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Metabolic Syndrome in Yup'ik Eskimos: The Center for Alaska Native Health Research (CANHR) Study

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Abstract

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Objective: This study investigated the prevalence of metabolic syndrome and its defining components among Yup'ik Eskimos.

Research Methods and Procedures: A cross-sectional study design that included 710 adult Yup'ik Eskimos ≥18 years of age residing in 8 communities in Southwest Alaska. The prevalence of metabolic syndrome was determined using the recently updated Adult Treatment Panel III criteria.

Results: The prevalence of metabolic syndrome in this study cohort was 14.7%, and varied by sex with 8.6% of the men and 19.8% of the women having metabolic syndrome. This is lower than the prevalence of 23.9% in the general U.S. adult population. The most common metabolic syndrome components/risk factors were increased waist circumference and elevated blood glucose. High-density lipoprotein (HDL) cholesterol levels in Yup'ik Eskimos were significantly higher, and triglycerides lower than levels reported in National Health and Nutritional Examination III.

Discussion: Compared with other populations, metabolic syndrome is relatively uncommon in Yup'ik Eskimos. The higher prevalence among Yup'ik women is primarily explained by their large waist circumference, suggesting central body fat accumulation. Further increases in metabolic syndrome risk factors among Yup'ik Eskimos could lead to increases in the prevalence of type 2 diabetes and cardiovascular disease, once rare in this population.

Key words: type 2 diabetes, cardiovascular disease, triglyceride, glucose, insulin

Introduction

The prevalence of obesity, type 2 diabetes (T2D),[1] and cardiovascular disease in Alaskan Eskimos has historically been low, but recent data indicate a more rapid increase in these disorders compared with other populations (1,2). While T2D prevalence among Alaska Eskimos is approximately one half that of American Indians or all U.S. ethnic groups combined, the percentage change in T2D prevalence in the last 13 years is significantly greater in Alaskan Eskimos (119%), than for American Indians (82%), or all U.S. races combined (75%) (personal communication; Alaska Native Tribal Health Consortium Diabetes Program). Available epidemiological data on overweight and obesity for all Alaska Native groups indicate that increased obesity prevalence parallels changes in diabetes prevalence (3). Increased consumption of market foods, reduced physical activity, stress, depression, smoking, and alcohol consumption have all been thought to contribute to an increased

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[1] Nonstandard abbreviations: T2D, type 2 diabetes; WHO, World Health Organization; ATPIII, Adult Treatment Panel III criteria; IDF, International Diabetes Foundation; CANHR, Center for Alaska Native Health Research; NHANES, National Health and Nutritional Examination; CRP, C-reactive protein; HDL, high-density lipoprotein.

prevalence of chronic diseases in Alaskan Eskimo populations; however, the relative roles of these factors are unknown.

Metabolic syndrome is characterized by a constellation of traits that have been shown in combination to be risk factors for T2D and cardiovascular disease. The most frequently cited defining criteria for metabolic syndrome are the World Health Organization (WHO) criteria (4) and the Adult Treatment Panel III criteria (ATPIII) (5). Recently, the International Diabetes Foundation (IDF) introduced a "worldwide" definition for metabolic syndrome (6). All criteria include abdominal obesity, an index of insulin resistance/glucose intolerance, dyslipidemia, and hypertension.

We sought to determine the prevalence of metabolic syndrome and its component risk factors in Yup'ik Eskimos. We used the updated ATPIII criteria (7) for three reasons: First, the WHO criteria require administration of an oral glucose tolerance test, and these data are not available for our study population. Second, the IDF criteria introduced ethnic-specific thresholds for waist circumference that are not defined for Alaska Natives. Third, the American Heart Association and the NIH continue to support the use of the ATPIII criteria recently published in a joint scientific statement (8).

An estimated 47 million people in the United States meet the criteria for metabolic syndrome (9), and the prevalence widely varies among different ethnic groups within the United States (10) and throughout the world (11). Evaluations of change in the individual components defining metabolic syndrome indicate that the prevalence is increasing (10). The prevalence of metabolic syndrome has not been reported in Alaskan Eskimos in general, or Yup'ik Eskimos, in particular. A recent report evaluated the prevalence of metabolic syndrome in Greenlandic Inuit, who are ethnically and culturally similar to Alaskan Yup'ik Eskimos (also Inuit), and determined the ATPIII and WHO prevalence to be 17.9% and 20.7%, respectively (12).

