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# The fetal cerebro-placental ratio in diabetic pregnancies is influenced more by the umbilical artery rather than middle cerebral artery pulsatility index

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ABSTRACT

*Objective:* This study aimed to assess the relationship between the cerebro-placental ratio (CPR) and intrapartum and perinatal outcomes in pregnancies complicated by pre-existing insulin dependent diabetes (pT1DM) mellitus, pre-existing non-insulin dependent diabetes mellitus (pT2DM) and gestational diabetes mellitus (GDM).

*Study design:* This was a retrospective cohort study of 1281 women with diabetes mellitus birthing at the Mater Mothers' Hospital in Brisbane between 2007 and 2015. The CPR in non-anomalous singleton fetuses was measured between 34 + 0 and 36 + 6 weeks gestation and compared between types of DM treatment groups and correlated with intrapartum and perinatal outcomes.

*Results:* Of the study cohort, 9.7% (124/1281) had pT1DM, 5.3% (68/1281) had pT2DM and 85.0% (1089/1281) had GDM. Of women with pT2DM and GDM, 61.8% (42/68) and 28.9% (315/1089) respectively, required insulin during pregnancy. Women with pT1DM had an increased odds of having a CPR <5th centile (OR 3.73, 95%CI: 1.90-6.96, p = 0.0001) or a CPR <10th centile (OR 3.01, 95% CI: 1.80–4.91, p < 0.0001) respectively. The odds of a UA PI >90th centile (OR 2.69, 95% CI: 1.60–4.39, p = 0.0001) was higher in the pT1DM cohort. There was however no significant difference in the mean MCA PI between the three groups. Stratification by CPR centiles (<10th centile vs. ≥10th centile) demonstrated a lower birth weight in the CPR <10th centile cohort for all DM categories. The proportion of neonates with birth weights <10th centile were higher in the CPR <10th centile cohort with the GDM cohort having an odds ratio of 8.28 (95% CI 4.22–16.13, p < 0.0001) of this complication. The CPR <10th centile cohort also had a greater proportion of adverse composite neonatal outcome regardless of type of DM.

*Conclusions:* Regardless of the type of DM, a low CPR was associated with poorer neonatal outcomes. Women with pT1DM also had the highest mean UA PI and lowest mean CPR despite no difference in the mean MCA PI between the three groups.



## Introduction

Diabetes mellitus (DM) is a significant contributor to adverse obstetric and perinatal outcomes. Its prevalence is increasing with pre-existing DM affecting approximately 1% of Australian pregnancies and gestational diabetes mellitus (GDM) complicating a further 7% of all maternities [1]. There is now clear and unequivocal evidence that adverse pregnancy outcomes are strongly linked to maternal hyperglycaemia, both in the peri-conception period and throughout gestation [2,3]. Although strict glycemic control does improve outcomes [4], there is still a higher rate of complications in women with DM and poorer perinatal outcomes, as well as exacerbation of existing maternal comorbidities, including hypertension, thyroid disease, pre-eclampsia and eclampsia [2,5].

Given the increased risk of late pregnancy complications particularly stillbirth, some international guidelines [6] now recommend planned delivery (either caesarean birth or induction of labour) no later than 39 + 0 weeks gestation for pregnant women with type 1 or type 2 DM with no other complications and no later than 41 + 0 weeks for women with GDM. These guidelines also recommend assessment of fetal wellbeing late in pregnancy although the type of monitoring is often not specified.

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The cerebro-placental ratio (CPR) is the ratio of the Middle Cerebral Artery Pulsatility Index (MCA PI) to the Umbilical Artery Pulsatility Index (UA PI). It represents the severity of increased cerebral perfusion resulting from fetal hypoxia and is associated with a myriad of adverse perinatal outcomes [7]. Although there is relatively little research regarding the utility of the CPR in a diabetic cohort, recent data suggests that a low CPR (<10th centile) regardless of GDM treatment was associated with worse perinatal outcomes, increased rates of low birth weight and higher preterm birth rates [8]. The objective of this study thus was thus to assess the relationship between the CPR and outcomes in pregnancies complicated by pre-existing Type 1 DM (pT1DM), pre-existing Type 2 DM (pT2DM) as well as women with GDM and to determine if the CPR measured at 34 + 0–36 + 6 weeks gestation is predictive of adverse obstetric and perinatal outcomes. To our knowledge, there have been no studies assessing the value of the CPR in these specific cohorts.

## Methods

This was a retrospective cross-sectional study of women with pregnancies complicated by DM birthing at the Mater Mothers' Hospital in Brisbane, Australia between January 2007 and December 2015. The Mater Mothers' Hospital is a major tertiary centre and the largest maternity hospital in Australia with a birth rate of approximately 10,000 births per annum. Previous prospectively collected maternal demographic data was cross-referenced against the institution's ultrasound and neonatal databases to correlate outcomes. The study protocol was assessed and approved by the hospital's Human Research Ethics Committee (Reference number HREC/14/MHS/37).

All women with a non-anomalous singleton fetus and DM regardless if pre-existing or gestational, who underwent an ultrasound scan between 34 + 0–36 + 6 weeks gestation with recorded data for **both** the MCA PI and UA PI (to enable calculation of the CPR) were eligible for inclusion in this study. At the Mater Mothers' Hospital all women with DM in pregnancy receive serial scans for growth and wellbeing with the final scan before delivery generally taking place between 34 + 0 and 36 + 6 weeks gestation.

