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Relationships between plasma adiponectin and body fat distribution, insulin sensitivity, and plasma lipoproteins in Alaskan Yup'ik Eskimos: the Center for Alaska Native Health Research study

Anna V. Goropashnaya[a,*], Johanna Herron[a], Mary Sexton[a], Peter J. Havel[b], Kimber L. Stanhope[b], Rosemarie Plaetke[a], Gerald V. Mohatt[a], Bert B. Boyer[a]

[a]*Center for Alaska Native Health Research, Institute of Arctic Biology, University of Alaska Fairbanks, Fairbanks, AK 99775-7000, USA*
[b]*Department of Molecular Biosciences, School of Veterinary Medicine, and Department of Nutrition, University of California Davis, Davis, CA 95616, USA*

Abstract

Adiponectin, a protein secreted by adipose tissue, has antiatherogenic, anti-inflammatory, and insulin-sensitizing actions. We examined the relationship between plasma adiponectin and adiposity, insulin resistance, plasma lipids, glucose, leptin, and anthropometric measurements in 316 adult men and 353 adult women Yup'ik Eskimos in Southwest Alaska. Adiponectin concentration was negatively associated with body mass index, percentage of body fat, sum of skin folds, waist circumference, triglycerides, insulin resistance (homeostasis model assessment of insulin resistance [HOMA-IR]), fasting insulin, and leptin in both men and women, and also with glucose in women. Adiponectin concentration correlated positively with high-density lipoprotein cholesterol concentration, and also with low-density lipoprotein cholesterol in women. Insulin-sensitive individuals (HOMA-IR <3.52, n = 442) had higher plasma adiponectin concentrations than more insulin-resistant individuals (HOMA-IR ≥3.52, n = 224): 11.02 ± 0.27 μg/mL vs 8.26 ± 0.32 μg/mL, $P < .001$. Adiponectin concentrations did not differ between groups of participants with low and high level of risk for developing coronary heart disease. No difference in plasma adiponectin levels was found among Yup'ik Eskimos and whites matched for sex, age, and body mass index. In conclusion, circulating adiponectin concentrations were most strongly associated with sum of skin folds in Yup'ik men and with high-density lipoprotein cholesterol levels, sum of skin folds, waist circumference, and insulin and triglycerides concentrations in Yup'ik women.

1. Introduction

Obesity is a risk factor for the development of type 2 diabetes mellitus, hypertension, hyperlipidemia, and cardiovascular disease [1]. Adipose tissue is an endocrine organ that secretes a number of hormones and metabolites that participate in the regulation of insulin sensitivity and energy metabolism [2,3].

Adiponectin is a 244–amino acid protein that is secreted specifically by adipose tissue [4]. This collagen-like cytokine has antiatherogenic [5], anti-inflammatory [6], and insulin-sensitizing actions [3]. Unlike most hormones produced by adipose tissue, circulating concentrations of adiponectin are decreased in obese animals and humans [3,7]; and low levels of adiponectin are predictive of the development of both cardiovascular disease [8-11] and type 2 diabetes mellitus [12].

Results of several studies suggest that increased intraabdominal fat contributes to reduced circulating adiponectin levels [13-16]. Individuals with coronary artery disease and/or type 2 diabetes mellitus also have lower plasma adiponectin levels than age- and body mass index (BMI)–matched nondiabetic individuals without coronary artery disease [5,17]. However, in Pima Indians with type 2 diabetes mellitus of duration of more than 10 years, serum adiponectin concentrations were higher than in those with impaired glucose regulation or diabetes of less than 10 years [18]. Plasma adiponectin levels, as well as the relationships between adiponectin and anthropometric

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* Corresponding author. Tel.: +1 907 474 1533; fax: +1 907 474 5700.
E-mail address: fnag@uaf.edu (A.V. Goropashnaya).

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measurements of body fat distribution, vary with ethnicity [12,19-22]. In addition, ethnic differences in the predictive value of circulating adiponectin concentrations and coronary heart disease (CHD) have been reported [23]. Studies in populations with different body fat distribution patterns are needed to obtain further understanding of the role of adiponectin in metabolic diseases in humans. Moreover, population groups with unusually high or low prevalence of type 2 diabetes mellitus or CHD might be especially useful in investigating the role of adiponectin in the pathogenesis of obesity and comorbidities.

