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Relationship between depressive symptoms and diabetes among native Hawaiians

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Abstract

Increased prevalence of depression has been reported among diabetes patients. We examined this association between diabetes and depressive symptoms in a population-based study where glucose tolerance status was determined with World Health Organization (WHO) criteria. Fasting plasma glucose (FPG) was determined from blood collected from 574 native Hawaiians. The Centers for Epidemiological Studies — Depression (CES-D) scale was used to assess depressive symptoms in association with diabetes history and hemoglobin A1c (HbA1c). A significant association was observed between depressive symptoms and HBA1c that persisted after adjusting for age, BMI, gender, education, and after exclusion of participants reporting a history of diabetes. Diabetes history was no longer associated with CES-D depressive symptoms after adjusting for HbA1c. These results support the hypothesis

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that depressive symptoms associated with diabetes may be partially explained by a shared neuroendocrinological disturbance.

Keywords: Type 2 diabetes; Glucose intolerance; Depressive symptoms; Depression; Native Hawaiians; Pacific Islanders

1. Introduction

Controlled studies have suggested that individuals with type 2 diabetes (Weyerer et al., 1989; Leedom et al., 1991; Palinkas et al., 1991; Eaton et al., 1996) may be at an increased risk for depression or depression-like symptoms. Most studies examining the association between diabetes and depression have been based on clinical samples; however, the association between the two disorders was also observed in several community-based samples (Weyerer et al., 1989; Palinkas et al., 1991; Eaton et al., 1996).

It has been proposed that depression among individuals with diabetes and other chronic illnesses may be reactive in nature, occurring in response to psychosocial hardships (i.e. physical disability, dietary restriction) related to their illness (Lustman et al., 1983a). However, others have proposed that some of the depressive symptoms among patients with diabetes may be organic in origin, caused by metabolic changes associated with diabetes (Popkin et al., 1988). Fluctuations in serum glucose levels may partially explain the high prevalence of depressive symptoms among patients with diabetes; hyperglycemia may produce stress-like arousal, which might be perceived as severe anxiety and/or depression-like symptoms (Lustman et al., 1983b). Experimental induction of hyperglycemia has been shown to increase plasma cortisol concentrations, which could precipitate mood changes in some patients with diabetes (Cameron et al., 1984).

Previous studies, both clinical and community-based, have included only persons with diabetes history. Furthermore, known risk factors for both disorders such as age, gender or obesity may have confounded the findings of previous studies (Gavard et al., 1993). The purpose of the current study was to examine whether the prevalence of depressive symptoms is increased among native Hawaiians with type 2 diabetes, and if so, whether the increased occurrence of depressive symptoms is explained by poor glycemic control as measured by hemoglobin A_{1c} (HbA1c). To avoid confounding that may have affected other studies, we adjusted for known history of diabetes and other chronic illness, as well as other biologic and sociodemographic risk factors for depression.

2. Methods

2.1. Participants

Methods of the NHHR Project have been described elsewhere (Mau et al., 1997). In brief, the NHHR Project was a cross-sectional study of diabetes and cardiovas-

cular risk factor prevalence among native Hawaiians living in two rural communities, North Kohala on the Island of Hawaii and Waimea/Kekaha on the Island of Kauai. A combined total of approximately 1100 Native Hawaiian adults were identified in the two communities, of whom 581 (approximately 53%) completed the full interview and clinical examination. Eligibility criteria were as follows: native Hawaiian ancestry, 30 years of age or older, and a resident of the North Kohala or West Kauai district. A native Hawaiian is defined as any individual with ancestors that lived in Hawai'i prior to initial Western contact in 1778. Native Hawaiian ancestry was determined by self-report and verified by a brief genealogical interview. All participants were either native speakers of English or fluent in English since early childhood.

2.2. Population characteristics

Ages of the 581 participants ranged from 30 to 85 with a mean age of 47 years (SD = 12.6). A total of 60% of all participants were female. The mean educational attainment was 12.3 years (SD = 2.3) and the distribution is as follow: 14% were non-high school graduates, 54% were high school graduates, and 32% had at least some college or technical training. Mean body mass index (m/kg^2) was 31 ± 7.0, and the prevalence of obesity (BMI ≥ 30) was 49%.

2.3. Evaluations

Blood samples were collected from all participants after an overnight fast of 10–12 h. Individuals not taking insulin or oral diabetic medication underwent a 2-h, 75 g oral glucose tolerance test (OGTT). Participant without a prior diagnosis of diabetes were classified according to WHO criteria for glucose tolerance (World Health Organization and Expert Committee on Diabetes, 1985). All plasma glucose levels were assayed in the NHHR Laboratory using the glucose oxidase method on a YSI autoanalyzer.

