WITH CHILD

EHAWAWISIT

Diabetes in Pregnancy Amongst Women of the Métis Nation of Alberta

UNIVERSITY OF ALBERTA

MÉTIS NATION of ALBERTA

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A MESSAGE
FROM THE PRESIDENT

Bringing a new life into the world can be a wonderfully complicated journey, particularly for Métis women. As the President of the Métis Nation of Alberta, I am pleased to share with you our health report *Diabetes in Pregnancy Amongst Women of the Métis Nation of Alberta*. In conjunction with our reports *Ehawawisit (With Child): The Epidemiology of Maternal and Neonatal Health among the Métis in Alberta: A Population-Based Retrospective Cohort Study*, and *Ehawawisit (With Child): Experiences and Perspectives of Métis Women on Pregnancy, Birth, and Motherhood*.

This report demonstrates the inequalities among the health of our Métis mothers related to gestational diabetes, compared to the non-Métis population. This work is an important step forward in understanding the health of Métis mothers and shows us where there is work to be done.

I would like to acknowledge and thank our partners, Dr. Maria Ospina and the Ehawawisit research team for their continued support and expertise in the development and completion of this project and in the development of this report.

Sincerely,

Audrey Poitras
President, Métis Nation of Alberta

1.0 BACKGROUND

Métis are a distinct Indigenous people in Canada whose beginnings can be traced back to marriages between European (primarily French and Scottish) fur traders and First Nations peoples.[1] Over time they combined features of both cultures and created new cultural elements to form their own unique identity. As a result, Métis people have developed their own culture, history, and language (Michif). The Métis Nation of Alberta (MNA) defines a Métis person as a "person who self-identifies as Métis, is distinct from other Aboriginal peoples, is of historic Métis Nation Ancestry, and who is accepted by the Métis Nation".[2]

Métis people can be found across the country with the number of self-identified Métis people in Canada being 587,545.[3] Many of which can be found in Alberta, where there are 114,375 self-identified Métis. Thus constituting the second largest Métis population in Canada after Ontario.[3] Currently, the MNA has approximately 50,000 registered Citizens in the Métis Nation of Alberta Registry (MNAR).

1.1 Pre-existing Diabetes Mellitus

Pre-existing diabetes mellitus (pre-existing DM) is predominantly characterized by type 2 diabetes with a smaller portion of women having type 1 diabetes diagnosed before pregnancy or overt diabetes diagnosed at the beginning of pregnancy.[4] Type 1 diabetes develops due to the destruction of pancreas beta cells that produce insulin resulting in insulin deficiency causing hyperglycemia, weight loss, and ketoacidosis.[5] Type 2 diabetes most often occurs after the age of 35 and is characterized by the development of insulin resistance or the pancreas' inability to produce enough insulin.[5]

Screening for overt diabetes in the first trimester should be done for pregnant women who have risk factors for diabetes.[4] Some risk factors for early screening include being over 40 years of age, having an immediate family member with type 2 diabetes, having vascular risk factors (e.g., obesity, smoking), having a previous medical condition associated with type 2 diabetes (e.g., pancreatitis, human immunodeficiency virus), use of drugs associated with type 2 diabetes (i.e., glucocorticoid steroids, antipsychotics), and organ damage related to type 2 diabetes (i.e., retinopathy).[6] Early screening can be done using a hemoglobin A1C test or fasting plasma glucose (FPG).[4] If values of hemoglobin A1C are ≥6.5% or the FPG is ≥7.0 mmol/L then a diagnosis of diabetes is made.[4]

Pre-existing DM has been associated with greater rates of preeclampsia, caesarean section, preterm birth, increased birth weight, congenital abnormalities, and perinatal mortality.[7-9] There is also evidence suggesting the offspring of women with pre-existing DM during pregnancy have an increased risk of developing type 2 diabetes.[10,11] Children of mothers with type 2 diabetes during pregnancy also have been found to have an increased likelihood of hospitalization for neurological/ developmental disorders, asthma, and infections.[12]

1.2 Gestational Diabetes Mellitus

Gestational Diabetes Mellitus (GDM) is classified as a glucose intolerance that arises during pregnancy above the expected range of normal glucose values that naturally occur in pregnancy.[4,13] Diabetes Canada recommends all pregnant women are screened at 24-28 weeks gestation with a 50g non-fasting oral

glucose challenge test. If the one-hour plasma glucose is ≥11.1 mmol/L, then a GDM diagnosis is made; however, if values are ≥7.8 mmol/L, then a 75g fasting oral glucose tolerance test is ordered.[4] A FPG of ≥ 5.3mmol/L, or a one-hour plasma glucose of ≥10.6mmol/L or a two-hour plasma glucose ≥9.0 mmol/L are indicative of GDM diagnosis.[5]

GDM is associated with poor adverse maternal and perinatal outcomes including preeclampsia, caesarean section, babies being large for gestational age, preterm birth, and neonatal intensive care unit admission.[14,15] The treatment of GDM during pregnancy can reduce the risk for adverse perinatal outcomes.[16] Both mothers with GDM and their offspring have an increased risk of developing type 2 diabetes later in life.[10,11,17]

1.3 Management of Diabetes in Pregnancy

The primary treatment for type 1 diabetes is insulin administration. Diabetes Canada recommends women with type 1 diabetes should continue with glucose monitoring and insulin treatment during pregnancy.[4,5] The primary treatment of GDM is diet and exercise counselling; insulin or metformin treatment is added if glycemic control cannot be maintained.[4] The first-line treatment for type 2 diabetes includes diet, exercise, and oral antihyperglycemic medications (i.e. metformin).[5,18] Insulin can also be used as a treatment for type 2 diabetes to improve glycemic control.[5] If metformin or glyburide oral hyperglycemic medications were taken during conception, then they can also be taken during pregnancy and insulin can be added to improve glycemic control.[4]

1.4 Diabetes among the Métis

In Canada, the small amount of research on diabetes among Métis people has focused on the burden of type 1 and type 2 diabetes among non-pregnant Métis people.[19-21] In Alberta the age-standardized prevalence of diabetes among Métis was 10.7% in 2016, and the rate was 1.5 times greater among Métis than non-Métis in Alberta.[21] Research conducted in the other provinces making up the Métis Homeland found the prevalence of diabetes is greater among Métis in Manitoba (12.0%) and Ontario (11.2%), compared to their non-Métis counterparts (8.9%, 9.0%).[19,20] Métis people with diabetes have also been found to have a greater number of adverse events, including a greater number of limb amputations compared to the non-Métis population.[20,21] Diabetes during pregnancy among the Métis, both pre-existing DM and GDM was not evaluated separately in this research. To address this knowledge gap, a population-based cohort study assessing the burden and outcomes of pre-existing DM and GDM among Métis women is needed.

