Can J Diabetes xxx (2023) 1–5

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

Original Research

Progression From Gestational Diabetes Mellitus to Type 2 Diabetes Mellitus Among First Nations Women in Northwest Ontario: A Retrospective Cohort Study

Ruben Hummelen MD, PhD, CCFP [a]; Sumeet Sodhi MD, MPH, CCFP [b]; Jenna Poirier BSc [c]; Janet Gordon COO [d]; Shanthive Asokan CCRA, MPhil, MSc, SCR Analyst [e]; Cai-lei Matsumoto MSc, RN [c]; Len Kelly MD, MClinSci, FCFP, FRRM [e,*]

[a] *Division of Clinical Sciences, Northern Ontario School of Medicine, Sioux Lookout, Ontario, Canada*
[b] *Department of Family and Community Medicine, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada*
[c] *Sioux Lookout Northern Ontario School of Medicine Local Education Group, Sioux Lookout, Ontario, Canada*
[d] *Sioux Lookout First Nations Health Authority, Sioux Lookout, Ontario, Canada*
[e] *Sioux Lookout Meno Ya Win Health Centre, Sioux Lookout, Ontario, Canada*

Key Messages

- First Nations women in northwest Ontario with gestational diabetes (GDM) are at increased risk for the development of type 2 diabetes (T2DM).
- In this retrospective cohort study, 39% of women with GDM developed T2DM at 6-year follow up, which is a 3-fold higher rate than that for women without GDM.
- Our findings are in contrast to provincial estimates of a 19% progression to T2DM at 9 years after GDM diagnosis.

ARTICLE INFO

Article history:
Received 9 May 2022
Received in revised form
7 March 2023
Accepted 9 May 2023

Keywords:
diabetes
First Nations
gestational
pregnancy
T2DM

Mots clés:
Diabète
Premières nations
Gestationnel
Grossesse
T2DM

ABSTRACT

Objective: Our aim in this study was to identify the incidence of type 2 diabetes mellitus among First Nations women in northwest Ontario with a history of gestational diabetes mellitus (GDM).
Methods: This work was a retrospective cohort study of women diagnosed with GDM using a 50-gram oral glucose challenge test or a 75-gram oral glucose tolerance test from January 1, 2010 to December 31, 2017 at the Sioux Lookout Meno Ya Win Health Centre. Outcomes were assessed based on glycated hemoglobin (A1C) measurements performed between January 1, 2010 and December 31, 2019.
Results: The cumulative incidence of T2DM among women with a history of GDM at 2 years was 18% (42/237) and 39% (76/194) at 6 years. Women with GDM who developed T2DM were of similar age and parity and had equivalent C-section rates (26%) compared to those who did not develop T2DM. They had higher birthweights (3,866 grams vs 3,600 grams, $p=0.006$) and rates of treatment with insulin (24% vs 5%, $p<0.001$) and metformin (16% vs 5%, $p=0.005$).
Conclusions: GDM confers a significant risk for the development of T2DM in First Nations women. Broad community-based resources, food security and social programming are required.

RÉSUMÉ

Objectifs : Nous avions pour objectif de décrire l'incidence du diabète sucré de type 2 chez les femmes des Premières Nations du Nord-Ouest de l'Ontario qui avaient des antécédents de diabète sucré gestationnel (DSG).
Méthodes : Une étude de cohorte rétrospective auprès de femmes qui avaient reçu un diagnostic de DSG à la suite d'un test de provocation au glucose (50 g) ou d'une épreuve d'hyperglycémie provoquée (75 g de

* Address for correspondence: Len Kelly MD, MClinSci, FCFP, FRRM, Sioux Lookout Meno Ya Win Health Centre, Box 489, Sioux Lookout, Ontario P8T 1A8, Canada.
Email address: lkelly@mcmaster.ca

1499-2671/
https://doi.org/10.1016/j.jcjd.2023.05.003

glucose) du 1er janvier 2010 au 31 décembre 2017, au Sioux Lookout Meno Ya Win Health Centre. Nous avons évalué les issues à partir des mesures de l'A1c réalisées du 1er janvier 2010 au 31 décembre 2019.
Résultats : L'incidence cumulée du DT2 chez les femmes ayant des antécédents de DG à 2 ans était de 18 % (42/237) et de 39 % (76/194) à 6 ans. Les femmes atteintes de DG qui ont développé un DT2 étaient d'âge et de parité similaires et avaient des taux de césarienne équivalents (26 %) par rapport à celles qui n'ont pas développé de DT2. Ils avaient des poids de naissance plus élevés (3 866 grammes contre 3 600 grammes, p = 0,006) et des taux de traitement à l'insuline (24 % contre 5 %, p < 0,001) et à la metformine (16 % contre 5 %, p = 0,005).
Conclusions : Le diabète gestationnel constitue un risque significatif de survenue du DST2 chez les femmes des Premières Nations. D'importantes ressources communautaires, une sécurité alimentaire et des programmes sociaux sont nécessaires.

