ORIGINAL RESEARCH

Impact of diabetes on maternal-fetal outcomes in Manitoba: Relationship with ethnic and environmental factors

Naji Aljohani MD¹
Brenda M. Rempel MD¹
Sora Ludwig MD^{1,4}
Margaret Morris MD²
Mary Cheang BSc³
Robert Murray PhD³
Sharon Bruce PhD³
Garry X. Shen MD PhD¹

Department of Internal Medicine¹, Department of Obstetrics, Gynecology and Reproductive Sciences², Department of Community Health Sciences³, University of Manitoba, and Manitoba Health and Healthy Living⁴, Winnipeg, MB, Canada

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Abstract

Purpose: To examine the impact of gestational diabetes mellitus (GDM) on maternal-fetal outcomes in Manitoba.

Methods: The rates of macrosomia, stillbirth, cesarean section (C/S) and shoulder dystocia (S/D) in 324,605 births in Manitoba during 1985-2004, and their relationships with diabetes and demographical factors were analyzed.

Results: The incidence of macrosomia, stillbirth, C/S and S/D were 15.3%, 0.57%, 16.0%, and 1.2%, respectively. The rates of macrosomia were elevated in mothers with GDM, type 2 DM (T2DM), rural living, First Nations (FN) status, or ≥ 35 years of age. Increased rates of stillbirth were associated with women with T2DM, FN status or ≥ 35 years, but not those with GDM. C/S and S/D were increased in women with GDM or T2DM. FN status in combination with GDM increased the risk of S/D.

Conclusions: GDM, T2DM, advanced maternal age, FN status or rural living affected pregnancy outcomes in Manitoba.

Gestational diabetes mellitus (GDM) is the most common metabolic disease during pregnancy. GDM is associated with future obesity and type 2 diabetes

mellitus (T2DM) in mothers or offspring.¹⁻³ Previous studies demonstrated that the incidence of macrosomia, fetal mortality and cesarean section was increased in women with GDM compared to those without GDM.⁴⁻¹² Increased prevalence of GDM was detected among several ethnic groups, including North American Indians, Canadian First Nations (FN), Australian Aboriginals, South-East Asians, African Americans and Hispanic Americans.^{13,14} FN people are the largest minority in Manitoba and the majority live in rural areas of the province. The impact of ethnicity or environmental factors on pregnancy outcome in Manitoba remains unclear.

Our recent study demonstrated that the prevalence of GDM in Manitoba increased progressively during the time frame of 1985-2004. In addition, we identified several independent predictors for GDM in the province, including First Nations (FN) status, advanced maternal age and a history of GDM.¹⁵ The present study examined the impact of GDM, T2DM, FN status, maternal age and rural/urban living on

macrosomia, stillbirth, cesarean section and shoulder dystocia in Manitoba within the twenty-year period.

Methods

Source of data

Non-identifiable data of 324,605 births from 165,969 women in Manitoba between January, 1985 and December, 2004 were retrieved from a prenatal database collected by and stored at Manitoba Health and Healthy Living, the provincial health department. The database was generated from prenatal forms, which has been required by the province for every pregnancy to be prepared from prenatal care provider since 1985. The study was approved by the Health Information Privacy Committee of the Manitoba Health and Healthy Living and the Research Ethics Board of the University of Manitoba.

Screening for and diagnosis of DM

Screening and diagnosis of GDM were conducted according to the latest Canadian criteria for each time period. Specifically, no national guideline was available for the screening or diagnosis of GDM before 1992. In 1992, the Society of Obstetricians and Gynecologists of Canada recommended screening all pregnant women for GDM with a 50 g glucose challenge test (GCT) at the 24th week of pregnancy, and a 100 g oral glucose tolerance test (OGTT) to verify the results.¹⁶ The Canadian Diabetes Association (CDA) modified the guidelines for GDM in 1998, recommending screening for GDM in all pregnant women at 24th-28th week of pregnancy using GCT. The results were verified using a 75 g OGTT.¹⁷ No major modification was made in the 2003 CDA Clinical Practice Guidelines¹⁸ for the screening or diagnosis of GDM compared with the recommendations in 1998.¹⁷ The diagnosis of T2DM was made based on abnormal fasting plasma glucose or OGTT according to CDA guidelines.^{17, 18}

Pregnancy outcomes

Macrosomia was defined as a birth weight >4,000 g.¹⁹ Other variables included shoulder dystocia, stillbirth (an infant ≥ 500 g or ≥ 20 weeks of gestation showing no sign of life at delivery)²⁰, cesarean section, birth weight, maternal age (age at first prenatal visit), self-declared FN status, rural or urban living. The latter was determined according to postal codes following the criteria of Statistics Canada on the definition of urban and rural regions (<http://www.umanitoba.ca/centres/mchp/concept/dict/urban-rural.html>). Body weights or heights of pregnant women were not available in the database.