2.0 METHODS

2.1 Study Population

All singleton births in Alberta from 2006-2016 were included in this study. Métis births were identified through probabilistic data linkage between the MNAR database and the Alberta Health Care Insurance Plan (AHCIP).[22] All births not identified as Métis were classified as the non-Métis population and are included as a comparison group. Deterministic data linkage was used to link the rest of the study databases using de-identifiable personal health numbers.[23]

2.2 Data Sources

	**MÉTIS NATION OF ALBERTA REGISTRY (MNAR)**	Maintained by the MNA and includes demographic information on all MNA Citizens in Alberta.
	**ALBERTA HEALTH CARE INSURANCE PLAN (AHCIP)**	Captures demographic information on everyone in Alberta that is covered by universal healthcare. Specifically, it includes information on the migration of people into the province, data of birth, gender, address, and cancellation of coverage.[24]
	**ALBERTA PERINATAL HEALTH PROGRAM (APHP)**	A validated clinical database that captures information about all births (hospital births and those delivered by registered midwives) in Alberta.[25-27] The two-part delivery form includes information on pre-pregnancy maternal characteristics, information about the current pregnancy and the delivery.[26,27]
	**DISCHARGE ABSTRACT DATABASE (DAD)**	Contains information on all hospital admissions in Alberta. This includes both maternal and perinatal hospital admissions. Diagnoses made in hospital are recorded using the International Classification of Disease 10th Revision (Canadian Version).[24]
	**PHARMACEUTICAL INFORMATION NETWORK (PIN)**	Captures information about all drugs dispensed from pharmacies in Alberta. Included in this database is the drug identification number, the dosage, and anatomical therapy code (ATC). Drugs dispensed in hospitals are not included in this database.[24]
	**PAMPALON MATERIAL AND SOCIAL DEPRIVATION INDEX (PMDI)**	Contains information from the 2006 Canadian Census. A principal component analysis is used to create two independent small area level measures of material and social deprivation.[28] Material deprivation is representative of the correlated census variables education, employment, and income. Social deprivation is representative of the correlated census variables; number of single-family homes, number of people widowed, single, or divorced, and the proportion of people living alone within that dissemination area. Both material and social deprivation are categorical variables with five quintiles ranging from the most privileged (Q1) to the most deprived (Q5).[28] The PMDI database also includes information on maternal area of the residency (urban or rural). Area of the residency is assigned based on population density, distance from services, local infrastructure and the movement patterns of people that live in the area, and the type of work. At the time of delivery, the mothers postal code is used to assign area of residency.[29]

2.3 Identification of Diabetes in Pregnancy

Diabetes type was classified using information captured on the delivery record and inputted into the APHP. Pre-existing DM was defined as those that had reported "diabetes controlled by diet," "insulin use" and/or "retinopathy documented" on their antenatal risk assessment. GDM was defined as those women that had "Gestational Diabetes" documented as an issue in their current pregnancy. In Alberta using the APHP to classify GDM has previously been used as the gold standard.[25]

2.4 Identification of Study Covariates and Diabetes Medications

The study covariates include maternal age at the indexed birth, pre-pregnancy weight (<45kg or >91kg), antenatal risk assessment score, substance use during pregnancy (alcohol and drug use), pre-existing hypertension, material deprivation, social deprivation, and area of residency (urban or rural). The antenatal risk assessment score is classified as low (i.e., <3), moderate (i.e., 3-6), and high (i.e., >6) based on the antepartum score that captures information on past obstetrical history, pre-pregnancy characteristics, and issues during the current pregnancy. Maternal postal code at the time of birth was used to assign the dissemination area linked to the census variables used to calculate material and social deprivation and to assign area of residency. Both material and social deprivation are comprised of five quintiles, ranging from the most privileged (Q1) to the most deprived (Q5). Insulin use (i.e., insulin dispensed within four months of birth) was identified in the PIN database using the ATC ('A10A').

2.5 Identification of Maternal Outcomes of Diabetes in Pregnancy

The two main maternal outcomes examined are pregnancy induced hypertension and caesarean sections. Women were classified as having pregnancy-induced hypertension if "gestational hypertension" was identified as a problem in the current pregnancy but were not classified as having pre-existing hypertension. A caesarean section was identified if the delivery method was recorded as being a caesarean section on the delivery record.

A number of secondary maternal outcomes were also assessed. These include preeclampsia (pregnancy-induced hypertension and proteinuria), obstetric hemorrhage (intrapartum; ICD-10: O67-O679 and postpartum; ICD-10: O72-O724), induction of labor, and maternal death at delivery. If the number of events is less than five, the outcome is not reported due to privacy concerns.

2.6 Identification of Neonatal Outcomes of Diabetes in Pregnancy

The two main neonatal outcomes assessed are preterm birth and being born large for gestational age. Preterm birth was defined as a birth before 37 weeks gestation. Size for gestational age was calculated using Canadian sex-specific reference (<10th percentile was defined as small for gestational age, and >90th percentile was defined as large for gestational age).[30]

Secondary neonatal outcomes that were assessed include congenital anomalies, birth injuries (ICD-10: P10-P159), admission to the neonatal intensive care unit, small for gestational age, induced preterm birth, spontaneous preterm birth, birth weight, stillbirth, and neonatal death (death within 28 days of birth). If the number of events is less than five, the outcome is not reported due to privacy concerns.

2.7 Statistical Analysis

Study outcomes and covariates are described using frequencies and proportions for categorical and means with standard deviations for continuous variables. Study covariate comparisons between Métis and non-Métis births were done using a t-test for continuous variables or Chi² test/Fishers exact test for categorical variables.

Crude period prevalence estimates were calculated for the whole study period for the proportion of births complicated by pre-existing DM and GDM among the Métis and non-Métis birth cohorts (i.e., the number of Métis births with GDM/number of Métis births). Age standardized prevalence estimates were calculated for the whole study period and annually using the direct standardization methods using a reference population of all births in Canada by age group in 2006.[31]

A multivariable analysis adjusting for theoretically important study covariates comparing outcomes among Métis and non-Métis births was done.[4,32-35] Covariates assessed for their potential confounding effects include maternal age, smoking, parity, pre-pregnancy weight, pre-pregnancy hypertension, material deprivation, social deprivation, insulin prescriptions, and area of residency (urban or rural).

Multilevel mixed logistic regression models with random effects were used to adjust for multiple singleton births to the same mother within the ten-year study period.[36] Model fit was assessed using the maximum likelihood ratio, and intraclass correlation coefficients were calculated to quantify the variance in outcome attributable to differences between mothers.[36]

The summary statistic used are adjusted odds ratios with 95% confidence intervals comparing Métis births to non-Métis births. Analysis was done using SAS software v. 9.4 (SAS Institute., Cary, NC, USA) and STATA Statistical Software (Release 15. College Station, TX: StataCorp LLC).

