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Fetal vascular adaptation before and after treatment of severe maternal anemia after 32 weeks of pregnancy

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Abstract
Introduction: Anemia among pregnant women is a serious global health concern. It is well known that pregnant women are susceptible to haematological abnormalities that may affect any women of child bearing age. Distribution of fetal blood flow (between the placenta and cerebral region) is determined by the ratio between the cerebral resistance index (CRI) and umbilical resistance index (URI). The combination of increased placental resistance and decreased cerebral resistance, measured using Doppler ultrasonography, is quantified by calculating the cerebral-to-umbilical artery resistance ratio.
Aim: of study is to improve perinatal morbidity and mortality by adequately and timely correction of severe maternal anemia.
Materials and Methods: 30 patients fulfilling inclusion and exclusion criteria selected from the labour room of MCSG, SMS Medical College, Jaipur, with hemoglobin level < 7g/ dl. All the patients underwent Color Doppler sonography at admission further blood transfusion & Iron transfusion was according to Hb level and follow-up done after 10 & 20 days of transfusion. Continuous variables will be summarized as mean and SD and will be analysed by unpaired and paired T test. Nominal and categorical variables will be summarized as proportion (%) and will be analysed by using chi square test and Fisher exact test.
Observations: The study shows that the ratio of mean CRI/ mean URI was 1.22 ± 0.14 at the time of admission and 1.36 ± 0.11 after 10 days of admission that was increased by 0.15 ± 0.02 from the day of admission and it was statistically significant (P<0.001). After 20 days of admission, it was 1.50 ± 0.15, increased by 0.29 ± 0.03 from the day of admission that was statistically significant. In this study, 50% newborns were low birth weight (<2.5kg) and 50% were normal birth weight (>2.5kg). This shows, uteroplacental insufficiency was the cause of low birth weight babies. One more cause would be preterm birth.
Conclusion: Anaemia in pregnancy is one of the causes of poor perinatal outcome like high risk of low birth weight, IUGR babies, low APGAR scores and NICU admissions and overall increases perinatal mortality and morbidity. Hence proper antenatal care and counselling can reduce the occurrence of anaemia in pregnancy. Close monitoring of the fetal umbilical and cerebral circulation by Doppler examination in anemic pregnancies allows the measurement of the amplitude of the fetal vascular response and the fetal recovery as well.

Keywords: Colour Doppler, umbilical artery resistance (URI), cerebral artery resistance (CRI)

Introduction
Anemia among pregnant women is a serious global health concern. According to World Health Organization (WHO) report, about 32.4 million pregnant women suffer from anemia worldwide, of which 0.8 million women are severely anemic. Moreover, 50% cases of anemia are attributable to iron deficiency anemia (IDA) [1]. The centres for disease control and prevention (CDC) defined anemia in iron supplemented pregnant women using cut-off of the 5th percentile-11 g/dl in first and thirst trimester and 10.5 g/dl in the second trimester [2]. Severe maternal anemia reduces the oxygen supply to the growing fetus, leading to the redistribution of fetal blood flow. In the presence of fetal hypoxemia, fetal blood flow becomes centrally distributed to preserve cerebral oxygenation, known as the brain-sparing reflex; this plays a major role in fetal adaptations to oxygen deprivation. Distribution of fetal blood flow (between the placenta and cerebral region) is determined by the ratio between the cerebral resistance Index (CRI) and umbilical resistance index (URI) [3]. UA Doppler is most commonly used for the monitoring and timing of delivery of the fetus compromised by FGR [4]. Increase impedance in the umbilical artery becomes evident only when at least sixty percent of the placental bed is obliterated [5].

Aim: To study the relationship to foetal vascular status to maternal anemia.

Materials & Methods

This hospital based interventional longitudinal study was conducted in the Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur (Rajasthan) from April 2017 to August 2018. The study was started after hospital ethical committee approval. 30 patients who were willing to participate in study (after taking written consent) were recruited from labour room those admitted for blood transfusion. A detailed history, general and systemic examination was done. All the patients underwent Doppler sonography and further management was done according to hemoglobin level. A repeat complete blood profile will be performed 10 and 20 days after treatment initiation. Fetal Doppler assessments of the umbilical and middle cerebral arteries will be performed 10days and 20days after the start of treatment for patients whose anemia had been successfully treated (Hb > 10gms).