Statistical methods

Chi-squared testing was used to assess the differences in pregnancy outcomes in women with and without GDM or T2DM, and between subgroups (e.g. FN versus non-FN women). The Student *t*-test was applied to assess the differences of continuous variables with normal distributions (e.g. birth weights) between two groups. Bonferroni approach was used for multiple univariate tests. The normal significance level was taken as 0.01. All *P*-values were two-tailed. Interactions between potential contributing factors and outcomes, and the likelihood of risk were examined using multivariate logistic regression modeling. Adjusted odds ratios (OR) and the 95% confidence intervals (CI) were calculated as previously described.²¹ Statistical analyses were performed using SAS v 9.1 software (SAS Institute Inc., Cary, NC).

Results

During 1985-2004, GDM was detected in 2.9% of pregnancies (9,474/324,605 births) in Manitoba. Among the pregnant women, 12.3% had self-declared FN status and 40.5% were living in rural areas. Close to one tenth (9.6%) of pregnant women in the province were ≥ 35 years of age at their first prenatal visit. Among FN pregnant women, 4.6% were ≥ 35 years of

TABLE 1. Maternal ages of women in Manitoba (1985-2004)

Groups	Maternal ages				
	General	Non-FN	FN	Urban	Rural
Total (yr)	27.0 ± 5.6	27.5 ± 5.5	23.7 ± 5.5*	27.7 ± 5.5	26.2 ± 5.5 ⁺
< 35 yr (%)	90.4	89.7	95.4*	88.7	92.5 ⁺
≥ 35 yr (%)	9.6	10.3	4.6*	11.3	7.5 ⁺

FN: First Nations. Values of maternal age at first prenatal visit are presented in mean ± SD; total: n = 324,605; non-FN: n = 284,785; FN: n = 39,820; urban: n = 178,201; rural: n = 131,423). *: $P < 0.01$ versus non-FN; +: $P < 0.01$ versus urban.

age compared with 10.3% of non-FN pregnant women in that age group ($P < 0.01$). The proportion of pregnant women aged 35 years or older was greater in urban (11.5%) than in rural (7.5%, $P < 0.01$) areas in the province (Table 1).

Birth weights of newborns from mothers with FN status or living in rural areas were greater than non-FN or urban living pregnant women ($P < 0.01$). Women <35 years of age had newborns with greater birth weights than mothers ≥35 years of age ($P < 0.01$). Pregnant women living in rural areas in both <35 or ≥35 years of age groups had newborns with higher birth weights than did urban living women in corresponding age groups ($P < 0.01$). FN women <35 years of age, but not ≥35 years, delivered newborns with greater birth weights compared to non-FN women ($P < 0.01$) (Table 2).

Macrosomia was detected in 15.3% (n = 49,790) of newborns in Manitoba during the 20-years. The incidence of macrosomia was higher in pregnant women with GDM than in those without GDM in total (general) or all subgroups of pregnant women (FN, non-FN, rural, urban living, ≥35 and <35 years of age) ($P < 0.01$). The incidence of macrosomia was higher in women with FN status, living in rural areas or ≥35

years of age than in pregnant women who were non-FN, living in urban areas or <35 years ($P < 0.01$, Table 3).

Stillbirth occurred in 0.57% (n = 1,855) of all deliveries in the province during the 20-years. A higher incidence of stillbirth was detected in FN pregnant women than in non-FN women, and women who were ≥35 years of age versus younger pregnant women ($P < 0.01$). There was no difference in stillbirth between women with and without GDM during their index pregnancies in general or the subgroups (Table 3). The incidence of stillbirth was almost identical between GDM (0.58%) and non GDM (0.57%) women.

