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Prevalence of impaired glucose tolerance and the components of metabolic syndrome in Canadian Tsimshian Nation youth

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Introduction: Canadian Aboriginal people have been disproportionately affected by obesity and type 2 diabetes (T2D). Our objective was to determine the prevalence of obesity, glucose intolerance and the components of metabolic syndrome (MetS) in Tsimshian Nation youth living in 3 remote coastal communities.

Methods: A medical history, anthropometric measurements and an oral glucose tolerance test were performed in youth aged 6–18 years. We defined “overweight” by a body mass index (BMI) at the 85th percentile or higher and “obese” by a BMI at the 95th percentile or higher, by age and sex. We used the International Diabetes Federation criteria for MetS.

Results: Of the 224 eligible youth, 192 (85%) participated in the study. Nineteen percent were overweight, 26% were obese and 36% had central obesity (waist circumference $\geq$ 90th percentile for age and sex). No new cases of T2D were identified. The prevalence of impaired fasting glucose (IFG 5.6–6.9 mmol/L) and impaired glucose tolerance (IGT 2-hr glucose 7.8–11.0 mmol/L) were 19.3% and 5.2%, respectively. Five of the 10 youth with IGT had a fasting glucose less than 5.6 mmol/L. The prevalence of MetS was 4.7% and increased to 8.3% when pediatric hypertension norms were applied.

Conclusion: Tsimshian Nation youth have a high prevalence of central obesity, impaired glucose homeostasis and other components of MetS. The oral glucose tolerance test may be a more appropriate screening test to identify IGT in Aboriginal youth.

Introduction : Les populations autochtones du Canada sont affectées de manière disproportionnée par l'obésité et le diabète de type 2. Nous avons pour objectif de mesurer la prévalence de l'obésité, de l'intolérance au glucose et des différents éléments du syndrome métabolique chez des jeunes de la nation Tsimshian vivant dans trois villages côtiers isolés.

Méthodes : Nous avons procédé à une anamnèse, à des mesures anthropométriques et à des tests d'hyperglycémie provoquée par voie orale (HGPO) chez des jeunes âgés de 6 à 18 ans. Nous avons défini l'embonpoint par l'atteinte d'un indice de masse corporelle (IMC) se situant dans le 85e percentile ou plus et l'obésité, par l'atteinte d'un IMC se situant dans le 95e percentile ou plus, selon l'âge et le sexe. Nous avons appliqué les critères de la Fédération internationale du diabète en ce qui concerne le syndrome métabolique.

Résultats : Parmi les 224 jeunes admissibles, 192 (85 %) ont participé à l'étude. Dix-neuf pour cent d'entre eux avaient de l'embonpoint, 26 % étaient obèses et 36 % présentaient une obésité abdominale (tour de taille $\geq$ 90e percentile selon l'âge et le sexe). Aucun nouveau cas de diabète de type 2 n'a été repéré. La prévalence de l'hyperglycémie modérée à jeun (HMJ : 5,6-6,9 mmol/L) et de l'intolérance au glucose (résultat HGPO : 7,8–11,0 mmol/L) a été de 19,3 % et de 5,2 %, respectivement. Parmi les 10 jeunes qui présentaient une intolérance au glucose, 5 avaient une glycémie à jeun inférieure à

5,6 mmol/L. La prévalence du syndrome métabolique était de 4,7 % et passait à 8,3 % lorsque l'on appliquait les critères de l'hypertension pédiatrique.

Conclusion : Les jeunes de la nation Tsimshian présentent une prévalence élevée d'obésité centrale, d'hyperglycémie modérée et d'autres éléments du syndrome métabolique. Les épreuves d'hyperglycémie provoquée pourraient être les tests de dépistage de l'intolérance au glucose les plus appropriés chez les jeunes Autochtones.

