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Cerebro placental ratio (CPR) as a tool for predicting neonatal outcomes in pregnancy complicated by overt and gestational diabetes

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Abstract

Background and Aim: Diabetes mellitus is one of common disease which is complicating pregnancy worldwide. Adverse neonatal outcomes associated with diabetes are of wide range. Cerebroplacental ratio (CPR) is a simple tool that can be calculated by Doppler hence using CPR as tool to predict neonatal outcome would be great scope in future. Hence present study aimed at to evaluate the cerebroplacental ratio (CPR) as a predictor of neonatal outcomes in pregnancies complicated by diabetes mellitus.

Materials and Methods: It's a prospective observational study at our tertiary care centre of 100 pregnant women who are diagnosed with overt or gestational diabetes mellitus. Cerebroplacental ratio is calculated. 100 cases were subdivided into 2 groups by calculating CPR Z score.
i)   Z score positive group with individual CPR ratio greater than mean (70 cases)
ii) Z score negative group with individual CPR ratio lesser than mean (30 cases)

Results: Cerebroplacental ratio less than 1.3 (negative Z score) is associated with bad neonatal outcome. Mean gestational age of delivery is lower (less than 37 weeks) in negative CPR Z score group in compared to more than 38 weeks in positive CPR Z score group. Pulsatility index of MCA is significantly lower in negative group than positive group with mean index of 1.23 in negative group and 1.55 in positive group. Pulsatility UA index is significantly higher in negative group than positive group with mean index 0.978 in negative group and 0.62 in positive group. Mean CPR z score is 1.224 for negative group and 2.57 score for positive group. Negative Z score group falls below 11th percentile and positive z score group falls above 86th percentile. Antenatal complications is significantly higher in negative group especially IUGR and oligohydramnios than positive group. Intrapartum complications are also significantly higher in negative group especially fetal distress. Bad neonatal outcomes are less in positive CPR Z score group like admission to NICU, low Apgar, and low birth weight.

Conclusion: Doppler cerebroplacental ratio is a better predictor of adverse perinatal outcome compared to Pulsatility index of umbilical artery or Pulsatility index of middle cerebral artery in singleton high risk pregnancy. There is no significant association between cerebroplacental ratio and pregnancy complicated by overt or gestational diabetes mellitus but CPR ratio less than 1.3 is associated with worse neonatal outcome. CPR ratio is less in pregnancy complicated by overt diabetes compared to gestational diabetes. Patients treated with insulin had less CPR ratio compared to patients on oral hypoglycaemic agents than on medical nutrition therapy. A less CPR ratio is associated with early gestational age of delivery. Ante partum complications like IUGR, oligohydramnios, Intrapartum fetal distress and postpartum complications like NICU admission, low birth weight and low Apgar are associated with low CPR ratio.

Keywords: Overt, diabetes mellitus, gestational diabetes mellitus, cerebroplacental ratio, pulsatility index middle cerebral artery, umbilical artery

Introduction

Diabetes mellitus is one of common disease which is complicating pregnancy worldwide. Neonatal outcomes associated with diabetes are of wide range. For example small to large to gestational age, neonatal hypoglycemia, respiratory distress syndrome as well increased risk for pre-eclampsia, cesarean, preterm delivery etc.

Cerebro placental ratio is a simple tool that can be calculated by Doppler hence using CPR as tool to predict neonatal outcome would be great scope in future.

Doppler ultrasound velocimetry of umbilical and fetal vessels has become established method of antenatal monitoring, hence allowing the non-invasive assessment of neonatal circulation and its perinatal outcome [1].

Its indices provide important information on the hemodynamics of the fetus [2]. Umbilical arteries (UA) and middle cerebral artery (MCA) are the common vessels assessed by Doppler

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ultrasound other than uterine vessels [3-5].

Several studies have reported higher sensitivities and specificities for PI index of middle cerebral artery/PI index of umbilical artery (MCA/UA)/ cerebroplacental ratio (CPR) Doppler ratio compared with umbilical artery velocimetry alone for the prediction of the fetal prognosis [6-9].

The CPR is emerging as an important predictor of adverse pregnancy outcome. Fetuses with an abnormal CPR that are appropriate for gestational age have a higher incidence of fetal distress in labor requiring emergency caesarean delivery, a lower cord pH, and an increased admission rate to the newborn intensive care unit when compared with fetuses with a normal CPR [10].