Introduction

Women who experience gestational diabetes mellitus (GDM) are at increased risk for development of type 2 diabetes (T2DM) [1]. Women with GDM can develop T2DM at up to 10-fold the rate of those with normal gestational glucose tolerance [2,3]. Due to multiple determinants of socioeconomic and health inequities, Indigenous women in Canada are particularly at risk [4,5]. GDM is 2- to 3-fold more prevalent in First Nations women in northwest Ontario (12% vs 4%) compared with the provincial norm [6–9].

Identifying women who are likely to progress to T2DM provides insight into population-specific risk and presents an opportunity for focussed individual and community surveillance and management. In this study we examine the development of T2DM in women who have had GDM in a primarily First Nations population in northwest Ontario.

Methods

In this retrospective cohort study we assessed the incidence of T2DM in women diagnosed with GDM using a 50- or 75-gram oral glucose tolerance test from January 1, 2010 to December 31, 2017 at the Sioux Lookout Meno Ya Win Health Centre (SLMHC). This 60-bed general hospital provides inpatient, outpatient and obstetric services to a primarily First Nations population of 30,000 in 26 remote communities and the town of Sioux Lookout [10].

Prenatal care and GDM screening in the remote communities is initiated at local nursing stations and all 50- and 75-gram glucose tolerance screens are processed at the SLMHC laboratory. These test results were reviewed and GDM was diagnosed according to Diabetes Canada's diagnostic criteria at the time of screening (Table 1). If women had multiple pregnancies during the 8-year study period, the pregnancy in which GDM was first diagnosed was used in the data and subsequent pregnancies by the same mother during the study period were excluded.

The incidence of T2DM was assessed using glycated hemoglobin (A1C) values, which were accessed from the provincial laboratory database from January 1, 2010 to December 31, 2019. The data included A1C testing before, during or after pregnancy. T2DM was defined solely as the presence a single A1C value of ≥6.5%. Data collected included maternal age, parity, gestational age, birth weight, cesarean section delivery, diabetes treatment and A1C results. Patients were excluded from the study if they had a pre-existent diagnosis of type 1 or type 2 diabetes in their prenatal chart or had an A1C of ≥6.5% before or during pregnancy. Data analysis was limited to women with postpartum A1C testing. Maternal and newborn data were collected through a manual review of hospital charts.

To establish relative risk, a cohort of women was established who had a 50-gram oral glucose challenge test or a 75-gram oral glucose tolerance test from January 1, 2010 to December 31, 2017 and tested negative for GDM. From this cohort, 2 age-matched women in 5-year age categories (≤19, 20 to 24, 25 to 30, 30+ years) were selected with a random number generator (www.calculator.net) for each woman with GDM. If the patient met the exclusion criteria, a new random number was generated. Women without GDM who did not have an A1C done postpartum were excluded from the analyses. Women with and without GDM were followed from their index pregnancy to the time of their last A1C measured before December 31, 2019. Follow up ranged between 24 and 118 months. Data were analyzed using SPSS version 21 (IBM Corp, Armonk, New York, United States). Continuous data were tested for significant differences with alpha=0.05 using independent two-sample t tests with unequal variances assumed. Categorical data were tested for significance with alpha=0.05 using Fisher's exact test. Kaplan–Meier analyses were used to assess the cumulative incidence of T2DM among women with and without a history of GDM and tested using a log-rank test.

