THE NEXT GENERATION STUDY: AN UPDATE ON THE BIOLOGICAL RISK FACTORS FOR TYPE 2 DIABETES IN INDIGENOUS CHILDREN IN MANITOBA

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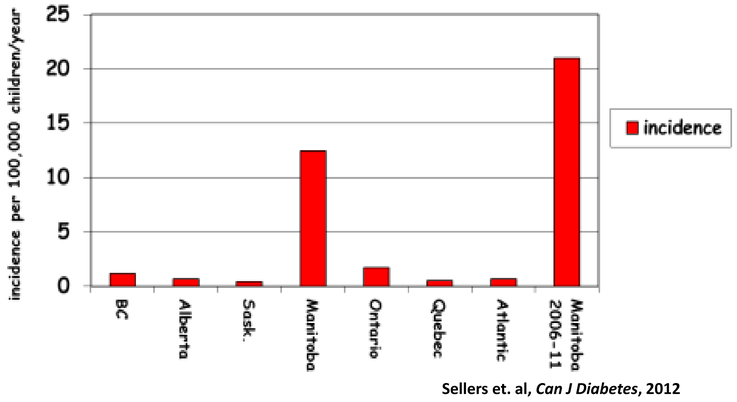
Background

- Childhood onset type 2 diabetes (T2D) is increasing at alarming rates.
- The first recognized case was in Manitoba in 1985.
- Incidence rates in Manitoba is 12-20x higher than any other province in Canada [1].
- A private polymorphism (HNF1α G319S) was found in the Oji-Cree is associated with childhood onset T2D[2] which decreases their insulin secretion.[3]
- Exposure to diabetes in utero is identified as a significant risk factor for childhood onset T2D.



Sellers et. al, *Can J Diabetes*, 2012

Objectives

This study aims to:

1. Discover modifiable risk factors within the natural history to plan for an early life intervention.
2. Prevent, delay, and intervene in at-risk children.

Methods

POPULATION:

- Indigenous children in Manitoba born to a parent with childhood onset T2D

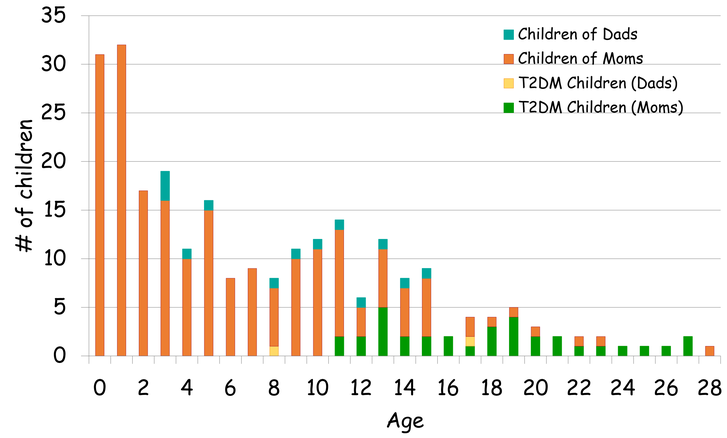
DESIGN:

- Annual environmental exposure questionnaires (i.e., smoking, SES, family history of T2D, food frequency)
- Annual clinical and laboratory assessments
- Breastfeeding questionnaire for moms with children <3y

Age	Annual Assessment
3rd Trimester (maternal sample)	• HbA1C • Inflammatory markers • Epigenetic markers • Urine ACR • HNF1α phenotype (once)
Birth	• Cord blood for inflammatory and epigenetic markers • Gestational age • Weight, length • Presence of congenital anomalies • HNF1α phenotype (once)
1-6 yrs	• Urine for ACR • Height, weight • Presence of acanthosis nigricans
7-18 yrs	• Urine for ACR • Height, weight, waist circumference • Presence of acanthosis nigricans • Serum for HbA1c, glucose, liver enzymes, inflammatory and epigenetic markers • OGTT (q2yrs) • HNF1α phenotype (if not done before)

Results

- The Next Gen cohort now consists of 133 parents (126 mothers, 7 fathers) and 254 children (131 female, 123 male).
- 1st trimester miscarriage, stillbirth and neonatal death rates in the cohort were 27.7%, 11.6%, and 3.6% respectively.
- 55% of newborns were large for gestational age.
- 20% had major congenital anomalies.
- 11.3% of the cohort's children aged 7-9 years were overweight and 80.7% are obese, while 29% and 40% are overweight and obese, respectively, in the age group 14-17 years.
- 38 children (15%) in our cohort was diagnosed with T2D. Of these children, the HNF1α G319S status was S/S (n=8, 21%), S/G (n=22, 58%), and G/G (n=6, 16%).
- 44% of the cohort are >12y, and 21% of them have been diagnosed with T2D.



Child's diagnosis	Born to T2D mom	Born to T2D dad
T2D*	36 (95%)***	2 (5%)
IGT**	6 (86%)	1 (14%)

*T2D median age: 11.04 years
**IGT= Impaired Glucose Tolerance, a form of pre-diabetes
***4 excluded in median age of T2D (no date of Dx)

Conclusions

- Intergenerational in utero exposure to T2D is associated with pregnancy complications, anomalies, increased birth weight, and increased risks of childhood onset T2D.
- The rates of childhood-onset T2D in our birth cohort is much higher than national rates (1.54/100,000 children/year). [1]
- The children who developed T2D earlier in life had a higher chance of carrying an HNF1α G319S allele, suggesting that a combination of genetics and in-utero exposure to T2D is involved in the development of childhood T2D.

Acknowledgements

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References

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