Fasting Glucose, Diagnosis of Type 2 Diabetes, and Depression: The Vietnam Experience Study

Catharine R. Gale, Mika Kivimaki, Debbie A. Lawlor, Douglas Carroll, Anna C. Phillips, and G. David Batty

Background: Recent findings suggest that both low and very high fasting blood glucose concentrations may be linked with depression, though whether type 2 diabetes is associated with depression may depend on awareness of the diagnosis. We explored the association between fasting glucose and type 2 diabetes (undiagnosed and diagnosed) and depression in middle-aged men.

Methods: Participants were 4293 US veterans who underwent an examination during which fasting blood glucose was measured, major depression diagnosed using DSM-III criteria, and depressive symptoms assessed with Minnesota Multiphasic Personality Inventory (MMPI) clinical scale for depression.

Results: Compared with those with normal fasting glucose, men with undiagnosed type 2 diabetes had nearly double the odds of major depression, odds ratio (95% confidence interval) 1.80 (1.01, 3.22), and men with diagnosed diabetes had triple the odds of major depression, 3.82 (1.68, 8.70), after adjustment for confounding variables. Men with undiagnosed or diagnosed diabetes had higher MMPI depression scores. There was no curvilinear association between fasting glucose and depression ($p > .45$).

Conclusions: These findings do not support a U-shaped association between fasting glucose and depression. They suggest that the positive association between type 2 diabetes and depression extends beyond those who are aware they have the disease.

Key Words: Depressive symptoms, diagnosis, fasting glucose, major depression, type 2 diabetes

The relationship between glycemia and depression is unclear (1). Findings that risk of depression is increased in people receiving medication for type 2 diabetes but not in those whose diabetes is managed without drugs or is undiagnosed (2–4) suggest that the stresses of managing the disease may have more effect on mood than the degree of hyperglycemia. A recent study reported that depression may be more prevalent not only among individuals with very high fasting glucose but also in nondiabetics with low glucose levels (5). These observations merit further investigation.

We examined the cross-sectional association of fasting blood glucose and type 2 diabetes (undiagnosed and diagnosed) with two measures of depression using data from the Vietnam Experience Study in which participants underwent a detailed assessment of psychological and physical health.

Methods and Materials

The Vietnam Experience Study has been described previously (6–9). In brief, 18,313 ex-military personnel were drawn randomly from records of United States veterans; 15,288 participated in a telephone survey at which time they provided information about medical history, medications, socioeconomic position, and lifestyle. A random sample were invited to a medical examination; 4462 attended (69.3% of those invited). Information on intelligence at enlistment (7) and ethnicity was extracted from records.

Ethical approval for the study protocol was given by the US Office for Technology Assessment, the Department of Health and Human Sciences Advisory Committee, the Agent Orange Working Group Science Panel, and a review panel from the US Centers for Disease Control.

At the examination, blood samples were taken in the morning; participants had fasted from 7:00 PM the previous day. Levels of triglycerides and cholesterol fractions were ascertained using a Kodak Ektachem 700 AutoAnalyzer (Eastman Kodak, Rochester, New York) (9). Serum glucose level was determined with an adaptation of the glucose oxidase-peroxidase-chromogen-coupled system for glucose determination in biological fluids (9). Cortisol level was measured from blood using a double-antibody radioimmunoassay (Leeco Diagnostics, Southfield, Minnesota) (9). Blood pressure, height, and weight were assessed (9). Body mass index (BMI; kg/m^2) was calculated.

The Diagnostic Interview Schedule (DIS) (10) was used to assess the prevalence of psychiatric conditions according to the DSM-III (11) criteria of the American Psychiatric Association. Participants completed the Minnesota Multiphasic Personality Inventory (MMPI), which consists of 566 true-false statements and measures 10 clinical psychopathology scales (12). The DIS and the MMPI were administered by psychology technicians under the supervision of a clinical psychologist. We used DIS data on the prevalence of major depression in the year before examination and the MMPI clinical scale for depression. Higher scores on the latter indicated greater depression.

