ORIGINAL RESEARCH PAPER

Radiodiagnosis

CHANGES IN THE FETAL DOPPLER INDICES DURING LAST TRIMESTER OF PREGNANCY IN CASE OF MATERNAL ANEMIA

KEY WORDS: Changes in the fetal Doppler indices , last trimester of pregnancy , maternal anemia

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ABSTRACT

Maternal anemia is common medical disorder during pregnancy in developing countries like India. WHO, defines anemia in pregnant women as haemoglobin concentration of less than 11 g/dl[1]. Maternal anemia is suspected to markedly reduced the oxygen supply to the fetus, which may be responsible for fetal blood flow redistribution, despite there being no evidence of placental insufficiency[2]. Doppler ultrasound is capable to detect beginning hemodynamic alterations, therefore the method can be utilized in the early detection of maternal and fetal complications. The current study aims to evaluate the effect of different degree of maternal anemia on fetal vascular adaptations by Doppler parameters in umbilical artery and middle cerebral artery in the last trimester of pregnancy.

Methodology: This is a prospective study was conducted on 200 pregnant women for a period of 1 year from February 2019 to July 2020 in Gajra Raja Medical College and Kamla raja hospital who attended obstetrics OPD or indoor department who fulfilling the inclusion criteria required for the study and who agreed to participate after consent approval.

Results: We observed that all the parameters of umbilical artery (PI, RI and S/D ratio) increases , all the parameters of MCA (PI, RI and S/D ratio) decreases and CPR decreases , as the severity of anemia increases in both control and different anemic groups (according to the gestational age) , however maternal anemia has no effect on MCA PSV.

Conclusion: With proper monitoring of the fetal umbilical and cerebral circulation by Doppler examination in the anemic pregnancy, quantify the fetal vascular response and fetal well being to deliver not only a healthy baby but a neurologically healthy baby.

INTRODUCTION

Anemia is most common medical disorders during pregnancy in developing countries like India which encounters serious global health concern. It causes many adverse effects on the mother and the fetus and it contributes significantly to high maternal mortality. Anemia in general is characterized by a decrease in number of red blood cells or less than the normal quantity of hemoglobin[3]. WHO, defines anemia in pregnant women as haemoglobin concentration of less than 11 g/dl and categorized into mild, moderate and severe category in which haemoglobin concentration is from 10.9-10 g/dl , 9.9-7 g/dl and less 7g/dl respectively.[1] Doppler ultrasonography has given insight to the fetal hemodynamics. Doppler velocimetry necessitates the computed analysis of flow patterns, along with the quantitative description of Doppler results by the Resistance and Pulsatility indices. The introduction and the clinical application of the normal reference values of the Doppler velocimetry provides appropriate interpretation of the physiologic fetal blood flow patterns which is the prerequisite of the diagnostic accuracy of the Doppler ultrasound in obstetrics. Abnormal velocity waveforms and indices obtained from the umbilical and fetal middle cerebral arteries may have significance in predicting adverse perinatal outcome of the pregnancy. Consequently it is fundamental for the recognition of early stage fetal hypoxic compromise by understanding the normal reference values of Doppler indices in the fetal middle cerebral artery and in the umbilical artery so that timely intervene the condition that will result in the significant reduction of fetal as well as maternal morbidity and mortality. So the ultimate goal is to delivered not only a healthy baby but neurologically healthy baby and a healthy mother.

MATERIAL AND METHODS

This study will be conducted in Department of Radio diagnosis G R Medical College and J.A. Group of Hospitals, Gwalior in close association with Department of obstetrics and gynecology. All the women attending obstetrics outpatient clinic and inpatient ward of Kamla Raja hospital, fulfilling the inclusion criteria required for the study and who agreed to participate after consent approval.

Sample size:

A total of 200 patients shall be included in the study. They were randomized into two groups: Group one: anemic pregnant females (study group) including 150 women divided according to degree of anemia in 3 sub groups namely mild, moderate and severe (50 women in each sub groups). Group two: non anemic pregnant females (control group) including 50 women.