First Nations heritage was determined based on self-report on provincial antenatal forms, the presence of an on-reserve address or having a "status band number" (denoting Indigenous registration with the Canadian government) on the hospital chart. Ethics approval was granted by the SLMHC research review and ethics committee. In compliance with principles guiding research with Indigenous peoples, the study was completed in partnership with

Table 1
Diagnostic and testing criteria for GDM

	2 step (50 g/75 g)			1 step (75 g)	Screening	
	50-g GCT	50 g→75 g GCT/OGTT	75-g OGTT*	75-g OGTT*	Population, timing	Protocol
2006–2012	≥10.3	7.8–10.2	≥5.3 / 10.6 / 8.9	NA	High risk: 24–28 weeks	2 step
2013–2018	≥11.1	7.8–11.0	≥5.3 / 10.6 / 9.0	≥5.1 / 10.0 / 8.5	Low risk: 24–28 weeks; high risk: first trimester	1 or 2 step

GCT, gestational diabetes screen; *NA*, not applicable; *OGTT*, oral glucose tolerance test.
* 75-g OGTT values: ≥fasting / 1 hour / 2 hours.

Table 2
Characteristics, pregnancy outcomes and diabetes status of women with and without gestational diabetes who received a postpartum A1C

	Women with GDM	Women without GDM	p Value
Total	237	329	
Indigenous/non-Indigenous	234 / 3	283 / 46	
Age, years, mean ± SD	27.2±6.4	27.4±6.4	0.8
Parity, average ± SD	2.2±2.0	1.8±1.8	0.01
Outcomes			
Gestational age at delivery, median ± SD	38±1.6	39±1.5	<0.001
Birth weight * median ± SD	3,626±637	3,459±609	<0.001
Cesarean section, n (%)	61 (26)	90 (27)	0.7
Diabetes			
Time to first A1C, months, median (range)	17 (0–99)	32 (0–108)	<0.001
Follow up, months, median (range)	75 (24–118)	74 (24–117)	0.14

A1C, glycated hemoglobin; *GDM*, gestational diabetes mellitus; *SD*, standard deviation; *T2DM*, type 2 diabetes.
* Data available for 229 women with GDM and 321 women without GDM.

the Sioux Lookout First Nations Health Authority, who oversaw the study, agreed to publication and participated in authorship [11,12].

Results

From January 1, 2010 to December 31, 2017, 346 pregnancies diagnosed with GDM met the inclusion criteria. Postpartum A1C diabetes testing was available on 65% (n=237) of these pregnancies. Within the cohort, 3 women did not identify as Indigenous (Table 2). Of the 771 age-matched women without GDM, postpartum A1C testing occurred in 43% (329 of 771).

Among those with a history of GDM at 2 years, 18% (42 of 237) of the women had developed T2DM compared with 2% (7 of 329) of those without a history with GDM. At 6 years, 39% (76 of 194) of the women with GDM had developed T2DM compared with 14% (30 of 214) of those without GDM (p<0.001, log-rank test) (Tables 3 and 4, and Figure 1).

Within the GDM cohort, women who developed T2DM were of similar age and parity and had equivalent cesarean section rates (26%) compared with those who did not develop T2DM. They had higher birth weights (3,866 vs 3,600 grams, p=0.006) and rates of insulin (24% vs 5%, p<0.001) and metformin (16% vs 5%, p=0.005) use (Table 3).

Discussion

GDM adds significantly to the risk of developing T2DM in First Nations women in northwest Ontario. Among women with GDM, 39% (76 of 194) had developed T2DM at the 6-year follow up compared with 14% (30 of 214) of those without GDM. These values are in contrast to the provincial rate of development of T2DM after GDM of 19% by 9 years [13].

Our findings are consistent with earlier research documenting a higher incidence of T2DM development after GDM among Indigenous women [14–17]. In a 2015 Manitoba study the prevalence of T2DM was higher for First Nations women: 22% vs 2% at 5 years and 47% vs 6% at 10 years after GDM [14]. By the end of the Manitoba study, with a total follow-up period of up to 30 years, 76% of First Nations women with GDM had progressed to T2DM compared with 56% of non–First Nations women [14]. In the James Bay Cree population, 29% of women with GDM developed T2DM within 8 years [17]. In northern Ontario, a 1998 study of 61 First Nations women with GDM in northern Ontario documented an 80% progression rate by 3 years [16].

Australian Indigenous populations are similarly affected. In a 2016 study of 578 Indigenous women with GDM, 42% had developed T2DM at 7 years, compared with 14% of non-Indigenous women [15]. Similarly high rates of progression to T2DM in geographic and genetically distinct Indigenous populations point to shared adverse determinants of health. Poverty, food insecurity, social inequities and transgenerational trauma contribute to the colonial effects on prevalence of diabetes in Indigenous peoples [18–22].

