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Original Research

# Prenatal, Obstetric and Perinatal Factors Associated with the Development of Childhood-Onset Type 2 Diabetes

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#### ABSTRACT

*Objective*: To explore associations among prenatal, obstetric and perinatal factors and the development of childhood-onset type 2 diabetes.

Methods: This retrospective, case-control study utilized administrative data housed at the Manitoba Centre for Health Policy. De-identified health records were examined from a sample of 270 children (aged 10 to 17 years at time of diagnosis) with type 2 diabetes and 1341 children without type 2 diabetes matched for age, sex and geographic location. Patients and control subjects were linked to their de-identified biological mothers' health records. Prenatal, obstetric and perinatal factors were investigated. Univariate and multivariable conditional regression analyses were conducted to identify key factors associated with the development of type 2 diabetes in children.

Results: The mean age at diagnosis was 13.1 years, and 61% of patients were girls. The majority (71.1%) of children with type 2 diabetes resided in rural areas. Exposure to maternal pregestational diabetes increased the odds of childhood-onset type 2 diabetes nearly 6-fold, and exposure to gestational diabetes carried a 4-fold increased risk. Breastfeeding was found to be protective, decreasing the risk of childhood-onset type 2 diabetes (odds ratio = 0.52, 95% confidence interval = 0.36-0.74). Low maternal income was significantly associated with development of childhood-onset type 2 diabetes (odds ratio = 0.67,

*Conclusions:* Health and social policies and programs are needed to provide financial, educational and clinical resources that target women whose pregnancies are affected by poverty, type 2 diabetes or gestational diabetes. Breastfeeding should be encouraged to aid in the prevention of childhood-onset type 2 diabetes.

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#### RÉSUMÉ

Objectif: Examiner les associations entre les facteurs prénatals, obstétricaux et périnatals et le développement du diabète de type 2 chez l'enfant.

Méthodes: Pour la présente étude cas-témoins, nous avons utilisé les données administratives du Centre manitobain des politiques en matière de santé. Nous avons examiné les dossiers médicaux dépersonnalisés d'un échantillon de 270 enfants (âgés de 10 à 17 au moment du diagnostic) atteints du diabète de type 2 et de 1341 enfants non atteints du diabète de type 2 appariés selon l'âge, le sexe et la zone géographique. Les patients et les sujets témoins ont chacun été reliés au dossier médical dépersonnalisé de leur mère biologique. Les facteurs prénatals, obstétricaux et périnatals ont été examinés. Des analyses univariées et multivariées par régression conditionnelle ont été réalisées pour déterminer les principaux facteurs associés au développement du diabète de type 2 chez les enfants.

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Résultats: L'âge moyen au moment du diagnostic était de 13,1 ans ; 61 % des patients étaient des filles. La majorité (71,1 %) des enfants atteints du diabète de type 2 habitaient en milieu rural. L'exposition au diabète prégestationnel augmentait la probabilité du diabète de type 2 chez l'enfant de presque 6 fois, et l'exposition au diabète gestationnel entraînait une augmentation du risque de 4 fois. Nous avons observé que l'allaitement protégeait puisqu'il faisait diminuer le risque du diabète de type 2 chez l'enfant (ratio d'incidence approché=0,52, intervalle de confiance à 95 %=0,36-0,74). Un faible revenu faible chez la mère était significativement associé au développement du diabète de type 2 chez les enfants (ratio d'incidence approché=6,67, intervalle de confiance à 95 %=3,01-14,79).

Conclusions: Des politiques et des programmes sociaux et de santé sont nécessaires pour offrir des ressources financières, éducatives et cliniques qui s'adressent aux femmes enceintes qui sont exposées à la pauvreté, au diabète de type 2 et au diabète gestationnel. Il faudrait encourager l'allaitement pour contribuer à la prévention du diabète de type 2 chez l'enfant.

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#### **Key Messages**

Type 2 diabetes is an emerging disorder in children, and the incidence is rising rapidly. In this study, we utilized retrospective data to further our understanding of the developmental origins of childhood-onset type 2 diabetes. Associations among prenatal, obstetric and perinatal risk factors for childhood-onset type 2 diabetes were found.

