

Original Research

Higher Protein Intake Is Associated with Diabetes Risk in South Asian Indians: The Metabolic Syndrome and Atherosclerosis in South Asians Living in America (MASALA) Study

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Objective: Despite a high prevalence of type 2 diabetes in South Asian Indians, the impact of diet in this high-risk ethnic group has not been fully explored. The association of macronutrient intake and diabetes in South Asian Indians was examined in this cross-sectional study.

Methods: A population-based cohort of 146 South Asian Indians aged 45–79 years without existing cardiovascular disease living in the San Francisco Bay Area was recruited between August 2006 and October 2007. Macronutrient intake was assessed with a food-frequency questionnaire developed and validated in South Asians. Diabetes was defined by use of a hypoglycemic medication, a fasting plasma glucose level ≥ 126 mg/dL, or a 2-hour post-challenge glucose level ≥ 200 mg/dL. The association between energy-adjusted macronutrient intake and diabetes was explored using multivariable logistic regression models.

Results: Forty-one (28%) participants had type 2 diabetes; 20 were unaware of this diagnosis and were classified as having diabetes by laboratory testing. In a model fully adjusted for age, sex, waist circumference, and hypertension, there was a 70% increase in the odds of diabetes per standard deviation in gram of protein intake/day (standardized OR 1.70 [95% CI 1.08, 2.68], $p = 0.02$). There was a trend toward increased protein intake and diabetes in the subset of participants with previously unknown, laboratory-diagnosed diabetes. Results did not vary significantly by sex, body mass index, or dietary pattern.

Conclusions: Higher level of protein intake was associated with increased odds of diabetes in this cohort of South Asian Indians. Diet may be a modifiable lifestyle factor in this high-risk ethnic group.

INTRODUCTION

Ethnicity is a well-known risk factor for type 2 diabetes. Studies have demonstrated an increased prevalence of metabolic syndrome and diabetes mellitus in the South Asian population compared to other ethnic groups [1]. A population-based study in India demonstrated a 15.5% prevalence of diabetes [2]. By using fasting glucose testing and self-report of treated diabetes, a recent population-based sample of South

Asian Indians in the United States found a diabetes prevalence of 17% in individuals >18 years of age [3].

Diet and nutritional intake are modifiable risk factors in the development of diabetes. Generally, studies show that dietary patterns characterized by a high consumption of vegetables, fruits, fish, poultry, and whole grains are inversely associated with diabetes risk, whereas dietary patterns characterized by a high intake of red or processed meats, refined grains, fried foods, and sweets demonstrate a positive association with

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The authors have no conflicts of interest to disclose.

Abbreviations: FFQ = Food Frequency Questionnaire, MASALA = Metabolic Syndrome and Atherosclerosis in South Asians Living in America, MESA = Multi-Ethnic Study of Atherosclerosis, SHARE = Study of Health Assessment and Risk in Ethnic Groups.

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diabetes. These studies have been primarily conducted in white European cohorts [4,5]; however, similar associations between protein intake and diabetes have been noted in ethnically diverse groups as well [6–8].

To further explore the association between diet and risk of diabetes in immigrant South Asian Indians, cross-sectional data collected from a population-based cohort of 150 South Asian Indians living in the San Francisco Bay Area was analyzed. The association between macronutrient intake and diabetes, as well as the effects of age, sex, waist circumference, and hypertension, were explored.

MATERIALS AND METHODS

Subjects

This study was a cross-sectional analysis of 150 South Asian Indians recruited from the San Francisco Bay Area between August 2006 and October 2007 for the Metabolic Syndrome and Atherosclerosis in South Asians Living in America (MASALA) study. The sampling strategy and recruitment procedures have been previously described [9]. Briefly, this study was modeled on the Multi-Ethnic Study of Atherosclerosis (MESA) [10]. To be eligible, participants had to be between age 45 and 79 years, self-identified as South Asian Indian, and have no cardiovascular disease. Excluded were those under cancer treatment, with impaired cognitive ability, life expectancy <5 years, with plans to move, or living in a nursing home. Also excluded were persons who could not speak or understand Hindi or English. We randomly sampled South Asian Indians using surname lists from a commercial marketing company (Genesys Marketing System Group, Washington, PA) for a goal of recruiting 150 participants. Participants were invited to a single session to complete the clinical measurements and laboratory tests described below.

