

Non-insulin-dependent diabetes mellitus among First Nations children

New entity among First Nations people of northwestern Ontario

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OBJECTIVE To describe the emergence of a new clinical form of non-insulin-dependent diabetes mellitus (NIDDM) among First Nations children.

DESIGN Case series developed through retrospective review of a computerized diabetes registry and of records from a hospital and clinic.

SETTING Sioux Lookout Zone Hospital, a secondary care referral hospital for 28 remote First Nations communities in northwestern Ontario, affiliated with the University of Toronto's Sioux Lookout Program.

PARTICIPANTS Eighteen First Nations youths younger than 16 years identified via the Sioux Lookout Diabetes Program registry and via hospital discharge records from 1978 to 1994. Three of the 18 subjects were excluded because data essential to the study were missing from their records.

MAIN OUTCOME MEASURES Prevalence of NIDDM in this population, clinical presentation at diagnosis, and associated risk factors (including family history, obesity, and clinical management).

RESULTS Age-adjusted prevalence was 2.5/1000 in this population, the highest yet reported for NIDDM in this age group. Ratio of female to male subjects was 6:1. Typical patients were asymptomatic, obese adolescents who were not prone to ketosis and whose families had a strong history of NIDDM.

CONCLUSIONS Non-insulin-dependent diabetes mellitus can occur during childhood, particularly among First Nations people.

OBJECTIF Décrire l'émergence d'une nouvelle forme clinique de diabète non insulino-dépendant (DNID) chez les enfants des Premières Nations.

CONCEPTION Série de cas accumulée par une revue rétrospective d'un registre informatisé des cas de diabète et des dossiers d'un hôpital et d'une clinique.

CONTEXTE L'hôpital régional Sioux Lookout, un centre hospitalier de référence pour soins secondaires desservant 28 communautés éloignées des Premières Nations dans le Nord-Ouest de l'Ontario, et rattaché au programme Sioux Lookout de l'Université de Toronto.

PARTICIPANTS Dix-huit jeunes de moins de 16 ans appartenant aux Premières Nations et identifiés par le registre du programme diabétique de Sioux Lookout et par les dossiers de congés hospitaliers entre 1978 et 1994. Trois des 18 sujets furent exclus parce que leurs dossiers ne contenaient pas les données essentielles à l'étude.

PRINCIPALES MESURES DES RÉSULTATS Prévalence du DNID dans cette population, présentation clinique au moment du diagnostic et facteurs de risques associés (incluant antécédents familiaux, obésité et prise en charge clinique).

RÉSULTATS Corrigée en fonction de l'âge, la prévalence fut de 2,5/1000 dans cette population ; c'est le taux le plus élevé de DNID jamais rapporté dans ce groupe d'âge. Le ratio femme : homme fut de 6 : 1. Les patients typiques étaient des adolescents asymptomatiques et obèses qui n'étaient pas enclins à la cétose et dont les antécédents familiaux étaient chargés de DNID.

CONCLUSIONS Le diabète non insulino-dépendant peut survenir pendant l'enfance, particulièrement chez les individus des Premières Nations.

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NON-INSULIN-DEPENDENT DIABETES MELLITUS (NIDDM) was relatively unknown among First Nations* patients in North America before the 1940s.¹

Over the past four decades, prevalence has risen dramatically.

In 1985, Young et al² reported the overall prevalence of diabetes as 28/1000 in communities located in northeastern Manitoba and northwestern Ontario. The highest age-specific rate occurred among 45- to 64-year-olds, with a prevalence of 125.5/1000. Recently, Fox, Harris, and Whalen-Brough³ conducted a follow-up chart review in the Sioux Lookout Zone (SLZ) of northwestern Ontario. Age-specific rates were higher than those reported by Young et al,² with a crude prevalence of 38.3/1000 and an age-adjusted prevalence of 66.5/1000.³ Onset of NIDDM also occurred at an earlier age in this population; median age of onset was 43.0 for male and 40.5 for female subjects.