INTRODUCTION

The rising prevalence of childhood obesity within the last decade has been associated with a corresponding increase in the incidence of type 2 diabetes (T2D) and the cluster of cardiovascular disease (CVD) risk factors (central obesity, impaired fasting glucose, dyslipidemia and hypertension) known as the metabolic syndrome (MetS). Among Canadians, Aboriginal people have been disproportionately affected by both obesity and T2D.¹ Furthermore, while the overall rates of CVD and associated mortality have been declining in North America, the opposite has been true among Aboriginal populations.^{2,3}

Current literature suggests that the atherosclerotic process may begin in childhood and that obesity and the components of MetS track from childhood to adulthood.⁴ With the high prevalence of obesity being documented among Aboriginal children, the burden of obesity-related diseases among Aboriginal adults will likely continue to rise as the current generation of children enters adulthood, carrying with it the associated CVD risk factors acquired in childhood. More worrisome still is that childhood-onset T2D and CVD risk factors may translate into an epidemic of premature complications in young Aboriginal adults.^{4,5}

Currently, epidemiologic data characterizing the prevalence of obesity, abnormal glucose metabolism and the components of MetS in Aboriginal children living in western Canada is limited.⁶ Existing Canadian pediatric data are largely based on the Ojibwa-Cree population living in central Canada.⁷⁻¹⁰ We were invited by 3 remote coastal Aboriginal communities, belonging to the Tsimshian Nation of British Columbia to determine the scope of these health issues among their youth.

The communities

We have a long-standing relationship with the Tsimshian Nation, which includes the communities of Hartley Bay (Gitga'at), Kitkatla (Gitksaahla)

and Port Simpson (Lax Kw'alaams). This relationship was established through a community-driven cooperative program, "Brighter Smiles," initially developed for the reduction of dental caries and well-child surveillance.¹¹ Hartley Bay, Kitkatla and Port Simpson are remote Aboriginal fishing communities on the Pacific Coast of British Columbia. The villages are located about 650-km northwest of Vancouver, and 160-km south of Prince Rupert, and are accessible only by boat or float plane. The cumulative population of the 3 villages ranges from 1000 to 1400.

Following identification by the Brighter Smiles team of a child with asymptomatic T2D, the 3 communities requested diabetes screening for all of their youth. The objective of this screening initiative was to determine the prevalence of obesity, abnormal glucose metabolism and the components of MetS among Tsimshian youth between the ages of 6 and 18 years, in order to provide the requisite information to work collaboratively to develop sustainable prevention and treatment programs.

Study design

Youth attended the village health clinic after a 12-hour fast, and compliance was ascertained by interview on arrival. A medical history screening for symptoms of diabetes and a detailed family history for T2D, gestational diabetes and the microvascular complications of T2D and CVD were obtained. History was substantiated by a first-degree family member whenever possible. Methodology for anthropometric measurements including height, weight and waist circumference are described elsewhere.¹² A physician examined each participant for the presence of acanthosis nigricans.

An intravenous saline lock was inserted in the dorsum of the participant's hand for blood collection, following application of topical anesthetic cream (EMLA, AstraZeneca) to avoid multiple venipunctures. Blood was collected at baseline for glucose, insulin and lipid profile (total cholesterol, triglycerides, high-density lipoprotein [HDL] and low-

density lipoprotein [LDL]). Participants then drank a 1.75 g/kg (maximum 75 g) glucose oral solution (ratio-GLUCOSE 75 g/300 mL, orange flavoured) and 2 hours later, blood for glucose was collected. After the study visit, participants were provided with a nutritious breakfast. All blood was immediately spun, aliquoted and stored in a -20°C freezer, and frozen samples were transported by float plane to the BC Children's Hospital for analysis.