The University of California, San Francisco, Institutional Review Board approved the study protocol, and all study participants provided written informed consent.

Clinical Measurements

Participants completed face-to-face, interviewer-administered questionnaires to ascertain medical history, smoking, alcohol use, and physical activity. Physical activity was measured using the Typical Week Activity Survey. Macronutrient intake was assessed with the Study of Health Assessment and Risk in Ethnic (SHARE) groups South Asian Food Frequency Questionnaire (FFQ), which was developed and validated in South Asians [11]. Briefly, the FFQ included 163 items, of which 61 were unique to the South Asian diet. The FFQ asked participants to describe their usual eating habits over the last 12 months, including frequency and serving size.

Using the Food Processor nutrient analysis software (version 6.11, 1996, ESHA, Salem, OR), diet records were then analyzed for nutrient composition. For each participant, the mean nutrient intake was calculated by summing across all food items the product of the frequency of consumption of each food, the portion size, and the nutrient composition of that item. Energy-adjusted nutrient intake was determined by using regression analyses to compute residuals of nutrient intake, thereby controlling for confounding and extraneous variation from total energy intake [12]. Four participants were excluded because they did not satisfy the *a priori* criteria of reporting daily energy intake of 800–4200 kcal/24 hours. Intake of fat, carbohydrates, and protein was expressed in 3 ways: absolute intake, percent of total caloric intake, and energy-adjusted intake.

Participants' weight was measured on a digital clinical scale (Acme Scale Co., San Leandro, CA) and height was measured with a stadiometer (Holtain Ltd., Crosswell, Crymych, Pembrokeshire, Wales, Britain). Waist circumference was measured using a Gullick II tape measure (Country Technology Inc., Gay Mills, WI) at the site of maximum circumference midway between the lower ribs and the anterior superior iliac spine. Three seated blood pressure measurements were obtained with an automated blood pressure monitor (Philips-Agilent V24C, Andover, MA). Mean systolic and diastolic blood pressures were calculated from the second and third blood pressure measurements. Hypertension was defined as blood pressure $\geq 140/90$ mm Hg or the use of antihypertensive medications.

Diabetes Outcome

A 12-hour fasting blood sample was obtained from each participant. Each participant was then given a 75-g oral glucose load and another blood sample was taken after 120 minutes. Plasma glucose was measured using an automated analyzer (YSI 2300 STAT Plus, YSI Life Sciences, Yellow Springs, OH). A participant was categorized as having diabetes if he or she reported use of a hypoglycemic medication, had a fasting plasma glucose ≥ 126 mg/dL, or had a 2-hour post-challenge glucose ≥ 200 mg/dL [12]. All other participants were categorized as not having diabetes.

Statistical Analyses

Associations of baseline covariates with diabetes status were assessed using the Kruskal-Wallis test for continuous variables and the χ^2 test for categorical variables. To determine macronutrient association (specifically protein) with diabetes status, multivariable logistic regression models were used. Energy-adjusted protein intake approximated a normal distribution, so it was treated as a continuous variable. The model was initially adjusted for age and sex, and then further adjusted for waist circumference and hypertension. Using the fully

Table 1. Baseline Characteristics of MASALA Participants by Diabetes Status, 2006–2007^a

