



Understanding the High Prevalence of Diabetes in U.S. South Asians Compared With Four Racial/Ethnic Groups: The MASALA and MESA Studies

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OBJECTIVE

We compared South Asians with four other racial/ethnic groups in the U.S. to determine whether sociodemographic, lifestyle, or metabolic factors could explain the higher diabetes prevalence and whether insulin resistance and β -cell dysfunction occurred at younger ages and/or lower adiposity levels compared with other groups.

RESEARCH DESIGN AND METHODS

We performed a cross-sectional analysis of two community-based cohorts, the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study and the Multi-Ethnic Study of Atherosclerosis (MESA); all participants had no known cardiovascular disease and were between 44 and 84 years of age. We compared 799 South Asians with 2,611 whites, 1,879 African Americans, 1,493 Latinos, and 801 Chinese Americans. Type 2 diabetes was classified by fasting plasma glucose ≥ 126 mg/dL or use of a diabetes medication. Insulin resistance was estimated by the homeostasis model assessment (HOMA) and β -cell function was measured by the HOMA- β model.

RESULTS

South Asians had significantly higher age-adjusted prevalence of diabetes (23%) than the MESA ethnic groups (6% in whites, 18% in African Americans, 17% in Latinos, and 13% in Chinese Americans). This difference increased further after adjustment for potential confounders. HOMA of insulin resistance (HOMA-IR) levels were significantly higher and HOMA- β levels were lower among South Asians compared with all other racial/ethnic groups after adjustment for age and adiposity.

CONCLUSIONS

The higher prevalence of diabetes in South Asians is not explained by traditionally measured risk factors. South Asians may have lower β -cell function and an inability to compensate adequately for higher glucose levels from insulin resistance.

The prevalence of type 2 diabetes is increasing worldwide, with lifestyle and behavioral factors promoting obesity cited as the primary culprit (1). South Asians, including individuals originating from India, Pakistan, Nepal, Sri Lanka, and Bangladesh, have a very high prevalence of diabetes (2,3), and the South Asian

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subcontinent is forecast to have the greatest burden of diabetes worldwide by 2030 (4,5). Insulin resistance and abnormalities of insulin secretion in pancreatic β -cells are the main defects that lead to type 2 diabetes. South Asians have high rates of insulin resistance (6,7), but more recent studies have shown that South Asians may have an early decline in β -cell function as well (8,9), a phenomenon with more genetic underpinnings (10).

In a pilot study of a community-based population of Asian Indians, we previously reported that the prevalence of diabetes was higher than in other U.S. ethnic groups (11). Here we report the prevalence of impaired fasting glucose (IFG) and diabetes in a larger community-based South Asian population called the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. The MASALA study was created with similar methods and measurements as the Multi-Ethnic Study of Atherosclerosis (MESA) to make valid and efficient cross-ethnic comparisons (12). We sought to determine whether this higher diabetes prevalence in South Asians was explained by lifestyle factors, adiposity measures, or other metabolic covariates, including fasting insulin. We also examined the effect of age and adiposity on insulin resistance and β -cell function in South Asians compared with the four MESA racial/ethnic groups.

RESEARCH DESIGN AND METHODS

MASALA Study Design and Setting

The MASALA study is a community-based cohort of South Asian men and women from two clinical sites (San Francisco Bay Area at the University of California, San Francisco [UCSF], and the greater Chicago area at Northwestern University [NWU]). The baseline examination was conducted from October 2010 through March 2013. The institutional review boards of UCSF and NWU approved the MASALA study protocol.

Eligibility Criteria

Study methods have been previously reported (12). In brief, to be eligible for the MASALA study, participants had to 1) self-identify to be of South Asian origin and have at least three grandparents born in one of the following countries: India, Pakistan, Bangladesh, Nepal, or Sri Lanka; 2) be between 40 and 84 years of

age; and 3) have the ability to speak and/or read English, Hindi, or Urdu. We used identical exclusion criteria to MESA (13), which included having a physician-diagnosed heart attack, stroke, or transient ischemic attack, heart failure, angina, or use of nitroglycerin or those with a history of cardiovascular procedures such as coronary artery bypass graft surgery, angioplasty, valve replacement, pacemaker or defibrillator implantation, or any surgery on the heart or arteries. Those with current atrial fibrillation or in active treatment for cancer were excluded. Those with life expectancy <5 years due to a serious medical illness, with impaired cognitive ability as judged by the reviewer, planning to move out of the study region in the next 5 years, or living in a nursing home or on a waiting list were also excluded. Due to computed tomography scanner limitations, those weighing >300 lbs were excluded.