Shoulder dystocia occurred in 1.20% (n = 3,889) of deliveries during the studied period in Manitoba. Higher incidences of shoulder dystocia were detected in pregnant women with GDM than in those without GDM in total and all studied subgroups ($P < 0.01$). FN pregnant women had a lower incidence of shoulder dystocia than non-FN women ($P < 0.01$). No difference in shoulder dystocia was detected between pregnant women living in rural and urban areas, or ≥35 and <35 years of age (Table 3).

TABLE 2. Comparisons of birth weights of newborns from First Nations (FN), non-FN, rural or urban living women in age groups

Groups	Birth weight (g)				
	General	Non-FN	FN	Urban	Rural
General	3,437 ± 623	3,430 ± 616	3,496 ± 666*	3,404 ± 617	3,495 ± 620 ⁺
<35 yr	3,441 ± 617 ^x	3,432 ± 610 ^x	3,500 ± 660 ^{x*}	3,407 ± 609 ^x	3,494 ± 611 ^{x+}
≥35 yr	3,409 ± 676	3,407 ± 669	3,429 ± 747	3,381 ± 653	3,475 ± 677 ⁺

Mean ± SD, *: $P < 0.01$ versus non-FN; +: $P < 0.01$ versus urban; x: $P < 0.01$ versus ≥35 year of age.

Table 3. Impact of GDM and T2DM on maternal-fetal outcomes

Groups	Case (%)			
	Macrosomia	Stillbirth	S/D	C/S
General	49,790 (15.3)	1,855 (0.57)	3,889 (1.2)	51,863 (16.0)
GDM	2,524 (26.7)*	55 (0.58)	251 (2.7)*	2,448 (25.8)*
Non-GDM	47,266 (15.0)	1,800 (0.57)	3,638 (1.2)	48,415 (15.7)
FN	7,995 (20.1)+	353 (0.89) +	360 (0.90)+	5,011 (12.6)+
GDM	931 (33.7)*	20 (0.72)	71 (2.6)*	615 (22.3)*
Non-GDM	7,064 (19.1)	333 (0.9)	289 (0.78)	4,396 (11.9)
Non-FN	41,795 (14.7)	1,502 (0.53)	3,529 (1.2)	46,852 (16.5)
GDM	1,593 (23.8)*	35 (0.52)	180 (2.7)*	1,833 (27.3)*
Non-GDM	40,202 (14.5)	1,467 (0.53)	3,349 (1.2)	45,019 (16.2)
Rural	23,135 (17.6) ^x	765 (0.58)	1,510 (1.2)	20,203 (15.4) ^x
GDM	1,269 (31.0)*	23 (0.56)	97 (2.4)*	992 (24.2)*
Non-GDM	21,886 (17.2)	742 (0.58)	3,349 (1.2)	19,211 (15.1)
Urban	24,433 (13.7)	948 (0.53)	2,241 (1.3)	29,310 (16.5)
GDM	1,077 (22.4)*	22 (0.46)	138 (2.9)*	1,323 (27.5)*
Non-GDM	23,356 (13.5)	926 (0.53)	2,103 (1.2)	27,987 (16.1)
≥35 yr	4,897 (15.8)	257 (0.83)#	444 (1.4)	7,483 (24.1)#
GDM	405 (22.0)*	9 (0.49)	38 (2.1)*	608 (33.1)*
Non-GDM	4,492 (15.4)	248 (0.85)	406 (1.4)	6,875 (23.5)
<35 yr	44,893 (15.3)	1,598 (0.54)	3,445 (1.2)	44,380 (15.1)
GDM	2,119 (27.8)*	46 (0.60)	213 (2.8)*	1,840 (24.1)*
Non-GDM	42,774 (15.0)	1,552 (0.54)	3,232 (1.1)	42,540 (14.9)
T2DM	105(26.5)*	10(2.5)*	20(5.0)*	151(38.0)*
Non-T2DM	49,656(15.3)	1,844 (0.6)	3,857(1.2)	51,633 (15.9)*

GDM : Gestational diabetes mellitus; T2DM: type 2 diabetes mellitus; FN: First Nations; S/D: shoulder dystocia ; C/S: cesarean section.

*: $P < 0.01$ versus non-GDM or non-T2DM; +: $P < 0.01$ versus non-FN ; x: $P < 0.01$ versus urban; #: $P < 0.01$ versus <35 years of age.

