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Birth outcomes in women with gestational diabetes managed by lifestyle modification alone: The PANDORA study

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ABSTRACT

Aims: To assess outcomes of women in the Pregnancy and Neonatal Diabetes Outcomes in Remote Australia (PANDORA) cohort with gestational diabetes mellitus (GDM) managed by lifestyle modification compared with women without hyperglycaemia in pregnancy.

Methods: Indigenous (n = 97) and Europid (n = 113) women managed by lifestyle modification were compared to women without hyperglycaemia (n = 235). Multivariate linear and logistic regressions assessed whether GDM-lifestyle women had poorer outcomes compared to women without hyperglycaemia.

Results: Women with GDM-lifestyle had higher body mass index and lower gestational weight gain than women without hyperglycaemia. On univariate analysis, gestational age at delivery was lower and induction rates were higher in women with GDM-lifestyle

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than without hyperglycaemia. On multivariable regression, GDM-lifestyle was associated with lower gestational age at delivery (by 0.73 weeks), lower birthweight z-score (by 0.26, p = 0.007), lower likelihood of large for gestational age (LGA) [OR (95% CI): 0.55 (0.28, 1.02), p = 0.059], and greater likelihood of labour induction [2.34 (1.49, 3.66), p < 0.001] than women without hyperglycaemia.

Conclusion: Women with GDM managed by lifestyle modification had higher induction rates and their offspring had lower birthweight z-scores, with a trend to lower LGA than those without hyperglycaemia in pregnancy. Further studies are indicated to explore reasons for higher induction rates.

1. Introduction

Rates of gestational diabetes mellitus (GDM) have increased dramatically during the last decade [1] with rates up to 17.8% worldwide now reported [2]. In the Northern Territory (NT) of Australia, 11.9% of all pregnancies are complicated by GDM. Thirty-three percent of all births in the NT are to Indigenous Australian women [3]. Rates of type 2 diabetes in pregnancy and GDM are 10 times and 1.5 times higher respectively in Indigenous women than in non-Indigenous women [4]. Pregnancy complications of GDM include macrosomia, preeclampsia and perinatal morbidity and mortality [5,6], with long term increased risk of diabetes, obesity and cardiovascular disease in both mother and child [7,8]. Recognition and treatment of women with GDM significantly reduces the rate of serious adverse maternal and neonatal outcomes [9,10].

The diagnosis of GDM may influence pregnancy and delivery management decisions which include birth location, timing and mode of delivery. A limited number of observational studies have addressed pregnancy outcomes in women with GDM treated with lifestyle modification alone [11,12]. We are aware of only one report since the introduction of the World Health Organization (WHO) and International Association of the Diabetes and Pregnancy Study Groups (IADPSG) diagnostic criteria for GDM [13]. Using the IADPSG criteria, Kgosidialwa et al. reported diet and exercise for those with GDM may be successful in lowering rates of large for gestational age and macrosomia without increasing small for gestational age rates. In addition, they demonstrated that women with GDM and a body mass index less than 25 kg/m^2 had similar outcomes to those without hyperglycaemia in pregnancy. However, 84% of those with GDM in that study were of white ethnicity and all received care at a multidisciplinary clinic where they were reviewed by a team including an obstetrician, endocrinologist, and midwife/diabetes nurse specialist at each visit. Each patient also received an hour-long individual consultation with a dietician at the time of diagnosis and had access to additional consultations if needed. These results may differ in women of other ethnicities and those with limited access to specialised care [13]. With limited research focused on those with GDM managed by lifestyle modification, universal clinical guidelines for the management of these women have not been well established [14,15].

The Pregnancy and Neonatal Diabetes Outcomes in Remote Australia Study (PANDORA) is an observational longitudinal birth cohort study recruited from the NT Diabetes in Pregnancy Clinical Register. The current study aims to assess maternal characteristics and birth outcomes of women in PANDORA with GDM managed by lifestyle modification alone and compare these to PANDORA women without hyperglycaemia in pregnancy. Our findings may then inform clinical guidelines regarding the most appropriate antenatal care and labour management for these mothers.

