

Review article

Role of MCA-PSV in managing fetal anemias of non-alloimmunized origin

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Abstract

The news that a fetus is normal and healthy on obstetric ultrasound scan brings immeasurable joy and satisfaction to the would be parents. However, this serene bounty can get haunted if the fetus develops signs of anemia. Although red blood cell alloimmunization remains one of the major causes of anemia in the fetus, never the less multiple other causes have been reported in non-alloimmunized pregnancies and are the focus of this article. Color Doppler ultrasound shows abnormal rise in peak systolic velocity of the middle cerebral artery (MCA-PSV) in presence of fetal anemia. This article discusses how measurement of middle cerebral artery peak systolic velocity helps in managing and monitoring such fetuses and emphasizes the need to routinely use this criterion along with other fetal biometry markers in all obstetric ultrasound scans for early detection of such mishaps before they become life threatening to the fetus as well as the mother. In right hands; this method is highly effective and economical as it is non invasive and therefore repeatable as per the need, even at bedside. Stress is also laid on the correct method of obtaining the values of fetal MCA-PSV and using the concept of multiples of median for their comparisons at different gestational ages.

Key words- Fetal anemia, Middle cerebral artery peak systolic velocity, Doppler Ultrasound

Introduction

All around the world, routinely not much is spoken about an entity called fetal anemia to the expectant parents. But nobody can deny the importance of early diagnosis and timely management of fetal anemias. The fact that around 10% of newborns, 31% low birth weights and 39% premature births, need blood transfusions when compared to control group¹ strongly points out that anemia is quite common in fetuses and newborns; and that it still remains under reported as it is mostly unsuspected. Therefore improved neonatal outcomes² are possible only by early detection and prompt intervention by means of intrauterine transfusion or labor induction for

neonatal therapy. Therefore, a diagnostic delay can result in an increased intra and perinatal morbidity and mortality rates.

Common causes of fetal anemia in non-alloimmunized pregnancies

1. Homozygous alpha-thalassemia-1 is inherited as an autosomal recessive entity and is the most severe form of alpha-thalassaemias. The affected fetus can develop anemia right from first trimester itself³. South-east Asia, the Middle-East Mediterranean basin and Africa are the commonly affected geographical locations. The risk of recurrence is 25 % per pregnancy.

Alpha-thalassemia is due to the defective synthesis of alpha-globin chains, principally because of a deletion of one, two, three or four genes. Homozygous alpha-thalassemia-1 results from a deletion of all four genes. The diagnosis can be confirmed by DNA analysis of the amniotic fluid. Cordocentesis confirms the presence of fetal anemia⁴.

In fetal anemia, the MCA-PSV increases due to following two mechanisms⁴:

- 1) Reduced hematocrit lowers blood viscosity and thereby increases blood flow velocities
- 2) Fetal anemia reduces the oxygen carrying capacity of the blood, so the cardiac output has to be increased proportionately to compensate for this.

Fetal anemia is better reflected by measurements of increased MCA-PSV than by other parameters like liver length and spleen perimeter in homozygous alpha thalassemia-1⁴. Infact the use of MCA-PSV enables a faster diagnosis of fetal anemia so that the results of DNA analysis of amniotic fluid can be awaited to find the underlying cause. MCA-PSV also helps in deciding the proper time for cordocentesis and intrauterine transfusion. Successful outcome has been reported after intrauterine transfusion, though it is not a standard treatment^{4, 5}.

MCA-PSV rise is also very useful as it indicates the necessity to transfuse even before fetal hydrops sets in, because once fetal hydrops develops, the intrauterine transfusion is less effective and has increased risks⁴.

2. Massive fetomaternal hemorrhage (FMH) has the potential to result in severe fetal anemia resulting in hydrops and even death. FMH results when > 80 – 150 mL of the fetoplacental blood enters into the

maternal circulation⁶⁻⁹. It is seen in 1 in 1000 to 1 in 3000 deliveries. Not only does it result in significant postnatal morbidity in the form of anemia, respiratory distress and even central nervous system damage, but it also has the potential to elevate the perinatal mortality range from 33% to 50%⁶⁻⁷. In such condition acute hypovolemia and reduced oxygen-carrying capacity of blood results in hypoxemia and causes fetal damage.

FMH leading to fetal anemia has already been suspected and successfully proved in patients giving history of decreased or absent fetal movements, by demonstrating elevated MCA-PSV¹⁰. The increased MCA-PSV and reversal of end-diastolic velocity in the middle cerebral artery is not altered by maternal oxygen therapy to the mother, but get reversed only after correction of fetal anemia¹¹.

3. Fetal Parvovirus B19 infection is an important cause of fetal anemia, hydrops and even intrauterine deaths¹². Serum IgM antibodies or positive polymerase chain reaction (PCR) results strongly suggest recent infection in the mother. For the fetus to be labeled as being infected, demonstration of viral DNA in amniotic fluid or fetal blood by means of PCR is a must¹³.

In parvovirus B19 infected fetuses elevated MCA PSV above 1.29 MoM has a high sensitivity (100%) and specificity (100%) in detecting fetal anemia¹³. Thus study of MCA PSV is an effective and efficient tool in managing such pregnancies and also in planning any invasive procedures as it can be treated successfully antenatally¹⁴.

