Metabolism
Clinical and Experimental

VOL 52, NO 2 FEBRUARY 2003

Alcohol Intake and Glycemia in American Indians: The Strong Heart Study

Weiquan Lu, Kathleen A. Jablonski, Helaine E. Resnick, Arvind K. Jain, Kristina L. Jones, Adrienne M. Gottlieb, Thomas K. Welty, Elisa T. Lee, Richard R. Fabsitz, and Barbara V. Howard

The goal of this study was to explore the relationship between alcohol intake and glycemia and type 2 diabetes in American Indians aged 45 to 74 years. Data were obtained from participants in the Strong Heart Study, a longitudinal study of 13 American Indian communities in 3 geographic areas in the United States. Alcohol consumption was determined by self-reported alcohol intake history. Participants previously diagnosed with diabetes were excluded from the analysis. Analysis of covariance (ANCOVA) was used to estimate the adjusted means of blood glucose for alcohol intake categories. Logistic regression was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) to estimate the association between alcohol intake and type 2 diabetes in the cross-sectional analysis and between alcohol intake and glucose intolerance using longitudinal data. Fasting and 2-hour plasma glucose concentrations showed an inverse J-shaped curve across categories of alcohol intake. Using never drinkers as the referent group in cross-sectional analysis, light drinkers had a significantly lower risk of having diabetes (OR, 0.66; 95% CI, 0.44 to 0.99); among drinkers, heavy drinkers had a higher, although not significant, prevalence of diabetes. Longitudinal analysis showed no significant worsening of glucose tolerance across levels of alcohol intake. Subanalyses stratified by body mass index (BMI) did not show differences between obese and non-obese participants in the relationship between alcohol intake and glucose tolerance. Although plasma glucose concentration showed a shallow, inverse J-shaped association across levels of increasing alcohol intake in American Indians aged 45 to 74 years, alcohol intake did not appear to significantly increase the risk for worsening glucose tolerance. Thus, alcohol intake does not appear to be a determinant of diabetes risk in this population.

THE POSSIBLE INFLUENCE of alcohol intake on worsening of glucose tolerance and development of type 2 diabetes is a subject of debate. Although a positive association between alcohol intake and type 2 diabetes has been reported in some cross-sectional and prospective studies,[1-4] an inverse association has been observed in others.[5-7] Studies on alcohol intake and glucose metabolism also show inconsistent results according to the amount and duration of alcohol consumption.[8,9] Some prospective studies reported a U-shaped relationship, with an elevated risk of developing type 2 diabetes in non-drinkers and heavy drinkers compared with light or moderate drinkers.[10,11]

American Indians have disproportionately high rates of diabetes and impaired glucose tolerance (IGT) compared with the general US population.[12,13] Although the prevalence of current drinking is lower among middle-aged to elderly American Indians than age-matched national rates, binge drinking is common among those who drink alcohol, and alcohol intake has been tentatively linked to a variety of health problems in American Indians.[14-16] This study explores both cross-sectional and prospective associations between alcohol consumption and blood glucose concentrations and type 2 diabetes in American Indians in the Strong Heart Study.

MATERIALS AND METHODS

Initiated in 1988, the Strong Heart Study is a longitudinal, population-based study of cardiovascular disease (CVD) and its risk factors in 13 American Indian communities in Arizona, Oklahoma, and South and North Dakota.[15] The study methods and laboratory techniques of

From the MedStar Research Institute and Washington Hospital Center, Washington, DC; Aberdeen Area Tribal Chairmen's Health Board, Rapid City, SD; Center for American Indian Health Research, University of Oklahoma Health Sciences Center, Oklahoma City, OK; and the Epidemiology and Biometry Program, National Heart, Lung, and Blood Institute, Bethesda, MD.

Submitted December 14, 2001; accepted August 26, 2002.

Supported by cooperative agreement grants (#U01-HL41642, #U01HL41652, and #UL01HL41654) from the National Heart, Lung, and Blood Institute. The opinions herein are those of the authors and do not necessarily reflect the view of the Indian Health Service.

Address reprint requests to Barbara V. Howard, PhD, MedStar Research Institute, 6495 New Hampshire Ave, Suite 201, Hyattsville, MD 20783.