Characteristic	n/N	Diabetes (n = 41)	No Diabetes (n = 105)	p Value ^b
Age (years)	146/146	58 ± 7	57 ± 8	0.28
Sex, n (%)				
Male	73/146	28 (68)	45 (43)	0.006
Female	73/146	13 (32)	60 (57)	
≥B.S. (education), n (%)	115/146	30 (73)	85 (81)	0.30
≥\$75,000 (family income), n (%)	98/146	25 (61)	73 (70)	0.32
Body mass index (kg/m ²)	146/146	27.1 ± 4.6	25.8 ± 4.6	0.05
Waist circumference (cm)	146/146	102 ± 11	94 ± 12	0.003
Male		100 ± 10	97 ± 9	0.09
Female		105 ± 14	92 ± 14	0.004
Physical activity (mets/wk), median (IQR)	146/146	1050 (548–2250)	1418 (683–2760)	0.31
Male		1103 (484–2044)	1470 (683–2475)	0.32
Female		1050 (788–3008)	1331 (648–2801)	0.69
Current smoking, n (%)	5/146	0 (0)	5 (5)	0.16
Alcohol (≥7 drinks/wk), n (%)	15/146	5 (12)	10 (10)	0.63
HDL-cholesterol (mg/dL)	146/146	45 ± 11	50 ± 14	0.04
Triglycerides (mg/dL)	146/146	149 ± 76	126 ± 56	0.16
Hypertension, n (%)	61/146	29 (71)	32 (30)	<0.001

^a Values represent mean ± standard deviation unless otherwise noted.

^b p Values comparing the overall groups by diabetes status, calculated by χ^2 test or Kruskal-Wallis test as appropriate. Significant values shown in bold-faced type.

B.S. = Bachelor of Science degree, HDL = high-density lipoprotein, IQR = interquartile range, MASALA = Metabolic Syndrome and Atherosclerosis in South Asians Living in America.

adjusted model, which includes age, sex, waist circumference, and hypertension, the association between protein intake and diabetes was also examined in the subset of 20 participants with previously unknown, laboratory-diagnosed diabetes. These participants were not aware of their diabetes status prior to enrollment in the study. In addition, subgroup analyses based on sex, body mass index (BMI), dietary patterns, and type of protein consumed were performed on all 146 participants. Stata (version 10, 2007, StataCorp, College Station, TX) was used for all statistical analyses.

RESULTS

Of all eligible persons, 150/248 (60.5%) were enrolled in the study. The average age of the 146 participants was 57 ± 8 (mean ± SD) years. Ninety-nine percent of the participants were immigrants, averaging 24 ± 11 years of residence in the United States. Forty-one (28%) participants had type 2 diabetes, of whom 20 (49%) were unaware of their diagnosis prior to enrollment in the study.

Table 1 shows the association of baseline covariates with diabetes status. Sex, waist circumference, high-density lipoprotein cholesterol, and hypertension were significantly associated with diabetes.

Table 2 illustrates the association of dietary intake with diabetes. Total energy intake was similar among those with diabetes (1935 ± 732 kcal/day) and without diabetes (1911 ±

681 kcal/day). Twenty-nine participants adhered to a lacto-vegetarian diet, 32 were lacto-ovo-vegetarian, and 85 consumed a diet that included meat. Overall macronutrient consumption was 52 ± 6% carbohydrates, 28 ± 5% total fat, and 15 ± 3% protein. Macronutrient intake is represented in 3 ways—absolute intake, percent of total energy intake, and energy-adjusted intake. Energy-adjusted protein intake was higher among participants with diabetes (74 ± 17 g/day) than in those without diabetes (69 ± 14 g/day) ($p = 0.03$). Further categorization of source of protein intake (animal, fish, or vegetable) did not seem to be associated with diabetes status. Neither energy-adjusted carbohydrate nor energy-adjusted total fat intake was significantly associated with diabetes. Total fiber intake was not associated with diabetes status ($p = 0.61$).

Table 3 shows sequential logistic regression models of the association between energy-adjusted protein intake and diabetes among the participants. In an unadjusted logistic regression model, there was 47% increase in odds of diabetes per standard deviation in gram of protein intake/day (standardized OR 1.47 [95% CI 1.02, 2.12], $p = 0.04$). In a model adjusted for age and sex, the association was intact (standardized OR 1.85 [95% CI 1.20, 2.84], $p = 0.005$). In a fully adjusted model for age, sex, waist circumference, and hypertension, the association remained robust (standardized OR 1.70 [95% CI 1.08, 2.68], $p = 0.02$).

