Original Article

ID: JCDR/2012/3411.3964:0035

Radiology Section

An Indian Study of a Novel Non-invasive Method of Screening for Foetal Anaemia

SUSHIL. G. KACHEWAR, SIDDAPPA.G. GANDAGE, HEMANT. J. PAWAR

ABSTRACT

Purpose: The assessment of foetal Middle Cerebral Artery Peak Systolic Velocity (MCA-PSV) is useful in non-invasively diagnosing foetal anaemias, irrespective of their cause. A study was therefore undertaken to find out its effectiveness in the local obstetric population.

Materials and methods: Doppler ultrasound measurements of foetal MCA-PSV were done in 1200 pregnant women who were referred for antenatal ultrasound between 12-40 weeks of gestation. The statistical analysis was done by using Microsoft Excel 2007 and SPSS software, version 12.

Results: A statistically significant ($p < 0.05$) positive correlation was found to exist between the gestational age and MCA-PSV. 14 foetuses had their MCA-PSV elevated enough to label them as being anaemic. Iso-immunization was seen in 4 foetuses, severe maternal hypertension in 4, foetal parvo virus B19 infection in 3 and thalassemia in 3. Also, a disturbed MCA waveform pattern (The K-G waveform) was transiently seen in few cases with normal MCA-PSV values (The Pravara Effect).

Conclusion: Foetal MCA-PSV can objectively demonstrate foetal anaemia in pregnant patients, irrespective of the underlying cause. Every effort must therefore be made to use this non-invasive test to look for foetal anaemia in the obstetric population.

Key Words: Foetal Anaemia, Middle cerebral artery, Non-invasive test, Color Doppler Ultrasound, KG Waveform, Pravara Effect, Mind

INTRODUCTION

The accurate figures of foetal anaemia are scarce throughout the world, as those who are afflicted are often unreported, undiagnosed and even unsuspected. It is possible that many unexplained intra-uterine deaths may in fact be due to the yet undiagnosed foetal anaemia. The inadequate knowledge about the availability of a rapid and effective non invasive diagnostic test also plays a vital role in this grim scenario.

Until recently, everyone relied on invasive measures like cordocentesis to obtain foetal blood and amniocentesis to obtain liquor for spectrophotometry, to assess the presence of foetal anaemia. But, the mounting evidence that the elevated values of foetal Middle Cerebral Artery Peak Systolic Velocities **(MCA-PSV)** can indicate foetal anaemia has ushered in a new angle to the entire perspective on foetal anaemia. This test soon became popular due to its non-invasive nature and it is now being routinely used for the non-invasive assessment and the follow up of foetal anaemias [1-4]. As very few studies have been reported [1,5] on this topic from the developing world, we undertook a prospective, cross sectional study on foetal MCA-PSV to evaluate its utility in the local community and also to validate whether the value of the foetal MCA-PSV increased with the advances in pregnancy, as had been reported earlier, [1- 6].

MATERIALS AND METHODS

After prior approval from the institutional ethical and research committees, this study was carried out in the ultrasound section. An informed written consent was obtained from each participant.

1200 women who had singleton pregnancies with a gestational age between 12 to 40 weeks were randomly selected for the study.

The foetal MCA-PSV was recorded by a single observer who had more than ten years of experience in ultrasound, by using a Siemens G-60 Doppler ultrasound machine. With the patient lying supine and at ease on the bed, a transverse section of the foetal head was obtained on the B mode imaging by using a 3.5 MHz curvilinear transducer. The colour mode was then switched on and the foetal MCA was localized near the circle of Willis. After the visualization of the entire length of the MCA, a pulse Doppler was used to sample it just after its origin from the internal carotid arteries, while the angle of insonation was kept at nearly zero degrees. After obtaining a steady waveform, the image was freezed and the peak of the systolic velocity was measured [Table/Fig 1]. The entire process took around 5-15 minutes.

