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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.

its origin at the circle of Willis. The UA Doppler waveforms were recorded from a free loop of cord. The CPR was calculated by dividing the MCA PI by the UA PI.

Outcomes analysed included mode of, and indication for, delivery, birth weight, birth weight centile (<10th or >90th centile), preterm birth (<37 weeks gestation) and adverse perinatal outcome. Adverse perinatal outcome was defined as a composite measure of ***any*** of perinatal death (fetal or neonatal), Neonatal Critical Care Unit (NCCU) admission, severe respiratory distress, Apgar score <7 at 5 min, significant hypoglycaemia requiring treatment, acidosis at birth (pH ≤ 7.0 or lactate ≥6 mmol/L). Outcomes were also stratified according to the CPR centiles (<10th vs. ≥10th centile).

Given the retrospective nature of this study and the difficulty in applying a rigorous definition to the diagnosis of fetal compromise we adapted a pragmatic approach and used the primary indication for delivery/intervention as recorded in the perinatal database and cross-referenced this with the operative notes. The diagnosis of fetal compromise would generally have been made on the basis of an abnormal fetal heart pattern, fetal scalp pH or lactate, fully accepting the limitations of this methodology in our analysis.

Kruskal-Wallis tests were used for comparisons of medians where data showed a skewed distribution and ANOVA was used for comparisons of means between groups where the data was normally distributed. Proportions were compared using Chi-square test or Fisher's exact test where expected frequencies were <5. Statistics are reported as mean (Standard Deviation (SD)) or median (Inter-quartile Range (IQR)) for normally and non-normally distributed variables respectively or as the number of observations with the percentage of total. Multivariate analysis was performed by logistic regression and odds ratio (OR) reported with 95% confidence intervals for the pT1DM group or the CPR <10th centile group vs. the other groups combined as appropriate. ORs were adjusted for birth weight and gestational age at delivery, with the exception of birth weight outcomes which were adjusted for gestational age only. Data were analyzed using R Commander (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $p < 0.05$. No adjustment was made for multiple comparisons.

Results

The final study population meeting all the inclusion criteria comprised 1281 women with diabetes mellitus. Of these, 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.

Table 1 displays the maternal demographics for the diabetes cohort. The mean maternal age and median BMI were significantly different between the diabetes groups ($p < 0.0001$), with the lowest age and BMI recorded in patients with pT1DM. Ethnicity also varied between the groups, with a higher proportion of Caucasian women in the pT1DM group compared to the pT2DM and GDM cohorts (87.9% vs 48.5% vs 38.7%, $p < 0.0001$). Parity, the use of reproductive technologies, smoking, hypertension/PET and thyroid disease were also significantly different between groups. Higher proportions of smoking, hypertension and thyroid disease was observed in the pT1DM group.

The mean CPR and mean UA PI were significantly different between diabetes groups ($p < 0.0001$), with the lowest mean CPR and highest mean UA PI recorded in the pT1DM cohort. Furthermore, the proportion of fetuses with a CPR <5th and <10th centiles was significantly different between groups (11.3% vs. 2.9% vs. 3.5%, $p = 0.001$ and 19.4% vs. 8.8% vs. 8.0%, $p = 0.0002$ respectively). 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 also significantly higher in the pT1DM cohort. There was however no significant difference in the mean MCA PI between the three groups ($p = 0.081$).

Table 2 describes the perinatal outcomes for the groups. The mean gestational age at delivery was lowest in the pT1DM group. This was associated with an almost 6-fold increased rate of delivery before 37 weeks in the pT1DM group compared to the other groups (OR: 5.77, 95% CI: 3.88–8.74, $p < 0.0001$). Birthweight was also significantly different between groups with the highest mean birthweight in the pT1DM cohort. There was no significant difference in the proportion of neonates with birth weights <10th centile, but a significantly higher proportion of babies were large for gestational age in the pT1DM group (OR 3.82, 95% CI: 2.34–6.15,

Table 2
Perinatal outcomes stratified by DM type.

