

An Advancing Avalanche—The Emergence of Complications in Indigenous Youth with Type 2 Diabetes

Elizabeth AC Sellers

*Department of Pediatrics and Child Health, Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada;
Children's Hospital Research Institute of Manitoba, Winnipeg, Manitoba, Canada*

Abstract

Youth-onset type 2 diabetes (diagnosed <18 years of age) is increasing around the world. Indigenous populations are disproportionately affected. The classic microvascular complications of diabetes are now emerging in this population and early data suggest that complications may occur early and more aggressively in youth-onset versus adult-onset disease. Of concern are the transgenerational effects of youth-onset diabetes, with increasing rates of pregestational exposure to diabetes, a potent risk factor for the development of youth-onset type 2 diabetes.

Keywords

Type 2 diabetes, youth, adolescent, Indigenous, complications

Disclosure: Elizabeth AC Sellers has nothing to disclose in relation to this article. This article is a short opinion piece and has not been submitted to external peer reviewers. No funding was received in the publication of this article.

Open Access: This article is published under the Creative Commons Attribution Noncommercial License, which permits any noncommercial use, distribution, adaptation, and reproduction provided the original author(s) and source are given appropriate credit.

Received: March 21, 2016 **Published Online:** April 15, 2016 **Citation:** *US Endocrinology* 2016;12(1):16–7 DOI: <http://doi.org/10.17925/USE.2016.12.01.16>

Correspondence: Elizabeth AC Sellers, University of Manitoba, FE-307 685 William Avenue, Winnipeg, MB, Canada, R3E 0Z2. E: esellers@exchange.hsc.mb.ca

An avalanche is “a sudden arrival or occurrence of something in overwhelming quantities”.¹ Is this an accurate description of the emerging complications seen in those with youth-onset type 2 diabetes? Type 2 diabetes of youth onset (diagnosed <18 years of age) is increasing around the world.² However, incident rates vary markedly between populations with Indigenous populations bearing a particularly high burden. In Canada, Indigenous youth represent approximately 45% of youth-onset type 2 diabetes, despite comprising less than 10% of the Canadian childhood population.³ Similarly, Native American youth have an incidence rate three to four times higher than non-Hispanic white youth in the US.⁴ The youngest reported case of type 2 diabetes is in an Indigenous child from the Torres Strait, who was diagnosed at the age of five.⁵

Early data suggest that complications may occur early and more aggressively in youth-onset versus adult-onset disease.⁶ Data on both the acute and chronic complications of type 2 diabetes of youth-onset are just now emerging and, given the increased burden in Indigenous children, much of the data available are for the Indigenous population. The morbidity of these children is high, and the majority of youth with type 2 diabetes have, at a minimum, two major health concerns—diabetes and obesity. Many have additional comorbidities such as dyslipidemia, hypertension, and fatty liver disease.³

The classic long-term microvascular complications of diabetes have now been described in young adults with youth-onset type 2 diabetes. Renal health is a particular concern in Indigenous youth as this population is

also at increased risk for primary non-diabetic renal disease.^{7–9} Thus, Indigenous youth with type 2 diabetes may have both diabetes and an underlying primary renal disease, placing them at significant risk for poor renal outcomes. Micro- and macroalbuminuria are frequently present at diagnosis of youth-onset type 2 diabetes. For example, albuminuria was present at diagnosis in 22% of Pima Indian youth, 29% of Canadian First Nation (FN) youth and in 14% of New Zealand Maori youth.^{7,10,11} Progression also appears to be rapid, with albuminuria described in 58% of Pima youth and 62% of Maori youth within 10 years of diagnosis.^{10,11} In a recent Canadian study, persistent, non-orthostatic albuminuria was present in 9.8% of FN children compared with 1.8% of non-FN children with type 2 diabetes.¹² FN children from Manitoba with type 2 diabetes had a four-fold increased risk of renal failure compared with youth with type 1 diabetes controlled for age at diagnosis, glycated hemoglobin (HbA1c), era of diagnosis, and body mass index z-score, and a 23-fold increased risk of renal failure compared to age-, sex, and geographically matched control children without diabetes.¹³

Other microvascular complications are also reported at high rates among those with youth-onset type 2 diabetes. Increased rates of neurological complications in those with type 2, compared with type 1 diabetes begin to appear by five years post-diagnosis and ophthalmologic complications begin to differ 10 years post-diagnosis. Major complications (defined as amputation, blindness, or dialysis) remained rare in youth-onset type 1 diabetes 20 years post-diagnosis, but occurred in 26% of youth-onset type 2 diabetes 10 years post-diagnosis and in almost 50% 20 years post-diagnosis.¹⁴

Shockingly, mortality data are now available. In Manitoba, the mortality rate of youth-onset type 2 diabetes 20 years post-diagnosis has been shown to be 22.5%, comparing unfavorably with youth-onset type 1 diabetes of 2.4%.¹⁴ In Australia, the mortality rate in youth-onset type 2 diabetes was double that of youth-onset type 1 diabetes with a median follow up of 20 years.¹⁵ In these reports, youth with type 2 diabetes were predominantly indigenous youth.