Maternal age and parity were not factors in the development of T2DM in our GDM cohort. This differs from findings from non-Indigenous populations [22–25]. This difference may reflect the high baseline First Nations diabetes prevalence, particularly for women 20 to 34 years of age [26,27].

Insulin use was associated with T2DM development—a likely marker of increased GDM severity when conservative measures fail to achieve glycemic control. This finding is consistent with a 2006 Australian study that demonstrated the need for bedtime insulin, reflected persistent fasting hyperglycemia in GDM pregnancy and was highly predictive for the development of subsequent T2DM [28].

In the context of remote First Nations communities in northwest Ontario, culturally appropriate, community-driven initiatives are needed to address fundamental issues such as poverty and food insecurity, which affect the health of women during pregnancy. The 2019 First Nations Food, Nutrition and Environment Study showed higher food costs and a 38% rate of food insecurity in remote

Table 3
Characteristics of patients with GDM who developed T2DM

	Women with GDM who developed T2DM (n=82)	Women with GDM who did not develop T2DM (n=155)	p Value
Age at delivery, mean ± SD	27.8±6.8	26.9±6.3	0.4
Parity, mean ± SD	2.4±2.0	2.2±2.0	0.4
Cesarean section, n (%)	21 (26%)	40 (26%)	1.0
Birth weight, mean ± SD, g	3,866.1±715.9 (n=76)	3,600.2±575.9 (n=153)	0.006
Insulin, n (%)	20 (24%)	7 (5%)	<0.001
Metformin, n (%)	13 (16%)	7 (5%)	0.005

GDM, gestational diabetes mellitus; *SD*, standard deviation; *T2DM*, type 2 diabetes.

Table 4
Duration of follow up for women with and without GDM

Years of follow up						
	2	4	6	8	10	Total
With GDM						
With T2DM	42	15	19	5	1	82
Without T2DM	0	30	47	42	36	155
Without GDM						
With T2DM	7	14	9	4	2	36
Without T2DM	0	46	92	59	96	293

GDM, gestational diabetes mellitus; *SD*, standard deviation; *T2DM*, type 2 diabetes.

Ontario First Nations communities, who controlled neither food quality nor access [21].

The health of children from GDM pregnancies is negatively impacted, with increased rates of obesity, diabetes and cardiovascular disease [29–31]. Addressing diabetes in pregnancy is therefore an important opportunity to affect population health of present and future generations.

Limitations

The most important limitation in this study was the unavailability of reliable maternal weight data, an established risk factor associated with diabetes in pregnancy and postpartum T2DM [32,33]. Initial maternal weights were often not recorded or measured at different time-points during the pregnancy.

The second limitation is the sole convenience use of a single A1C for identification of T2DM. In addition, the frequency of A1C tests may have changed during the study period, likely increasing after 2013 when it was acknowledged as a diagnostic criteria for T2DM [34]. We assumed that patients diagnosed with T2DM by other postpartum glucose testing methods would have had an A1C performed upon diagnosis, but any patients without one would have been missed. The rates reported may therefore be an underrepresentation of the true prevalence. The high percentage of women without GDM who developed T2DM during the study period is likely a reflection of various clinical indications that led to the A1C testing. Due to this selection bias, the incidence rate of T2DM among women without GDM in our study population is likely lower.

A third limitation is that some women diagnosed with GDM may have had pre-existing T2DM. Hence, a diagnosis of T2DM postpartum may not have represented a progression from GDM. This effect could have increased the incidence of T2DM among women with GDM in our cohort. Women with an A1C of $\geq$6.5% before pregnancy were excluded from our study, so we expect this effect to have been limited.

In conclusion, the presence of GDM increases the risk for developing T2DM by 3-fold for First Nations people in northwest Ontario. Addressing the prevalence of GDM provides opportunities for decreasing the subsequent development of T2DM in this and future generations and will require broad community-based resources and social programming.

Acknowledgments

This study was supported by a NOAMA Clinical Innovation Fund Grant.

Author Disclosures

Conflicts of interest: None.

Author Contributions

Hummelen designed the study. Sodhi contributed to study design and critically read drafts. Poirier performed literature searches and summaries and critically read each draft. Asokan performed data collection. Matsumoto performed data analysis. Gordon provided First Nations supervision and input. Kelly contributed to study design, supervised data collection and wrote the drafts.

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