In the present study, we examined the relationship between plasma adiponectin concentration and BMI, percentage of body fat (%BF), body fat distribution, insulin resistance, and plasma lipids in Yup'ik Eskimos from Southwest Alaska. The prevalence of obesity in Yup'ik men is similar to that seen in men in the National Health and Nutrition Examination Survey (NHANES) III cohort, and Yup'ik women show higher prevalence of obesity than women in the NHANES (unpublished); but Yup'ik Eskimos currently have a relatively low prevalence of cardiovascular disease [24] and type 2 diabetes mellitus [25]. They also have relatively low levels of plasma triglycerides and elevated high-density lipoprotein cholesterol (HDL-C) levels (unpublished). The aims of this study were to evaluate associations between adiponectin and BMI, %BF, anthropometric measurements, insulin resistance, and plasma lipids in Yup'ik Eskimos and to compare adiponectin levels in individuals with normal (NFG) and impaired fasting glucose (IFG) to determine potential relationships between plasma adiponectin levels and protection from type 2 diabetes mellitus and cardiovascular disease in this study population.

2. Participants and methods

2.1. Participants

The participants are from the Center for Alaska Native Health Research (CANHR) study [26] consisting of Yup'ik Eskimos residing in several rural communities in the Yukon-Kuskokwim Delta region of Southwest Alaska. The participants were recruited from December 2003 through March 2007. In this analysis, nonpregnant Yup'ik Eskimo participants 18 years or older were included. There were 669 adult Yup'ik Eskimos (316 men and 353 women) aged 18 to 94 years who met the inclusion criteria. The CANHR study is approved by the Institutional Review Board (IRB) at the University of Alaska Fairbanks, the Alaska Area IRB, the National Indian Health Service IRB, and the Yukon-Kuskokwim Health Corporation Human Studies Committee.

2.2. Blood parameters

All blood samples were drawn after at least an 8-hour fast, samples were centrifuged, and plasma was stored at −15°C in the field and then transferred to −80°C within 2 weeks. Adiponectin was assayed with a radioimmunoassay kit using an I^{215}-iodinated murine adiponectin tracer, multispecies adiponectin rabbit antiserum, and human adiponectin standards from Linco Research (St Charles, MO). The intra- and interassay coefficients of variation were 7.1% and 12.1%, respectively. Insulin and leptin were assayed with radioimmunoassay kits from Linco Research. Intra- and interassay coefficients of variation were 5.8% and 10.4%, respectively, for insulin assays and 6.7% and 11.1%, respectively, for leptin assays.

High-density lipoprotein cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides were measured with a Poly-Chem System Chemistry Analyzer (Polymedco, Cortlandt Manor, NY). Laboratory intra- and interassay coefficients of variation were 3.6% and 3.9%, respectively, for HDL-C and 3.2% and 4.1%, respectively, for triglycerides.

Plasma glucose concentrations were measured using a lipid and glucose analyzer (LDX; Cholestech, Hayward, CA). We used the diagnostic and classification criteria issued by the American Diabetes Association (Clinical Practice Recommendations 2004) to interpret the values of fasting plasma glucose: NFG was considered to be less than 100 mg/dL, IFG was considered to be at least 100 mg/dL and less than 126 mg/dL, and fasting blood glucose of at least 126 mg/dL met the threshold for the diagnosis of type 2 diabetes mellitus. Clinically diagnosed diabetic patients or individuals on glucose- or lipid-lowering medications were not included in this analysis.

The estimate of insulin resistance by the homeostatic model assessment ratio (HOMA-IR) was calculated with the formula described by Matthews et al [27]: HOMA-IR = fasting insulin (in microunits per milliliter) ∗ fasting glucose (in millimoles per liter)/22.5. We calculated the Framingham risk score for CHD according to Wilson et al [28].

