at the proximal third of the MCA. MCA Doppler indices are considered abnormal when the values are below 5th percentile. Cerebroplacental ratio (CPR) is calculated by the ratio of MCA pulsatilitty index and UmA pulsatility index.

Statistical analysis

Summarization of continuous variables like gestational age and ratio was done using mean and standard deviation. ANOVA test and Pearson correlation coefficient was calculated to find the correlation between quantitative variables. Statistical significance is checked at 5% level of significance (p value<0.05). The statistical software SPSS 15.0 was used for analysis of the data and Microsoft word and Excel were used to generate graphs and tables.

RESULTS

Patients were divided based on haemoglobin values with value 10-10.9 g/dl were considered under mild anaemia group, 7-9.9 g/dl in moderate anaemia group and <7 g/dl were in severe anaemia group as depicted in Table 1.

Maximum number of patients are noted in mild anaemia group i.e. 245 (61.25%), followed by 120 (30%) in moderate and 35 (8.75%) in severe anaemia group. Maximum pregnant patients belonged to younger age group of 20-25 years with maximum (131) in mild anaemia category. Pregnant women's gravidity and gestational age at the time of ultrasound were correlated with severity of anaemia as shown in Figure 1 and 2. Most patients were primigravida at the time of scan and were of mild anaemia category. Gestational age at the time of scan ranged from 28-40 weeks and we found that 170 out of 400 patients were primigravida with maximum in mild category. However, none of the above factor was found to have a significant correlation with the severity of anaemia in pregnant female (p>0.005).

Table 2 depicts the distribution between the three studied groups regarding UA resistive index, pulsatility index and peak systolic velocity. UmA resistive index ranged from 0.40-0.80 in mild anaemia group, 0.50-0.80 in moderate anaemia group and 0.51-0.97 in severe anaemia group. UmA pulsatility index ranged from 0.60-1.80 in mild anaemia group, 0.70-1.30 in moderate anaemia group and 0.80-1.73 in severe anaemia group. UmA peak systolic velocity (cm/s) ranged from 19-74 in mild anaemia group, 21-89 in moderate anaemia group and 16-63 in severe anaemia group. In this study, mean UmA RI and PI increases with the severity of anaemia with maximum value seen in severe anaemia. There is significant association between mean UmA RI and PI with anaemia severity (p<0.05). UmA PSV shows no correlation with the maternal anaemia.

Table 3 depicts the distribution between the three studied groups regarding mean values of MCA (middle cerebral artery) resistive index, pulsatility index and peak systolic velocity. MCA resistive index ranged from 0.60-0.94 in mild anaemia group, 0.60-0.90 in moderate anaemia group and 0.48-0.81 in severe anaemia group. MCA pulsatility index ranged from 1.20-1.30 in mild anaemia group, 1.10-2.80 in moderate anaemia group and 0.90-2.00 in severe anaemia group. MCA peak systolic velocity (cm/s) ranged

from 25-75 in mild anaemia group, 26-94 in moderate anaemia group and 24-68 in severe anaemia group. In this study, mean MCA RI, PI and PSV decreases with the severity of anaemia with maximum value seen in severe anaemia. There is significant association between mean MCA RI and PI with anaemia severity ($p<0.05$). But, MCA PSV shows no correlation with the maternal anaemia. Cerebroplacental ratio ranged from 0.94-3.10 in mild anaemia group, 0.90-2.54 in moderate anaemia group and 0.64-2.0 in severe anaemia group. CPR was found to be decreasing with severity of anaemia, maximum mean value of 1.77±0.26 was seen in mild anaemia group. Significant decrease of mean CPR with anaemia severity progression was found (Table 4).

Table 1: Distribution of pregnant patients on basis of haemoglobin values.

Anaemia	Range (g/dl)	N	Percentage (%)	Mean±SD (g/dl)
Mild	10-10.9	245	61.25	10.5±0.30
Moderate	7-9.9	120	30	9.1±0.57
Severe	<7	35	8.75	6.3±0.59
Total		400	100	

Table 2: Distribution and comparison of mean value of umbilical artery resistive index, pulsatility index and peak systolic velocity with severity of anaemia.

