International Journal of Advanced Research in Gynaecology and Obstetrics
Volume 1, Issue 2 - 2023, Pg. No. 10-17
Peer Reviewed & Open Access Journal

Research Article

# Correlation of Middle Cerebral Artery Doppler Velocimetry and Perinatal Outcomes in Intra Uterine Growth Restricted Babies

Bishan Dhiman[1], Shriya Ganju[2], Nishi Sood[3]

[1]Professor and Head, [2]Junior Resident, [3]Assistant Professor, Department Obstetrics and Gynaecology, Kamla Nehru State Hospital for Mother and Child, Shimla,Himachal Pradesh, India.

## I N F O

**Corresponding Author:**
Shriya Ganju, Department Obstetrics and Gynaecology, Kamla Nehru State Hospital for Mother and Child, Shimla, Himachal Pradesh, India.
**E-mail Id:**
shriya.ganju@gmail.com
**How to cite this article:**
Dhiman B, Ganju S, Sood N. Correlation of Middle Cerebral Artery Doppler Velocimetry and Perinatal Outcomes in Intra Uterine Growth Restricted Babies. Int J Adv Res Gynaecol Obstet. 2023;1(2):10-17.

Date of Submission: 2023-03-20
Date of Acceptance: 2023-04-15

## A B S T R A C T

*Objective:* To correlate foetal Middle Cerebral Artery (MCA) Doppler velocimetry indices in clinically diagnosed cases of Intra Uterine Growth Restriction (IUGR) with perinatal results.

*Materials and Methods:* This study was performed using Doppler MCA among 120 consecutive clinically suspected singleton IUGR pregnancy cases. As per the inclusion criteria, the subjects who were at 34-40 weeks of gestation were selected for the study. The mode of delivery of the participants was noted along with the adverse perinatal outcomes (if any) they had to experience, such as perinatal mortality, hypoglycaemia, asphyxia etc. Follow-up of the participants was ensured till delivery. SPSS 16.0 was used to analyse the obtained data.

*Result:* This study did not include 3 babies who had congenital anomalies at birth. Among these 120 women, three babies were born with congenital malformations. They were excluded from the study. In 117 study women, the Doppler revealed abnormal values of MCA PI (< 1.5), MCA S/ D ratio (< 4) and MCA RI (< 0.59) in 81 (69.2%), 69 (58.9%) and eight (6.8%) antenatal mothers respectively. Statistically significant correlations were observed with MCA PI and low birth weight ($p < 0.001$), MCA S/ D ratio and mode of delivery by caesarean section ($p < 0.05$). Among the neonates, 43 suffered from respiratory distress syndrome and hence needed admission to NICU. There were six perinatal mortalities.

*Conclusion:* MCA Doppler parameters offer an important non-invasive tool to assess foetal well-being in utero and can help to reduce the risk of prenatal mortality by timely intervention at delivery.

**Keywords:** Foetal Growth Restriction, Middle Cerebral Artery, Doppler Parameters, Perinatal Outcome

## Introduction

The prevalence of intrauterine growth restriction (IUGR), a complicated foetal growth condition, has increased in today's world.[1] IUGR is defined as the estimated foetal weight less than the 10th percentile for that corresponding gestational age.[2] It should always be kept in mind that though IUGR seems to be similar to Small for Gestational Age (SGA), there is a very important difference between the two. SGA considers only the birth weight of a neonate, while the term IUGR is applicable only in cases where a neonate shows characteristics of malnutrition from birth.[3]

It has been observed that at a global level, approximately 24% of neonates are affected by IUGR,[4] and in the Asian continent, about 75% of newborns are affected by this condition.[5,6] As per a recent UNICEF survey and the National Neonatal Perinatal database report, the prevalence of IUGR among hospital-born neonates in India has been estimated at about 25%-30% and 9.65%, respectively.[4,7]