In the subset of 20 participants who had previously unknown, laboratory-diagnosed diabetes, higher protein intake

Table 2. Dietary Intake of MASALA Participants by Diabetes Status, 2006–2007^a

	Diabetes			No Diabetes			<i>p</i> Value ^b
	Overall (n = 41)	Men (n = 28)	Women (n = 13)	Overall (n = 105)	Men (n = 45)	Women (n = 60)	
Calories (kcal/day)	1935 ± 732	1922 ± 808	1965 ± 562	1911 ± 681	2067 ± 673	1794 ± 669	0.94
Dietary type, n (%)							0.47
Lacto-vegetarian	6 (15)	5 (18)	1 (8)	23 (22)	9 (20)	14 (23)	
Lacto-ovo-vegetarian	8 (20)	3 (11)	5 (38)	24 (23)	12 (27)	12 (20)	
Non-vegetarian diet	27 (66)	20 (71)	7 (54)	58 (55)	24 (53)	34 (57)	
Protein (g/day)							
Absolute	75 ± 38	74 ± 42	79 ± 29	68 ± 28	68 ± 23	69 ± 32	0.58
Percent	15.2 ± 2.7	14.9 ± 2.9	15.8 ± 2.4	14.3 ± 2.6	13.1 ± 2.0	15.1 ± 2.7	0.05
Energy-adjusted	74 ± 17	73 ± 18	77 ± 14	69 ± 14	62 ± 12	73 ± 13	0.03
Animal protein	32 ± 15	32 ± 16	33 ± 13	29 ± 16	24 ± 14	33 ± 17	0.29
Fish protein	4 ± 6	3 ± 5	4 ± 8	2 ± 3	1 ± 2	2 ± 3	0.28
Vegetable protein	38 ± 8	38 ± 7	39 ± 9	37 ± 8	37 ± 9	38 ± 7	0.47
Carbohydrates (g/day)							
Absolute	275 ± 98	270 ± 102	286 ± 90	282 ± 100	305 ± 104	264 ± 94	0.75
Percent	50.5 ± 4.7	50.6 ± 4.8	50.2 ± 4.9	52.7 ± 5.7	53.2 ± 6.0	52.2 ± 5.5	0.03
Energy-adjusted	272 ± 32	269 ± 33	279 ± 32	282 ± 34	285 ± 41	280 ± 27	0.10
Fat (g/day)							
Absolute	60 ± 24	60 ± 26	62 ± 17	60 ± 25	62 ± 26	58 ± 24	0.78
Percent	28.2 ± 3.7	27.9 ± 3.5	28.8 ± 4.3	27.9 ± 5.0	26.8 ± 5.3	28.7 ± 4.7	0.73
Energy-adjusted	60 ± 7	59 ± 6	61 ± 9	60 ± 11	57 ± 14	61 ± 9	0.99

^a Values represent mean ± standard deviation unless otherwise noted.

^b *p* Values comparing the overall groups by diabetes status, calculated by *t*-test or Kruskal-Wallis test as appropriate. Significant values shown in bold-faced type. MASALA = Metabolic Syndrome and Atherosclerosis in South Asians Living in America.

was also associated with a 65% increase in standardized odds ratio of diabetes ($p = 0.08$). Secondary analysis showed that combined animal protein intake (animal and fish) was more likely to be associated with diabetes ($p = 0.07$) than was vegetable protein intake ($p = 0.26$). Sex, BMI, and dietary patterns did not show an interaction with energy-adjusted protein intake.

DISCUSSION

In a population-based cohort of South Asian Indians living in the San Francisco Bay area, the prevalence of type 2

diabetes was 28%. This prevalence is higher than that reported in other studies in the literature due to the older age of the participants and the fact that the diagnosis of diabetes included a 2-hour glucose challenge test.

Currently, there are no good estimates of dietary patterns among South Asian Indians living in the United States. This study demonstrated that higher dietary protein intake was associated with higher odds of diabetes in a sample of South Asian Indians living in the San Francisco Bay Area; however, it could not be determined whether animal or fish or vegetable protein was responsible for this increased risk.

This association between protein intake and diabetes is supported in the literature among the white European

Table 3. Sequential Models Showing the Association between Energy-Adjusted Protein Intake (per standard deviation of g/day) and Diabetes among MASALA Participants, 2006–2007

	Standardized Odds Ratio	95% Confidence Interval	<i>p</i> Value ^a
Unadjusted model	1.47	1.02–2.12	0.04
Minimally adjusted model ^b	1.85	1.20–2.84	0.005
Fully adjusted model ^c	1.70	1.08–2.68	0.02
Previously unknown, laboratory-diagnosed diabetes	1.65	0.95–2.87	0.08

^a Significant values shown in bold-faced type.

