Clinical variables associated with depression in patients with type 2 diabetes

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Summary

Background: the aim of the study was to evaluate the relationship between type 2 diabetes (T2DM), depression and depressive symptoms and their clinical impact on T2DM.
Methods: the authors evaluated 214 outpatients, 105 with diabetes (T2DM group) and 109 non-diabetics (control group), with ages ranging between 50 and 75 years (T2DM group 65.1 ± 5.6 years, control group 63.4 ± 5.8 years). Use of antidepressant treatment or score ≥ 16 on the Beck depression inventory (BDI) was considered depression. Complications of diabetes and total symptom score (TSS) for peripheral neuropathy were reported by patients.
Results: diabetes group had a higher frequency of depression (35.2%) compared to controls (21.1%) (p=0,021), with 2.4 times increased risk of depression. The presence of depressive symptoms was also higher in T2DM group (mean BDI 9.5 ± 8.8 *versus* 6.9 ± 6.2; p=0.039). Symptoms of diabetic neuropathy were higher in depressed subjects. The metabolic control and presence of complications in T2DM group were not associated with depression.
Conclusion: T2DM led to an increased risk of depression, but this did not influence the metabolic control or the presence of other complications.

Keywords: diabetes mellitus, depression, diabetes complications, diabetic neuropathies.

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic disease with high prevalence, estimated at 9.8% of the global population.[1] Several studies have shown an association between T2DM and depression, which is present in 11 to 31% of diabetic patients.[2] These individuals have a 24% higher risk than the general population to manifest depression at some point in life, and this risk may be even higher in those diagnosed with depression in the past.[3]

The association of these diseases appears to be related to worsening of various clinical factors associated with T2DM, such as worse glycemic control, amplification of symptoms[4] and a higher prevalence of complications.[5] Furthermore, patients with T2DM and depressive symptoms have worse physical and cognitive performance,[6] reduced adherence to dietary and drug recommendations,[4] and worse quality of life.[7] Such individuals also represent higher health care costs[6] and have an increased risk of mortality from all causes.[8]

Depression has a significant impact not only on clinical outcomes but also on psychological and social factors, and is connected with gradual worsening of health status[9] and accelerated cognitive decline.[10] Because of these negative consequences, some clinical guidelines recommend the evaluation of psychological status and depressive symptoms in patients with T2DM.[11] However, these recommendations are not carried out effectively in clinical practice. The treatment of these comorbidities jointly is increasingly considered essential for the clinical management of these individuals.[4]

In the present study, the authors evaluated the association between depression and depressive symptoms in individuals with T2DM compared to the general population, and the impact of these symptoms on clinical

and laboratory parameters, and on complications of the disease.

Methods

This is a cross-sectional study, conducted from September 2012 to September 2013. The sample consisted of 214 outpatients, with 105 diagnosed with T2DM and 109 non-diabetics. Participants eligible for the study group were those aged 55-75 years with a previous diagnosis of T2DM. The control group consisted of individuals of the same age range without diabetes of any cause, and with fasting blood glucose levels below 100 mg/dL, obtained no later than six months prior to the interview. In both groups, mourning (loss of a close friend or family member in the previous year) was considered as an exclusion criterion for influencing the diagnosis of depressive symptoms.

This study was approved by the Committee of Ethics on human research of the Universidade Comunitária da Região de Chapecó. All participants read and signed a free and informed consent.

The presence of depression was determined by the use of antidepressant medications in order to treat depression, confirmed by medical record review; or a score ≥16 on the Beck depression inventory (BDI), which is an instrument used for the purpose of diagnosing depression. The first BDI scale dates from 1961, designed by Beck et al.[12] Later, changes were made over the years. Currently, it is widely used in research and clinical practice. It has been properly translated and validated for the Brazilian population,[13] and it has also been validated for patients with T2DM.[14] The instrument consists of 21 items on symptoms and attitudes, with intensities ranging 0-3. The items refer to sadness, pessimism, sense of failure, lack of satisfaction, guilt, feeling of punishment, self-deprecation, self-accusation, suicidal ideation, crying spells, irritability, social withdrawal, indecisiveness, distortion of body image, inhibition to work, sleep disorder, fatigue, loss of appetite, weight loss, somatic concern and decreased libido.