Of equal or, perhaps even greater concern, is a 'new' complication of youth-onset type 2 diabetes that is now emerging—the transgenerational effects of intrauterine exposure to type 2 diabetes. With the increasing incidence of youth-onset type 2 diabetes, more youth will be diagnosed prior to their childbearing years and thus their offspring will be exposed to pregestational type 2 diabetes. In The Pima population, siblings born following a pregnancy complicated by diabetes have been shown to be at higher risk for the development of type 2 diabetes and at a younger age than their siblings who were not exposed to diabetes in utero.¹⁶ In Canadian FN children, offspring exposed to pregestational type 2 diabetes had a 14-fold increased risk for the development of youth-onset type 2 diabetes compared with offspring who were not exposed to diabetes in utero.¹⁷ The Next Generation or NextGen Cohort is a research cohort composed of the offspring of young FN women in Manitoba who had youth-onset type 2 diabetes diagnosed prior to their pregnancies. By definition, all offspring

were exposed to pregestational type 2 diabetes. This cohort appears to be at very high risk for youth-onset type 2 diabetes, perpetuating the vicious cycle of exposure. To date, approximately 50% of the NextGen cohort >12 years of age have developed type 2 diabetes (personal communication, Brandy Wicklow, Winnipeg, 2016). In addition, exposure to pregestational diabetes is associated with an increased risk of congenital renal anomalies.¹⁸

Little is known about the psychosocial health of youth with type 2 diabetes, though early reports suggest this is a concern.^{19,20} These issues may have significant effects on adherence to management regimes and ability to provide self-care. We must understand these issues in order to best support youth and their families living with type 2 diabetes.

Youth-onset type 2 diabetes is associated with very significant morbidity and mortality in young adulthood and Indigenous youth are disproportionately affected. Indeed, we are now seeing an 'avalanche' of complications in youth-onset type 2 diabetes. 'Avalanche prevention' will require an increased understanding of the disease and the complex bio-psycho-social interactions that limit access to healthcare, healthy diets, and physical activity opportunities and influence ability to self-manage. Diabetes and complication prevention will also likely involve intervention at many stages, including in the pre-conception period. The avalanche is gathering speed—the time for action is now. ■

- Collins English Dictionary. Available at: www.collinsdictionary.com/dictionary/english/avalanche (accessed March 18, 2016).
- Pulgaron E, Delamater AM, Obesity and type 2 diabetes in children: epidemiology and treatment, *Curr Diab Rep*, 2014;14:508.
- Amed S, Dean HJ, Panagiotopoulos C, et al., Type 2 Diabetes, Medication-Induced Diabetes and Monogenic Diabetes in Canadian Children: A Prospective National Surveillance Study, *Diabetes Care*, 2010;33:786–91.
- Dabelea D, DeGroat J, Sorrellman C, et al., Diabetes in Navajo youth, *Diabetes Care*, 2009;32(Suppl 2):S141–S147.
- Kevat D, Wilson D, Sinha A, A 5-year old girl with type 2 diabetes, *Lancet*, 2014;383:1268.
- Pinhas-Hamiel O, Zeitler P, Acute and chronic complications of type 2 diabetes mellitus in children and adolescents, *Lancet*, 2007;369:1823–31.
- Sellers EAC, Blydt-Hansen, Dean HJ, et al., Macroalbuminuria and renal pathology in First Nation youth with type 2 diabetes, *Diabetes Care*, 2009; 32:786–90.
- Bulloch B, Postl BD, Ogborn MR, Excess prevalence of non diabetic renal disease in native American children in Manitoba, *Pediatr Nephrol*, 1996;10:702–4.
- White A, Wong W, Sureshkumar P, Singh G, The burden of kidney disease in Indigenous children of Australia and New Zealand, epidemiology, antecedent factors and progression to chronic kidney disease. *J Paediatr Child Health*, 2010;46:504–9.
- Fagot-Campagna A, Knowler WC, Pettitt DJ, Type 2 diabetes in Pima Indian children: cardiovascular risk factors at diagnosis and 10 years later, *Diabetes*, 1998;47(Suppl 1):A155.
- McGrath NM, Parker GN, Dawson P, Early presentation of type 2 diabetes mellitus in young New Zealand Maori, *Diabetes Res Clin Pract*, 1999;43:205–9.
- Sellers EAC, Hadjiyannakis S, Amed S, et al., Persistent Albuminuria in Children with Type 2 Diabetes: A Canadian Paediatric Surveillance Program Study, *J Pediatr*, 2016;168:112–7.
- Dart AB, Sellers EAC, Martens PJ, et al., High Burden of Kidney Disease in Youth-Onset Type 2 Diabetes, *Diabetes Care*, 2012;35:1265–71.
- Dart A, Martens P, Rigatto C, et al., Earlier onset of complications in youth with type 2 diabetes, *Diabetes Care*, 2014;37:436–43.
- Wong J, Constantino M, Yue DK, Morbidity and mortality in young-onset type 2 diabetes in comparison to type 1 diabetes: where are we now?, *Curr Diab Rep*, 2015;15:566.
- Dabelea D, Hanson RL, Lindsay RS, et al., Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships, *Diabetes*, 2000;49:2208–11.
- Young TK, Martens PJ, Taback SP, et al., Type 2 diabetes mellitus in children: prenatal and early infancy risk factors among native Canadians, *Arch Pediatr Adolesc Med*, 2002;156:651–5.
- Dart A, Ruth C, Sellers EAC, Dean H, Pre-gestational and Gestation Diabetes are Associated with Congenital Anomalies of the Kidney and Urinary Tract, *Am J Kidney Dis*, 2015;65:684–91.
- Hood KK, Beavers DP, Yi-Frazier J, et al., Psychosocial burden and glycemic control during the first 6 years of diabetes: results from the SEARCH for Diabetes in Youth Study, *J Adolesc Health*, 2014;55:498–504.
- Levitt Katz LE, Swami S, Abraham M, et al., Neuropsychiatric disorders at the presentation of type 2 diabetes mellitus in children, *Pediatric Diabetes*, 2005;6:84–89.