Original Research Paper

Volume - 16 | Issue - 01 | January - 2026 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Obstetrics & Gynaecology

STUDY OF THE ROLE OF CEREBRO-PLACENTAL RATIO IN EVALUATION OF PREGNANCIES WITH GESTATIONAL DIABETES MELLITUS

Dr. Shreepad V. Karhade

Dr. Ashwini Jaybhaye

Dr.Prasad K. Kulat

Dr. Mugdha Parasnis

KEM Hospital, Sardar Moodliar Road, Rasta Peth, Pune, Maharashtra, India-411011

ABSTRACT **Objectives:** This study evaluated the role of the cerebro-placental ratio (CPR) in predicting adverse perinatal outcomes in pregnancies complicated by gestational diabetes mellitus (GDM), regardless of small for gestational age (SGA) status. **Material and Methods:** A cross-sectional observational study was conducted at K.E.M. Hospital, Pune, involving 100 singleton diabetic pregnant women in their third trimester (>30 weeks). Participants underwent detailed clinical evaluations, laboratory investigations, and Doppler velocimetry of the umbilical artery (UA) and middle cerebral artery (MCA). Adverse outcomes were defined by factors such as perinatal death, cesarean section for fetal distress, 5-minute APGAR scores <7, hypoglycemia, and NICU stays >24 hours. **Results:** Caesarean section was the primary mode of delivery (88%), with non-reactive CTG being a leading indication for emergency procedures (48.1%). Abnormal Doppler values were found in a minority of patients: 9% for UA PI, 12% for MCA PI, and 12.9% for CPR in cases with macrosomia. Significant associations ($p<0.05$) were found between: Abnormal UA PI: NICU admission, hypoglycemia, and respiratory distress syndrome (RDS). Abnormal MCA PI: RDS only. Abnormal CPR: NICU admission, 5-minute APGAR <7, and hypoglycemia. The type of GDM intervention significantly influenced outcomes, with RDS and hypoglycemia associated with insulin use. **Conclusion :** While abnormal Doppler values are not frequent in GDM, they are significant predictors of adverse neonatal outcomes. UA Doppler PI outperformed MCA PI as a predictor. Specifically, abnormal CPR is a valuable indicator for hypoglycemia and low APGAR scores, supporting the routine use of Doppler monitoring in high-risk GDM pregnancies.

KEYWORDS : Doppler, Cerebro placental ratio (CPR), GDM, Fetal distress.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common antenatal pregnancy complications. GDM is actually a condition of carbohydrate intolerance that starts or is first recognized during pregnancy [1]. Gestational diabetes mellitus is defined by the WHO as hyperglycemia first detected during pregnancy that does not meet diagnostic criteria for diabetes mellitus[2]. Approximately 7% of all pregnancies are complicated by GDM. The prevalence may range from 1 to 14% of all pregnancies. About 90% of patients with diabetes diagnosed during pregnancy are cases of GDM[1].

Diabetes mellitus in pregnancy, which is divided into two categories of pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM), complicates approximately 6–7% of pregnancies in the . A previous study of 3674 patients across 7 cities in India estimated that the prevalence of GDM was 16.55% in India using the WHO 1999 method[3]. A variety of factors may contribute to this variability, including differences in the genetics and population across India, as well as differences in screening practices.

GDM has both maternal and neonatal complications. Uncontrolled GDM has profound effects on fetal growth and neonatal health. Diabetes mellitus is related to increased rates of perinatal morbidity and mortality. Pregnancies affected by diabetes mellitus are more likely to be associated with complications, such as increased rate of cesarean section, macrosomia, hyperbilirubinemia, shoulder dystocia, congenital anomalies, and birth trauma[4]. Neonatal complications consist of hypoglycemia, hypocalcemia, hyperbilirubinemia, polycythemia, operative delivery, shoulder dystocia, macrosomia, birth injury, asphyxia, and respiratory distress syndrome (RDS)[4].

