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Type 2 diabetes after a pregnancy with gestational diabetes among first nations women in Australia: The PANDORA study

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ABSTRACT

Aims: To determine among First Nations and Europid pregnant women the cumulative incidence and predictors of postpartum type 2 diabetes and prediabetes and describe postpartum cardiovascular disease (CVD) risk profiles.
Methods: PANDORA is a prospective longitudinal cohort of women recruited in pregnancy. Ethnic-specific rates of postpartum type 2 diabetes and prediabetes were reported for women with diabetes in pregnancy (DIP), gestational diabetes (GDM) or normoglycaemia in pregnancy over a short follow-up of 2.5 years (n = 325). Pregnancy characteristics and CVD risk profiles according to glycaemic status, and factors associated with postpartum diabetes/prediabetes were examined in First Nations women.
Results: The cumulative incidence of postpartum type 2 diabetes among women with DIP or GDM were higher for First Nations women (48%, 13/27, women with DIP, 13%, 11/82,

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Indigenous health

GDM), compared to Europid women (nil DIP or GDM p < 0.001). Characteristics associated with type 2 diabetes/prediabetes among First Nations women with GDM/DIP included, older age, multiparity, family history of diabetes, higher glucose values, insulin use and body mass index (BMI).

Conclusions: First Nations women experience a high incidence of postpartum type 2 diabetes after GDM/DIP, highlighting the need for culturally responsive policies at an individual and systems level, to prevent diabetes and its complications.

1. Introduction

The prevalence of gestational diabetes (GDM) and type 2 diabetes are increasing globally, in parallel with rising obesity [1]. GDM is associated with future type 2 diabetes [2] and First Nations peoples worldwide are reported to be at particularly high risk [3,4]. However, reported rates of type 2 diabetes after GDM vary considerably, ranging between 0.3% and 67% [2,5–7], and reported risk factors for type 2 diabetes among women with a history of GDM remain unclear. Large *meta*-analyses have reported differing conclusions as to whether ethnicity is an important determinant of type 2 diabetes after GDM [5,6], however, findings are limited both by the lack of comparison between ethnic groups within the same study and a lack of First Nations participants. Furthermore, existing evidence relies on retrospective analysis of administrative datasets with incomplete capture of postpartum diabetes screening. Given the high burden and early onset of type 2 diabetes among First Nations peoples, it is important to quantify the risk of diabetes after pregnancy. This current study is the first prospective study on the cumulative incidence of type 2 diabetes among Australian First Nations and non-First Nations women with and without a history of GDM.

Aboriginal and Torres Strait Islander peoples, collectively referred to herein as the First Nations people of Australia, are culturally and linguistically diverse, have inhabited the Australian continent for over 60,000 years, and now comprise 3% of the Australian population. In the Northern Territory (NT), Australia, First Nations people comprise 30% of the population, with 80% living in remote communities [8]. The Pregnancy and Neonatal Diabetes Outcomes in Remote Australia (PANDORA) study is a prospective observational birth cohort study of women with and without hyperglycaemia in pregnancy across the NT. This current study is the follow-up of a subset of PANDORA participants at median 2.5 years postpartum (Wave 1 follow-up). This follow-up study aimed to (i) prospectively assess the cumulative incidence of type 2 diabetes after GDM or diabetes in pregnancy (DIP), (ii) assess the cardiovascular disease (CVD) risk factor profile at follow-up among those with postpartum type 2 diabetes and prediabetes compared to those without these outcomes, and (iii) determine risk factors for progression to type 2 diabetes and prediabetes.

2. Material and methods

2.1. Participants

Details of the PANDORA study have been published [9], with further detail in Supplementary Methods. Participants (n = 1139) were First Nations and non-First Nations women with (i) hyperglycaemia in pregnancy (n = 904: pre-existing type 1 diabetes, type 2 diabetes, DIP and GDM) recruited in pregnancy from the NT Diabetes in Pregnancy Register and (ii) normoglycaemia recruited from antenatal clinics (n = 235). The study was approved by the Human Research Ethics Committee of the NT Department of Health and Menzies School of Health Research, and the Central Australian Human Research Ethics Committee. Informed consent was obtained.

A subgroup of women who participated at baseline were invited to participate in the Wave 1 follow-up study between 18-months to 4-years postpartum. Women eligible for Wave 1 included those who self-identified as Aboriginal and/or Torres Strait Islander or Europid ancestry (n = 860). Of the 860 eligible women, 371 were not invited to participate in Wave 1 for the following reasons (i) logistical feasibility: women who resided in some extremely remote locations or had moved outside the NT (n = 247), (ii) funding: awarded for Wave 1 sample size of n = 400. Among the 489 women invited, 416 (85%) participated (Supplementary Fig. 1).

