Retrospective study for correlation of fetal middle cerebral artery PSV and fetal anemia using newborn hemoglobin and blood indices

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Abstract---To establish relation between fetal MCA’s PSV in 3rd trimester and fetal anemia as non-invasive method. The study was done retrospectively, including 40 pregnant women who had raised PSV of MCA (Multiple of Median (MoM) >1.5) blood flow in third trimester and was correlated with the new born's Hemoglobin and Blood indices (MCV and MCH). Forty fetuses who had MCA’s PSV more than 1.5 MoM(coming out to be around 66.50 ± 12.35 cm/seconds), after delivery, blood samples of these 40 neonate were taken, of which 37 were anemic based on hemoglobin and blood indices using reference range from study done by kumar et al8. Sensitivity was 92.5% and specificity around 88 %. Doppler spectral analysis of PSV of MCA is very reliable for predicting fetal anemia. MoM of PSV of Fetal MCA correlates very well with MoM of Neonatal Hemoglobin. Thus, fetal MCA’s PSV is very potential to replace invasive method for diagnosis of fetal anemia.

Keywords---Fetal MCA’S PSV, Multiple of Median (MoM), fetal hemoglobin, blood indices.
**Introduction**

Fetal anemia is a well-known cause of morbidity and mortality for the fetus in-utero as well as after birth. Active management is needed in these cases depending on the availability of resources. Diagnosing fetal anemia earlier can be of great difference which can help in timely intervention with options like intra-uterine transfusion and post-partum neonatal care. Even if these facilities are not available, out timely diagnosis can give the patient and doctors window for timely referral to higher or tertiary centres where advanced treatment (NICU) and intense neonatal care is available. Causes of fetal anemia include:

<table>
<thead>
<tr>
<th>Cause</th>
<th>Description</th>
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<tbody>
<tr>
<td>Alloimmunization</td>
<td>This occurs when the baby inherits certain blood antigens or proteins from the father that the mother does not have. The mother’s immune system may create antibodies that attack and destroy the fetal red blood cells.</td>
</tr>
<tr>
<td>Infection</td>
<td>Several maternal infections may cause fetal anemia like B19 parvovirus, CMV, toxoplasma, syphilis and etc.</td>
</tr>
<tr>
<td>Blood loss</td>
<td>Direct loss of blood will lead to anemia.</td>
</tr>
<tr>
<td>Structural abnormalities</td>
<td>Defective heart of blood vessels structures will lead to anemia.</td>
</tr>
<tr>
<td>Inherited</td>
<td>Include G6PD deficiency, pyruvate kinase disease, alpha thalassemia, lysosomal storage disorders, mucopolysaccharidosis type VII and etc.</td>
</tr>
<tr>
<td>Others</td>
<td>Aneuploidy, TTTS, feto-maternal hemorrhage and etc.</td>
</tr>
</tbody>
</table>

If these causes are not treated, it can lead to serious complications as mentioned below:

- Fetal hydrops and stillbirth.
- Hepatosplenomegaly.
- Neonatal jaundice.
- Neonatal kernicterus.

However, the standard and traditional tests to evaluate the need for fetal transfusion is serial amniocentesis for the determination of bilirubin levels in amniotic fluid. Hemolysis will lead to accumulation of its products like bilirubin in the amniotic fluid, hence its level will correlate with severity of hemolysis which is ongoing, which in turn can be detected by spectrophonometry. However, all these invasive procedures have a significant risk of causing miscarriage, premature rupture of membrane and preterm delivery. By establishing the correlation between fetal MCA’s PSV and fetal anemia, and using the MoM of PSV of MCA and Fetal hemoglobin MoM, we can provide a non-invasive method for diagnosis which is also fast and has no risk of complications related to the traditional invasive methods.

An anemic fetus has high cardiac output and low blood viscosity, resulting in high velocity blood flow, which is used in prediction of anemia. Doppler USG assessment of fetal MCA PSV for the diagnosis of fetal anemia is promising and current practise standard leading to impact on neonatal death, reducing it
considerably as reported in recent years. The objective of our study is to establish relation between fetal middle cerebral artery’s peak systolic velocity in third trimester near time of delivery (37 weeks) and fetal anemia as a non-invasive method in non hydropic fetuses, so that timely recommendation or referral to higher centers or tertiary centers can be made, which drastically improves neonatal morbidity and mortality.

**Material and Method**

The study was performed in the department of Radiodiagnosis, Dhiraj Hospital, S.B.K.S. Medical Institute and Research Centre, Pipariya, Vadodara on GE Logic P9 USG machine. The study was done in the period from November 2021 to April 2022. It is a retrospective hospital based study. Only those patients who were willing to participate in study were included. 40 patients who were in 37th or more gestation age (3rd trimester) were selected from daily ANC OPD who showed increased level of PSV of fetal MCA (equal to or more than 1.5 MOM of reference) on fetal doppler screening. Assessment consisted of ultrasound fetal biometry examination and excluding any structural abnormalities, liquor AFI assessment, umbilical artery doppler study and doppler blood flow velocity studies of the MCA. Hydrops was defined as fluid collection in body cavities or skin edema, and hydropic fetuses were excluded from the study. Fetal MCA doppler was done taking an axial section of brain (including thalami and CSP) the angle kept while getting spectrum was 0’ insonation angle. The circle of willis was visualized and then the middle cerebral artery which was proximal to the probe was assessed around its origin from internal carotid artery. Atleast three measurements were taken and the highest one was recorded in our study. The reference test for the diagnosis of fetal anemia was measurement of peak systolic velocity of the MCA more than 1.5 multiple of median (MoM) using reference produced by Mari and his colleagues$^{3,6}$. Practical approach is to convert actual values into MoM to account for changes in gestational age, internet based calculator is available at www.perinatology.com. These 40 patient’s neonatal blood reports were then correlated to our doppler study. The Fetal hemoglobin MoM was also calculated and plotted against MoM of Fetal MCA PSV MoM.
Results

