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Fat Distribution and Insulin Resistance in Young Adult Nonobese Asian Indian Women

Magdalene Szuszkiewicz-Garcia, M.D.,[1,2] Rong Li, M.D.,[2] Scott M. Grundy, M.D., Ph.D.,[1,2] Nicola Abate, M.D.,[3,4] and Manisha Chandalia, M.D.[3,4]

Abstract

Although Asian Indian (people of Indian subcontinent descent) men are shown to have higher total and truncal body fat as well as greater insulin resistance compared to white men matched for total body fat and age, data in women are not conclusive. The objective of this study was to compare total and regional fat distribution and insulin sensitivity between healthy young premenopausal Asian Indian and white women of similar body mass index (BMI). Twenty Asian Indian women (65% immigrants and 35% first generation living in Dallas) and 31 white women of similar age and BMI [age 24 ± 3 vs. 25 ± 4; BMI 22 ± 4 vs. 23 ± 5; mean ± standard deviation (SD) in Asian Indian and white, respectively] without diabetes were evaluated with anthropometric measurements, underwater weighing for percentage of total body fat mass, magnetic resonance imaging of whole abdomen for measurement of abdominal subcutaneous and intraperitoneal fat mass, and euglycemic–hyperinsulinemic clamp study for measurement of insulin sensitivity. There were no differences in waist or hip circumference, total body subcutaneous abdominal or intraperitoneal fat mass, fasting plasma glucose, and insulin levels between Asian Indian women and white women. The peripheral glucose disposal rate (Rd) during hyperinsulinemic–euglycemic clamp was found to be almost identical in the two study groups (median value of 6.9 and 6.8 mg/min per kg of body weight, for Asian Indians and whites, respectively). For similar total or regional fat content, the glucose disposal rate was comparable in the two study groups. In conclusion, we demonstrate that young Asian Indian women do not have excess abdominal or intraperitoneal fat or insulin resistance for similar BMI compared to white women of European descent.

Introduction

Type 2 diabetes is reaching epidemic proportions among persons of Asian Indian descent, both in their country of origin as well as in western countries of migration.[1] An ethnic predisposition to insulin resistance may contribute to diabetes susceptibility.[2–5] Previously, we have reported that young Asian Indian men tend to have increased body fat content, particularly in the subcutaneous abdominal area, and have excessive insulin resistance when compared to white men, even in the absence of generalized or regional obesity (including visceral obesity).[5,6] It is assumed that similar susceptibility to insulin resistance exists in young Asian Indian women as well. However, no detailed studies are available to assess insulin resistance independent of body fat content and distribution in Asian Indian women compared to white women of European descent similar to that available in men.

Recently, we reported that Asian Indian women but not men had lower high-density lipoprotein cholesterol (HDL-C) compared to whites,[7] which suggests that independent evaluations are needed in Asian Indian women for other risk factors as well. Therefore, in this study, we examined the characteristics of body fat content and distribution in young Asian Indian women and their relationship to insulin resistance and compared the results to age and body mass index (BMI)-matched white women as a continuation of our evaluation done in similar aged Asian Indian men in the previous studies using similar methods.[5,6]

Methods

The study and public advertisements for this study were approved by Institutional review board of the University of Texas Southwestern Medical Center (UTSW) (Dallas, TX). A written informed consent was obtained from every

[1]Department of Internal Medicine, [2]Center for Human Nutrition, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas.
[3]Department of Internal Medicine, [4]Division of Endocrinology and Metabolism, University of Texas Medical Branch, Galveston, Texas.

participant. Participants were recruited by public advertisements (flyers) placed in colleges, churches, temples, and Asian Indian grocery stores in the Dallas–Fort worth Metroplex. Fifty-one women (20 Asian Indians, 13 new immigrants, all immigrated as adults, and 7 first generation and 31 whites) without a history of diabetes were enrolled. Fifty percent of Asian Indians and 48% of whites had a family history of diabetes in either parents or grandparents. Each participant was administered a questionnaire on demographics and personal history. Subjects with impaired glucose tolerance or diabetes were excluded by both fasting glucose and 2-h glucose concentrations during an oral glucose tolerance test, following American Diabetes Association (ADA) guidelines.[8] Qualified subjects were provided a prepackaged isocaloric diet with 30% fat, 55% carbohydrate, 15% protein, and 300 mg cholesterol for 4 days from the UTSW metabolic kitchen. On day 4, the subjects were studied by hyperinsulinemic–euglycemic clamp.