^b Adjusted for age and sex.

^c Adjusted for age, sex, waist circumference, and hypertension.

MASALA = Metabolic Syndrome and Atherosclerosis in South Asians Living in America.

population and other ethnic groups. A population-based study of 6814 white, African American, Hispanic, and Chinese adults demonstrated that a dietary pattern characterized by high intake of tomatoes, beans, refined grains, high-fat dairy, and red meat was associated with an 18% greater risk of diabetes [6]. These findings were not modified by race or ethnicity. Another case-control study concluded that among residents of Vietnam, significantly higher intakes of protein, especially animal protein, were observed in diabetic compared to control subjects [7]. In Calcutta, India, a study of the dietary intake of 200 individuals (80 lean controls, 70 lean diabetics, and 50 obese diabetics) revealed a significant increase in the amount of total protein consumed per day by obese individuals with diabetes (62.4 g) compared to lean controls (60.4 g) [8]. However, given the variation in which protein intake is reported and the difference in study methodologies, it is difficult to make a direct assessment regarding the increased odds of diabetes per gram of protein as compared to other ethnic groups. Within the South Asian ethnic group, another study utilized the same South Asian FFQ and found an inverse relationship between protein intake and abdominal obesity [13]. Although the present study did not address abdominal obesity, waist circumference was adjusted for in the multivariable logistic regression model.

The role of dietary protein in the pathogenesis of diabetes may be mediated through several possible mechanisms, including saturated fats, nitrites, and advanced glycation end products. Previous studies demonstrated that a diet high in red meat and processed meats is associated with diabetes [4,5]. Nitrites are used in processed meats as a preservative and have been shown to be associated with type 1 diabetes in children [14], as well as reduced insulin secretion in rats [15]. Advanced glycation end products, known to cause oxidative stress *in vitro* [16], are found in meat and high-fat products [17]. This could, in turn, lead to inflammation, which may play a role in diabetes development [18].

The main limitation of the cross-sectional design of this study involves the possibility of reverse causality. Among the 21 participants with a known diagnosis of diabetes, it is possible that they increased protein intake and decreased carbohydrate intake as a direct result of their diabetes diagnosis, which could account for the findings of this study. The questionnaires administered did not ascertain whether diet had been modified. However, in an effort to address this limitation, additional analyses were performed on the subset of 20 participants who were not aware of their diabetes status prior to enrollment in the study. These participants were classified with diabetes based on elevated fasting or 2-hour glucose results obtained for the study, and thus could not have made dietary changes as a result of diabetes prior to the study. In this subset of participants, there was a trend toward

increased odds of diabetes and higher protein intake, which supports the main finding of this study.

Other limitations of this study include the small sample size and the assessment of macronutrient intake, which is subject to recall bias. The FFQ requires participants to recall food intake over the last 1 year, which is very difficult. However, FFQs are used in many epidemiologic studies. The study may also have limited generalizability. It excluded participants who did not speak English or Hindi; thus, the dietary patterns may not reflect South Asian Indians who speak another dialect. Although the data were collected from 150 South Asian Indians living in the San Francisco Bay Area, the cohort's high socioeconomic status parallels that of South Asian Indians in the United States as described in a recent Pew Charitable Trusts survey [19] and the Census 2000 data [20]. Therefore, the results from this study plausibly apply to the South Asian Indian population living elsewhere in the United States.

Future studies include dietary pattern analyses to better understand nutrition in this population. Protein consumption will also be further evaluated to determine whether red meat or processed meats are the main contributors to the association between protein intake and diabetes. The cohort is anticipated to have follow-up visits, which will allow for exploration of dietary changes and diabetes status.

CONCLUSIONS

Higher levels of protein intake were associated with increased odds of diabetes in a sample of South Asian Indians, aged 45–79 years, living in the San Francisco Bay area. Diet may be a modifiable risk factor in this high-risk ethnic group.

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