3.0 RESULTS

3.1 Data Merging

After the removal of multiple births and merging of the databases the resulting study population was 483,300 births in the 10-year study period. The cohort sizes are 7,977 Métis births and 475,323 non-Métis births (Figure 1).

3.2 Characteristics of Métis and Non-Métis Births with Pre-existing Diabetes Mellitus and Gestational Diabetes Mellitus

Métis women with pre-existing DM were on average two years younger than non-Métis women with pre-existing DM (30.1yr and 32.1yr). A greater proportion of Métis women with pre-existing DM had a pre-pregnancy weight of > 91kg (41%), smoked during pregnancy (29%), lived in rural areas (33%), and were classified as having a high-risk pregnancy (53%) compared to non-Métis women with pre-existing DM (23%, 15%, 23%, and 41%) (Table 1).

Métis women with GDM also were on average younger than non-Métis with GDM (30.1 yr and 32.3 yr). A greater proportion of Métis women with GDM had a pre-pregnancy weight > 91kg (33%), smoked during pregnancy (32%), lived in rural areas (28%), were taking insulin during their pregnancy (37%), had a multiparous birth (29%), were classified as a high risk pregnancy (19%), and were assigned to the most deprived quintile of material deprivation, compared to non-Métis women with GDM (17%, 11%, 15%, 26%, 25%, 14% and 23% respectively) (Table 1).

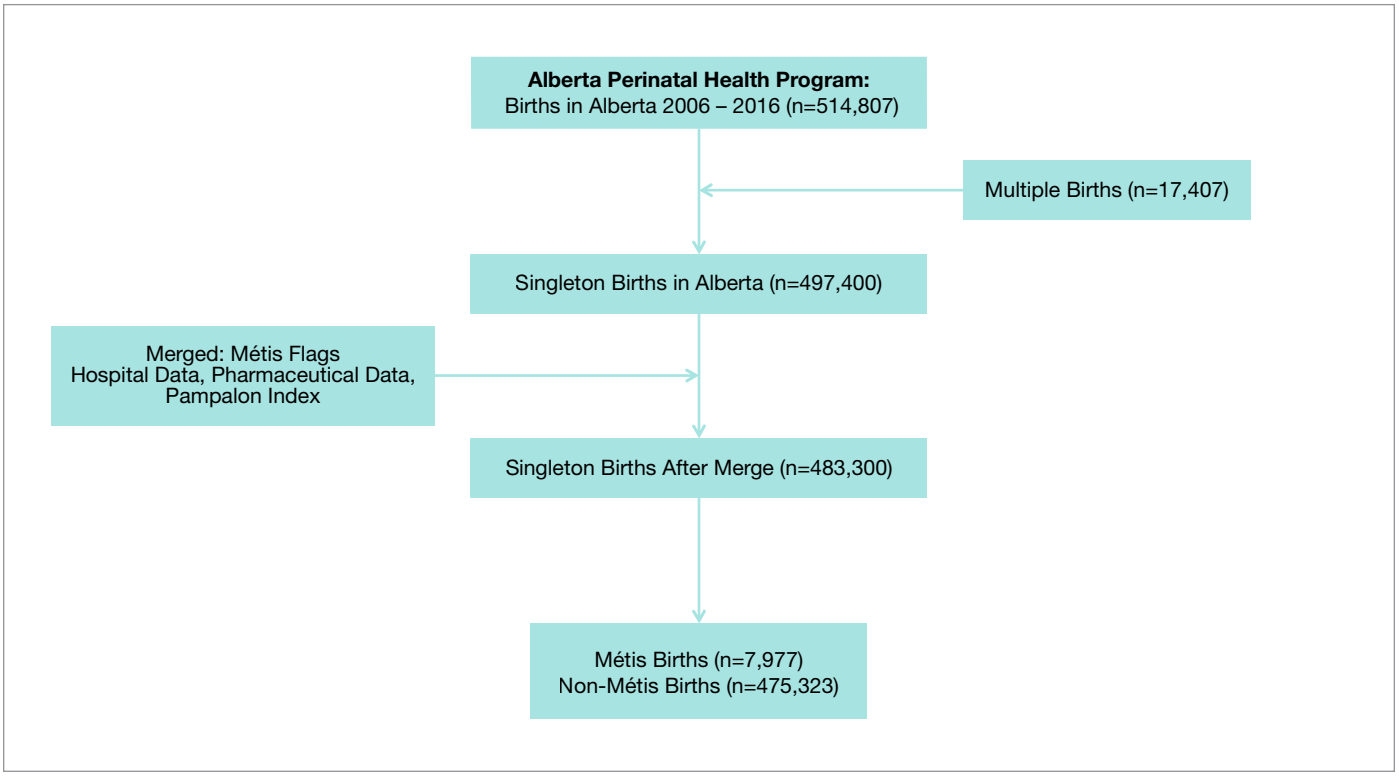


Figure 1. Study Flow

3.3 Prevalence of Pre-existing DM

During the ten-year study period the crude prevalence of pre-existing DM was 1.4% and 1.2% among non-Métis births. After the prevalence was age standardized it was 1.8% among Métis births and 1.1% among non-Métis women (Table 2). After adjusting for important study covariates and birth clusters, Métis women have a 74% increased risk for having pre-existing DM during pregnancy compared to non-Métis women (Figure 2).

During the ten-year study period the age-standardized prevalence of pre-existing DM increased from 1.2% in 2006, to 2.5% in 2016 among Métis births. Among non-Métis births the age-standardized prevalence of pre-existing DM increased from 1.0% to 1.4% over the ten-year study period (Figure 3).

Table 1. Characteristics of Métis and Non-Métis Births with Pre-existing DM and GDM