Laboratory measurements

Plasma glucose concentration was measured by Glu Microslides, Vitros 950/250 chemical system (Ortho Clinical Diagnostics). Total cholesterol and triglycerides were measured by Vitros analyzer (Ortho Clinical Diagnostics). Low-density lipoprotein was calculated using the Friedewald formula.¹³ High-density lipoprotein was measured by phosphotungstic acid precipitation followed by enzymatic colorimetric assay (Bayer Advia 1650). Plasma insulin was measured by the Beckman-Coulter Access Immunoassay System. Insulin resistance was estimated using the homeostasis model assessment of insulin resistance (HOMA-IR).¹⁴ A level of 2.28 was used as the threshold to indicate insulin resistance.¹⁵ Pubertal status was ascertained by serum estradiol and total testosterone levels. Serum estradiol concentration was measured by Pantex estradiol ^{125}I Kit (catalogue no. 047) and serum total testosterone was measured by DSL-4100 testosterone radioimmune assay (Diagnostic Systems Laboratories, Inc.). Girls with a serum estradiol of 60 pmol/L or less and boys with a serum total testosterone level of 2.4 nmol/L or less were categorized as prepubertal, and the remainder was considered pubertal.¹⁶

Diagnostic criteria

Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) and then standardized for sex and age.¹⁷ We defined "overweight" by a BMI at the 85th percentile or higher and "obesity" by a BMI at the 95th percentile or higher (corresponding to BMI z scores of 1.04 and 1.64, respectively).¹⁸ Metabolic syndrome was defined using the International Diabetes Federation (IDF) criteria,¹⁹ which include waist circumference greater than or equal to the 90th percentile for age and sex (or adult cutoff if lower) and 2 additional criteria comprising of triglycerides 1.7 mmol/L or higher, HDL cholesterol 1.03 mmol/L or lower, fasting glucose

5.6 mmol/L or higher or known T2D, and hypertension (systolic ≥ 130 mm Hg or diastolic ≥ 85 mm Hg). To account for pediatric norms, we also used the National High Blood Pressure Education Program Working Group's²⁰ pediatric definitions for elevated blood pressure (≥ 90 th percentile).

To align with IDF criteria, we used the American Diabetes Association²¹ criteria to classify the participants as having normal fasting glucose (< 5.6 mmol/L), impaired fasting glucose (IFG 5.6–6.9 mmol/L), impaired glucose tolerance (IGT 2-hour oral glucose tolerance test [OGTT] glucose of 7.8–11.0 mmol/L) or T2D (fasting glucose ≥ 7.0 mmol/L or 2-hour OGTT glucose ≥ 11.1 mmol/L). We also determined the number of youth who met the 2008 Canadian Diabetes Association (CDA)²² definition for IFG (6.1–6.9 mmol/L) as a means of comparing our results with those of previously published studies (see Discussion).

Analysis

We designed our study to estimate prevalences with a measure of precision and to generate hypotheses. Thus the analyses are descriptive and exploratory, not inferential. Given the small populations in each community, we conducted community comparisons for age, BMI z score, fasting glucose and insulin resistance using 95% confidence intervals (CIs). Because there were no clinically or statistically significant differences between communities, the data were combined for the later analyses. Sex differences for demographic, clinical and metabolic parameters were analyzed with means or proportions plus differences between means and proportions with appropriate CIs.

Approval

Our study was approved by the Children's and Women's Hospital Research Review Committee and the University of British Columbia Clinical Research Ethics Board. This was a community-based participatory action research project that was approved by the elected Band Council, the hereditary band chiefs and elders, the community health directors and health representatives of each village. Parents or caregivers gave written informed consent and youth gave written assent. The process for obtaining community approval, consent and study logistics^{23,24} as well as preliminary data from the first community to complete screening (Hartley Bay)¹² have been previously published.

RESULTS

Of the 224 eligible youth, 193 were screened, representing a participation rate of 85%. The index case of T2D was not considered eligible for screening and therefore not included in these results. Data from 192 youth are presented because 1 adolescent was excluded from analysis after completion of screening, as it was disclosed that she was pregnant. Twenty-four youth did not consent to participate, 3 had consented but were absent on testing day, 1 did not fast and could not be rescheduled, and 3 could not complete testing. Demographic, clinical and metabolic characteristics of participants are summarized in Table 1.