Body composition studies

Height and weight were measured by standard procedures. Waist and hip circumferences were measured, as mentioned in our earlier publications.[5,6] Skin fold thickness was measured three times and averaged at five different anatomical sites (subscapular, diagonal and vertical; chest; midaxillary; abdominal, horizontal and vertical; suprailiac, diagonal and vertical) using a Lange Skin fold caliper (Cambridge Scientific Instruments Inc. Cambridge, MD), as previously reported.[5,6] Truncal (sum of subscapular, chest, midaxilla, abdominal, and suprailiac skinfolds) and peripheral (sum of triceps, biceps, thigh, and calf skinfolds) skinfold thickness values were calculated. Body composition was determined using underwater weighing, as previously reported.[5,6] Magnetic resonance imaging (MRI) was used to measure intraabdominal (visceral) and abdominal subcutaneous adipose tissue volume in 16 subjects in each group, as previously described.[5] In brief, MRI studies were performed using a 1.5 T imaging device (Philips Gyroscan Intera, Holland). The entire abdominal region was scanned using contiguous axial 10-mm slices. Fat volume was measured on each slide by mapping subcutaneous and intraabdominal adipose tissue compartment using computerized imaging. Volume was converted into adipose tissue mass assuming adipose tissue density of 0.9196 kg/L. Similar measurements were done for young Asian Indian men and white men in our previous study.[6]

Hyperinsulinemic–euglycemic clamps

On the morning of study day 4, breakfast was withheld, and the euglycemic–hyperinsulinemic clamp procedure was performed after an overnight fast. The details of this procedure were described previously.[5,6] An insulin infusion rate of 80 mU/m^2 per min was used to assure complete suppression of the hepatic glucose output during the hyperinsulinemic phase of study. The rate of glucose disposal (Rd) was calculated by subtracting the urinary glucose excretion from the Ra and using space correction. The data on Rd were computed in mg/min per kg of lean body mass.

Biochemical analysis

Insulin was measured by radioimmunoassay at Linco Research Inc. (St. Louis, MO). The plasma concentrations of free fatty acids were measured by enzymatic colorimetric assay (Roche Diagnostics, Mannheim, Germany).

Statistical analysis

The Mann–Whitney U-test was used to compare Asian Indian and white groups. Spearman correlation coefficients were used to assess association between continuous variables. Statistical analysis was performed using SAS version 9.1 (SAS Institute, Cary, NC).

Results

The general characteristics of the two study groups are summarized in Table 1. Asian Indian and white women were well matched for most of the parameters. Median ages were

Table 1. General Characteristics, Body Composition, and Metabolic Parameters of Asian Indian and White Nondiabetic Women

