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Factors associated with glycemia and microvascular complications among James Bay Cree Indian diabetics of Quebec

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Abstract

We conducted a chart review of physician diagnosed diabetics to obtain plasma glucose levels (fasting plasma glucose and glycosylated hemoglobin) over a retrospective 30 month time span and data on the presence or absence of current renal or ophthalmic microvascular complications. Multiple logistic regression was used to determine factors associated with the presence of microvascular complications. Poor glycemic control reflected by a need of insulin therapy (odds ratio (OR)=2.7, confidence internal (CI): 1.1,6.7), increased serum triglyceride levels (OR=4.5,CI:2.0,9.9) and duration of illness of more than five years (OR=3.0,CI: 1.2,7.8) were found to be associated with the presence of microangiopathies. Process of care and temporary reversion to traditional lifestyle and diet did not influence glycemic control. Our results points towards a need for an increased awareness of lipid disorders in diabetic patients and a better understanding of how social and psychological factors are related to metabolic outcomes.

Diabetes has been recognized as increasingly prevalent and as a relatively new disease in North American Indian tribes (1-2). In Canada, non-insulin dependent diabetes mellitus (NIDDM) is also becoming a major burden among the native population (2-6) including the James Bay Cree Indians of Quebec (7). Longitudinal studies have enabled the identification of risk factors for diabetes among American Indians such as the Pima in Arizona (8-11) and tribes living in Oklahoma (12). In Canada, a cross sectional study with the Cree and Ojibwa nations of northern Ontario (13) also looked at various determinants. Of these, age, serum triglycerides and obesity indices were the most important independent predictors of glucose levels. From a public health point of view it is important to discover the role of and effect of various risk factors leading to the development of NIDDM or its vascular complications within the Indian population. Interventions on these factors may prevent progression to a later stage within the natural history of the disease. Genetic susceptibility and family history as risk factors for NIDDM are not modifiable but factors affecting glycemic control in known diabetics and development of microangiopathies, which is the most specific and frequent complication in the James Bay Cree diabetics (14), may be. The present study was undertaken as a first attempt to identify potential determinants of glucose levels and microvascular complications in the James Bay Cree Indian diabetics which may be not only unique to this population but also amenable to change through appropriate prevention programs.

METHODS

Study setting

The cultural and historical background of the eastern James Bay Cree Indians of Quebec and their health care system have been described elsewhere (15-16). This northern nation was composed of eight different settlements numbering 8,840 individuals. Currently, health services to these communities are the responsibility of the Cree Board of Health and Social Services, under the Ministry of Health and Social Services of Quebec (16). The Cree Board is directly responsible for the administration of a hospital, clinics in seven communities, and a social service center. Patients in need of tertiary medical care are evacuated by plane to hospitals in Montreal. The health services offered in the communities are the only source of primary health care, and medical records are maintained in the local facilities.

Case finding and data collection

A prevalence study was performed during the summer of 1989 (7). NIDDM subjects were obtained from a chronic disease registry maintained in each community clinic. Then medical chart review was done to confirm the diagnosis using the biochemical criteria of the World Health Organization (17). Those not meeting the criteria were not considered. We also excluded subjects defined as gestational diabetes, secondary diabetes or impaired glucose tolerance. Current data collected from the medical files during July and August 1989 included sociodemographic, anthropometric, and care process information as well as family history and lifestyle factors (7,14). No assessment of physical activity or dietary profile including alcohol use was carried out. Data on blood sugar and lipids were obtained from charts for the period from January 1987 to June 1989. Data collection was performed by the principal investigator with the help of a research assistant. In order to minimize bias and maximize collection of complete and accurate data, we pre-tested the data collection sheet in one of the communities. This preliminary step provided us with a clear operational definition of the inclusion-exclusion criteria of the variable collected and a standard procedure to minimize inter-observer variations.

Variable definition

Overall obesity indices were constructed from measurements of height and weight. Overweight was defined as a Body Mass Index (BMI; weight (KG) divided by height in meters squared) of over or equal to 26. Obesity was considered for those with a BMI > 30 (18). A microvascular complication was defined as diabetic nephropathy and/or retinopathy from a written diagnosis confirmed by a consulting physician in the reviewed chart and had to be recorded after the time of diagnosis of NIDDM. A person with no history of physician diagnosed hypertension or use of antihypertensive drugs was considered normotensive. Diabetics who spent more than 120 days per year for the last two years in traditional native activities such as hunting, trapping and fishing as determined by the local trapping association, were categorized as bush living. Local trapping associations record how many days people spend in native activities as they provide a guaranteed income through an income security program to individuals spending more than four months in the bush. Traditional way-of-life has been shown to influence metabolic features of diabetes (19). Presence of glycemic follow-up was defined at the use by health professionals or by the diabetic person of more than one follow-up technique for

blood or urine sugar, such as fasting plasma glucose, glycosylated hemoglobin, self monitoring device and urine analysis. Mode of treatment was divided into three categories: diet only, diet with oral hypoglycemic medication, and diet with insulin. Family history of NIDDM was considered for those cases with first degree relatives harboring the disease. Other variables included age, sex, current smoking, and length of illness from time of diagnosis.