Inclusion criteria - a) All singleton pregnant women after 32 weeks of gestational age admitted in labour room with severe anemia (hemoglobin level < 7gm/ l) b) All women who give consent to be part of study.

Exclusion criteria -Pregnant women with- a) History of recent blood transfusion b) Multiple gestation c) Antepartum haemorrhage d) Gestational diabetes e) Pregnancy induced hypertension f) Heart disease g) Pregnancy with congenital anomalies h) Chronic medical disorder I) intrauterine foetal death j) Rh negative pregnancy

Statistical analysis: Continuous variables will be summarized as mean and SD and will be analysed by unpaired and paired T test. Nominal and categorical variables will be summarized as proportion (%) and will be analysed by using chi square test and Fisher exact test. *P* value < 0.05 will be taken as significant.

Results & Discussion

The mean age of participants was 25.43years (SD±2.64). 70% study subjects belonged to 25-29 years of age group. The mean gestational age at the time of admission was 34 weeks (SD±1.39). This shows severe anemia generally presents in third trimester because of increase requirement of iron & maximum hemodilution occurs. Major population belonged to lower middle socioeconomic status (63.3%) followed by Middle (36.7%).63.3% study subjects were unbooked & 36.7% were booked. This shows, education status of Rajasthan, especially in rural areas, despite implementation of JSSY majority of anemic mothers will come directly in third trimester for check-up and they don't receive proper iron & folic acid supplementation during pregnancy due to lack of knowledge about health facilities. 54.3 belonged to rural area whereas 46.7% were from the urban area. 80% study subjects belonged to Hindu religion and 20% belonged to Muslim religion. This shows the demographic profile of Rajasthan which is a Hindu dominant state. One more reason could be non-vegetarian diet. Most of Muslim population takes non- vegetarian diet that is rich in vitamin B12 and prevent from megaloblastic anemia that is the major contributor of dimorphic anemia.

Table 1: Hemoglobin level of study subjects at different follow up time

Hb (mg/dl)	Admission		After 10 days		After 20 days	
	N	%	N	%	N	%
<4 (very severe)	4	13.3	0	0	0	0
4 -7(severe)	26	86.7	22	73.3	0	0
7-10(moderate)	0	0	8	26.7	30	100
P value	-		<0.001 (S)		<0.001 (S)	

Table 1 shows Hemoglobin level of study subjects at different follow up time. 13.3% study subjects belonged to very severe anemia and 86.7% belonged to severe anemia at the time of admission. After 10 days of admission, 73.3% were severe anemic & 26.7% subjects were moderately anemic (*P* value < 0.001) that was statistically significant in comparison to admission and after 20 days of admission all study subjects were moderately anemic (*P* value < 0.001) that was significant in comparison to admission).

Table 2: Mean Cerebral Resistance Index (CRI) on USG Doppler of study subjects at different follow up time

Time point	CRI	Change in CRI	P value in comparison to admission
Admission	0.82 ± 0.06	-	-
After 10 days	0.85 ± 0.06	0.02 ± 0.01	0.006
After 20 days	0.87 ± 0.07	0.05 ± 0.01	<0.001 (S)
Repeated measures ANOVA -- *P* = <0.001 (S)			

Table 2 shows Cerebral Resistance Index (CRI) on USG Doppler of study subjects at different follow up time. In this, the mean value of CRI was 0.82 ± 0.06 at the time of admission that was increased by 0.02 ± 0.01 after 10 days of admission that was statistically not significant (P value 0.006). After 20 days of admission it was 0.87 ± 0.07 and increased by 0.05 ± 0.01 in comparison to admission that was statistically significant (*P*<0.001). This showed, severe maternal anemia induced significant hemodynamic changes at the level of brain due to hypoxia-induced cerebral vasodilatation affecting the fetus during severe anemia. The increase in cerebral resistance after the transfusion and that the situation was restored quickly by units of red blood transfusion to the patient or intravenous iron. So the chances of low Apgar score, meconium and perinatal morbidity& mortality will decrease. Eram Ali *et al*. (2016) [6] done in Lady Hardinge Medical College, New Delhi, found that The Mean middle cerebral artery resistance index of anemic subjects was 0.67 ± 0.074 and after 4 weeks of admission it was 0.72 ± 0.07 that the difference was statistically significant (*P* value <0.001) in comparison to admission.

