Depression, Diabetes, and Glycemic Control in an American Indian Community

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Objective: American Indians have a high prevalence of diabetes and its complications, and so it may be clinically important to identify psychiatric risk factors for the development of diabetes and its complications in this population. The objectives of this cross-sectional study were (1) to determine whether depression and diabetes are associated in the Pima Indians and (2) to determine if depression is associated with variables indicating risk for development of diabetes or diabetic complications.

Method: Adults (aged ≥ 18 years) who attended research examinations in the Gila River Indian Community in Arizona from July 2003 through January 2007 were included. A sample of 2902 individuals (1121 with diabetes, 1781 without diabetes) was evaluated with the depression module of the Patient Health Questionnaire (DSM-IV criteria), physical examination, and laboratory tests.

Results: The prevalence of depression was slightly, but not significantly, higher among participants with diabetes than those without diabetes (12.8% vs. 9.4%, p = .053). Among participants with diabetes, mean glycosylated hemoglobin levels were significantly higher among depressed individuals than among those who were not depressed (9.0% vs. 8.4%, p = .02), even when controlling for age, sex, duration of diabetes, and body mass index (p = .03). In participants without diabetes, mean glycosylated hemoglobin levels were similar among depressed and nondepressed participants (5.4% vs. 5.4%, p = .24).

Conclusion: Overall, participants with diabetes had a slightly, but not significantly, higher prevalence of depression than those without diabetes. Among those with diabetes, depression was associated with worse glycemic control. Treatment of depression in Pima Indians with diabetes may improve glycemic control and thereby reduce the risk of diabetic complications.

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Depression has been associated with diabetes[1] and poor glycemic control[2] in previous reports. There are also significant health care costs associated with depression in diabetes.[3,4] Most published reports as well as a recent meta-analysis have shown that depression is more common in individuals with diabetes than in those without diabetes.[1,5,6] Several prospective studies have shown that individuals with depression were approximately twice as likely to develop type 2 diabetes than those who were not depressed,[7–11] suggesting that depression is itself related to development of diabetes. One of these studies suggests that this association may be mediated through changes in central adiposity,[9] although another study reported that depression predicted development of diabetes independent of central adiposity.[11] Depression has also been associated with hyperglycemia,[2] diabetic complications,[12] and increased mortality[13] in individuals with diabetes.

The relationship between depression and diabetes may be complicated by sociodemographic factors, such as education, race, ethnicity, social support, socioeconomic status, and access to health care. One recent study of a national sample reported that depression predicted the development of future diabetes in individuals with low education levels, but not in those with high education levels.[14] The relationship of depression and diabetes has not been well studied in ethnic minority groups.[15] Although previous reports have generally shown that depression is more common among individuals with diabetes than among

those without diabetes, this association was not found in some recent studies of ethnic minority groups. In 3 studies including Hispanic participants[16–18] and in a study of a multiethnic sample,[19] depression was not associated with diabetes. However, consistent with previous reports, a recent study in Hispanic individuals with diabetes showed that hyperglycemia was associated with depression.[20] The relationship between depression and diabetes, therefore, may vary by ethnic group. Further studies of depression and diabetes in ethnic minority communities are important because diabetes represents a significant health burden in these populations.[21,22] Psychiatric diagnoses that might co-occur with either diabetes or risk factors for diabetic complications, such as hyperglycemia, warrant careful examination. Not only is there a disparity in the prevalence of diabetes between whites and ethnic minority groups,[22] but there may also be disparities in depression treatment. Recent studies have shown that Hispanics and African-Americans with diabetes were less likely to receive depression treatment than whites.[19,20,23]

There have been few published reports on the relationship between depression and diabetes in American Indians. One recent study reported that a past diagnosis of depression (although not a current depression diagnosis) was associated with current diagnosis of diabetes in 2 American Indian reservation populations.[24] In another report including people with diabetes from the national Behavioral Risk Factor Surveillance System (BRFSS), the prevalence of mental health rated "not good" was significantly higher among American Indians than among whites.[25] Both of these studies relied on self-report for diagnosis of diabetes, and neither report assessed markers for metabolic risk such as glycosylated hemoglobin (HbA_{1c}) and cholesterol. Authors of both reports call for further studies on the association between diabetes and psychiatric disorders in American Indian populations. The prevalence of diabetes among American Indians has increased substantially in recent years and is a significant public health issue.[26] American Indians, along with other ethnic minority groups in the United States, have a higher prevalence of diabetes and diabetic complications than whites.[22] For this reason, it is clinically important to identify possible psychiatric diagnoses, such as depression, that might co-occur with diabetes and diabetic complications in American Indians.

The Pima Indians in particular have a very high prevalence of type 2 diabetes.[27] In this study, we compared the prevalence of depression in Pima Indians with and without diabetes as diagnosed according to the 1997 American Diabetes Association criteria.[28] We also examined whether depression was associated with markers of metabolic risk such as HbA_{1c} and cholesterol in subjects with and without diabetes. Results from the pilot phase of this study, in which depression was assessed in face-to-face interviews with 541 persons, were published previously.[29] In the current report, depression was determined using a self-administered questionnaire. We report a large population-based study of depression and diabetes among American Indians in the United States.