INCLUSION CRITERIA –

- Gestational age between 24-40 weeks of singleton pregnancy (calculated by their last menstrual period or by earlier ultrasound).
- Fetus is alive.
- Normal fetal ultrasound parameters.

EXCLUSION CRITERIA -

- Experiencing labor.
- Any major congenital fetal anomalies.
- Any hemoglobinopathies, hemolytic anemia, anemia of chronic infection.
- Intra uterine fetal growth retardation, oligohydramnios or polyhydramnios.
- Maternal diseases like diabetes, pre-eclampsia, bronchial asthma, etc

EQUIPMENT AND PROTOCOL:

The study was performed using real time grey scale and colour Doppler ultrasound using convex probes of frequency ranging from 3 to 5 MHZ with the following USG machine , ALOKA IPF-1701B, ESAOTE MODEL5 6400 LC185EXN and MINDRAY DC-30.

STATISTICAL ANALYSIS:

The results of the descriptive analysis were presented in numbers, percentages and as Mean ± SD (Min-Max). for

expected cell count <5 Fisher's Exact /Chi-square test were applied to see the association. Pearson's correlation coefficient was calculated to find the correlation between quantitative variables. Chi-square/ Fisher Exact test and Pearson's correlation were used to find the association between ultrasonography and hormonal parameters. 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.

OBSERVATION AND RESULTS

Table1: Distribution & comparison of patients according to the maternal age

(a)

Age (Yrs)	Non-Anemic (Control Group) (N=50)		Anemic group					
			Mild (N=50)		Moderate (N=50)		Severe (N=50)	
	n	%	n	%	n	%	n	%
<20	7	14	6	12	8	16	6	12
20-25	20	40	21	42	22	44	17	34
26-30	18	36	17	34	12	24	15	30
>30	5	10	6	12	8	16	12	24
Chi-square=6.172						p-value=0.723		

(b)

Age (Yrs)	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	18-34	18-35	18-35	18-36
Mean	**25.08**	**24.74**	**24.74**	**26.24**
S.D.	**4.208**	**4.384**	**4.694**	**4.822**
f value =1.234		p-value=0.299		

Table2: Distribution & comparison of patients according to the order of pregnancy

(a)

Gravida	Non-Anemic (Control Group) (N=50)		Anemic group					
			Mild (N=50)		Moderate (N=50)		Severe (N=50)	
	n	%	n	%	n	%	n	%
G1	23	46	26	52	25	48	16	32
G2	20	40	13	26	12	26	14	28
G3	5	10	7	14	8	16	12	24
>G3	2	4	4	8	5	10	8	16
Chi-square=14.130				p-value=0.118				

(b)

Gravida	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	1-4	1-4	1-4	1-4
Mean	**1.76**	**1.78**	**1.86**	**2.24**
S.D.	**0.80**	**0.97**	**1.03**	**1.08**
f value =2.637		p-value =0.051		

Table3: Distribution & comparison of patients according to the Mean Gestational age (MGA)at the time of ultrasound

(a)

MGA (in completed weeks)	Non-Anemic (Control Group) (N=50)		Anemic group					
			Mild (N=50)		Moderate (N=50)		Severe (N=50)	
	n	%	n	%	n	%	n	%
24-32	35	70	36	72	30	60	34	68
33-36	14	28	12	24	16	32	13	26
>36	1	2	2	4	4	8	3	6
Chi-square=3.243				p-value=0.790				

(b)

MGA (incompleted weeks)	Non-Anemic (Control Group)(N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	24-37	24-37	24-37	24-37
Mean	**30.40**	**30.44**	**31.64**	**29.92**
S.D.	**3.15**	**3.79**	**3.31**	**3.84**
fvalue=2.15		p-value =0.096		

Table4: Distribution & comparison of patients according to the Gestational age at which the delivery occurs

(a)

GA (in completed weeks)	Non-Anemic (Control Group)(N=50)		Anemic grouap					
			Mild (N=50)		Moderate (N=50)		Severe (N=50)	
	n	%	n	%	n	%	n	%
<28	0	0	0	0	0	0	0	0
28-32	0	0	1	2	3	6	3	6
33-36	7	14	10	20	11	22	15	30
≥37	43	86	39	78	36	72	32	64
Chi-square=8.637		p-value=0.195						