UmA Doppler indices		Anaemia			P value
		Mild (n=245)	Moderate (n=120)	Severe (n=35)	
UmA RI	Range	0.40-0.80	0.50-0.80	0.51-0.97	0.000
	Mean±SD	0.59±0.05	0.62±0.06	0.68±0.09	
UmA PI	Range	0.60-1.80	0.70-1.30	0.80-1.73	0.000
	Mean±SD	0.89±0.13	0.96±0.14	1.15±0.21	
UmA PSV*	Range	19-74	21-89	16-63	0.252
	Mean±SD	39.32±16.89	41.93±9.17	39±9.96	

Note: *PSV values are expressed as cm/s; p value is significant if <0.05.

Table 3: Distribution and comparison of mean value of middle cerebral artery resistive index, pulsatility index and peak systolic velocity with severity of anaemia.

MCA Doppler indices		Anaemia			P value
		Mild (n=245)	Moderate (n=120)	Severe (n=35)	
MCA RI	Range	0.60-0.94	0.60-0.90	0.48-0.81	<0.001
	Mean±SD	0.76±0.05	0.74±0.06	0.65±0.08	
MCA PI	Range	1.20-1.30	1.10-2.80	0.90-2.00	<0.000
	Mean±SD	1.58±0.16	1.53±0.27	1.30±0.21	
MCA PSV*	Range	25-75	26-94	24-68	0.104
	Mean±SD	50±9.3	48.36±10.3	46.8±11.1	

Note:*PSV values are expressed as cm/s; P value is significant if <0.05.

Table 4: Association between mean cerebroplacental ratio and different anaemia groups.

CPR	Anaemia		
	Mild (n=245)	Moderate (n=120)	Severe (n=35)
Range	0.94-3.10	0.90-2.54	0.64-2.0
Mean	1.77	1.66	1.16
SD	0.26	0.36	0.31
P value<0.053 (significant)			

Note: P value is significant if <0.05.

Figure 4 shows CPR<1 in a pregnant female with severe anaemia on colour Doppler assessment. Pearson correlation was applied to the all the Doppler indices with haemoglobin values where all parameters showed a positive correlation with Hb except UmA pulsatility index and resistive index which had a negative correlation and

no correlation was found between UmA and MCA peak systolic velocity (Table 5). On Color Doppler ultrasonography (a) umbilical artery showed normal end diastolic flow and normal PI value, (b) MCA PI value was decreased and on calculation cerebroplacental ratio was <1. Patients were distributed in the three categories based on their normal and abnormal Color Doppler indices value and then compared with each other. UmA Doppler indices will be considered abnormal if values are above 95th percentile. UmA Doppler indices will be considered abnormal if values are above 95th percentile. CPR is considered abnormal if its value is below <1. These are depicted in Table 6.

Table 5: Correlation between haemoglobin and MCA PSV, MCA RI, MCA PI, UA PSV, UA RI, UA PI AND CPR level.

Parameters		MCA PSV	MCA PI	MCA RI	UmA PSV	UmA PI	UmA RI	CPR
Hb	Pearson correlation	0.093 No	0.325 Positive	0.407 Positive	0.006 No	-0.455 Negative	- 0.363 Negative	0.407 Positive
	P value	0.06	0.000	0.000	0.911	0.000	0.000	0.000