2. Materials and methods

2.1. Participants

All NT women aged 16 years and over with hyperglycaemia in pregnancy, including type 1 diabetes, type 2 diabetes and GDM who resided and gave birth in the NT between November 2011 and February 2017 were eligible for inclusion on the NT Diabetes in Pregnancy Clinical Register. Women on this register who consented to be involved in further research were then invited to participate in the PANDORA study. The details of this process have been previously described [16]. Exclusion criteria for this analysis included type 1 diabetes, type 2 diabetes and GDM requiring insulin or oral hypoglycaemic agents. Following local clinical guidelines, all women with GDM who were managed by lifestyle modification alone in PANDORA should have received dietary and physical activity advice following their diagnosis. Women in this group did not receive any insulin or oral antidiabetic medication and may include women who declined these treatments or who were not treated at all. The primary intervention for women newly diagnosed with GDM is to modify diet and physical activity with the aim of achieving good glycaemic control, managing weight gain within Institute of Medicine (IOM) recommendations [17] and encouraging generally healthy lifestyles beyond pregnancy. Women who do not achieve optimal glucose levels with lifestyle modification or who have pregnancy complications including macrosomia or small for gestational age are commenced on insulin or oral antidiabetic therapy. From 2014 to 2017, medication was generally considered if fasting and two-hour post prandial glucose values were greater than or equal to 5.1 mmol/L and 6.8 mmol/L respectively on two or more occasions in a week [18]. Prior to 2014, medication was generally considered if fasting and

two-hour post-prandial values were greater than or equal to 5.5 mmol/L and 7.0 mmol/L respectively [19].

A group of women without hyperglycaemia in pregnancy with normal 75 gm oral glucose tolerance test (OGTT) was recruited to PANDORA through antenatal clinics from December 2012 to February 2017. This group was representative of women who birthed in NT in terms of age and geographic location.

Summary data from the Northern Territory Midwives' Data Collection 2012 (MDC) on women aged 16 years and above who resided and birthed in the NT from 1st January 2012 to 31st December 2012, without hyperglycaemia in pregnancy, was provided to the research team. MDC is a population-based census of all births in the NT. From 2012, most information was captured directly in electronic format; information on births that did not involve being admitted to hospital was submitted by paper form. Women without hyperglycaemia in pregnancy in PANDORA were compared with MDC to assess how representative they were of this population. The MDC group included two women who were also recruited in the PANDORA group of women without hyperglycaemia (babies born in December 2012). On comparison of women without hyperglycaemia in pregnancy in PANDORA and women without hyperglycaemia in pregnancy in MDC, the PANDORA women were more likely to be Indigenous (49.8% vs. 32.5%, $p < 0.001$), have higher reported alcohol use (24.3% vs. 5.3%, $p < 0.001$), lower rates of previous caesarean section (9.4% vs. 14.9%, $p = 0.021$), higher rates of induction (27.7% vs. 22.5%, $p = 0.043$), lower rates of preeclampsia (0.4% vs. 3.5%, $p < 0.001$) and fewer cases of postpartum haemorrhage (22.1% vs 25.1%, $p < 0.001$) (Supplementary Table A). There were no other significant differences. Note that the higher proportion of Indigenous women in PANDORA than MDC was by design, as only Indigenous and Europid women were eligible for the PANDORA group without hyperglycaemia. The difference in reported alcohol use may be due to methodological differences as PANDORA women were asked specifically if any alcohol was consumed during the pregnancy, whereas MDC data may be entered by health professionals without specifically asking women the amount or frequency of alcohol consumption.

2.2. *Diagnostic criteria for gestational diabetes*

During the course of the PANDORA study, diagnostic criteria for GDM were changed, with a gradual increase in implementation of new guidelines throughout the NT between 2012 and 2014. Hence, women with GDM were diagnosed by either the 1998 Australian Diabetes in Pregnancy Society (ADIPS) guidelines [19] or new guidelines of universal 75gm OGTT and revised glucose cut-points as recommended by WHO [20]. All the women without hyperglycaemia in pregnancy in PANDORA had fasting glucose levels $\leq$5.0 mmol/L (normal glucose tolerance on both criteria).