The exact fetal hemoglobin status can be known only through cordocentesis or amniocentesis, but both are

invasive technique and associated with complications that can lead to intrauterine fetal demise. But as validated in a study¹³, MCA-PSV measurements can modify the management in such pregnancies, thereby avoiding unnecessary cordocentesis and at the same time detecting and confirming all positive cases of anemia.

In cases of intrauterine infections¹⁵, severe fetal anemia and tense ascites are seen mostly in Parvovirus B19 infection; and cytomegalovirus, toxoplasmosis and Treponema pallidum have milder anemia. Ventriculomegaly or microcephaly and hyperechogenic bowel are more common findings of cytomegalovirus and toxoplasmosis.

4. Haemoglobin (Hb) H Quong Sze disease has also been reported¹⁶ to present with cardiomegaly and increased MCA-PSV but without hydropic features. In these cases, the final diagnosis of HbH Quong Sze was confirmed by chorionic villus sampling and β -globin genotyping.

5. The twin-twin transfusion syndrome (TTTS) arises out of abnormal vascular communications in placenta causing imbalance in blood transfer amongst fetuses and is seen in 10% of all monochorionic twins¹⁷. It can cause anemia in the donor twin. This anemia can be demonstrated noninvasively by rise in MCA-PSV of the donor twin. Infact, MCA-PSV can be used for monitoring such cases as it demonstrates the beneficial result of intraoperative transfusion for donor fetus, after sequential selective laser photocoagulation of communicating vessels¹⁸.

MCA-PSV can predict anemia within 24 hours of the death of one monochorionic twin, in twin-to-twin-transfusion syndrome; and hence is believed to be a

reliable noninvasive diagnostic tool which also has immense use in counseling and planning invasive assessment in such cases¹⁹.

In most of the cases with severe fetal anemia, intrauterine blood transfusion is a proven therapy especially when the cause is known. But in cases with markedly elevated MCA-PSV with undetermined cause of anemia expectant management and serial follow up appears to be a reasonable alternative²⁰.

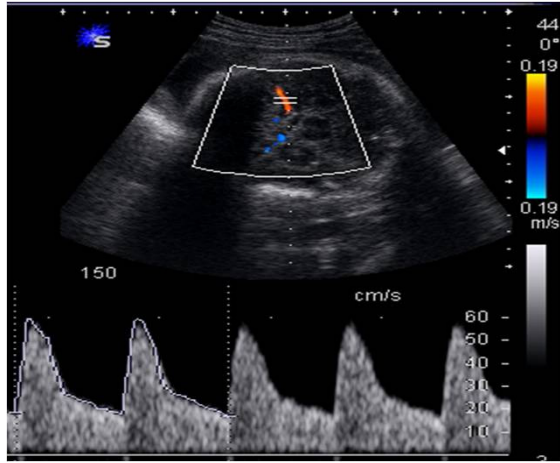
Methods to diagnose fetal anemia:

They are broadly classified as invasive methods and non-invasive methods. Amniocentesis followed by spectrophotometric analysis and ultrasound-guided cordocentesis are the invasive methods. Both are associated with certain complications²¹⁻²² and can even result in fetal death. Measurement of MCA-PSV is the non-invasive method of assessing fetal anemia. Although it is an indirect method, when MCA-PSV rises > 1.5 times the normal median value for a given gestational age; significant fetal anemia is seen^{2,10}.

The technique of measuring MCA-PSV:

On ultrasound study of fetal head, transverse section at the base of skull demonstrates the middle cerebral artery arising from internal carotid artery on either side from the circle of Willis on color flow Doppler. In this imaging plane the longitudinally oriented proximal and distal middle cerebral arteries lie parallel to the ultrasound beam and hence can be insonated at an angle of zero degrees so that accurate and actual MCA-PSV can be measured. Proximal MCA-PSV when measured just after its origin from the circle of Willis has the best reproducibility²³.

Fig.1 shows the MCA-PSV measurement in 26 weeks fetus with anemia.



How to use MCA-PSV in fetal anemia in alloimmunized pregnancies:

MCA-PSV value >1.5 times the multiple of median (MoM) for a given gestational age of fetus, suggests moderate to severe anemia, with a sensitivity of 100% and a false positive rate of 12%²⁴.

On using this technique satisfactory results²⁵ are demonstrated in the developing nations as well due to which MCA-PSV measurements are being used with to decide when the transfusions should be carried out. Moreover, it has also been observed that the degree of fetal anemia following transfusion can also be evaluated, because MCA-PSV value falls down to almost normal level following successful blood transfusion.

Although normal reference range values of fetal MVA-PSV are now available²⁴ for global use, certain reports suggest that loco-regional differences exist between normal reference values²⁶.

Benefits of using MCA-PSV:

1. Noninvasive nature; hence harmless to mother or fetus.
2. Wide repeatability.
3. Bedside availability.
4. Acceptable inter and intra observer variability.
5. Superior to spectrophotometry in the prediction of fetal anemia².

Conclusions and Suggestions

Fetal MCA-PSA has now been established as the method to identify the presence of fetal anemia of any cause. Although standard global reference range is available, it is suggested that the local range be first compared with the published standard values and only then be followed. Unacceptable discrepancy in the two reference ranges calls for scientific construction of the local reference ranges of MCA-PSV for successful utilization as life saving decisions are based on its interpretations.

A confirmed prediction of severe fetal anemia enables optimal therapy, either intrauterine blood transfusion or a timely delivery with full preparation for resuscitation of a severely anemic newborn.

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