The retrospective variables, over the period of 30 months prior to current data collection were: mean values of all fasting plasma glucose (FPG), glycosylated hemoglobin (HbA_1), total cholesterol and triglycerides obtained at diabetic clinic visits over those 30 months. Glucose, cholesterol and triglyceride levels were determined through enzymatic methods. The level of glycosylated hemoglobin was measured by means of chromatography. We considered these indices as an integrated reflection of the current glycemic and lipid situation. The number of visits to the medical clinic for diabetic follow-up and the number of respective blood tests performed in order to obtain these different metabolic measurements was also recorded within the same time interval. The frequency of visits was calculated for a yearly basis in order to adjust for differences in time of diagnosis. A retrospective assessment was also needed in order to assess the presence of symptoms of diabetes at time of diagnosis as recorded in the medical chart.

Data analysis

Analysis of data was done in two steps. First, bivariate associations were evaluated either with t-test, chi-square, analysis of variance or simple linear regression. Choice of test depended on the measurement level of the variables being compared (20). Based on associations observed in bivariate analyses, multivariate models were constructed. Multiple linear regression (21) was used with the dependent continuous variable glucose level (FPG and HbA_1). The principal independent variables of interest for glucose level were current mode of treatment, mean number of visits to clinics per year in the prior 30m months, and glycemic follow-up. We considered these three variables as related to process of care.

Multiple logistic regression was used to determine factors associated with the presence of microvascular complications, controlling for potentially confounding factors such as age, sex, smoking, hypertension and BMI level. All data entry, management, and analysis were performed on a microcomputer with a software SYSTAT (Version 3.2, 1988, Evanston, IL, U.S.A.). All probabilities reported are for two-tailed tests at the 0.05 level.

RESULTS

A total of 230 NIDDM cases were identified for a crude prevalence of 5.2 % for the 20 years and older age group (7). Mean age at diagnosis was 48.3 years and mean duration of illness since diagnosis as of July 1989 was 60.4 months. According to our current definition 77.3 % of the NIDDM cases were overweight and 65.4 % were obese. A more complete description of the nature of the population recorded in the charts has been described elsewhere (14).

Glucose level

Initial bivariate analyses compared mean levels of the two glycemic indices (FPG, HbA_1) between different categories of potential influential factors (Table I). There were no sex differences and no increase with age was recorded for FPG or HbA_1. Significantly higher levels were observed for both indices when insulin was the current mode of treatment. Duration of illness since diagnosis was positively associated with increased levels of FPG and HbA_1. The presence of at least one symptom of diabetes at the time of diagnosis was associated with higher level of mean HbA_1.

To investigate which of the principal independent variables of interest related to process of care were significantly associated with glucose levels considering other independent variables as covariates or potential confounders, multivariate linear regression was performed (Table II). Current mode of treatment and total cholesterol levels were associated with both glycemic measures. Triglyceride levels were also significantly associated ($p < 0.05$) with HbA_1, while age was for FPG. Sex and BMI were not found significant in bivariate and multivariate analyses. Squared multiple r values which reflect the portion of the overall variance explained by the regression model were low and ranged between 18 and 24 %.

TABLE I. Mean glycosylated hemoglobin and fasting plasma glucose by risk factors among James Bay Cree Indians with N1DDM.

	Glycosylated Hemoglobin (%)		Fasting plasma Glucose (mmol/1)	
Risk factor	Number of subjects	Overall mean (p value)	Number of subjects	Overall mean (p value)
Age		(.87)		(.73)
20-39	21	8.0	30	11.0
40-59	100	8.1	119	10.4
60+	55	7.9	71	10.3
Sex		(.24)		(.32)
Men	56	8.2	56	10.6
Women	120	7.9	154	10.2
Mode of treatment		(.001)		(.001)
Diet	34	6.9	38	8.2
Diet and oral med.	107	8.2	143	10.4
Diet and insulin	35	8.4	39	12.1
Glycemic follow-up		(.84)		(.14)
Single technique	14	8.1	29	11.1
Multiple technique	162	7.9	191	10.3
Symptoms at time of diagnosis		(.002)		(.14)
Yes	65	8.5	82	10.7
No	111	7.6	138	10.1
Positive family history of type II diabetics		(.72)		(.86)
Yes	66	7.9	87	10.4
No	110	8.0	133	10.3
Current cigarette smoking		(.10)		(.88)
Yes	28	8.5	37	10.3
No	148	7.9	183	10.4
Hypertension		(.80)		(.20)
Yes	74	8.0	95	10.6
No	102	7.9	125	10.1
Bush living		(.80)		(.12)
Yes	79	7.9	97	10.0
No	97	8.0	123	10.6
Length of illness		(.001)		(.001)
<5 years	101	7.5	137	9.7
≥5 years	75	8.4	88	11.3

TABLE II. Predictors of mean glycosylated hemoglobin and mean fasting plasma glucose.