Clinical Measurements

All visits were conducted by trained bilingual study staff, and all consent forms were translated into Hindi and Urdu. We gathered information on participant demographic data, tobacco use, alcohol consumption, and medication use. Intentional exercise in metabolic equivalents (MET)-minutes per week was assessed using the Typical Week's Physical Activity Questionnaire (14).

Seated resting blood pressure was measured three times using an automated blood pressure monitor (V100 Vital Signs Monitor; GE Medical Systems, Fairfield, CT), and the average of the last two readings was used for analysis. Hypertension was defined as self-reported treatment for hypertension or a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. Participant weight was measured on a standard balance beam scale or digital weighing scale and height using a stadiometer, and BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured using a flexible tape measure at the site of maximum circumference midway between the lower ribs and the anterior superior iliac spine.

After a requested 12-h fast, blood tests were obtained. Fasting plasma glucose was measured by the glucose oxidase method; total cholesterol, triglycerides,

and HDL cholesterol were measured by enzymatic methods (Quest, San Jose, CA, and Chicago, IL) and LDL cholesterol was calculated (15). Diabetes was classified if a participant was using a glucose-lowering medication or had a fasting plasma glucose ≥ 126 mg/dL. IFG was defined for those with fasting glucose between 100 and 125 mg/dL, and normal glucose was <100 mg/dL (16). Fasting serum samples were batched for insulin measured by the sandwich immunoassay method (Roche Elecsys 2010; Roche Diagnostics, Indianapolis, IN). The homeostasis model assessment of insulin resistance (HOMA-IR) was used to measure insulin resistance and calculated as insulin_0 ($\mu\text{IU/mL}$) \times glucose_0 (mmol/L)/22.5, and HOMA- β was used to measure β -cell function and was calculated as $20 \times \text{insulin}_0$ ($\mu\text{IU/mL}$)/ glucose_0 (mmol/L) $- 3.5$ (17). Individuals taking diabetes medications were excluded from the analyses of HOMA-IR and HOMA- β due to bias in the measurement with treatment effects.

MESA Study Methods

The study design, eligibility, and methods for MESA have been previously published (13). MESA includes individuals from four racial/ethnic groups (whites, African Americans, Latinos, and Chinese Americans). We used data from the baseline MESA examination (2000–2002) for this analysis. Identical questionnaires for sociodemographic characteristics and physical activity and protocols for seated blood pressure and anthropometry were used as described above for the MASALA study.

Serum glucose was measured from fasting samples by the glucose oxidase method (Ortho Clinical Diagnostics, Johnson & Johnson). Serum insulin was measured from baseline samples with the Beckman Access assay. To harmonize this insulin assay with newer-generation assays with the Roche Elecsys assay that were used in future MESA exams (as well as the MASALA study), a calibration study was performed to calculate a formula for serum insulin values that correlated with the Roche method. The calibration formula is as follows: calibrated insulin = $1.656 + [0.208 \times (\text{Beckman Access assay result} \times 6)]$.

Similar definitions were used for diabetes, impaired and normal fasting glucose, and HOMA-IR and HOMA- β . We excluded six MESA participants from

this analysis who had fasting glucose levels <64 mg/dL and were not taking diabetes medications since HOMA- β could not be calculated.

To have a similar age range of participants from both the MASALA and MESA studies, individuals in the MASALA study <44 years of age were excluded from this analysis, leaving a total of 799 South Asians who were compared with the four MESA racial/ethnic groups (2,611 whites, 1,879 African Americans, 1,493 Latinos, and 801 Chinese Americans).

Statistical Analyses

Baseline characteristics of the MASALA participants and each of the MESA racial/ethnic groups were summarized using descriptive statistics as appropriate. The crude, age-/site-/sex-adjusted, and fully adjusted prevalence of normal, IFG, and diabetes within each race/ethnicity and for each sex was estimated using multinomial logistic regression models, followed by regression standardization (18). Fully adjusted models included

age, sex, clinical site, educational attainment, family income, current smoking, alcohol use, exercise, BMI, waist circumference, HDL cholesterol, triglycerides, hypertension, and fasting insulin. We purposely did not adjust for HOMA-IR or HOMA- β because fasting glucose is a common component of these surrogate measures and the outcome of this analysis, complicating interpretation.

