Comparison of Middle Cerebral Artery Doppler and Cord Blood Hemoglobin in the Diagnosis of Fetal Anemia among Rh-negative Pregnant Women

Farzana Burki,[1] Abdul Jalil Khan,[2] Naeem ullah,[3] Shahnaz Parveen,[1] Hina Javed,[2] Kashif Muqarrab,[4] Ihsan Ullah,[7] Sheraz Fazid[8]

Abstract

Background: Most prevalent cause of fetal anemia is Rh incompatibility between the mother's and the fetus's blood types, where antibodies from the mother damage the fetus's red blood cells causing fetal hemolytic anemia.
Objective: To compare the Doppler of the middle cerebral artery of the fetus and cord blood hemoglobin to diagnose fetal anemia among Rh-negative women in the last trimester of pregnancy.
Methodology: This was a cross-sectional study conducted at the Gynecology & Obstetrics Department, Mercy Teaching Hospital Peshawar, from February 2020 to May 2021. A total of 126 Rh-negative blood group women were included who were in the last trimester of the pregnancy. Ethical approval was obtained from Ethics Committee and informed written consent was taken from the study participants. Middle cerebral artery Doppler peak systolic velocity was checked at 28th, 32nd, and 34th week of gestation. If middle cerebral artery Doppler peak systolic velocity changes were present, then patients were closely monitored and managed appropriately for post-delivery assessment of cord blood fetal anemia. A pre-designed structured proforma was used to collect patient details.
Results: Mean age of 126 pregnant mothers was 28±7 years, and the mean parity was 4.57±2. The overall frequency of fetal anemia among Rh-negative women predicted by middle cerebral artery Doppler peak systolic velocity was 59 (46.8%), while anemia on cord blood sampling after delivery was found in 43 (34.1%) of babies. No anemia was found in 83 (65.8%) study participants. The sensitivity and specificity of middle cerebral artery Doppler were 100% and 84% respectively.
Conclusion: Middle cerebral artery Doppler can be a simple noninvasive method to detect fetal anemia before the development of hydrops fetalis with high sensitivity and specificity.
Keywords: Doppler peak systolic velocity, Fetal Anemia, Hydrops fetalis, Middle cerebral artery, Rh-negative
Article Citation: Burki F, Khan AJ, Ullah N, Parveen S, Javed H, Muqarrab K, Ullah I Fazid S. Comparison of Middle Cerebral Artery Doppler and Cord Blood Hemoglobin in the Diagnosis of Fetal Anemia among Rh-negative Pregnant Women, Pakistan. JSZMC 2022;13(1):3-6.
DOI: https://doi.org/10.47883/jszmc.v13i01.212

Introduction

Anemia develops when circulating red blood cells and hemoglobin levels decrease below the normal level.[1] Fetal anemia is considered an important cause of morbidity and fetal death. The most prevalent cause of fetal anemia is Rh-incompatibility between the mother and the fetus blood types, known as iso-immunization. In this condition, the antibodies from the mother damage the fetus's red blood cells causing fetal hemolytic anemia.[1] During pregnancy, red blood cells from the fetus cross into the mother's bloodstream through the placenta. If the mother is Rh-negative, her immune system treats Rh-positive fetal cells as foreign and starts producing IgG antibodies against them leading to fetal hemolytic anemia.[2,3]
A severe manifestation of fetal anemia is the immune hydrops also called Rh-disease. In severe conditions, fetal hematocrit value falls below 15% (Hb <5g/dl), resulting in generalized edema, ascites, pericardial effusion, and pleural effusion leading to hydrops fetalis.[2] Untreated fetal hydrops is usually not survivable and lead to the death of the fetus in-utero or newborn due to severe anemia and tissue hypoxia.[4] The overall prevalence of disease caused by Rh-incompatibility is around 276/100,000 births worldwide. Out of the total Rh-disease cases, around 50% of the babies die or may develop some kind of serious complication like brain damage if not treated in time. The developed world has improved perinatal and neonatal care so the prevalence of Rh incompatibility in these countries has decreased to 2.5/100,000 live births. However, the condition in the developing world is still worse and they need a lot of improvement in their perinatal care to overcome this problem.[5]

1.Gynaecology Department, Peshawar Medical College, Peshawar, Pakistan.
2.Family Medicine, Khyber Medical University Peshawar, Pakistan.
3.Community Medicine Department, Saidu Medical College, Swat, Pakistan.
4.Technical Officer, WHO, KP, Pakistan.
5.Institute of Pathology and Diagnostic Medicine, Khyber Medical University Peshawar, Pakistan.
6.Institute of Public Health & Social Sciences, Khyber Medical University Peshawar, Pakistan.