HbA1c was chosen as a marker for glycemic control because it is not subjected to daily fluctuations as are fasting or 2-h post challenge plasma glucose. HbA1c was assessed by affinity chromatography using a minicolumn (BioRad, Hercule, CA). Each individual with a HbA1c $\geq 7.0\%$ was classified as chronically hyperglycemic. The chosen cut-point for HbA1c is the American Diabetes Association (ADA) recommended level for glycemic control for patients with diabetes (American Diabetes Association, 1997).

An extensive medical history was obtained during the interview segment. Participants were asked whether they were ever diagnosed with diabetes, hypertension, high cholesterol, heart disease, or ever had a heart attack or stroke. Medical history obtained during the examination was confirmed by a record review conducted at the offices of participants' primary care physicians. Individuals were measured for weight, height, waist and hip circumference using standardized protocols.

In addition to obtaining clinical and biochemical measurements, examiners also collected sociodemographic and health risk behavior data. Participants completed a

series of self-report questionnaires, including a six-item social support scale and the short form of the Center for Epidemiological Studies — Depression (CES-D) scale. The CES-D short form is an 11-item self-report scale of depressive symptoms based on a 20-item scale developed by the Center for Epidemiological Studies (Radloff, 1977). Of the 11 items, six items assess somatic symptoms (e.g. 'restlessness', 'concentration'), while the remaining five assess cognitive-affective symptoms (e.g. 'felt fearful', 'felt lonely'). The validity and reliability of both short and long forms of this instrument have not been tested among native Hawaiians. However, the validity and reliability of the CES-D have been documented among various other ethnic groups (Radloff, 1977; Roberts, 1980; Kohout et al., 1993). In our study, the alpha coefficient for the CES-D (0.76) was consistent with a high degree of internal consistency.

Low levels of social support have been shown to be associated with depression (Brugha et al., 1990). Perceived social support was measured using a scale adapted from one used by the Honolulu Heart Study (1991) in order to adjust for this correlate of depressive symptoms. The alpha coefficient for the six items selected for the modified social support scale was 0.79 (Cronbach's alpha).

2.4. Statistics

General linear modeling was used to compare continuous data on CES-D total scores by chronic disease history. Adjustments were made for age, gender, level of social support, and body mass index (BMI). The association between each categorical risk factor and prevalence of depressive symptoms was also evaluated using multiple logistic regression. Prevalence odds ratios (POR) were calculated to elucidate the relative strength of each associated variable. The exponential of the estimated logistic regression parameters were used for the odds ratio calculations. Established cutoff scores for the CES-D short form (12 or greater) (Kohout et al., 1993) were used to categorize participants as exhibiting high or exhibiting low levels of depressive symptoms. To estimate the significance of the association between factors, 95% confidence limits were calculated . Multiple logistic regression models were used to adjust for age, gender, level of social support, and BMI. All statistical analyses were performed using SAS statistical software (SAS Institute, Cary, NC).

3. Results

Overall, 78 participants (14.9%) had high levels of depressive symptoms estimated with the CES-D. Prevalence of type 2 diabetes was 20%; however, only 8% of the participants reported a prior history of diabetes. An additional 15% were classified with impaired glucose tolerance. Among participants reporting a prior history of type 2 diabetes, both mean CES-D scores (8.01 ± 5.02) and depressive symptom prevalence (26.9%; POR = 2.45, 95% CI 1.24–4.87) were significantly higher compared with participants with no prior history of chronic illness (6.52 ± 4.73; 13.1%). However, neither mean CES-D scores nor depressive symptom prevalence were

Table 1
Relative odds of depressive symptom prevalence among native Hawaiians according to glycemic control (hemoglobin A1c at or above 7%)

	CES-D ≥ 12			
	N	Frequency (%)	Odds ratio	95% CI
HbA1c < 7	463	57 (12.3%)	1.00	–
HbA1c ≥ 7	61	21 (34.4%)	3.82	2.10–6.95

higher among participants with other previously diagnosed chronic diseases such as hypertension, high cholesterol, heart disease, or ever had a heart attack or stroke (6.21 ± 5.21; 15.2%). The association between CES-D score and diabetes history remained significant even after adjusting for age and social support.