	Asian Indian mean ± SD (median)	*White mean ± SD (median)*	p
N	20	31	
Age (years)	24 ± 3 (24)	25 ± 4 (24)	0.5
BMI (kg/m^2)	22 ± 4 (22)	23 ± 5 (22)	0.7
Total body fat (%)	28 ± 9 (26)	24 ± 9 (22)	0.2
Waist circumference (cm)	77 ± 11 (77)	77 ± 11 (73)	0.9
Hip circumference (cm)	91 ± 18 (94)	99 ± 9 (98)	0.1
Truncal skin folds (cm)	116 ± 57 (111)	96 ± 38 (86)	0.2
Peripheral skin folds (cm)	83 ± 36 (64)	80 ± 23 (82)	0.7
Abdominal subcutaneous fat (g)[a]	3204 ± 2063 (2375)	3202 ± 2460 (2193)	0.9
Intraperitoneal fat (g)[a]	557 ± 384 (393)	590 ± 367 (444)	0.8
Fasting plasma glucose (mg/dL)	87 ± 8 (86)	87 ± 7 (88)	0.8
Fasting plasma insulin (IU/mL)	11 ± 5 (11)	12 ± 7 (10	0.9
Peripheral glucose disposal rate (Rd) (mg/min per kg body weight)	7.2 ± 2.7 (6.9)	6.8 ± 1.9 (6.8)	0.8

Data are expressed as mean ± standard deviation (SD) (median). The Mann–Whitney U-test was used to compute *p* values.
p value for Rd is shown after statistical adjustment for total body fat mass.
[a]Abdominal fat was measured in 16 subjects in each group.

24 years for both groups. There were no significant differences in BMI, waist circumference, hip circumference, and total body fat mass between the groups. Sixteen subjects for each study group had MRI performed, and the results show comparable mass of subcutaneous abdominal fat (median of 2375 and 2193 g for Asian Indians and whites, respectively) and intraperitoneal fat (median of 393 and 444 g for Asian Indians and whites, respectively). Fasting plasma glucose and insulin levels were similar. Most importantly, the peripheral Rd during hyperinsulinemic–euglycemic clamp was found to be almost identical in the two study groups (median value of 6.9 and 6.8 mg/min per kg lean body mass, for Asian Indians and whites, respectively).

The relationships between BMI and measures of body fat content and distribution are depicted in Fig. 1A. The correlations were comparable in the two study groups. Asian Indian women tend to have similar total and abdominal subcutaneous and intraperitoneal fat when compared to white women of similar BMI. The relationship between total body or regional fat content and glucose disposal rate during hyperinuslinemic–euglycemic clamps is depicted in Fig. 1B. Asian Indian and white women had a comparable decrease in glucose disposal rate with increasing total or regional fat content. For similar total or regional fat content, the glucose disposal rate was comparable in the two study groups.

Discussion

The two most important findings of our study are: (1) Contrary to what has been observed by us and others in young Asian Indian men compared with white men, young Asian Indian women do not have excessive insulin resistance relative to total body or abdominal fat content compared with white women. (2) When matched for BMI, young Asian Indian women have similar total and abdominal body fat to white women. These are very important and novel findings because young Asian Indian men have higher total and truncal fat content for similar BMI values and also have excessive insulin resistance, even after matching for total and abdominal fat when compared with white men.[5,6] To our knowledge, this is the first study using precise techniques for measurement of total and regional body fat as well as insulin resistance comparing young Asian Indian women with age and BMI-matched white women. One prior study comparing Asian Indians with whites included a very small number of women, with the limitation of analyzing men and women