Average HOMA-IR and HOMA- β levels for each racial/ethnic group were estimated using linear models adjusting for age, sex, site, BMI, waist circumference, fasting glucose, smoking status, physical activity levels, and alcohol use. Because HOMA-IR and HOMA- β are right skewed, these measures were log transformed for analysis, and then the results were back transformed to the measured scale. Linear models adjusting for site and sex were also used to examine the association between the HOMA measures and age among participants not using diabetes medications within each racial/ethnic

group. Specifically, we regressed log-transformed HOMA values on a three-knot restricted cubic spline in age and then plotted the back-transformed fitted values against age. We also used this approach to examine the associations between HOMA and BMI and waist circumference, by race/ethnicity and then by sex, adjusting for age and site. Tests for interaction were used to determine whether the associations between HOMA and age, BMI, and waist circumference differed by race/ethnicity or sex. Scatter plots were used to assess the potential influence of outliers.

All analyses were conducted in SAS version 9.3 (SAS Institute, Cary, NC) and Stata version 12.1 (Stata Corporation, College Station, TX).

RESULTS

Table 1 shows the baseline characteristics of the MASALA and MESA participants by racial/ethnic group. South Asians were significantly younger than the MESA groups and had higher educational

Table 1—Baseline characteristics of MASALA and MESA participants by race/ethnicity

	South Asian, <i>n</i> = 799	White, <i>n</i> = 2,611	African American, <i>n</i> = 1,879	Latino, <i>n</i> = 1,493	Chinese American, <i>n</i> = 801
Male sex (%)	53	48	45	48	48
Age (years)	57 ± 9	63 ± 10	62 ± 10	61 ± 10	62 ± 10
Immigrants to U.S. (%)	99	7	9	69	96
Education ≥Bachelor (%)	87	50	34	10	39
Family income ≥\$75,000 (%)	71	36	16	7	17
Current smoker (%)	3	12	18	14	6
Alcohol use ≥1 drink/week (%)	33	64	52	47	21
Exercise (MET-min/week)*	945 (330–1,837)	1,852 (874–3,360)	1,665 (630–3,570)	1,204 (424–2,730)	1,260 (607–2,422)
BMI (kg/m ²)	26 ± 4	28 ± 5	30 ± 6	29 ± 5	24 ± 3
Waist circumference (cm)	93 ± 10	98 ± 14	101 ± 15	101 ± 13	87 ± 10
Systolic blood pressure (mmHg)	126 ± 16	124 ± 20	132 ± 22	127 ± 22	125 ± 22
Diastolic blood pressure (mmHg)	73 ± 10	70 ± 10	75 ± 10	72 ± 10	72 ± 10
Hypertension (%)†	43	39	59	42	37
LDL cholesterol (mmol/L)	2.87 ± 0.83	3.03 ± 0.78	3.00 ± 0.85	3.10 ± 0.85	2.97 ± 0.75
HDL cholesterol (mmol/L)*	1.24 (1.03–1.50)	1.29 (1.06–1.58)	1.29 (1.06–1.58)	1.16 (1.01–1.40)	1.24 (1.03–1.45)
Triglycerides (mmol/L)*	1.34 (1.00–1.78)	1.29 (0.87–1.85)	1.02 (0.74–1.39)	1.52 (1.08–2.17)	1.40 (0.98–1.94)
Fasting glucose (mmol/L)*	5.38 (5.00–6.05)	4.83 (4.50–5.27)	5.05 (4.61–5.66)	5.11 (4.66–5.77)	5.11 (4.77–5.61)
Fasting insulin (pmol/L)*	60 (42–88)	45 (33–66)	53 (37–77)	57 (39–83)	46 (36–65)
HOMA-IR (μIU/mL, mmol/L)*‡	2.3 (1.5–3.5)	1.6 (1.1–2.4)	1.9 (1.3–2.9)	2.0 (1.4–3.2)	1.8 (1.3–2.6)
HOMA-β (μIU/mL/mmol/L)*‡	111 (75–156)	118 (86–167)	118 (82–171)	124 (85–181)	101 (75–144)
Diabetes medication use (%)	18	4	14	14	10
Glucose category§					
Normal	55	83	68	67	70
IFG	24	11	15	15	17
Diabetes	21	6	18	18	13

*Median (interquartile range) shown for skewed variables. †Hypertension defined by systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or use of an antihypertensive medication. ‡Excludes those using any diabetes medications. §IFG defined by fasting glucose 100–125 mg/dL; diabetes defined by fasting plasma glucose ≥126 mg/dL and/or use of a diabetes medication.