2.3. Anthropometric measurements

Body mass index was calculated from weight and height measurements (in kilograms per square meter), and %BF was estimated with a Tanita (Arlington Heights, IL) TBF-300A bioelectrical impedance analyzer. Visceral adiposity was estimated using waist circumference measurement [29]; and subcutaneous fat accumulation was evaluated using the sum of 4 skin folds: triceps, subscapular, abdominal, and thigh [30]. Measurements of waist circumference and skin folds were made by trained individuals and according to the protocols described in the *NHANES III Anthropometric Procedures Manual* [31].

2.4. Statistical analysis

Statistical analyses were performed with SPSS software version 14.0 (SPSS, Chicago, IL). Descriptive statistical analysis was conducted to determine the frequency distribution of variables, location (mean), and dispersion parameters (standard error and range). The nonparametric 2-sided Mann-Whitney test was applied to test differences between

groups, with the exact version used when the samples size was less than 30.

The following transformations were used to normalize distributions: square root of adiponectin; inverse BMI; inverse waist circumference; and log10 of fasting plasma glucose, plasma insulin, leptin, triglycerides, HDL-C, LDL-C, and HOMA-IR values.

Relationships between adiponectin and metabolic and anthropometric variables were examined using linear regression analysis. To test for significant differences between Pearson correlation coefficients of adiponectin with covariates, we tested the equality of pairs of correlations [32,33].

To compare adiponectin concentrations between groups of individuals with higher and lower degrees of insulin sensitivity, we defined a HOMA-IR cutoff value (ie, 3.52) as the lower limit of the top quintile of HOMA-IR distribution values in individuals with BMI not exceeding 25 and with no metabolic disorders [34]. In these participants (n = 88), the limits of HOMA-IR values of the 5 quintiles were as follows: 0.60 to 1.77, 1.78 to 2.09, 2.10 to 2.55, 2.56 to 3.51, and 3.52 to 6.36. Other studies suggested lower HOMA-IR cutoff values: 2.77 [34], 2.68 [35], or 2.50 [36]; and we used the lowest cutoff value for comparison of adiponectin levels in participants with higher and lower degrees of insulin sensitivity.

Because the number of participants with CHD was only 15 in the present study, we calculated a Framingham score for CHD [28] in all individuals and compared adiponectin plasma concentrations in participants with low and high risk indices of −2 vs greater than or equal to 6 (2% and ≥11% risk for developing CHD, respectively).

To evaluate whether adiponectin concentrations in Yup'ik Eskimos differ from those in whites, we compared adiponectin levels from 20 male and 21 female individuals (Yup'ik and white). All samples were measured in the same radioimmunoassay. Men and women were pairwise matched for age and BMI; that is, each Yup'ik individual was matched with a white individual of similar age and BMI. Measurements in white individuals were performed on plasma samples collected at baseline from a nutritional supplements study conducted in Dr Havel's laboratory at the University of California, Davis (unpublished).

3. Results

Anthropometric and metabolic characteristics of Yup'ik Eskimos are presented in Table 1. On average, individuals were 40 years old; and age did not differ by sex. Compared with men, women had a significantly higher BMI, %BF, sum of skin folds, insulin, HDL-C, HOMA-IR, and leptin (absolute and adiposity corrected) values. Only glucose levels were significantly higher in men compared with women. Waist circumference, plasma adiponectin, triglycerides, and LDL-C concentrations did not differ between men and women.

Table 1
Sex differences in Yup'ik Eskimos for selected anthropometric and metabolic characteristics