In 1988, Dean and Moffatt⁴ estimated diabetes prevalence and identified 15 definite cases of diabetes among Manitoba First Nations children younger than 15 years. Unlike Young et al,² they attempted to segregate subjects into the two distinct diabetic conditions, insulin-dependent diabetes mellitus (IDDM) and NIDDM. Dean and Moffatt⁴ noted that it is challenging to distinguish between the two conditions in a First Nations child presenting with hyperglycemia. Within their sample of 15 subjects, six were clearly IDDM, five NIDDM, and four probably NIDDM patients. Clinical manifestations at initial presentation of NIDDM in young patients occasionally mimic those of IDDM.⁵

This paper highlights NIDDM in the pediatric First Nations population of northwestern Ontario to emphasize growing prevalence and to raise awareness among health care professionals of the clinical challenge of NIDDM in the young.

* First Nations is used throughout this article to refer to the indigenous and aboriginal inhabitants of Canada and their descendants.

METHODS

The study population included 28 remote communities within the SLZ, located in the subarctic boreal forest of northwestern Ontario. More than 14 000 Cree and Ojibway people live in this 385 000-km² area.

Health care services are provided by the Medical Services Branch of Health Canada. Each community has a nursing station or health clinic on site, which is staffed by community health nurses or community health representatives. The health care activities of the nursing stations in the isolated communities are coordinated from the SLZ hospital. The University of Toronto's Sioux Lookout Program provides 24-hour medical coverage at the hospital and telecommunications with the northern communities. Each of the 14 staff physicians are assigned two or three communities where they are responsible for spending 1 week monthly; the remainder of their time is spent at the SLZ hospital providing on-call services and patient clinics.

The Sioux Lookout Diabetes Program registry and discharge records from the hospital during the study period, 1978 to 1992, were used to identify cases. All patients younger than 16 with diabetes (excluding patients with gestational diabetes) were considered for inclusion so as to be consistent with the Manitoba data.⁵ Particular attention was given to symptoms at diagnosis, familial aggregation, and basic blood chemistry parameters. Family history of diabetes was determined by chart review and included information on siblings, parents, grandparents, and first- and second-degree relatives.

Obesity was estimated by means of calculating body mass index (BMI) using height and weight data collected by community nurses and recorded on clients' charts. Measurements were obtained by using a standard weight scale with an extendable height-measurement arm. The calculated values were compared with standardized percentile curves for white children and adolescents from the United States⁶ because similar standardized data for First Nations children are unavailable. The 95th percentile BMI is used as a

conservative limit for defining obesity among children.⁶ (Normal standards used in this study are thus of value for their relative estimate of adiposity only.)

Crude prevalence was calculated using current data from the Sioux Lookout Diabetes Program registry on Epi Info⁷ for the numerator and Immunization and Population statistics from Medical Services Branch, SLZ, for the total population estimates for the denominator.⁸ Population statistics used for estimating prevalence of NIDDM were the most recent available at the time of the study.

RESULTS

A total of 18 subjects (17 female, 1 male) were identified as having received a diagnosis of diabetes mellitus before their 16th birthday. Dates of diagnosis spanned a period from June 1978 to

August 1992. Three of these subjects were excluded from the analysis because data from chart review and from communicating with nursing stations serving their communities were inadequate. The remaining 15 subjects (14 female, 1 male) were aged 7 to 15 years (mean age 11.7 years) at the time of diagnosis (*Table 1*⁶).

Family history of diabetes could not be confirmed for one of the 15 subjects. One of the remaining 14 subjects had no identifiable relatives with diabetes; the remaining 13 (92.9%) had a family history of diabetes. Of these, nine (69.2%) had a strong family history of NIDDM, with at least one first-degree relative affected. The remaining four had second-degree relations (grandparents, aunts, or uncles) with NIDDM. Each of the eight subjects with an affected parent had a maternal association.