Table 2—Prevalence of IFG and diabetes in five ethnic groups with sequential adjustment for covariates, MASALA and MESA studies

	South Asian, n = 799	White, n = 2,611	African American, n = 1,879	Latino, n = 1,493	Chinese American, n = 801
Crude IFG prevalence (%)	24.3 (21.3–27.2)	11.2 (10.0–12.4)†	14.8 (13.2–16.4)†	15.5 (13.6–17.3)†	17.1 (14.5–19.7)†
Crude DM prevalence (%)	21.1 (18.3–24.0)	6.0 (5.1–7.0)†	17.7 (15.9–19.4)*	17.7 (15.7–19.6)*	13.1 (10.8–15.4)†
Age-, sex-, and site-adjusted DM prevalence (%)	23.2 (18.3–28.1)	5.9 (4.9–6.8)†	18.0 (15.9–20.0)	17.0 (14.9–19.3)*	13.2 (10.6–15.8)†
Fully adjusted DM prevalence (%)‡	26.7 (21.2–32.3)	6.3 (5.3–7.3)†	16.4 (14.5–18.3)*	14.5 (12.6–16.3)†	16.0 (12.9–19.1)†
Men n = 422		n = 1,256	n = 837	n = 720	n = 388
Crude IFG prevalence (%)	27.0 (22.8–31.2)	13.6 (11.7–15.5)†	17.4 (14.9–20.0)†	17.5 (14.7–20.3)†	21.1 (17.1–25.2)
Crude DM prevalence (%)	26.8 (22.5–31.0)	7.6 (6.1–9.0)†	19.5 (16.8–22.2)*	19.0 (16.2–21.9)*	13.9 (10.5–17.4)†
Age- and site-adjusted DM prevalence (%)	31.0 (23.5–38.4)	7.0 (5.5–8.4)†	18.6 (15.6–21.5)*	20.5 (16.9–24.1)*	14.3 (10.4–18.2)†
Fully adjusted DM prevalence (%)‡	32.5 (24.4–40.6)	7.1 (5.6–8.6)†	17.7 (14.8–20.5)*	17.8 (14.6–21.1)†	18.8 (13.9–23.8)*
Women n = 377		n = 1,355	n = 1,042	n = 773	n = 413
Crude IFG prevalence (%)	21.2 (17.1–25.3)	9.0 (7.5–10.5)†	12.7 (10.6–14.7)†	13.6 (11.2–16.0)*	13.3 (10.0–16.6)*
Crude DM prevalence (%)	14.8 (11.3–18.4)	4.6 (3.5–5.8)†	16.2 (14.0–18.5)	16.4 (13.8–19.0)	12.3 (9.2–15.5)
Age- and site-adjusted DM prevalence (%)	15.5 (9.5–21.5)	4.8 (3.6–6.0)†	17.4 (14.6–20.3)	14.2 (11.5–16.8)	12.2 (8.7–15.8)
Fully adjusted DM prevalence (%)‡	22.4 (14.3–30.4)	5.6 (4.2–6.9)†	15.2 (12.7–17.7)	11.7 (9.5–13.8)*	12.9 (9.2–16.7)*

Data are presented for the overall study populations, then separately by sex. First data are presented as crude rates and then with age, sex, and site adjustment and finally with full covariate adjustment. DM, diabetes. *0.001 ≤ P < 0.05 for comparison with South Asians. †P < 0.001 for comparison with South Asians. ‡Adjusted for age, sex, clinical site, education, family income, smoking, alcohol use, exercise, BMI, waist circumference, HDL cholesterol, triglycerides, hypertension, and fasting insulin.

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attainment and family income and less current tobacco use. South Asians also had lower physical activity levels than all of the MESA groups. The Chinese Americans had the lowest mean BMI and waist circumference, followed by the South Asians, whites, and Latinos, with African Americans having the highest BMI. South Asians had higher fasting median glucose and insulin values, higher HOMA-IR, lower HOMA-β, higher diabetes medication use, and significantly higher prevalence of IFG (24%) and diabetes (21%) than all four MESA racial/ethnic groups.