2.3. *Data collection*

PANDORA data were collected prospectively from medical records (weight, height, birth outcomes) and by participant questionnaire. Maternal body mass index (BMI) was calculated using the first available weight and height in pregnancy. Gestational weight gain (GWG) was determined by subtracting the first weight in pregnancy from the last weight measured in the pregnancy. Birthweight z-score (standard deviation score) was adjusted for gestational age at birth and gender using Australian centile charts [21]. Large for gestational age (LGA) and small for gestational age (SGA) were defined as a birthweight >90th centile and <10th centile respectively, according to gender-specific growth percentiles for infants born in an Australian population [21,22]. Severe adverse events was a composite outcome defined as one of: death (maternal, stillbirth and neonatal), delivery prior to 32 weeks, prolonged hospitalisation greater than five days in higher level neonatal care or any condition which resulted in significant disability/incapacity or required medical intervention to prevent permanent damage. Outcomes of postpartum haemorrhage, shoulder dystocia, respiratory distress syndrome and APGAR scores have been defined previously [23,24]. This study was approved by the joint Menzies School of Health Research – Northern Territory Department of Health Human Research Ethics Committee, including the Aboriginal sub-committee, and the Central Australian Human Research Ethics Committee. Women in the PANDORA study provided informed consent to participate.

2.4. *Statistical analysis*

Statistical analyses were performed using Stata v15 (Stata Corporation, College Station, TX). Women of "other" ethnic groups (neither Indigenous Australian nor Europid) and six women with twin pregnancies were excluded from analysis of the GDM-lifestyle group, as these women were not eligible for inclusion in the group without hyperglycaemia. Maternal characteristics of PANDORA women with GDM managed by lifestyle modification were compared to women without hyperglycaemia in pregnancy. We reported frequencies and percentages for categorical variables, the mean and standard deviation for normally distributed continuous variables and the median and interquartile range for continuous variables not normally distributed. P-values were derived to test differences in distribution of participants' characteristics using Chi-squared test for categorical factors and Students *t*-test for normally distributed continuous factors. The Wilcoxon rank-sum test was used to compare medians in not normally distributed variables. Linear regression models were used to assess the association of GDM managed by lifestyle modification versus no hyperglycaemia in pregnancy for continuous neonatal outcomes (birthweight z-score, gestational age at delivery). Logistical regression models were used for binary neonatal outcomes (LGA, SGA, induction of labour, caesarean section, serious adverse event). Covariates included in each multivariate model were maternal age, ethnicity, BMI, parity, smoking, employment, caesarean section and gestational age at birth as these were known prior to be important factors associated with these neonatal outcomes [23]. There were no significant interactions with ethnicity for each outcome, thus multivariate models are presented for Indigenous and Europid women combined. To investigate the potential

Table 1 – Characteristics and pregnancy outcomes of women with GDM managed by lifestyle modification, and women without hyperglycaemia in pregnancy.