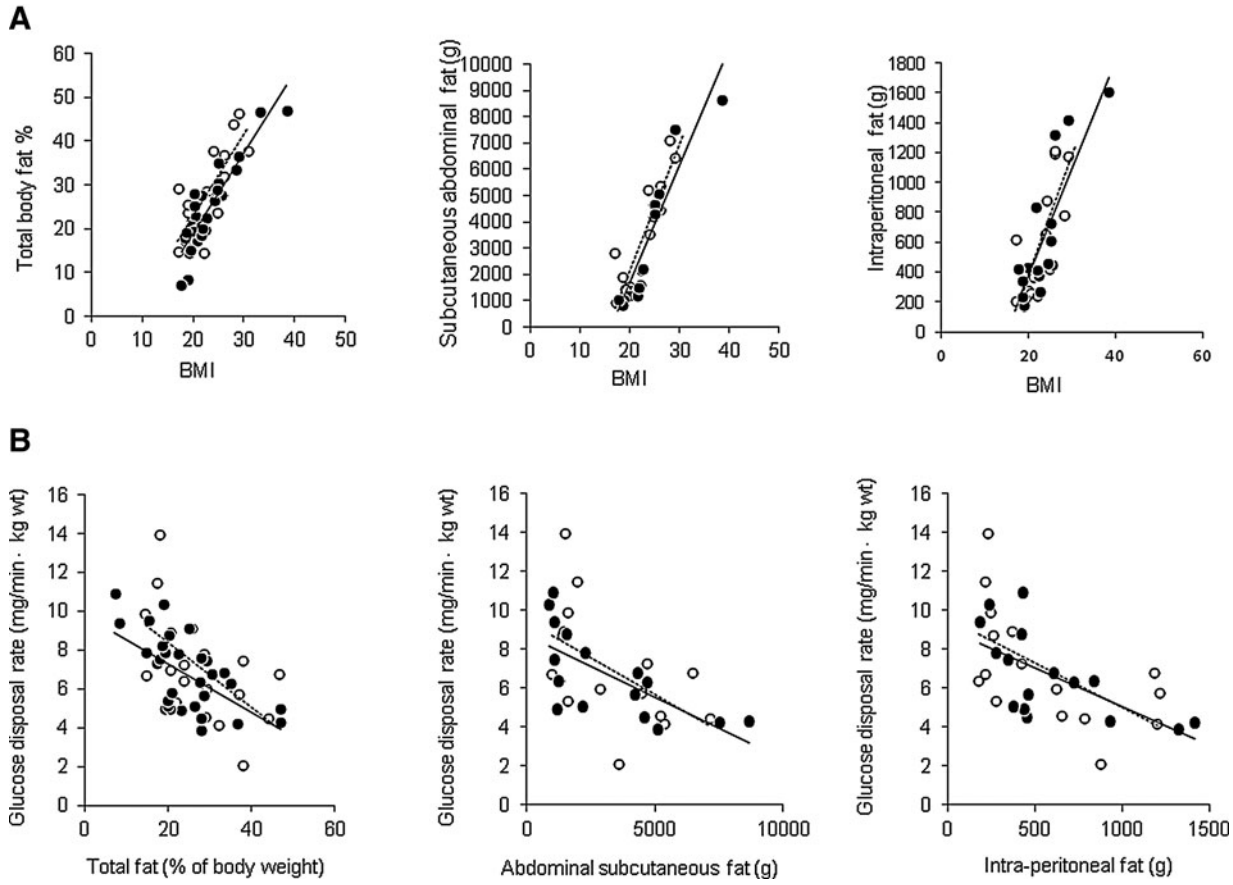

FIG. 1. **(A)** Relationship between body mass index (BMI) and total and regional body fat distribution. Spearman correlation coefficients and p values for Asian Indians and whites, respectively, are as follows: Total body fat: $r=0.70$, $p=0.009$, and $r=0.86$, $p<0.0001$; subcutaneous abdominal fat: $r=0.79$, $p=0.0003$, and $r=0.98$, $p<0.001$; intraperitoneal fat: $r=0.78$, $p=0.0003$, and $r=0.74$, $p=0.001$. **(B)** Relationship between glucose disposal rate and total and regional body fat. Spearman correlation coefficients and p values for Asian Indians and whites, respectively, are as follows: Total body fat: $r=-0.58$, $p=0.009$, and $r=-0.59$, $p=0.0004$; abdominal subcutaneous fat: $r=-0.49$, $p=0.05$, and $r=-0.80$, $p=0.0002$; intraperitoneal fat: $r=-0.64$, $p=0.007$, and $r=-0.75$, $p=0.0009$. (Open circle, dotted line) Asian Indians; (dark circle and solid line) whites.