	Men		Women	
	n	Mean ± SE	n	Mean ± SE
Age (y)	316	40 ± 0.90	353	40 ± 0.85
BMI (kg/m^2)†	315	26.0 ± 0.23	351	29.3 ± 0.36
%BF†	315	21.6 ± 0.40	351	35.7 ± 0.47
Waist circumference (cm)	313	89.6 ± 0.68	351	91.9 ± 0.82
Sum of skin folds (mm)†	307	58.9 ± 1.83	346	118.2 ± 2.15
Glucose (mmol/L)*	316	5.22 ± 0.03	353	5.13 ± 0.03
Insulin (μU/mL)†	314	13.1 ± 0.39	352	15.5 ± 0.48
Leptin (ng/mL)†	316	3.67 ± 0.19	352	16.5 ± 0.52
Leptin/BMI†	315	0.13 ± 0.11	351	0.53 ± 0.25
Leptin/%BF†	315	0.15 ± 0.10	351	0.44 ± 0.20
Adiponectin (μg/mL)	316	9.77 ± 0.28	353	10.4 ± 0.31
Triglycerides (mg/dL)	316	86.2 ± 3.18	351	80.6 ± 1.94
HDL-C (mg/dL)†	316	58.1 ± 0.94	351	65.3 ± 0.97
LDL-C (mg/dL)	316	143.8 ± 2.27	351	138.6 ± 1.96
HOMA-IR†	314	3.07 ± 0.10	352	3.61 ± 0.13

* $P \leq .05$.
† $P \leq .001$.

The correlations of adiponectin with selected anthropometric and metabolic variables are shown separately for men and women in Table 2. Most of the correlations were of a similar magnitude and in the same direction for men and women alike. For both men and women, adiponectin had a moderate negative correlation with BMI, %BF, waist circumference, the sum of skin folds, triglycerides, insulin, HOMA-IR, and leptin. For both men and women, adiponectin had moderate positive correlations with HDL-C. The correlation of adiponectin with LDL-C was weaker, but positive and significant for women; the same correlation was not significant for men. Age was not correlated with adiponectin (Table 2), although BMI, %BF, and waist circumference increased with age (data not shown). Linear regression analysis among selected variables indicated that the sum of skin folds and BMI had the strongest correlation with adiponectin in men, and HDL-C and the sum of skin folds in women (Table 2). We tested for significant differences between the strongest correlations (Pearson correlation coefficients >.2 and <−.2), and the results are shown in Table 3. In men, only the correlation coefficient of adiponectin and the sum of skin folds differed from the correlation coefficients of adiponectin and other variables (BMI, %BF, insulin, HOMA-IR, triglycerides, and leptin). Thus, adiponectin had the strongest correlation with the sum of skin folds in men (Table 2). In women, the correlation between adiponectin and HDL-C was not different from those observed for the waist circumference, %BF, the sum of skin folds, insulin, HOMA-IR, triglycerides, or leptin (Table 3). Only 2 correlations were significantly different from the others: the correlations of adiponectin with the waist circumference and with the sum of skin folds were significantly stronger than the correlation of adiponectin and BMI (Table 2). Thus, for women, when compared with the waist

Table 2
Pearson correlation coefficients by sex of plasma adiponectin[a] with selected anthropometric and metabolic variables

Variable	Transformation	Men	Women
BMI	−(Inverse)	−0.344†	−0.306†
%BF	–	−0.297†	−0.337†
Waist circumference	−(Inverse)	−0.341†	−0.367†
Sum of skin folds	–	−0.412†	−0.369†
HDL-C	Log10	0.343†	0.400†
LDL-C	Log10	−0.076	0.092*
Triglycerides	Log10	−0.245†	−0.335†
Insulin	Log10	−0.237†	−0.316†
Glucose	Log10	−0.031	−0.189†
HOMA-IR	Log10	−0.228†	−0.325†
Leptin	Log10	−0.307†	−0.333†
Age	–	0.040	0.074

[a] Square-root transformed.
* $P \leq .05$.
† $P \leq .001$.

circumference and the sum of skin folds, BMI has a significantly weaker correlation with adiponectin.

We found a weak but significant negative association between adiponectin and fasting plasma glucose levels in women (Table 2). Plasma adiponectin levels tend to differ in women with NFG and IFG: 10.68 ± 0.36 μg/mL (n = 285) vs 9.23 ± 0.62 μg/mL (n = 67), $P = .052$. Plasma adiponectin concentrations did not differ in men with NFG (9.67 ± 0.33 μg/mL, n = 239) and IFG (10.11 ± 0.53 μg/mL, n = 73), $P = .334$. Because the number of individuals with diabetic values of fasting glucose was small (1 woman and 4 men), we did not include them in the analysis.