Correspondence: Dr. Abdul Jalil Khan, Assistant Professor, Family Medicine Department, Khyber Medical University Peshawar, Pakistan.
Email: jalilkhan@kmu.edu.pk **Received:** 17-02-2022 **Published:** 10-03-2022

The management of pregnancies complicated by Rhesus isoimmunization involves invasive procedures like amniocentesis and cordocentesis. These procedures are usually associated with multiple complications like rupture of membranes, infections, fetal bleeding which further worsen hemolysis and fetal loss. This has prompted many investigators to use a non-invasive test to diagnose fetal anemia. Middle cerebral artery peak systolic velocity (MCA-PSV) is a very good method for identifying fetuses having a risk of anemia.[6,7]

MCA-PSV is a valid and sensitive non-invasive way to detect fetal anemia and follow fetuses at risk in-utero. The middle cerebral artery blood velocity increases with advancing gestational age and is a safe method of detecting anemia in pregnancies complicated by maternal blood group isoimmunization. This is an easy method to predict anemia and has high sensitivity, as cerebral vessels respond early to the fetal anemic state.[8,9]

The aim of this study was to predict fetal anemia among Rh-negative women by using a non-invasive test i.e., middle cerebral artery doppler ultrasound so that other invasive tests like cordocentesis, amniocentesis can be omitted and to ensure timely management.

Methodology

This was a cross-sectional study done at Gynecology and Obstetrics Department, Mercy Teaching Hospital Peshawar, from February 2020 to May 2021. The sample size was calculated by using the WHO sample size formula. The prevalence of severe fetal anemia was 20% with a confidence interval of "95%" with a margin of error of "7%", which gave a total sample of 126 cases. A non-probability consecutive sampling technique was used.

Ethical approval was taken from the Institutional Ethical Committee and informed written consent was sought from all participants. Women who had Rhesus antigen-negative blood group, whose husbands had Rhesus antigen-positive blood group, and having a gestational age of 24 weeks onward were included in the study. A complete history and examination were done during the antenatal period. Fetal anemia was predicted by doing middle cerebral artery Doppler peak systolic velocity and patients were managed according to gestational age and severity of anemia either by inducing labor or referring the patient for intrauterine blood transfusion. The diagnosis was confirmed by doing cord blood sampling after delivery to know the newborn hemoglobin level.

Middle cerebral artery Doppler peak systolic velocity was done at 28th, 32nd, and 34th week of gestation.

In cases where middle cerebral artery Doppler peak systolic velocity was normal at 34 weeks, regular antenatal follow-up was carried out till 38th week. However, if middle cerebral artery Doppler peak systolic velocity changes were present, then patients were closely monitored and managed. In order to eliminate inter-observer bias ultrasound was performed by the same Sonologist. A pre-designed structured proforma was used to collect patient details.

All the analysis was done using SPSS version 20.0. Mean and standard deviation was computed for numeric variables like parity and gestational age, while frequencies and percentages were computed for categorical variables like fetal anemia. Fetal anemia was stratified among parity and gestational age. To compare between anemia on middle cerebral artery Doppler peak systolic velocity and laboratory method, a hemoglobin level of the fetal cord blood was done after delivery. The sensitivity and specificity of both methods were calculated. All the results were presented in the form of tables and charts.

Results

A total of 126 pregnant women in their last trimester having Rh-negative blood group were observed. Among these 7 (5.56%) had a gestational age of less than 35 weeks, 57 (45.24%) had 35-37 weeks while 62 (49.21%) had above 37 weeks. Age distribution of the study population showed that the average age of the participants was 28.52±7.46 years. Most of the participants were in the age group 21-34 years while15.9% were below the age of 20 years.

When we analyzed fetal anemia based on the maternal gestational age, the present study showed that the gestational age of the Rh-negative mothers has no role in fetal anemia as shown by the statistically non-significant (p-value=0.755) in table-I.

