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ORIGINAL ARTICLE

A cross-sectional survey of depression, anxiety, and cognitive function in patients with type 2 diabetes

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Abstract To evaluate the prevalence of depression in outpatients with type 2 diabetes and its possible correlation with anxiety, cognitive function, and clinical variables. The Zung Self-Rating Depression and Anxiety Scales and the Mini-Mental-State Examination were administered to 249 non-insulin-treated (NIT) and 249 insulin-treated (IT) outpatients with type 2 diabetes, aged 40–80, in a cross-sectional survey. Compared with a reported prevalence of 6–13% in the general population, 104 (20.9%) patients had either a score indicative of depression or were on anti-depressant medication. Assuming that medication might modify the responses to questionnaires, the latter patients were excluded from further analysis. IT patients had higher age, known duration of diabetes, HbA1c, more foot ulcers, retinopathy, microalbuminuria and practised more self-monitoring of blood glucose ($P < 0.01$ all) but a slightly lower mean depression score ($P = 0.004$) and similar anxiety or cognitive function. At multivariate analysis, depression was associated with anxiety ($P < 0.001$), age ($P < 0.001$), gender (men having lower scores than women, $P = 0.042$), and insulin treatment, IT patients being less depressed than NIT ($P < 0.001$), but none of the clinical variables. Anxiety correlated with age ($P < 0.001$). The association between depression and anxiety became progressively weaker with increasing age. These data confirm increased prevalence of depression in a population of patients with type 2 diabetes who did not show impaired cognitive function. The lack of correlation with disease duration, metabolic control, and complications suggests that depression may not appear/worsen with diabetes and/or its complications but rather supports suggestions that it might predate both.

Keywords Depression · Anxiety · Cognitive function · Type 2 diabetes · Metabolic control

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Introduction

Background

Several reports suggest that people with diabetes are almost twice as likely to suffer from depression and anxiety as the general population [1–4]. Emotional problems may influence patient adherence to lifestyle and treatment recommendations, be associated with decreased quality of life, impaired self-care behaviors, and poorer glycemic control [5] and contribute to increase health care costs [2]. In particular, self-management can be hindered by the presence of diabetes-specific emotional problems such as fear of hypoglycemia, worries about complications and not accepting diabetes [6].

Interestingly, recent evidence suggests that, rather than diabetes increasing the risk of depression, the opposite may be true [7, 8]. A recent meta-analysis [9] showed that the prevalence of diabetes among people with depression is

about 60%, much higher than the increased risk of depression among people with diabetes.

Finally, a number of studies has reported that cognitive decline is accelerated in patients with diabetes, independently of common cardiovascular risk factors [10] and may be associated with poor metabolic control in patients with type 2 diabetes [11]. However, cognitive function, depression, and anxiety have not been studied together and with clinical data in people with type 2 diabetes.

In this study, we aimed at assessing the prevalence and severity of depression in a population of outpatients with type 2 diabetes and its possible correlation with anxiety, cognitive function, and clinical variables.

Patients and methods

In total, 498 outpatients with type 2 diabetes, aged 40–80, routinely followed in our diabetes clinic, gave their informed consent to participate in the study, which conformed with the Declaration of Helsinki principles. Of these, 249 (NIT) were treated by lifestyle recommendations alone ($n = 22$) or with oral hypoglycemic agents but not insulin ($n = 227$), and 249 (IT) received insulin as part of their glucose-lowering treatment. Both groups were enrolled separately and consecutively as they attended the clinic. Body weight, glycated hemoglobin (HPLC), fasting blood sugar (glucose-oxidase), blood pressure, serum creatinine, total and HDL cholesterol, triglyceride, microalbuminuria/creatininuria ratio were measured, and foot and fundus examination (digital color photography) were performed in all patients (Table 1).

Questionnaires

Depression and anxiety were assessed by the relevant Zung questionnaires [12] and cognitive status by the Mini-Mental State Examination (MMSE) [13].