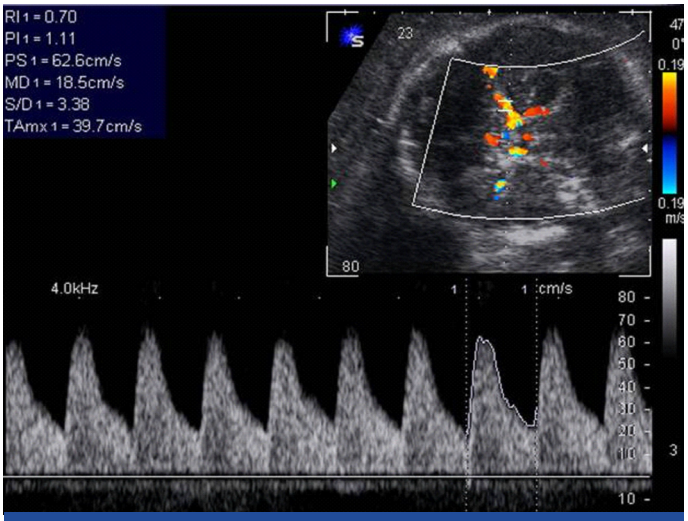
The data was compiled and statistically analyzed by using Microsoft Excel 2007 and SPSS software, version 12. The correlation between MCA-PSV and the gestational age was assessed by using the Karl Pearson`s Correlation Coefficient (r) and the 't'-test as a test of significance. The MCA-PSV values were compared with the standard published international values to evaluate whether foetal anaemia was present or not.

RESULTS

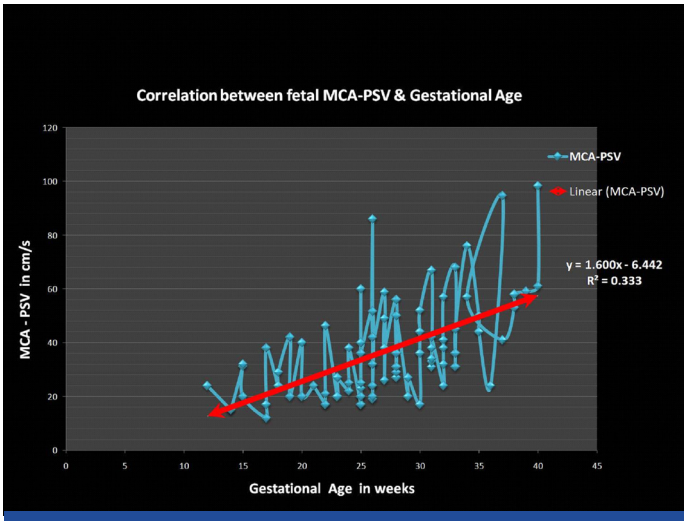
The scatter diagram [Table/Fig 2] shows the correlation between the gestational age of the foetus and its MCA-PSV. As shown by the upward slope of the line, a positive correlation was found to

exist between the two, indicating that there was an increase in the MCA-PSV as the pregnancy advanced. This correlation was statistically significant ($p < 0.05$).

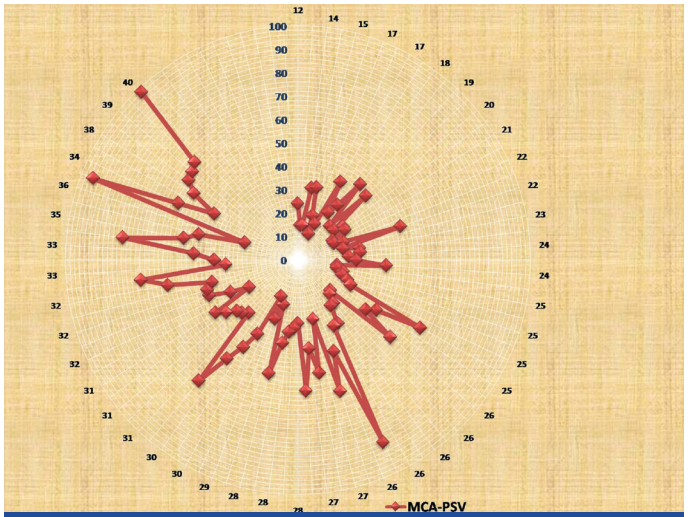
In this study, 14 foetuses had their MCA-PSV elevated enough



[Table/Fig-1]: Correct method to measure fetal MCA-PSV at origin of proximal MCA.