Variable	pT1DM (n = 124)	pT2DM (n = 68)	GDM (n = 1089)	p-value	OR (95% CI) ‡	p-value
Gestation at delivery (weeks) [SD] §	36.7 [1.1]	37.3 [1.0]	38.0 [1.2]	<0.0001	NA	
Delivery <37 weeks (n, %)*	87 (70.2)	31 (45.6)	304 (27.9)	<0.0001	5.77 (3.88–8.74)	<0.0001
BW (g) [SD] §	3515.1 [610.8]	3292.5 [587.0]	3227.8 [535.7]	<0.0001	NA	
BW <10th centile (n, %)*	4 (3.2)	3 (4.4)	55 (5.1)	0.72†	0.19 (0.051–0.52)	0.003
LGA (BW ≥ 90th centile) (n, %)*	33 (26.6)	13 (19.1)	111 (10.2)	<0.0001	3.82 (2.34k6.15)	<0.0001
Apgar score <7 at 5 min (n, %)*	3 (2.4)	2 (2.9)	21 (1.9)	0.63†	0.55 (0.12–1.84)	0.38
Acidosis (pH ≤ <7.0 or Lactate>6) (n, %)*	11 (8.9)	4 (5.9)	68 (6.2)	0.47†	1.81 (0.83–3.66)	0.11
NCCU admission (n, %)*	66 (53.2)	14 (20.6)	186 (17.1)	<0.0001	2.91 (1.85–4.57)	<0.0001
Respiratory distress (n, %)*	40 (32.3)	9 (13.2)	160 (14.7)	<0.0001	1.43 (0.89–2.25)	0.13
Hypoglycaemia (n, %)*	52 (43.0)	13 (19.4)	129 (11.9)	<0.0001	2.59 (1.64–4.04)	<0.0001
Perinatal Death (n, %)*	0 (0)	0 (0)	5 (0.5)	NA	NA	NA
Composite adverse neonatal outcome (n, %)*	91 (74.6)	27 (39.7)	349 (32.2)	<0.0001	3.39 (2.16–5.42)	<0.0001

§ Mean (SD)—data analysed by 1-way ANOVA.
*Number (percentage)—data analysed by Chi-squared test or Fisher's exact test where indicated (†).
‡ Odds ratios are for the Insulin-treated group compared to other treatment groups.
BW—birth weight, LGA—large for gestational age, NCCU—neonatal intensive care unit, SD—standard deviation, OR—Odds Ratio, 95% CI—95% Confidence Interval.
OR adjusted for birthweight and gestational age at delivery with exception of delivery <37 weeks which is unadjusted and birth weight <10th centile and LGA which are adjusted for gestational age only.

Table 3
Intrapartum and perinatal outcomes stratified by DM type and CPR centile categories.

	pT1DM (n = 124)					pT2DM (n = 68)					GDM (n = 1089)				
	CPR <10th centile (n = 24)	CPR ≥10th centile (n = 100)	p-value	OR (95% CI)	p-value	CPR <10th centile (n = 6)	CPR ≥10th centile (n = 62)	p-value	OR (95% CI)	p-value	CPR <10th centile (n = 87)	CPR ≥10th centile (n = 996)	p-value	OR (95% CI)	p-value
Mean gestation at delivery (weeks) [SD]§	36.3 [1.3]	36.9 [1.0]	0.016			37.3 [0.8]	37.3 [1.0]	0.99			37.1 [1.5]	38.1 [1.2]	<0.0001		
Mean BW (g) [SD] §	3446.1 [698.7]	3531.7 [590.5]	0.54			3210.3 [598.5]	3300.5 [590.25]	0.72			2717.9 [613.2]	3272.1 [505.0]	<0.0001		
Mode of Delivery (n, %) *															
SVD	3 (12.5)	19 (19.0)	0.56†	0.58 (0.12–1.99)	0.43	0 (0.0)	25 (40.3)	0.078†	NA	NA	44 (50.6)	480 (47.9)	0.63	1.21 (0.75–1.92)	0.44
Instrumental	1 (4.2)	9 (9.0)	0.69†	0.49 (0.03–2.94)	0.51	1 (16.7)	7 (11.3)	0.54†	1.47 (0.070–11.54)	0.74	12 (13.8)	126 (12.6)	0.74	1.22 (0.60–2.31)	0.56
CS	20 (83.3)	72 (72.0)	0.25	1.92 (0.63–7.26)	0.28	5 (83.3)	30 (48.4)	0.20†	5.39 (0.80–10.71)	0.14	31 (35.6)	396 (39.5)	0.48	0.74 (0.45k1.21)	0.24
Elective CS	11 (45.8)	41 (41.0)	0.67	1.22 (0.48–3.06)	0.67	1 (16.7)	15 (24.2)	1†	0.62 (0.031–4.28)	0.68	16 (18.4)	205 (20.5)	0.65	0.89 (0.47–1.58)	0.69
Emergency CS	9 (37.5)	31 (31.0)	0.54	1.30 (0.48–3.38)	0.59	4 (66.7)	15 (24.2)	0.047†	6.67 (1.15–53.17)	0.042	15 (17.2)	191 (19.1)	0.68	0.73 (0.39–1.31)	0.31
NRFS	3 (12.5)	5 (5.0)	0.18†	4.08 (0.74–20.19)	0.085	0 (0.0)	4 (6.5)	1†	NA	NA	6 (6.9)	37 (3.7)	0.15†	1.15 (0.39–2.88)	0.79
Other	6 (25.0)	26 (26.0)	0.92	0.79 (0.25–2.22)	0.67	4 (66.7)	11 (17.7)	0.019	11.87 (1.87–104.86)	0.012	9 (10.3)	154 (15.4)	0.21	0.58 (0.26–1.18)	0.16
BW <10th centile (n, %)*	2 (8.3)	2 (2.0)	0.17†	2.21 (0.21–21.75)	0.48	1 (16.7)	2 (3.2)	0.25†	6.25 (0.26–82.12)	0.17	26 (29.9)	29 (2.9)	<0.0001	8.28 (4.22–16.13)	<0.0001
Delivery <37 weeks (n, %)*	18 (75.0)	69 (69.0)	0.56	1.35 (0.51–4.01)	0.56	3 (50.0)	28 (45.2)	1†	1.21 (0.21–7.01)	0.82	46 (52.9)	258 (25.7)	<0.0001	3.24 (2.08–5.06)	<0.0001
Composite neonatal outcome score (n, %)*	21 (87.5)	70 (70.0)	0.11	2.19 (0.59–1.07)	0.27	3 (50.0)	24 (38.7)	0.68†	1.78 (0.27–11.46)	0.53	48 (55.2)	301 (30.2)	<0.0001	2.09 (1.28–3.39)	0.003