METHOD

Description of Participants

Since 1965, residents of the Gila River Indian Community in Arizona, primarily from the Pima or the closely-related Tohono O'odham tribes, have participated in a longitudinal population-based study of diabetes and risk factors for diabetes conducted by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).[27] All residents of Community Districts 1 through 5 aged 5 years or older are invited to attend research examinations every 2 years whether or not they have diabetes. This is accomplished by door-to-door recruitment visits to all households in these districts. The study is also open to walk-in participants, some of whom live outside the study area. The sample reported here includes adults aged 18 years or older who were examined from July 2003, when screening for depression using the depression module of the Patient Health Questionnaire (PHQ-9) began, through January 2007.

Informed Consent/Ethics Review

This study was approved by the Institutional Review Board of the NIDDK and by the Gila River Indian Community. The investigators report study progress and results to each of these entities annually. Each participant provided written informed consent.

Measures

Depression. Depression was assessed with the PHQ-9.[30] This self-administered questionnaire was selected in consultation with Pima Indian clinic staff, who felt it was more appropriate than other depression screening tools for the study population. These staff primarily recommended the PHQ-9 because they felt its reading level was appropriate for the study population. Infrequently, when participants requested help in completing the PHQ-9, clinic staff orally administered the questionnaire. The PHQ-9 was also selected for this study because it is used routinely in the community's behavioral health clinic in evaluating people for depression, is easy to administer, and follows the diagnostic criteria for depression described in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV), of the American Psychiatric Association.[31] Following DSM-IV diagnostic criteria, the 9 symptoms included in the PHQ-9 are (1) loss of interest (anhedonia), (2) feeling down or depressed (dysphoria), (3) sleep disruption, (4) loss of energy, (5) changes in appetite, (6) feeling guilty or worthless, (7) trouble concentrating, (8) psychomotor agitation or retardation, and

Table 1. Participants in Study of Depression and Diabetes by Age, Sex, and Residence

Age	Residents in Study Area at Midpoint Census, N	Participants Examined, N		Ratio of Residents Examined/ Census[a]
		Not Residing in Study Area	Residing in Study Area	
18–34 y				
Male	1154	109	448	0.39
Female	1194	193	653	0.55
35–44 y				
Male	604	58	255	0.42
Female	659	102	322	0.49
≥ 45 y				
Male	827	38	221	0.27
Female	1006	83	420	0.42
Total	5444	583	2319	0.43

[a]This ratio is not a true fraction; the numerator is not a subset of the denominator (midpoint census) because the census population changes over time.

(9) suicidal ideation. The self-administered questionnaire asks respondents to rate how often they have experienced each of the 9 symptoms of depression during the last 2 weeks by circling one of the following responses: 0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day. Participants were classified as depressed if they reported experiencing 5 or more symptoms on "more than half the days" or "nearly every day," with 1 of the symptoms required to be anhedonia or dysphoria. When participants reported anhedonia or dysphoria for "more than half the days" or "nearly every day," the score for the questionnaire was totaled for all 9 questions. In the absence of both anhedonia and dysphoria for "more than half the days" or "nearly every day" the participant was given a score of 0. Since each symptom can be rated on a scale of zero to 3, the total PHQ-9 score for participants reporting at least 1 of the screening symptoms ranges from 2 to 27. This scoring scheme was first introduced by the creators of the PHQ-9.[30] Participants who reported 1 or more symptoms of depression were referred to mental health services when appropriate. Antidepressant and diabetes medicine use was determined by self-report and confirmed by medical chart review.

Diabetes-related clinical variables. Each participant also received a physical examination, medical history interview, and anthropometric measurements. Body mass index (BMI) was calculated from height and weight measured with participants wearing light clothing and no shoes. A 75-g oral glucose tolerance test was performed, in which plasma glucose concentrations were determined after an overnight fast and 2 hours postload. Glucose was measured by the glucose oxidase method with a glucose analyzer (Beckman Coulter, Inc., Fullerton, Calif.). Participants were classified as having diabetes according to the 1997 American Diabetes Association criteria[28] (fasting plasma glucose ≥ 126 mg/dL or 2-hour plasma glucose ≥ 200 mg/dL) or a previously documented clinical diagnosis. The stable fraction of total HbA_{1c} was measured by high-performance liquid chromatography.[32] Fasting triglyceride and cholesterol concentrations in serum were quantified on a Chiron Diagnostics Express Plus/550 Express (Ciba-Corning, Irvine, Calif.) from fasting samples. High-density lipoprotein (HDL) cholesterol was isolated using dextran sulfate/magnesium sulfate precipitation with an Express Plus (Ciba-Corning, Irvine, Calif.), and non-HDL cholesterol was calculated by subtracting the HDL cholesterol from the total cholesterol. Blood pressure was measured supine to the nearest 2 mm Hg (first and fourth Korotkoff sounds) with a large cuff and a mercury sphygmomanometer. Mean arterial pressure was computed as [(2 × diastolic blood pressure) + systolic blood pressure]/3. Cigarette smoking was determined by self-report. Participants who reported smoking at least 1 cigarette per day on average were classified as currently smoking.