Women with type 2 diabetes diagnosed prior to pregnancy (n = 78), and women without data on postpartum diabetes/prediabetes status (n = 13) were excluded for this analysis, resulting in 325 women with (i) DIP (27 First Nations and 4 Europid), (ii) GDM (82 First Nations and 90 Europid) or (iii) normoglycaemia in pregnancy (60 First Nations and 62 Europid) included. Preferential sampling was employed to ensure adequate numbers of women from each of the baseline glycaemia in pregnancy groups were followed-up.

2.2. Data measurements

At baseline, demographic, clinical and biochemical data were obtained from medical records and questionnaires. GDM screening and diagnostic guidelines changed worldwide during the study. Women with GDM were identified by either

the 1998 Australian Diabetes in Pregnancy Society (ADIPS) two-step screening guidelines [10] or by a universal 75-g OGTT with revised glucose cut-points as recommended by the International Association of the Diabetes and Pregnancy Study Group (IADPSG) [11] and World Health Organization (WHO) [12] (Supplementary Methods). Among the PANDORA cohort with GDM, 10.3% satisfied only the 1998 ADIPS glucose thresholds, 11.5% satisfied only the WHO glucose thresholds and 76.6% satisfied both [13]. Considering IADPSG and WHO guidance regarding diabetes first detected during pregnancy, women diagnosed with GDM, but meeting glucose or HbA_{1c} values diagnostic of type 2 diabetes outside of pregnancy, were subclassified as having "diabetes in pregnancy" (DIP) [12]. Due to small numbers, women with DIP were included in the GDM group for all analyses involving Europid women and for First Nations women when analysing the primary outcome.

Breastfeeding data were collected at 6-months postpartum. Predominant breastfeeding was defined as an infant being fed human milk as the only form of milk at 6-months postpartum [14]. During Wave 1, participants were invited to attend a physical examination (anthropometric and blood pressure (BP) measurements, non-fasting blood and midstream urine collection) and completion of questionnaires. Primary care and hospital electronic medical records were reviewed, and private pathology companies were contacted. If a postpartum HbA_{1c} or OGTT had been performed as part of clinical practice these results were included.

2.3. Outcomes

The primary outcome was postpartum type 2 diabetes or prediabetes. Type 2 diabetes was defined in accordance with WHO criteria as (i) a diagnosis of type 2 diabetes after pregnancy, established from medical records or self-report, or (ii) $HbA_{1c} \geq 6.5\%$ (48 mmol/mol) at Wave 1 study visit, or (iii) in women who did not have an HbA_{1c} at Wave 1 visit (n = 24): a postpartum $HbA_{1c} \geq 6.5\%$ and/or fasting plasma glucose $\geq$ 7.0 mmol/L or 2-hour plasma glucose $\geq$ 11.1 mmol/L from medical records [15]. Prediabetes was defined in accordance with WHO criteria as (i) HbA_{1c} 6.0% to 6.4% (42 to 47 mmol/mol) from the Wave 1 study visit, or (ii) in women who did not have an HbA_{1c} from the study visit: postpartum HbA_{1c} 6.0 to 6.4% and/or fasting plasma glucose $\geq$ 6.1 mmol/L and < 7.0 mmol/L and/or 2-hour plasma glucose $\geq$ 7.8 mmol/L and < 11.1 mmol/L [16,17] from medical records, and (iii) without an established diabetes diagnosis from medical records or self-report.

Secondary outcomes involved characterising CVD risk. Risk factors assessed included obesity (waist circumference $\geq$ 80 cm); dyslipidaemia (non-fasting HDL cholesterol < 1.0 mmol/L and triglycerides $\geq$ 2 mmol/L or taking lipid lowering medication) [18]; hypertension (systolic BP $\geq$ 140 mmHg and/or diastolic BP $\geq$ 90 mmHg or taking antihypertensive medications) [19]; and either microalbuminuria (urinary albumin to creatinine ratio (ACR) of 3.5–35 mg/mmol) or macroalbuminuria (urinary ACR > 35 mg/mmol) [20].

2.4. Statistical methods

Statistical analysis was conducted using Stata v15 (Stata Corporation, College Station, TX, USA). Differences in maternal characteristics according to ethnicity (First Nations vs. Europid) and diabetes in pregnancy status (normoglycaemia vs. GDM) were determined using Pearson-chi square tests for categorical variables and Student's unpaired t-tests for normally distributed continuous variables. Differences in rates of those who did and did not have postpartum diabetes/prediabetes by ethnicity and pregnancy glycaemic status were determined using Fischer's Exact test.