The primary aim of the Center for Alaska Native Health Research (CANHR) study is to identify behavioral, genetic, and nutritional risk factors contributing to obesity and T2D in Yup'ik Eskimos residing in Southwest Alaska (13). Because metabolic syndrome increases an individual's risk for T2D, we also sought to determine the prevalence of metabolic syndrome in Yup'ik Eskimos as a secondary analysis.

Research Methods and Procedures

Recruitment of study participants started in December 2003 and continued through March 2006. All residents from 8 communities were invited to participate. Communities were stratified by size and key cultural factors representative of the diversity of the region. The age distribution of the study population reflects the age distribution among eligible participants based on the U.S. 2000 census (Kolmogorov Smirnov test, $p > 0.05$). All participants were consented using protocols approved by the University of Alaska Institutional Review Board, the National and Area Indian Health Service Institutional Review Boards, and the Yukon Kuskokwim Human Studies Committee.

We enrolled a total of 907 participants and 872 participants completed the study. The analysis for this report is based on participants who identified themselves as nonpregnant Alaska Natives, ≥18 years old, and having fasted at least 8 hours. Data for all 5 metabolic syndrome components were available for 710 adult Yup'ik Eskimos. Anthropometric measurements were obtained by trained observers using previously published protocols implemented in the National Health and Nutritional Examination (NHANES) III survey (14). Leptin was assayed with a radioimmunoassay kit using an I^{125}-iodinated human leptin tracer and human leptin standards from Linco Research, Inc. (St. Charles, MO), and the intra- and inter-assay variations were 6.6% and 12.0%, respectively. Adiponectin was assayed with a radioimmunoassay kit using a I^{125}-iodinated murine adiponectin tracer, a multi-species adiponectin rabbit antiserum, and human adiponectin standards from Linco Research. The adiponectin intra- and inter-assay variations were 5.1% and 9.1%, respectively. Insulin was assayed with a radioimmunoassay kit using a I^{125}-iodinated insulin tracer, anti-human insulin-specific antibody, and human insulin standards from Linco Research, and the intra- and inter-assay variations were 5.8% and 10.2%, respectively. C-reactive protein (CRP) was measured with an Immulite Analyzer and high sensitivity CRP reagents from Diagnostic Products Corporation (Los Angeles, CA). Manufacturer's intra- and inter-assay variations were 2.8% and 3.3%, respectively. Low-density lipoprotein cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were measured with the Poly-Chem System Chemistry Analyzer (Polymedco Inc., Courtlandt Manor, NY) in the Nutritional Assessment Laboratory, School of Medicine, University of California at Davis. Laboratory intra- and inter-assay variations were 3.6% and 3.9%, respectively, for HDL-cholesterol; 1.8% and 6.2%, respectively, for cholesterol; and 3.2% and 4.1%, respectively, for triglycerides. Fasting blood glucose was measured on a Cholestech LDX analyzer and glycosylated hemoglobin was measured on a Bayer HbA1c DCA 2000+ analyzer (Bayer AG, Leverkusen, Germany).

Waist circumference was measured with a Gulick II 150-cm tape measure (Country Technologies, Inc., Gays Mills, WI) immediately below the lowest lateral portion of the rib case, and percentage body fat was estimated by electrical bioimpedance using a Tanita TBF-300A body fat analyzer (Tanita Corp., Arlington Heights, IL). We classified individuals with the metabolic syndrome according to the new ATPIII criteria (7). We also calculated prevalence in our Yup'ik Eskimo participants using IDF South Asian/Chinese waist circumference cut-off recommendations

(≥90 cm for males and ≥80 cm for females) and Europid cut-off criteria (≥94 cm for males and ≥80 cm for females) (6). Cardiovascular disease risk was estimated according to the Framingham criteria including low-density lipoprotein cholesterol (15).