Sixty percent of participants ($n = 116$) had a positive family history of T2D and 46% ($n = 88$) had a positive family history of CVD (myocardial infarction, stroke or dyslipidemia). Thirty-five percent of participants ($n = 68$) had evidence of acanthosis nigricans on physical examination. Prevalence of obesity by community is presented in

Figure 1. Overall, 45% (95% CI 38.3–52.4) of participants had a BMI at the 85th percentile or higher: 19% of participants were overweight (17.5% of boys and 21.1% of girls) and 26% of participants were obese (23.7% of boys and 28.4% of girls). The distribution of glucose metabolism by community is summarized in Figure 2. Given the shared genealogy among the villages and lack of statistical differences between communities for clinical and metabolic parameters (see Analysis), data were subsequently pooled for analysis.

The overall rates of IFG and IGT were 19.3% and 5.2%, respectively. Boys were 2 times more likely to have IFG compared with girls (relative risk [RR] 2.0, 95% CI 1.1–3.8). Table 2 describes the characteristics of the 10 youth confirmed to have IGT. Girls appeared to be more insulin resistant than boys (RR 1.6, 95% CI 0.9–2.8), but this did not reach statistical significance. Pubertal status significantly contributed to the level of insulin resistance seen, where 25.9% of children with insulin resistance (HOMA-IR ≥ 2.28) were pubertal com-

Table 1. Demographic, clinical and metabolic characteristics of Tsimshian Nation youth

Variable	Mean (95% CI)*			Mean difference (95% CI)
	Total, <i>n</i> = 192*	Boys, <i>n</i> = 97*	Girls, <i>n</i> = 95*	
Demographic				
Age, yr	12.0 (11.6–12.4)	12.1 (11.5–12.7)	11.9 (11.3–12.5)	
Sex, %		50.5	49.5	
Clinical				
BMI z score	1.0 (0.9–1.1)	0.9 (0.7–1.1)	1.1 (0.9–1.2)	−0.2 (−18.6 to 18.2)
Overweight, % (95% CI)	19.3‡(13.7–24.9)	17.5‡(10.6–26.6)	21.1§ (13.4–30.6)	−3.6 (−14.7 to 7.6)
Obese, % (95% CI)	26.0¶(19.8–32.2)	23.7**(15.7–33.4)	28.4††(19.6–38.6)	−4.7 (−17.1 to 7.7)
Prepubertal, % (95% CI)	44.7 (37.8–51.8)	55.6 (45.2–65.8)	33.7 (24.3–44.1)	−22.0 (−35.7 to −8.3)
Pubertal, % (95% CI)	55.2 (48.2–62.8)	44.3 (34.2–54.8)	66.3 (55.9–75.7)	22.0 (8.3–35.7)
Metabolic				
Fasting glucose, mmol/L	5.25(5.2–5.3)	5.3 (5.19–5.36)	5.2 (5.15–5.28)	0.1 (0.0–0.2)
Fasting insulin, pmol/L	49.2 (43.9–54.6)	43.0 (35.7–52.0)	55.6 (47.7–63.4)	−12.6 (−23.2 to −2.0)
HOMA-IR score	1.7 (1.5–1.9)	1.5 (1.2–1.7)	1.9 (1.6–2.2)	−0.4 (−78.0 to −0.02)
Triglyceride, mmol/L	1.0 (0.88–1.02)	0.8 (0.76–0.93)	1.1 (1.0–1.2)	−0.3 (−0.4 to −0.2)
HDL-C, mmol/L	1.5 (1.45–1.55)	1.5 (1.37–1.52)	1.5 (1.39–1.53)	0.0 (−0.1 to 0.1)
LDL-C, mmol/L	1.8 (1.7–1.9)	1.7 (1.6–1.8)	1.9 (1.8–2.0)	−0.2 (−0.36 to −0.03)

BMI = body mass index; CI = confidence interval; HDL-C = high-density-lipoprotein cholesterol; HOMA-IR = homeostasis model assessment of insulin resistance; LDL-C = low-density-lipoprotein cholesterol.