Appropriate management of diabetes mellitus in pregnancy requires planned fetal surveillance. Although diagnostic tests such as fetal scalp blood sampling or umbilical cord blood sampling are available for the assessment of fetal well-being, they are all invasive methods with a high sampling failure rate, requiring membrane puncture or rupture. Instead, screening of fetal distress is applied to detect a fetus at risk[5]. Diagnosing, monitoring and controlling of GDM as well as assessment of fetal well-being may reduce the impact of diabetes on the fetus and decrease neonatal complications[6].

Doppler ultrasound examination measures the blood flow through arteries and veins, such as umbilical and middle cerebral arteries. Doppler assessment of placental and fetal circulations is a non-invasive method for the evaluation of fetal well-being in high-risk pregnancies (e.g., pre-eclampsia and intrauterine growth retardation). However, application of Doppler ultrasound examination in diabetic pregnancies has revealed conflicting results[7]. In fact, despite the widespread use of these techniques, only few studies have investigated their effectiveness in improving perinatal outcomes in diabetic women[4].

The use of Doppler studies of the umbilical artery has been demonstrated to reduce perinatal adverse outcome in non-diabetic pregnancies[8], but its use in diabetic pregnancies has shown conflicting results. While umbilical artery (UA) Doppler studies have been shown to be more predictive of adverse outcome than cardiotocography and biophysical profile in diabetic pregnancies[9], fetal compromise would occasionally still be observed despite normal Doppler studies[10]. Thus, the precise value of Doppler studies in the monitoring of GDM pregnancies remains controversial.

In pregnancies with suspected fetal growth restriction, the use of umbilical artery Doppler has been demonstrated to reduce the number of perinatal deaths and unnecessary obstetric interventions. In the context of diabetic pregnancies, however, the applications of umbilical artery Doppler remain controversial.

An UA Doppler ultrasound does not induce any stress on the fetus during the test but a perinatologist must perform the test. Abnormal umbilical artery Doppler is a marker of utero-placental insufficiency and consequent intrauterine growth restriction (IUGR). Abnormal waveforms include elevated systolic/diastolic (S/D) umbilical arterial ratio, as well as absent and reversed end-diastolic velocimetry. The use of routine UA Doppler ultrasound in low-risk women has not been supported[11].

The middle cerebral artery (MCA) is the most studied cerebral artery

because it is simple to sample, consistent and reproducible, and provides information on the cerebral blood flow in normal and growth restricted fetuses[12]

Overt MCA changes appear as increased diastolic velocity, and an altered cerebro-placental ratio (MCA PI/ UA PI) will thus be observed. Changes in cerebro-placental ratio (CPR) may be at least partly pressure-dependent, reflecting structural placental deficiencies, whereas brain-sparing is attributed to hypoxia induced cerebro-vascular dilatation[13].

In these pregnancies over 34 weeks of gestation, placental functional decline may be more dominant than structural decline. Thus MCA changes in brain-sparing may appear in small fetuses with near-normal umbilical artery Doppler[14,15]. Such findings are again more likely to occur in women with pre-existing diabetes mellitus with vasculopathy than in those with gestational diabetes mellitus.

The present study was designed to evaluate the role of middle cerebral artery and umbilical artery Doppler and cerebro-placental ratio in the third trimester in assessment of fetal wellbeing in diabetic pregnant females.

MATERIAL AND METHODS

The present study was conducted in the Department of Obstetrics and Gynecology, King Edward Memorial Hospital and Research Centre, Pune.

Singleton diabetic pregnant females in the third trimester (> 30 weeks).

All study cases were precisely dated based on reliable menstrual dates that were consistent with early examination or early ultrasonography (</= 20 weeks). This was a Cross-sectional observational study. **Sample size –** 100.