Statistical Analysis

Descriptive statistical analysis was performed to determine frequency distribution of variables, location (mean), and dispersion parameters (standard deviation, standard error, and range). The non-parametric Mann-Whitney test was applied to test differences between men and women within the CANHR sample (16). The direct method was applied to adjust for age and sex for estimating the prevalence of the metabolic syndrome (17). Univariate ANOVA was performed to correct for age, sex, and BMI in the analyses of the components of metabolic syndrome. All statistical tests were two-sided with a significance level of $p = 0.05$. Partial correlation coefficients were estimated for the components defining metabolic syndrome and after correcting for BMI, age, and sex. Before including these covariates in the analysis, their significant effects were evaluated with univariate ANOVA. Statistical analyses were performed with SPSS version 14.0 (SPSS, Inc., Chicago, IL). We extracted and analyzed data from the NHANES III (1988 to 1994). The data were processed and distributed with permission from the Population Research Institute, Simple On-line Data Archive for Population Studies (16). All NHANES biochemical measures, except for fasting glucose, were taken from serum instead of plasma. BMI was calculated as recommended by the NHANES III Public-Use Data Files Errata. Identical inclusion/exclusion criteria were applied to the NHANES and CANHR sample.

Results

A comparison between our study population and NHANES sample regarding age, anthropometric, and metabolic characteristics is presented in Table 1. Participants' age ranged between 18 and 94 years, and their age distribution was not different from that of the general population residing in participating villages. Fifty-three point nine percent of the participants were female, and the ages of men and women participating in the study were not significantly different regarding age (Mann-Whitney, $p = 0.580$).

On average, women were shorter, significantly more overweight (as estimated by BMI and percentage body fat), and had greater waist circumference than men. Men had higher systolic and mean arterial pressure than women. Total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels were not significantly different between men and women; however, women did have higher HDL cholesterol levels than men. Women also had significantly higher plasma leptin and insulin concentrations than men. Glucose, high sensitivity CRP, and adiponectin concentrations were not significantly different between men and women.

The age-adjusted prevalence of metabolic syndrome in Yup'ik Eskimos was 16.9%, and the prevalence for women was 20.7%, compared with 9.6% for men. In comparison, using the South Asian/Chinese IDF criteria, the age-adjusted prevalence of metabolic syndrome, increased to 22.3% for women and 10.8% for men. Finally, using the Europid waist circumference cut-off, the prevalence of metabolic syndrome was 22.3% for women and 8.6% for men. In the remainder of the study, we only present results based on the most recent ATPIII criteria.

The presence of additional metabolic parameters associated with obesity, T2D, atherosclerotic cardiovascular disease, and metabolic syndrome were also evaluated. These endophenotypes included leptin as a marker for obesity, and CRP and adiponectin as measures of the pro-inflammatory status and cardiovascular disease risk (18). Fasting plasma insulin concentrations and homeostasis model assessment of insulin resistance values were studied to evaluate the degree of insulin resistance. The results from this analysis are presented as a function of the number of metabolic syndrome components present (Table 2). These 4 groups are significantly different regarding sex, age, and BMI (ANOVA, all $p \leq 0.05$); therefore, Table 2 presents mean values adjusted for these covariates. The average age for the participants without any metabolic syndrome risk factors was 34 years (range, 18 to 75 years), compared with 40 years (range, 18 to 94 years) for individuals with 1 risk factor, 46 years (range, 18 to 82 years) for participants with 2 risk factors, and 52 years (range, 18 to 91 years) for those with metabolic syndrome. There was a clear trend for plasma adiponectin levels to decrease with increasing numbers of abnormal metabolic syndrome components; plasma leptin, insulin, homeostasis model assessment of insulin resistance values, and Framingham Risk scores increased with increasing numbers of risk factors. However, not all pairwise comparisons were significant (Table 2). No clear trend could be observed between groups for plasma CRP concentrations.

Discussion

The prevalence of metabolic syndrome among Yup'ik Eskimos (14.7%) is lower than that observed in NHANES III (23.9%), Greenlandic Eskimos (17%) (12), and several other Native American and non-Native groups (10,11). The mean age of the participants with metabolic syndrome was 52 years and is similar to NHANES III (57 years) and Greenlandic Inuit (54 years) with metabolic syndrome (12). A large waist circumference is the most common risk factor for metabolic syndrome in Yup'ik Eskimos and was more common in women than men (59.3% of women vs. 15.9%