0026-0495/03/5202-0001$35.00/0
doi:10.1053/meta.2003.50020

the study have been detailed elsewhere.[15,17] Briefly, the study population for the baseline examination included 4,549 American Indians aged 45 to 74 years between July 1989 and January 1992 at 3 study centers: Arizona, Oklahoma, and South and North Dakota. Participants were resident members of the following tribes: the Pima (Akimel O'odham)/Maricopa (Pee Posh)/Papago (Tohono O'odham) of central Arizona in the Gila River, Salt River, and Ak Chin Indian communities; the 7 tribes of Southwestern Oklahoma (Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa, and Wichita); the Oglala and Cheyenne River Sioux in South Dakota; and the Spirit Lake Community in the Fort Totten area of North Dakota. Participation rates of all age-eligible tribal members were 72% in the Arizona center, 62% in the Oklahoma center, and 55% in the South/North Dakota center.[17-19] Participants were similar to non-participants in age and self-reported frequency of diabetes. The study protocol was approved by the Indian Health Service Institutional Review Board (IRB), by the IRBs of the participating institutions, and by the participating American Indian communities. Baseline clinical examinations (1989 to 1992) consisted of a personal interview, physical examination, and laboratory tests; all survey methods and procedures in the second examination (1993 to 1995) were similar to those used at baseline.

The personal interview assessed demographic information, including education, marital status, family health history, personal medical history, American Indian heritage, and lifestyle factors, such as physical activity, smoking, and alcohol consumption. Parental diabetes was noted if 1 or both parents had diabetes. Hypertension was defined as systolic blood pressure $\geq$ 140 mm Hg or diastolic blood pressure $\geq$ 90 mm Hg or use of antihypertension medication. "Income sufficient" was defined as income equaling or exceeding expenses. Physical activity was assessed with a validated questionnaire with which participants were queried about the type, weekly frequency, and hours of leisure-time physical activity. An estimate of an individual's physical activity level was the reported leisure time (including walking for exercise) activity averaged over the past year and defined as hours per week.[20]

Alcohol intake was determined by self-reported alcohol intake history, the type of alcoholic beverages consumed, frequency of alcohol consumption, and average quantity consumed per day and per week. Alcohol intake was converted to drinks: 1 drink of alcohol was defined as 12 oz of beer, 4 oz of wine, or 1 shot of hard liquor. Interviewers were trained to convert other quantities of alcoholic beverages into numbers of drinks. For this analysis, participants were categorized as never-drinkers, former drinkers, or current drinkers. Former drinkers had stopped consuming alcohol for $\geq$ 12 months. Individuals were classified as current drinkers if they had consumed any alcohol during the previous year. Current drinkers were then ranked according to number of drinks consumed per week as light drinkers ($<$4 drinks), moderate drinkers (4 to 12 drinks), or heavy drinkers ($>$12 drinks). Binge drinking was quantified as the number of times participants drank $\geq$ 5 drinks on a single occasion in the past month or year, as well as the usual number of "binge" drinks consumed per day.

After obtaining informed consent, blood samples were drawn from participants in the morning after at least a 12-hour overnight fast. Glucose, plasma fibrinogen, insulin, lipids and lipoproteins, creatinine, and glycosylated hemoglobin (HbA_{1c}) were measured in fasting blood samples. A 75-g oral glucose tolerance test (OGTT) was performed on all participants, except for diabetic persons treated with insulin or oral hypoglycemic agents or participants with a fasting glucose $\geq$ 225 mg/dL as determined by an Accu Check II (Baxter Healthcare, Grand Prairie, TX).[12] Laboratory methods were published previously.[15,17]

World Health Organization (WHO) criteria were used for defining diabetes status[21] based on fasting and 2-hour plasma glucose, as well self-reported diabetes history by questionnaire. Diabetic participants were determined to have (1) known diabetes if they were taking insulin or oral hypoglycemic agents or had fasting plasma glucose (FPG) $\geq$ 126 mg/dL or 2-hour blood glucose $\geq$ 200 mg/dL and a history of diabetes; or (2) new diabetes if they had a FPG $\geq$ 126 mg/dL or 2-hour blood glucose $\geq$ 200mg/dL and no history of diabetes; (3) normal glucose tolerance (NGT) if they had a FPG $<$126 mg/dL and 2-hour blood glucose $<$140 mg/dL; or (4) impaired glucose tolerance (IGT) if they had a FPG $<$126 mg/dL and 2-hour blood glucose 140 to 199 mg/dL and no history of diabetes. In order to assess whether obesity modulates the association between alcohol intake and glycemia, we conducted subanalyses among obese and non-obese participants. Obesity was defined, according to WHO/National Institutes of Health criteria, as a body mass index (BMI) $\geq$ 30 kg/m^2.[22,23]