Table 2 shows the prevalence of diabetes comparing South Asians to each of the MESA racial/ethnic groups overall and by sex. After adjusting for age, sex, and study site, there was a larger difference in diabetes prevalence between the South Asians (23%) and the other groups. Further adjustment for potential explanatory variables that could explain the association between race/ethnicity and diabetes, including education, family income, smoking, alcohol use, exercise, BMI, waist circumference, HDL, triglycerides, hypertension, and fasting insulin, increased the adjusted

prevalence of diabetes in South Asians (27%) and widened the differences between South Asians and each racial/ethnic group. In sex-stratified analyses, South Asian men had a significantly higher prevalence of IFG and diabetes than men and women in all other ethnic groups. In unadjusted analyses, South Asian women had a significantly higher prevalence of IFG than women in other ethnic groups, but had a similar prevalence of diabetes compared with African American, Latino, and Chinese American women. In fully adjusted analyses for women, South Asian women had a

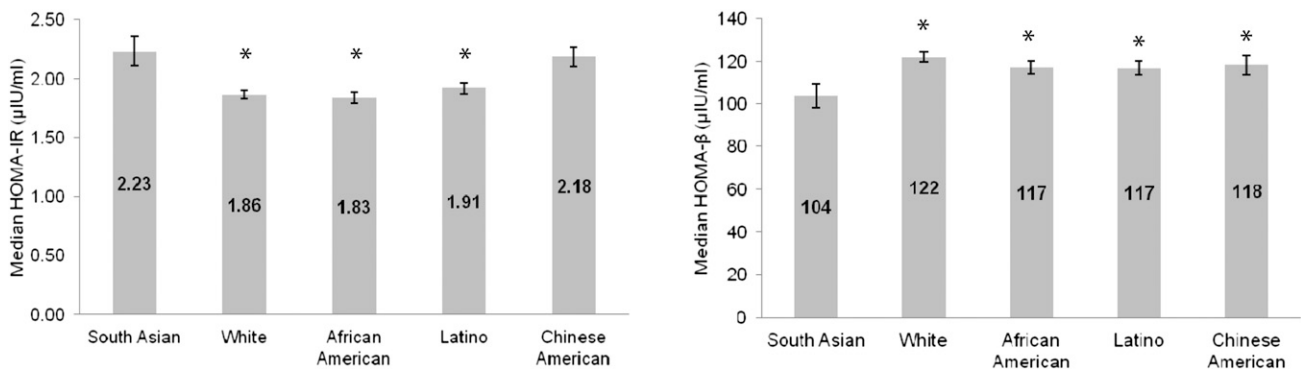


Figure 1—Median (95% CI) HOMA-IR and HOMA-β values adjusted by sex, age, clinical site, fasting glucose level, BMI, waist circumference, physical activity levels, smoking, and alcohol use; excludes those on any diabetes medications; the MASALA and MESA studies. *P < 0.001 in comparison to South Asians.

higher diabetes prevalence compared with all other groups except for African Americans. Within each racial/ethnic group, after full covariate adjustment, men had a significantly higher diabetes prevalence compared with women.

Figure 1 displays the adjusted medians for HOMA-IR and HOMA- β by racial/ethnic group among participants who were not taking diabetes medications. South Asians had a higher HOMA-IR and lower HOMA- β compared with the other racial/ethnic groups, and this difference persisted after adjusting for

their main determinants, including fasting glucose value. The only adjusted interethnic comparison that was not significantly different was between South Asians and Chinese Americans for HOMA-IR outcome. Figure 2 shows the spline curves for insulin resistance (A) and β -cell function (B) over the age distribution for each racial/ethnic group, adjusted for sex and clinical site. Race/ethnicity significantly modified the association between age and insulin resistance (P for interaction = 0.001), but the association between age and

HOMA- β was similar for each racial/ethnic group (P for interaction = 0.27). Additionally, in all ethnic groups, the association between age and HOMA-IR was stronger in men than in women (P for interaction = 0.02). In contrast, although South Asians had the lowest levels of HOMA- β compared with all other groups, the gradual decline in β -cell function by age was common to all racial/ethnic groups and to both men and women.