Analyses of risk factors for postpartum type 2 diabetes/prediabetes were assessed only among First Nations women due to the small number of diabetes/prediabetes outcomes among Europid women. Among First Nations women, baseline characteristics and follow-up CVD risk profiles were compared across three groups: (i) women with normoglycaemia in pregnancy and at postpartum (at median 2.5 years follow-up), (ii) women with GDM/DIP in pregnancy and normoglycaemia postpartum and (iii) women with GDM/DIP in pregnancy and diabetes/prediabetes postpartum. To make direct comparisons between each group, we used Pearson-chi square tests for categorical variables, Student's unpaired t-tests and Wilcoxon rank sum tests for normally and non-normally distributed continuous variables, respectively. Body mass index (BMI) in pregnancy and gestational weight gain were presented as means adjusted for gestational age using linear regression. Differences in cardiometabolic risk factors were adjusted for time to follow-up also using linear regression.

Among First Nations women with GDM/DIP, unadjusted and age-adjusted logistic regression models were performed to assess factors associated with postpartum type 2 diabetes/prediabetes. Due to small numbers, multivariable regression results are only presented in brief (expanded in Supplementary Results). Sensitivity analyses were performed excluding women with DIP.

3. Results

3.1. Participant characteristics

Characteristics of participants in Wave 1 (n = 338 excluding those with pre-existing type 2 diabetes), including parity, BMI and category of hyperglycaemia, were similar to the larger eligible cohort who did not participate (n = 384). First Nations women who participated in Wave 1 were younger than those who did not participate (27 years vs. 29 years, P = 0.014). Conversely, Europid women who participated in Wave 1 were older than those who did not participate (32 years vs. 31 years, P = 0.046) (Supplementary Table 1).

Ethnicity and baseline diabetes status of this cohort (n = 325) are reported in Table 1 and are consistent with the larger PANDORA baseline cohort as previously reported [21]. Among women with GDM/DIP, a higher proportion of First Nations women met glycaemic criteria for DIP (25%, 27/109) compared to non-First Nations women (4%, 4/109, P > 0.001).

Table 1 – Characteristics of Pandora Wave 1 cohort by maternal ethnicity and glycaemic status in pregnancy.

	First Nations Women			Europid Women	
	DIP (n = 27)	GDM (n = 82)	Normoglycaemia in pregnancy (n = 60)	GDM/DIP (n = 94)	Normoglycaemia in pregnancy (n = 62)
Maternal characteristics:					
Age at baby's DOB, years	28 (5.5)	29 (5.6)	25 (4.6)	32 (6.0)	32 (5.4)
Urban residence, n (%)	7 (26)	28 (34)	14 (23)	91 (97)	62 (100)
Year 12 education, n (%)	9 (33)	39 (48)	31 (53)	80 (86)	57 (92)
Employed full or part time, n (%)	7 (26)	22 (27)	11 (18)	64 (68)	44 (71)
Nulliparity, n (%)	7 (26)	18 (22)	27 (45)	41 (44)	32 (52)
Family history diabetes, n (%)	17 (65)	40 (49)	21 (37)	40 (45)	9 (15)
Pregnancy Characteristics:					
1st recorded BMI, kg/m^2	30.5 (7.1)	28.9 (7.4)	24.2 (6.4)	28.7 (6.8)	27.3 (5.7)
Gestational weight gain, kg	8.0 (5.5)	6.8 (5.1)	9.7 (5.2)	7.3 (5.8)	10.6 (4.1)
Gestational age first weight, weeks	12.9 [9, 22.9]	12.2 [8.1, 16.9]	13.6 [7.4–19.3]	14.2 [12.4–17.4]	16.1 [14.0–17.1]
Gestational age last weight, weeks	36.4 [34.6, 37.7]	36.4 [34.0, 37.7]	36.6 [35.4–38.7]	37.0 [36.0–38.3]	38.1 [36.6–39.4]
Sedentary lifestyle during pregnancy, n (%)[a]	7 (43)	15 (23)	18 (49)	29 (36)	18 (35)
Gestational age at OGTT, weeks	26.7 [18.9, 28.0]	26.1 [19.0, 28.7]	28.1 [25.7–29.3]	27.4 [26.3–28.7]	27.6 [27.0–28.3]
OGTT results:					
Fasting glucose, mmol/L	6.0 (1.75)	4.9 (0.74)	4.2 (0.4)	4.7 (0.7)	4.3 (0.3)
1-hour glucose, mmol/L	11.1 (2.4)	9.8 (1.5)	7.1 (1.5)	9.4 (1.7)	7.0 (1.5)
2-hour glucose, mmol/L	9.9 (2.6)	8.1 (1.5)	6.0 (1.1)	8.5 (1.5)	5.7 (1.2)
Early diagnosis GDM (<20 weeks), *n* (%)	6 (22)	22 (27)	–	18 (19)	–
Use of insulin during pregnancy, *n* (%)	17 (63)	24 (29)	–	31 (32)	–
Smoking in pregnancy, n (%)	11 (41)	31 (38)	24 (41)	13 (14)	11 (18)
Postpartum Characteristics:					
Predominant breastfeeding at 6 months, n (%)[b]	18 (72)	60 (73)	43 (73)	50 (53)	36 (58)
Time to review, years	2.9 [2.2, 3.6]	2.7 [2.2, 3.4]	2.3 [1.9–2.7]	2.6 [2.4–3.0]	2.0 [1.9–2.6]
Postpartum BMI, kg/m^2[c]	29.8 (5.9)	29.3 (7.3)	26.2 (7.5)	29.1 (7.3)	27.8 (5.8)
Postpartum waist circumference, cm[c]	103.3 (14.7)	101.9 (14.8)	94.4 (16.2)	94.6 (16.6)	92.9 (14.0)