Uteroplacental insufficiency is the principal pathology of IUGR. It may be primary, or caused by foetal infections, foetal chromosomal anomalies, or a maternal disorder.[8-10] Growth retardation results from abnormalities found in placental circulation that cause an increase in blood flow resistance thereby leading to a reduction in the speed in feeding arteries. This primarily occurs during diastole and causes a rise in various Doppler indices like pulsatility index. Thus, Doppler velocimetry, helps to understand the pathophysiological process leading to growth restriction and in detecting uteroplacental insufficiency and in monitoring fetal health. In the present study, the authors studied the Resistive index (RI), Systolic/ Diastolic (S/ D) ratio, and Pulsatility index (PI) of the MCA waveform indices and correlated with adverse foetal outcomes.

## Materials and Methods

This observational, prospective, non-interventional study was performed from August 2017 to July 2018 in the Obstetrics and Gynaecology Department of our tertiary care hospital. After obtaining informed consent, 120 consecutive patients with singleton pregnancies who were attending the OPD, were between the 34th and 40th week of gestation and were clinically suspected of IUGR, were included in this research. The college committee gave the approval for the study.

The inclusion criteria were antenatal mothers with i) singleton pregnancies ii) gestational age between 34 and 40 weeks and iii) willingness to take part in the research. The criteria for exclusion included i) multiple pregnancies and ii) congenital abnormalities in the foetus.

Poor increase in maternal weight, as well as fundal height less than the gestational period, form the basis of diagnosing IUGR clinically. Following the completion of a standard B-mode Doppler velocimetry procedure and identification of MCA, a GE LOGIQ PE6 scanner with a 3.5 MHz transducer was used to study the Doppler waveform in patients who were clinically suspected of IUGR. The origin of the MCA from the circle of Willis lies in the anterior wing of the sphenoid bone located in the sylvian fissure in proximity to the internal carotid artery near the skull base. Spells of apnoea and foetal inactivity were used to record MCA flow velocity waveforms while visualising MCA caudally to the trans-thalamic plane. The cut-off level for MCA PI<1.5[11], MCA RI <0.59[12] and S/ D ratio of <4 was considered abnormal.[13]

Follow-up was done for each participant from clinical diagnosis to delivery. Their mode of delivery was recorded. The following factors were taken into consideration while making a decision regarding delivery: i) reversal/ absence of diastolic flow ii) abnormal foetal heart tracing iii) unfavourable maternal conditions iv) severe foetal growth restriction with Amniotic Fluid Index (AFI) below five v) abnormal biophysical profile. The birth weight was recorded immediately within six hours after delivery. An Apgar score below seven after five minutes of birth was taken as abnormal. Ponderal index of <2 was considered as IUGR.[14] Any adverse perinatal outcome in terms of asphyxia, hypoglycemia, perinatal death or stay in NICU was noted.

Statistical Package for Social Sciences (SPSS) version 16.0 was utilised for the management and statistical analysis of obtained data.[15] P values below 0.05 were considered to be statistically significant.

## Result

The ages of participants varied from 18 to 35 years with the mean value being 21.8 years. At the first Doppler velocimetry test, the average gestational age was 35.2 weeks. All subjects revealed acceptable waveforms. Three newborns were not included in the study due to congenital anomalies. Among all participants, 70% (n=83) had a rural background and 44% (n=51) were primi gravida. Table 1 depicts the associated risk factors and oligohydramnios (n=21; 18%), being the commonest finding. In the past history, stillbirths occurred in 15% (n=10) of cases as shown in Table 2.

There were 116 live births and one fresh stillbirth. The mean value of birth weight was found to be 1.92 kg, the minimum value being 900 grams. One neonate weighed 3 kg at birth. Amongst these 116 live births, 70% (n = 81) had a weight between 1.5-2.4 kg. Among 39 term live births, the ratio of normal to low birth weight was 1:2. The late preterm births accounted for 78 births out of which 61 (79%) had a low birth weight; less than the 10th centile (Table 3).