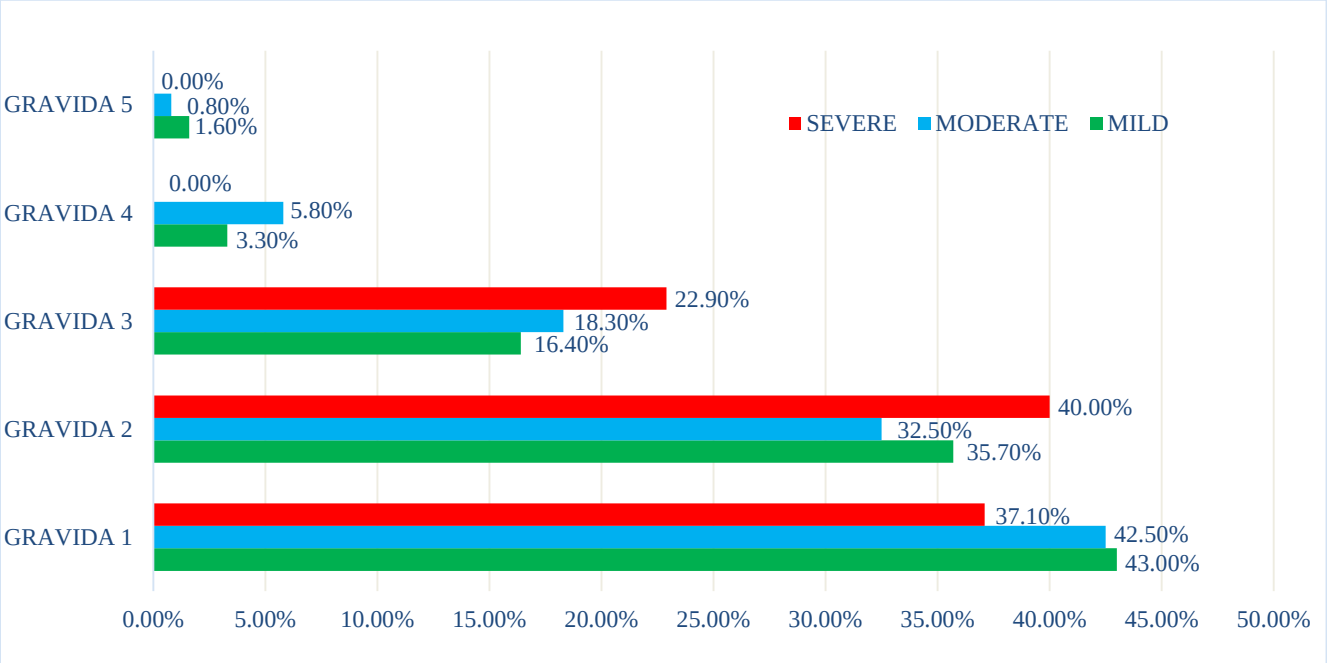

Figure 1: Distribution and comparison of pregnant patients according to gravida with severity of anaemia.

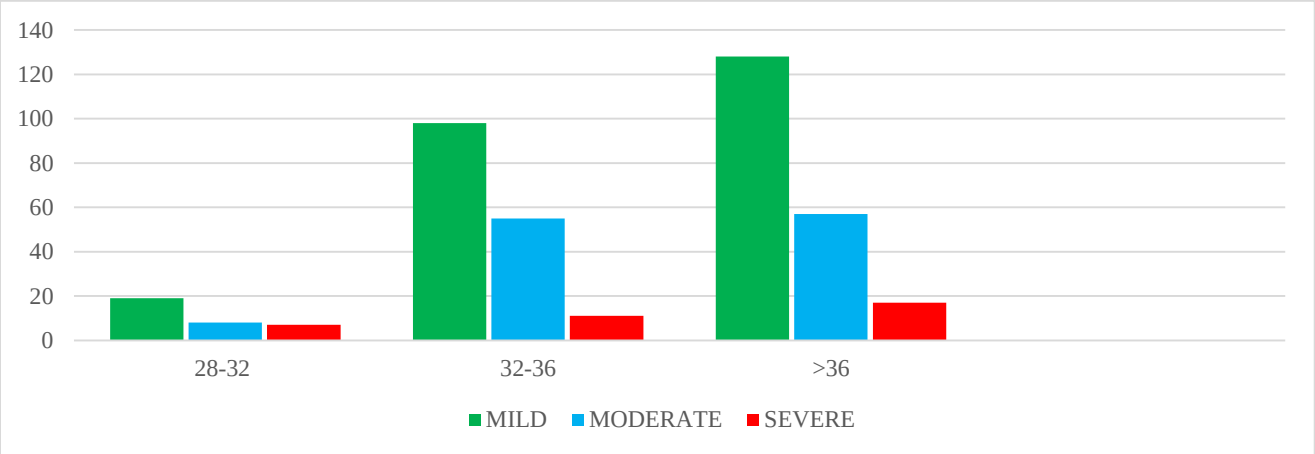

Figure 2: Distribution and comparison of pregnant patients as per mean gestational age (MGA) at the time of ultrasound with severity of anaemia.

Table 6: Distribution and comparison of various foetal Doppler indices with severity of anaemia.