We found that insulin-sensitive individuals (HOMA-IR <3.52, n = 442) had higher plasma adiponectin concentrations than the insulin-resistant individuals (HOMA-IR ≥3.52, n = 224): 11.02 ± 0.27 μg/mL vs 8.26 ± 0.32 μg/mL, $P < .001$. The difference remained significant when we used HOMA-IR values of less than 2.50 (11.41 ± 0.36 μg/mL, n = 255) vs greater than or equal to 2.50 (9.27 ± 0.25 μg/mL, n = 411), $P < .001$ [36].

Plasma adiponectin concentrations did not differ between groups of individuals with a Framingham score of −2 for CHD (9.60 ± 0.34 μg/mL, n = 223) vs greater than or equal to 6 (9.94 ± 0.54 μg/mL, n = 94), $P = .831$. Plasma adiponectin levels were slightly higher in Yup'ik Eskimos compared with age- and BMI-matched whites, but the differences were not statistically significant for men ($P = .94$) or for women ($P = .74$) as shown in Table 4.

4. Discussion

4.1. Adiponectin and adiposity

In the present population-based study of Yup'ik Eskimos, we found that adiponectin was inversely correlated with adiposity assessed by either BMI or %BF, consistent with previously reported results [16,21,22,37-41]. Our results showed significant inverse correlations between waist circumference and adiponectin levels that are consistent with recent studies reporting that the amount of intraabdominal fat modulates circulating adiponectin levels [13-15].

Central obesity and intraabdominal fat accumulation have been shown to be more strongly associated with decreased adiponectin levels than subcutaneous fat [13,16]. In our Yup'ik study population, waist circumference, a measure of central adiposity, did not differ between women and men,

Table 3
Differences in *Z* scores by sex for 2 correlations: adiponectin with correlate A vs adiponectin with correlate B

Adiponectin correlated with		Difference in *Z* scores	
Correlate A	Correlate B	Men	Women
HDL-C	Waist circumference	0.030	0.557
HDL-C	BMI	−0.015	1.533
HDL-C	%BF	0.647	1.027
HDL-C	Sum of skin folds	−1.117	0.533
HDL-C	Insulin	1.522	1.394
HDL-C	HOMA-IR	1.622	1.715
HDL-C	Triglycerides	1.553	1.123
HDL-C	Leptin	0.514	1.119
Waist circumference	BMI	−0.142	2.998*
Waist circumference	%BF	1.873	1.729
Waist circumference	Sum of skin folds	−1.894	−0.076
Waist circumference	Insulin	1.608	1.021
Waist circumference	HOMA-IR	1.801	1.463
Waist circumference	Triglycerides	1.543	0.608
Waist circumference	Leptin	0.918	0.980
BMI	%BF	1.922	−1.813
BMI	Sum of skin folds	−1.977*	−2.671‡
BMI	Insulin	1.651	−0.196
BMI	HOMA-IR	1.812	−0.383
BMI	Triglycerides	1.608	−0.521
BMI	Leptin	0.946	−0.858
%BF	Sum of skin folds	3.113‡	1.314
%BF	Insulin	−0.920	−0.407
%BF	HOMA-IR	−1.089	−0.240
%BF	Triglycerides	−0.814	−0.036
%BF	Leptin	0.285	−0.126
Sum of skin folds	Insulin	2.793‡	1.049
Sum of skin folds	HOMA-IR	2.910‡	0.894
Sum of skin folds	Triglycerides	2.760‡	0.622
Sum of skin folds	Leptin	2.945‡	1.191
Insulin	Homa-IR	0.709	−0.984
Insulin	Triglycerides	−0.124	−0.338
Insulin	Leptin	−1.145	−0.339
HOMA-IR	Triglycerides	−0.264	−0.181
HOMA-IR	Leptin	−1.318	−0.162
Triglycerides	Leptin	−1.016	0.037

* $P \leq .05$.
‡ $P \leq .01$.