	Indigenous women			Europid women		
	GDM managed by lifestyle modification *n* = 97	Women without hyperglycaemia in pregnancy *n* = 117	p-value	GDM managed by lifestyle modification *n* = 113	Women without hyperglycaemia in pregnancy *n* = 118	p-value
Age – years	28.1 (5.7)	25.1 (4.7)	<0.001	30.6 (5.5)	30.4 (5.0)	0.76
Nulliparity	27 (27.8)	49 (41.9)	0.033	59 (52.2)	61 (51.7)	0.94
Weight at earliest date – kg	71.8 (20.9)	65.7 (16.1)	0.021	76.0 (18.1)	73.1 (16.3)	0.20
Gestational age at above weight – weeks	14.4 (7.3)	14.9 (7.3)	0.62	15.8 (6.4)	16.0 (4.8)	0.81
BMI at earliest date – kg/m^2	27.2 (7.2)	24.7 (6.0)	0.009	27.7 (6.2)	25.9 (5.2)	0.022
BMI groups – kg/m^2						
<25	34 (39.1)	67 (59.3)		44 (42.3)	60 (51.3)	
25–29.9	25 (28.7)	27 (23.9)		27 (26.0)	37 (31.6).	
≥30	28 (32.2)	19 (16.8)	0.009	33 (31.7)	20 (17.1)	0.039
Gestational age at final weight – weeks	35.0 (8.9)	36.6 (5.7)	0.16	36.2 (7.2)	37.8 (1.9)	0.042
Gestational weight gain – kg	7.8 (10.2)	10.2 (5.6)	0.060	7.8 (4.8)	11.4 (4.6)	<0.001
GWG above IOM guidelines	6 (7.9)	18 (19.1)	0.036	12 (16.0)	28 (30.8)	0.03
GWG above IOM guidelines by BMI group (kg/m^2)						
<18.5	0	1 (6.7)	NA	0	0	NA
18.5–24.9	1 (5.0)	6 (13.6)	0.42	2 (6.5)	4 (8.9)	0.99
25–29.9	2 (9.1)	6 (30.0)	0.12	3 (15.8)	15 (48.4)	0.0033
≥30	3 (12.5)	5 (33.3)	0.22	7 (28.0)	9 (64.3)	0.027
GA at 1st antenatal visit – weeks	11.1 (6.4)	11.0 (6.4)	0.91	7.5 (3.4)	6.5 (2.5)	0.0095
Gestational age at OGTT – weeks	26.4 (6.0)	26.8 (4.9)	0.67	27.4 (4.4)	26.5 (3.1)	0.096
Gestational age at OGTT						
<24 weeks	22 (22.9)	17 (14.7)		14 (12)	16 (13.6)	
24–28 weeks	29 (30.2)	39 (33.6)		37 (32.7)	68 (57.6)	
28 + weeks	45 (46.9)	60 (51.7)	0.3	62 (54.9)	34 (28.8)	<0.001
OGTT result – mmol/L						
Fasting	4.8 (0.9)	4.2 (0.36)	<0.001	4.5 (0.6)	4.2 (0.30)	<0.001
1 hr	9.4 (1.7)	7.2 (1.5)	<0.001	9.2 (1.5)	6.7 (1.4)	<0.001
2 hr	7.9 (1.7)	6.0 (1.07)	<0.001	8.5 (1.2)	5.7 (1.1)	<0.001
GA at first ultrasound – weeks	14.0 (6.9)	13.4 (6.4)	0.47	10.0 (3.6)	9.2 (3.2)	0.073
Family history of DM	46 (52.0)	38 (33.9)	0.011	34 (30.6)	17 (14.5)	0.004
Antenatal smoking						
Yes	49 (50.5)	46 (39.3)		16 (14.2)	20 (17.0)	
No	46 (47.2)	70 (59.8)		97 (85.8)	98 (83.0)	
Not stated	2 (2.1)	1 (1.0)	0.17	0	0	0.56

Antenatal alcohol						
Yes	15 (15.5)	12 (10.3)		34 (30.1)	45 (38.1)	
No	79 (81.4)	104 (88.9)		79 (69.9)	73 (61.9)	
Not stated	3 (3.1)	1 (0.9)	0.23	0	0	0.20
Preeclampsia	0	0		3 (2.7)	1 (0.9)	0.36
Previous caesarean section	15 (15.5)	8 (6.8)	0.097	9 (8.0)	6 (5.1)	0.9

Continuous variables are described with mean and SD, categorical variables with frequencies and percent.
Sample size (Indigenous women with GDM-lifestyle and without hyperglycaemia in pregnancy, Europid women with GDM-lifestyle and without hyperglycaemia in pregnancy): First weight, n = 87, n = 114, n = 107, n = 117; Gestational age at above weight, n = 87, n = 114, n = 107, n = 117; BMI and BMI groups, n = 87, n = 113, n = 104, n = 117; Gestational age at final weight, n = 85, n = 98, n = 78, n = 91; Gestational weight gain, n = 77, n = 96, n = 77, n = 91; GWG above IOM guidelines, n = 76, n = 94, n = 75, n = 91; GWG above IOM guidelines: BMI < 18.5, BMI 18.5–24.9, BMI 25–29.9, BMI ≥ 30n = 10, n = 15, n = 2, n = 0, n = 20, n = 44, n = 31, n = 45, n = 22, n = 20, n = 19, n = 31, n = 24, n = 15, n = 25, n = 14; Gestational age at OGTT, n = 94, n = 116, n = 113, n = 118; Fasting glucose, n = 84, n = 115, n = 112, n = 118; 1hr glucose, n = 80, n = 102, n = 103, n = 110; 2hr glucose, n = 93, n = 116, n = 113, n = 118; Family history of DM, n = 88, n-112, n = 111, n = 117.