Data are mean (standard deviation), median [interquartile range] or *n* (%). As only 4 Europid women met diagnostic criteria for DIP, data were combined with women with GDM.

For First Nations women with DIP, GDM and normoglycaemia respectively: education, n = 26, n = 78, n = 59; family history, n = 26, n = 72, n = 57; 1st recorded BMI, n = 24, n = 80, n = 60; gestational weight gain, n = 22, n = 75, n = 53; sedentary lifestyle pregnancy, n = 16, n = 65, n = 37; fasting glucose, n = 21, n = 82, n = 60; 1-hour glucose, n = 18, n = 71, n = 53; 2-hour glucose n = 21, n = 82, n = 60; smoking, n = 77, n = 78, n = 59; breastfeeding, n = 25, n = 82, n = 59; postpartum waist circumference, n = 24, n = 78, n = 57.

For Europid women with and without GDM/DIP, respectively: education, n = 93, n = 62; family history, n = 92, n = 62; 1st recorded BMI, n = 90, n = 60; gestational weight gain, n = 73, n = 44; sedentary lifestyle, n = 80, n = 52; fasting glucose, n = 93, n = 62; 1-hour glucose, n = 86, n = 60; 2-hour glucose n = 94, n = 62; smoking, n = 94, n = 62; breastfeeding, n = 94, n = 62; postpartum BMI, n = 84, n = 52; postpartum waist circumference, n = 83, n = 51.

Abbreviations. DIP, diabetes in pregnancy (diagnosed in pregnancy but meeting the diagnostic glucose/HbA1c values for type 2 diabetes outside of pregnancy). GDM, gestational diabetes. DOB, date of birth. OGTT, 75 g oral glucose tolerance test.

a. Sedentary lifestyle defined as 2 or more hours /day watching TV and/or DVDs.

b. Predominant breastfeeding defined as an infant being fed human milk as the only form of milk at 6-months postpartum.

c. Excluding 24 women who were $\geq$ 6 weeks pregnant at time of measurement.

First Nations women were more likely than Europid women to have breastfed for 6 months (72% vs. 55%, P = 0.002), and have a higher mean waist circumference (99.6 vs. 94.0 cm, P = 0.003), although there was no difference in mean postpartum BMI (28.4 vs. 28.6 kg/m^2, P = 0.756). First Nations women with GDM/DIP had higher mean postpartum BMI (29.6 vs. 26.2 kg/m^2, P = 0.005) and waist circumference (102.4 vs. 94.4 cm, P = 0.002) than First Nations women without GDM/DIP. Adjustment for time to follow-up did not alter these outcomes (data not shown).

3.2. *Postpartum diabetes/prediabetes*

The cumulative incidence of postpartum type 2 diabetes among those with DIP or GDM, over a median of 2.5 years follow-up, was high among First Nations women (48%, 13/27 among those with DIP and 13%, 11/82 among those with GDM). No Europid women developed diabetes. For prediabetes, among First Nations women, 4% (1/27) of women with DIP and 13% (11/82) with GDM developed prediabetes. Among Europid women, no women with DIP and 6% (5/90) with GDM developed prediabetes. Among women with normoglycaemia in pregnancy, 3% (2/60) and 2% (1/60) of First Nations women had postpartum type 2 diabetes and prediabetes, respectively, compared to nil (0/62) Europid women (Fig. 1). The postpartum follow-up period was shorter for women with normoglycaemia, compared to those with GDM/DIP (median time to review 2.2 years [1.9, 2.6] vs. 2.7 years [2.3, 3.2]).

Of the 24 First Nations women with GDM/DIP who were then diagnosed with postpartum type 2 diabetes, 18 (75%) had postpartum screening within 6-months of delivery (either an OGTT or an HbA_{1c} between 4 and 6 months postpartum). Six of these screened women (33%) were diagnosed with type 2 diabetes while the remaining 12 women (66%) had normoglycaemia (10 women) or prediabetes (2 women) on initial postpartum screening and were subsequently diagnosed with type 2 diabetes.