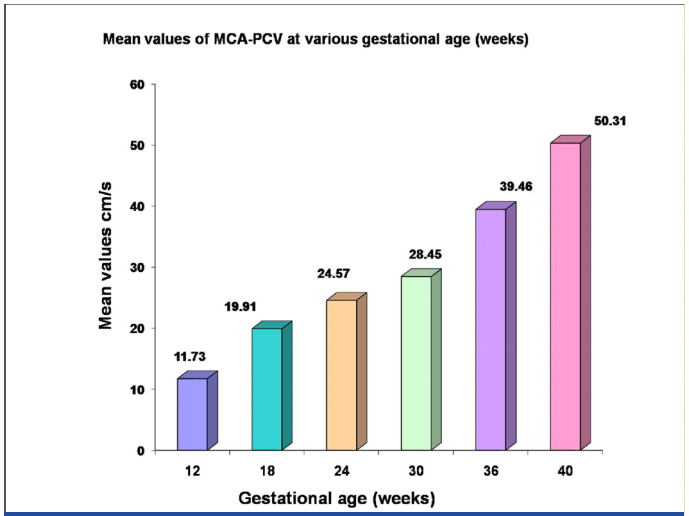
[Table/Fig-2]: Scatter diagram showing correlation between fetal MCA-PSV in cm/s and gestational age in weeks.



[Table/Fig-3]: Radar diagram showing focal elevations of fetal MCA-PSV in anemic cases at given gestational age shown as circles of different circumferences.

Gestational Age(weeks)	Observed MCA-PSV value cm/s	Cut Off value3 of MCA-PSV	Aetiology
15	32	30.3	Thalassemia
17	38	33.2	Parvo virus B19 infection
19	42	36.5	Parvo virus B19 infection
20	40	38.2	Thalassemia
22	46.3	41.9	Severe maternal hypertension
26	51.7	50.4	Iso-immunization
26	66	50.4	Iso-immunization
27	59	52.8	Iso-immunization
27	58.8	52.8	Thalassemia
28	56.0	55.4	Parvovirus B19 Infection
31	66.9	63.6	Severe maternal hypertension
34	76	70	Iso-immunization
37	94.7	84.0	Severe maternal hypertension
40	98.3	96.6	Severe maternal hypertension

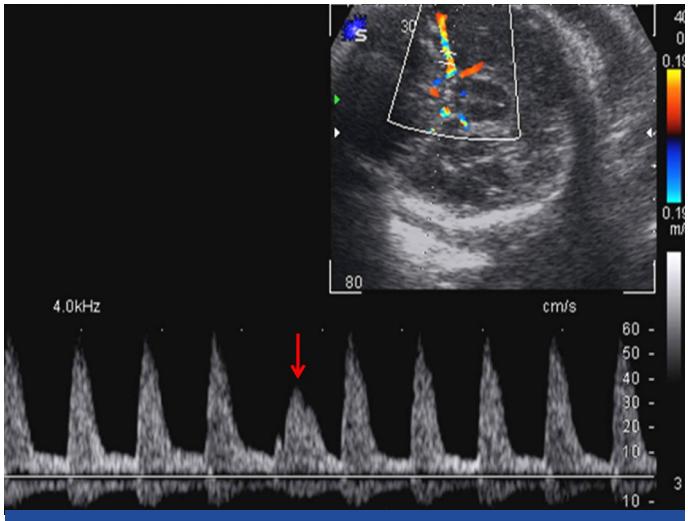
[Table/Fig-4]: Table showing anemic fetuses detected in this study and causes found subsequently.



[Table/Fig-5]: Scatter diagram showing mean fetal MCA-PSV in cm/s at various gestational ages in fetuses with normal outcome.

to label them as being anaemic. These cases with anaemia had focally elevated values as has been demonstrated in the Radar diagram [Table/Fig 3].