CS—Caesarean Section, BW—birth weight, SD—standard deviation, OR—Odds Ratio, 95% CI—95% Confidence Interval.
OR adjusted for birth weight and gestational age at delivery with exception of delivery <37 weeks which is unadjusted and birth weight <10th centile and LGA which are adjusted for gestational age only.
§Mean (SD)—data analysed by 1-way ANOVA.
*Number (percentage)—data analysed by Chi-squared test or Fisher's exact test where indicated (†).

$p < 0.0001$) respectively. Significantly poorer perinatal outcomes were also observed in the pT1DM cohort with higher rates of NCCU admission, respiratory distress and hypoglycaemia compared to the other diabetes groups, corresponding to a 3-fold increased rate of composite adverse outcome (OR 3.39, 95% CI: 2.16–5.42, $p < 0.0001$).

Stratification by CPR centiles (<10th centile vs. ≥10th centile) demonstrated a lower birth weight in the CPR <10th centile cohort for all DM categories (Table 3). The proportion of women requiring an emergency caesarean section for non-reassuring fetal status was also increased in both the pT1DM and GDM cohorts. In addition, the proportion of neonates with birth weights <10th centile were also higher in the CPR <10th centile cohort with the GDM cohort, associated with 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. The GDM cohort with CPR <10th centile was also at significantly increased risk of preterm birth (<37w) (OR 2.09, 95% CI 1.28–3.39, $p = 0.003$).

Comment

The results of our study suggest that fetuses in women with pT1DM and pT2DM have a lower mean CPR and higher mean UA PI compared to those with GDM, with the lowest mean CPR and highest mean UA PI seen in the pT1DM cohort. We did not find a significant difference in the MCA PI between the three DM cohorts, suggesting that the low CPR in the pT1DM group is likely to be mediated by increased resistance in placental perfusion reflected by the higher mean UA PI in this cohort. This finding is biologically plausible given that women with pre-existing DM are more likely to have greater end organ microvascular disease including the utero-placental circulation. There are numerous morphological abnormalities described in placental structure and development in women with pre-existing diabetes mellitus attributable to maternal hyperglycaemia and increased TNFα production seen in these placentae which reduce trophoblast proliferation and endovascular invasion, thus directly impairing placental development and function [3]. In addition, elevated levels of leptin, Insulin-like

Growth Factors (IGF) and matrix metalloproteinases stimulate extensive production of extracellular matrix and result in basement membrane thickening, erythrocyte deformation and increased intra-placental blood viscosity. These result in increased capillary branching and surface area, dilatation and congestion of vessels, increased diffusion distance, edematous villous stroma, villous tree maturation defects and intra- and extra-villous fibrinoid and glycogen deposition [3,9–12]. These abnormalities are most evident in T1DM compared to T2DM and GDM placentae [9,11]. In addition, raised levels of glycosylated haemoglobin (a marker of glycaemic control) has been linked to increased UA resistance [13] with higher UA PI levels seen in T1DM patients compared to T2DM and GDM patients [14].