*Unless otherwise indicated.

† $n = 37$.

‡ $n = 17$.

§ $n = 20$.

¶ $n = 50$.

** $n = 23$.

†† $n = 27$.

pared with 11.2% who were prepubertal (95% CI -25.3 to -4.0).

Prevalence of the components of MetS is summarized in Figure 3. Central obesity was the most common component of the MetS found in this cohort. Overall, 35.9% of participants had a waist circumference greater than or equal to the 90th percentile. Girls were significantly more centrally obese relative to boys (RR 1.7, 95% CI 1.1–2.5). The overall prevalence of MetS was 4.7%. Based on pediatric norms, 26.6% of participants had hypertension, and no significant difference between sexes was present. When the IDF criteria were adjusted to reflect pediatric blood pressure norms,²⁰ the prevalence of MetS increased to 8.3%.

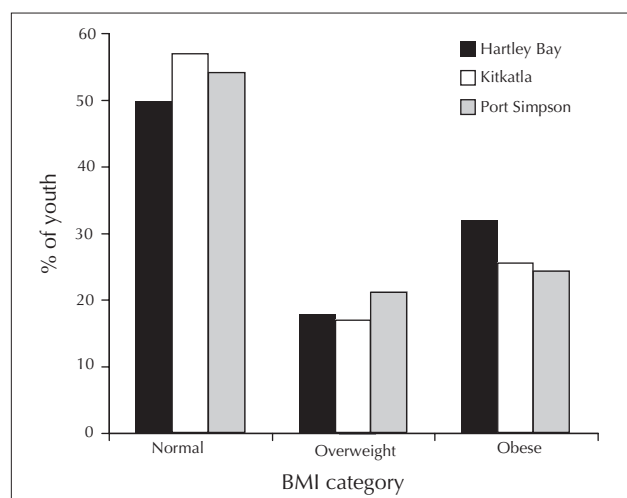


Fig. 1. Body mass index (BMI) of Canadian Tsimshian Nation youth, by community. Normal weight = BMI less than the 85th percentile; overweight = BMI at the 85th–95th percentile; obese = BMI at the 95th percentile or higher.

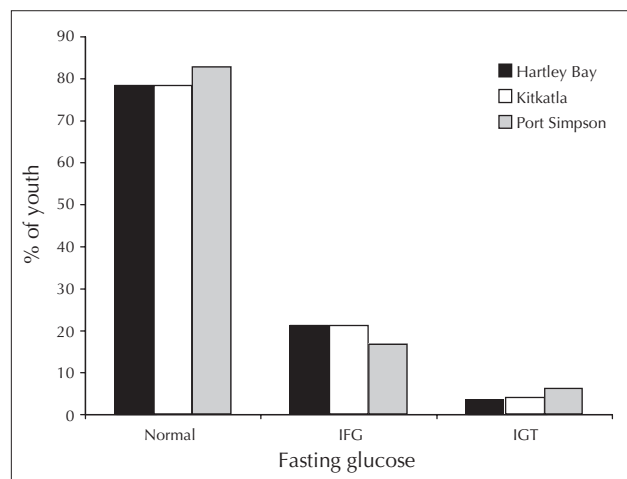


Fig. 2. Glucose metabolism of Canadian Tsimshian Nation youth, by community. The American Diabetes Association criteria were used to classify the participants as having normal fasting glucose (< 5.6 mmol/L), impaired fasting glucose (IFG 5.6–6.9 mmol/L) and impaired glucose tolerance (IGT 2-h oral glucose tolerance test glucose of 7.8–11.0 mmol/L).