**Table 1.Associated Antepartum Risk Factors in IUGR**

| S. No. | Antepartum Risk Factors | Number (N = 117) | Percentage (%) |
|---|---|---|---|
| 1. | Oligohydramnios | 21 | 18.0 |
| 2. | Preeclampsia | 19 | 16.0 |
| 3. | Anaemia | 4 | 4.0 |
| 4. | Gestational diabetes mellitus | 3 | 2.5 |
| 5. | Intra hepatitis cholestasis | 3 | 2.5 |
| 6. | Antepartum haemorrhage | 2 | 2.0 |
| 7. | Premature rupture of membranes | 1 | 0.5 |
| 8. | Heart disease | 1 | 0.5 |
| 9. | Multiple associated complications | 28 | 24.0 |
| 10. | No associated complications | 35 | 30.0 |

**Table 2.Significant Past Obstetric History in the Study Population**

| S. No. | Past Obstetric History | Number (N = 66) | Percentage (%) |
|---|---|---|---|
| 1. | Stillbirth | 10 | 15 |
| 2. | Spontaneous abortions > 2 | 5 | 7 |
| 3. | Neonatal deaths | 4 | 6 |
| 4. | Preterm labour | 1 | 2 |
| 5. | Congenital malformation | 1 | 2 |
| 6. | None | 45 | 68 |

**Table 3.Birth Weight Distribution of Neonates**

| S. No. | Category | Birth weight (kg) | Term (N = 39) n (%) | Preterm (N = 78) n (%) | Total (N = 116) n (%) |
|---|---|---|---|---|---|
| 1. | Extremely low | < 1 | 0 (0) | 2 (1) | 2 (1) |
| 2. | Very low | 1-1.4 | 6 (15) | 5 (8) | 11 (10) |
| 3. | Low | 1.5-2.4 | 20 (51) | 61 (79) | 81 (70) |
| 4. | Normal | ≥ 2.5 | 13 (34) | 10 (12) | 23 (19) |

**Table 4.Middle Cerebral Artery Doppler Indices and Mode of Delivery**

| S. No. | Mode of Delivery | Middle Cerebral Artery Doppler Indices | | | | | |
|---|---|---|---|---|---|---|---|
| | | MCA PI | | MCA RI | | MCA SD Ratio | |
| | | ≥ 1.5 n (%) | < 1.5 n (%) | ≥ 0.59 n (%) | < 0.59 n (%) | ≥ 4 n (%) | < 4 n (%) |
| 1. | Vaginal | 22 (62) | 42 (50) | 60 (55) | 4 (50) | 31 (64) | 33 (47) |
| 2. | LSCS | 13 (38) | 40 (50) p = 0.083 | 49 (45) | 4 (50) p = 0.52 | 17 (36) | 36 (53) p < 0.05 |
| 3. | Total | 35 (100) | 82 (100) | 109 (100) | 8 (100) | 48 (100) | 69 (100) |

## Doppler Velocimetry Parameters

Abnormal MCA PI was observed at 69.2% (n = 82/ 117). In these 82 study subjects, 87% (n = 72) delivered low birth weight neonates, which was statistically significant (p < 0.001).

**Table 5.Middle Cerebral Artery Doppler Indices and Perinatal Outcome**

| S. No. | Middle Cerebral Doppler Artery Indices | Reference Values | Perinatal Outcome | | |
|---|---|---|---|---|---|
| | | | Apgar < 7 at 5 minutes (N = 28) n (%) | NICU admission(N = 43) n (%) | Perinatal mortality (N = 6) n (%) |
| 1. | MCA PI | ≥ 1.5 | 7 (30) | 7 (16) | 1 (17) |
| | | < 1.5 | 21 (70) | 36 (84) | 5 (83) |
| | | p value | 0.315 | 0.004 | 0.534 |
| 2. | MCA RI | ≥ 0.59 | 24 (86) | 40 (93) | 6 (100) |
| | | < 0.59 | 4 (14) | 3 (7) | 0 (0) |
| | | p value | 0.035 | 0.744 | 0.562 |
| 3. | MCA S/ D | ≥ 4 | 12 (43) | 13 (30) | 1 (17) |
| | | < 4 | 16 (57) | 30 (70) | 5 (83) |
| | | p value | 0.855 | 0.061 | 0.321 |