3.3. *BMI and weight*

First Nations women were stratified into (i) normoglycaemia in pregnancy and postpartum normoglycaemia at Wave 1 follow-up, (ii) GDM/DIP in pregnancy and postpartum normoglycaemia and (iii) GDM/DIP in pregnancy and postpartum diabetes/prediabetes. Three women with normoglycaemia in pregnancy and postpartum diabetes/prediabetes were excluded from this analysis. Mean first recorded BMI in pregnancy was progressively higher across the three groups. Women with GDM/DIP at baseline and postpartum diabetes/prediabetes at follow-up (as compared to those with GDM/DIP and postpartum normoglycaemia) had a higher BMI and waist circumference at follow-up (Supplementary Table 2).

3.4. *Cardiovascular risk at follow-up*

First Nations women with GDM/DIP and postpartum diabetes/prediabetes were more likely to have an adverse

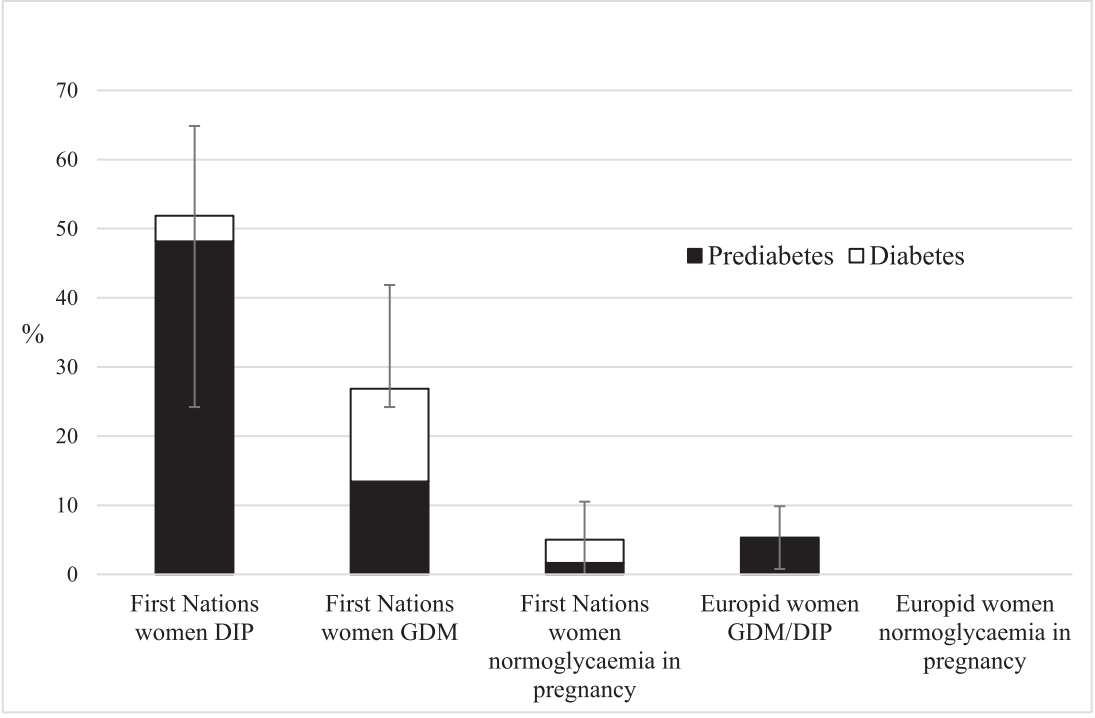

Fig. 1 – Postpartum type 2 diabetes and prediabetes among First Nations and Europid women, with DIP, GDM or normoglycaemia in pregnancy over a median of 2.5 years follow-up. White = diabetes, black = prediabetes. Error bars are 95% confidence intervals. 4 Europid women met diagnostic criteria for DIP and data were combined with women with GDM. Abbreviations: **DIP, diabetes in pregnancy (diagnosed in pregnancy but meeting the diagnostic glucose/HbA1c values for type 2 diabetes outside of pregnancy); GDM, gestational diabetes.**