DISCUSSION

Across Canada, the prevalence of overweight and obese children in non-Aboriginal populations is rising, with the overall prevalence reported to be 26%.²⁵ In comparison, Tsimshian Nation youth on the remote Pacific Coast of British Columbia were found to have almost double (45% overall: 41% of boys, 49% of girls) the prevalence of overweight and obese youth. Obesity and central obesity among

Table 2. Characteristics of Tsimshian Nation youth with impaired glucose tolerance

Age, yr	Sex	Glucose intolerance	Fasting BG*	2-h BG†	BMI, percentile‡	Acanthosis nigricans
10.8	F	IGT	5.4	7.8	98.4	Yes
10.0	F	IGT	5.1	8.5	72.6	No
12.0	F	IGT	5.2	8.5	48.2	No
11.4	M	IGT	5.1	7.9	94.7	Yes
15.6	M	IGT	5.4	7.8	97.8	Yes
12.6	F	IFG + IGT	5.6	8.2	50.0	No
13.4	M	IFG + IGT	6.3	8.5	77.0	Yes
12.6	F	IFG + IGT	5.8	8.1	> 99.0	Yes
11.7	M	IFG + IGT	6.1	7.8	98.4	Yes
11.8	M	IFG + IGT	5.7	8.5	88.2	Yes

BG = blood glucose; BMI = body mass index; F = female; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; M = male.

*Blood glucose measured after 12-hour fast.

†Blood glucose measured 2 hours after a standard oral glucose tolerance test.

‡Body mass index percentile for age and sex.

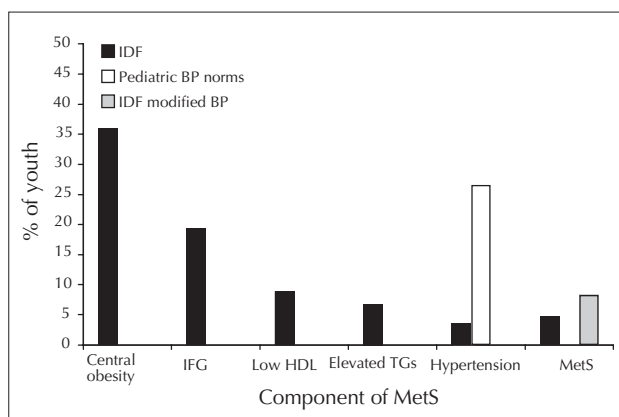


Fig. 3. Prevalence of the components of metabolic syndrome (MetS) among Canadian Tsimshian Nation youth. The components of MetS as defined by the International Diabetes Federation (IDF): central obesity (waist circumference at the 90th percentile or higher for age and sex [or adult cutoff if lower]), and 2 additional criteria comprising of triglycerides (TG) 1.7 mmol/L or higher, high-density lipoprotein (HDL) cholesterol 1.03 mmol/L or lower, impaired fasting glucose (IFG) 5.6 mmol/L or higher or known type 2 diabetes and hypertension (systolic $\geq$ 130 mm Hg or diastolic $\geq$ 85 mm Hg). Pediatric blood pressure (BP) norms reflect the National High Blood Pressure Education Program Working Group, where hypertension is defined at the 90th percentile or higher for age, sex and height percentile. International Diabetes Federation modified BP represents prevalence of MetS when pediatric BP norms are used.

these youth is also higher than that reported previously in other Aboriginal communities in Canada. For example, overall prevalence of overweight children in the Sandy Lake First Nation²⁶ was 27.7% in boys and 33.7% in girls; the prevalence of central obesity was 23% in this population versus 36% in the Tsimshian Nation youth. Similarly, in Mohawk children²⁷ aged 5–12 years, 29.5% of boys and 32.8% of girls were overweight or obese. The prevalence of overweight and obese youth in the Tsimshian Nation, however, is below that reported for the St. Theresa Point First Nation of Manitoba, where 64% of girls and 60% of boys exceeded the 85th percentile, and 40% of girls and 34% of boys exceeded the 95th percentile.²⁸