Parameters	Mild n (%)		Moderate n (%)		Severe n (%)		P value
	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal	
MCA PSV (cm/s)	128 (52.2)	117 (47.7)	68 (56.6)	52 (43.3)	22 (62.8)	13 (37.1)	0.42
MCA PI	195 (79.5)	50 (20.4)	61 (50.8)	59 (49.1)	14 (40)	21 (60)	0.001
MCA RI	157 (64)	88 (35.9)	59 (49.1)	61 (50.8)	3 (8.5)	32 (91.4)	0.001
UA PSV (cm/s)	206 (84)	39 (16)	109 (91)	11 (9)	31 (88.6)	4 (11.4)	0.45
UA PI	67 (27.3)	178 (72.6)	20 (16.6)	100 (83.3)	2 (5.71)	33 (94.2)	0.003
UA RI	65 (25.7)	180 (73.4)	21 (17.5)	99 (82.5)	4 (11.4)	31 (88.5)	0.002
CPR	244 (99.6)	1 (0.4)	116 (96.6)	4 (3.3)	23 (65.7)	12 (34.2)	0.001

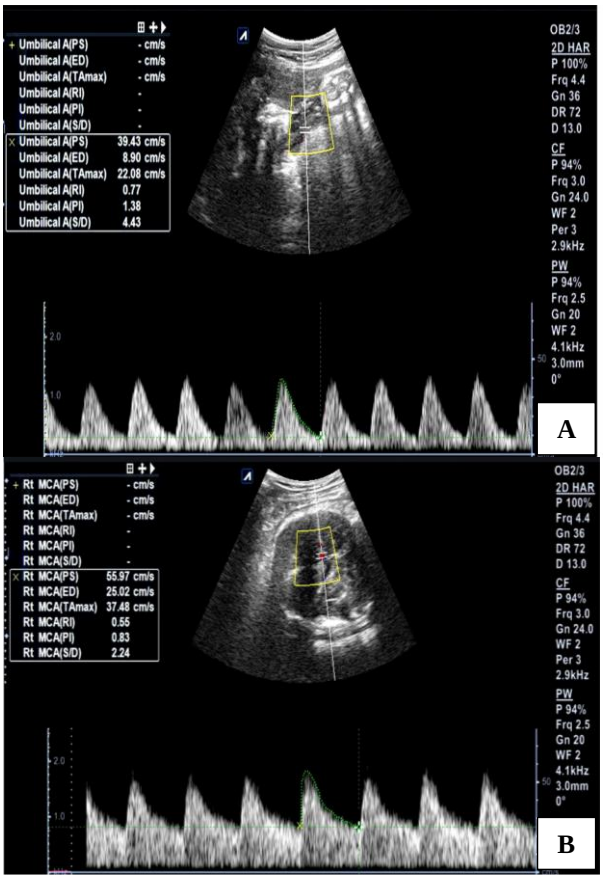

Figure 3: A 23 years old multigravida with gestational age 34 weeks 5 days with 4.1 g/dl Hb (severe anaemia) On Color Doppler ultrasonography (A) umbilical artery showed normal end diastolic flow and normal PI value; and (B) MCA PI value was decreased and on calculation cerebroplacental ratio was<1.

DISCUSSION

Globally, anaemia is considered a serious global public health problem that particularly affects young children and pregnant women. Varying degrees of maternal anaemia results in different types of compensatory mechanisms in foetus which may or may not result in adverse perinatal outcome. Increased risk of IUGR, premature delivery and perinatal mortality are found to be associated with maternal anaemia. Umbilical artery and MCA represent the distribution of foetal blood flow at level of placental and foetal brain, respectively. Color Doppler sonography has become the foremost investigation to detect any abnormality regarding hemodynamic environment of foetus caused due to foetal hypoxia as a result of maternal anaemia.