Some of the 4,549 eligible participants refused the OGTT, and a small number of blood samples were lost during shipping to the laboratory (n = 245); therefore, diabetes status was determined for 4,304 of the participants examined. To avoid confounding by lifestyle changes made after diagnosis, the 1,698 participants with known diabetes were excluded from this study, as well as an additional 5 participants for whom no alcohol data were available. Thus, data from 2,601 of the 4,549 Strong Heart Study participants were used in this analysis. The second examination was conducted between 1993 and 1995; average follow-up time between the baseline and second examination was approximately 4 years, and 88% of the surviving participants were re-examined.

Data were analyzed using the SAS statistical package (SAS Institute, Cary, NC). Because of the skewed distributions, insulin and triglyceride levels were logarithm transformed before being used in the analysis as continuous variables. The associations between alcohol intake and baseline characteristics and suspected risk factors were assessed by multiple regression analysis for continuous variables and by logistic regression analysis for categorical variables. All analyses were adjusted for gender and age. Analysis of covariance (ANCOVA) was used to calculate means of fasting and 2-hour glucose for each category of alcohol intake after adjustment for age, gender, and study center. Pair-wise tests on the adjusted means were computed to determine if the means significantly differed from one another. To evaluate the consistency of the association between plasma glucose concentrations and alcohol intake by sex, first-order interaction terms were added to the multiple regression model.

Logistic regression was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) to estimate the association between alcohol intake and type 2 diabetes in the cross-sectional analysis and alcohol intake and the progression of glucose intolerance using longitudinal data. A specific alcohol intake category was compared with the corresponding data in the reference category after adjusting for the possible simultaneous effects of potential confounders, such as age, gender, BMI, smoking status, physical activity, insulin, total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides.

RESULTS

Baseline characteristics are shown by alcohol intake category in Table 1, with 47.1% of participants self-reporting as current drinkers. The mean weekly alcohol intake among current drinkers was 7.9 drinks per week (standard deviation, 13.0); the distribution of alcohol intake was substantially skewed, with a median of 2 drinks. Overall, a significantly higher proportion of men than women were current drinkers, with the gender disproportion increasing with increasing levels of alcohol intake. After adjustment for gender and age, the tests for trend across alcohol categories for each variable suggested significant associations for all baseline characteristics except parental diabetes, total cholesterol, and fibrinogen. Smoking and leisure time physical activity increased with alcohol intake, whereas age and the proportion of currently married partici-

Table 1. Baseline Characteristics of Participants Without Previously Diagnosed Diabetes by Alcohol Intake Category in American Indians: The Strong Heart Study

Characteristics	Alcohol Intake					*P* for Trend
	Never	Former	Light (≤3 drinks/wk)	Moderate (4-12 drinks/wk)	Heavy (≥12 drinks/wk)	
Participants (n)	365	1,011	657	282	286	
Age (yr)	59 (60)	56 (56)	54 (54)	54 (54)	53 (53)	<.0001†
Gender (male%)	14 (13)	42 (42)	45 (46)	59 (60)	70 (71)	<.0001‡
Currently married (%)	49 (55)	54 (55)	48 (47)	34 (31)	33 (28)	<.0001‡
Parental diabetes (%)	33 (36)	39 (40)	41 (39)	36 (35)	46 (43)	.3801‡
Body mass index (kg/m^2)	31 (31)	31 (31)	30 (30)	29 (29)	30 (30)	<.0001†
Waist circumference (cm)	106 (105)	105 (105)	101 (101)	100 (100)	102 (103)	<.0001†
Current smoker (%)	17 (20)	34 (35)	45 (44)	50 (49)	61 (59)	<.0001‡
Physically active (h/wk)	5 (6)	7 (7)	8 (7)	8 (8)	9 (8)	<.0001†
Hypertension (%)	20 (18)	20 (19)	21 (22)	26 (27)	28 (30)	<.0001‡
Income sufficient (%)	77 (77)	74 (74)	76 (76)	69 (69)	67 (67)	.0262‡
High school education (%)	46 (51)	61 (62)	66 (64)	52 (50)	51 (48)	.0461‡
Insulin (μU/mL)*	16 (15)	15 (15)	12 (12)	11 (11)	11 (11)	<.0001†
Total cholesterol (mg/dL)	190 (190)	192 (192)	197 (197)	189 (190)	193 (193)	.2798†
HDL cholesterol (mg/dL)	48 (45)	44 (44)	49 (49)	50 (51)	51 (54)	<.0001†
Triglycerides (mg/dL)*	115 (116)	116 (116)	112 (111)	106 (105)	110 (109)	.0134†
Fibrinogen (mg/dL)	297 (288)	288 (287)	283 (284)	277 (281)	284 (291)	.8571†