The causes of anaemia in these patients are shown in [Table/Fig 1]. Iso-immunization was seen in 4 patients, severe maternal hypertension in 4, foetal parvo virus B19 infection in 3 and thalassemia in 3. The mean foetal MCA-PSV which was found at various gestational ages in the foetus with its normal outcome, is shown in the Bar diagram [Table/Fig 5]. In this study, we also came across a disturbed MCA waveform pattern (named as the K-G waveform- after Kachewar and Gandage; the researchers in this



[Table/Fig-6]: The Kachewar-Gandage waveform (K-G wave) of the Pravara Effect.

project) that was transiently seen in few cases with normal MCA-PSV values [Table/Fig 6]. The foetus however was not anaemic. As this effect in which the foetal MCA velocity waveform was disturbed while the foetal haemoglobin was within normal limits was first documented successfully at our institute, we would like to label it as the 'Pravara Effect' (after the name of our Medical University).

DISCUSSION

A study [7] which was done to assess the need of blood transfusions in various categories of newborns, showed that 39% premature babies, 31% low birth weight babies, and 10% of the newborns required blood transfusions as compared to a control group. This implies that foetal anaemia was quite common and hence a timely diagnosis would ensure a satisfactory outcome. The compliance and monitoring would be better if this foetal anaemia could be suspected, suggested, graded and even diagnosed non-invasively.

The commonly known causes of foetal anaemias are red blood cell alloimmunization, parvo virus B-19 infection, the twin-twin-transfusion syndrome and foeto-maternal haemorrhage [1-7]. Unusually severe haemolytic diseases of newborns with the ABO Rh incompatibility have been reported from India, Sri Lanka and Bangladesh, which often require multiple exchange transfusions [8-10]. Severe haemolytic diseases due to the anti C and anti E antibodies in two Rh D positive women, have been reported postnatally, [11] thereby showing that severe haemolytic disease due to an alloantibody other than anti D is also possible.

Not long ago, amniocentesis and cordocentesis were exclusively used for quantifying foetal anaemias. But inherent complications of amniocentesis like foeto-maternal haemorrhage may even worsen the severity of the disease, [12].Cordocentesis is known to have a higher risk for foetal loss than amniocentesis and foeto-maternal haemorrhage and an increased sensitization is possible after a transplacental puncture, [13]. Procedure-related pregnancy loss, foetal bradycardia, bleeding, a premature rupture of membranes and enhanced risks of infection due to an intravascular access for the direct measurement of foetal haemoglobin and for transfusions have also been reported, [3].

Hence, a global search was on for a satisfactory non-invasive method to assess foetal anaemia. The doppler ultrasound based quantification of MCA-PSV was shown to be a more sensitive, specific and a non-invasive test than other parameters like intrahepatic umbilical venous maximum velocity, liver length, and spleen perimeter [14,15]. The confidence in the foetal MCA PSV has reached such levels that invasive diagnostic techniques can safely be avoided if the MCA flow velocity is found to be normal [16]. Moreover, the changes in the foetal cerebral arteries are more useful and reliable than those in the umbilical arteries, [17].

The global acceptance of the Doppler ultrasound based foetal MCA-PSV measurement as a non-invasive method of foetal haemoglobin estimation stems from the very fact that it is quick easy, and widely reproducible and that it has minimal inter or intra observer variability. It is the reduced viscosity of the blood in foetal anaemia which manifests as an elevation in the peak systolic velocity, so as to provide adequate nutrients and oxygen to the brain. The peak velocity is thus inversely related to the haemoglobin value and to the results from the increased cardiac output, [3,18].

The inverse correlation between foetal haemoglobin and MCA-PSV is weaker to begin with, when the foetus is normal or mildly anaemic and it gradually becomes stronger and statistically significant with the increasing severity of the anaemia [3]. These elevated values gradually reduce and even fall in the normal range when the foetal aneamia is adequately treated, so that ultimately the number of the unnecessary and invasive amniocentesis and cordocentesis prescriptions for diagnosing foetal anaemia can be effectively reduced, [19].