A. INCLUSION CRITERIA

1. Diabetic pregnant females
2. Singleton pregnancy with no other congenital abnormality
3. Gestational age > 30 weeks
4. With no history of rupture of membranes

B. EXCLUSION CRITERIA

1. Multiple pregnancy
2. Fetuses with anatomical defects
3. Pregnant females with other medical disorders

This cross-sectional observational study comprised 100 women who were monitored and delivered in K.E.M. Hospital, Pune . All cases were subjected to detailed history taking, complete general examination with special attention to history of diabetic condition, diabetic complications and treatment, and obstetric examination, laboratory investigations (including complete blood picture, fasting and 2 hours postprandial blood sugar, liver function tests, kidney function tests, and complete urine analysis), and interval ultrasonographic biometry. Doppler velocimetry of the UA and MCA were performed during their routine growth assessment scans after 30 weeks.

Mode of the delivery was recorded, and also the indication for elective/ emergency cesarean section, if performed.

Adverse or abnormal perinatal outcome was defined as any perinatal complications such as: perinatal death, cesarean section for fetal distress, meconium staining of amniotic fluid, 5-minute APGAR score <7, hypoglycemia (glucose level <45mg/dL), or stay in neonatal intensive care unit for >24 hours.

Ultrasound equipment capable of high resolution gray-scale, pulsed wave and colour Doppler modes was used, (GE Voluson E6 and Mindray DC 8) using 3.5 MHZ probe.

All recordings were obtained in the absence of fetal breathing and fetal movements. For each vessel, an average of three consecutive Doppler waveforms was used for statistical analysis.

The APGAR score was used in the evaluation of fetal condition after birth. The score includes the heart rate, respiratory effort, muscle tone, reflexes and color. In general, the higher the score (up to 10), the better the condition of the infant. The 1 minute APGAR score determines if immediate resuscitation is needed. A score of 7 or higher indicates good infant condition and no need for aid for more than nasopharyngeal suction. Mild to moderate depressed infants score between 4 to 7 at 1 minute. Severely depressed infants score 0 to 4.

All adverse outcomes including fetal macrosomia and polyhydramnios, as well as adverse neonatal outcomes were recorded.

RESULTS AND DISCUSSION:

In the present study, more than one third of patients were of 25-29 years age (47%), followed by 30-34 years (32%), 35-39 years (11%), 20-24 years (5%) and ≥40 years (5%). The mean age of patients was 24.35±3.27 years. More than one third of patients were primigravida (44%), followed by multigravida (34%) and prior spontaneous abortions (22%). Majority of patients had Cesarean Section as mode of delivery (88%), while 12% patients delivered vaginally.

Table 1. : Distribution of cases according to mode of delivery

Mode of delivery	Current study
Vaginal delivery	12%
Elective CS	34%
Emergency CS	54%

Table 2.: Distribution of cases according to indications of CS

Indication for CS	Current study
Abnormal Doppler	23.5%
Non-reactive CTG during labour	18%

On comparing the indications for elective cesarean sections, it was found that out of 34 patients, 26 (76.4%) underwent elective CS due to previous cesarean sections, while 8 (23.5%) cases were due to abnormal Doppler values.

On comparing the indications for emergency cesarean sections, it was found that out of 54 cases, 26 (48.1%) were due to non-reactive CTG during labour.

Cerebro-placental ratio is the ratio of the MCA to UA Doppler systolic to diastolic ratios. CPR compares the resistance to blood flow in the umbilical artery and the MCA. It measures the proportion of flow supplying the brain and the placenta. It is heart rate-independent and has a significant single cutoff value of 1 (CPR is normal if it >1). In redistribution of blood flow to the brain CPR becomes < 1. The CPR ratio is a possibly better predictor of adverse outcome than the ratio in either of the vessels on their own[16].

Table 3.: Comparison of Abnormal Doppler values

	Current study
Abnormal UA PI	9%
Abnormal MCA PI	12%

CPR ratio varies from 1.41 at 21 weeks to a peak of 2.36 at 33 weeks. Subsequently there is a fall in the CPR to 1.97 at 39 weeks. It is important to note that in normal fetuses, the CPR is always >1, irrespective of the gestational age[17]. In this study, UA and MCA Doppler were abnormal in 9% and 12% patients respectively.