NOTE. Data are means or %, observed (adjusted). Adjusted for age and gender, except age only adjusted for gender and gender for age.
*Geometric mean.
†Multiple regression model.
‡Logistic regression model.

pants decreased across alcohol intake categories. Insulin concentrations tended to decrease and HDL cholesterol and hypertension tended to increase with increasing alcohol intake, but triglycerides showed no definite tendency by alcohol intake. There was an inverse relationship between alcohol intake and socioeconomic factors, ie, income sufficiency and high school education decreased with increased alcohol intake. Current drinkers had a lower BMI and smaller waist circumference than never and former drinkers.

The baseline mean 2-hour and fasting glucose concentrations across categories of alcohol intake are shown in Fig 1. The relationship between 2-hour/fasting glucose concentrations and alcohol intake shows shallow inverse J-shaped curves with increasing alcohol intake level. The lowest glucose concentrations were in light and moderate drinkers. Among the pair-wise comparisons, there were statistically significant differences in means between never and light drinkers and moderate drinkers ($P = .037$ and $P = .0079$, respectively) for 2-hour glucose. Fasting glucose concentrations were significantly different between never and light drinkers ($P = .048$). Compared with light and moderate drinkers, heavy drinkers had higher levels of glucose, but the differences were not significant. These results were consistent in men and women and independent of age, BMI, smoking status, study center, and physical activity. At the baseline examination, 515 participants were newly diagnosed with diabetes. Using never drinkers as the referent group,

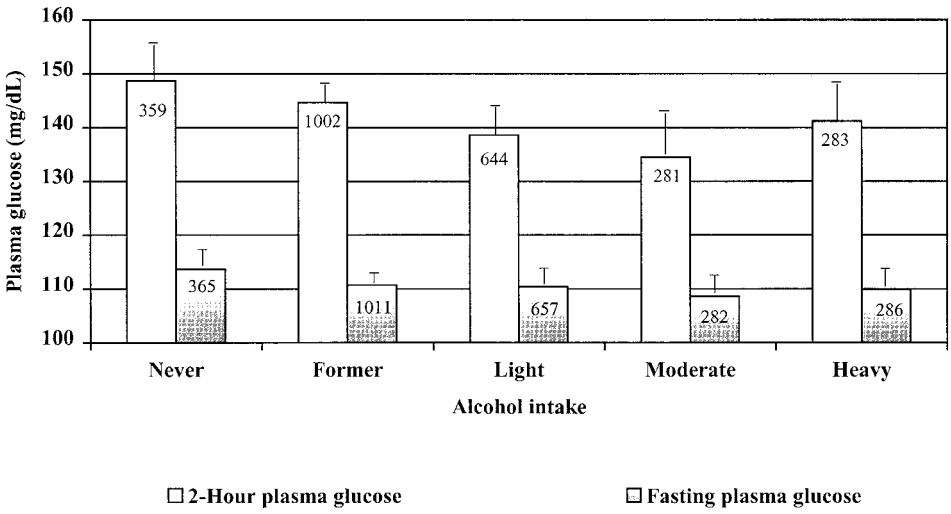

Fig 1. Mean concentrations of fasting glucose and 2-hour glucose by category of alcohol intake: The Strong Heart Study.

Table 2. Cross-Sectional Association of Alcohol Intake and Diabetes in American Indians: The Strong Heart Study