**Table 6.MCA PI Performance Indicators for Prediction of IUGR**

| S. No. | Parameter | MCA PI (%) |
|---|---|---|
| 1. | Sensitivity | 79.17 |
| 2. | Specificity | 42.86 |
| 3. | Positive predictive value | 86.36 |
| 4. | Diagnostic accuracy | 72.62 |

Table 4 depicts the correlation of MCA Doppler indices with mode of delivery. Statistically significant association was seen with abnormal MCA S/ D ratio (< 4) and caesarean delivery ($p < 0.05$).

Out of the 28 neonates having Apgar score below seven at five minutes after birth, 21 (70%) had an abnormal MCA PI and 4 (14%) had an abnormal MCA RI and 16 had an abnormal MCA S/ D ratio as shown in Table 5. In 43 NICU admissions, 36 (84%) had an abnormal MCA PI. This was found to be statistically significant ($p < 0.004$). Significantly, five (83%) out of six perinatal deaths had abnormal values of MCA PI and MCA S/ D ratio. An abnormal MCA S/ D ratio, suggestive of brain sparing effect, was seen in four subjects who had an absent end diastolic flow in the umbilical artery. Three of these patients underwent a caesarean delivery for foetal distress whereas one delivered a fresh stillborn vaginally. The three live-born neonates whose birth weights were below 2.5 kg were admitted to the NICU, with one perinatal mortality. Table 6 depicts the performance indicators of MCA PI.

## Discussion

This research included women who were in the age group of 18-35 years with 42% of subjects in the 21-25-year range similar to studies conducted by Malik and Saxena on 100 subjects, having 47% of subjects in the 21-25-year range.[16]

In our study, 44% were primigravidae and 56% were multi gravidae as noted in the other studies also.[17]

Several studies have reported the association of risk factors in IUGR (Table 7). Our study reports oligohydramnios in 17.9%, pregnancy-induced hypertension in 16.2%, gestational diabetes mellitus in 2.5% and heart disease in 0.8% of participants. Geetha and Prasad,[17] Vishwekar et al.[18] and Sharma and Chandani[19] reported that hypertension induced by pregnancy was found to be correlated with IUGR in 42%, 48%, and 50% respectively. The usage of a grey-scale ultrasound for the diagnosis of IUGR may be the cause of the variation. Oligohydramnios is reported by several authors to be associated with IUGR ranging from 20% to 25%, indicative of the foetus's hypoxic condition in case of IUGR pregnancies.[16-19] Bora et al.[20] and Dhand et al.[21] observed pregnancy-induced hypertension in 20% and 14.4% of antenatal mothers, comparable to our study (16.2%). Here too, the clinical diagnosis pointed towards IUGR.

In the present study, 17.9% (n = 21) had bad obstetric history (BOH). Several authors report variable associations of BOH in IUGR as shown in Table 8. History of recurrent abortions reported by Bora et al.[20] and Dhand et al.[21] was 5% and 5.7% respectively, similar to the 4.2% noted in our study.[20,21] However, the incidence of previous stillbirths noted by these authors was lower; 2% and 2.4% respectively. The higher percentage (8.5%) may be because of the 57% multigravidae enrolled in our study.