Deterioration in placenta function during pregnancy results in compensatory hemodynamic changes in the fetus, with increased blood flow to the brain and other essential organs [24].

This redistribution of cardiac output is typically seen in small for gestational age fetuses, or any fetus that fails to reach its growth potential regardless of gestation [24].

Small for gestational age neonates, with birth weight below 10th percentile, may be constitutionally small or growth restricted due to impaired placenta ion, fetal abnormalities or adverse environmental effects, such as congenital infection [26].

In fetal growth restriction (FGR) due to impaired placenta ion, both perinatal outcome and long term neurodevelopment was worse than in constitutionally small fetuses [26].

Hence after identification of SGA fetuses and exclusion of those with fetal abnormalities, prenatal diagnosis aims to detect the FGR group and, through close surveillance, to define the best time, place and mode of delivery [26].

An important modality for achieving this objective is by Doppler assessment of impedance to flow in the Umbilical artery, fetal middle cerebral artery and the ratio of their Pulsatility index (PI) in these vessels, defined as CPR [26].

The main advantage of Doppler studies over other methods because it's a noninvasive, easily repeatable and is safe to the fetus.

Doppler ultrasound plays an important role in screening for defective placentation and decreased oxygenation and its complications in high risk pregnancies.

Pathophysiology of high risk pregnancies and its management can be understood better with the assessment of fetal circulation. Using Doppler, compromised fetus can be identified and timely delivery can be planned which is important in decreasing the mortality and morbidity of the fetus. Decision regarding risk of prolonging the pregnancy (stillbirth) and the risk of prematurity can be assessed using Doppler in high risk pregnancy.

Impaired placentation occurs   mostly in a vascular disorder like hypertension, diabetes, IUGR, collagen vascular diseases like SLE and APLA. Fetal compromise can also occur with decreased fetal oxygenation due to CF maternal anaemia and rheumatic heart diseases. It starts with tertiary villi and ends with fetal cardiovascular manifestations.

Aims
The aim of the study is to evaluate the predictive value of cerebroplacental ratio (CPR) by Doppler and to correlate it with Neonatal outcomes in pregnancies complicated by diabetes mellitus.

Objectives
The objective of my study would be to evaluate the
1. Variations in CPR in Pregnancies complicated by gestational diabetes mellitus and overt diabetes mellitus.

2. Changes in CPR in patients with GDM in different modes of treatment.
3. Significance of CPR in antepartum, Intrapartum and Neonatal period.

Materials and Methods
The cases admitted in wards of department of Obstetrics and Gynecology who are diagnosed to have Overt and Gestational diabetes mellitus. 100 cases were taken from the period of November 2019 to October 2021.

Inclusion Criteria
a) Patients diagnosed with gestational diabetes mellitus.
b) Patients diagnosed to have overt diabetes mellitus

Exclusion Criteria
High risk pregnancies: including multiple gestations, cardiopulmonary disease, and pregnancy induces hypertension, previous caesarean, renal disease.

Precise description of methodology of the proposed research
After approval from ethical committee study was conducted after obtaining informed consent from the patient during the period of November 2019 to October 2021. The cases admitted in wards of department of Obstetrics and Gynecology who were diagnosed to have Gestational diabetes mellitus was included in the study. A detailed history is taken and examination is done along with systemic examination and basic investigations.

USG obstetrics with fetal Doppler is done after 34 weeks to calculate cerebroplacental ratio.

Pulsatility index of Umbilical artery, Pulsatility index of middle cerebral artery are obtained by Doppler and cerebroplacental ratio is calculated. Patients are followed according to the protocol of the institution.

Table 1: Doppler changes and follow up

PI of MCA	PI of UA	Follow up
Normal	Normal	After 2 weeks
Normal	Increased	After a week
Decreased	Increased	Twice a week

CPR ratio less than 1.5 was planned for termination of pregnancy. Patient were followed through antepartum, Intrapartum and postpartum period to know the outcomes of neonates.

Results
Age distribution
The age distribution in the present study was in the range of 19 to 40 years. There was no significant difference among the CPR Z score negative and positive group. The mean age was 26.3 for negative group and 26.6 for positive group.

A study done by Cl. Flatley et al. revealed the mean age group of women included in the study cohort was 28.5 years of age.