	PRE-EXISTING DM (n, %)		GDM (n, %)	
	MÉTIS (n=112)	NON-MÉTIS (n=5,509)	MÉTIS (n=384)	NON-MÉTIS (n=25,285)
Maternal Age	30.09 (5.4)	32.12 (5.4)*	30.85 (5.7)	32.26(5.1)*
Pre-pregnancy Weight > 91kg	46 (41.1%)	1,274 (23.1%)*	125 (32.55%)	4,258 (16.8)*
Smoking During Pregnancy	32 (28.6%)	824 (15.0)*	122 (31.8)	2,861 (11.3)*
Pre-pregnancy Hypertension	14 (12.5)	395 (7.2)	8 (2.1)	302 (1.2)
Substance Use	5 (4.5)	130 (2.4)	10 (2.6)	389 (1.5)
Rural	36 (32.7)	1,238 (22.6)*	107 (27.6)	3,622 (14.5)*
Insulin Use	58 (51.8)	2,616 (47.5)	133 (36.6)	6,497 (25.7)*
Multiparous (2-4 births)	20 (17.9)	1359 (24.8)	122 (29.2)	6,218 (24.7)*
High Risk Pregnancy	59 (52.7)	2,273 (41.3)*	73 (19.0)	3,641 (14.4)*
MATERIAL DEPRIVATION				
Least Deprived	10 (9.4)	912 (17.6)*	27 (7.3)	4,522 (18.8)*
2	12 (11.3)	996 (19.2)*	71 (19.1)	4,610 (19.1)
3	24 (22.6)	991 (19.1)	87 (23.5)	4,694 (19.5)*
4	25 (23.6)	1,057 (20.4)	77 (20.8)	4,829 (20.1)
Most Deprived	35 (33.0)	1,225 (23.6)*	109 (29.4)	5,431 (22.6)*
SOCIAL DEPRIVATION				
Least Deprived	15 (14.2)	658 (12.7)	47 (12.7)	3,127 (13.0)
2	14 (13.2)	1,025 (19.8)	46 (12.4)	5,328 (22.1)*
3	23 (21.7)	1,211 (23.4)	90 (24.3)	5,393 (22.4)
4	29 (27.4)	1,193 (23.0)	113 (30.5)	5,219 (21.7)*
Most Deprived	25 (23.6)	1,094 (21.1)	75 (20.2)	5,019 (20.8)

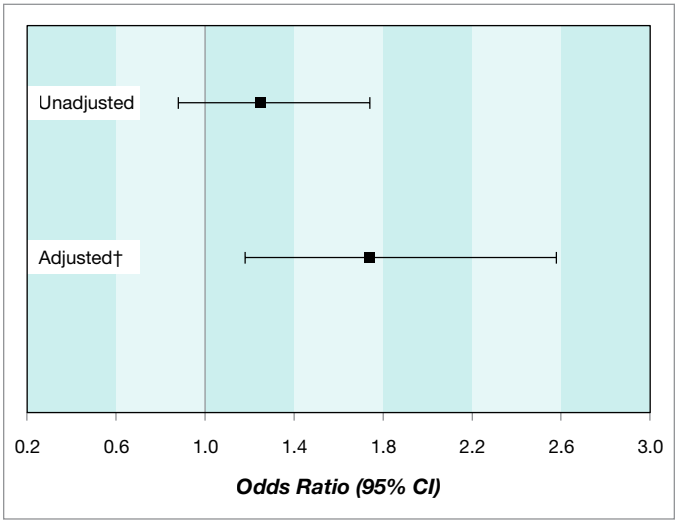
** Statistically significant P<0.05*

Table 2. The Prevalence of Pre-existing DM Among Métis and Non-Métis Births

	MÉTIS (n, %)	NON-MÉTIS (n, %)
Pre-existing DM	112 (1.42%)	5,509 (1.17%)
Age Standardized†	6,227 (1.8%)	4,111 (1.1%)

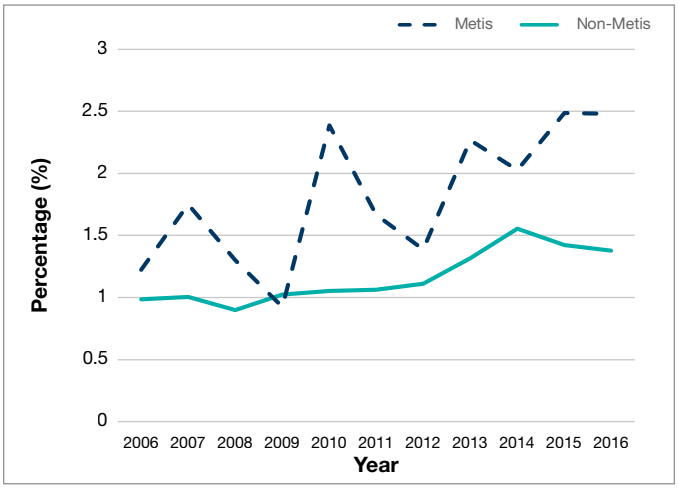
†*Standardized to the number of births in Canada by age group in 2006.*

Figure 2. Adjusted and Unadjusted Odds Ratios of Pre-Existing DM Comparing Métis and Non-Métis Births



†*Adjusted for maternal age, material and social deprivation, area of residency, pre-existing hypertension, and multiple births to the same mother over the ten-year study period.*

Figure 3. Age-Standardized Prevalence of Pre-existing DM Over the Ten-year Study Period



‡*Standardized to the number of births in Canada by age group in 2006.*

3.4 Maternal and Neonatal Outcomes of Pre-existing DM

After adjusting for important study covariates and cluster of births there was no significant difference in the risk for pregnancy induced hypertension among Métis births compared to non-Métis births (14% and 10%, aOR 1.45 95% CI: 0.71, 2.96). Similarly, there were no differences between Métis and non-Métis births complicated with pre-existing DM for risk of caesarean section, preterm birth, and having a baby born large for gestational age (Table 3 and Figure 4).

Among the secondary outcomes, Métis births with pre-existing DM also had 3.5 times increased risk of having preeclampsia during pregnancy compared to non-Métis women (9.8% and 3.4%, OR 3.51 95% CI: 1.60, 7.69) (Table 4).

Due to the small number of events, further adjustments were not made. There were no differences between Métis and non-Métis for the risk of induction of labour, obstetric hemorrhage, small for gestational age, birth weight, induced preterm birth, spontaneous preterm birth, and admission to the neonatal intensive care unit (Table 4).

Table 3. Maternal and Neonatal Outcomes of Pre-existing DM

	MÉTIS (n, %)	NON-MÉTIS (n, %)	UNADJUSTED OR†	ADJUSTED OR†
Pregnancy Induced Hypertension	16 (14.3)	556 (10.1)	1.66 (0.81, 3.39)	1.45 (0.71, 2.96)[a]
Caesarean Section	59 (52.7)	2,630 (47.7)	3.27 (0.20, 55.0)	3.53 (0.48, 26.13)[b]
Preterm Birth	30 (26.8)	1,098 (19.8)	1.72 (0.92, 3.21)	1.30 (0.68, 2.51)[c]
Large for Gestational Age	35 (31.3)	1,481 (26.9)	1.54 (0.76, 3.12)	0.99 (0.50, 1.96)[d]

† *Adjusted for multiple births to the same mother over the ten-year study period.*

[a] *Adjusted for pre-pregnancy weight > 91kg and multiple births to the same mother over the ten-year study period.*

[b] *Adjusted for maternal age, parity, smoking, material and social deprivation and multiple births to the same mother over the ten-year study period.*

[c] *Adjusted for smoking, material deprivation and multiple births to the same mother over the ten-year study period.*

[d] *Adjusted for maternal age, parity, insulin use, pre-pregnancy weight >91kg and multiple births to the same mother over the ten-year study period.*