(b)

GA (in completed weeks)	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	35-40	32-42	31-40	31-39
Mean	**37.76**	**38.72**	**37.18**	**36.62**
S.D.	**1.25**	**2.50**	**2.03**	**2.08**
fvalue=9.99		p-value =0.00		

Table5: Comparison of Haemoglobin between different studied groups

Hb% (in g/dl)	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	11.0-13.8	10.0-10.9	7.0-9.9	5.2-6.9
Mean	**12.16**	**10.62**	**8.92**	**6.26**
S.D.	**0.77**	**0.49**	**0.80**	**0.56**
f value =712.19		p-value =0.0001		

Table6 : Umbilical artery Doppler changes:-

(a)Resistive index-

Um RI	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	0.51-0.70	0.52-0.72	0.56-0.74	0.60-0.78
Mean	**0.60**	**0.63**	**0.66**	**0.70**
S.D.	**0.09**	**0.05**	**0.05**	**0.04**
f value =26.56		p-value =0.0001		

(b) Pulsality index

Um PI	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	0.72-0.86	0.60-0.91	0.68-0.99	0.75-1.88
Mean	**0.79**	**0.78**	**0.78**	**1.35**
S.D.	**0.03**	**0.08**	**0.08**	**0.30**
f value =152.321		p-value =0.000		

(c) Systolic/Diastolic ratio

Um S/D	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	2.01-2.19	2.14-2.26	2.16-3.60	2.19-4.80
Mean	**2.11**	**2.19**	**2.85**	**3.21**
S.D.	**0.04**	**0.03**	**0.36**	**0.81**
f value =71.79		p-value =0.000		

Table7: Middle cerebral artery Doppler changes

(a) Resistive index

MCA RI	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	0.80-0.98	0.78-0.96	0.76-0.91	0.58-0.82
Mean	0.88	0.86	0.84	0.67
S.D.	0.04	0.05	0.04	0.06
f value =186.55 p-value =0.00				

(b)Pulsality index

MCA PI	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	1.40-1.78	1.28-1.75	1.13-1.70	1.10-1.68
Mean	1.60	1.54	1.44	1.39
S.D.	0.17	0.14	0.14	0.16
f value =20.17 p-value =0.0001				

(C)Systolic/Diastolic ratio

MCA S/D	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	2.89-4.80	2.78-4.75	2.76-4.71	2.60-4.2
Mean	3.69	3.68	3.75	3.07
S.D.	0.58	0.60	0.59	0.44
f value =16.53 p-value =0.0001				

(d)Peak systolic velocity

MCA PSV (in cm/sec)	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	30.0-50.9	31.5-50.7	30.5-50.5	30.2-51.0
Mean	41.79	40.94	38.93	40.79
S.D.	5.27	5.10	5.67	5.03
f value =2.607 p-value =0.053				

Table 8: Cerebroplacental ratio(CPR)- MCA PI/UmA PI

CPR	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	0.89-2.36	1.44-2.70	1.16-2.29	0.63-1.80
Mean	2.01	1.99	1.85	1.09
S.D.	0.22	0.29	0.28	0.27
f value =132.609 p-value =0.000				

Table 9: Amniotic fluid Index/Volume (AFI) - by 4 quadrant method at the time of Doppler

AFI (in cm)	Non-Anemic (Control Group) (N=50)	Anemic group		
		Mild (N=50)	Moderate (N=50)	Severe (N=50)
Range	8.5-15.6	8.2-15.9	8.5-13.1	7.5-11.2
Mean	11.36	11.80	11.08	8.84
S.D.	2.08	1.65	1.50	1.36
f value =13.285 p-value =0.00				

Table 10: Maternal complications

Complications	Non-Anemic (Control Group) (N=50)		Anemic group					
			Mild (N=50)		Moderate (N=50)		Severe (N=50)	
	n	%	n	%	n	%	n	%
PPH	2	4	3	6	5	10	8	16
Infections	4	8	7	14	8	16	13	26
Caesarean delivery	6	12	9	18	12	24	15	30
ICU admission	2	4	5	10	8	16	16	32
Maternal Death	0	0	1	2	3	6	4	8