Overall, the results of this study are in harmony with those of other studies, in that the MCA-PSV increases with the advancing gestational age [2, 5, 6, 20, 21, 22]. In our study, elevated MCA-PSV values were seen in 14 patients and they were labeled as anaemic. Their causes are shown in [Table/Fig 4].

The strength of this study was that it was the first regional study to demonstrate the successful utilization of the non invasive method of foetal MCA-PSV Doppler measurement to diagnose foetal anaemia, although few case reports had been reported earlier [23,24]. The usage of this method enables the visualization of the cases which result in intra and perinatal mortality and morbidity, with fresh eyes. The strength of this study was that it was population based and that a representative sample from the rural population was involved. An internationally standardized protocol was followed in this research project. The measurements were made as they were made by other researchers.

However, we feel that this study should be conducted on a wider scale and in populations who reside in different geographic localities. We feel that this is the first regional study on this topic as till date, we have not come across any such study from this geographic locality. Moreover, this study adds a new dimension to the current literature on the foetal MCA velocity waveform in the form of the contribution of the K-G wave [6] and the Pravara effect [6].

CONCLUSION

The positive correlation between the MCA-PSV values and the gestational age which has been described in international studies, was confirmed by this regional study. The successful utilization of this non invasive test adds a silver lining to the management of foetal anaemia. The identification of the K-G wave and the description of the Pravara effect indicate that although a lot has been done globally on this topic, still there are certain dimensions

of the foetal MCA waveform that are lying unexplored. There is therefore a scope for more research.

REFERENCES

[1] Tan KBL, Fook-Chong SMC, Lee SL, Tan LK. Foetal peak systolic velocity in the middle cerebral artery: an Asian reference range. *Singapore Med J* 2009; 50(6): 584-6.

[2] Kurmanavicius J, Streicher A, Wright EM, Wisser J, Muller R, Royston P, et al. Reference values of foetal peak systolic blood velocity in the middle cerebral artery at 19-40 weeks of gestation. *Ultrasound Obstet Gynaecol* 2001; 17: 50-3.

[3] Mari G, Deter RL, Carpenter RL, Rahman F, Zimmerman R, Moise KJ, et al. Non-invasive diagnosis by Doppler ultrasonography of foetal anaemia due to maternal red-cell alloimmunization. Collaborative Group for Doppler Assessment of the Blood Velocity in Anemic Fetuses. *N Engl J Med* 2000; 342:9–14.

[4] Hernandez-Andrade E, Scheier M, Dezerega V, Carmo A, Nicolaides KH. Foetal middle cerebral artery peak systolic velocity in the investigation of non-immune hydrops. *Ultrasound Obstet Gynaecol* 2004; 23: 442-45.

[5] Kachewar SG, Gandage SG, Kulkarni DS. A local Indian scenario of foetal middle cerebral artery peak systolic velocities. *Japanese Journal of Radiology* 2011; 29: 725-9.

[6] Kachewar SG, Gandage SG. The foetal 'mind' as a reflection of its inner self: evidence from colour doppler ultrasound of foetal MCA. *Mens Sana Monogr 2012; 10:98-108.*

[7] Nardozza LM, Camano L, Moron AF, Pares DBS, Shinen RA, Torloni MR. Pregnancy outcome for Rh-alloimmunized women. *Int J Gynaecol Obstet*. 2005; 90:103-6.

[8] Marwaha N, Dhawan HK, Thakral B, Kaur R, Basu S, Parmar V. Severe ABO haemolytic disease of the newborn with a positive direct anti-globulin test. *Indian J Pathol Microbiol* 2009; 52:292-5.

[9] Haque KM, Rahman M. An unusual case of ABO-haemolytic disease of the newborn. *Bangladesh Med Res Counc Bull* 2000; 26:61-4.

[10] Lucas GN. Neonatal jaundice due to ABO incompatibility in Sri Lanka. *Indian J Paediatr* 1996; 63:381-4.

[11] Thakral B, Agrawal SK, Dhawan HK, Saluja K, Dutta S, Marwaha N. The first report from India on haemolytic disease of newborns due to the anti C and anti E antibodies in Rh (D) positive mothers. *Haematology* 2007; 12:377-80.