Table 1. Anthropometric and biochemical measures by gender

		CANHR			
	NHANES III	Total CANHR	Females	Males	*p*
Sex (*n*)	10,843	710	383	327	
Age (yr) (mean ± SD)	47 ± 21	41 ± 16	41 ± 16	40 ± 16	0.58
Height (cm)* (mean ± SD)	166.4 ± 10.0	160.8 ± 8.7	155.7 ± 6.3	166.9 ± 7.2	≤0.001
Weight (kg) (mean ± SD)	74.7 ± 18.0	72.3 ± 15.2	71.9 ± 16.8	72.7 ± 13.1	0.122
BMI (kg/m^2)* (mean ± SD)	27.0 ± 5.8	28.0 ± 6.0	29.7 ± 6.9	26.0 ± 4.1	≤0.001
Percentage body fat* (mean ± SD)	Not available	29.6 ± 10.8	36.3 ± 8.8	21.7 ± 7.1	≤0.001
Waist circumference (cm)† (mean ± SD)	92.4 ± 14.5	91.4 ± 14.3	92.8 ± 15.9	89.9 ± 12.1	0.021
n (%) with abnormal value‡		278 (39.2)	226 (59.0)	52 (15.9)	
Blood pressure					
Mean arterial pressure* (mean ± SD)	89.0 ± 13.0	88.0 ± 10.3	86.9 ± 11.3	89.3 ± 9.4	≤0.001
Systolic BP* (mean ± SD)	122.7 ± 20.7	121.5 ± 14.8	119.0 ± 15.8	124.4 ± 12.9	≤0.001
n (%) with abnormal value§		161 (22.7)	75 (19.6)	86 (26.3)	
Diastolic BP (mean ± SD)	72.2 ± 12.6	71.2 ± 10.3	70.9 ± 10.8	71.7 ± 9.6	0.102
n (%) with abnormal value		69 (9.7)	41 (10.7)	28 (8.6)	
Biochemical measures					
Cholesterol (mg/dL) (mean ± SD)	203.3 ± 44.0	220.0 ± 46.2	220.9 ± 45.0	219.0 ± 47.7	0.497
HDL (mg/dL)* (mean ± SD)	50.9 ± 15.1	61.9 ± 17.8	65.1 ± 18.3	58.1 ± 16.5	≤0.001
n (%) with abnormal value‖		90 (12.7)	69 (18.0)	21 (6.4)	
LDL (mg/dL) (mean ± SD)	127.0 ± 38.5	141.3 ± 38.5	139.2 ± 36.9	143.7 ± 40.3	0.224
Triglyceride (mg/dL) (mean ± SD)	135.1 ± 105.8	84.4 ± 48.4	82.7 ± 40.1	86.4 ± 56.7	0.866
n (%) with abnormal value**		48 (6.8)	25 (6.5)	23 (7.0)	
Fasting glucose (mg/dL) (mean ± SD)	101.5 ± 31.6	94.2 ± 13.3	94.0 ± 15.1	94.5 ± 10.8	0.065
n (%) with abnormal value††		170 (23.9)	85 (22.2)	85 (26.0)	
Insulin (μU/mL)* (mean ± SD)	11.1 ± 8.0	14.7 ± 8.3	15.9 ± 9.2	13.2 ± 6.8	≤0.001
Adiponectin (μg/mL) (mean ± SD)	Not available	10.1 ± 5.5	10.3 ± 6.0	9.7 ± 5.0	0.37
Leptin (ng/mL)* (mean ± SD)	Not available	11.0 ± 10.2	17.1 ± 10.1	3.8 ± 3.5	≤0.001
C-reactive protein (mg/dL) (mean ± SD)	0.48 ± 0.80	0.36 ± 1.01	0.27 ± 0.57	0.49 ± 1.40	0.11

CANHR, Center for Alaska Native Health Research; NHANES, National Health and Nutritional Examination; SD, standard deviation; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

* Mann-Whitney $p \leq 0.001$ by gender within CANHR population.

† Mann-Whitney $p \leq 0.05$ by gender within CANHR population.

‡ Women, waist circumference ≥88 cm; men, waist circumference ≥102 cm.

§ Women and men: systolic blood pressure ≥130 mm Hg; women and men: diastolic blood pressure ≥85 mm Hg.

‖ Women: HDL ≤50mg/dL, Men: HDL ≤40 mg/dL.

** Women and men: triglyceride ≥150 mg/dL.

†† Women and men: fasting glucose ≥100 mg/dL.

of men). Higher HDL cholesterol and normal plasma triglyceride concentrations contribute to the overall low prevalence of metabolic syndrome in this population. This favorable lipid profile may be explained, in part, by a diet rich in salmon and marine mammals that are high in polyunsaturated fatty acids (19).