Another study done by M. Pe´Rez-Cruz et al. revealed that age distribution was 29.4 for the study group and 30.2 in the IUGR group, which was not statistically significant.

Distribution of parity
In the present study, 60% of them were multiparty, and 40% were null parity. There is almost equal distribution, among the primigravida and multigravida.

A study done by Flatley Cl, et al, 53.4% of women was nulliparous.

Another study done my M. PE´REZ-CRUZ *et al*, 57% of women was nulliparous in control group, and 67% of women were nulliparous in high risk group. No significant difference between both groups.

Type of Diabetes mellitus
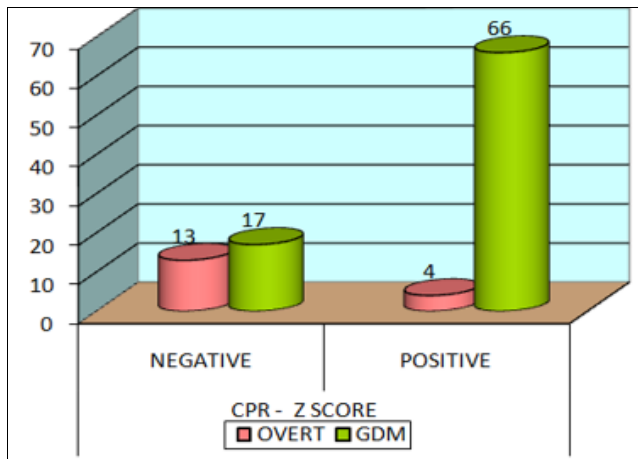
Fig 1: Comparison of type of Diabetes

Table 2: Comparison of type of diabetes

Type of diabetes	CPR - Z score	
	Negative	Positive
OVERT	13	4
GDM	17	66
Total	30	70
P value	< 0.001 Significant	

Out of 30 CPR Z score negative cases, 13 had overt and 17 cases had GDM treatment and out of 70 positive cases, 4 had overt and remaining 66 cases had GDM.

Type of treatment

Table 3: Type of treatment

Treatment	CPR - Z score	
	Negative	Positive
MNT	7	44
OHA	3	15
Insulin	20	11
Total	30	70
P value	< 0.001 Significant	
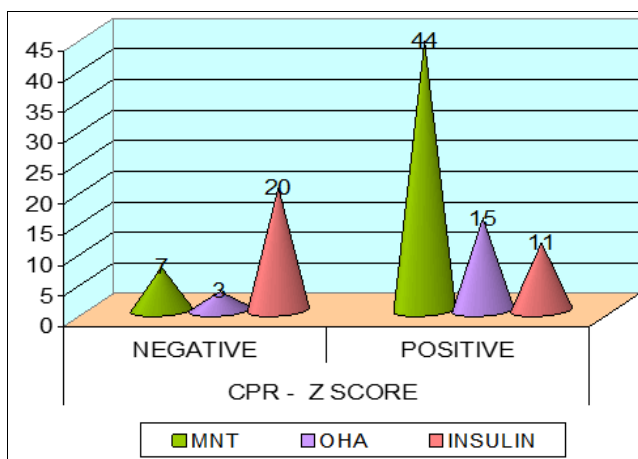
Fig 2: Comparison of Treatment

Out of 30 negative score cases, 20 cases had taken insulin, but in positive group only 11 cases had taken insulin out of 70 cases.

Gestational Age
Mean gestational age is significantly lower in CPR Z score negative cases when compared with positive cases. 36.94 mean weeks for negative group and 37.82 in positive group cases.

Pulsatility (MCA) index
Pulsatility index of MCA is significantly lower in negative group than positive group. Mean score 1.23 in negative group and 1.55 in positive group.

Pulsatility (UA) index
Pulsatility index of UA is significantly higher in negative group than positive group. Mean score 0.978 in negative group and 0.62 in positive group.

CPR Z score
Mean CPR z score is 1.224 for negative group and 2.57 score for positive group. There is highly statistically significant difference for both groups.

Table 4: Significance of CPR score

| CPR score	CPR - Z score	
	Negative	Positive
≤ 1.8	29	1
> 1.8	1	69
Total	30	70
Mean	1.224	2.566
SD	0.391	0.444
P value	< 0.001 Significant	

CPR Percentile
Negative Z score group falls below 11th percentile and positive z score group falls above 86th percentile.