The Zung Self-Rating Depression Scale includes 20 items on a scale that rates four common characteristics of depression: the pervasive effect, the physiological equivalents, other disturbances, and psychomotor activities. There are 10 positively worded and 10 negatively worded questions. Each question is scored on a scale of 1 to 4, and scores range from 20 to 80. The four possible outcomes are as follows: 20–49 normal range, 50–59 mildly depressed, 60–69 moderately depressed, 70 and above severely depressed.

The Zung Self-Rating Anxiety Scale is also a self-administered 20-question test scored on a scale of 1–4. Fifteen questions are worded toward increasing anxiety and 5 toward decreasing anxiety levels. The scores range from 20 to 80: 20–44 normal range, 45–59 mild-to-moderate anxiety levels, 60–74 marked to severe anxiety, 75–80 extreme anxiety.

The MMSE includes 30 items and assesses orientation, attention, immediate and short-term recall, language, and the ability to follow simple verbal and written commands. Cognitive performance varies by age and educational level, with an inverse relationship between MMSE scores and age, ranging from a median of 29 for individuals 18 to 24 years of age, to 25 for those 80 years of age and older. The median MMSE score is 29 for individuals with at least 9 years of schooling, 26 for those with 5 to 8 years of schooling, and 22 for those with 0 to 4 years of schooling.

If the patients had literacy problems, the questionnaires were completed with the help of a health operator.

Statistical methods

Descriptive data are shown as absolute frequencies of the different modalities for categorical data and as mean ± SD for continuous variables. Chi-square test for categorical variables and *t* test or Mann–Whitney test for independent data for continuous variables were carried out to assess whether significant differences could be demonstrated between IT and NIT groups.

Multivariate analysis models were used in which depression, anxiety, and MMSE scores were dependent variables and, respectively, anxiety and MMSE, depression and MMSE and depression and anxiety, together with age, gender, disease duration, HbA1c, and NIT/IT were independent variables. As a significant interaction coefficient between age and depression was estimated, indicating a weaker effect of depression with increasing age, the above-mentioned regression models were subsequently applied stratifying by age (<50, 50–59, 60–69, 70–80).

A *P* value of less than 0.05 was taken as significant. All analyses were performed with Stata 9.2.

Results

Overall, 57 (11.4%) patients had a score indicative of mild depression, 8 (1.6%) of moderate depression, none of severe depression, and 39 (7.8%) were taking anti-depressant drugs at the time of study (Table 2). Thus, the overall prevalence of depression was 20.9%. Assuming that medication might modify the responses to questionnaires, patients on anti-depressants were excluded from further analysis. Only 38 patients (7.6%) had a score suggestive of mild anxiety, 6 (1.2%) of moderate anxiety, and 1 (0.2%) of severe anxiety. Both scores were significantly higher in women than men (41.6 vs. 34.8 for depression and 40.0 vs. 33.7 for anxiety, both $P < 0.001$), although differences by gender disappeared when considering only higher scores (>50).