#### Introduction

Childhood-onset type 2 diabetes is an emerging disorder in children and adolescents, but until 1990, it was seldom reported (1, 2). Prevalence rates vary greatly around the world, with United States estimates as high as 5000 new cases per year (3). In Canada, a minimum incidence of 1.54 per 100,000 children <18 years of age has been reported (4). In several parts of the world, including Canada, the incidence of type 2 diabetes now exceeds that of type 1 diabetes in children (5, 6). In Manitoba, the annual incidence of childhood-onset type 2 diabetes is 20-fold higher than that in other areas of Canada and has increased dramatically from 9.03 to 20.55 per 100,000 children <18 years of age each year from 2006 to 2011 (5).

The increasing rate of childhood-onset type 2 diabetes is a major health concern. The impact of this disease on youth of ethnic and racial minorities and in disenfranchised groups is disproportionately greater than that on youth without a similar background (1). Evidence suggests that complications occur earlier and more aggressively than in either type 1 diabetes or adult-onset type 2 diabetes, and end-stage complications have been reported in the third and fourth decades of life for those diagnosed with childhood-onset type 2 diabetes (7). In addition, the early age at onset contributes to an increasing number of young women with type 2 diabetes (2) and an increasing number of pregnancies complicated by pregestational diabetes.

Exposure to maternal gestational diabetes or pregestational type 2 diabetes has been shown to increase the risk of childhood-onset type 2 diabetes in offspring, as well as the risk of adult-onset type 2 diabetes and gestational diabetes in those offspring (8–12). Exposure to pregestational type 2 diabetes in utero appears to present a particular risk. In a cohort study of offspring of women with pregestational type 2 diabetes, 43% of those between 12 and 19 years of age had already developed type 2 diabetes (13). Although the association between diabetes during pregnancy and type 2 diabetes in offspring is consistent across studies, the relative importance of gestational and pregestational diabetes has not previously been explored in a single study.

Therefore, the objective of this study was to explore the relative associations between gestational and pregestational diabetes exposure in utero and the risk for type 2 diabetes in offspring within the context of important prenatal, obstetric and perinatal

confounders. The use of retrospective data in this study serves to further our understanding of the developmental origins of childhood-onset type 2 diabetes. Associations with the development of childhood-onset type 2 diabetes that were found in previous studies—such as breastfeeding, diabetes exposure in pregnancy, socioeconomic status (SES), geographic location and birth weight—will be further evaluated in this large cohort of youth with type 2 diabetes.

#### Methods

This retrospective case-control study used data from the Population Health Research Data Repository (henceforth called "The Repository") at the Manitoba Centre for Health Policy. A cohort of children with type 2 diabetes was identified from the pediatric diabetes database of the Diabetes Education Resource for Children and Adolescents (DER-CA) and included all children diagnosed with type 2 diabetes from 1986 to 2011. Inclusion criteria were as follows: 1) diagnosis of type 2 diabetes between the ages of 10 and 17 years, 2) valid Manitoba personal health information number (PHIN) and 3) an accessible Manitoba hospital birth record. A control group was created, and subjects were matched for age, sex and area of residence. A case-to-control ratio of 1:5 was utilized to maximize power. The index date for age matching was the age at the time of diagnosis of type 2 diabetes. Geographic matching was achieved using the first 3 digits of the 6-digit Manitoba postal code. Geographic residence, marked by postal code, was chosen as a marker for SES, which has been previously described as similar income levels in like postal codes (14). All youth in this study were then linked to their biological mothers' health records by using their PHIN within the Manitoba Health Registry. Approvals were obtained from the Education and Nursing Research Ethics Board, Faculty of Nursing, University of Manitoba, and the Manitoba Health Information Privacy Committee.

#### Data sources

Data were collected from 4 linked databases, all of which are housed at The Repository. This population health research data repository is a comprehensive collection of population-based administrative, registry, survey, social and other data relating to residents of Manitoba. The databases accessed were 1) Manitoba Health Insurance Plan, 2) Social Administrative Database—Healthy Child Manitoba, 3) the Drug Program Information Network and 4) the DER-CA database.

The Manitoba Health Services Insurance Plan contains physician reimbursement claims, hospital discharge abstracts, registration files and records of all dispensed prescriptions. Files can be linked at the person level by utilizing the PHIN. Records are linkable across administrative health databases and create a longitudinal record for each patient.

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