To our knowledge, there is no MetS prevalence data available in non-Aboriginal Canadian children. The prevalence of MetS in Tsimshian youth (4.7%–8.3%) is difficult to compare with other Canadian Aboriginal communities because of the lack of a consensus definition for MetS.²⁹ With that in mind, the prevalence of MetS in Sandy Lake First Nation children has been reported to vary from 5.4 to 18.6%.^{30,31} Although the most prevalent component in Sandy Lake First Nation children was low HDL,³¹ the most prevalent components in Tsimshian Nation youth were central obesity followed by IFG. In a small subset of Western Cree children of Alberta, Kaler and colleagues⁶ used a definition of MetS similar to that used in our study, reporting an overall prevalence of 40.5%, with central obesity also determined to be the most prevalent component (65.5%).

Although no additional cases of T2D, aside from our index case, were identified as a result of this study, the prevalence of IFG and IGT was high in this group of youth. The prevalence of IFG corresponds to that reported in the Western Cree of Alberta (25%), where the same cutoff value was used.⁶ When the 2008 CDA cutoff for IFG (6.1–6.9 mmol/L) was applied to this cohort of children, the prevalence was 2.1%. This rate is comparable to that previously published (2.7%) in Ojibwa–Cree children in the St. Theresa Point First Nation.⁸

To our knowledge, ours is the first study to report the prevalence of IGT in a Canadian cohort of school-aged Aboriginal youth. Previous Canadian Aboriginal screening studies have used fasting glucose with oral glucose tolerance testing limited primarily to adult screening initiatives that included some youth aged 15 years or older.^{32,33} The 2008 CDA guidelines²² recommend considering an OGTT for screening if the fasting glucose is 5.6–6.0 mmol/L

and there is 1 or more risk factor for diabetes. The specific guidelines for screening for T2D in youth recommend consideration of an OGTT if the youth is extremely obese ($\geq$ 99th percentile) and has risk factors such as high-risk ethnic origin, family history of T2D or intrauterine exposure to T2D. Of the 10 Tsimshian youth confirmed to have IGT, only 50% had a fasting glucose 5.6 mmol/L or higher. As well, none of the 5 youth with IGT and a fasting glucose less than 5.6 had a BMI at the 99th percentile or higher. Our findings are consistent with a report of 1376 obese white Italian children in which 96% of children with IGT had fasting plasma glucose levels less than 5.5 mmol/L.³⁴ These data would suggest that fasting glucose may not be useful in the detection of impaired glucose intolerance that might be identified only by performing an OGTT.

The early detection of obesity, impaired glucose metabolism and the components of MetS in these youth has provided the communities with the impetus to develop primary prevention strategies for T2D and CVD-related complications. We are working collaboratively with these communities to develop culturally and environmentally appropriate lifestyle-modification programs. Future steps include a request by the communities to implement and evaluate school-based programs and to gather more extensive physical activity, physical fitness and nutritional information. We regard this partnership to be a long-term commitment with an ongoing evaluation component to gain a better understanding of the natural history of disease progression in these youth. Our goal is to develop programs that will involve the whole community and effect change that the community would be willing to implement, and be enthusiastic about sustaining for generations to come.

Limitations

This is a cross-sectional study, and therefore, longitudinal follow-up of these youth is required to understand the prognostic significance of the high prevalence of the components of MetS as well as impaired glucose metabolism in their future T2D and CVD risk. Although these data cannot be extrapolated to other Aboriginal communities in British Columbia, these findings may provide the impetus for other communities to undertake screening initiatives.

CONCLUSION

Tsimshian Nation youth living on the remote Pacific

Coast of northern British Columbia were found to have a high prevalence of central obesity, impaired glucose homeostasis, as well as other components of the MetS, particularly hypertension. International Diabetes Federation criteria in children underestimated the prevalence of MetS for this population because the current definition does not account for pediatric blood pressure norms. Oral glucose tolerance testing may be a more appropriate screening test to identify IGT in Aboriginal youth.

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Competing interests: None declared.

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