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Diagnostic Accuracy of Fetal Middle Cerebral Artery Peak Systolic Velocity in the Detection of Fetal Anaemia Keeping Neonatal Haemoglobin Estimation at Birth as the Gold Standard

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ABSTRACT

***Objective*:** To assess whether monitoring the peak systolic velocity (PSV) in the middle cerebral artery (MCA) was a useful, non-invasive method for predicting anaemia in fetuses.
Study Design: Cross-sectional study.
***Place and Duration of Study*:** Department of Radiology, Armed Forces Institute of Radiology, Rawalpindi Pakistan, from Feb and Aug 2022.
Methodology: Fifty pregnant women who did not have hydropic babies were included. The peak systolic velocity (PSV) was measured in the middle cerebral artery (MCA). A positive result was determined when the MCA-PSV value exceeded 1.5 multiples of the median (MoM). The blood samples obtained from neonates were forwarded to the hospital laboratory to estimate haemoglobin levels shortly after birth. The outcome of the method (MoM) was observed and subsequently compared with neonatal haemoglobin levels.
Results: 60% of neonates were anaemic according to middle MCA-PSV while the haematology laboratory reported 74% of neonates as anaemic according to cut-off haemoglobin of less than 13.5gm/dl. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the MCA-PSV in detecting the anaemia were 93.75%, 61.1%, 81.08%, 84.62%, and 82%, respectively.
***Conclusion*:** MCA-PSV Doppler is deemed valuable as a diagnostic technique for fetal anaemia, albeit secondary to the primary approach of neonatal haemoglobin estimation upon birth.

Key Words: Anaemia, Fetus, Middle cerebral artery (MCA), Neonatal haemoglobin estimation.

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INTRODUCTION

During pregnancy, maternal alloimmunization may occur if the mother produces an immune response to an RBC antigen obtained from the father that is novel to her and is passed on to the fetus.[1] When maternal antibodies penetrate the placenta and attach to antigens on fetal erythrocytes, it may cause hydrops fetalis, hemolysis, and potentially fetal mortality. Any pregnant woman whose red blood cell antibody levels are growing, regardless of whether or not she has ever had an impacted pregnancy, should be evaluated by a fetal medicine specialist.[2,3] The likelihood of survival increases to over 90% if anemia is detected early and intrauterine blood transfusions are administered. The most reliable method for gauging fetal anaemia and, by extension, the need for transfusion is the measurement of fetal haemoglobin (Hb) by blood collection.[4] However, serial amniocentesis for assessing bilirubin concentration in amniotic fluid is the gold standard test for determining whether or not a fetal transfusion is necessary. The degree of hemolysis is correlated with the amount of bilirubin present in the amniotic fluid, which accumulates due to hemolysis.[5]

Most recently, it has been found that higher blood flow velocities in the fetal MCA are associated with fetal anaemia.[6] To delay the need for intrusive testing until transfusion is essential, many non-invasive approaches for predicting fetal anaemia have been evaluated. Since then, it has been detailed how measuring the blood flow velocity in the MCA of the growing baby is one of the most capable among non-invasive approaches. Fetal anaemia is characterized by elevated blood-flow velocities owing to the increased heart rate and low blood viscosity, suggesting that such measurements might be useful in predicting the occurrence of fetal anaemia before birth.[7,8] Brenned *et al*. demonstrates that variations in heart rate and blood-flow velocities manifest as an amplified peak systolic velocity in the MCA in the presence of fetal

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anaemia.[9] This research aims to determine whether or not non-invasively monitoring PSV in the MCA may be used to forecast fetal anaemia because of maternal red-cell alloimmunization in fetuses that are not hydropic.

METHODOLOGY

The cross-sectional study was carried out at the Armed Forces Institute of Radiology and Imaging Rawalpindi Pakistan, from February to August 2022, after the approval from the Institutional Review Board (certificate number 0064). The sample size was calculated using the WHO sample size calculator, taking the reported prevalence of ABO incompatibility of 17%.[2]

Inclusion Criteria: Pregnant women aged 25 and 45 years, with gestation age >32 weeks, >1 parity, singleton gravidity, and diagnosed rhesus alloimmunization were included.

