The Next Generation Birth Cohort: Screening for Dysglycemia and Albuminuria in High Risk Children

Yash Rawal[1], Elizabeth A. C. Sellers[1,2], Allison Dart[1,2], Christy Pylypjuk[1,2], and Brandy A. Wicklow[1,2]
[1]Children's Hospital Research Institute of Manitoba, University of Manitoba; [2]Pediatrics and Child Health, University of Manitoba

Background

- Childhood onset type 2 diabetes (T2D) is increasing worldwide[1].
  - At risk for early onset kidney disease[2]
  - Albuminuria is a marker of early kidney disease[3]
- Which children are at the highest risk?
  - Children of First Nation Heritage[4]
  - Children exposed to pregestational diabetes in utero[5]
- Despite epidemiological and prospective cohort evidence characterizing children at onset of type 2 diabetes, little is understood about the early pre-clinical course of childhood onset type 2 diabetes.

Research question

In First Nations children exposed to T2D in utero, is there evidence of early kidney and Beta cell dysfunction prior to the diagnosis of T2D?

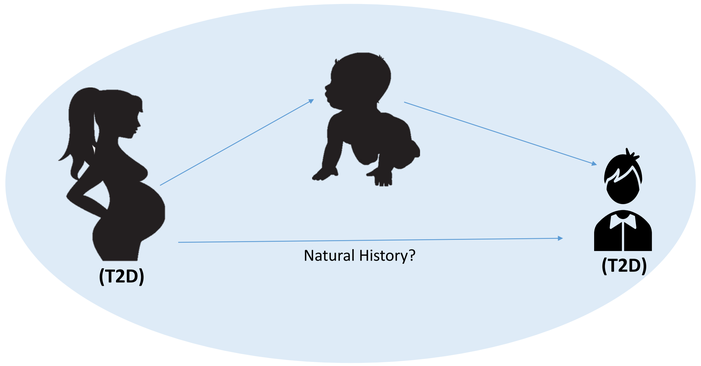

Figure 1. *Natural History of Type 2 Diabetes (T2D)?*

Methods

POPULATION:

- First Nation children living in Manitoba exposed to type 2 diabetes in utero
- Recruited into the Next Generation longitudinal birth cohort prenatally[6]

DESIGN:

- A cross sectional sub-analysis of data from the Next Generation Cohort - a prospective cohort of First Nation children exposed to T2D in utero.

- All participates have an annual urine albumin to creatinine ratio starting at age 1 year.
- Starting at age 7 years, participants undergo an annual OGGT.
- We reviewed the results of these tests in the 2 to 3-year period prior to diagnosis for children who have developed T2D and in an age matched group of children from the Next Generation Cohort who have not developed diabetes.
- Descriptive analysis included proportions, means and medians.

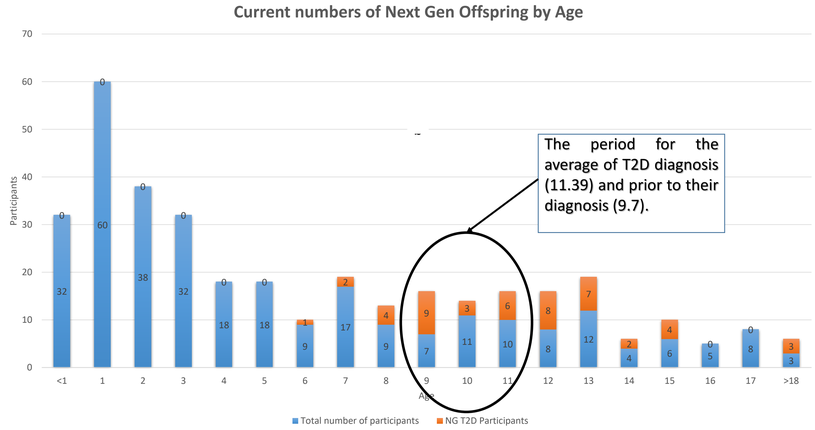

Figure 2. Next Generation Birth Cohort – Total number of children enrolled in the study and the proportion of children that have T2D.

Results

		Prior T2D (n = 46)	No diabetes (n = 72)
Sex		17 (37%) male	41 (57%) male
Average Age		9.74 (2.34)	9.28 (2.23)
Albuminuria (mg/mmol)		1 (2%)	2 (3%)
A1C ≥ 6(%)		6 (13%)	0 (0%)
Blood Glucose (75g OGTT) (mmol/L)	IFG	4 (9%)	2 (3%)
	IGT	6 (13%)	9 (13%)

Table 1. Characteristics of children who developed T2D prior to developing diabetes compared to age matched children who have not developed diabetes

Child's diagnosis		T2D (n = 46)	No diabetes (n = 72)
Sex		17 (37%) male	41 (57%) male
Average Age		11.39 (2.22)	11.01 (2.93)
Albuminuria (mg/mmol)		10 (22%)	6 (8%)
A1C ≥ 6(%)		4 (100%)	4 (6%)
Blood Glucose (75g OGTT) (mmol/L)	IFG	N/A	3 (4%)
	IGT	N/A	11 (15%)

Table 2. Characteristics of children at diagnosis of T2D and age matched children who have not developed diabetes

Discussion and Conclusions

- Children are diagnosed with T2D without a significant period of preceding dysglycemia and albuminuria (less than 2 years).
- Children develop albuminuria co-incident with T2D onset.
- Children without T2D showed some evidence of albuminuria and dysglycemia which increased over time.
- This study suggests rapid and early onset of dysglycemia and renal dysfunction in offspring exposed to T2D in utero which may inform screening practices and prevention strategies.

Acknowledgements

Thank you to all our participants, Northern medical staff and collaborators!

References

1 – D'Adamo & Caprio. Diabetes Care. 2011, 34(SUPPL. 2).

2 – Dart, et al. Diabetes Care. 2012, 35(6), 1265–1271.

3 – Lorenzo, Saracho, Zamora, Rufino, & Torres. NEPHROL DIAL TRANSPL. 2010, 25(3), 835–841.

4 – Amed et al. Diabetes Care. 2010, 33(4), 786–91.

5 – Wicklow et al. JAMA Pediatr 2018; 172: 724-731.

6 – Jabar, Colatruglio, Sellers, Kroeker, & Wicklow. Dev. Orig. Health Dis. 2019, 10, 24–30.