Additional endophenotypes associated with obesity, insulin resistance, and cardiovascular disease included plasma leptin concentrations, which were increased, whereas plasma adiponectin levels were decreased with increasing numbers of metabolic syndrome components. CRP levels were not significantly elevated with increasing components for

Table 2. Endophenotypes associated with metabolic syndrome in Yup'ik Eskimos

		Mean ± standard error (range)*				Non-significant pairwise comparisons†
		N = (153–242)	*N* = (158–223)	*N* = (103–138)	*N* = (90–102)	
Measurement	**Covariates‡**	**0 risk factors**	**1 risk factor**	**2 risk factors**	**≥3 risk factors**	**$p \geq 0.05$**
Leptin (ng/mL)	Sex, age, and BMI	9.60 ± 0.38 (0.20 to 29.80)	10.56 ± 0.35 (0.60 to 42.60)	11.72 ± 0.47 (0.80 to 45.70)	14.14 ± 0.59 (0.80 to 48.40)	0–1 and 1–2
Insulin (μU/mL)	Age and BMI	13.32 ± 0.51 (2.90 to 45.10)	14.20 ± 0.47 (3.50 to 81.40)	13.73 ± 0.62 (3.70 to 53.5)	20.22 ± 0.78 (7.60 to 79.80)	0–1, 0–2, 1–2
Adiponectin (μg/mL)	Sex, age, and BMI	11.08 ± 0.38 (1.20 to 33.80)	10.03 ± 0.34 (0.90 to 35.8)	9.73 ± 0.46 (0.30 to 39.6)	7.89 ± 0.58 (0.70 to 30.30)	0–1, 0–2, 1–2
C-reactive protein (mg/dL)	Sex	0.35 ± 0.09 (0.00 to 4.95)	0.27 ± 0.08 (0.00 to 7.09)	0.56 ± 0.10 (0.01 to 15.00)	0.33 ± 0.12 (0.00 to 3.50)	0–1, 0–2, 0–3, 1–3, 2–3
Framingham Risk Score	Sex and age	0.25 ± 0.19 (−2.00 to 10.00)	1.36 ± 0.25 (−2.00 to 13.00)	2.78 ± 0.40 (−2.00 to 12.00)	5.36 ± 0.53 (−2.00 to 17.00)	0–1 and 1–2
HOMA-IR	Age and BMI	2.56 ± 0.08 (0.54 to 9.35)	3.18 ± 0.10 (0.80 to 16.88)	3.61 ± 0.16 (0.89 to 13.08)	6.14 ± 0.36 (1.91 to 22.07)	0–1, 0–2, 1–2

HOMA-IR, homeostasis model assessment of insulin resistance. Number (*N*) of individuals varies because hormone and cytokine measurements were not made for all individuals.
* Mean estimates are adjusted for significant covariates ($p < 0.05$).
† Pairwise significance are based on estimated marginal means (ANOVA). Significance values were corrected for multiple testing (Bonferroni, nominal level 0.05). The numbers (m-n) refer to the tested groups with m or n risk factors.
‡ Covariates significant in Univariate ANOVA ($p < 0.05$)

metabolic syndrome; nevertheless, the Framingham risk score did increase in parallel with an increasing number of metabolic syndrome defining components further suggesting an increased risk for cardiovascular disease.

Despite a high prevalence of increased central adiposity, particularly in women, Yup'ik Eskimos seem to be somewhat protected from metabolic syndrome. Like their Greenlandic Inuit Eskimo counterparts, Yup'ik Eskimos have lower triglycerides, lower fasting glucose, and higher HDL cholesterol levels (20) compared with northern Europeans. A traditional diet rich in polyunsaturated fatty acids may play a role in protecting Yup'ik Eskimos from dyslipidemia and hyperglycemia associated with metabolic syndrome, while at the same time reducing pro-inflammatory cytokines and increasing adiponectin levels. Maintaining a traditional Yup'ik diet and encouraging an active lifestyle may ultimately serve to curb potential increases in the prevalence of metabolic syndrome and also prevent the onset of T2D atherosclerotic cardiovascular disease in Yup'ik Eskimos and other Inuit groups.

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