Table 4. Secondary Outcomes of Métis and non-Métis births with Pre-existing DM

	MÉTIS (n, %)	NON-MÉTIS (n, %)	OR or BETA COEFFICIENT (95% CI)†
Preeclampsia (superimposed)	11 (9.8)	189 (3.4)	3.51 (1.60, 7.69)*
Induction of Labour	51 (62.2)	2,321 (57.5)	1.26 (0.69, 2.32)
Obstetric Hemorrhage	10 (8.9)	567 (10.3)	0.81 (0.37, 1.78)
Small for Gestational Age	10 (8.9)	374 (6.8)	1.50 (0.57, 3.99)
Birth Weight	3342.2 (731.1)	3363.8 (842.5)	-4.39 (-147.76, 138.97)
Induced Preterm Birth	10 (7.0)	359 (7.0)	1.55 (0.68, 3.54)
Spontaneous Preterm Birth	13 (12.4)	375 (7.3)	2.00 (0.97, 4.15)
NICU Admission	19 (18.6)	1,079 (20.6)	0.87 (0.38, 1.97)

* *Statistically significant P<0.05*

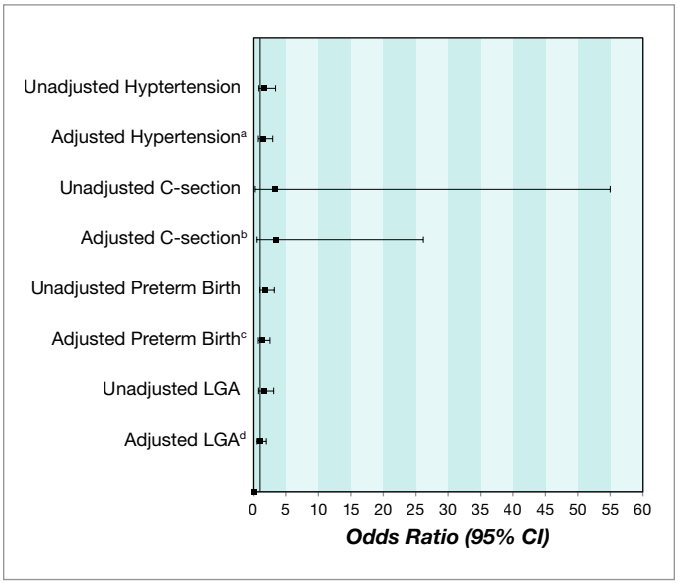
† *Adjusted for multiple births to the same mother over the ten-year study period.*

Table 5. The Prevalence of GDM Among Métis and Non-Métis Births

	MÉTIS (n, %)	NON-MÉTIS (n, %)
GDM Prevalence	384 (4.86%)	25,285 (5.36%)
Age Standardized†	22,294 (6.3%)	18,889 (5.3%)

† *Standardized to the number of births in Canada by age group in 2006.*

Figure 4. Maternal and Neonatal Outcomes of Pre-existing DM



a *Adjusted for pre-pregnancy weight > 91kg and multiple births per mother for the ten-year study period*

b *Adjusted for maternal age, parity, smoking, material and social deprivation and multiple births to the same mother over the ten-year study period.*

c *Adjusted for smoking, material deprivation and multiple births to the same mother over the ten-year study period.*

d *Adjusted for maternal age, parity, insulin use, pre-pregnancy weight >91kg and multiple births to the same mother over the ten-year study period.*

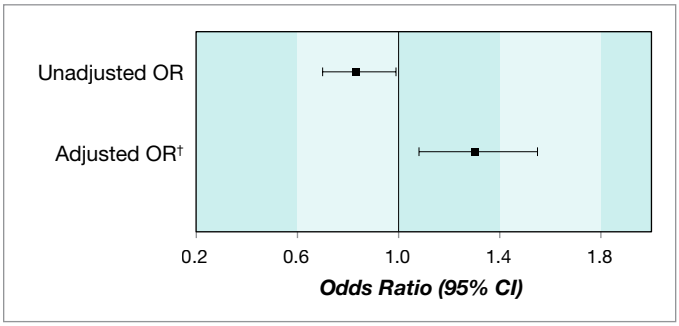
LGA=large for gestational age

3.5 The Prevalence of GDM

The overall crude prevalence of GDM during the ten-year study period was 4.9% among Métis births and 5.4% among non-Métis births (Table 5). The age-standardized prevalence of GDM among Métis births is 6.3% and among non-Métis it was 5.3% (Table 5). The Métis cohort is younger than the non-Métis cohort at the time of birth leading to the crude prevalence being lower among Métis births. Métis women have a 30% increased risk of having GDM compared to non-Métis women after adjusting for theoretically important covariates and birth clusters (aOR 1.30, 95%CI: 1.08, 1.55) (Figure 5).

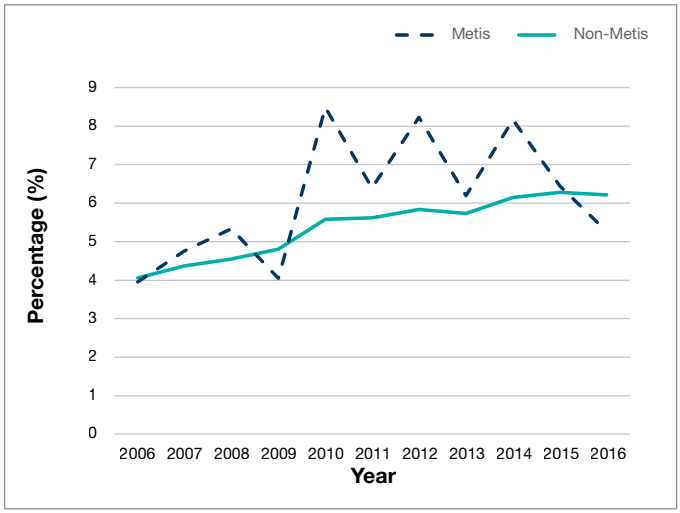
During the ten-year study period, the age standardized prevalence of GDM increased from 4.1% in 2006 to 5.3% in 2016 among Métis births. Among non-Métis births the age-standardized prevalence increased from 4.1% in 2006 to 6.2% in 2016 among non-Métis births (Figure 6).