There were three DM cohorts: pT1DM, pT2DM and GDM. Demographic data collected included maternal age, parity, body mass index (BMI), ethnicity (Caucasian, Asian, Indigenous, Indian or other), smoking status, maternal disease (thyroid disease, hypertension) and mode of conception. Indigenous ethnicity refers to patients identifying as being of Aboriginal or Torres Strait Islander origin. Gestational age was calculated using the last menstrual period or earliest ultrasound examination or by correlation with both. Doppler parameters were recorded in the absence of fetal breathing movements. An automated tracing method incorporating at least three waveforms was employed and repeated three times to obtain the mean PI. The angle of insonation was maintained at <30°. The MCA, either right or left, depending on waveform quality, was imaged using colour Doppler and its waveform recorded from the proximal third of the vessel distal to

**Table 1**
Maternal demographics, intrapartum outcomes and ultrasound characteristics stratified by DM type.

| Variable | pT1DM (n = 124) | pT2DM (n = 68) | GDM (n = 1089) | p-value |
|---|---|---|---|---|
| Maternal age (years)§ | 29.1 [5.2] | 33.6 [5.9] | 32.5 [5.2] | <0.0001 |
| BMI (kg/m$^2$)^ | 25.4 [22.4–29.2] | 30.9 [27.6–37.7] | 25.9 [22.1–30.8] | <0.0001 |
| Ethnicity* | | | | |
| Caucasian | 109 (87.9) | 33 (48.5) | 421 (38.7) | <0.0001 |
| Asian | 2 (1.6) | 9 (13.2) | 259 (23.8) | <0.0001† |
| Indigenous | 2 (1.6) | 5 (7.4) | 6 (0.6) | <0.001† |
| Indian | 0 (0) | 4 (5.9) | 148 (13.6) | <0.0001† |
| Other | 8 (6.5) | 13 (19.1) | 236 (21.7) | <0.001 |
| Parity* | | | | |
| 0 | 60 (48.4) | 19 (27.9) | 430 (39.5) | 0.020 |
| ≥1 | 64 (51.6) | 49 (72.1) | 659 (60.5) | 0.020 |
| ART* | 4 (3.2) | 0 (0) | 65 (6.0) | 0.042† |
| PET/Hypertension* | 34 (27.4) | 34 (35.3) | 105 (9.7) | <0.0001 |
| Thyroid disease* | 20 (16.1) | 2 (2.9) | 95 (8.7) | <0.01† |
| Smoking* | 34 (27.4) | 15 (22.1) | 126 (11.6) | <0.0001 |
| Total length labour (mins)^ | 418.5 [250.5–599] (n = 50) | 227 [133–313] (n = 38) | 276.0 [167–443] (n = 753) | <0.001 |
| Mode of Delivery* | | | | |
| SVD | 22 (17.7) | 25 (36.8) | 524 (48.1) | <0.0001 |
| Instrumental | 10 (8.1) | 8 (11.8) | 138 (12.7) | 0.33 |
| CS | 92 (74.2) | 35 (51.5) | 427 (39.2) | <0.0001 |
| Elective CS | 52 (41.9) | 16 (23.5) | 221 (20.3) | <0.0001 |
| Emergency CS | 40 (32.3) | 19 (27.9) | 206 (18.9) | <0.001 |
| NRFS | 8 (6.5) | 4 (5.9) | 43 (3.9) | 0.26† |
| Other | 32 (25.8) | 15 (22.1) | 163 (15.0) | <0.01 |
| Gestation at US (weeks)§ | 35.4 [0.8] | 35.588 [0.863] | 35.633 [0.882] | 0.021 |
| CPR§ | 1.86 [0.60] | 1.94 [0.50] | 2.08 [0.55] | <0.0001 |
| UA PI§ | 0.94 [0.21] | 0.87 [0.17] | 0.85 [0.17] | <0.0001 |
| MCA PI§ | 1.66 [0.38] | 1.63 [0.35] | 1.71 [0.34] | 0.081 |
| CPR <5th centile* | 14 (11.3) | 2 (2.9) | 38 (3.5) | 0.001† |
| CPR <10th centile* | 24 (19.4) | 6 (8.8) | 87 (8.0) | <0.001 |
| UA PI >90th centile* | 23 (18.5) | 7 (10.3) | 82 (7.5) | <0.001 |
| MCA PI <5th centile* | 8 (6.5) | 5 (7.4) | 44 (4.0) | 0.19† |

§Mean [SD]—data analysed by 1-way ANOVA.
^Median [25th centile—75th centile]—data analysed by Kruskal-Wallis.
*Number (Percentage)—data analysed by Chi-squared test or Fisher's exact test where indicated (†).
BMI—Body Mass Index, ART—Assisted Reproductive Techniques, PET—Pre-eclampsia, CS—Caesarean Section, SVD—Spontaneous Vaginal Delivery, NRFS—Non-Reassuring Fetal Status, SD—standard deviation, IQR—Interquartile Range, CPR—Cerebroplacental Ratio, UA—Umbilical Artery, MCA—Middle Cerebral Artery, PI—Pulsatility Index.