In this study, forty fetuses had undergone doppler study who had middle cerebral artery PSV more than 1.5 multiple of median (MoM) using reference study produced by Mari and his colleagues\textsuperscript{3,6}, coming out to be around 66.50 ± 12.30 cm/seconds (normal range being around 49 ± 14.20 cm/seconds). After delivery, blood samples of these 40 neonates were taken out of which 37 were anemic based on hemoglobin and blood indices. The fetal hemoglobin MoM was also calculated and plotted against MoM of Fetal MCA PSV MoM. The MoM (multiple of median) of MCA for fetuses with normal Hb was 1.22 ± 0.21 while that for anemic fetuses was 1.62 ± 0.08 (P ≤ 0.001). There is a linear correlation observed between MoM of MCA’s PSV and hemoglobin of fetal blood (MoM)-

<table>
<thead>
<tr>
<th>FETAL MCA PSV MOM</th>
<th>NEONATAL HEMOGLOBIN (g/dl)</th>
<th>NEONATAL Hb MoM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>15-17</td>
<td>1.6</td>
</tr>
<tr>
<td>1.6</td>
<td>13-15</td>
<td>1.7</td>
</tr>
<tr>
<td>1.7</td>
<td>11-13</td>
<td>1.8</td>
</tr>
<tr>
<td>1.8</td>
<td>9-11</td>
<td>1.9-2.0</td>
</tr>
</tbody>
</table>

FIG - A
FIG-B

A) Axial section of fetal brain at 37 weeks showing spectral indices of fetal MCA, PSV of which measures 84 cm/sec (correlates with approx. 1.8 MoM ),
B) The neonatal blood investigation revealed significantly reduced Hb to be 13.2 g/dl and significantly deranged blood indices.
Here, we have found out that risk of anemia was higher in fetuses with peak systolic velocity greater than 1.5 MoM (taken from our reference study\textsuperscript{3,6}) showing inverse correlation of MoM and Hemoglobin. As we have taken MoM of MCA's PSV reference, we have used similar reference study for MoM for fetal hemoglobin levels which also states that values greater than 1.5 MoM is anemic. Fetuses with PSV values less than 1.5 MoM did not have anemia or were very mild cases and didn't need any interventions. The fact that this study didn't predict mild anemia is not clinically important as no intervention is indicated in these fetuses, whereas moderate and severe anemia which we are predicting, need proper management. Sensitivity of increased peak velocity of systolic blood flow in MCA for prediction of fetal anemia was 92.5% and specificity came out to be around 88%.

**Discussion**

Middle cerebral artery's (MCA) doppler velocimetry has played a major role in the fetal medicine in the last 2 decades, both in anemic fetuses and intrauterine growth-restricted (IUGR). The most likely physiological explanation is that in an anemic fetus, high cardiac output and low blood viscosity, results in high velocity blood flow, which then is picked on colour and power doppler. The peak systolic velocity in the middle cerebral artery decreases when the fetal hematocrit rises. Finding are suggestive of that hemoglobin and hematocrit concentration values are in reciprocal relation to velocity of cerebral blood flow. Therefore, the use of measurements of peak systolic velocity as described here would be beneficial and decrease the number of fetal and neonatal deaths. Our findings coincided with the work of previous researchers who demonstrated that MCA-PSV measurement is essential in the diagnosis, evaluation, and management of the cases of fetal and neonatal anemia.

Also, Amy & Kenneth\textsuperscript{9} showed that the peak systolic velocity of the MCA was effective in the detection of fetal anemia in a variety of pathologic states. They have showed that this non-invasive method for detection of anemic fetus has helped maternal fetal specialist to intervene timely in diseases like hemolytic anemia and infections. Although it's a new method, it is soon becoming a gold standard method for the diagnosis of fetal anemia. Our results were compared with hemoglobin levels of 40 cases whose blood samples were taken at birth. MCA-PSV had a sensitivity of 92.5% and a specificity of 80.6% for the detection of severe anemia. Brennand showed by comparing hemoglobin levels in 165 fetuses at either fetal blood sampling, or sampling at delivery that the sensitivity and accuracy of the middle cerebral artery Doppler (sensitivity of 88%, specificity of 82%) were substantially greater than amniocentesis (sensitivity of 76%, specificity of 77%) for the detection of anemia. We observed a linear relationship of fetal/neonatal Hb MoM and MCA PSV MoM in our study. Thus raised MCA PSV MoM was directly correlating with raised Fetal / neonatal Hb Mom. Hydropic fetuses were excluded from this study. This is because we wished to assess how effective the measurement of MCA Doppler velocity is at predicting fetal anemia in borderline cases, in which the decision to sample the fetal blood is not clear.
Conclusion

In conclusion, predicting fetal anaemia by PSV of MCA is a fast, better and far safer method. It has immense potential to replace the traditional invasive amniocentesis method to predict or diagnose fetal anemia. As well the inverse linear relationship of MoM of PSV of MCA and fetal or neonatal Hemoglobin helps to predict the severity of anemia. Its widespread use is on the near horizon and it will help in reducing risk of still births and also give immense boost to new born survival rates as well. By timely intervention or timely referral to tertiary centre, it is of great help to reduce new born morbidity and mortality as well.

References