Statistical Analyses

Analysis of covariance was used to compare normally distributed clinical variables in the groups with or without diabetes, adjusted for age and sex. Log transformation was used for variables that were not normally distributed, such as serum triglycerides, total cholesterol, and cholesterol subfractions. Analyses for the prevalence of depression in participants with and without diabetes were stratified by sex and compared with the Fisher exact test. General linear models controlling for age and sex were used to compare clinical variables by depression status in both groups with or without diabetes. Least squares means were adjusted for age and sex, and, where appropriate, models were adjusted further for BMI and diabetes duration. Multivariate linear regression was used to control for potential confounding variables when examining the relationship between depression and HbA_{1c} levels. For continuous variables, interaction terms were assessed with logistic regression where models included the main effects with and without interaction terms, and the significance was assessed by likelihood ratio tests. Categorical variables were analyzed by the Mantel-Haenszel procedure,[33] and interactions were tested using the Breslow-Day test. When interaction terms were statistically significant, overall main effects were not estimated.

RESULTS

Table 1 shows study participants by age, sex, and residence, as well as the total number of residents in the study area during the census estimated at the midpoint of the study period. The census does not measure diabetes or depression status. Therefore, we cannot comment on how the prevalence of depression or diabetes in the study sample compares to that of the general population residing in the study area. Participants in the study included

Table 2. Clinical Characteristics of Participants With or Without Diabetes[a]

Variable	Men (N = 1129)			Women (N = 1773)			Overall p Value for Diabetes
	No Diabetes (N = 735)[b]	Diabetes (N = 394)[c]	p Value for Diabetes	No Diabetes (N = 1046)[d]	Diabetes (N = 727)[e]	p Value for Diabetes	
Age, y	32.0 ± 11.1	44.2 ± 12.7	< .01	31.3 ± 11.0	45.6 ± 13.1	< .001	…[f]
BMI, kg/m^2	33.6 ± 7.9	35.0 ± 8.7	< .001	35.6 ± 8.6	37.5 ± 9.4	< .001	< .001
HbA_{1c}, %	5.4 ± 0.4	8.7 ± 2.5	< .001	5.4 ± 0.4	8.5 ± 2.4	< .001	< .001
Fasting glucose, mg/dL	93.3 ± 9.5	182.7 ± 78.1	< .001	90.8 ± 9.5	181.1 ± 80.1	< .001	< .001
MAP, mm Hg	91.7 ± 11.0	96.8 ± 13.8	< .001	84.0 ± 10.6	89.8 ± 11.9	< .001	< .001
Total cholesterol, mg/dL[g]	177 (152, 199)	181 (154, 208)	.02	165 (145, 189)	173 (150, 196)	< .001	< .001
HDL cholesterol, mg/dL[g]	43 (37, 54)	42 (35, 50)	< .01	46 (39, 56)	45 (38, 54)	< .001	< .001
Non-HDL cholesterol, mg/dL[g]	129 (104, 154)	134 (108, 160)	.01	117 (98, 138)	124 (104, 151)	< .001	< .001
Triglycerides, mg/dL[g]	113 (77, 170)	139 (95, 219)	< .01	102 (72, 144)	141 (100, 202)	< .01	< .001
Oral hypoglycemic use, N (%)	0 (0)	213 (54.1)	NA	0 (0)	500 (69.1)	NA	NA
Insulin use, N (%)	0 (0)	70 (17.8)	NA	0 (0)	202 (27.8)	NA	NA
Current smoking, N (%)[h]	212 (29.1)	85 (21.7)	< .01	228 (21.9)	88 (12.1)	< .001	< .001

[a]Unless otherwise stated, data are expressed as mean ± standard deviation (SD). The p values for diabetes association are computed with general linear models adjusted for age within sex groups, except for age, where the p values are unadjusted. Overall p values for diabetes are computed with general linear models adjusted for age and sex.
[b]Missing data for BMI (13 subjects), HbA_{1c} (2 subjects), MAP (2 subjects), total cholesterol and HDL and non-HDL cholesterol (1 subject), serum triglycerides (9 subjects), and current smoking (7 subjects).
[c]Missing data for BMI (10 subjects), HbA_{1c} (25 subjects), fasting glucose (27 subjects), total cholesterol (23 subjects), HDL and non-HDL cholesterol (33 subjects), serum triglycerides (32 subjects), oral hypoglycemic use (3 subjects), and current smoking (2 subjects).
[d]Missing data for BMI (12 subjects), HbA_{1c} (1 subject), MAP (3 subjects), total cholesterol (1 subject), HDL and non-HDL cholesterol (2 subjects), serum triglycerides (9 subjects), and current smoking (5 subjects).
[e]Missing data for BMI (11 subjects), HbA_{1c} (35 subjects), fasting glucose (43 subjects), MAP (2 subjects), total cholesterol (36 subjects), HDL and non-HDL cholesterol (43 subjects), serum triglycerides (47 subjects), and current smoking (2 subjects).
[f]The interaction term for diabetes and sex was statistically significant for this model. Interaction terms were calculated using general linear modeling. In the presence of a statistically significant interaction, a single p value for a diabetes effect is not meaningful and therefore is not shown.
[g]Data are expressed as median (25th, 75th percentile). The p values for diabetes association are computed by general linear modeling for log (variable) adjusted for age within sex groups. Overall p values for diabetes association are computed by general linear modeling for log (variable) adjusted for age and sex.
[h]The p values for diabetes association are computed by logistic regression adjusted for age within sex groups. Overall p values for diabetes association are computed by logistic regression adjusted for age and sex.
Abbreviations: BMI = body mass index, HbA_{1c} = glycosylated hemoglobin, HDL = high-density lipoprotein, MAP = mean arterial pressure, NA = not applicable.