Table 1 Clinical data of the patients studied

	All patients ($n = 498$)	Insulin-treated ($n = 249$)	Non-insulin-treated ($n = 249$)	Difference IT versus NIT
Gender (F/M)	236/262	122/127	114/135	NS
Age (years)	67.58 ± 7.72	68.96 ± 7.14	66.20 ± 8.05	$P < 0.01$
Schooling° (0/1/2/3/4)	26/206/143/100/22	20/116/65/41/6	6/90/78/59/16	$P < 0.01$
Occupation^ (0/1/2/3/4/5/6)	48/382/12/16/6/14/17	28/200/4/4/3/3/7	20/182/8/12/3/11/10	$P = 0.05$
Status* (1/2/3/4/5)	22/85/9/12/365	9/53/3/6/178	13/32/6/6/187	NS
Known diabetes duration (years)	17.03 ± 8.25	20.27 ± 8.03	13.77 ± 7.11	$P < 0.01$
Family history for_DM (no/yes)	167/306	82/167	85/139	NS
Smoking status (no/yes/former)	263/57/178	124/24/101	139/33/77	NS
Hypertension (yes/no)	411/87	214/35	197/52	$P < 0.05$
Menopause (no/current/over)	6/15/215	0/8/114	6/7/101	$P < 0.05$
Owning glucose meter (no/yes)	45/453	2/247	43/206	$P < 0.01$
Self-monitoring blood glucose (no/yes)	59/439	3/246	56/193	$P < 0.01$
Self-monitoring > 1/day (no/yes)	323/175	92/157	231/18	$P < 0.01$
BMI	28.41 ± 5.12	28.18 ± 4.80	28.65 ± 5.42	NS
Total cholesterol (mmol/l)	4.83 ± 0.95	4.65 ± 0.93	5.01 ± 0.94	$P < 0.01$
HDL cholesterol (mmol/l)	1.26 ± 0.38	1.28 ± 0.41	1.24 ± 0.34	NS
Triglyceride (mmol/l)	1.69 ± 1.05	1.70 ± 0.14	1.68 ± 1.03	NS
Fasting blood glucose (mmol/l)	9.00 ± 3.12	9.63 ± 3.74	8.38 ± 2.18	$P < 0.01$
HbA1c (% of total Hb)	8.16 ± 1.39	8.46 ± 1.48	7.85 ± 1.23	$P < 0.01$
Foot ulcers (never/previous/active)	467/26/4	221/23/4	246/3/0	$P < 0.01$
Retinopathy (no/mild/moderate-severe)	240/110/127	80/62/103	160/48/24	$P < 0.01$
Microalbuminuria (no/micro/macro)	306/105/18	151/82/14	155/23/4	$P < 0.01$

° 0 = no formal schooling; 1 = primary education; 2 = middle school; 3 = high school; 4 = university education

^ 0 = housewife; 1 = retired; 2 = blue collar; 3 = self-employed; 4 = craftsman; 5 = white collar; 6 = other

* 1 = single; 2 = widower; 3 = divorced; 4 = separated; 5 = married

Table 2 Zung Depression, Zung Anxiety, and MMSE scores in the patients studied (39 people taking anti-depressants are not included)

	All patients ($n = 459$)	Non-insulin treated ($n = 232$)	Insulin treated ($n = 227$)	*P*
Depression				NS
None (20–49)	394 (85.8%)	198 (85.3%)	196 (86.3%)	
Mild (50–59)	57 (12.4%)	31 (13.4%)	26 (11.5%)	
Moderate (60–69)	8 (1.7%)	3 (1.3%)	5 (2.2%)	
Severe (70–80)	–	–	–	
Depression (mean ± SD)	38.6 ± 8.9	39.7 ± 8.3	37.5 ± 9.3	0.004*
Anxiety				NS
None (20–49)	421 (91.7%)	211 (91.0%)	210 (92.5%)	
Mild (50–59)	32 (7.0%)	17 (7.3%)	15 (6.6%)	
Moderate (60–69)	5 (1.1%)	4 (1.7%)	1 (0.4%)	
Severe (70–80)	1 (0.2%)	–	1 (0.4%)	
Anxiety (mean ± SD)	36.4 ± 8.5	36.2 ± 8.3	36.2 ± 8.3	NS*
MMSE (mean ± SD)	24.8 ± 3.3	25.1 ± 3.4	24.6 ± 3.2	NS*

* Mann–Whitney test

The average MMSE score in the whole sample was 24.83 ± 3.34 which, considering the age and schooling of the patients (Table 1), was not indicative of cognitive impairment.

NIT patients differed from IT patients for age, schooling, known duration of diabetes, fasting blood glucose, HbA1c, presence of hypertension, foot ulcers, retinopathy, microalbuminuria, self-monitoring practice, and frequency

(all $P < 0.05$) and had a slightly higher average depression score (39.7 ± 8.3 vs. 37.5 ± 9.3, $P = 0.004$). However, when stratified by severity of symptoms, the two groups did not differ for depression, anxiety, or cognitive function (Table 2).

On multivariate analysis, depression was associated with anxiety ($P < 0.001$), age ($P < 0.001$), gender (men having lower scores than women, $P = 0.042$), and insulin treatment, IT patients being less depressed than NIT ($P < 0.001$).