The association between BMI and HOMA-IR showed a log-linear relationship

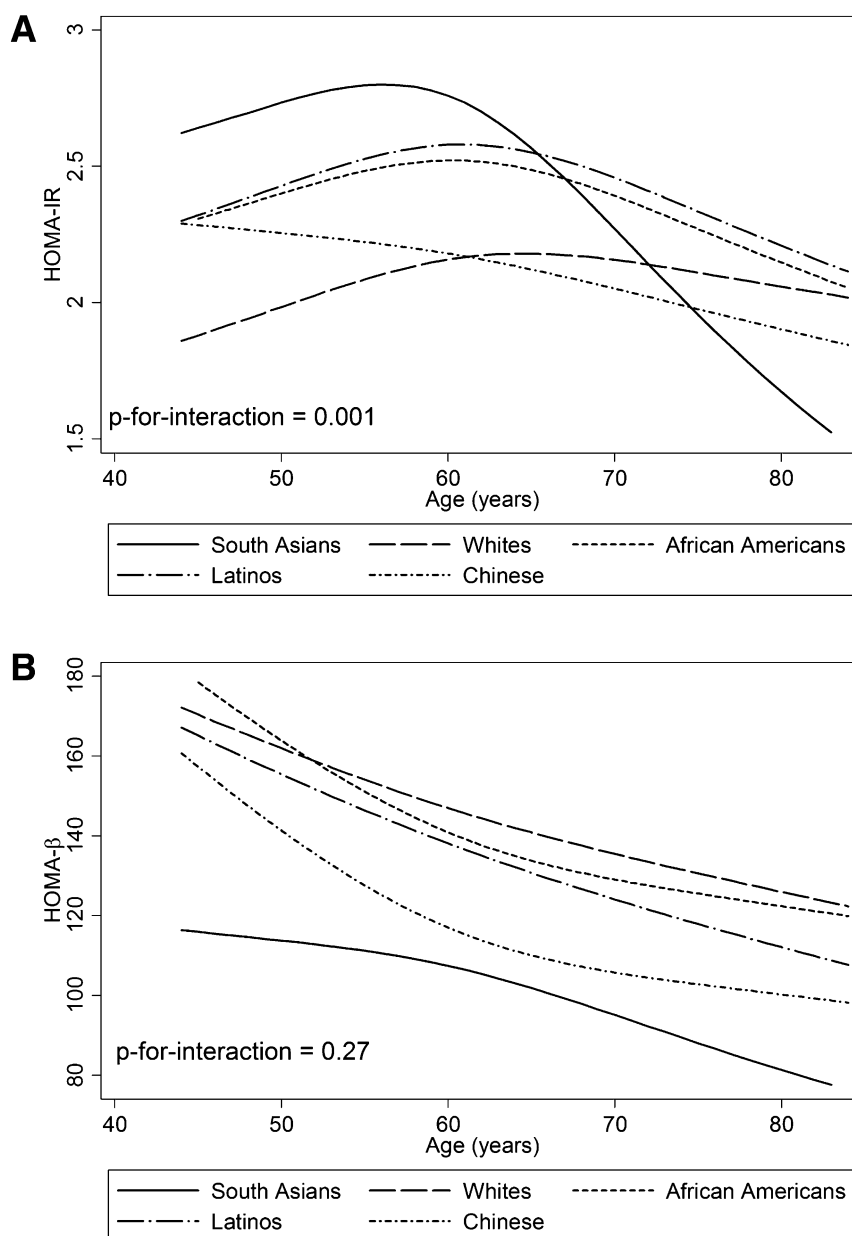


Figure 2—Association between age and insulin resistance (A) and β -cell function (B) in the five racial/ethnic groups adjusted for sex and clinical site; excludes those on any diabetes medications; the MASALA and MESA studies.

in most racial/ethnic groups, but South Asians had a distinct nonlinear pattern, with faster increases in HOMA-IR in the region with BMI <30 kg/m² but slower increases above that level (P for interaction <0.001) (Fig. 3A). On average, the trend in HOMA-IR was steepest for Chinese Americans. HOMA- β was lowest among South Asians at any given BMI (P for interaction <0.001) (Fig. 3B), and on average, the trend was steepest among Chinese Americans. These relationships were more significant in men than women in all racial/ethnic groups (P for interaction by sex <0.001). Plotting HOMA-IR and HOMA- β against waist circumference revealed similar results in the four MESA ethnic groups but somewhat different patterns in the South Asians (Fig. 3, lower panels). In particular, trends among South Asians in both metabolic measures accelerated across the range of waist circumference,

in contrast to their decelerating trends in the region with BMI >30 kg/m².