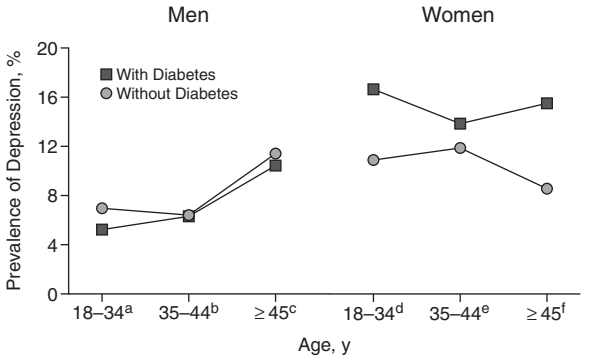
both individuals residing in the study area, as well as those residing out of the study area. The ratio of study participants residing in the study area to the total number of study area residents at the midpoint of the study period is shown by age and sex (Table 1). The ratio for participation is higher among women and in younger age groups, as we expected based on previous experience. Therefore, results are stratified by sex or adjusted for age and sex.

Table 2 shows clinical characteristics of the sample by diabetes status and sex. During the period of July 2003 through January 2007, a total of 3427 adults aged 18 years or older attended the research clinic at least once. The first such examination was analyzed for persons seen more than once during this period. Participants were excluded from the present sample if they had not completed the PHQ-9 questionnaire (N = 237), had no previous or current diagnosis of diabetes and were missing either a fasting or 2-hour glucose (N = 235), or both of the above (N = 53). Therefore, 2902 participants are included in the sample presented here. Of these participants, 2319 (80%) lived in the study area. Clinical characteristics (age, BMI, HbA_{1c}, fasting glucose, mean arterial pressure, total cholesterol, HDL cholesterol, non-HDL cholesterol, and triglycerides) for participants residing in or out of the study area were similar (data not shown).

The prevalence of depression (as measured by PHQ-9 score) in the total sample was 10.7%, and was higher in women than in men (12.8% vs. 7.5%, p < .001). Women were almost twice as likely to have depression as men in a logistic regression model controlled for age (odds ratio [OR] = 1.78, 95% confidence interval [CI] = 1.37 to 2.32). The prevalence of depression increased slightly with age, but this association was not statistically significant among either men (18–34 years: 6.6%, 35–44 years: 6.4%, ≥ 45 years: 10.8%, p = .07) or women (18–34 years: 12.1%, 35–44 years: 12.7%, ≥ 45 years: 13.9%, p = .61).

Participants with diabetes had a higher prevalence of depression than those without diabetes, but this association was not statistically significant (12.8% vs. 9.4%, age- and sex-adjusted OR = 1.31, 95% CI = 1.00 to 1.77, p = .053). However, there was a statistically significant association between diabetes and depression in women (15.4% vs. 10.9%, age-adjusted OR = 1.51, 95% CI = 1.09 to 2.10, p = .01) though not in men (7.9% vs. 7.4%, age-adjusted OR = 0.93, 95% CI = 0.55 to 1.55, p = .77)

Figure 1. Prevalence of Depression by Age, Sex, and Diabetes Status



[a]Men aged 18–34 years with diabetes, N = 95; without diabetes, N = 462.
[b]Men aged 35–44 years with diabetes, N = 127; without diabetes, N = 186.
[c]Men aged ≥ 45 years with diabetes, N = 172; without diabetes, N = 87.
[d]Women aged 18–34 years with diabetes, N = 168; without diabetes, N = 678.
[e]Women aged 35–44 years with diabetes, N = 172; without diabetes, N = 252.
[f]Women aged ≥ 45 years with diabetes, N = 387; without diabetes, N = 116.

(Figure 1). Despite the apparent sex difference in the association, there was no statistically significant interaction of sex and diabetes in their association with depression ($p = .25$).

Clinical characteristics by depression and sex are shown for persons without diabetes in Table 3A and for persons with diabetes in Table 3B. Among those without diabetes, depression was statistically significantly associated with lower fasting plasma glucose in men, but otherwise was not associated with measures of lipids or glycemia. In participants with diabetes, diabetes duration was positively associated with depression while there was no association between depression and BMI. Pharmacologic treatment for diabetes was more common in subjects with depression than those without depression. Among the participants with diabetes, measures of glycemia and lipid profiles were worse in subjects with depression ($p < .05$), adjusted for age and sex. Cigarette smoking was associated with depression among participants without diabetes, while there was no consistent association between depression and smoking among those with diabetes.