	Alcohol Intake				
	Never	Former	Light (≤3 drinks/wk)	Moderate (4-12 drinks/wk)	Heavy (≥12 drinks/wk)
Total					
Diabetic	98	194	116	50	57
Nondiabetic	267	817	541	232	229
OR (95% CI)*	1	0.77 (0.56-1.06)	0.64 (0.44-0.94)	0.76 (0.46-1.24)	0.89 (0.52-1.52)
OR (95% CI)†	1	0.72 (0.52-1.00)	0.66 (0.44-0.99)	0.74 (0.44-1.26)	0.86 (0.48-1.54)
Non-obese					
Diabetic	31	60	44	20	28
Nondiabetic	133	431	336	158	139
OR (95% CI)*	1	0.66 (0.38-1.13)	0.60 (0.32-1.12)	0.70 (0.31-1.61)	1.39 (0.60-3.24)
OR (95% CI)†	1	0.66 (0.38-1.16)	0.61 (0.32-1.18)	0.76 (0.32-1.80)	1.38 (0.55-3.51)
Obese					
Diabetic	67	134	72	30	29
Nondiabetic	134	386	205	74	90
OR (95% CI)*	1	0.83 (0.56-1.23)	0.69 (0.43-1.11)	0.78 (0.42-1.47)	0.65 (0.32-1.32)
OR (95% CI)†	1	0.77 (0.51-1.16)	0.72 (0.43-1.21)	0.72 (0.36-1.45)	0.64 (0.29-1.41)

*Adjusted for age, gender, BMI, smoking status, physical activity, and study center.

†Adjusted for the covariates in *, above, plus waist circumference, hypertension, insulin, HDL cholesterol, and triglycerides.

logistic regression analyses were performed to calculate the ORs for the cross-sectional association between type 2 diabetes and categories of alcohol intake (Table 2). After adjustment for age, gender, BMI, smoking status, physical activity, and study center, overall OR for the association of alcohol intake with diabetes status was 0.75 (95% CI, 0.56 to 0.99). When waist circumference, hypertension, insulin, HDL cholesterol, and triglycerides were entered into the model, the association was only slightly changed, ie, overall OR was 0.72 (0.54 to 0.98). When using categories of alcohol intake, light drinkers had a significantly lower OR for diabetes of 0.64 (0.44 to 0.94). Former and moderate drinkers also had a lower prevalence of diabetes compared with never drinkers, but the ORs did not reach statistical significance. Heavy drinkers had a slightly elevated OR compared with former and moderate drinkers, but this OR was also not significant. Additional adjustments for waist circumference, hypertension, insulin, HDL cholesterol, and triglycerides did not significantly change the associations between alcohol intake and type 2 diabetes. A subanalysis of the effect of obesity on the association between alcohol intake and diabetes did not reveal significant differences between the groups, although the OR was somewhat elevated in non-obese heavy drinkers.

Of the 1,697 nondiabetic patients (1,186 with NGT and 511 with IGT) for whom alcohol data were obtained in the first examination, 300 participants developed diabetes at the second examination; the 4-year cumulative incidence of diabetes was 17.7%. Risk for worsening glucose tolerance (progression of NGT to IGT, NGT to diabetes, or IGT to diabetes) over follow-up was not significantly associated with alcohol intake. For non-obese participants, a decreased incidence of worsening glucose tolerance was observed in light drinkers, but the association was not statistically significant (Table 3). We repeated these analyses using incident WHO-defined diabetes, with similar results (overall OR is 0.87; 95% CI, 0.59 to 1.28).

DISCUSSION

In the present study, we analyzed the relationships between alcohol intake and plasma glucose and alcohol intake and diabetes in 2,601 American Indians 45 to74 years of age. We found that both fasting and 2-hour plasma glucose concentrations had an inverse J-shaped relationship across categories of alcohol intake, in which never drinkers had significantly higher mean plasma glucose levels and heavy drinkers had nonsignificantly higher levels compared with light and moderate drinkers. In cross-sectional analysis, light drinkers had a significantly lower risk of having diabetes than never drinkers. In contrast, longitudinal analyses revealed no significant risk of worsening glucose tolerance across levels of alcohol intake groups. The relationships were not influenced by obesity.

Previous epidemiologic studies that examined the association between alcohol and type 2 diabetes showed inconsistent results. Some studies reported positive associations,[1-4] some reported inverse associations,[5-7] and still others found no statistically significant association between alcohol intake and the risk of diabetes.[24-27] In a population-based, cross-sectional study of 3,128 Swedish men aged 35 to 56 years, the ORs for diabetes were 2.1 (CI, 1.0 to 4.5) in heavy drinkers (>12 drinks per week) and 0.7 (CI, 0.3 to 1.8) in moderate drinkers (7 to 12 drinks per week) compared with occasional drinkers after adjustment for family history, smoking, physical activity, and BMI.[4] The Physicians Health Study, an evaluation of 20,951 individuals aged 40 to 84 years who were free of diabetes, CVD, and cancer at baseline, found that light and moderate alcohol intake decreased the risk of type 2 diabetes compared with rare or never drinking, in which relative risk (RR) was 0.74 (CI, 0.59 to 0.93) for those reporting alcohol use of 2 to 4 drinks per week, 0.67 (CI, 0.51 to 0.89) for those reporting alcohol use of 5 to 6 drinks per week, and 0.57 (CI, 0.45 to 0.73) for those reporting alcohol use of 1 or more drinks per day (there were too few heavy drinkers in the study to ana-