Table 4
Adiponectin concentrations (in micrograms per milliliter) in Alaskan Yup'ik Eskimos and whites matched for age and BMI

	Yup'ik		White	
	n	Mean ± SD	n	Mean ± SD
Men	20	8.15 ± 3.26	20	8.09 ± 2.60
Women	21	10.11 ± 5.22	21	9.62 ± 4.31

although BMI and %BF were higher among women. This result might be due to a greater accumulation of subcutaneous fat among women. This is supported by our observation that the sum of skin fold thicknesses in Yup'ik women was twice as high as that in Yup'ik men, and this difference in subcutaneous adipose deposition does not appear to influence circulating adiponectin concentrations because we found no difference between men and women. Several other obesity studies on the Inuit have used waist circumference as a proxy for visceral fat and obtained similar results to those reported in this study [42-44]. However, wide variations in fat distribution exist among different ethnic groups using waist circumference as a proxy for visceral fat [30,45-47]. In the meantime, the observed associations between waist circumference and visceral fat should be viewed with caution.

Although we did not measure adipocyte size in this study, we hypothesize that adipocyte hypertrophy leads to decreased circulating adiponectin concentrations because large, insulin-resistant adipocytes with greater triglyceride stores secrete less adiponectin than smaller, insulin-sensitive adipocytes [3].

We had a wide age range of 18 to 94 years among our participants, with the average age for both men and women being 40 years. Despite predictions that plasma adiponectin levels decrease with age because of an increase in BMI, % BF, and visceral adiposity accumulation, we did not find a significant association between adiponectin concentrations and age, although BMI, %BF, and waist circumference in all participants were positively associated with age. Contrary to our observations, Cnop et al [16] showed that plasma adiponectin levels were modestly but significantly positively associated with age.

4.2. Adiponectin and insulin resistance

Japanese, Pima Indians, and whites with diabetes have lower plasma adiponectin levels than nondiabetic individuals of the same ethnicity [17,21]; however, Looker et al [18] showed that adiponectin levels increased with the duration of type 2 diabetes mellitus in Pima Indians. Although an oral glucose tolerance test was not conducted in the present study, we did assess fasting plasma glucose and plasma insulin levels and evaluated insulin resistance by calculating HOMA-IR levels. Homeostasis model assessment of insulin resistance is less accurate than the glucose clamp or the oral glucose tolerance test; however, this limitation is mitigated when a large number of participants are examined as in the present study [34]. Yup'ik Eskimos with elevated HOMA-IR values had lower adiponectin concentrations than individuals with low HOMA-IR values. Interestingly, plasma adiponectin levels did not differ in participants with NFG and IFG, suggesting that adiponectin concentrations are more closely associated with insulin resistance than with moderately elevated plasma glucose levels. This result is consistent with the results of Hotta et al [48] who observed that plasma adiponectin levels begin to decline at an early stage of obesity in rhesus monkeys in parallel with the decrease in insulin sensitivity and before the appearance of frank hyperglycemia.

Our results demonstrated that adiponectin concentrations were inversely correlated with triglycerides, insulin, and insulin resistance, consistent with results from other studies in various populations [16,21,22,39,40]. Based on the known actions of adiponectin, it seems biologically plausible that circulating adiponectin concentrations are determinants of insulin sensitivity [3] rather than insulin sensitivity affecting adiponectin production. This would be similar to the relationship between circulating adiponectin and HDL-C concentrations as proposed by Cnop et al [16] in which adiponectin was hypothesized to increase HDL-C production rather than the converse. Nonetheless, the metabolic sequelae leading to insulin resistance and type 2 diabetes mellitus need to be definitively determined in interventional mechanistic study designs.

Individuals with low plasma adiponectin concentrations at baseline are more likely to develop type 2 diabetes mellitus than those with high concentrations [12,49-51]. This was shown in individuals with both normal and impaired glucose tolerance at baseline. Observations of this nature can only be made in studies where participants are repeatedly measured over time. Longitudinal measurements in the participants of the present study over the next several years may reveal whether low adiponectin levels are predictive of the development of type 2 diabetes mellitus in Yup'ik Eskimos.