Among participants with diabetes, depression was associated with a higher mean HbA_{1c} (9.0% in those with depression vs. 8.4% in those without depression, $p = .02$). This difference remained statistically significant even after controlling for age, sex, duration of diabetes, and body mass index ($p = .03$). No difference in HbA_{1c} was found in participants without diabetes (5.4% in those with depression vs. 5.4% in those without depression, $p = .24$). The PHQ-9 depression score was also analyzed as a continuous variable in relation to HbA_{1c} (Table 4). HbA_{1c} was positively associated with the depression score in participants with diabetes but not in those without diabetes. The association between depression score and HbA_{1c} in participants with diabetes remained statistically significant in a multivariate linear regression model controlled for age, sex, duration of diabetes, and BMI (β coefficient = .036% HbA_{1c} per unit of the depression score, $p = .003$).

Use of antidepressant medication was reported by 144 individuals (5.0% of the total sample) of whom only 37 (25.7%) were currently depressed according to the PHQ-9 score. Thus, the prevalence of depression, including that which is successfully treated, may be higher than the prevalence of depression by PHQ-9 score. The results described above did not change when participants taking antidepressant medication were excluded from the sample (data not shown).

DISCUSSION

The prevalence of depression in this sample was 10.7%, which is higher than that in the general population. The National Comorbidity Survey Replication reported a prevalence of 6.6% (95% CI = 5.9% to 7.3%), although in that study, depression was assessed using a more detailed questionnaire/interview than the PHQ-9.[34] The prevalence of depression was also higher than that in the general population when the sample was split into groups by diabetes status. In this sample, the prevalence of depression in participants with diabetes was 12.8% and was 9.4% in participants without diabetes. In the National Health Interview Survey, the depression prevalence among individuals with diabetes was 9.3% and was 6.1% among individuals without diabetes.[35] As in the general United States population, the prevalence of depression was also higher among women than among men in our sample.[36]

There have been few previous reports directly assessing the prevalence of depression among American Indians.[37] In the American Indian Service Utilization, Psychiatric Epidemiology, Risk and Protective Factors Project (AI-SUPERPFP), a population-based study of 3084 tribal members from 2 American Indian reservations, the prevalence of any episode of depression occurring during the previous 12 months was 2.8% among men and 4.9% among women.[38] The prevalence of depression in the current report was higher among both men (7.5%) and women (12.8%). However, it is difficult to directly compare the results reported here with those in the AI-SUPERPFP because that study used a more detailed questionnaire for assessing depression and a different time frame (i.e., 12 months) than in the current report (the last 2 weeks). A recent study of the elderly with diabetes compared the prevalence of depression among American

Table 3. Clinical Characteristics by PHQ-9 Depression Category and Sex[a]

A. Participants Without Diabetes

Variable	Men (N = 735)			Women (N = 1046)			Overall
	No Depression (N = 681)[b]	Depression (N = 54)[c]	p Value for Depression	No Depression (N = 932)[d]	Depression (N = 114)[e]	p Value for Depression	p Value for Depression
Age, y	31.9 (31.0 to 32.7)	33.3 (30.3 to 36.2)	.37	31.3 (30.6 to 32.0)	31.9 (29.9 to 33.9)	.56	.32
BMI, kg/m^2	33.6 (32.9 to 34.2)	34.0 (31.8 to 36.3)	.67	35.7 (35.1 to 36.2)	35.4 (33.8 to 36.9)	.66	.93
MAP, mm Hg	91.7 (90.9 to 92.5)	91.1 (88.4 to 93.9)	.77	84.0 (83.4 to 84.7)	83.9 (82.0 to 85.8)	.84	.73
HbA_{1c}, %	5.4 (5.3 to 5.4)	5.3 (5.2 to 5.4)	.50	5.4 (5.4 to 5.4)	5.4 (5.3 to 5.4)	.60	.41
Fasting glucose, mg/dL	93.5 (92.8 to 94.2)	89.9 (87.5 to 92.4)	.01	90.9 (90.3 to 91.5)	90.8 (89.1 to 92.5)	.88	…[f]
Total cholesterol, mg/dL[g]	175 (152, 199)	173 (154, 186)	.46	166 (145, 189)	164 (143, 186)	.37	.24
HDL cholesterol, mg/dL[g]	43 (37, 54)	43 (38, 53)	.66	46 (39, 56)	46 (38, 54)	.45	.39
Non-HDL cholesterol, mg/dL[g]	130 (105, 154)	126 (103, 148)	.57	117 (98, 138)	115 (97, 139)	.52	.39
Triglycerides, mg/dL[g]	113 (77, 169)	110 (76, 176)	.68	102 (74, 142)	106 (66, 157)	.44	.41
Current smoking, N (%)[h]	191 (28.3)	21 (38.9)	.11	190 (20.5)	38 (33.6)	< .01	< .001