The ≥16 cutoff score in BDI was adopted to detect depression, while lower scores were considered non-depressed individuals. The cutoff point (≥16) showed the best balance between sensitivity and positive predictive value in a diabetic population, identifying more than 70% of patients with depression with 71% certainty.[13,14]

Structured interviews were conducted including the following variables: name, gender, age, marital status, education, duration of T2DM, and medicines used. To assess signs and symptoms associated with poor glycemic control, individuals were asked whether or not they presented in recent weeks polyuria, excessive thirst, increased appetite, weight loss, fatigue, blurred vision or infections. The items counted a point for each positive response. The evaluation of T2DM complications has also been performed by means of an interview with the patient's self-report, investigating the presence of cardiovascular disease, cardiovascular events, diabetic retinopathy, foot ulcer or amputation history, and peripheral vascular disease. For the evaluation of peripheral neuropathy, the authors used the Portuguese version of the total symptoms score (TSS), which scores the typical symptoms of peripheral neuropathy (burning, pain, numbness and paresthesia), further classified according to intensity. The diagnosis of neuropathy was determined as a TSS score ≥2.

Anthropometric measurements included height and weight of patients, with calculation of body mass index (BMI) in Kg/m². To measure the blood pressure, an aneroid pressure apparatus was used. Plasma concentrations of fasting glucose, glycated hemoglobin, total cholesterol, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c) and triglycerides were searched in electronic medical records, which included tests performed at the municipal laboratory, performed at up to six months prior to the interview. Tests carried out in another laboratory were not accepted.

Statistical analysis

Data analysis was performed using SPSS software version 20.0®. The adopted confidence interval (CI) was 95% with significance level of 5% ($p<0.05$).

For analysis of the qualitative variables, the authors used the chi-square test and the likelihood ratio test.[15] The comparison of age and BDI scores between groups was performed using Student's t test and Mann-Whitney test,[15] respectively. The same tests were used to verify the relationship between the characteristics of individuals with the presence of depression.

Odds Ratios (OR) were estimated with 95% CIs as a measure of association for both univariate tests and multiple analysis.

Results

Characteristics of individuals in the T2DM and control groups are presented in Table 1. Compared with the control group, individuals in the T2DM group were older ($p=0.032$) and less educated ($p=0.022$). Previous history of depression did not differ between groups ($p=0616$), and was present in 37.3% of subjects in the T2DM group and in 33.9% of the non-diabetic population. The same

occurred with a family history of depression, which was positive in 34 and 44% of patients, respectively (p=0.138). The average duration of T2DM diagnosis was 11.6±8.5 years. Regarding treatment of this disease, 46.5% used only oral medication, and the remainder used insulin associated with oral therapy.

TABLE 1 Demographic and clinical characteristics of the T2DM group (n=105) and the control group (n=109).

	Groups				
Variable	**T2DM**		**Control**		**p**
	n	**%**	**n**	**%**	
Gender					**0.224**
Female	68	64.8	79	72.5	
Male	37	35.2	30	27.5	
Age (years)					**0.032**
Average ± SD*	65.1±5.6	63.4±5.8			
Median (min.; max.)	65 (55; 75)	63 (55; 75)			
Marital status					**0.564**
Single	14	13.6	20	18.3	
Married	67	65.0	67	61.5	
Widowed	21	20.4	19	17.4	
Education					**0.022**
Illiterate	13	12.5	7	6.6	
Incomplete primary	64	61.5	58	54.7	
Complete primary	13	12.5	22	20.8	
Incomplete secondary	9	8.7	3	2.8	
Complete secondary	5	4.8	12	11.3	
University-level	0	0.0	4	3.8	
Positive history of depression					**0.616**
Yes	38	37.3	37	33.9	
No	64	62.7	72	66.1	
Family history of depression					**0.138**
Yes	34	34.0	48	44.0	
No	66	66.0	61	56.0	

*SD: standard deviation.

Compared with the control group, subjects with T2DM had a higher prevalence of depression (35.2 *versus* 21.1%, p=0.021) and higher scores on the BDI (mean 9.5 ± 8.8 *versus* 6.9 ± 6.2, p=0.039), with 2.4 times increased chance of depression (OR 2.4, 95CI 1.1-5.0) (Table 2).