Table 3. Prospective Association of Alcohol Intake and Worsening Glucose Tolerance in American Indians: The Strong Heart Study

	Alcohol Intake				
	Never	Former	Light (≤3 drinks/wk)	Moderate (4-12 drinks/wk)	Heavy (≥12 drinks/wk)
Total					
Worsening*	80	215	120	58	56
Non-worsening†	145	456	328	120	119
OR (95% CI)‡	1	0.97 (0.68-1.38)	0.89 (0.59-1.33)	1.18 (0.68-2.03)	1.21 (0.64-2.30)
OR (95% CI)§	1	0.90 (0.63-1.30)	0.90 (0.59-1.37)	1.28 (0.73-2.27)	1.18 (0.61-2.28)
Non-obese					
Worsening*	33	83	58	35	26
Non-worsening†	76	262	217	84	80
OR (95% CI)‡	1	0.92 (0.54-1.57)	0.70 (0.39-1.24)	1.34 (0.62-2.87)	1.83 (0.68-4.91)
OR (95% CI)§	1	0.89 (0.51-1.56)	0.74 (0.41-1.35)	1.67 (0.72-3.88)	1.97 (0.70-5.570)
Obese					
Worsening*	47	132	62	23	30
Non-worsening†	69	194	111	36	39
OR (95% CI)‡	1	0.96 (0.60-1.55)	1.11 (0.63-1.97)	1.02 (0.46-2.26)	0.76 (0.31-1.85)
OR (95% CI)§	1	0.90 (0.55-1.47)	1.08 (0.60-1.94)	1.00 (0.44-2.26)	0.68 (0.26-1.74)

Abbreviations: NGT, normal glucose tolerance; IGT, impaired glucose tolerance.

*Progression of NGT to diabetes, NGT to IGT, or IGT to diabetes.

†Glucose tolerance remained the same or improved.

‡Adjusted for age, gender, BMI, smoking status, physical activity, and study center.

§Adjusted for the covariates in ‡, above, plus waist circumference, hypertension, insulin, HDL cholesterol, and triglycerides.

lyze).[7] In a cross-sectional study of 3 populations at high risk for type 2 diabetes, alcohol intake was not significantly associated with prevalence of type 2 diabetes or IGT in 8,700 people not previously known to have diabetes.[24] In South Australian Aborigines, a population known to have a high level of alcohol intake and a high prevalence of type 2 diabetes, no differences in alcohol intakes among normal, borderline diabetic, or diabetic individuals were found.[25] In our study, both cross-sectional and longitudinal associations were examined using the same cohort of individuals.

In the current study, our data showed that both fasting and 2-hour plasma glucose concentrations had an inverse J-shaped relationship across the categories of alcohol intake. Several previous studies have reported a U-shaped relationship between alcohol intake and diabetes, ie, an elevated risk of type 2 diabetes in nondrinkers and heavy drinkers.[10,11] A U-shaped association between alcohol intake and type 2 diabetes was found in a prospective study of 8,633 men aged 30 to 79 years, with a higher risk of developing diabetes in nondrinkers and heavy drinkers compared with moderate drinkers.[9] The British Regional Heart Study also found a shallow U-shaped relationship between alcohol intake and diabetes, in which moderate drinkers had a significantly lower relative risk of type 2 diabetes compared with occasional drinkers after adjustment for age and BMI.[11]