B. Participants With Diabetes

Variable	Men (N = 394)			Women (N = 727)			Overall
	No Depression (N = 363)[i]	Depression (N = 31)[j]	p Value for Depression	No Depression (N = 615)[k]	Depression (N = 112)[l]	p Value for Depression	p Value for Depression
Age, y	44.1 (42.7 to 45.4)	46.3 (41.7 to 50.8)	.35	45.8 (44.7 to 46.8)	44.7 (42.3 to 47.1)	.44	.81
BMI, kg/m^2	35.0 (34.0 to 35.9)	33.8 (30.6 to 36.9)	.35	37.5 (36.7 to 38.2)	38.0 (36.3 to 39.7)	.64	.88
Diabetes duration, y	9.0 (8.2 to 9.8)	10.8 (8.0 to 13.5)	.29	10.4 (9.7 to 11.0)	13.8 (12.4 to 15.3)	< .001	< .001
MAP, mm Hg	96.7 (94.7 to 98.7)	98.9 (92.0 to 105.7)	.41	90.6 (89.0 to 92.1)	89.4 (85.8 to 93.1)	.28	.83
HbA_{1c}, %	8.7 (8.4 to 8.9)	9.3 (8.4 to 10.3)	.18	8.4 (8.2 to 8.6)	8.9 (8.4 to 9.3)	.08	.03
Fasting glucose, mg/dL	181.4 (173.0 to 189.9)	204.6 (174.8 to 234.4)	.13	178.5 (172.1 to 184.9)	198.3 (182.9 to 213.7)	.02	.006
Total cholesterol, mg/dL[g]	181 (154, 208)	168 (138, 210)	.66	172 (149, 195)	185 (158, 212)	< .01	.03
HDL cholesterol, mg/dL[g]	42 (35, 51)	39 (33, 46)	.12	45 (38, 54)	44 (38, 52)	.64	.23
Non-HDL cholesterol, mg/dL[g]	134 (109, 160)	123 (105, 172)	.76	123 (103, 149)	134 (110, 162)	< .01	< .01
Triglycerides, mg/dL[g]	139 (94, 213)	169 (109, 302)	.25	137 (96, 200)	164 (119, 213)	.01	.01
Oral hypoglycemic use, N (%)[h]	197 (54.3)	16 (51.6)	.78	413 (67.5)	87 (77.7)	.03	.09
Insulin use, N (%)[h]	60 (16.5)	10 (32.3)	.03	161 (26.2)	41 (36.6)	.02	.002
Current smoking, N (%)[h]	73 (20.2)	12 (38.7)	.02	77 (12.6)	11 (9.8)	.39	…[f]

[a]Unless otherwise stated, data are least squares means (95% CI). Least squares means and p values for depression difference are computed with general linear models adjusted for age within sex groups, except for the age variable, where the p value is unadjusted. Overall p values for depression are computed with general linear models adjusted for age and sex, except for the age variable, where the model is only adjusted by sex. For the age variable, unadjusted means and 95% confidence intervals are shown.

[b]Missing data for BMI (11 subjects), MAP (2 subjects), HbA_{1c} (1 subject), total cholesterol and HDL and non-HDL cholesterol (1 subject), serum triglycerides (8 subjects), and current smoking (7 subjects).

[c]Missing data for BMI (1 subject), HbA_{1c} (1 subject), and serum triglycerides (1 subject).

[d]Missing data for BMI (11 subjects), MAP (3 subjects), HbA_{1c} (1 subject), total cholesterol (1 subject), HDL and non-HDL cholesterol (2 subjects), serum triglycerides (6 subjects), and current smoking (4 subjects).

[e]Missing data for BMI (1 subject), serum triglycerides (3 subjects), and current smoking (1 subject).

[f]Interaction terms for diabetes and sex were statistically significant for these models. Interaction terms were calculated using general linear modeling. In the presence of a statistically significant interaction, a single p value for a diabetes effect is not meaningful and therefore is not shown.

[g]Data are median (25th, 75th percentile). The p values for depression difference are computed for log (variables) by general linear models adjusted for age within sex groups. Overall p values for depression are computed for log (variables) by general linear models adjusted for age and sex.

[h]The p values for depression difference are computed by logistic regression adjusted for age within sex groups. Overall p values for depression are computed by logistic regression adjusted for age and sex.

[i]Missing data for BMI (10 subjects), HbA_{1c} (20 subjects), fasting glucose (23 subjects), total cholesterol (19 subjects), HDL and non-HDL cholesterol (28 subjects), serum triglycerides (27 subjects), and current smoking (2 subjects).

[j]Missing data for HbA_{1c} (5 subjects), fasting glucose (4 subjects), total cholesterol (4 subjects), and HDL cholesterol, non-HDL cholesterol, and serum triglycerides (5 subjects).

[k]Missing data for BMI (9 subjects), MAP (1 subject), HbA_{1c} (25 subjects), fasting glucose (32 subjects), total cholesterol (26 subjects), HDL and non-HDL cholesterol (31 subjects), serum triglycerides (35 subjects), oral hypoglycemic use (3 subjects), and current smoking (2 subjects).

[l]Missing data for BMI (2 subjects), MAP (1 subject), HbA_{1c} (10 subjects), fasting glucose (11 subjects), total cholesterol (10 subjects), and HDL cholesterol, non-HDL cholesterol, and serum triglycerides (12 subjects).