Figure 5. Adjusted and Unadjusted Odds Ratio of GDM Comparing Métis and Non-Métis Births



† *Adjusted for maternal age, material and social deprivation, area of residency, and pre-existing hypertension.*

Figure 6. Age-Standardized Prevalence of GDM over the Ten-Year Study Period



‡ *Standardized to the number of births in Canada by age group in 2006.*

3.6 Maternal and Neonatal Outcomes of GDM

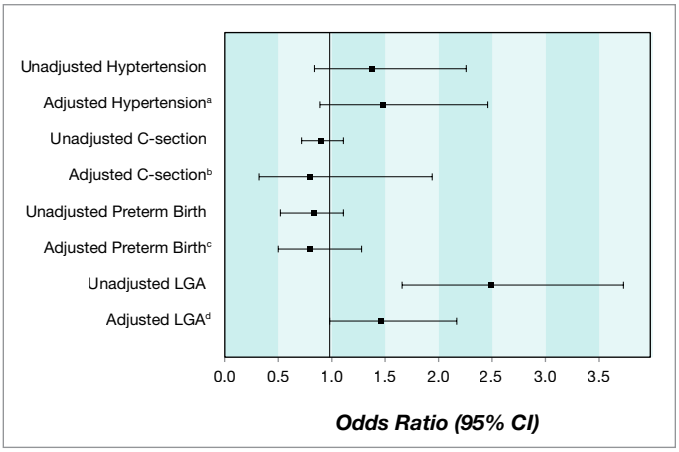
After adjusting for important study covariates and cluster of births, Métis women with GDM have 48% increased risk of having a baby that is born large for gestational age compared to non-Métis (23% and 14%, aOR: 1.00, 2.19) (Table 6 and Figure 7). There were no differences between Métis and non-Métis births with GDM for risk of pregnancy induced hypertension, caesarean section, and preterm birth (Table 6 or Figure 7).

Further differences were identified between Métis and non-Métis births in the secondary maternal and neonatal outcomes. Births to Métis women with GDM have reduced risk of having a baby that is small for gestational age (5.6% and 9.1% OR: 0.45, 95%CI: 0.26, 0.80), and for having an obstetric hemorrhage (6.0% and 10.2%, OR: 0.53, 95%CI: 0.33, 0.85) compared to non-Métis GDM births (Table 7).

Births to Métis women with GDM were found to have an increased risk for having a baby that has a congenital anomaly compared to non-Métis women (3% and 1%, OR: 3.46, 95% CI: 1.68, 7.12). Métis births complicated with GDM were on average 157g heavier than births to non-Métis with GDM (ß: 156.5, 95%CI: 93.7, 219.4) (Table 7).

There were no differences for the risk of induction of labor, induced preterm, spontaneous preterm, admission to the neonatal intensive care unit, birth injury, still birth, and neonatal death between Métis and non-Métis births complicated by GDM (Table 7).

Figure 7. Main Maternal and Neonatal Outcomes of GDM Among Métis and Non-Métis Births



[a] *Adjusted for maternal age, smoking, parity, material and social deprivation and multiple births to the same mother over the ten-year study period*

[b] *Adjusted for maternal age, parity, area of residency, material and social deprivation and multiple births to the same mother over the ten-year study period.*

[c] *Adjusted for maternal age, smoking, material deprivation and multiple births to the same mother over the ten-year study period.*

[d] *Adjusted for maternal age, pre-pregnancy weight >91kg, parity, area of residency, material and social deprivation and multiple births to the same mother over the ten-year study period.*

LGA= large for gestational age

Table 6. Main Maternal and Neonatal Outcomes of GDM among Métis and Non-Métis births

	MÉTIS (n, %)	NON-MÉTIS (n, %)	UNADJUSTED OR†	ADJUSTED OR†
Pregnancy Induced Hypertension	44 (11.5)	2,391 (9.5)	1.40 (0.86, 2.28)	1.50 (0.91, 2.48)[a]
Caesarean Section	140 (36.5)	9,734 (38.5)	0.92 (0.74, 1.13)	0.82 (0.34, 1.96)[b]
Preterm Birth	38 (9.9)	2,754 (10.9)	0.85 (0.54, 1.13)	0.82 (0.52, 1.30)[c]
Large for Gestational Age	88 (22.9)	3,606 (14.3)	2.51 (1.68, 3.75)*	01.48 (1.00, 2.19)*[d]

† *Adjusted for multiple births to the same mother over the ten-year study period.*

[a] *Adjusted for maternal age, smoking, parity, material and social deprivation and multiple births to the same mother over the ten-year study period.*

[b] *Adjusted for maternal age, parity, area of residency, material and social deprivation and multiple births to the same mother over the ten-year study period.*

[c] *Adjusted for maternal age, smoking, material deprivation and multiple births to the same mother over the ten-year study period.*

[d] *Adjusted for maternal age, pre-pregnancy weight >91kg, parity, area of residency, material and social deprivation and multiple births to the same mother over the ten-year study period.*

Table 7. Secondary Maternal and Neonatal Outcomes of Métis and Non-Métis births with GDM

	MÉTIS (n, %)	NON-MÉTIS (n, %)	OR or BETA COEFFICIENT (95% CI)†
Preeclampsia (superimposed)	10 (2.6)	216 (1.6)	1.24 (0.60, 2.58)
Induction of Labour	190 (62.3)	11,332 (56.6)	1.35 (0.98, 1.87)
Obstetric Hemorrhage	23 (6.0)	2,578 (10.2)	0.53 (0.33, 0.85)*
Congenital Anomaly‡	11 (2.9)	216 (0.9)	3.46 (1.68, 7.12)*
Small for Gestational Age	20 (5.6)	2,297 (9.1)	0.45 (0.26, 0.80)*
Birth Weight	3,463.3 (576.4)	3308.9 (594.5)	156.5 (93.70, 219.42)*
Induced Preterm Birth	17 (4.5)	922 (3.8)	1.22 (0.68, 2.17)
Spontaneous Preterm Birth	13 (3.5)	1,131 (4.6)	0.71 (0.36, 1.40)
NICU Admission	37 (10.2)	3,243 (13.3)	0.69 (0.46, 1.04)
Birth Injury	8 (2.1)	845 (3.36)	0.61 (0.29, 1.26)

**Statistically significant p<0.05*

‡Not all regions in Alberta have consistent reporting of congenital anomalies

4.0 DISCUSSION

The results of this study indicate Métis women have an increased prevalence and risk of having pre-existing DM compared to non-Métis women after adjusting for study covariates including age, and material and social deprivation. However, although Métis women have an increased risk for having pre-existing DM, there were no differences identified between Métis and non-Métis for the main maternal (pregnancy induced hypertension and caesarean section) and neonatal (preterm birth and large for gestational age) outcomes.

Although the crude prevalence of GDM was not greater among Métis women, after age-standardization, the prevalence of GDM was greater among Métis women compared to non-Métis women. After adjusting for important study covariates and cluster of births, Métis women had an elevated risk of having GDM compared to non-Métis women.