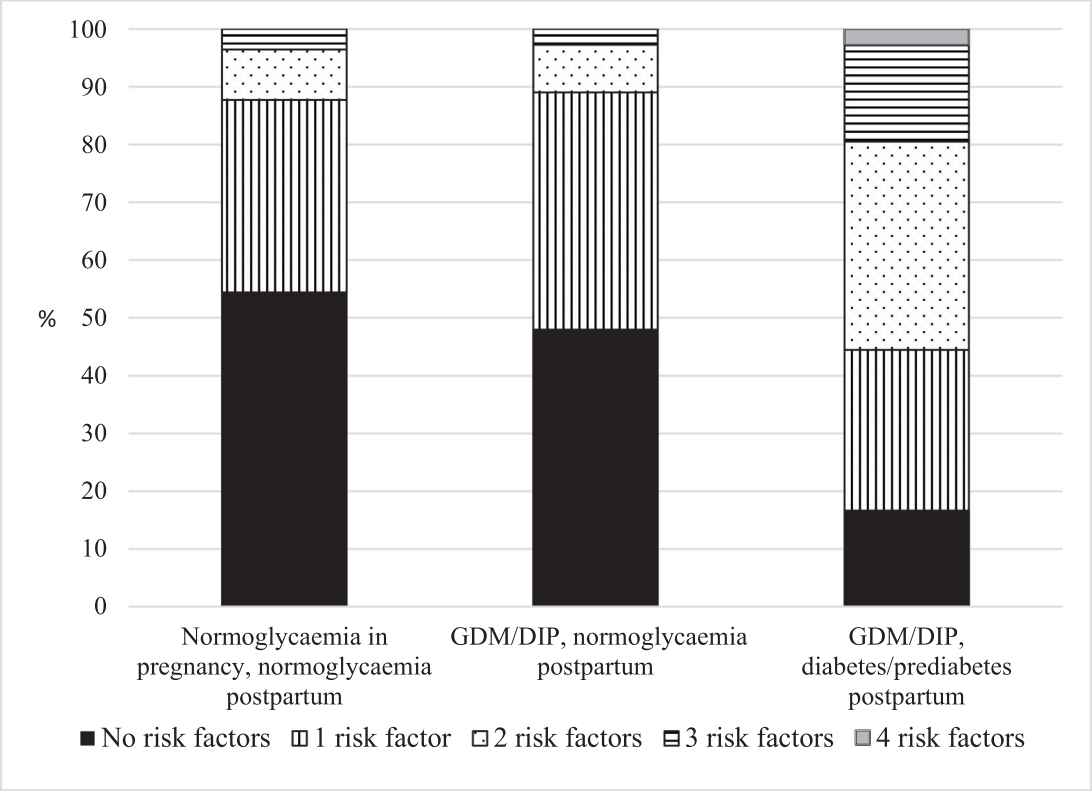

Fig. 2 – Number of postpartum cardiovascular risk factors stratified by diabetes status in pregnancy and at postpartum among First Nations women. Black = no risk factors, vertical stripes = 1 risk factor, dots = 2 risk factors, horizontal stripes = 3 risk factors, white = 4 risk factors. Risk factors: obesity; waist circumference ≥ 80 cm, dyslipidaemia; HDL cholesterol < 1.0 mmol/L and non-fasting triglycerides ≥ 2 mmol/L or taking lipid lowering medication, hypertension; systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg or taking antihypertensive medication, and either microalbuminuria (urinary albumin to creatinine ratio (ACR) of 3.5–35 mg/mmol) or macroalbuminuria (urinary ACR > 35 mg/mmol). P value for number of risk factors: normoglycaemia in pregnancy vs. GDM/DIP with normoglycaemia postpartum: 0.589; normoglycaemia in pregnancy vs. GDM/DIP with diabetes/prediabetes postpartum: <0.001; GDM/DIP with normoglycaemia postpartum vs. GDM/DIP with postpartum diabetes/prediabetes: <0.001. Abbreviations: **DIP, diabetes in pregnancy (diagnosed in pregnancy but meeting the diagnostic glucose/HbA_{1c} values for type 2 diabetes outside of pregnancy); GDM, gestational diabetes.**

cardiovascular profile compared to First Nations women with GDM/DIP and postpartum normoglycaemia, as well as compared to First Nations women with normoglycaemia in pregnancy and postpartum (Fig. 2, Supplementary Table 2). Adjustment for timing of postpartum follow-up did not alter differences observed between groups for cardiovascular risk factors (data not shown).

3.5. *Maternal factors associated with postpartum diabetes/prediabetes*

Among First Nations women with GDM/DIP, age was a strong predictor for postpartum diabetes/prediabetes. Other risk factors were family history, multiparity, higher fasting and 1-hour glucose levels during pregnancy, insulin use during pregnancy, not smoking in pregnancy (no longer associated when adjusted for BMI) and higher BMI in pregnancy (Table 2). On multivariable analysis, with age, parity, 1-hour glucose in pregnancy and BMI in pregnancy entered into the model, only 1-hour glucose remained independently associated with postpartum diabetes/prediabetes (Supplementary Fig. 2).

4. Discussion

In this prospective study of Australian First Nations and Europid women with and without GDM or DIP, we report three key findings. Firstly, among First Nations women with GDM/DIP, 22% were subsequently diagnosed with postpartum type 2 diabetes despite relatively young maternal age and a median of only 2.5 years follow-up. Secondly, First Nations women with GDM/DIP and subsequent postpartum diabetes/prediabetes had a more adverse cardiometabolic profile compared to women with normoglycaemia (in pregnancy and postpartum) and women with GDM/DIP and postpartum normoglycaemia. Thirdly, among First Nations women with GDM/DIP, older age, multiparity, family history, higher glucose values in pregnancy, insulin use and BMI were associated with postpartum diabetes/prediabetes.