There is now good data, both from prospective [15,16] and retrospective studies [17,18] demonstrating that a low CPR is associated with suboptimal growth at term, increased rates of intrapartum compromise and emergency caesarean, poor condition at birth and increased rates of neonatal unit admission. In addition, a low CPR may also reflect a failure of a fetus to reach its genetic growth potential at term [19,20] despite having a normal birth weight. Fetuses with reduced feto-placental reserves prior to labour have a decreased ability to tolerate the normal but progressive hypoxic stress caused by intrapartum uterine contractions which can reduce uterine blood flow by as much as 60% [21]. The CPR therefore reflects suboptimal placental function and associated fetal cardiovascular compensation and thus appears to be a better predictor of outcome than either the UA PI or MCA PI individually [7]. Hence, it is likely to be a good modality for assessment of fetal wellbeing given the previously described specific placental abnormalities seen in diabetic pregnancies.

Our results also indicate a correlation between mode of delivery and perinatal outcomes and a putative increase in diabetes severity (GDM–pT2DM–pT1DM), such that GDM women had the highest rates of SVD and pT1DM women had the highest rates of CS delivery, both elective and emergency. Women with pT1DM had significantly higher rates of preterm birth, large for gestational age (LGA) babies, NCCU admission, respiratory distress and hypoglycaemia compared to the other groups. Further, there may be a link between the observed larger proportion of CPR <10th centile and poorer neonatal outcomes in the pT1DM cohort, with a trend toward higher rates of the composite adverse neonatal outcome in babies with low CPR. Poorer outcomes with CPR <10th centile were also noted in the other DM cohorts, albeit at a lower proportion to those in the pT1DM group.

The novel observation of our study is the positive correlation between CPR and diabetes severity. We report a significantly lower mean CPR in pT1DM women compared with the pT2DM and GDM cohorts. To our knowledge this finding has not previously been reported. Our results are in contradistinction to that of Bachanek et al. [22] and To & Mok [23] who found that there was no difference in the UA PI in pT1DM or GDM pregnancies respectively compared to controls. However, our findings are in agreement with Fadda et al.'s smaller study where it was shown that abnormal UA and MCA Doppler indices and a low CPR in GDM pregnancies were associated with adverse perinatal outcomes [24]. Consistent with a recent study in women with pT1DM, showing that macrosomic fetuses had lower UA PIs [13], we too found that LGA fetuses (>90th centile) had higher mean CPRs compared to smaller fetuses. It is interesting that although the pT1DM cohort had the highest mean UA PI, this cohort also had the highest birth weights. Fetal growth is dependent on a number of factors including placental function and the availability of substrates as well as the influence of various adipogenic and growth hormones. It is possible although speculative, that fetal metabolic and endocrine factors outweigh the limitations on growth posed by suboptimal placental function in some diabetic cohorts.

The strengths of this study include the large number of cases stratified according to type and onset of DM from a single tertiary centre and the inclusion of clinically relevant outcomes. Limitations were primarily intrinsic to the retrospective nature of the study. Spanning nine years, the study period was associated with evolution in hospital policy and practice with particular emphasis of the changing diagnostic criteria for GDM, potentially affecting the relationship between diabetes status, Dopplers and outcomes. In addition, inter- and intra-sonographer variability was not known and not all outcomes of interest were reliably recorded. We were also unable to confirm adequacy of treatment and glycaemic control, the gestation at which the diagnosis of GDM had been made and the duration of treatment, all factors which could have confounded our findings. Despite these limitations we have shown that the changes in CPR in diabetic pregnancies regardless of type or onset appears to be mediated primarily by the umbilical artery resistance.

Conclusions

Our findings add to the increasing data on the utility of the CPR in risk stratification of late gestation pregnancies complicated by DM and may assist in clinical management. Further prospective studies are required to establish the utility of the CPR in the management of these pregnancies.

Conflicts of interests

All authors report no conflicts of interests.

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