**Table 7.Antepartum Risk Factors Associated with IUGR**

| S. No. | Authors | Year | Study Population | Maternal Risk Factors Associated with IUGR | | | |
|---|---|---|---|---|---|---|---|
| | | | | Pregnancy-induced hypertension (%) | Oligo hydramnios (%) | Heart disease (%) | Gestational diabetes mellitus (%) |
| 1. | Dhand H et al.[21] | 2011 | 121 | 14.4 | - | 1.6 | - |
| 2. | Bora MK[20] | 2015 | 100 | 20.0 | - | 2.0 | 4.0 |
| 3. | Geetha M, Prasad KJ[17] | 2016 | 100 | 42.0 | 24.0 | - | - |
| 4. | Sharma DD, Chandani CK[19] | 2016 | 60 | 50.0 | 25.0 | 3.3 | - |
| 5. | Vishwekar PS et al.[18] | 2016 | 100 | 48.0 | 20.0 | 1.0 | - |
| 6. | Present study | 2018 | 117 | 16.2 | 17.9 | 0.8 | 2.5 |

**Table 8.Bad Obstetric History and IUGR**

| S. No. | Authors | Year of Study | Study Population | BOH (%) | Risk Factors in Past Pregnancy | | |
|---|---|---|---|---|---|---|---|
| | | | | | Stillbirths (%) | Recurrent abortions (%) | Preterm deliveries (%) |
| 1. | Dhand et al.[21] | 2011 | 121 | - | 2.4 | 5.7 | - |
| 2. | Allam and Taiseer[22] | 2015 | 201 | 2.5 | - | - | - |
| 3. | Bora et al.[20] | 2015 | 100 | - | 2.0 | 5.0 | - |
| 4. | Geetha and Prasad[17] | 2016 | 100 | 36.0 | - | - | - |
| 5. | Present study | 2018 | 117 | 17.9 | 8.5 | 4.2 | 2.0 |

The distribution of newborns with IUGR as per their birth weight has been shown in Table 9. It was seen that newborns with low birth weights were more in number which could be explained because of 78 preterm births in comparison to other studies reporting it to be around 48%.[17,19] Moreover, it was reported by Sparks et al. that the sensitivity of diagnosing IUGR on clinical assessment was below 35%.[23]

The performance indicators of MCA PI have been shown in Table 10. The sensitivity, specificity, positive predictive value and diagnostic accuracy noted in our study were 79.17%, 42.8%, 86.3% and 72% respectively are comparable to studies done by Vishwekar et al.[18] and Geetha and Prasad.[17] However, Sharma and Chandani[19] noted the specificity and positive predictive value to be 93.7% and 91.6% and Khanduri et al.[24] report it as 92.6% and 93.8% respectively which was higher than in the present study. In these studies, patients were recruited at an early gestation period and multiple Doppler assessments were carried out to improve the overall specificity and positive predictive value of MCA PI. Amongst the subjects who had an abnormal MCA PI, 75% had an Apgar score less than 7 at 5 minutes, 83% were admitted to the NICU and 9% had a perinatal mortality similar to the study conducted by Bano et al.[25] Table 11 depicts the relation between an abnormal MCA PI and incidence of NICU admission was statistically significant ($p < 0.004$). In 59% of IUGR subjects with abnormal MCA PI, caesarean deliveries were performed. This finding was similar to that noted by Singh et al. with 61.5% caesarean deliveries.[26]

**Table 9.Birth Weight Distribution and IUGR**

| S. No. | Author | Year | Study Population | Extremely Low (≤ 1 kg) (%) | Very Low (1-1.4 kg) (%) | Low (1.5-2.4 kg) (%) | Average (≥ 2.5 kg) (%) |
|---|---|---|---|---|---|---|---|
| 1. | Malik and Saxena[16] | 2012 | 100 | - | - | 29.0 | - |
| 2. | Geetha and Prasad[17] | 2016 | 100 | 3.0 | 18.0 | 48.0 | 31.0 |
| 3. | Sharma and Chandani[19] | 2016 | 60 | 6.0 | 33.3 | 48.3 | 8.3 |
| 4. | Present study | 2018 | 117 | 4.0 | 10.0 | 70.0 | 19.0 |