Table-I: Stratification of fetal anemia over gestational age (n=126)

Gestational age Weeks	Fetal Anemia		Total	P-value
	Yes	No		
<35	4 (57.1%)	3 (42.9%)	7 (100%)	0.755
35-37	25 (43.9%)	32 (56.1%)	57 (100%)	
>37	30 (48.4%)	32 (51.6%)	62 (100%)	
Total	59 (46.8%)	67 (53.2%)	126 (100%)	

This study identified an increased frequency of anemia in mothers with higher parity as compared to low parity. There was a statistically significant (p-value=0.001) association between maternal parity and fetal anemia as shown in table-II.

Table-II: Distribution of fetal anemia based on maternal parity (n=126)

Maternal Parity	Fetal Anemia		Total	P-value
	Yes	No		
<4	10 (25.0%)	30 (75.0%)	40 (100%)	0.001
4-7	46 (55.4%)	37 (44.6%)	83 (100%)	
>7	3 (100.0%)	0	3 (100%)	
Total	59 (46.8%)	67 (53.2%)	126 (100%)	

The overall predicted frequency of fetal anemia among Rh-negative women using MCA-PSV was found to be 47 (46.8%), while 67 (53.2%) had no fetal anemia as shown in table-III.

Table-III: Predicted fetal Anemia on middle cerebral artery Doppler peak systolic velocity

Doppler report	Frequency	Percent
Predicted Anemia	59	46.8
Normal	67	53.2

Table-III shows that 43 (34.1%) cases had anemia of different severity on the fetal cord blood hemoglobin after delivery of the baby, while 83 (65.8%) had no anemia.

Table-IV: Frequency and severity of fetal anemia after delivery on cord blood Hb level

Anemia Status	Frequency	Percent
Severe anemia (Hb:<5g/dl)	4	3.2
Moderate anemia (Hb: 5-7 g/dl)	12	9.5
Mild anemia (Hb: 8-10 g/dl)	27	21.4
Normal level (>10g/dl)	83	65.9

To find the sensitivity and specificity of MCA-DPV, we compared the results obtained from Doppler with the laboratory results of anemia shown in table-III and IV respectively. On comparing the 59 (46.8%) cases of fetal anemia as predicted by the middle cerebral artery Doppler peak systolic velocity with 43 (34.1%) newborn anemia determined by the cord blood sampling, there were 16 false-positive cases. The sensitivity and specificity of MCA-DSV were then calculated by using a 2 by 2 table were 100% and 83.8% respectively.

Discussion

Fetal anemia is a life-threatening condition and the commonest cause is Rh-incompatibility between mother and the fetus blood types. Fetal hemolytic anemia is one of the leading causes of anemia in-utero which is most commonly caused by Rh-D alloimmunization. An early in-utero diagnosis and management are needed to prevent morbidity and mortality associated with this condition.[6]

The present study was aimed to find the usefulness of MCA-DSV for early detection of fetal anemia in-utero. The study participants were 126 women having Rh-negative blood groups, with different gestational ages. The average age of the study participants was 28.52±7.46 years. Most of the participants were in the age group between 21-34 years. Our study is supported by another study having 111 participants and most of the participants were in this age group.[10]

The present study also showed that maternal age has no role (p-value=0.755) in the fetal Hb levels and anemia. We observed anemia in fetuses of different age groups of mothers. Our findings are supported by different studies where maternal age has no role in hydrops fetalis and anemia,[7] however, some studies showed that maternal age favors iron deficiency which causes maternal anemia leading to fetal anemia and low birth weight.[11,12] Similarly, when we analyzed fetal anemia among Rh-negative women, it was seen in 47 (46.8%) of participants while 67 (53.2%) had no fetal anemia. However, after birth, analysis of fetal cord blood hemoglobin showed that 43 (34.1%) of babies had anemia while 83 (65.8%) were normal. A study conducted by Fatemeh Rahimi-Sharbaf et al, showed that around 80% of fetuses with severe diseases could be detected by MCA-PSV which supports our findings to some extent.[13]

When we compared the results of MCA-DSV, the

sensitivity and specificity of the test were very significant. On comparing the 59 (46.8%) cases of fetal anemia as predicted by the MCA-PSV with 43 (34.1%) newborn anemia determined by the cord blood sampling, there were 16 false-positive cases. The sensitivity and specificity were 100% and 83.8% respectively. Our findings are supported by different studies in the literature. A small sample study showed that the sensitivity of MCA-DSV for prediction of fetal anemia was 90.5% and specificity was 78.6%.[14] Another study showed sensitivity, specificity of 86.8%, 90.3%, respectively [15] which support our findings of the present study. The present study showed that MCA-DSV is a good non-invasive method for the detection of fetal anemia. Although our findings are encouraging, this is a small sample size study and the results could not be generalized. Furthermore, large sample size studies at multiple hospitals are suggested for further refinement. Another limitation of the study was the lack of facilities available for intra-uterine blood transfusion across the province, so blood transfusion was not done at that stage.