A previous study demonstrated that American Indians have high rates of obesity and insulin resistance, with insulin resistance increasing with obesity.[15] Among healthy subjects, light and moderate alcohol drinking were reported to be associated with increased insulin sensitivity and decreased fasting plasma insulin levels.[28-30] Therefore, if light or moderate alcohol intake enhances insulin sensitivity and improves glucose disposal, the association between alcohol intake and glucose tolerance may be stronger in non-obese individuals, who are less insulin resistant. In the current study, we assessed whether obesity had a modulating effect on the association of alcohol intake and glucose tolerance and found that obesity did not appear to modify the relationship between alcohol intake and diabetes prevalence in cross-sectional data, or alcohol and progression of glucose tolerance in longitudinal analysis. In contrast, the Osaka Health Survey, which enrolled 6,362 Japanese men aged 35 to 61 years who did not have diabetes, impaired fasting glucose, hypertension, or liver cirrhosis at study entry, revealed that daily heavy alcohol consumption ($\geq$ 50.1 mL/d) was strongly and positively associated with risk of type 2 diabetes (RR = 2.48; 95% CI, 1.31 to 4.71) compared with no alcohol intake (after adjustment for confounding variables) in lean men (BMI $\leq$ 22). Whereas, among men with a BMI $\geq$ 22.1, moderate drinking (29.1 to 50 mL/d) was associated with a decreased risk of diabetes, with a multiple-adjusted RR of 0.58 (0.39 to 0.87).[31]

It has been reported that moderate alcohol intake may increase insulin sensitivity and lower insulin resistance. Compared with moderate drinkers, heavy drinkers, nondrinkers, and light drinkers have been reported to have higher insulin resistance, whereas moderate alcohol intake is shown to improve glucose disposal rates or response to ingested carbohydrates.[28-30,32] In the Insulin Resistance and Atherosclerosis Study, an inverse U-shaped relationship between alcohol intake and insulin sensitivity was observed.[33] This observation may explain the finding in the current study of lower glycemic levels in the light and moderate drinkers.

In this study, both cross-sectional and longitudinal associations were examined. The alcohol intake variables represented current and past drinking habits. In the cross-sectional analysis, we excluded participants who had previously diagnosed diabetes, because they may have reduced their alcohol intake after they were diagnosed with diabetes. Alcohol consumption data

were collected before diagnosis of new diabetes in the baseline examination. In the prospective study, we analyzed the participants who were free of diabetes at baseline; therefore, drinking habits and the recall of alcohol intake would not have been influenced by disease status. We also considered the possible confounding that could have occurred among nondrinkers, because this group could include individuals who stopped consuming alcohol because of preexisting disease or an alcohol problem. Thus, in the analysis, we divided nondrinkers into never drinkers and former drinkers to minimize the effect of these possible confounders. We could not do subanalyses for former drinkers who may have been heavy drinkers, moderate drinkers, or light drinkers, because of lack of detailed data, but our analyses on the relationship between glucose and current alcohol intake provide additional evidence for alcohol moderation.

In epidemiologic studies, self-reported alcohol intake information has been consistently underreported.[34] Binge drinking ($\geq$ 5 drinks on 1 occasion) is a relatively common pattern of drinking among American Indians. Current drinkers reported that binge drinking accounted for 53% of their drinking during the past month or 71% of their drinking during the past year. Similar trends were seen when light and moderate drinkers who reported binge drinking in the past month were excluded from the analysis; those who had $>$10 binges in the past month were also similar to heavy drinkers in terms of baseline characteristics and prevalence of diabetes. To further confirm the association between alcohol intake and glycemia observed in this population, systematic analysis of those with a high intake of alcohol is needed.

In conclusion, plasma glucose concentrations show a shallow, inverse J-shaped association across levels of increasing alcohol intake in American Indians aged 45 to 74 years, with light and moderate drinkers having significantly lower glucose concentrations. However, in longitudinal analyses, risk for worsening glucose tolerance was not significantly associated with alcohol intake. The subanalysis, in which the model is stratified by obesity, suggests that association of alcohol intake and glycemia were not modified by obesity. Thus, although alcohol intake may cause other problems, it does not appear to be a major determinant of diabetes in this population.

ACKNOWLEGMENT

The authors acknowledge the assistance and cooperation of the AkChin Tohono O'odham (Papago)/Pima, Apache, Caddo, Cheyenne River Sioux, Comanche, Delaware, Spirit Lake Community, Fort Sill Apache, Gila River, Pima/Maricopa, Kiowa, Oglala Sioux, Salt River Pima/Maricopa, and Wichita Indian communities, without whose support this study would not have been possible. The authors also wish to thank the Indian Health Service hospitals and clinics at each center, and Betty Jarvis, RN, Tauqeer Ali, MD, and Marcia O'Leary, RN, directors of the Strong Heart Study clinics and their staffs. We also gratefully acknowledge the editorial assistance of Ellen Shair, MA, ELS.

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