Table11: Fetal complications

Complications	Non-Anemic (Control Group) (N=50)		Anemic group					
			Mild (N=50)		Moderate (N=50)		Severe (N=50)	
	n	%	n	%	n	%	n	%
LBW (<2500 gm)	8	16	11	22	14	28	17	34
Preterm Delivery (<37Week)	7	14	11	22	14	28	18	36
Low APGAR Score(<7) at 5 min	5	10	8	16	12	24	15	30
NICU admission	9	18	12	24	16	32	19	38
Perinatal /early neonatal death	2	4	5	10	7	14	9	18

DISCUSSION

In our study, most of the women were in age group 20-25 year in both control (non- anemic) and different anemic groups which is 20(40%) , 21(42%) , 22(44%) and 17(34%) in control group , mild , moderate and severe anemia groups respectively , as this is the appropriate age for pregnancy in developing countries like India. There was no statistical significant difference in the mean age in between non anemia and different anemia groups(p>0.05). This agrees with result of **Mohamad Ihab et al**[4] who suggests that maternal age were independently associated with maternal anemia.

In this study, most of the patients were primiparous in both control and different anemic groups, which is 23(46%), 26(52%), 25(50%) and 16(32%) in control group , mild , moderate and severe anemia groups respectively. There was no statistical significant difference in the mean parity in between non anemia and different anemia groups(p>0.05). This agrees with result of **Judith Angelitta**[5] who suggests that parity were independently associated with maternal anemia.

Most of the women in our study came for USG in 24-32 week of pregnancy in both control and different anemic groups, which is 35(70%), 36(72%), 30(60%) and 34(72%)in control group, mild , moderate and severe anemia groups respectively. There was no statistical significant difference in the Mean gestation age in between non anemia and different anemia groups(p>0.05). This agrees with result of **Abdel Mageed Ismail et al**[3] who suggests that mean gestational age were independently associated with maternal anemia.

In our study, maximum number of women delivered full term (on or after the 37 weeks) of pregnancy in both the groups. We observed that number of preterm delivery (<37 weeks) increases as the severity of anemia increases which is 7(14%), 11(22%) , 14(28%) and 18(36%) in control group, mild, moderate and severe anemia groups respectively. There was statistically significance noted between control and different studied groups (p<0.05) regarding gestational age at delivery. There are many studies like **Levy et al**[6] which conclude that higher rates of preterm deliveries noted in anemia complicated pregnancy.

Hemoglobin in non-anemia group ranged from 11.0-13.8 , mild anemia group ranged from 10.0-10.9 , moderate ranged from 7.0-9.9 and severe anemia ranged from 5.2-6.9. There was a significant decrease in hemoglobin level in anemic more than non-anemic, these result obeying the inclusion and exclusion criteria.

We observed that all the parameters of umbilical artery (PI, RI and S/D ratio) **increases** as the severity of anemia increases in both control and different anemic groups (according to the gestational age). In our study, there was statistical significant noted in the UmA PI, RI & S/D in between non anemia and different anemia groups (p<0.05) as these values are increased as the severity of anemia is increased. This agreed

with the results of **Abdel Mageed Ismail et al**[3] who showed the similar results. Normally as the pregnancy advanced umbilical artery PI, RI and S/D is gradually decreased (due to increased diastolic flow). **Acharya et al**[7]**, Kurmanavicius et al**[8] and **Maj. Satyabrat et al**[9] described that UmA PI & RI shows a gradual fall over gestation period. In Anemia complicated pregnancy, these values are increased as the severity of anemia is increased (possibly due to increased placental resistance). **Mohamad Ihab et al**[4] and **Ghada A. Abdel Moety et al**[10] showed that after (10 days & at the time of delivery) treatment of anemia there was significant decrease in UmA RI.