confounding effect of GWG, a sensitivity analysis was carried out and regression analyses performed in a subset of participants who had this variable recorded.

3. Results

Of the 713 women with GDM in PANDORA, 319 (45%) had GDM managed with lifestyle modification alone, of whom 103 were excluded due to ethnicity and six were excluded due to twin pregnancy, thus 97 Indigenous women and 113 Europid women with GDM were included. Women diagnosed with GDM by ADIPS criteria only (n = 24), WHO criteria only (n = 32), or both criteria (n = 160) did not differ for age or delivery mode, but maternal BMI was higher for women diagnosed by WHO criteria alone (mean, 95% CI: ADIPS alone 27.5 [25.5–29.5] kg/m^2; WHO alone 31.2 [28.7–33.5] kg/m^2; both criteria 26.9 [25.9–27.8] kg/m^2; p = 0.006).

3.1. *Maternal characteristics*

Among both Indigenous and Europid groups, women with GDM managed by lifestyle modification had higher BMI and less GWG (and were more likely to have GWG within the IOM guidelines) than women without hyperglycaemia in pregnancy (Table 1). Among Indigenous women, those with GDM were older and less likely to be nulliparous than those without hyperglycaemia. Ninety percent of the women with GDM managed by lifestyle modification reported an improved diet following the diagnosis of GDM; this included 60% of women who reported reduced consumption of sugar sweetened drinks, up to 40% who reported increased consumptions of vegetables, fruit or fish, and up to 30% who reported reduced intake of bread, pasta and rice.

3.2. *Pregnancy outcomes*

On univariate analysis, Europid women with GDM managed by lifestyle modification had increased rates of labour induction (47.8% vs. 28.8%, p = 0.003) compared with those without hyperglycaemia in pregnancy (Table 2). Among both Indigenous and Europid women, babies of those with GDM managed by lifestyle modification were born at earlier gestation and of lower birthweight (but no difference in birthweight z-score on univariate analysis) than babies of mothers without hyperglycaemia. APGAR scores at 1 and 5 min, and rates for shoulder dystocia and serious adverse events were not significantly different. There were lower rates of respiratory distress syndrome among babies born to Indigenous mothers with GDM (compared to Indigenous mothers without hyperglycaemia).

3.3. *Multivariable analysis*

On multivariable analyses (Table 3) including adjustments for maternal age, ethnicity, BMI, parity, smoking, employment, caesarean section and gestational age at delivery, GDM managed by lifestyle modification was significantly associated with lower gestational age at delivery (by 0.73 weeks), lower mean birthweight (by 111 g), and lower birthweight z-score (reduced by 0.26 SD units), when compared to those without

Table 2 – Pregnancy outcomes of women with GDM managed by lifestyle modification, and women without hyperglycaemia in pregnancy.