Table 3: Umbilical Artery Resistance index (URI) on USG Doppler of study subjects at different follow –up time

Time point	URI	Change in URI	P value in comparison to admission
Admission	0.68 ± 0.06	-	-
After 10 days	0.62 ± 0.05	0.06 ± 0.01	<0.001 (S)
After 20 days	0.57 ± 0.05	0.11 ± 0.01	<0.001 (S)
Repeated measures ANOVA - *p* <0.001 (S)			

Table 3 shows Umbilical Artery Resistance index (URI) on USG Doppler of study subjects at different follow – up time. In my study, the mean value of URI at admission was 0.68 ± 0.06 that is increased by 0.06 ± 0.01 after 10 days of admission that was statistically significant. After 20 days of admission it was 0.57 ± 0.05 that was increased by 0.11 ± 0.01 in comparison to admission that was statistically significant. This indicates that uterine artery resistance index was increased due to preplacental hypoxia, blood supply to the fetus was decreased, the fetus had to adapt by increasing its blood flow redistribution towards the brain. Ghada a. Abdel Moety *et al.* (2012) [7] showed that mean umbilical artery resistance index at admission was 1.09; it was 0.87 after 10 days of admission and 0.65 at the time of delivery. There was a significant difference after 10 days.

Table 4: CRI /URI Ratio in study subjects at different follow up time

Time point	CRI / URI Ratio	Change in CRI / URI Ratio	P value in comparison to admission
Admission	1.22 ± 0.14	-	-
After 10 days	1.36 ± 0.11	0.15 ± 0.02	<0.001 (S)
After 20 days	1.50 ± 0.15	0.29 ± 0.03	<0.001 (S)
Repeated measures ANOVA – p <0.001 (S)			

Table 19 shows CRI /URI Ratio in study subjects at different follow up time. In this, the ratio of mean CRI/ mean URI was 1.22 ± 0.14 at the time of admission and 1.36 ± 0.11 after 10 days of admission that was increased by 0.15 ± 0.02 from the day of admission and it was statistically significant (P<0.001). After 20 days of admission, it was 1.50 ± 0.15, increased by 0.29 ± 0.03 from the day of admission that was statistically significant.

For quantifying the fetal hemodynamic response, we used the C/U ratio cut-off value, which is usually quite constant (C/U=1.1) during normal pregnancy and allows for the quantification of the blood flow redistribution. In this study, C/U ratio was increased at different follow up time because of umbilical artery resistance decreased due to increased blood flow to umbilical artery after blood transfusions. Similarly Mohamad Ihab *et al.* (2017) [8] C/U ratio compared among mild(A) moderate(B), severe(C) anemic subjects, The mean C/U ratio on admission was less than 1.1 in Group (B) and Group (C) while Group (A) showed a normal C/U ratio and this difference was statistically significant between all groups.

After 10 days of treatment, the mean C/U ratio improved in the 3 groups and was highest in Group (C).

Conclusion

Anaemia in pregnancy is one of the causes of poor perinatal outcome like high risk of low birth weight, IUGR babies, low APGAR scores and NICU admissions and overall increases perinatal mortality and morbidity. Hence proper antenatal care and counselling can reduce the occurrence of anaemia in pregnancy. Close monitoring of the fetal umbilical and cerebral circulation by Doppler examination in anemic pregnancies allows the measurement of the amplitude of the fetal vascular response and the fetal recovery as well. It can conclude that the correction of fetal blood flow redistribution following treatment suggests that fetal oxygenation returned to normal parameters following treatment.

The present study demonstrated that, in Cases of severe maternal anemia, the fetus is in a compromised state and that close monitoring of the fetal umbilical and cerebral circulation using Doppler ultrasonography allows fetal vascular responses and recovery to be measured, perinatal outcome can Improved.

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