We found 245 out of 400 patients (61.25%) in mild anaemia group, followed by 120 (30%) patients in moderate anaemia group and least patients 35 (8.75%) in severe anaemia group. This prevalence results were similar with the results obtained by Suryanarayan et al where he found 71.4% patients were in mild, 24.1% in moderate and 4.3% in severe anaemic group.[4] However, Sinha et al found moderate anaemia to be most prevalent in his study.[5]

In current study, the age of patients ranged from 18-39 years of age with maximum number of patients in 20-25 years age group followed by 26-30 years age group. In 20-25 years age group maximum number of patients i.e. 131 (53.4%) were seen in mild anaemia group. The mean age of patients was 25.14±4.14 years in mild anaemia group, 24.36±4.14 years in moderate anaemia group and 24.2±3.5 years in severe anaemia group. No association of maternal age with anaemia was found. Our findings are similar to the results obtained in the study done by Stefanovic et al who reported that the maternal age and gestational age were similar in both moderate and severely anaemic pregnant women.[6]

We found primigravida females to be more common in our study with number 170 (42.5%) followed by 140 (35.2%) females with 2 pregnancies. Most of the primigravida belonged to mild anaemia group with 106 (43%) pregnant females. No association of gravidity of female with anaemia was found. This correlated well with the study done by Suryanarayana et al and Singh et al where they did not find a significant association between gravidity and anaemia.[4,7]

Most of the women were found to be of more than 36 weeks of gestation with 128 (52.2%) in mild, 57 (47.5%) in moderate and 17 (48.5%) in severe anaemia groups. No significant association of anaemia with the gestation age

of women was found in our study. These findings were similar to the study done by Lumbanraja et al.[8]

Umbilical artery resistive index showed a rising trend with the severity of anaemia in our study. The UmA RI in mild anaemia group had a mean value 0.59±0.05, mean value in moderate anaemia group was 0.62±0.06 and mean value in severe anaemia group was 0.68±0.09. The increasing trend of UmA RI showed statistical significance between different anaemia groups as the severity of anaemia is increased. UA impedance is measured in terms of resistive index or RI which decreases with the progression of pregnancy. The decrease in vascular resistive allows continuous flow through out cardiac cycle. In pregnancies complicated by anaemia there is reduction in end diastolic flow causing rise in resistive and thus with increasing severity there is rise in resistive. The results are in consonance with the findings obtained in Abdel Mageed et al and Abdel Samie et al study.[10,16] Also, the results correlated well with the study done by Rafiq et al where mean UmA RI was more in severe anaemia group (0.64±0.01) than moderate anaemia group (0.617±0.03) which decreased after treatment ($p<0.05$).[12] Similar decrease in UmA RI after treatment of maternal anaemia was found in study done by Mohamad Ihab et al and Ghada A et al.[11] Mean value of umbilical artery pulsatility index in mild anaemia group was found to be 0.89±0.13, 0.96±0.14 in moderate anaemia and 1.15±0.21 in severe anaemia group. UmA PI values in different anaemia groups showed statistically significant difference ($p<0.05$) with the increasing severity of anaemia. PI is calculated by the ratio of difference of systolic and diastolic velocity with maximum velocity. Thus, due to rise in the end diastolic volume during severe anaemia the decrease in PI values was appreciable. Similar results were seen in study done by Abdel Samie et al with mean UmA PI higher in severe anaemia group at 1.11±0.275 than mild or moderate anaemia groups ($p<0.000$).[10] Studies done by Ghada A et al and Rafiq et al showed similar results.[11,12] Harneet et al, Kurmanavicius et al and Srikumar et al described that UmA PI and RI shows a gradual fall over gestation period with a strong negative correlation.[13-15] In our study, we found umbilical artery peak systolic velocity (PSV in cm/sec) mean value in mild anaemia group at 39.32±16.89, in moderate anaemia group at 41.93±9.17, in severe anaemia group at 39±9.96. However, the data was not statistically significant. Similar study done by Kessous et al found no association of UmA PSV with the outcome.[9]

In our study, middle cerebral artery resistive index had a decreasing trend with severity of anaemia. Mean value of MCA RI in mild anaemia group was 0.76±0.05, in moderate anaemia group was 0.74±0.06 and in severe anaemia group 0.65±0.08. The results in our study correlated well with findings of Abdel Mageed et al study where a progressive significant decline ($p<0.05$) was seen with anaemia severity and in control group.[16] Ali A et al also found MCA RI significantly lower in the anaemia group than in the control group.[17] Cerebral circulation is high resistive flow which gradually rises with progression of pregnancy. But in maternal anaemia case, the foetal cerebral circulation shows vasodilatation in order to maintain the foetal oxygenation at satisfactory levels. The most profound effect is seen in severe maternal anaemia.