together, thus raising the question of whether the described ethnic differences in insulin sensitivity were driven by the men in the group.[9] Two other studies using dual-energy X-ray absorptiometry (DXA) for measuring body fat reported a higher percentage of body fat in Asian Indian women compared with white women, and one of thee studies included postmenopausal women.[10,11] We acknowledge that our sample size is small for any generalization regarding body fat distribution in Asian Indian women, but differences in techniques for measuring the body fat of the subjects may play a role in these discrepancies.[12]

Our study contributes to filling the gap in current data regarding the relationship between obesity, fat distribution, and insulin resistance for young women in general and young Asian Indian women in particular. The assumption has been that data obtained in men could be extrapolated to women. For example, there is now a prevailing consensus that Asian Indians have higher total body fat and truncal fat compared to whites with similar BMI values that is reflected in lower cutoffs of BMI for determining overweight and obese individuals in Asian Indian population compared with white populations.[13] While this appears to be true for men, as shown by previous studies including ours,[6] no specific studies have reported data comparing Asian Indian women with white women only. Most of the literature on ethnic differences in body fat and insulin sensitivity and their impact on diabetes and cardiovascular disease in Asian Indians appears to be dominated by data obtained either in men or combining men and women together. Such data do not provide adequate insight into potential differences between men and women. Our data show that there are no significant differences between young Asian Indian and white women with regard to BMI and total as well as abdominal fat distribution. More studies are needed to establish if indeed lower BMI cutoffs are required in Asian Indian women to assess metabolic risk related to obesity.

We realize that our study has limitations because it is a cross-sectional study conducted in a small number of young subjects. However, rigorous methods were used to assess body composition and insulin sensitivity that are not feasible in a larger number of subjects. By comparing a well-matched group and using the same techniques as in our previous studies in young Asian Indian and white men, we have been able to demonstrate that young Asian Indian women are similar in body fat distribution and insulin sensitivity compared to age- and BMI-matched white women. Results of our study cannot be generalized to women of all ages, particularly older postmenopausal women, because young premenopausal women were studied here. However, the important point of the study is that young Asian Indian women did not have higher body fat or insulin resistance as seen in migrant Asian Indian men of similar age.[5,6] It is likely that Asian Indian women develop higher body fat and insulin resistance compared to white women of similar BMI later in life, but then the mechanisms are likely to be different than those in Asian Indian men. Although our subjects were healthy, young, active women in both groups, one other limitation of the study is that physical activity was not measured in the subjects.

Despite these limitations, our results raise the important question of gender difference in susceptibility to insulin resistance in young Asian Indians. It is postulated that estrogen may have a protective effect in Asian Indian women against excessive insulin resistance seen in Asian Indian men.[14] It would be desirable to evaluate this question further, perhaps with studies in older postmenopausal Asian Indian women for insulin resistance compared to postmenopausal white women of similar BMI. We have now demonstrated that Asian Indian women behave significantly differently with respect to HDL-C compared to Asian Indian men with a similar social environment.[7]

Understanding the mechanisms involved in these gender differences independently of dietary and environmental influences may allow us to better target our therapeutic effort for prevention of type 2 diabetes and cardiovascular disease. If Asian Indian women of all ages are shown to not have increased total and truncal fat relative to BMI or excessive risk of insulin resistance for similar body fat, and their risk of type 2 diabetes is driven by obesity similar to white women, then targeting weight management and healthy lifestyle may have a larger impact in Asian Indian women compared to Asian Indian men. This information will be of great significance from a public health policy point of view. Further studies, both epidemiological and mechanistic, are needed in women of different ethnicities and ages to establish their risk for type 2 diabetes as well as cardiovascular disease.

In conclusion, we have demonstrated that young adult Asian Indian women and white women with similar BMI values do not differ in total or central body fat distribution or degree of insulin resistance. This lack of ethnic difference in Asian Indian women is distinct from that reported in Asian Indian men.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Manisha Chandalia, M.D.
University of Texas Medical Branch
8.138 Medical Research Building
301 University Boulevard
Galveston, TX, 77555-1060

E-mail: manisha.chandalia@utmb.edu