Body mass index values were available for 13 of the 15 subjects analyzed. Of these, all had a

Table 1. Patient characteristics at time of diagnosis

SUBJECT NO.	SEX	AGE	BODY MASS INDEX	BMI PERCENTILE*
1	F	9	22.35	>90
2	F	8	24.6	>95
3	F	11	24.68	>90
4	F	7	23.18	>95
5	M	13	27.16	>95
6	F	13	37.91	>95
7	F	15	25.39	>75
8	F	12	Unavailable	Unavailable
9	F	10	30.78	>95
10	F	12	20.23	>50
11	F	12	38.53	>95
12	F	14	33.56	>95
13	F	13	35.54	>95
14	F	12	Unavailable	Unavailable
15	F	15	36.79	>95

* Percentages are adjusted for age and sex.⁶

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BMI greater than the 50th percentile for age and sex. Ten (71.4%) had a BMI greater than the 95th percentile and were thus classified as "obese" at diagnosis⁶ (Table 1).

At the time of diagnosis, eight of the 15 subjects (53.3%) had non-classic symptoms, while seven (46.7%) presented with polyuria and/or polydipsia.

Eight patient charts documented testing for ketones in the urine. Only four of these demonstrated significant ketonuria. At the time of diagnosis, fasting plasma glucose levels varied from 5.4 to 18.4 mmol/L and random plasma glucose (RPG) levels varied from 8.8 to 34.1 mmol/L. Total glycosylated hemoglobin levels for seven subjects ranged from 11.0% to 31.5%. Using clinical and blood chemistry findings documented in the charts at diagnosis, all subjects had diagnoses consistent with the National Diabetes Data Group criteria for NIDDM⁹ (Tables 2 and 3).

Twelve of the 15 subjects responded to treatment that did not involve insulin therapy. The remaining three subjects received insulin during the study period. Of these three subjects, one (subject 4) had a clinical diagnosis more consistent with IDDM due to symptoms of diabetic ketoacidosis at the time of diagnosis as well as recurring episodes of diabetic ketoacidosis and a family history of autoimmune disease (a sibling with Hashimoto's thyroiditis). Moreover, the father of subject 4 was not a First Nations person. Insulin-dependent diabetes mellitus in First Nations populations is more common among children of mixed racial backgrounds.⁵ In addition, subject 4 required treatment with insulin from the time of diagnosis. Although treatment for the other two subjects involved continual insulin therapy, their courses were clinically consistent with a diagnosis of NIDDM.

Table 2. Clinical features and test results at time of diagnosis

SUBJECT NO.	CHIEF COMPLAINT	POLYURIA	POLYDIPSIA	DIABETIC KETOACIDOSIS (PH 6.8-7.3)	WEIGHT CHANGE
1	Infection	Y	Y	N	Unavailable
2	Infection	Y	N	N	N
3	Infection	Y	Y	N	Unavailable
4	Symptoms	Y	Y	Y	Y
5	Infection	Y	N	N	Y
6	Pain	N	N	N	N
7	Incidental	N	N	N	N
8	Infection	Y	Y	N	Unavailable
9	Incidental	N	N	N	N
10	Incidental	Y	Y	N	N
11	Infection	Y	N	N	N
12	Asymptomatic	N	N	N	Unavailable
13	Symptoms	Y	Y	N	Y
14	Unavailable	Unavailable	Unavailable	Unavailable	Unavailable
15	Asymptomatic	N	N	N	N

Of the 15 cases with charted treatment histories, 12 were consistent with a diagnosis of NIDDM, two with that of insulin-requiring NIDDM, and one with that of IDDM. During follow-up appointments, mean glycosylated hemoglobin values ranged from 4.7% to 20.7%.

Prevalence was determined using data from 1994. At that time 14 First Nations children younger than 16 years were registered with the Sioux Lookout Diabetes Program registry as NIDDM patients. Using SLZ immunization and population statistics from the same year, age-adjusted prevalence was calculated to be 2.5/1000. When analyzed by sex, prevalence of NIDDM in the young was found to be 4.24/1000 in female and 0.72/1000 in male subjects, with a 6:1 ratio of females to males younger than 16 affected by NIDDM.

DISCUSSION

An important limitation of this study is that data were collected via chart reviews. Medical chart reviews are prone to missing data due to the different recording procedures of health care personnel. Given this limitation, the number of cases of NIDDM identified likely underestimates the true number of cases. Our results clearly show, however, that NIDDM is emerging as a serious clinical entity among First Nations children in northwestern Ontario.