Abbreviations: BMI = body mass index, HbA_{1c} = glycosylated hemoglobin, HDL = high-density lipoprotein, MAP = mean arterial pressure, PHQ-9 = depression module of the Patient Health Questionnaire.

Table 4. Multivariate Linear Regression Models for HbA_{1c} (%)

A. Participants Without Diabetes		
Variable	Regression Coefficient	p Value
Intercept	5.08	
Depression score[a]	–0.001	.49
Sex (women compared with men)	0.01	.70
Age[b]	0.01	< .001
B. Participants With Diabetes		
Variable	Regression Coefficient	p Value
Intercept	9.46	
Depression score[a]	0.04	< .01
Sex (women compared with men)	–0.29	.06
Age[b]	–0.01	.03

[a]Depression module of the Patient Health Questionnaire (PHQ-9).
[b]Age was measured in years, so the unit for the age regression coefficient = %/year.
Abbreviation: HbA_{1c} = glycosylated hemoglobin.

Indian, white, and African American participants using the Center for Epidemiologic Studies Depression Scale (CES-D) to assess depressive symptoms. While this study reported that the 181 American Indian participants had a higher prevalence of depressive symptoms (21%) than either of the other 2 racial groups, this difference was not statistically significant.[39] Since this study only included participants with diabetes, these data are difficult to compare with other estimates of depression prevalence in American Indians. The current report, on the other hand, presents data on the prevalence of depression in American Indians with and without diabetes.

In the pilot phase of the current study,[29] we found that the overall prevalence of depression was 16.3%, which is higher than the prevalence of depression reported here. This difference is most likely due to the different modes of administration of the questionnaire: in the pilot phase of the study, depression was assessed using a face-to-face interview tool (PRIME-MD), while in this report depression was assessed using a self-administered paper version of the same questionnaire (PHQ-9). In other studies, estimates of the prevalence of depression differed based on the mode of screening (interview versus self-administered), although usually, interview methods yielded lower estimates of depression prevalence than self-administered approaches.[40]

In the absence of a "gold standard" measure for depression, we are unable to say whether in this population the presence of depression was overestimated with the interview questionnaire, underestimated by the self-administered questionnaire, or whether the difference is explained by some unmeasured difference between the subjects included in the pilot study and those included in the current report. Pima Indian clinic staff who were presented with this finding suggested that because a segment of the study participants may have limited literacy, those individuals may have had greater comprehension of the questions when asked about depression symptoms in an oral interview. We attempted to minimize problems with literacy by selecting a questionnaire that uses simple language and by orally administering the questionnaire to those participants who requested assistance. However, literacy was not directly assessed in the study, and so we cannot draw any direct conclusions about the impact of literacy on the self-reported prevalence of depression. Clinic staff also suggested that concerns about confidentiality may have caused some research participants to be reluctant to admit to depression symptoms on a written questionnaire that they were filling out in a public waiting room, while participants may have been more willing to do so when interviewed in a private room. It was not possible to directly compare the different methods of depression assessment because there was no overlap between the 2 study phases. Further studies, perhaps using ethnographic methods, may be necessary to fully elucidate the reasons that interview screening yielded a higher prevalence estimate of depression in this population than a self-administered questionnaire.

Although a few clinical trials have assessed the efficacy of antidepressant medications in individuals with diabetes,[41–45] few cross-sectional reports on diabetes and depression have assessed the use of antidepressant medications. The prevalence of reported antidepressant medication in this sample was 5.0%, and there was little overlap between the group of participants with depression by PHQ-9 score and those taking antidepressants. Similar results were reported by the Diabetes Prevention Program.[46]

Diabetes and depression were significantly associated in women but not men, although there was not a significant sex interaction in this association. Due to the smaller numbers of depressed men (i.e., lower prevalence of depression in men than in women), the confidence interval around the odds ratio for the association of diabetes and depression is wide, consistent with the same degree of association as seen in women. Thus, this study is inconclusive regarding the association of diabetes and depression in men. Many previous reports have shown a higher prevalence of depression among individuals with diabetes.[1,3,5,6] However, there have been few studies of depression and diabetes in nonwhite populations.[15] It is possible that the relationship between depression and diabetes may vary by ethnicity: 3 studies in Hispanic populations and 1 in a multiethnic sample also did not find an association between depression and diabetes.[16–19] Consistent with the results reported here, diabetes was not associated with a current diagnosis of depression among American Indians in the AI-SUPERPFP study, although there was a significant association between a past diagnosis of depression and diabetes.[24] In a study of cognitive function and type 2 diabetes in elderly American Indians, those with diabetes had a slightly higher score on the CES-D scale than those without diabetes (17.2 ± 0.5 vs. 15.9 ± 0.4, $p = .04$).[47]

Diabetes is much more prevalent in our sample than in the general U.S. population.[27] The high prevalence of diabetes could make the psychosocial impact of the disease different in this community than in the general U.S. population. The lack of a statistically significant association between depression and diabetes in this sample also may indicate that certain social, cultural, or economic factors overshadow the association between depression and diabetes in this population. We cannot account for factors that might engender reactive depression, such as income and education, as these data were not collected. We also do not have data on eating habits or dietary interventions, but did find that for participants with both depression and diabetes, there was a greater use of both oral hypoglycemic agents and insulin than there was for participants with diabetes who were not depressed. This finding is expected, in light of the poorer glycemic control in the depressed subjects with diabetes.