Exclusion Criteria: Neonates with antenatal diagnosed malformations, intrauterine growth retardation, ectopic pregnancies, and mothers with a blood transfusion history were excluded.

Referrals were common when patients had elevated maternal serum antibodies or a prior obstetric history marked by anaemia in the fetus or newborn. Blood flow velocity assessments of the maternal chorionic artery and Doppler blood flow investigations of the umbilical artery and uterine artery were components of the assessment. Fetuses diagnosed with hydrops, the abnormal fluid buildup in body cavities or skin swellings, were excluded from the study. Twenty-nine patients had cordocentesis on their first appointment, and the rest were scheduled for follow-up; those whose evaluation indicated increasing anaemia had cordocentesis during their second visit. Before any cordocentesis was done, a Doppler ultrasound of the MCA was conducted. An axial brain segment was taken, exposing structures including the cavitas septi pellucid and the thalami. One side of the head was examined, allowing for a look at the beginning of the internal carotid artery as well as the middle cerebral artery and the circle of Willis. Since we discovered that the systolic velocity drops rapidly as one moves away from the vessel's point of origin, we ensured that the ultrasound beam never deviated more than 30 degrees from where the blood flowed. The apex of the wave was determined using peak systolic velocity (PSV). Doppler images were taken when there seemed to be no fetal body or respiratory movements, preventing an incorrect correlation between an increase in PSV and a faster fetal heart rate. The best of at least three readings was used as the ending value. The PSV of the MCA was measured to be more than 1.5 multiples of the median (MOM) as a reference test for fetal anaemia by Mari *et al*. To do a fetal transfusion, blood was drawn using cordocentesis from the fetal umbilical vein at the point where the placenta was inserted. If anaemia was suspected, an urgent complete blood count was taken from the fetal blood, and an intravascular transfusion was done. Umbilical cord blood haemoglobin testing was the reference standard for fetal anaemia diagnosis. According to the established reference range, haemoglobin (Hb) levels below 0.65 times the median for GA are considered to be indicative of fetal anaemia.[10]

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Diagnostic parameters were calculated using a 2x2 contingency table. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were determined by using the standard formulae.

RESULTS

The present research comprised 50 pregnant women with non-hydropic and alloimmunization fetuses. Among them, 37(74%) women had RhD, 8(16%) had RhC, and 5(10%) women had RhE antibodies. 37 of the 50 fetuses have anemia (7.15±1.09g/dL) and 13 of the 50 (14.09±0.43g/dL) were with normal haemoglobin (p-value <0.0001). Table-I shows the demographic and clinical parameters of the recruited participants in study participants. Mean maternal age in both the study groups was 33.07±5.54 and 31.84±3.99 years (p=0.406). The mean maternal BMI in both the study groups was 27.30±1.61 and 26.87±1.34 kg/m^2 (p=0.117). Mean gestational age in both the study groups was 34.53±1.39 and 34.15±1.28 weeks (p=0.175). The majority of the participants in both study groups were multiparous. 60% of neonates were anaemic according to middle MCA-PSV while the haematology laboratory reported 74% of neonates as anaemic according to cut-off haemoglobin of less than 13.5gm/dl. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the MCA-PSVin detecting the anaemia were 93.75%, 61.1%, 81.08%, 84.62%, and 82%, respectively, as shown in Table-II. Figure shows the ROC curve analysis of MCA-PSV in detecting anaemia with an area under curve 0.820.

Table-I: Clinical and Demographic Features of Study Participants (n=50)

Parameters	Women with Anaemia (n=37)	Women with no Anaemia (n=13)	*p*-value
Maternal Age (years)	33.07±5.54	31.84±3.99	0.406
Maternal BMI (kg/m2)	27.30±1.61	26.87±1.34	0.117
Gestation age (weeks)	34.53±1.39	34.15±1.28	0.175
Haemoglobin (g/dL)	7.15±1.09	14.09±0.43	<0.0001
Parity			0.190
1	6(16%)	3(23%)	
2	20(43%)	6(46%)	
3	19(41%)	4(31%)	