Among First Nations women with type 2 diabetes after GDM/DIP, a third of those screened within 6-months of birth already met criteria for diabetes, likely indicating unrecognised pre-existing type 2 diabetes in pregnancy. Importantly, two-thirds of women with early postpartum screening had

Table 2 – Factors associated with postpartum diabetes/prediabetes among First Nations women with GDM/DIP on unadjusted and age-adjusted logistic regression.

	UNADJUSTED		AGE ADJUSTED	
	Odds ratio (95% CI)	*P value*	Odds ratio (95% CI)	*P value*
Demographics:				
Maternal age at baby's DOB, years	1.69 (1.16, 2.49)	0.007		
Urban residence[a]	1.16 (0.49, 2.72)	0.735	0.94 (0.39, 2.31)	0.901
Completed year 12 education[b]	0.92 (0.40, 2.14)	0.853	0.60 (0.24, 1.52)	0.281
Employed full or part time[c]	0.60 (0.23, 1.57)	0.298	0.60 (0.22, 1.61)	0.309
Family history of diabetes[d]	3.00 (1.17, 7.67)	0.022	3.01 (1.14, 7.94)	0.026
Markers of hyperglycaemia in pregnancy:				
Fasting glucose, mmol/L	1.85 (1.14, 3.00)	0.013	2.10 (1.21, 3.61)	0.008
OGTT 1- hour, mmol/L	2.01 (1.37, 2.95)	<0.001	1.98 (1.35, 2.92)	0.001
OGTT 2-hour, mmol/L	1.16 (0.92, 1.45)	0.204	1.13 (0.90, 1.42)	0.307
Insulin during pregnancy	3.98 (1.71, 9.25)	0.001	3.33 (1.39, 7.96)	0.007
Early diagnosis GDM (<20 weeks)	1.31 (0.52, 3.39)	0.562	1.05 (0.40, 2.76)	0.926
Clinical:				
Multiparous	4.75 (1.32, 17.12)	0.017	3.33 (0.88, 12.34)	0.077
Smoking in pregnancy	0.38 (0.15, 0.95)	0.037	0.38 (0.15, 0.98)	0.045
Smoking in pregnancy adjusted for BMI	0.44 (0.16, 1.22)	0.114	0.45 (0.16, 1.29)	0.138
Predominant breastfeeding at 6 months[e]	0.80 (0.33, 1.93)	0.616	0.85 (0.34, 2.12)	0.719
Anthropometric:				
1st BMI in pregnancy, kg/m^2	1.23 (1.03, 1.48)	0.026	1.06 (0.998, 1.13)	0.060
1st BMI adjusted gestational age, kg/m^2	1.19 (0.97, 1.44)	0.049	1.04 (0.98, 1.11)	0.216
Gestational weight gain, kg	0.92 (0.85, 1.01)	0.084	0.94 (0.86, 1.03)	0.201
Gestational weight gain adjusted gestational age, kg	0.94 (0.86, 1.03)	0.202	0.97 (0.88, 1.08)	0.600

Of the 109 women including in this analysis, 27 women were classified as having DIP and 82 women classified as having GDM in the index pregnancy.
The odds ratio for age represents a 5-year increase and for BMI a 3 kg/m^2 increase.
[a]Compared to regional/remote residence.
[b]Compared to<12 years of school or equivalent.
[c]Compared to unemployed.
[d]In parent or sibling, compared to no family history.
[e]Predominant breastfeeding defined as an infant being fed human milk as the only form of milk at 6-months postpartum.

confirmed initial postpartum normoglycaemia prior to development of type 2 diabetes within the follow-up period. As expected, a higher proportion of First Nations women with DIP progressed to type 2 diabetes (48%) than First Nations women with GDM (13%). Conversely, 52% of women with DIP did not have type 2 diabetes postpartum. Thus, meeting standard OGTT or HbA1c criteria for type 2 diabetes during pregnancy (DIP) does not equate to a diagnosis of type 2 diabetes. Nevertheless, women with DIP are at high risk of progression to type 2 diabetes within a short timeframe, highlighting the importance of postpartum diabetes screening.

Systematic reviews report incidence rates of type 2 diabetes following GDM to be between 0.3% and 67% [2,5–7]. Such marked variation can partly be explained by varied definitions of GDM, screening rates and length of follow-up, although, given the lack of comparison between ethnic groups within the same study, it is also unclear how much of the variation can be explained by ethnicity [2]. Furthermore, the vast majority of studies included in these systematic reviews did not include First Nations participants. Addressing this gap in the literature, a Canadian study directly comparing First Nations women to non-First Nations women, reported a type 2 diabetes incidence of 22% five years postpartum in First Nations women and 17% in non-First Nations women after GDM [3]. In the only study of Australian First Nations women, the investigators report an incidence of 22% among First Nations women after GDM, compared to 4% in non-First Nations women, within 3 years postpartum among those screened [4]. The high cumulative incidence of type 2 diabetes development in a short timeframe in that retrospective study, in which less than half the cohort underwent postpartum screening, are now supported by the findings of this prospective study and support early postpartum screening recommendations.