In addition to the difference in ethnicity between our study population and participants included in most previous studies of depression and diabetes, our study also has methodological strengths compared with other reports. We assessed diabetes using an oral glucose tolerance test, whereas the majority of previous studies have used self-report methods[1,3,7,18,24] or diagnostic codes in health insurance databases[5,6] for diagnosis of diabetes. We also assessed depression symptoms directly using a screening questionnaire based on DSM-IV diagnostic criteria rather than relying on diagnostic codes in the medical record[5,6] or self-report of depression diagnosis or treatment.[3]

Although depression and diabetes were significantly associated only among women in this study, HbA_{1c} was significantly higher overall in individuals with diabetes who were depressed than in those who were not. These results are consistent with those reported in the pilot phase of this study.[29] This report not only provides further evidence that depression is associated with poor glycemic control, but also shows that the severity of depression (as measured by depression score, which is determined by number of depression symptoms and how often they are experienced) is positively correlated with HbA_{1c}. Although the PHQ-9 was devised as a screening tool for depression, previous studies have shown that higher scores are associated with more severe levels of depression, so we feel justified in using it here as a continuous measure.[30]

In addition, fasting plasma glucose and serum triglyceride concentrations were also higher in depressed individuals with diabetes. In individuals without diabetes, fasting plasma glucose was lower in depressed men than in those without depression, although there were no other significant associations between depression and measures of lipids or glycemia. In contrast to our findings, there was no relationship between depressive symptoms and HbA_{1c} in a study of elderly people with diabetes including American Indians.[39] This may reflect the older age of those study participants (all were ≥ 65 years of age), the better glycemic control in that sample (mean HbA_{1c} = 6.8%), and the use of a different tool for assessing depression.

In the current report, cigarette smoking was also associated with depression among participants without diabetes, consistent with the association between cigarette smoking and depression reported for the general U.S. population.[48] Therefore, the results reported here provide evidence that depression is associated with poor glycemic control in American Indians with diabetes across a wide age range. The AI-SUPERPFP, which is the other recent study to examine the relationship between depression and diabetes in American Indians, did not examine the association of depression with metabolic risk factors.[24] Our study indicates that identification and treatment of depression may be important in managing diabetes in American Indians.

The causes of the association between depression and hyperglycemia in individuals with diabetes cannot be determined from this cross-sectional study. On the one hand, it is possible that plasma glucose, HbA_{1c}, triglycerides, and total cholesterol are higher among depressed participants with diabetes in this sample because individuals who are depressed may have poor adherence to prescribed diabetes treatment or self-care (diet, exercise, seeking health care) regimens.[49,50] Depression, anxiety, and other psychiatric disorders can hinder patients from successfully managing their diabetes.[51–53] In this study, more participants with diabetes and depression were prescribed oral hypoglycemics and insulin than the nondepressed participants with diabetes. On the other hand, poor glycemic control or dyslipidemia could adversely affect the psychological well-being and quality of life of individuals with diabetes.[54,55] Managing diabetes is stressful for many patients, and it is possible that patients experience depression in reaction to being diagnosed with diabetes or hyperglycemia.[55] Finally, depression and hyperglycemia might act in a vicious cycle whereby depression worsens glycemic control, and poor glycemic control, in turn, results in mental distress.[2] One study has shown that treatment of depression with either medication or counseling improves glycemic control in patients with diabetes, at least in the short term,[41] although in studies with longer follow-up (12 months), results have been mixed.[43–45] The long-term effects of treatment with antidepressant medication on glycemic control are not known.[42,56]

That there was no association between glycemia and depression among participants without diabetes in the current report is not surprising, particularly for HbA_{1c}, which has such a limited range among participants without diabetes. However, HbA_{1c} in individuals without diabetes is clinically important because it predicts mortality.[57] If depression is indeed a risk factor for development

of diabetes, we might have expected to see higher glucose levels associated with more depression symptoms in the participants without diabetes.

Pima Indians with diabetes in this sample had a slightly higher prevalence of depression than those without diabetes, although this association was statistically significant only in women. In those with diabetes, depression was associated with elevated HbA_{1c} levels. This study adds to the sparse literature on depression and diabetes in American Indians. Previous studies in other populations have shown that depression is associated with hyperglycemia. We have confirmed that depression and hyperglycemia are also associated in American Indians, an ethnic minority group with a high prevalence of diabetes. Further studies are necessary to determine the precise mechanism(s) by which depression is associated with hyperglycemia and dyslipidemia. Among people with depression and diabetes, members of ethnic minority groups are less likely to be treated for depression.[19,20,23] This finding is of concern because ethnic minority groups such as the Pima Indians have a high prevalence of diabetes as well as depression, and depression treatment may improve glycemic control.[41] Further investigation is needed into whether treating depression in patients with diabetes improves glycemic control and the risk for later complications of diabetes, especially in American Indians and other ethnic minority groups.

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