ADIPOKINES AND INCIDENT TYPE 2 DIABETES IN AN ABORIGINAL CANADIAN POPULATION

Sylvia H. Ley[1], Stewart B. Harris[2], Philip W. Connelly[1,3], Mary Mamakeesick[4], Joel Gittelsohn[5], Robert A. Hegele[2], Ravi Retnakaran[1,6], Bernard Zinman[1,6], Anthony J. Hanley[1,6], [1]*University of Toronto, Toronto, ON,* [2]*University of Western Ontario, London, ON,* [3]*St Michael's Hospital, Toronto, ON,* [4]*Sandy Lake Health and Diabetes Project, Sandy Lake, ON,* [5]*Johns Hopkins Bloomberg School of Public Health, Baltimore, MD,* [6]*Mount Sinai Hospital, Toronto, ON.*

ABSTRACT

Interactions of adipokines in regulating the metabolic homeostasis have been suggested recently. Limited population-based data, however, are available on how adipokines in combination may contribute to the etiology of type 2 diabetes. In addition, only a few prospective studies on the associations of adipokines with type 2 diabetes have been reported from North American Aboriginal people, while none have been conducted among Aboriginal Canadians in whom type 2 diabetes is increasingly prevalent. The aim of this study was to investigate associations of adiponectin, leptin, C-reactive protein (CRP), interleukin 6 (IL-6), and serum amyloid A (SAA), individually or in combination, with risk of incident type 2 diabetes in an Aboriginal Canadian population. Of the 606 Sandy Lake Health and Diabetes Project cohort subjects who were free of type 2 diabetes at baseline, 540 (89.1%) participated in 10-y follow-up assessments. Concentrations of fasting adiponectin, leptin, CRP, IL-6, SAA, and covariates were measured at baseline. Fasting glucose and a 75-g oral glucose tolerance test were obtained at baseline and follow-up to determine incident type 2 diabetes, defined as clinically diagnosed type 2 diabetes or as fasting plasma glucose ≥7.0 mmol/l or 2-h postload plasma glucose ≥11.1 mmol/l. Low adiponectin, high leptin and low adiponectin-to-leptin (A/L) ratio at baseline were associated with increased risk of incident type 2 diabetes after adjustment for age, sex, triglyceride, HDL cholesterol, hypertension, and impaired glucose tolerance (IGT) (odds ratio [OR] 0.63 [95% CI 0.48-0.83], 1.50 [1.02-2.21], and 0.54 [0.37-0.77], respectively). When the models were additionally adjusted for waist circumference or BMI, however, only low adiponectin remained significantly associated with increased incident type 2 diabetes (OR 0.68 [0.51-0.90]). Combinations of leptin, CRP, IL-6, and/or SAA with adiponectin, assessed using either ratios or joint effects, did not improve type 2 diabetes prediction. In conclusion, low baseline adiponectin is associated with increased risk of incident type 2 diabetes independent of leptin, CRP, IL-6, SAA, and metabolic syndrome variables. The strong independent association between adiponectin and incident type 2 diabetes suggests that adiponectin may be involved in the etiology of type 2 diabetes.

INTRODUCTION

- Adipokines, defined as proteins secreted by adipose tissue, have been associated with insulin resistance and type 2 diabetes in cross-sectional studies.
- Reports have suggested that adipokines may interact to regulate metabolic and endocrine systems.
- Limited population-based data, however, are available on how adipokines in combination may contribute to the etiology of type 2 diabetes.
- No prospective study on the associations of adipokines with incident type 2 diabetes has been reported among Aboriginal Canadians who have a high prevalence of diabetes.
- The objective was to investigate associations of adiponectin, leptin, CRP, IL-6, and SAA, individually and/or in combination, with incident type 2 diabetes in Aboriginal Canadians.

STUDY DESIGN & METHODS

- The Sandy Lake Health and Diabetes Project is a population-based cohort study in an isolated Aboriginal community.
- Concentrations of fasting adiponectin, leptin, CRP, IL-6, SAA, and covariates were measured at baseline.
- Fasting and 2-h postload glucose were obtained at baseline and follow-up to determine incident type 2 diabetes, defined as clinically diagnosed type 2 diabetes or as fasting glucose ≥7.0 mmol/l or 2-h postload glucose ≥11.1 mmol/l.