In 1985 Young et al² first documented a prevalence of 0.5/1000 in Native children of the SLZ. A decade later, prevalence had reached 1.7/1000.³ Two years later, it had increased to an alarming 2.5/1000. Dean and Moffat⁴ reported a prevalence (0.9/1000) significantly higher than Young and colleagues but lower than rates

Table 3. Test results at time of diagnosis

SUBJECT NO.	URINE KETONES	RANDOM PLASMA GLUCOSE (normal >11.1 MMOL/L)	FASTING PLASMA GLUCOSE (normal 3.5-7.7 MMOL/L)	GLYCOSYLATED HEMOGLOBIN (normal 4.0%-8.5%)
1	Unavailable	24.1	18.4	Unavailable
2	Trace	22	15.3	15.0
3	Unavailable	20.2	12.2	11.6
4	4+	29.9	12.2	Unavailable
5	3+	24.7	16.2	11.0
6	None	Unavailable	12.2	Unavailable
7	4+	19	13.4	Unavailable
8	4+	15.4	14.2	15.7
9	Unavailable	11*	8.4*	Unavailable
10	Trace	12.1	9.2	8.6
11	Unavailable	12.1	5.4	8.0
12	Unavailable	Unavailable	14.2	Unavailable
13	Unavailable	31.5	16.1	24.4
14 [†]	Unavailable	Unavailable	Unavailable	Unavailable
15	None	12.2	Unavailable	Unavailable

* Blood values for subject 9 were determined after she was diagnosed as having diabetes.

[†] No clear data were available for subject 14, but the diagnosis of diabetes was confirmed.

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recently documented in the SLZ. In a follow-up study, Dean et al⁵ reported a minimum prevalence of NIDDM in First Nations children aged 7 to 14 years in Manitoba of 0.53/1000. These findings suggest a trend toward younger age at onset of NIDDM, which will have a profound effect on future health care programs for this population.

This study also identifies the need to define the type and clinical presentation of diabetes mellitus appropriately for this population. Whereas IDDM typically presents in childhood as an acute ketosis-prone condition occurring more commonly in thin white children, clinical characteristics of NIDDM in First Nations children include obesity, a strong family history of NIDDM, and an indolent, nonketotic, asymptomatic condition.

Literature describing this clinical entity is limited. In 1987, Winter et al¹⁰ described an atypical symptomatic diabetes syndrome in young black Americans. These patients had acute diabetic symptoms that were short in duration and reversible with insulin, but that displayed a course consistent with NIDDM months or years later. This course differs from the clinical presentation found among First Nations youth in the SLZ described in this study: that is, their condition was more likely to be asymptomatic and chronic, not requiring insulin. A similar clinical description was reported in 1987 for white people.¹¹

Several different approaches to diabetes in the young have been presented. In 1976, Fajans and colleagues¹² reported that slowly progressive, mild, or even asymptomatic diabetes occurs in children, adolescents, and young adults. They also reported that diabetic glucose tolerance and fasting hyperglycemia occurring in such young patients can be treated by sulfonylurea therapy for as long as 26 years, again presenting a clinical picture that conflicts with that usually associated with a youth-onset diabetic condition.

Onset of diabetes at maturity has been acknowledged in the literature as a clinical entity^{13,14} distinct from IDDM. Unlike IDDM, which occurs more commonly in the first and second decades of life, maturity-onset diabetes of the young (MODY) characteristically presents in the

third and fourth decades and is characterized by an autosomal dominant inheritance pattern. The MODY syndrome differs considerably from the one described in this population, as onset is during the first and second decades of life and does not appear to follow the same genetic pattern. The term NIDDM in the young can thus be applied to children and adolescents with a classic presentation of NIDDM where familial aggregation of NIDDM is unknown or does not have an autosomal dominant pattern.