Independent variable †	Glycosylated hemoglobin β	95% CI. ‡	Fasting plasma glucose β	95% CI
Mode of treatment				
- diet and insulin	0.74	(0.18-1.30)	1.9	(1.00-2.80)
- diet and oral medication	0.05	(0.01 - 0.09)	0.04	(0.02 - 0.06)
- diet only (referent)				
Mean total cholesterol	0.27	(0.02 - 0.52)	0.53	(0.20 - 0.86)
Mean triglycéride	0.25	(0.02-0.48)	----	----
Age	—	—	0.03	(0.01 - 0.05)
N	139		159	
Total r^2	0.18		0.24	

*From multiple linear regression model.

†Other variables tested but not found to be statistically significant were; sex, glycemic follow-up, mean number of visits to medical clinics, duration of illness, bush living, current smokers and body mass index.

‡ 95% confidence interval.

In all covariance models, the observed relationships were homogenous as no significant interactions were found between our variables of interest and the selected covariates. Bush living had no effect on the independent factors. The mean number of visits to the medical clinics for diabetic follow-up in our 30 months time frame, calculated on a yearly basis to account for different times of diagnosis, did not influence significantly the levels of glycemic measures. Although the number of test readings performed in order to obtain these mean glycemic values was taken into account as it could influence the resulting index, it did not influence the final mean figure in bivariate and multivariate analysis.

Microvascular complications

Overall microvascular complication rate was 19.6 % (14). Duration of illness since diagnosis, and insulin as the mode of treatment were significantly related to the presence of microvascular complications in NIDDM patients. Other metabolic variables such as total cholesterol, Triglycerides levels, HbA_1 and FPG showed also positive associations (Table III).

In considering the independent effects of different variables on microvascular complication status, a multiple logistic regression model was constructed to compare the risk of harboring microangiopathies as a function of age, sex, smoking, hypertension and BMI level. The net effect of this multivariate approach is seen by comparing the crude and adjusted odds-ratio (OR) estimates for the selected factors.

Retinopathy and nephropaty are 2.7 times (95 % confidence interval (C.I.): 1.1, 6.7) more frequent in those with long duration of diabetes (more than 5 years), and respectively 4.5 (CL: 2.0,9.9) and 3.0 (CL: 1.2, 7.8) times more frequent for above normal levels of Triglycerides and for insulin as current mode of treatment (Table IV).

TABLE III. Microvascular complications by risk factors among James Bay Cree Indians with NIDDM.

Risk factor 20	% with complications	Odds ratio	95% C.I.*	P†
Age				.16
20-39	6.3	1.0	referent	
40-59	16.9	3.2	(0.7 - 14.3)	
60+	20.8	4.1	(0.9-19.1)	
Sex				.69
Men	18.2	1.0	referent	
Women	16.0	0.9	(0.4- 1.8)	
Mode of treatment				<.001
Diet	2.5	1.0	referent	
Diet and oral med.	14.9	6.7	(0.9-51.2)	
Diet and insulin	35.7	21.1	(2.6 - 168.6)	
Current cigarette smoking				.68
No	16.2	1.0	referent	
Yes	18.9	1.2	(0.5- 2.9)	
Hypertension				.11
No	13.2	1.0	referent	
Yes	21.2	1.5	(0.8- 3.0)	
Length of illness				<001
<5 years	8.9	1.0	referent	
≥5 years	27.9	4.0	(1.9- 8.4)	
Triglycéride level				<.001
≤1.7 mmol/1	10.6	1.0	referent	
> 1.7 mmol/1	34.5	4.4	(2.1-9.2)	
Total cholesterol level				.05
≤6.2 mmol/1	15.0	1.0	referent	
> 6.2 mmol/1	31.8	2.6	(1.0-6.9)	
Glycosylated hemoglobin level				.01
≤ 9%	13.6	1.0	referent	
>9%	29.5	2.7	(1.2-5.7)	
Fasting plasma glucose level				.01
≤ 7. 8 mmol/1	5.5	1.0	referent	
> 7.8 mmol/1	20.1	4.3	(1.3 - 14.4)	
Body mass index				.06
<26	5.8	1.0	referent	
26-30	22.2	4.6	(1.0-19.9)	
>30	19.3	3.8	(1.1-13.2)	

95% confidence interval.
† p value by chi-square test.