[12] Bowman JM, Pollock JM. Transplacental foetal haemorrhage after amniocentesis. *Obstet Gynaecol*. 1985; 66: 749-54.

[13] MacGregor SN, Silver RK, Sholl JS. Enhanced sensitization after cordocentesis in a rhesus-isoimmunized pregnancy. *Am J Obstet Gynaecol*. 1991; 165:382-3.

[14] Dukler D, Oepkes D, Seaward G, Windrim R, Ryan G. Non-invasive tests to predict foetal anaemia: A study which compared the Doppler and ultrasound parameters. *Am J Obstet Gynaecol* 2003; 188:1310-1314.

[15] Hobbins JC. Use of ultrasound in complicated pregnancies. *Clin Perinatol* 1980; 7:397–411.

[16] Oepkes D, Meerman RH, Vandenbussche FP, Van Kamp IL, Kok FG, Kanhai HH. Ultrasonographic foetal spleen measurements in red blood cell-alloimmunized pregnancies. *Am J Obstet Gynaecol* 1993; 169:121–28.

[17] Arduini D, Rizzo G. Prediction of the foetal outcome in small for gestational age fetuses: comparison of the Doppler measurements which were obtained from different fetal vessels. *J Perinat Med*. 1992; 20: 29 -38.

[18] Fan FC, Chen RYZ, Schuessler GB, Chien S. Effects of haematocrit variations on the regional haemodynamics and oxygen transport in the dog. *Am J Physiol* 1980; 238:H545–H552.

[19] Stefos T, Cosmi E, Detti L, Mari G. Correction of foetal anaemia with MCA-PSV. *Obstet Gynaecol* 2002; 99: 211-5.

[20] Mari G, Abuhamad AZ, Cosmi E, Segata M, Altaye M, and Akiyama M. Middle cerebral artery peak systolic velocity: technique and variability. *J Ultrasound Med* 2005; 24:425-30.

[21] Scheier M, Hernandez-Andrade E, Carmo A, Dezerega V, Nicolaides KH. Prediction of foetal anaemia in rhesus disease by the measurement of foetal middle cerebral artery peak systolic velocity. *Ultrasound Obstet Gynaecol* 2004; 23:432-6.

[22] Tongsong T, Wanapirak C, Sirichotiyakul S, Tongprasert F, Srisupundit K. Middle cerebral artery peak systolic velocity of healthy foetuses in the first half of pregnancy. *J Ultrasound Med* 2007; 26:1013-7.

[23] Deka D, Sharma N, Dadhwal V, Suneeta M. Successful application of middle cerebral artery peak systolic velocity to time intra-uterine tranfusions in an Rh isoimmunised foetus. *J Obstet Gynaecol* India 2006; 56:6:534-36.

[24] Arora D, Bhattacharyya TK, Kathpalia SK, Kochar SPS, Sandhu GS, Goyal BK. Management of Rh-isoimmunised Pregnancies: Our Experience *MJAFI* 2007; 63(1): 7-11.

AUTHOR(S):

1. Dr. Sushil. G. Kachewar
2. Dr. Siddappa.G. Gandage
3. Mr. Hemant. J. Pawar

PARTICULARS OF CONTRIBUTORS:

1. Corresponding Author, Associate Professor, Department of Radio-diagnosis, RMC, PIMS
2. Professor and Head, Department of Radio-diagnosis, RMC, PIMS
3. Associate Professor & Head, Medical Statistics, RMC, PIMS, Loni, India.

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sushil Ghanshyam Kachewar,
MD, DNB (Radio-diagnosis)
Associate Professor, Rural
Medical College, PIMS, Loni, India.
Phone: 0091-9921160357
E-mail: sushilkachewar@hotmail.com

FINANCIAL OR OTHER COMPETING INTERESTS:

None.

Date of Submission: **Jan 10, 2012**
Date of Peer Review: **Jan 11, 2012**
Date of Acceptance: **Jan 13, 2012**
Date of Publishing: **May 31, 2012**