We have found that all the parameters of MCA (PI, RI and S/D ratio) **decreases** as the severity of anemia increases in both control and different anemic groups (according to the gestational age) which was statistically significant($p<0.05$). The MCA PI and RI values change throughout normal pregnancy. Previous studies done on MCA PI and RI by **Ebbing et al**[11]**, Mari et al**[12] and **Maj. Satyabrat et al**[9] 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. In Anemia complicated pregnancy, these values are decreased as the severity of anemia is increased (possibly due to decreased cerebral resistance due to hypoxia). This agreed with the results of **Abdel Mageed Ismail et al**[3] who showed the similar results.

We observed that maternal anemia has **no effect** on MCA PSV as there is no statistical significance in our study between non anemia and different anemia groups. **G. Marie et al 2000**[12] 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 fetal anemia.

In our study , CPR **decreases** as the severity of anemia increases in both control and different anemic groups (according to the gestational age). 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. In Anemia complicated pregnancy, CPR is decreased as the severity of anemia is increased (possibly due to increased placental resistance and cerebral vasodilatation due to hypoxia or centralization of blood flow, also known as fetal 'brain sparing effect'). In our study, there was statistical significant noted in the CPR between non anemia and different anemia groups ($p<0.05$) as the value is decreased as the severity of anemia is increased. This agreed with the results of **Abdel Mageed Ismail et al**[3] who showed the similar results. **Georgieff and colleagues**[2] in 1990 stated that maternal anemia is suspected to reduce the oxygen supply to the fetus which may be responsible for fetal blood flow redistribution despite there being no evidence of placental insufficiency. Distribution of fetal blood flow is determined by the CP ratio. This parameter is always >1.1 during normal pregnancy but decreases in cases of fetal hypoxia.

We have found that amniotic fluid index **decreases** as the severity of anemia increases in both control and different anemic groups (according to the gestational age) which was statistical significant ($p<0.05$). In our study oligohydramnios (AFI<5cm in 4 quadrant) is a exclusion criteria but, we have seen that the mean value of AFI is decreasing in moderate and severe anemic patients. **Dr Y. Gaur et al**[13] **2017** conclude that oligohydramnios is frequent in pregnant women with anemia.
In this study, we observed that maternal anemia is associated with various maternal and fetal complications which increases as the severity of anemia increases. Most of the PPH , infections and cesarean delivery were is severe anemia group which is 8(16%) , 13(26%) and 15(30%) respectively. Maximum number of patient admitted to ICU were in severe anemia group which is 16(32%) as compared to the 2(4%) in control group. Maximum number of maternal death were in severe anemia group which is 4(8%) as compared to the control group which is none

In our study, there are increased incidence of fetal complications associated with maternal anemia which increases as the severity of anemia increases. In our study most of the LBW babies , preterm deliveries and low APGAR score were in severe anemia group which is 17(34%), 18(36%) and 15(30%) respectively. Maximum number of neonate admitted to NICU were in severe anemia group which is 19(38%) as compared to the 9(18%) in control group. Most of the early neonatal/ perinatal death were also in severe anemia group which is 9(18%) as compared to the 2(4%) in control group.

There are many studies done on the maternal anemia and its maternal and fetal outcome which shows the similar results [2,3,6,10,14-20].

CONCLUSION

- On completion of the study, analysis of the demographic and obtained Doppler data was done. Among all , maternal age , parity and gestational age of ultrasound is not associated with maternal anemia.
- Preterm delivery is associated with severity of maternal anemia.
- All the parameters of umbilical artery (PI, RI and S/D ratio) **increases** with the severity of anemia.
- All the parameters of MCA (PI, RI and S/D ratio) **decreases** with the severity of anemia.
- Maternal anemia has **no effect** on MCA PSV.
- CPR **decreases** with the severity of anemia with the centralization of blood flow to reduce the resistance in MCA in response to fetal hypoxia.
- Amniotic fluid index **decreases** with the severity of anemia.
- Maternal anemia is one of the cause of poor maternal and perinatal outcome like LBW, low APGAR score, NICU admission, neonatal death, PPH, cesarean delivery and maternal death.
- With proper monitoring of the fetal umbilical and cerebral circulation by Doppler examination in the anemic pregnancy, quantify the fetal vascular response and fetal well being to deliver a neurologically healthy baby.

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