Mode of delivery
Out of 30 negative CPR z score cases, 21 cases delivered by LSCS but in positive group 33 cases delivered by LSCS out of 70 cases. There is no significant difference between both groups. P value 0.074 not significant.

Maternal complications
Maternal complications is significantly higher in negative group especially IUGR and oligohydramnios than positive group. 14 out of 30 had complications in negative group but in positive group only 11 complications out of 70 cases.
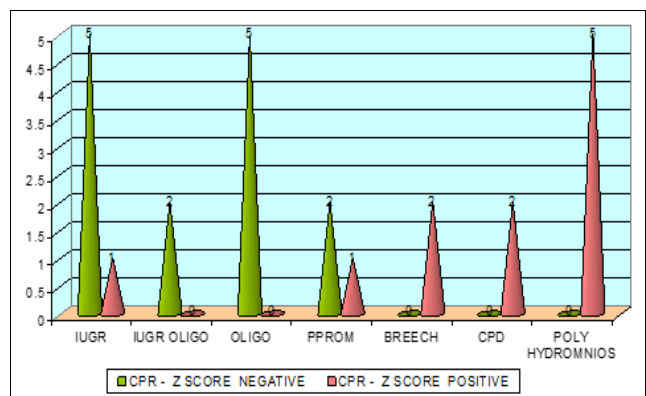
Fig 3: Maternal Complications - Antepartum

Intrapartum Complications

Table 5: Intrapartum Complications

Intrapartum	CPR - Z score	
	Negative	Positive
Fetal distress	11	7
Meconium	2	10
CORD 2 around neck	1	1
CPD	1	7
Failed induction	1	0
Perineal tear	0	2
Shoulder dystocia	0	2
Nil	14	41
Total	30	70
P value	0.031 Significant	

Intrapartum complications is significantly higher in negative group especially fetal distress than positive group. 16 complications out of 30 in negative group but in positive group only 29 complications out of 70 cases, p value 0.031 is significant.

No significant difference between both groups regarding post-partum complications.

Apgar 1 min score
Out of 30 negative score cases, 21 had low Apgar score babies, but in positive group 28 cases had low Apgar out of 70 cases. This difference is significantly higher in negative group. P value is 0.011 significant.

Apgar 5 min score
Out of 30 negative score cases, 12 had low Apgar score babies, but in positive group 13 cases had low Apgar out of 70 cases. This difference is significantly higher in negative group. P value 0.044 significant.

NICU admission
Out of 30 negative score cases, 21 babies need ICU admission, but in positive group only 21 babies need out of 70 cases. This difference is significantly higher in negative group. P value < 0.001 significant.

Birth weight
Out of 30 negative group, 10 babies had low birth weight <10% but in positive group only one baby have low birth weight.

Conclusion
Doppler cerebroplacental ratio is a better predictor of adverse perinatal outcome compared to Pulsatility index of umbilical artery or Pulsatility index of middle cerebral artery in singleton high risk pregnancy. There is no significant association between cerebroplacental ratio and pregnancy complicated by overt or gestational diabetes mellitus but CPR ratio less than 1.3 is associated with worse neonatal outcome. CPR ratio is less in pregnancy complicated by overt diabetes compared to gestational diabetes. Patients treated with insulin had less CPR ratio compared to patients on oral hypoglycemic agents than on medical nutrition therapy. A less CPR ratio is associated with early gestational age of delivery. Ante partum complications like IUGR, oligohydramnios, Intrapartum fetal distress and postpartum complications like NICU admission, low birth weight, and low Apgar are more associated with low CPR ratio. Doppler ultrasound velocimetry of umbilical and fetal vessels has become established method of antenatal monitoring, hence allowing the non-invasive assessment of neonatal circulation and its perinatal outcome.

In low risk cases, following up patients with Doppler, have less significance, compared to high risk cases.

In high risk cases, Doppler velocimetry should be done at 30 – 34 weeks, to detect FGR, since the morbidity and mortality associated with late onset FGR is high when, compared to early onset FGR.

Doppler velocimetry helps significantly in late onset FGR, for detection and follow up, and will also help in the decision of time of delivery, or to prolong the pregnancy.

Babies with abnormal CPR, will be followed up or monitored with daily AFI, and NST, but Doppler velocimetry becomes an important tool for decision of delivery after lung maturity.

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