Table-II: Diagnostic Parameters of Middle Cerebral Artery Peak Systolic Velocity (MCA PSV) in the Detection of Fetal Anaemia (n=50)

Parameters	HB <13.5 gm/dl	HB e″ 13.5 gm/dl
Anemia Present(e″1.5 MoM)	30(TP)	2(FN)
Anemia Absent(<1.5 MoM)	7(FP)	11(TN)
Sensitivity	93.75%	
Specificity	61.11%	
NPV	81.08%	
PPV	84.62%	
Accuracy	82%	

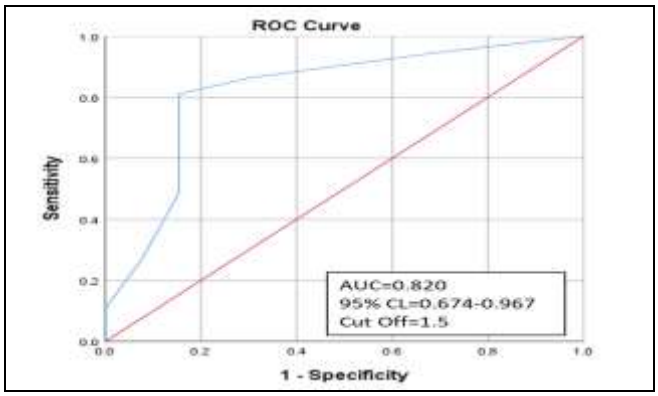

Figure: ROC Curve Analysis in the Diagnosis of Fetal Anemia through MCA_PSV

DISCUSSION

In the current investigation, the sensitivity, specificity, and accuracy of the MCA-PSV in identifying haemoglobin were found to be 93.75%, 61.11%, and 82%, respectively. Similar findings were also documented in the previous investigation.[11] In one study study, it was shown that the utilization of MCA-PSV (middle cerebral artery peak systolic velocity) with a normal median value (MOM) cutoff greater than 1.29 successfully identified 60% of the patients with moderate anaemia and 100% of the instances with severe anaemia.[12]

Conversely, when the MOM cutoff was set at a higher value of 1.5, no moderate anaemia cases were recognized, but 93% of the severe anaemia cases were identified. Hence, the sensitivity and specificity for diagnosing fetal anaemia vary across different thresholds of MCA-PSV.[13] In our investigation, an MCA-PSV value greater than 1.5 multiples of the median (MoM) was considered a positive result. However, data unequivocally indicates that the middle cerebral artery Doppler exhibits significantly higher sensitivity and accuracy than amniocentesis in detecting anaemia.[14] Doppler ultrasound can be utilized to evaluate the hemodynamic modifications made by the fetus in order to compensate. The measurement of peak systolic velocity in the fetal middle cerebral artery (MCA-PSV) can significantly improve the non-invasive prediction of fetal anaemia in fetuses at risk due to maternal Rhesus alloimmunization. There is a strong correlation between the fetal middle cerebral artery peak systolic velocity (MCA-PSV) and haemoglobin concentration and hematocrit levels. The measurement of middle cerebral artery peak systolic velocity (MCA PSV) has emerged as the established approach for diagnosing prenatal anaemia in various fetal conditions.[15] This modality is grounded on the observation that fetuses experiencing anaemia exhibit an elevated blood flow velocity, indicating a state of hyperdynamic circulation. One of the benefits of studying the middle cerebral artery (MCA) compared to other vessels is that it enables velocity measurements without the need for angle adjustment.[16] This is because the insonation angle in the MCA axial plane is about 0°, resulting in enhanced reproducibility.[17,18]

CONCLUSION

The measurement of the middle cerebral artery peak systolic velocity (MCA-PSV) in fetuses at risk of developing anaemia due to Rhesus alloimmunization offers a reliable and non-invasive clinical test for predicting the occurrence of fetal anaemia. However, it is important to note that the primary method for assessing fetal anaemia should still be assessing fetal haemoglobin levels at delivery. The future holds the potential for the widespread utilization of MCA Doppler assessment to diagnose fetal anaemia and other fatal illnesses.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SN & NA: Conception, study design, drafting the manuscript, approval of the final version to be published.

MUK & ARS: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MZA: Data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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