HbA1c concentrations were significantly correlated with CES-D scores among the study participants (Pearson's $r = 0.115$, $P = .009$), as were fasting glucose concentrations (Pearson's $r = 0.132$, $P = .003$); however, 2-h glucose concentrations were not significantly correlated with CES-D scores (Pearson's $r = -0.02702$, $P = .564$). Similarly, high HbA1c (≥ 7) was also associated with higher prevalence of CES-D assessed depressive symptoms (Table 1; POR = 3.82, 95% CI = 2.10–6.95). HbA1c was significantly associated with six of the 11 items, of which three assessed somatic symptoms, and three cognitive-affective symptoms. The association between high HbA1c and prevalence of CES-D depressive symptoms was statistically significant after adjusting for age, gender, social support and diabetes history in a multiple logistic regression model (Table 2; adjusted POR = 3.95, 95% CI = 1.72–9.08). Interestingly, we observed that the association between depressive symptoms and diabetes history was attenuated and no longer statistically significant after adjusting for HbA1c levels (POR = 0.95, 95% CI = 0.39–2.34).

Table 2
Relative odds of CES-D assessed depressive symptom prevalence among native Hawaiians according to glycemic control (hemoglobin A1c at or above 7%) after adjusting age, gender, high social support, education level, and diabetes history

Model	Odds ratio	95% CI
HbA1c	3.82	2.10–6.95
HbA1c (persons with diabetes history excluded)	4.97	2.12–11.65
HbA1c, age	4.21	2.25–7.87
HbA1c, age, gender	4.34	2.31–8.15
HbA1c, age, gender, BMI	4.00	2.11–7.57
HbA1c, age, gender, BMI, social support	3.37	1.74–6.51
HbA1c, age, gender, BMI, social support, education	3.20	1.64–6.23
HbA1c, age, gender, BMI, social support, education, diabetes history	3.95	1.72–9.08
HbA1c, age, gender, BMI, social support, education (persons with diabetes history excluded)	5.29	2.20–12.71

Since HbA1c is highly correlated with diabetes history, the multiple logistic regression model was repeated after excluding all participants with pre-existing diabetes in order to eliminate potential bias due to collinearity. The relationship between HbA1c and CES-D remained significant among the remaining participants (Table 2; POR = 5.29, 95% CI = 2.20–12.71).

4. Discussion

The findings of this study confirm that, when assessed with the CES-D, depressive symptoms may be more prevalent among persons with type 2 diabetes when compared with healthy individuals and individuals with other chronic health problems. Although CES-D scores were significantly higher among persons with diabetes history compared with persons reporting no illnesses, we did not observe high CES-D depressive symptoms among participants diagnosed with other chronic health conditions in the absence of diabetes. This would suggest that depressive symptoms among participants with diabetes were not purely reactive in nature, or there should be more similarity with persons with other chronic diseases.

The association of depressive symptoms with HbA1c after adjustment for medical history and social support further suggests that the relationship may be physiological in nature, perhaps due to arousal induced by hyperglycemia, which in turn may be attributed to anxiety or depression by the patient (Lustman et al., 1983b). Alternatively, stress or anxiety detected by the CES-D may lead to fluctuations in blood glucose that may result in elevated HbA1c levels. Further support for this conclusion may be inferred from the observation that depressive symptom prevalence was associated with HbA1c even after adjusting for known diabetes, the only individuals that would be expected to exhibit reactive depression. In fact, the results of multiple logistic regression suggest that hyperglycemia may completely explain the high prevalence of depressive symptoms among participants with known and newly identified diabetes.

The study reported here was cross-sectional in design; therefore, the temporal relationship between glycemic control and CES-D depressive symptoms cannot be determined. The Epidemiological Catchment Area (ECA) Program, which was longitudinal in design, reported higher type 2 diabetes incidence among individuals with depression (Eaton et al., 1996); however the difference was not statistically significant. The results of the ECA Program suggest that depression may be a risk factor for type 2 diabetes, or that both disorders share similar neuroendocrinological abnormalities; however, the study endpoint included only patients with self-reported, diagnosed diabetes. Therefore, the ECA study may have been subject to differential detection bias of type 2 diabetes among participants with follow-up for depression. We are currently conducting a longitudinal study that will detect new cases of diabetes developing subsequent to the first examination. This follow-up examination will allow a better determination of the temporal relationship between depressive symptoms and diabetes. Clarification of the direction of the causal relationship between diabetes and depressive symptoms may have important impli-

cations for early detection of diabetes, better glycemic control, and effective treatment of depression among patients with diabetes.

The present study is the first to report the relationship between glycemic control and depressive symptoms while adjusting for both biological and sociodemographic risk factors for depression. However, because native Hawaiians represent a unique population, similar studies are needed to elucidate the relationship between glycemic control and depressive symptoms among other ethnic groups.

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