Anxiety correlated with age ($P < 0.001$). The association between depression and anxiety became progressively weaker with increasing age. Stratifying by age, in fact, the coefficient decreased from 1.24 for age <50, $P = 0.02$, to 0.93 for ages 50–59, $P < 0.001$, 0.69 for ages 60–69, $P < 0.001$, and 0.59 for ages >70, $P < 0.001$. For ages >60, women had higher anxiety scores than men ($P < 0.01$).

None of the clinical independent variables correlated with MMSE, although this showed a trend to an inverse correlation with depression and anxiety.

Discussion

This study was designed to assess depression and anxiety together with cognitive function in a population of people with type 2 diabetes and to explore their possible associations with the clinical status of the patients. While confirming an increased prevalence of depression compared to the general population, we did not find evidence for increased anxiety or cognitive dysfunction. In addition, depression correlated with age, gender, and anxiety, as expected, but not with duration of diabetes, HbA1c, or the presence of vascular complications.

Using the Zung Depression tool, prevalence estimates of 12–13% were reported in general population samples from the United States [14, 15] and in 6.8% of men and 12.1% of women in Finland [16]. Data from Italy are limited to a small set of 26 HIV-negative intra-venous drug users aged 28.5 [17] (average Zung depression score 47.6), and a larger group of 255 elderly non-diabetic people aged 77.5 (average score 49.4) [18], both of which lay outside the age range of the patients in this study.

The 12-month prevalence of generalized anxiety disorder in the general American population is 18.1%, most cases being comorbid with clinical depression [19]. Using the Zung tool, 20% of consecutive patients followed in a family practice in the United States scored in the anxiety range [20].

Many studies have described depression and diabetes as comorbid conditions and explored the association of depression with metabolic variables [1–4]. It is not clear, however, which comes first. Strine et al. demonstrated that adults with current depression or a lifetime diagnosis of depression or anxiety are significantly more likely than those without either diagnosis to smoke, be obese or physically inactive and to binge drink or drink heavily [21]. The initial onset of major depressive disorder has been suggested to occur independently and precede the diagnosis of type 2 diabetes by many years [7]. According to a national 21-year follow-up study, symptoms of depression were found to predict diabetes independently and through established risk factors for diabetes, primarily in people of low socioeconomic status and high numbers of depressive symptoms [8]. On the other hand, psychosocial factors associated with the hardships imposed by chronic illnesses, such as diabetes, may themselves be responsible for concurrent depression and anxiety in some patients. Diabetes is a complex and demanding disease that can induce serious psychological stress. This, in turn, may disrupt glycemic control directly, through the effects of counter-regulatory hormones, or indirectly, via deterioration of self-care behaviors. Gonzales et al. demonstrated in a meta-analysis a significant association between depression and treatment non-adherence in patients with type 1 and type 2 diabetes, suggesting that non-adherence may represent an important pathway between depression and worse diabetes clinical outcomes [5].

The lack of correlation with disease duration, HbA1c, vascular complications or the need for insulin treatment suggests that mild-to-moderate depression may not have influenced health-related outcomes in our population sample. Cox et al. also found no significant differences for mood or cognitive symptoms between insulin regimens [22], and Koopmans et al. reported no association with vascular comorbidities in non-insulin-treated type 2 patients [23]. If anything, we observed a slightly lower average depression score among the patients with more severe diabetes. In a study of similarly stratified patients with type 2 diabetes, Fal et al. [24] report better quality of life among the insulin treated. Though cross-sectional in nature and therefore unsuited to reveal cause-relationship effects, our data support the possibility that depression may have predated the onset of diabetes.

Deterioration of cognitive function was also reported in association with poor metabolic control in patients with type 2 diabetes [11]. In this paper, we assessed mental status by the MMSE, a research tool widely used in epidemiological studies and to follow cognitive changes in clinical trials [13], and found no impairment in the population studied. Similar results were reported recently by van den Berg et al. [25] in a follow-up study, in which cognitive function was not found to differ from that of a matched non-diabetic population, both in terms of prevalence and progression rate over 4 years.

In conclusion, we found that depressive symptoms may show increased prevalence in type 2 diabetes but are of mild-to-moderate severity and do not appear to correlate with disease duration, metabolic control, use of insulin, or the presence of complications.

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Conflict of interests No potential conflict of interest relevant to this article was reported.

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