CONCLUSIONS

In a large community-based sample of South Asians without existing cardiovascular disease, we confirmed that South Asians have a significantly higher prevalence of prediabetes and diabetes than four other U.S. ethnic groups (11). Additionally, South Asian men have the highest diabetes prevalence overall, whereas South Asian women have a higher diabetes prevalence than white and Chinese American women but a similar prevalence to African American and Latino women. The broad disparity in diabetes among South Asians compared with the other ethnic groups was further widened after adjusting for all potential correlates of diabetes. South Asians have higher HOMA-IR levels and lower HOMA- β than all other

ethnic groups after adjusting for age and adiposity. These findings suggest that South Asians may have lower β -cell function and are unable to compensate for higher glucose levels due to insulin resistance, which ultimately leads to the dramatically higher rates of type 2 diabetes.

South Asians are known for having high type 2 diabetes prevalence in native (19,20) and diaspora settings (2,21,22). Studies that have directly compared diabetes prevalence in South Asians with other ethnic groups in North America have found higher diabetes rates among South Asians than most other ethnic groups (23–25). Similarly, we found that middle- to older-aged South Asians in the U.S. with higher socioeconomic attainment than South Asians living in other Western countries still have a significantly higher IFG and diabetes prevalence compared with

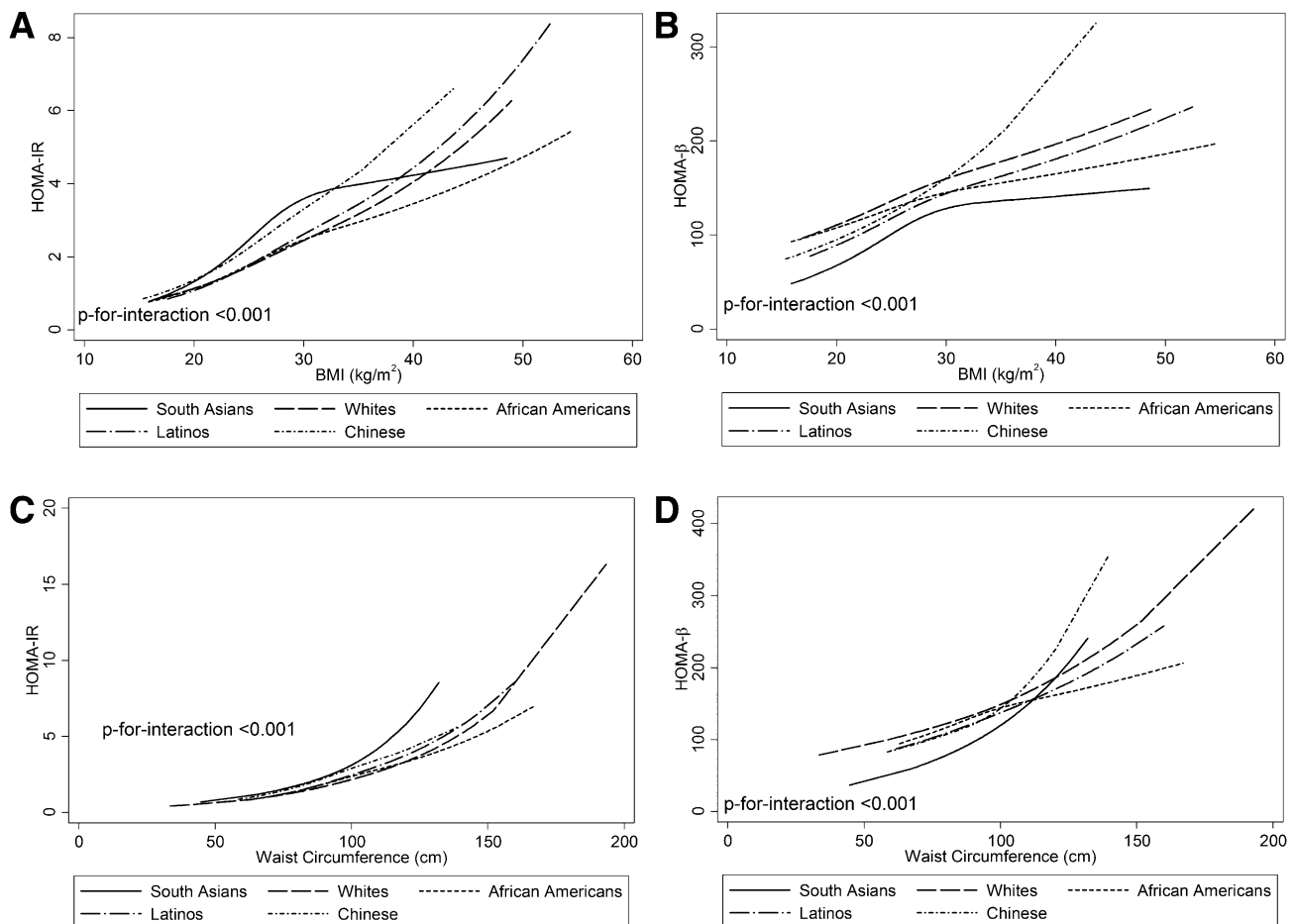


Figure 3—Association between BMI (A and B) and waist circumference (C and D) with insulin resistance (left panels) and β -cell function (right panels); adjusted for sex, age, and site; excludes those on any diabetes medications; MASALA and MESA studies. P for interaction <0.001 for each figure.

four other ethnic groups. Adjusting for sociodemographic, lifestyle, and metabolic covariates only enhanced the difference between South Asians and other ethnic groups, suggesting that other unmeasured factors, including biologic differences in the mechanisms of diabetes and a higher genetic burden (26), may be responsible.

We compared insulin resistance patterns by age and adiposity and found that South Asians have higher HOMA-IR levels compared with other ethnic groups. Although no prior studies have compared as many ethnic groups directly with South Asians, several have reported that South Asians have higher basal insulin levels and a higher insulin response to a glucose load than Europeans (27) and Chinese (28–30). Moreover, studies have found that a higher percentage of body fat and abdominal adiposity in South Asians (31) does not appear to explain these high levels of insulin resistance (32,33).

We also found that South Asians have lower β -cell function at all ages than other ethnic groups, although the decline with age appears to be similar to other groups. Whereas others have found reduced β -cell function in Asian Indians (9), others have noted that β -cell function declines more rapidly with age in Asian Indians than other ethnic groups (28). It is unclear whether there may be a genetic predisposition to lower β -cell mass and function, earlier β -cell loss from environmental factors, or quicker β -cell exhaustion from higher levels of insulin resistance or a complex combination of all of these factors among South Asians (34).