On evaluation, middle cerebral artery pulsatility index in mild anaemia group ranged from 1.20-1.30 with mean value 1.58±0.16, in moderate anaemia group ranged from 1.10-2.80 with mean value 1.53±0.27, in severe anaemia group ranged from 0.90-2.00 with mean value 1.30±0.21. Due to increased end diastolic volume with progression of anaemia the decrease in PI values was discernable. The decrease in MCA PI in our study was significant and corroborated well with findings of Mageed et al study, Ali et al and Samie et al results who also showed a decreasing trend of MCA PI with severity of anaemia.[16,19,10]

The MCA PI and RI values change throughout normal pregnancy. Previous studies done on MCA PI and RI by Ebbing et al, Mari et al, Tarzamni et al, Komwilaisak et al and Srikumar et al have shown a parabolic curve for MCA PI and RI with a plateau between 28 and 30 weeks likely due to increased requirement of brain during early and late pregnancy.[15,20-23] They also showed a strong negative correlation of MCA PI and RI with the gestation age after 30 weeks.

Middle cerebral artery peak systolic velocity (PSV in cm/sec) in mild anaemia group ranged from 25-75 with mean value 50±9.3, in moderate anaemia group ranged from 26-94 with mean value 48.36±10.3, in severe anaemia group ranged from 24-68 with mean value 46.8±11.1. There was no statistically significance in between different anaemia groups ($p>0.05$) regarding MCA PSV. These findings are similar to the findings obtained by Ali A et al showing no association of MCA PSV with anaemia.[17]

Mari et al 2000 said that Doppler assessment of the peak systolic velocity of MCA blood flow is a non-invasive method of monitoring alloimmunised pregnancies at risk of foetal anaemia.[18] They said that risk of anaemia was high in foetuses with a peak systolic velocity of 1.50 times the median or higher.

In our study, CPR was calculated using ratio of MCA PI with UA PI. In mild anaemia group mean value of CPR was 1.77±0.26, 1.66±0.36 in moderate anaemia group and 1.11±0.31 in severe anaemia group. There was statistically significance decline in mean value of CPR between different study groups. This ratio was found to be more reliable and accurate for the prediction of hypoxia, foetal growth retardation, and behaviour than the UA or MCA PI in the evaluation of various antenatal and perinatal complications.[24,25] CP ratio reflects the status of redistribution of the cardiac output to the cerebral circulation, which improves accuracy in predicating adverse outcome compared to MCA and UA Doppler alone. It should be >1 in normal foetuses but foetuses with hypoxia as in severe anaemia will have this ratio at <1

value. Thus, it is supposed to be more physiological in the measurement of centralization of foetal blood flow. CP ratio is proven to be an important adjunct parameter to help in monitoring perinatal and antenatal complications in pregnancies complicated with anaemia.[26] This agreed with the results of Megeed et al, Stefanović et al where CPR values were less than 1 in severe anaemia pregnant females.[6,16] Ali et al also detected decreased CPR value on admission of anaemic pregnant females which improved after treatment.[17]

CONCLUSION

With high prevalence of anaemia, continuous and intense monitoring of pregnant females has become imperative. Obstetrics Doppler has been a crucial parameter in discerning any foetal haemodynamic changes with high accuracy for the past few decades. The umbilical artery parameters (PI, RI) show an increasing trend with the decrease of haemoglobin values or increase in severity of anaemia while MCA PI and RI have shown a positive correlation with the haemoglobin values. Furthermore, the cerebroplacental ratio has also decreases with the severity of anaemia. It includes both the middle cerebral and umbilical artery pulsatility index as its components making it even a better parameter than MCA and UA parameters alone. In our study, low cerebroplacental ratio is a result of increased placental resistive and decrease in MCA resistive as a result of foetal hypoxia causing foetal cerebral vasodilatation. The early detection of these changes will prevent both mother and foetal complications as appropriate management can be further ensued. Thus, Doppler USG enables a better understanding of the hemodynamic changes and has therefore become one of the most important clinical tools for foeto-maternal surveillance in high-risk pregnancies. It can be credited with causing a significant decrease in perinatal mortality and morbidity.

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