Conclusion

Middle cerebral artery peak systolic velocity is a diagnostic technique that allows a rapid, noninvasive prediction of fetal anemia with high sensitivity and specificity dictating the urgency of treatment. It is a method that can serve as a first-line monitoring tool for fetal anemia, however, the availability of facilities for intra-uterine blood transfusion must be made available for effective management.

Authors Contribution: FB: Design of work, Acquisition and analysis of data and Drafting. **AJK, N & SP:** Conception of work Interpretation of data and revising. **HJ:** Conception of work, Interpretation of data and drafting. **KM:** Acquisition, Analysis of data and revising. **IU:** Design of work and drafting. **SF:** Interpretation of data and revising.

All authors critically revised and approve its final version.

Conflict of Interest: Author has declared no conflict of interest.

Sources of Funding: The source of funding was self.

Declaration: None

References

1. Nassar GN, Wehbe C. Erythroblastosis Fetalis. [Updated 2021 Jun 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513292/
2. Jagannathan-Bogdan M, Zon LI. Hematopoiesis. Development. 2013; 140(12):2463-7.
3. Pegoraro V, Urbinati D, Visser GHA, Di Renzo GC, Zipursky A, Stotler BA, et al. Hemolytic disease of the fetus and newborn due to Rh(D) incompatibility: A preventable disease that still produces significant morbidity and mortality in children. PloS one. 2020; 15(7):e0235807.
4. Urbaniak SJ, Greiss MA. RhD haemolytic disease of the fetus and the newborn. Blood Rev. 2000; 14(1):44-61.
5. Zipursky A, Paul VK. The global burden of Rh disease. Arch Dis Child Fetal Neonatal Ed. 2011; 96(2):F84-5.
6. Abbasi N, Johnson J-A, Ryan G. Fetal anemia. 2017; 50(2):145-53.
7. Maisonneuve E, Jayot A, Friszer S, Castaigne V, Cynober E, Pernot F, et al. Accuracy of Middle Cerebral Artery Doppler Assessment between 34 and 37 Weeks in Fetuses with Red Cell Alloimmunization. Fetal Diagnosis and Therapy. 2017; 42(3):225-31.
8. Andrei C, Vladareanu R. The value of reference ranges for middle cerebral artery peak systolic velocity in the management of rhesus alloimmunized pregnancies. Maedica (Bucur). 2012; 7(1):14-9.
9. Kennedy AM, Woodward PJ. A Radiologist's Guide to the Performance and Interpretation of Obstetric Doppler US. 2019; 39(3):893-910.
10. Mari G, Deter RL, Carpenter RL, Rahman F, Zimmerman R, Moise KJ, et al. Noninvasive Diagnosis by Doppler Ultrasonography of Fetal Anemia Due to Maternal Red-Cell Alloimmunization. 2000; 342(1):9-14.
11. Gomaa A-HG, Mohamed M, Radwan M, El Sheikh AM. Severity of Maternal Iron Deficiency Anemia and Risk for Low Birth Weight Babies. J Al-Azhar International Medical Journal. 2021; 2(1):24-7.
12. Rahimi-Sharbaf F, Shariat M, Mirzaie F, Dehghan P, Dastgardy E, Adabi K. Prediction of fetal anemia by different thresholds of MCA-PSV and Delta-OD in first and second intrauterine transfusions. Archives of Iranian medicine. 2012;15(3):162-5.
13. Sanni OB, Chambers T, Li JH, Rowe S, Woodman AG, Ospina MB, et al. A systematic review and meta-analysis of the correlation between maternal and neonatal iron status and haematologic indices. eClinicalMedicine. 2020;27.
14. El. Shourbagy S, Elsakhawy M. Prediction of fetal anemia by middle cerebral artery Doppler. Middle East Fertility Society Journal. 2012;17(4):275-82.
15. Shehbaz S. Diagnostic accuracy of fetal middle cerebral artery peak systolic velocity in detection of neonatal anemia in rhesus alloimmunization. Pak J Rad.2019; 29(3): 181-6.