In the present study, NICU Admission was seen among 62% babies, Hypoglycemia was seen among 46% babies and RDS was seen in 27% babies. In this study, out of 100 cases of GDM, 28% cases were on MNT (diet-controlled), 42% cases were on OHAs, 17% cases were on Insulin, and 13% cases were on both OHAs + Insulin. There was no significant association found between the type of GDM and abnormal UA Doppler, MCA Doppler or CPR values. However, there was a significant association found between GDM on OHAs and NICU admission of neonate (35.5%). RDS (12%) and Hypoglycemia (16%) were more in cases with GDM on insulin.

The results of this study indicated that both UA and MCA Doppler tests were significantly related with some adverse neonatal outcomes.

Table 4.: Adverse neonatal outcomes related to UA PI

Neonatal outcome	Current study (n=100)		
	Normal UA PI (n=91)	Abnormal UA PI (n=9)	p value
NICU admission	58.2%	100%	0.01*
APGAR at 5 min <7	1.1%	0%	0.75
Hypoglycemia	41.8%	88.9%	0.005*
RDS	23.1%	66.7%	0.007*

*Significant

Table 5.: Adverse neonatal outcomes related to MCA PI

Neonatal outcome	Current study (n=100)		
	Normal MCA PI (n=88)	Abnormal MCA PI (n=12)	p value
NICU admission	63.6%	50%	0.36
APGAR at 5 min <7	1.1%	0%	0.71
Hypoglycemia	46.6%	41.7%	0.74
RDS	30.7%	0%	0.02*

*Significant

There was a significant (p<0.05) association of NICU admission, hypoglycemia and RDS in babies with abnormal UA Doppler. Also, there was significant (p=0.02) association of RDS in babies with abnormal MCA Doppler. There was no significant difference in the mean gestational age at delivery of patients with abnormal UA Doppler (34.25 ± 1.48 weeks) as compared to patients with normal UA Doppler (35.85 ± 2.00 weeks), and also in those with abnormal MCA Doppler (36.14 ± 2.19 weeks) compared with those with normal MCA Doppler (35.64 ± 2.00 weeks).

In the present study, abnormal CPR was seen in 12.9% patients in whom fetal macrosomia was present. Abnormal UA, MCA and CPR was seen in 6%, 12% and 10% patients respectively in whom polyhydramnios was present. NICU admission, APGAR score at 5 MIN <7 and Hypoglycemia were significantly (p<0.05) associated with abnormal CPR.

Table 6: Adverse neonatal outcomes related to abnormal CPR values

Neonatal outcome	Current study (n=100)		
	Normal CPR (n=91)	Abnormal CPR (n=9)	P value
NICU admission	63.7%	44.4%	0.02*
APGAR at 5 min <7	1.1%	0%	0.02*
Hypoglycemia	48.4%	22.2%	0.001*
RDS	26.4%	33.3%	0.13

*Significant

CONCLUSION

There is now good data, both from prospective[18,19] and retrospective studies[20,21] linking low CPR with suboptimal growth at term, increased rates of intrapartum compromise and emergency CS, poor condition at birth and increased NICU admission. Fetuses with reduced feto-placental reserves prior to labour have decreased ability to tolerate the progressive hypoxic stress caused by intrapartum uterine contractions, which reduce uterine blood flow by up to 60%[22]. The CPR reflects suboptimal placental function and subsequent fetal cardiovascular compensation, and thus appears to be a better predictor of outcome than UA PI or MCA PI individually[23]. Hence, it is likely a good parameter for assessment of fetal wellbeing in diabetic pregnancies.

This study has demonstrated that abnormal Doppler values are found in very less number of GDM pregnancies, and is not related to the type of GDM. Abnormal UA PI is significantly associated with NICU admission, hypoglycemia and respiratory distress in neonates. Abnormal MCA PI is significantly associated only with respiratory distress in neonates and is therefore, not very useful in predicting adverse neonatal outcomes in such pregnancies. Abnormal CPR values are significantly associated with NICU admission, neonatal hypoglycemia and 5 minute APGAR score <7.

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