Confirmation of autosomal dominant inheritance in this limited review was impossible, as family history information is only sometimes available for second-degree relatives. Relatively new health care resources and record keeping are limiting factors in these isolated communities. The literature, however, describes NIDDM in Pima Indians younger than 25 years of age only when at least one parent is affected.^{11,15} Our study confirms this relationship for 58.3% of subjects and documents a maternal predominance. Familial aggregation of diabetes is clearly an important focus for any study exploring diabetes in the young.

The issues of misdiagnosis and of early detection in asymptomatic high-risk First Nations youth need to be addressed. Because physicians are unaware that NIDDM can present in children and adolescents, such patients could be misdiagnosed as having IDDM. No studies to date have determined how frequently this occurs. Failure to recognize that a young patient with diabetes could in fact have NIDDM and not IDDM can contribute to incorrect management and incorrect assignment of prognosis. Long-term prognosis is unknown at present for NIDDM. Early detection is likely a crucial factor in prognosis, because duration of hyperglycemia correlates with the prevalence of microvascular and macrovascular complications.^{16,17} Given this correlation, emphasis should be placed on recognizing the clinical presentation of NIDDM in any First Nations youth and initiating culturally appropriate interventions if available.

Because presenting symptoms vary, because asymptomatic diabetes is prevalent, and because

of associated complications, we agree with the criteria of Dean and colleagues⁵ for diagnosing diabetes in children. The National Diabetes Data Group criteria for diagnosing diabetes in asymptomatic children require both an elevated fasting glucose concentration (>7.8 mmol/L) and a sustained elevated glucose concentration during oral glucose tolerance tests on more than one occasion.⁹ Diagnosing nonpregnant adults requires only that fasting glucose concentration be elevated on more than one occasion. As Dean and colleagues⁵ suggest, the criteria are probably more appropriate and indicative of long-term morbidity for adults. Again, the natural history of impaired glucose tolerance in First Nations children must be further studied and clarified.

Obesity has become prevalent in this population, primarily because of changes from a nomadic to a more sedentary lifestyle, coupled with the introduction of high-fat, store-bought food. Experts disagree about adiposity in youth-onset NIDDM.¹⁸⁻²⁰ In this study, more than 70% of the SLZ youths with diabetes had BMI values greater than the 95th percentile compared with standardized percentile curves of BMI measurements for white children and adolescents. These curves have been used by other investigators comparing First Nations children and adolescents with NIDDM to the general population.^{21,22} Lifestyle could thus greatly affect the future health status of the SLZ population.

The challenge is to develop screening and educational programs for early detection of diabetes mellitus. Culturally appropriate diabetes education should be emphasized. In turn, strategies for encouraging patients to make healthy lifestyle choices rather than medical therapeutic approaches are crucial for First Nations populations.

The University of Toronto has recently established the Sioux Lookout Diabetes Program, which focuses on providing First Nations people who have diabetes mellitus with access to culturally appropriate education and care. The program is administered primarily by First Nations diabetes educators who conduct workshops in the

communities, as well as clinics for inpatient and outpatient referrals in Sioux Lookout.

Along with its regular program, a "Children with Diabetes" summer camp program was initiated with the aim of educating, in a culturally appropriate manner, First Nations youth living in remote communities. The camp focuses on increasing awareness of diabetes management through lifestyle changes, creating diabetic support groups, and fostering patient initiative for managing diabetes. Although the program has not yet been fully evaluated, many of the First Nations youth participating in the program have shown improved glucose control.

Currently, more than 40% of the SLZ population is younger than 16 years. Many of these children are at risk of developing diabetes unless their lifestyles change. With a large population genetically predisposed to diabetes, the increasing prevalence of NIDDM among First Nations youth indicates that diabetes and its associated long-term complications represent a growing problem. More research is needed on early identification and culturally appropriate management that minimizes the risk of long-term complications.

CONCLUSION

Primary care practitioners clearly need to be aware that NIDDM does occur in childhood, particularly in First Nations populations. The clinical presentation differs from IDDM in that it is generally not ketosis-prone, is often asymptomatic, and is more common among obese adolescents with a strong family history of NIDDM. Clinical management should focus on culturally appropriate lifestyle interventions and careful long-term follow up to monitor for the development of chronic complications. ■

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