	Indigenous women			Europid women		
	GDM managed by lifestyle modification *n* = 97	Women without hyperglycaemia in pregnancy *n* = 117	p-value	GDM managed by lifestyle modification *n* = 113	Women without hyperglycaemia in pregnancy *n* = 118	p-value
Induction of labour	37 (38.1)	31 (26.5)	0.068	54 (47.8)	34 (28.8)	0.003
Mode of delivery						
Vaginal delivery	55 (56.7)	72 (61.5)		59 (52.2)	71 (60.2)	
Forceps delivery	4 (4.1)	7 (6.0)		4 (3.5)	4 (3.4)	
Ventouse	3 (3.1)	6 (5.1)		14 (12.4)	9 (7.6)	
Planned caesarean section	16 (16.5)	10 (8.5)		16 (14.2)	20 (16.9)	
Unplanned caesarean section	19 (19.6)	22 (18.8)	0.43	20 (17.7)	14 (11.9)	0.46
Postpartum haemorrhage	33 (34.0)	25 (21.4)	0.038	14 (12.4)	27 (22.9)	0.037
Third and fourth degree tear[a]	0	3 (3.5)	0.16	1 (1.3)	3 (3.6)	0.41
Mean GA at delivery – weeks	38.8 (1.4)	39.5 (1.3)	<0.001	39.2 (1.4)	39.8 (1.2)	<0.001
Mean birthweight – grams	3249 (504)	3399 (539)	0.039	3360 (467)	3557 (504)	0.0023
Birthweight z-score	−0.14 (1.26)	−0.04 (1.08)	0.51	0.013 (0.89)	0.21 (1.05)	0.13
Gestational age at delivery – weeks						
<28	0	0		0	0	
28–36 + 6	6 (6.2)	6 (5.1)		7 (6.2)	3 (2.5)	
37–39 + 6	66 (68.0)	61 (52.1)		69 (61.1)	57 (48.3)	
>40	25 (25.8)	50 (42.7)	0.035	37 (32.7)	58 (49.2)	0.026
Birthweight – grams						
<1499	0	0		0	0	
1500–2499	5 (5.2)	4 (3.4)		5 (4.4)	3 (2.5)	
2500–2999	30 (30.9)	23 (19.7)		19 (16.8)	12 (10.2)	
3000–3499	33 (34.0)	40 (34.2)		46 (40.7)	42 (35.6)	
3500–3999	21 (21.6)	38 (32.5)		33 (29.2)	41 (34.7)	
>4000	8 (8.2)	12 (10.3)	0.23	10 (8.9)	20 (16.9)	0.17
SGA < 10th percentile	16 (16.5)	16 (13.7)	0.57	5 (4.4)	9 (7.6)	0.31
LGA > 90th percentile	11 (11.3)	12 (10.3)	0.80	11 (9.7)	18 (15.3)	0.21
Apgar score at 1 min						
0–3	2 (2.1)	6 (5.1)		1 (0.9)	3 (2.5)	
4–6	5 (5.2)	10 (8.5)		9 (8.0)	10 (8.5)	
7–10	90 (92.8)	101 (86.3)	0. 19	103 (91.2)	105 (89.0)	0.85
Apgar score at 5 min						
0–3	0	1 (0.9)		0	1 (1.0)	
4–6	2 (2.0)	4 (3.4)		1 (1.0)	3 (2.5)	
7–10	95 (98.0)	112 (95.7)	0.66	111 (99.0)[b]	114 (96.6)	0.74
Serious neonatal adverse effect	3 (3.1)	8 (6.8)	0.22	8 (7.1)	3 (2.5)	0.10
Shoulder dystocia	1 (1.0)	5 (4.3)	0.15	4 (3.5)	3 (2.5)	0.53
Respiratory distress syndrome	12 (12.4)	30 (25.6)	0.015	22 (19.5)	22 (18.6)	0.58
Special care nursey >5 days	3 (3.1)	8 (6.8)	0.08	8 (7.1)	2 (1.7)	0.13
Fetal deaths	0	0		0	0	

Continuous variables are described with mean and SD, categorical variables with frequencies and percent.

[a] Results have been given as a percentage of the total number of vaginal delivery for each respective group.

[b] Sample size (Europid GDM-lifestyle): n = 112.

Table 3 – Multiple regression analysis of women with GDM managed by lifestyle modification and women without hyperglycaemia in pregnancy in PANDORA.