A total of 51,863 (16.0% of all deliveries) of cesarean sections were performed during pregnancy in Manitoba between 1985 and 2004. Women with GDM had higher rates of cesarean section during deliveries than did women without GDM in general pregnant women or all subgroups ($P < 0.01$). Pregnant women with FN status, living in rural areas or <35 years of age received fewer cesarean sections than non-FN, urban living or ≥35 years of age pregnant women ($P < 0.01$, Table 3).

T2DM was diagnosed in 397 women before index pregnancies (0.12%). Significantly higher incidence of macrosomia, stillbirth, shoulder dystocia and increased requirement of cesarean section was detected

in pregnant women had a previous diagnosis of T2DM compared to those without T2DM ($P < 0.01$, Table 3).

Results of multivariate logistic regression analysis suggested that GDM was an independent predictor for macrosomia, cesarean section or shoulder dystocia ($P < 0.01$), but it did not increase the likelihood of stillbirth in Manitoba during the 20 years. FN women increased the likelihood of macrosomia or stillbirth, but had a lower risk for cesarean section or shoulder dystocia than non-FN women ($P < 0.01$). FN status in combination with GDM increased the risk of shoulder dystocia ($P < 0.01$). T2DM increased the risk of stillbirth, cesarean section or shoulder dystocia by 3-4-fold, and moderately, but significantly, increased the

TABLE 4. Multivariate logistical regression analysis results on adjusted odds ratios (OR), confidential intervals (CI) and interactions between factors on maternal-fetal outcomes

Factor	OR (95% CI)			
	Macrosomia	Stillbirth	C/S	S/D
GDM ^a	1.79(1.68-1.90)*	NS	1.88(1.80-1.98)*	2.16(1.84-2.53)*
FN	1.37(1.30-1.44)*	1.72(1.53-1.94)*	0.67(0.62-0.71)*	0.77(0.63-0.94)*
T2DM	1.68(1.33-2.13)*	3.46(1.84-6.51)*	3.60(2.90-4.46)*	4.73(2.89-7.72)*
≥35 yr	1.06(1.02-1.09)*	1.59 (1.39-1.82)*	1.70(1.65-1.75)*	1.15(1.03-1.27)*
Rural	1.30(1.27-1.32)*	NS	NS	NS
FN + GDM	1.19(1.08-1.32)*	-	-	1.64(1.21-2.23)*
FN + Rural	0.91(0.85-0.97)*	-	1.12(1.04-1.21)*	0.78(0.62-0.99)*
FN + ≥35 yr	-	-	-	0.58(0.33-0.99)*

C/S: cesarean section; S/D: shoulder dystocia; GDM: gestational diabetes mellitus; FN: First Nations; T2DM: type 2 diabetes mellitus; NS: not significant; -: no interaction.

Values expressed in the Table are OR (95% CI). ^a: GDM = 1, non-GDM = 0, same as following factors.

*: $P < 0.01$.

risk of macrosomia ($P < 0.01$). Advanced maternal age (≥ 35 years) increased the risk of macrosomia, stillbirth, cesarean section or shoulder dystocia ($P < 0.01$). Rural living increased the likelihood of macrosomia ($P < 0.01$), and but had no impact on stillbirth, cesarean section or shoulder dystocia (Table 4).

Discussion

The major novel findings generated from the present retrospective cohort database study are: 1) FN status and rural living were independent predictors for macrosomia in Manitoba; 2) GDM had a similar impact on macrosomia as T2DM; 3) FN women with GDM had an increased risk for shoulder dystocia; 4) non-FN pregnant women had higher incidence of shoulder dystocia than FN women; and 5) Rural living women and younger FN women (< 35 yr) had babies with greater birth weights compared to urban living women or FN women with advanced maternal ages.