We defined diabetes by a fasting glucose ≥7.0 mmol/L (13), self-reported physician diagnosis of diabetes, or use of diabetes medication. We subdivided diabetics into undiagnosed or diagnosed according to self-reported physician diagnosis. In nondiabetic participants, we classified impaired

From the Medical Research Council Epidemiology Resource Centre (CRG), University of Southampton, Southampton; and Department of Epidemiology and Public Health (MK), University College London, London, United Kingdom; Finnish Institute of Occupational Health (MK), Helsinki, Finland; Medical Research Council Centre for Causal Analyses in Translational Epidemiology (DAL), University of Bristol, Bristol; School of Sport & Exercise Sciences (DC, ACP), University of Birmingham, Birmingham; Medical Research Council Social and Public Health Sciences (GDB), University of Glasgow, Glasgow; and Centre for Cognitive Ageing and Cognitive Epidemiology (GDB), Department of Psychology, University of Edinburgh, Edinburgh, United Kingdom; and The George Institute for International Health (GDB), Sydney, Australia.

Address correspondence to Catharine R. Gale, Ph.D., MRC Epidemiology Resource Centre, Southampton General Hospital, Southampton SO16 6YD, UK; E-mail: crg@mrc.soton.ac.uk.

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fasting glucose (IFG) as fasting glucose between 5.6 mmol/L and 6.9 mmol/L.

We used analysis of variance (ANOVA), the χ^2 test, and the Kruskal-Wallis test to examine characteristics in relation to IFG and diabetes status. Minnesota Multiphasic Personality Inventory depression scores were transformed to normality using logarithms. We used linear and logistic regression to examine associations of IFG and diabetes with logged MMPI depression scores and DIS diagnosis of major depression, respectively. Models were adjusted for age, ethnicity, blood pressure, BMI, triglycerides, high-density lipoprotein (HDL) cholesterol, cortisol, smoking, alcohol consumption, intelligence, education, and household income. To test for a curvilinear trend, squared blood glucose was added to models containing the linear term.

Results

A total of 4293 men had complete data on diabetes status, depression measures, and the covariates. Of these, 11.5% had IFG and 5.3% had type 2 diabetes; 79.8% of men with diabetes were undiagnosed. Mean (SD) reported age at diagnosis was 33.3 (5.7) years. Mean (SD) fasting glucose was 5.23 (.94) mmol/L, range 1.94 mmol/L to 22.2 mmol/L.

Table 1 shows participant characteristics according to IFG and diabetes status. Compared with men with normal fasting glucose, those with IFG or diabetes tended to be older and nonwhite and have higher BMI, blood pressure, triglycerides, and cortisol and lower HDL cholesterol, IQ, and educational attainment. Men with undiagnosed diabetes were the least likely to smoke currently.

Table 2 shows the relation between fasting glucose and diabetes status and the two measures of depression. Compared with men with normal fasting glucose, men with undiagnosed diabetes scored 4.99% higher (95% confidence interval [CI] 1.71, 8.27) on the MMPI depression scale and men with diagnosed diabetes scored 11.1% higher (95% CI 4.69, 17.6), after adjustment for age and ethnicity. Additional adjustment for the other covariates had only slight attenuating effects. Men with IFG did not differ in depression scores from those with normal fasting glucose.

Compared with men with normal fasting glucose, men with diabetes were more likely to receive a diagnosis of major depression. After adjustment for age and ethnicity, the odds ratio (95% CI) for major depression was 1.67 (.99, 2.81) in men with undiagnosed diabetes and 3.39 (1.54, 7.43) in those with diagnosed diabetes. Further adjustment for clinical characteristics strengthened these associations and they were only slightly attenuated by additional adjustment for IQ, education, and income: the fully adjusted odds ratio was 1.80 (1.01, 3.22) in men with undiagnosed diabetes and 3.82 (1.68, 8.70) in those with diagnosed diabetes.