A greater proportion of Métis women with GDM were taking insulin during pregnancy suggesting the severity of GDM cases may be greater among Métis women because blood glucose could not be controlled with diet and exercise alone. This is consistent with the results that Métis women with GDM have an increased risk for having a baby born large for gestational age.[15] This is concerning because of the association between elevated birth weight and risk for type 2 diabetes later in life.[37]

The elevated risk among Métis women for having a baby born large for gestational age remained after adjusting for important study covariates including age, material and social deprivation, and insulin use during pregnancy. Blood glucose management during pregnancy can be influenced by many complex factors including emotional distress leading to undesirable eating patterns, an unstable home environment, economic, and social pressures.[38] It is important to note that although Métis women with GDM have an increased risk for having a baby born large gestational age, they did not have an increased risk for obstetric hemorrhage and birth injuries, both of which are related outcomes.[39]

Among the secondary outcomes, Métis women with pre-existing DM were identified as having an increased risk of having preeclampsia during pregnancy compared to non-Métis women. Previous research has identified pre-existing DM as a risk factor for preeclampsia and has found that women with pre-existing DM have a 3.7-fold increased risk of developing preeclampsia during pregnancy.[40] In addition, maternal obesity is also associated with an increased risk for developing preeclampsia.[40] A greater proportion of Métis women with pre-existing DM were identified as having a pre-pregnancy weight >91kg which could be a contributing factor to the increased risk for preeclampsia.

Métis women with GDM during pregnancy had an increased risk of having a baby experiencing a congenital anomaly. The elevated risk among births to Métis women with GDM could be due to a greater proportion of Métis women with GDM that have a pre-pregnancy weight >91kg or it could be due to uncontrolled blood sugars during pregnancy, both of which have been associated with an increased risk for congenital anomalies in pregnancies complicated by GDM.[41,42]

Due to the small number of events among GDM complicated Métis births no adjustments were made to further understand this association. These results should be interpreted with caution due to lack of consistent reporting in certain regions of Alberta.

In Canada, research examining diabetes in pregnancy among First Nations women has also found First Nations women have an elevated prevalence of diabetes in pregnancy.[43-46]

The results of genetic studies have not been able to provide a clear answer to the elevated risk First Nations women have for developing diabetes during pregnancy compared to non-Indigenous women,[47] and this increased risk is not exclusive to Indigenous women in Canada.[48-50] A greater prevalence of diabetes in pregnancy has also been identified in Aboriginal and Torres Strait Islanders (Australia) and Native Americans and Alaska Natives (United States of America), countries where Indigenous peoples experience a similar colonial history and social inequalities.[48-50]

The results of this study demonstrate Métis women have a residual risk for having both pre-existing DM and GDM compared to non-Métis women. This increased risk could be due to a combination of reasons including genetics, lifestyle, and environment factors (social determinants of health).[4,51] Exposure to unfavorable social determinants of health (i.e., low income, unemployment) is associated with an increased risk for developing diabetes in pregnancy.[52]

In addition to the social determinants of health, Indigenous peoples in Canada are survivors of colonialism which has been identified as a fundamental determinant to the health of Indigenous peoples worldwide.[53,54] Aspects of colonialism impacting the lives of Indigenous peoples include institutionalization, systemic racism, loss of culture, and a rapid transition away from a traditional lifestyle to a western one.[55] This has had detrimental implications for the mental, spiritual and physical wellbeing of Indigenous peoples.[55] The impact of colonialism and the social determinants of health could be contributing factors for the development of diabetes in pregnancy and greater diabetes risk profiles among Métis women compared to non-Métis women.

Clinicians engaging with Métis women should be aware of the elevated risk they have for both pre-existing DM and GDM. They should also be aware health inequalities Métis people experience are largely due to the history of colonialism and perpetuated social inequalities. Close management of blood sugars during pregnancy should be a focus due to the increased risk among Métis women for having a baby born large for gestational age. Programs and services to support Métis women who have pregnancies complicated with diabetes should be co-created and delivered in partnership with the MNA, so Métis culture and specific needs are meaningfully incorporated.

Strengths and Limitations of This Research

One of the main strengths of this research is the use of MNAR database to identify Métis births. The use of this database allows for identification of Métis births that have a verifiable connection to the Métis Homeland and Métis community in Alberta. Another strength is the use of the APHP database that has built in verification steps to ensure the accuracy of the data used to define study outcomes.[25]

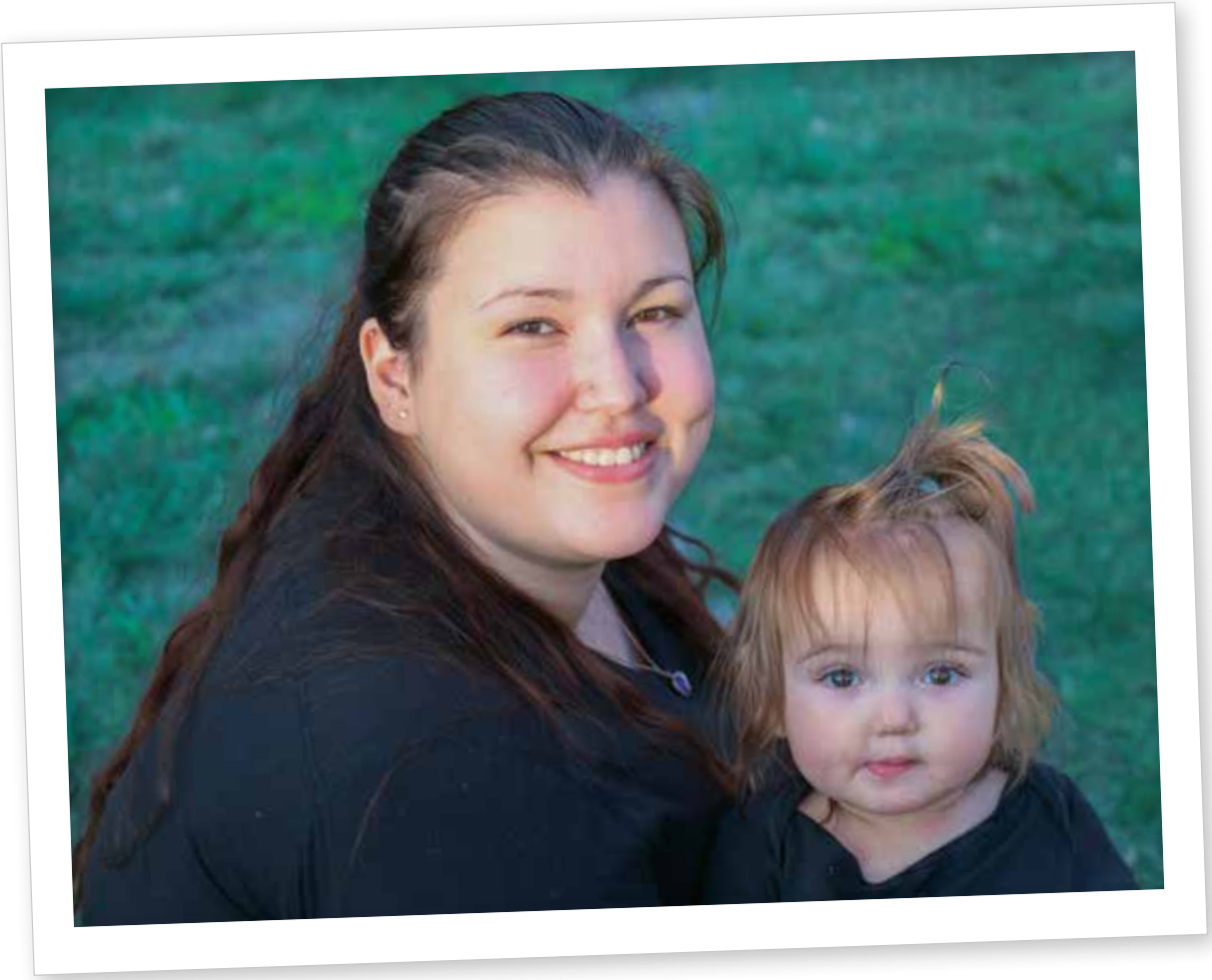
In addition to these strengths there are also some important limitations that should be considered when interpreting study results. The comparison group of non-Métis women included other Indigenous peoples in Alberta (First Nations and Inuit). This could result in a misclassification bias that would likely bias study estimates towards the null (no effect). Identification of Métis births was done using probabilistic data linkage, and it is possible some Métis births were misclassified and included in the non-Métis comparison group. The generalizability of study results is limited to MNA Citizens and should be applied with caution to those that self-identify as Métis but are not MNA Citizens.