RESULTS

Table 1 Baseline demographics and 10-y incident diabetes

Characteristic	No DM	Incident DM	p
n (%)	406 (82.5)	86 (17.5)	
Age (years)	25.4 ± 13.0	31.5 ± 12.4	<0.001
Sex, male/female	173/233 (83.6/81.8)	34/52 (16.4/18.3)	0.60

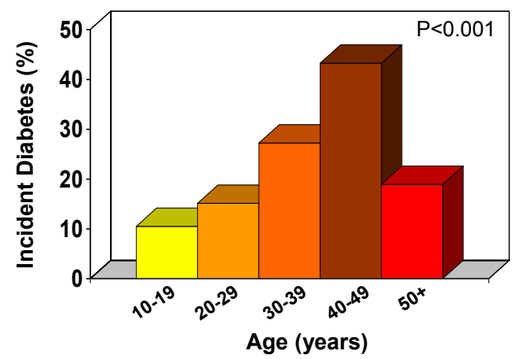

Figure 1 Baseline age groups and 10-y incident diabetes

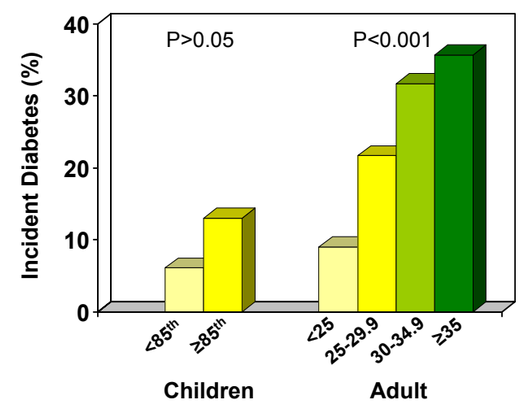

Figure 2 Baseline BMI and 10-y incident diabetes

Table 2 Adipokines and OR for diabetes risk per SD change

	SD	Model 1 OR (95% CI)	Model 2 OR (95% CI)
Adiponectin	0.49	0.63 (0.48-0.83)	0.68 (0.51-0.90)
Leptin	0.92	1.50 (1.02-2.21)	0.97 (0.58-1.62)
CRP	1.41	1.29 (0.96-1.73)	1.05 (0.76-1.36)
IL-6	1.00	1.11 (0.84-1.45)	1.03 (0.78-1.36)
SAA	0.88	1.14 (0.88-1.49)	1.07 (0.81-1.41)
A/L ratio	1.11	0.54 (0.37-0.77)	0.66 (0.42-1.02)

- Model 1: adjustment with age, sex, triglyceride, HDL-C, hypertension, and IGT
- Model 2: model 1 + waist circumference (WC)

Table 3 Adiponectin and incident diabetes with addition of leptin, CRP, IL-6, and/or SAA

	Adiponectin	C statistic
Base model	0.45 (0.25-0.81)	0.753
+ leptin	0.45 (0.25-0.81)	0.753
+ CRP	0.45 (0.25-0.81)	0.753
+ IL-6	0.45 (0.25-0.81)	0.753
+ SAA	0.46 (0.26-0.81)	0.754
+ leptin + CRP	0.45 (0.25-0.81)	0.753
+ leptin + CRP + IL-6	0.45 (0.25-0.81)	0.753
+ leptin + CRP + IL-6 + SAA	0.45 (0.25-0.81)	0.755

- OR (95% CI) per 1 unit change
- Base model: adiponectin, age, sex, triglyceride, HDL-C, hypertension, IGT, WC
- p≥0.05, C statistics for baseline vs. any subsequent models

CONCLUSIONS

- Low baseline adiponectin was independently associated with incident type 2 diabetes, while leptin, CRP, IL-6 and SAA were not associated with incident diabetes after adjustment for metabolic syndrome variables including obesity.
- Combinational effects of leptin, CRP, IL-6, and/or SAA with adiponectin did not improve diabetes prediction
- The strong association between adiponectin and incident type 2 diabetes independent of obesity suggests that adiponectin may be involved in the etiology of diabetes.

ACKNOWLEDGEMENTS & CORRESPONDENCE

Canadian Institutes for Health Research; Banting and Best Diabetes Centre

Anthony Hanley, Department of Nutritional Sciences, University of Toronto
150 College Street, Room 341, Toronto, ON, Canada M5S 3E2
Telephone: 1 416 978 3616 E-mail: anthony.hanley@utoronto.ca