**Table 10.Performance Indicators of Middle Cerebral Artery Pulsatility Index**

| S. No. | Authors | Year | Study Population | Performance Indicators of MCA PI | | | |
|---|---|---|---|---|---|---|---|
| | | | | Sensitivity (%) | Specificity (%) | PPV (%) | Diagnostic accuracy (%) |
| 1. | Gramenelli et al.[13] | 1992 | | | | | 54.4 |
| 2. | Khanduri et al.[24] | 2012 | 60 | 35.7 | 92.6 | 93.8 | 52.8 |
| 3. | Sharma and Chandani[19] | 2016 | 60 | 78.0 | 93.7 | 91.6 | - |
| 4. | Geetha and Prasad[17] | 2016 | 100 | 59.5 | 71.7 | 65.1 | 66.0 |
| 5. | Vishwekar et al.[18] | 2016 | 100 | 87.5 | 46.0 | - | 66.0 |
| 6. | Present study | 2018 | 117 | 79.17 | 42.8 | 86.3 | 72.0 |

**Table 11.Adverse Perinatal Outcome in Abnormal MCAPI**

| S. No. | Authors | Year ofStudy | Study Population | Apgar < 7 at 5 Minutes (%) | NICU Admission (%) | Mortality (%) |
|---|---|---|---|---|---|---|
| 1. | Bano et al.[25] | 2010 | 60 | 75 (p < 0.010) | 75 (p < 0.050) | 25 (p = 0.001) |
| 2. | Present study | 2018 | 117 | 75 (p = 0.315) | 83 (p = 0.004) | 9 (p = 0.534) |

**Table 12.Mode of Delivery in IUGR**

| S. No. | Author | Year of Study | Study Population | Vaginal Delivery (%) | LSCS (%) | p Value |
|---|---|---|---|---|---|---|
| 1. | Malik and Saxena[16] | 2012 | 100 | - | - | 0.090 |
| 2. | Singh et al.[26] | 2013 | 100 | 38.4 | 61.5 | 0.001 |
| 3. | Present study | 2018 | 117 | 41.0 | 59.0 | 0.001 |

**Table 13.Indication for Caesarean Section in IUGR**

| S. No. | Authors | Year of Study | Study Population | Indication for Caesarean Section | | | |
|---|---|---|---|---|---|---|---|
| | | | | Foetal distress (%) | Failed induction (%) | MSL* (%) | PoorBPP (%) |
| 1. | Parra-Saavedra et al.[27] | 2013 | 193 | 27.0 | - | - | - |
| 2. | Cruz Martine et al.[28] | 2015 | 327 | 37.9 | - | - | - |
| 3. | Geetha and Prasad[17] | 2016 | 100 | 46.0 | - | - | - |
| 4. | Sharma and Chandani[19] | 2016 | 60 | 32.0 | 18.9 | - | - |
| 5. | Present study | 2018 | 117 | 49.0 | 17.0 | 11.0 | 15.0 |

*MSL (Meconium stained liquor)

Caesarean Sections (CS) were performed in 49% of subjects for foetal distress (Tables 12 and 13). This was comparable to the 46% of caesarean sections performed for foetal distress.[17] IUGR foetuses have a lower placental reserve and less tolerance towards deprivation of oxygen in the intermittent contractions of labour leading to foetal distress and caesarean sections. The other reasons for CS were failed induction in 17%, poor biophysical profile (BPP < 6/10) in 15% and meconium-stained liquor in 11%.

Admission to NICU was needed in the case of 43 newborns because of varying reasons like respiratory distress syndrome (49%), hypoglycaemia (34%), neonatal jaundice (14%), and meconium aspiration syndrome (13%). Six perinatal mortalities were observed, one among which was a stillbirth. In the rest five, admitted to NICU perinatal deaths were attributable to respiratory distress.

## Conclusion

The present study showed that abnormal MCA Doppler indices played a vital role in the prediction of low birth weight and Apgar score, caesarean sections for foetal distress, and higher probability of NICU admissions in clinically diagnosed patients with IUGR. Evaluation of an

antenatal mothers early in their antenatal period with Doppler parameters offers a non-invasive comprehensive tool to assess the fetal well-being in utero.

**Source of Funding:** None

**Conflict of Interest:** None

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