There was a notable difference in the spline curves between BMI and waist circumference for both HOMA-IR and HOMA- β that was observed only among South Asians. Increases in HOMA-IR and HOMA- β plateau in the region above BMI of 30 kg/m², whereas both measures continue to increase across the range of waist circumference values. This inconsistency in the associations between these two surrogate measures of body adiposity may be due to sparse data with few South Asians having BMI >30 kg/m², but also underscores the findings of early studies where central adiposity was much more closely linked to insulin resistance and diabetes than BMI in South Asians (35). This finding also

provides further evidence that for assessing metabolic risk, waist circumference is a better measure of adiposity than BMI among South Asians.

Although we were able to compare glycemic status between South Asians and four other well-phenotyped U.S. ethnic groups, we were limited to using fasting glucose and insulin measures and did not have more sophisticated measures of insulin resistance or β -cell function. The cross-sectional design also limits us from comparing the relative strengths of insulin resistance or β -cell function as risk factors for diabetes. We also did not have comparable measures of dietary intake in both studies and were unable to determine whether diet may explain some of the ethnic differences in diabetes prevalence. Although the South Asians in MASALA are representative of middle-aged South Asians in the U.S. (12), the findings may not generalize to all South Asians in native or other diaspora settings with very different socioeconomic and environmental exposure.

In conclusion, South Asians have a significantly higher prediabetes and diabetes prevalence than other U.S. ethnic groups, which is not explained by known risk factors. South Asians have significantly higher insulin resistance and lower β -cell function than other ethnic groups. The biological and genetic mechanisms underlying these differences deserve further study. Prospective follow-up of the MASALA study cohort can assess whether insulin resistance and β -cell function explain the higher diabetes rates in South Asians.

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Author Contributions. A.M.K. conceived the project, researched data, and wrote the manuscript. D.H. contributed to the interpretation of the results and reviewed and edited the manuscript. E.V. supervised and contributed to the data analyses and reviewed and edited the

manuscript. S.K.E. performed the data analysis and reviewed and edited the manuscript. K.L. and M.J.B. reviewed and edited the manuscript. S.S.D. and F.Q. collected data and reviewed and edited the manuscript. N.R.K. contributed to the interpretation of the results and reviewed and edited the manuscript. A.M.K. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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