Several variables significantly associated with microvascular complications in the univariate analyses, such as FPG and HbA_1 levels, as well as total cholesterol were found not to bear any significant relationship to the presence of microangiopathies in the multivariate analysis. Age and sex were of no significant contribution. Another model composed of the three main effect variables and their interaction was also constructed. None of the interaction terms met the 0.05 significance level.

TABLE IV. Predictors of microvascular complications.*

Variables † (Comparison group)	Crude odds ratio	Adjusted odds ratio ‡	95% confidence interval
Mean triglycéride level (> 1.7 mmol/1, ≤1.7 mmol/1)	4.4	4.5	(2.0-9.9)
Length of illness (≥ 5 years, < 5 years)	4.0	2.7	(1.1-6.7)
Mode of treatment § (Diet and insulin, diet and oral medication)	3.9	3.0	(1.2-7.8)

*From multiple logistic regression model.

†Other variables included were; mean total cholesterol, mean fasting plasma glucose, and mean glycosylated hemoglobin.

‡For age, sex, current smoking, hypertension and body mass index.

§Grouped into two categories, diet only was placed in the second category.

DISCUSSION

Glycemic control

From our three variables of interest regarding process of care, only mode of treatment (need of insulin therapy) comes out consistently as an in-dependent influential factor. This observation may reflect the common clinical practice of placing patients in poorer control on more aggressive therapies rather than reflecting the competing hypothesis that patients treated with more aggressive therapies have worse metabolic control. In diabetes, a number of suggested methods of prevention, treatment and care are available but relationship between care process and patient out-come, as reflected by their glucose levels, are poorly correlated (22-24). A substantial proportion of the variance in glycemic control is not explained by the independent variables measured in this study as squared multiple r varies from 18 to 24 %. Our data is consistent with others (25-28) who concluded that differences in the process of care may not be associated with differences in glycemic outcome amongst diabetic patients. Factors such as social network, social support, cultural understanding and importance of the illness and family function are now being considered as important as proper medical treatment in community based multidisciplinary approaches to diabetes (29,30).

Furthermore, we expected that diabetic individuals who lived at least four months out of the year in the bush which is a temporary reversion to traditional lifestyle and diet that directly affect insulin sensitivity (increased physical activity, reduced energy intake and low-fat diet) would show a relationship with glycemic control (19, 31). Unpublished observations on 25 Cree Indians with NIDDM who spent more than 3 months in the bush showed that they lost more weight than a control group but showed no significant improvement in their glucose level. These observations seem to be related to increased physical activity. Furthermore their weight went back rapidly to their initial levels following the return to the community. Unfortunately our definition of bush living did not reflect individual dietary habits and degree of physical activity. Further studies should take into account these parameters.

Microvascular complications

Our results have to be tempered by the fact that microvascular disease was an aggregation of retinopathy and nephropathy; All by chart review. There is also a potential for misclassification as individuals who did not have a recorded physician's diagnosis simply may not have been tested for the complications. A cross sectional study of diabetes also fails to demonstrate temporal sequences and the effect of treatment on metabolic variables. Despite these limitations we found that three most powerful associations for microangiopathies after adjustment for potential confounders such as age, sex, current smoking, hypertension and BMI, were above normal level of Triglycerides (OR = 4.5), need of insulin therapy (OR = 3.0) and duration of diabetes of over 5 years (OR = 2.7). These relationships are independent of the effect of other variables. Risk of microvascular complications was also related in bivariate analyses with mean HbA^1 and FPG levels. Since mode of treatment in the form of a need for insulin therapy is strongly associated with poorer glucose status it was a stronger predictor of microangiopathies than FPG or HbA^1 levels in the multivariate analysis. Note that in a cross-sectional study the odds-ratios (relative risks) refer to the risk of having the disease and not of developing the disease. Our findings are consistent with other studies (3,32-34) which also looked at determinants of microvascular complications in native populations harboring diabetes.

CONCLUSION

This report is based upon hospital records which typically have poor information concerning diabetes, metabolic control, risk factors and complications. Nonetheless, poor glycemic control reflected by a need of insulin therapy, increased serum Triglyceride levels and duration of illness were found to be associated with the presence of microangiopathies. Our definition of process of care was not strongly associated with glycemic control, and temporary reversion to traditional lifestyle and diet as we measured it did not influence glycemic control. Finally, our results points towards a need for an increase awareness of lipid disorders in diabetic patients (35) and a better understanding of how social and psychological factors are related to metabolic outcomes.

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