	Women with GDM managed by lifestyle modification vs. women without hyperglycaemia in pregnancy			
	Age and ethnicity adjusted		Full model	
	β coeff & 95% CI	p-value	β coeff & 95% CI	p-value
Median gestational age at delivery (week)	−0.60 (−0.86, −0.35)	<0.001	−0.73 (−1.0, −0.47)	<0.001
Mean birthweight (kg)	−173 (−269, −78)	<0.001	−111 (−195,−27))	0.010
Birthweight z-score	−0.16 (−0.36, 0.042)	0.12	−0.26 (−0.45, −0.07)	0.007
	OR and 95% CI	p-value	OR and 95% CI	p-value
SGA < 10th percentile	0.92 (0.49, 1.73)	0.80	0.82 (0.40, 1.68)	0.59
LGA > 90th percentile	0.74 (0.41, 1.34)	0.32	0.55 (0.28, 1.02)	0.059
Induction of labour	2.1 (1.39, 3.10)	<0.001	2.34 (1.49, 3.66)	<0.001
Caesarean section	1.15 (0.74, 1.79)	0.53	1.18 (0.74, 1.89)	0.48
Serious neonatal adverse event and shoulder dystocia	0.94 (0.46, 1.92)	0.87	1.07 (0.51, 2.24)	0.87

*Full model for each outcome includes BMI, parity, smoking, employment, caesarean section and gestational age at birth as appropriate.

hyperglycaemia in pregnancy. GDM managed by lifestyle modification was associated with an increase in labour induction (OR 2.34, $p < 0.001$), no difference in SGA, and the odds of having an LGA newborn were 45% lower ($p = 0.059$) than the odds for those without hyperglycaemia in pregnancy.

On sensitivity analysis where GWG was included in the full multivariable models, associations between GDM and birth outcomes were attenuated, with only the relationship with lower gestational age and higher induction rates remaining significant (Supplemental Table B).

4. Discussion

In comparing maternal and birth outcomes among NT women with GDM managed by lifestyle modification and those without hyperglycaemia in pregnancy, we have reported two key findings. First, those with GDM managed by lifestyle modification had increased rates of induction of labour than those without hyperglycaemia in pregnancy. Second, median gestational age was earlier, and birthweight z-score was lower with a trend to lower LGA rates in offspring born to women with GDM managed by lifestyle modification after controlling for maternal age, ethnicity, BMI, parity, smoking, employment, caesarean section, and gestational age at birth as appropriate.

The diagnosis of GDM or the knowledge that it is present, has been reported to be associated with an increase in several interventions such as induction of labour or caesarean section [25]. Caregiver bias (an expectation of adverse outcomes due to GDM diagnosis) may reduce a caregiver's inclination to allow the woman to go past a certain gestation, and/or may lead to a lower threshold for operative delivery [25–27]. In our study, the results of GDM testing were openly disclosed to caregivers and women at diagnosis. Increased induction of labour likely contributed to the greater percentage of neonates delivered prior to 40 weeks gestation within the GDM group. The extent to which knowledge of GDM status may have contributed to this is unclear. Further work is required to explore reasons for higher rates of induction of labour in those with GDM managed with lifestyle modification.

After adjusting for important maternal characteristics, we reported that gestational age, birthweight z-score and LGA rates were lower among babies born to women with GDM managed by lifestyle modification than of babies born to those without hyperglycaemia in pregnancy. The lower gestational age in the GDM-lifestyle group is unlikely to be of clinical significance. The extent to which these results are due to treatment effect are uncertain. We note that GWG was lower in women with GDM managed by lifestyle modification than those without hyerglycaemia in pregnancy. Our findings support previous reports on the impact of lifestyle modification in GDM (WHO criteria) on neonatal size outcomes [13], and are able to demonstrate similar reduction in neonatal size in babies of women from diverse ethnic backgrounds. Birthweight z-score was assessed using Australian (adjusted for gender and gestational age) rather than ethnically customised centile charts [21]. No charts are available which include Indigenous ethnicity. Customised centile charts adjust within normal variance, and their use in the context of pathological variance remains unclear [28]. There is con-