In the subgroup with diabetes, compared with men with undiagnosed disease, men with diagnosed diabetes had depression scores that were 6.2% higher (−2.0, 14.5) and an odds ratio for major depression of 1.58 (.58, 4.29), after adjustment for age and ethnicity, but these differences were not statistically significant.

Men with IFG had a slightly lower prevalence of major depression than those with normal glucose tolerance. We tested for a curvilinear trend in the relations between fasting glucose concentration and the two measures of depression but there was no evidence of this (both $p > .45$).

Discussion

In this study of middle-aged men, type 2 diabetes was associated with higher scores on the MMPI clinical depression scale and increased odds of major depression. This association was not confined to men who were aware that they had diabetes:

Table 1. Characteristics of the Participants by Impaired Fasting Glucose and Type 2 Diabetes Status ($n = 4293$)

	Fasting Glucose		Type 2 Diabetes		
	Normal ($n = 3573$)	Impaired ($n = 492$)	Undiagnosed ($n = 182$)	Diagnosed ($n = 46$)	*p* Value for Difference
Age (Years), Mean (SD)	38.2 (2.51)	38.6 (2.47)	39.1 (2.42)	39.6 (2.48)	<.001
Ethnicity, Number (%)					
White	2962 (82.9)	404 (81.3)	128 (70.3)	26 (56.5)	<.001
Black	400 (11.2)	55 (11.2)	33 (18.1)	14 (30.4)	
Other	211 (5.9)	37 (7.52)	21 (11.5)	6 (13.0)	
IQ at Enlistment, Mean (SD)	101.6 (15.1)	99.4 (15.1)	98.3 (15.5)	95.3 (18.6)	<.001
Education (Grade Completed), Mean (SD)	13.4 (2.31)	12.9 (2.14)	13.1 (2.38)	12.8 (2.29)	.002
Household Income (US$ per Year), Number (%)					
<20,000	997 (27.9)	145 (29.5)	59 (32.4)	17 (37.0)	.612
−40,000	1790 (50.1)	248 (50.4)	87 (47.8)	20 (43.5)	
>40,000	786 (22.0)	99 (20.1)	36 (19.8)	9 (19.6)	
BMI, Mean (SD), kg/m^2	26.4 (4.15)	28.7 (4.98)	30.1 (5.55)	29.5 (6.53)	<.001
Systolic Blood Pressure (mm Hg), Mean (SD)	121.9 (11.4)	127.5 (12.7)	130.3 (13.9)	128.2 (16.6)	<.001
Diastolic Blood Pressure (mm Hg), Mean (SD)	83.3 (9.10)	87.3 (9.46)	89.8 (11.0)	86.9 (10.9)	<.001
Smoking Status, Number (%)					
Never	900 (25.2)	129 (26.2)	52 (28.6)	11 (23.9)	.006
Former	986 (27.6)	155 (31.5)	70 (38.5)	13 (28.3)	
Current	1687 (47.2)	208 (42.3)	60 (33.0)	22 (47.8)	
Alcohol Intake (Units per Week), Median (IQR)	2 (0–9)	2 (0–11)	2 (0–9)	1 (0–4)	.397
Triglycerides (mg/dL), Median (IQR)	86 (60–127)	106 (73–158)	149 (96–231)	105 (66–188)	<.001
HDL Cholesterol (mg/dL), Mean (SD)	45.0 (12.3)	44.0 (12.5)	41.1 (13.6)	41.4 (15.3)	<.001
Cortisol (mg/dL), Median (IQR)	17.1 (14–20.8)	19.9 (15.7–23.9)	20.0 (16.1–25.5)	18.5 (15.4–21.7)	<.001

BMI, body mass index; HDL, high-density lipoprotein; IQR, interquartile range; SD, standard deviation.