Within the APHP database, pre-existing DM is not broken down by diabetes type (type 1 or type 2), and therefore, we were unable to determine the proportion of diabetes cases that are made up of type 1 and type 2 diabetes. Social and material deprivation are area level measures, and it is possible the assigned material and social deprivation quintiles assigned to each birth may not accurately reflect the maternal material and social deprivation. This misclassification would likely affect both cohorts, Métis and non-Métis equally.

5.0 CONCLUSION

The results of this study identify Métis women have an increased risk for having both pre-existing DM and GDM during pregnancy compared to non-Métis women after adjusting for important study covariates and birth clusters. Métis women with GDM complicated pregnancies also have an increased risk for having a baby born large for gestational age. The reason that Métis women have an elevated risk for diabetes in pregnancy is unclear, but it could be due to social inequalities stemming from the complex history Métis have had in Canada.

Further research is needed to understand the pathways colonialism and social inequalities take to increase the risk for developing pre-existing DM and GDM among Métis women.



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APPENDIX A: GLOSSARY

Antenatal:
Before birth.[56]

Congenital Anomalies:
Structural or functional anomalies (for example, metabolic disorders) that occur during intrauterine life and can be identified prenatally, at birth, or sometimes may only be detected later in infancy, such as hearing defects.[57]

Covariate:
A measurable variable that has a statistical relationship with the response variable.[58]

Gestation:
The amount of time a baby is in the uterus.[56]

Gestational Hypertension:
Hypertension that develops for the first time at ≥20+0 weeks gestation.[59]

Fasting Plasma Glucose Test:
A test used to check for diabetes that measures glucose in the blood after someone has not eaten for at least 8 hours.[60]

Hemoglobin A1C Test:
A blood test that measures the amount of glucose (sugar) that is bound to red blood cells. People with diabetes tend to have higher levels of hemoglobin A1c.[61]

Hemorrhage:
Extreme bleeding.[56]

Hyperglycemia:
High blood sugar, caused by too little insulin or the body's inability to use insulin properly.[62]

Hypertension:
High blood pressure.[63]

Ketoacidosis:
A dangerous and sometimes fatal condition that occurs when the body can't produce enough insulin.[64]

Material Deprivation:
Occurring when an individual or household is unable to purchase material goods and activities that are common in the society in which they live.[65] In this study, material deprivation was assessed based on average household income, unemployment rate, and high school education rate.

Misclassification Bias:
Occurring when an individual is assigned to a different category than the one they should be in.[66] In our study, this would occur when a Métis mother is included in the non-Métis group.

Multiparous Birth:
The birth of two or more children during a single delivery.[67]

Non-Fasting Oral Glucose Challenge Test:
A test used to diagnose diabetes, especially gestational diabetes. It is a series of blood sugar measurements taken after drinking a sweet liquid containing glucose.[60]

Perinatal:
The period prior to and after giving birth.[68]

Placenta Previa:
A condition in which a baby's placenta covers the mother's cervix, either partially or fully, potentially causing severe bleeding during pregnancy and birth.[69]

Preeclampsia:
A complication during pregnancy where the pregnant woman has high blood pressure and damage to her organs (most commonly the liver and kidneys).[59]

Preterm Birth:
A live birth that occurs before 37 weeks gestation.[70]

Proteinuria:
High levels of protein in the urine which can lead to kidney damage.[71]

Quintile:
One of five ordered subgroups of data.[72]

Rural:
Defined by Alberta Health Services as 3 distinct categories, based on a number of variables including demographics, urbanization processes, and land use. The 3 categories are: (1) large rural centers and surrounding areas (population greater than 10,000 but less than 25,000); (2) rural areas (population less than 10,000, population density between 100 – 10,000 per square km, within 200km from a regional center, and a mixed land use and industry primarily based on farming and ranching, and Indigenous lands), and; (3) rural remote (population density less than 100 per square km, greater than 200km distance from a regional center, and land use and industry predominately based on oil and gas and forestry, and a larger proportion of Indigenous communities).[73]

Singleton Birth:
A delivery where only one baby is born.[74]

Social Deprivation:
Deprivation relating to social relationships; can include family, personal, and professional relationships.[65] In this study, measured based on marital status (partnered, single, widowed or divorced), proportion of population living alone, proportion of single parent households.

Social Determinants of Health:
The social and economic factors that can influence an individual's health, including but not limited to income, education, employment, discrimination, and historical trauma.[75]

Type 1 Diabetes:
An autoimmune disease causing the destruction of insulin-producing beta cells in the pancreas.[76]

Type 2 Diabetes:
A condition in which the body either doesn't make enough insulin, or the cells of the body do not respond to insulin made by the body.[76]

Urban:
Defined by Alberta Health Services as 4 distinct categories, based on a number of variables including demographics and urbanization processes. The 4 categories are: (1) metro centres and capital cities (population greater than 100,000, population density greater than 30,000 per square kilometer, includes tertiary care centers where there is a minimal travel distance to a wide variety of services); (2) metro influenced areas (areas in close proximity to metro centers and are deemed commuter cities, such as the communities surrounding Edmonton and Calgary); (3) urban (with populations greater than 50,000 and less than 100,000, population density greater than 20,000 per square km and where there is minimal travel distance to a wide variety of services), and; (4) urban influenced areas (local geographic areas surrounding urban centers).[73]

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