4.3. Adiponectin and CHD

Increased plasma lipid concentrations are associated with the elevated risk and incidence of cardiovascular disease [52]. Adiponectin is positively correlated with HDL-C and acts as an endogenous antiatherogenic factor [3,39,53-55]. We found a positive association between adiponectin and HDL-C in our Yup'ik study population; however, in a comparison of individuals with low risk vs high risk for CHD, based on their Framingham score, plasma adiponectin levels did not differ.

Adiponectin circulates in human plasma mainly as high–molecular weight (HMW) and low–molecular weight multimers [56]. Lara-Castro et al [57] reported that the HMW form, not total or HMW-to-total ratio, was primarily responsible for the observed relationships between adiponectin and metabolic syndrome traits (insulin sensitivity and abdominal fat but not total fat mass and BMI). Bobbert et al [58] showed that the HMW form of adiponectin was more closely correlated with HDL-C than total adiponectin. We did not measure the HMW form of adiponectin because there was no high throughput assay available at the time we initiated this study. Therefore, it is also possible that sex differences in the associations of adiponectin and different metabolic traits might be better explained with data on HMW multimeric values.

We found that women had more than 4-fold higher leptin concentrations than men in our study sample, and these differences remained when BMI and %BF were controlled. Our observations are similar to those reported by Havel et al [59]: plasma leptin was 4 times higher in normal-weight women than in men independent of age, reproductive status, and hormone replacement. Cnop et al [60] also found that leptin concentrations were 3-fold higher in obese women than in obese men, whereas the sex differences were 2-fold in lean individuals. As a whole, this group of studies suggests that women, regardless of the presence of obesity and insulin resistance, have much higher leptin values compared with men; but the explanation for this is not known.

4.4. Ethnic differences in adiponectin levels

Findings to date do not present a coherent picture of the relationship of adiponectin and ethnicity. Weyer et al [21] found that plasma adiponectin levels were lower in Pima Indians than in whites adjusted for age, sex, and %BF and that adiponectin was associated with insulin sensitivity irrespective of ethnic origin. Hulver et al [20] showed that plasma adiponectin concentrations did not differ among obese white, and obese and nonobese African American women. They also demonstrated that BMI, insulin, and HOMA-IR did not correlate with adiponectin among African Americans. These striking findings of the lack of association could be a result of ethnic differences. Kadowaki et al [61] reported higher levels of adiponectin in American men compared with Japanese men in all waist circumference tertile groups. Kanaya et al [23] found that older white Americans had higher circulating adiponectin concentrations compared with older blacks, although adiponectin levels were lower among whites with CHD than among whites without CHD. Although we used a small sample of age- and BMI-matched whites as a comparison group, we did not find significant differences in plasma adiponectin levels among Yup'ik Eskimos compared with whites. Because our sample size was small and individuals in our study were matched for BMI and not visceral adiposity, this conclusion should be taken with caution.

Despite significantly higher BMI and %BF in Yup'ik women than in men, plasma adiponectin concentrations did not differ between men and women in the Yup'ik population. Inconsistent findings have been reported in other studies of sex differences. In studies of Native Canadians [22], Japanese [39], African Americans [62], and whites [16], adiponectin levels were found to be significantly higher among female than male subjects. However, no difference in adiponectin concentrations between men and women has also been reported in whites [63]. In Pima Indians, despite differences in %BF, no difference in adiponectin levels between men and women was found [21]. These inconsistencies in findings might be a result of differences in intraabdominal fat accumulation in men and women in different studies.

In conclusion, in the present study, we observed that adiponectin levels in Yup'ik Eskimos are inversely correlated with waist circumference, triglycerides, insulin concentrations, and HOMA-IR, but positively correlated with HDL-C levels. We found that circulating adiponectin concentrations were most strongly associated with sum of skin folds in Yup'ik men and with HDL-C levels, sum of skin folds, waist circumference, and insulin and triglycerides concentrations in Yup'ik women. Future longitudinal studies of Yup'ik Eskimos are needed to determine whether decreased circulating adiponectin concentrations are predictive or an important risk factor for serious metabolic diseases such as type 2 diabetes mellitus and CHD.

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