In the above-mentioned Canadian study, differences in type 2 diabetes rates between First Nations and Non-First Nations women were partially explained by socioeconomic and environmental barriers [3]. The contribution of the impacts of colonisation and associated socioeconomic disadvantage on the development of diabetes was not specifically assessed in this study. Such factors likely play an important role in type 2 diabetes for First Nations peoples, with multiple contributors including access to health care, substandard housing, food insecurity, psycho-social stressors, as well as lack of economic opportunities [22,23]. This broader context needs to be considered in the provision of healthcare and design of strategies to reduce risk.

A history of GDM is an independent risk factor for CVD, even without a diagnosis of type 2 diabetes [24,25]. In this

study, First Nations women with GDM and postpartum diabetes/prediabetes had an adverse CVD profile. No clear differences in clinical characteristics were detected between women with GDM and subsequent postpartum normoglycaemia and women with normoglycaemia in both pregnancy and postpartum, possibly owing to the short follow-up period or small sample size. Alternatively, this may reflect the overall higher risk of CVD in First Nations women generally [26]. Consistent with this, three quarters of First Nations women with normoglycaemia in pregnancy in this study had at least one CVD risk factor at follow-up. While a diagnosis of GDM presents an opportunity to identify women at high risk of CVD, for Australian First Nations women, regardless of diabetes status, pregnancy presents an opportunity for engagement and identification of modifiable risk factors in the context of a population with a higher background CVD risk.

Among women with GDM, older age, multiparity, family history of diabetes, higher glucose values in pregnancy, insulin use and higher BMI are associated with postpartum diabetes/prediabetes. These findings are largely consistent with the literature [27,28]. Breastfeeding was not found to be protective. One systematic review found no evidence for maternal protection [27] while other studies report evidence for protection against maternal diabetes after GDM with breastfeeding [29,30]. The lack of observed benefit may be explained by the high rates of breastfeeding in the study population contributing to a lack of power to observe a difference, or by the short follow-up, as the reported benefits of breastfeeding were stronger in studies with longer follow-up [30].

Obesity is an important cardiometabolic risk factor. Consistent with previous literature [27,28], among First Nations women with GDM, in this study, women with postpartum diabetes/prediabetes had higher pregnancy and postpartum BMI and postpartum waist circumference than women who did not develop diabetes/prediabetes. Abdominal obesity is thought to better reflect visceral fat and is more strongly associated with type 2 diabetes than BMI [31]. This is important for First Nations women who have more adiposity for a given BMI, with a predominant central distribution, than Europid women [32]. In this study, First Nations women had a higher follow-up waist circumference than Europid women, but similar pregnancy BMI, gestational weight gain and follow-up BMI. These results provide further justification for targeting postpartum weight loss and the reduction of central obesity.

This is the first longitudinal prospective study of Australian First Nations women with and without a history of GDM. The prospective nature is a strength, with BMI in pregnancy and diabetes status of women accurately recorded. The following limitations should be considered. The follow-up period was shorter for women at lower risk of postpartum type 2 diabetes/pre-diabetes. Women with normoglycaemia during pregnancy were recruited later in PANDORA and thus were followed-up for a median 4-months shorter time period compared to women with GDM. In addition, First Nations women with GDM who did not develop postpartum diabetes/prediabetes had a median of 7-months shorter follow-up compared to First Nations women with GDM who did have this outcome. However, the difference in follow-up periods is not considered clinically significant; upon review of medical records, 23/24 women who had postpartum type 2 diabetes were already diagnosed prior to Wave 1. Whilst women who participated in Wave 1 were broadly representative of the eligible PANDORA cohort, First Nations women who participated were younger than those who did not participate and hence may be less likely to progress to type 2 diabetes.

Given the small number of outcomes, this study may not be powered to detect some key risk factors for postpartum diabetes. Furthermore, the observational nature of the study limits any inference of a causal relationship between risk factors and postpartum diabetes/prediabetes. Nevertheless, these factors may be useful for identifying which women to target for close follow-up and preventative strategies.

This study reports very high progression to type 2 diabetes for First Nations women early in the postpartum period. Results highlight the importance of early postpartum screening after GDM and the need for culturally responsive policies, both at an individual and systems level, to prevent diabetes and its complications for these women and their future pregnancies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability:

Data are available on request to the Partnership Steering Committee. They are not available on an online repository.

Ethics approval:

The study was approved by the Human Research Ethics Committee of the NT Department of Health and Menzies School of Health Research (HREC-2010-1487), and the Central Australian Human Research Ethics Committee (HREC-12-7).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2021.109092.

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