Macrosomia potentially contributes to childhood obesity and adolescent T2DM. Correlations between macrosomia and maternal GDM or T2DM were detected in the present and previous studies.^{4,11,12,14} Results of multivariate regression analysis indicated that

GDM (OR 1.79, CI 1.68-1.90) had similar risk for macrosomia to T2DM (OR 1.68, 1.33-2.13). The results of the present study indicate that FN status, rural living, and advanced maternal age increased the likelihood of macrosomia. It is possible that pregnant women with FN status or living in rural areas have less access to resources for recreational activities or healthy foods compared to non-FN or urban living women. Interestingly, FN women analyzed in combination with rural living had a reduced risk of macrosomia, which implies that FN women living in urban areas had a higher likelihood of macrosomic babies than FN women living in rural areas. Women with advanced maternal ages had lower average birth weights than younger women, and had a moderate, but significantly, higher incidence of macrosomia than women younger than 35 yr. This phenomenon may be partially explained by findings described in one of our recent reports that pregnant women ≥ 35 yr had higher prevalence of GDM than those < 35 yr in the province (5.9% versus 2.6%)¹⁵ and the relationship between GDM and macrosomia in the present study. The results of the present study demonstrated that the risk of macrosomia was associated with GDM, FN status,

rural living and advanced maternal ages in Manitoba during the last 20 years.

Previous studies demonstrated that increased incidence of stillbirth has been described in mothers with alcohol-related binge drinking²², sexually-transmitted diseases²³, GDM^{6, 24} or T2DM.¹⁴ Elevated rates of stillbirth were detected in North American Indians, but not among the Inuits, in the province of Quebec.¹² The results of the present study demonstrated that FN pregnant women had a 68% higher rate of stillbirth than non-FN pregnant women in Manitoba. Alcohol consumption²² and genetic disease²⁵ are potential contributors to stillbirth among FN women in Manitoba. The present large-scale retrospective study did not detect connection between GDM and stillbirth in Manitoba using Chi-square or multivariable logistical regression analysis. Mothers with T2DM had increased rates of stillbirth in the present study, which supports findings from previous reports.³

Shoulder dystocia is one of the threatened obstetric emergencies, which potentially leads to serious maternal-fetal consequences. Increased shoulder dystocia was described previously in mothers with diabetes or large babies.²⁴ Surgical procedures including cesarean section are often required for deliveries of newborns with high risk of shoulder dystocia. The results of the present study demonstrated that GDM, T2DM and advanced maternal ages increased the likelihood of shoulder dystocia. Interestingly, FN women had a reduced likelihood of shoulder dystocia in spite that they had higher rates of macrosomia and GDM.¹⁵ Besides, FN pregnant women in the province received a lower rate of cesarean section than non-FN pregnant women (12.6% versus 16.5%, $P < 0.01$), which may be partially due to less access to required medical services. The reduced rate of shoulder dystocia in FN women is likely independent from the less access of medical service. The results of the present study in FN women demonstrated that non-FN pregnant women were 2.2-times more likely to be of advanced maternal

ages than FN pregnant women. A previous study suggested that advanced maternal age contributed to shoulder dystocia.²⁶ Younger maternal age in FN pregnant women potentially contributes to the low incidence of shoulder dystocia in FN women in the present study. Possible influence of ethnic variations, such as pelvic structure or body composition, has not been excluded.

The results of multivariate logistic regression analysis indicated that FN, in combination with GDM, increased the likelihood of shoulder dystocia. FN in combination with rural living increased the requirement of cesarean section and reduced the odds of macrosomia or shoulder dystocia, which implies that FN women living in urban areas may be at a higher risk for macrosomic babies and shoulder dystocia or receiving less cesarean section than FN women living in rural areas.

In conclusion, GDM, T2DM, FN ethnicity, rural living and advanced maternal age are contributing factors for macrosomia, shoulder dystocia or cesarean section in Manitoba. T2DM, FN status and advanced maternal age, but not GDM, increased the likelihood of stillbirth. Higher rates of macrosomia and stillbirth in FN women may result partially from less access to proper obstetric care, particularly in rural aboriginal communities. Improvement of prenatal care for FN women may help to reduce maternal-fetal complications, obesity and T2DM in mothers and their children. It should be pointed out that the interpretation of data in the present study is limited by the lack of information on weight and height of pregnant women in the database. Maternal obesity is a known confounding factor for pregnancy outcomes.

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Correspondence to:

Garry X. Shen MD PhD
Diabetes Research Group
University of Manitoba
835-715 McDermot Ave
Winnipeg, Canada MB R3E 3P4
Tel: 204-789-3816
Fax: 204-789-3987
Email: gshen@ms.umanitoba.ca