cern that use of customised centile charts for Indigenous women and babies risks normalising disadvantage; as the effects of pathological processes and socio-economic factors, which contribute significantly to perinatal outcomes and fetal growth, become incorporated in the model as part of physiological adjustments to find normal values for this group [29]. We note that previous studies have reported increased rates of LGA in those with untreated GDM diagnosed by WHO criteria only compared with those without hyperglycaemia in pregnancy [30,31]. However, in our study all women who form the PANDORA group without hyperglycaemia screened negative for GDM by 1998 ADIPS and/or WHO criteria and displayed higher adjusted odds of LGA than women with GDM managed by lifestyle modification. The odds of having an LGA baby were 45% lower among women with GDM compared with women without hyperglycaemia on multivariate analysis (which did not reach statistical significance). This likely reflects confounding by variables included in the multivariate model such as maternal age, BMI and smoking. After adjusting for GWG, the strength of the inverse relationship between GDM-lifestyle and LGA was attenuated. These findings suggest in this observational cohort that dietary modification alongside physical activity, weight management, self-monitoring of blood glucose concentrations and education may partly contribute to reducing the odds of LGA. A carbohydrate controlled diet that provides adequate nutrition, as well as glycaemic control and avoids ketonuria is recommended to reduce the risk of adverse outcomes associated with GDM including LGA [32].

Among women with GDM managed by lifestyle modification, 31% were Indigenous women, whereas 50% of those with GDM on the NT Diabetes in Pregnancy Clinical Register identified as Indigenous [24]. The lower than expected representation of Indigenous women with GDM managed by lifestyle modification in PANDORA may be attributed to several factors. First, the Clinical Register GDM group includes women diagnosed with likely pre-existing diabetes for the first time in pregnancy [16]; for these women glycaemic control may be more challenging given the severity of their dysglycaemia, and may require pharmacological therapy. Second, there are contextual challenges in delivering lifestyle modification in disadvantaged settings in the NT where factors such as poverty, food insecurity, limited infrastructure for changes in exercise and limited access to a dietician are prevalent [33,34]. All these factors may have resulted in more women requiring intensive management including pharmacotherapy (metformin and insulin) rather than continuing with intensified dietary management.

Our study has some limitations. Firstly, due to the observational nature of this study we were not able to fully evaluate the independent impact of lifestyle modification on neonatal size and obstetric outcomes. Secondly, we were unable to confirm adherence with dietary advice and physical activity as we were not able to collect data on glucose levels during pregnancy. There was no documentation as to whether target glucose levels in women with GDM were achieved. Inadequate glycaemic levels may have contributed to clinical decisions regarding timing of birth, and may be one reason for the increased rates of induction of labour among women with GDM-lifestyle. Thirdly, it was not feasible to collect data on the details of the type of diet prescribed and physical activity advice provided to women. However, data on self-reported diet quality indicated that a high proportion of women with GDM-lifestyle reported improved nutrition following the GDM diagnosis. Fourthly, we may not have sufficiently controlled for the impact of GWG as the mean gestational age of first recorded weight was in early second trimester (15 weeks). The PANDORA group without hyperglycaemia is limited as a convenience sample with possible volunteer bias. However, the comparison to women without hyperglycaemia in pregnancy in MDC showed no differences in key maternal characteristics and birth outcomes of relevance to our findings.

5. Conclusion

In conclusion, women with GDM managed by lifestyle modification had higher induction rates, and their offspring had lower birthweight z-score, with a trend to lower LGA and no difference in SGA rates compared with women without hyperglycaemia in pregnancy. This may reflect the benefit of dietary education, physical activity, weight management and glycaemic monitoring. Reasons for higher rates of induction of labour in those with GDM managed with lifestyle modification are unclear and further research exploring this and other contributing factors warrant investigation. Factors such as caregiver bias and co-morbidities may play a role.

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Authors contributions

EC was involved in study design, literature search, data analysis, data interpretation, writing of the manuscript. DKL, FB and EB were involved in data analysis, data interpretation and writing of the manuscript. ILL, CW, JAB, JO, CC, HDM, MK, KD, XZ, ST, DW, PZ, ADHB, JES were involved in study design, data interpretation and writing of the manuscript. LJMB was involved in study design, supervision of data collection and analysis, data interpretation and writing of the manuscript. All authors approved the final manuscript.

Declaration of Competing Interest

We declare that we have no conflicts of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107876.

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