TABLE 2 Association and risk of depression between the T2DM group (n=105) and the control group(n=109).

	Depression							
Group	**Yes**		**No**		**OR**	**95CI**		**p**
	n	**%**	**n**	**%**		**Inferior**	**Superior**	
T2DM	37	35.2	68	64.8	2.40	1.10	5.00	0.021
Control	23	21.1	86	78.9	1.00			

The associations between glycemic control and lipid control *versus* depression were tested in the T2DM group. The assessment of glycated hemoglobin showed a tendency to higher values in depressed subjects (10.9 ± 17.7 *versus* 9.1 ± 2.5%), even though with no statistical difference (p=0.478). Fasting blood glucose levels (143.1 ± 66 *vs*. 160.7 ± 63.9 mg/dL), total cholesterol (197.6 ± 45.5 *vs*. 201 ± 50.9 mg/dL), HDL-c (42.2 ± 11.4 *vs*. 46.5 ± 13.3 mg/dL), LDL-c (109.9 ± 38.1 *vs*. 117.5 ± 33.9 mg/dL) and triglycerides (314.6 ± 627.1 *vs*. 231.2 ± 437 mg/dL) did not differ according to the presence of depression (p>0.05). Similarly, BMI was not associated with depression (p=0.316) with a mean of 31 ± 5.3 kg/m² in depressed and 29.7 ± 6.2 kg/m² in non-depressed subjects. Systolic and diastolic pressure did not differ between depressed and non-depressed subjects (p> 0.05) either. There was no relationship between greater amount of hyperglycemic symptoms and the presence of depression (mean 3.1 ± 1.2 in depressed subjects *versus* 2.8 ± 1.6, p=0.234).

The average score in the TSS questionnaire was higher in depressed subjects (mean 4.4 ± 3.2) compared to those without depression (mean 3.0 ± 2.5) (p=0.048); however, the presence of peripheral neuropathy did not differ according to this disorder.

The presence of depression and its association with self-reported macrovascular and microvascular complications are shown in Table 3.

TABLE 3 Presence of chronic complications in the T2DM group, between individuals with and without depression.

	Depression				
Variable	**Yes**		**No**		**p**
	n	**%**	**n**	**%**	
Cardiovascular disease					0.462
Yes	15	39.5	23	60.5	
No	21	32.3	44	67.7	

(Continue)

TABLE 3 (Cont.) Presence of chronic complications in the T2DM group, between individuals with and without depression.

Previous cardiovascular event					0.600
Yes	12	38.7	19	61.3	
No	24	33.3	48	66.7	
Retinopathy					0.063
Yes	17	47.2	19	52.8	
No	19	28.8	47	71.2	
Nefropathy					0.186
Yes	6	54.5	5	45.5	
No	30	32.6	62	67.4	
Peripheral vascular disease					0.154
Yes	14	45.2	17	54.8	
No	22	30.6	50	69.4	
Neuropathy					0.348
Yes	25	39.1	39	60.9	
No	12	30.0	28	70.0	

Discussion

The results of this study revealed that the diagnosis of T2DM is associated with a 2.4 times increased risk of depression compared to people without diabetes. This risk was close to that found by an important meta-analysis,[2] which showed a 2-fold greater chance of depression. However, the risk was lower to that found by a large cross-sectional study with more than 3,000 participants aged over 30 years, in which T2DM was associated with a 4.3 times greater chance of depression.[17] The prevalence of this disorder found in this series is slightly higher than that reported in a meta-analysis by Anderson et al.,[2] which revealed depression in 11-31% of diabetic patients. Similarly, another Brazilian study found a prevalence of 18.6% in individuals with T2DM.[18] Similar results were reported in a recent meta-analysis involving more than one hundred thousand participants, which revealed that individuals with T2DM have a 24% higher risk of developing depression,[3] consistent with the results demonstrated in this sample: diabetes is a risk factor for depression.

During the last 30 years, increasing evidence has shown that depression is an important comorbidity related to diabetes,[19] and that the combination of these diseases seems to affect the clinical management of T2DM. Ciechanowski et al.[4] noted that the number of individuals with glycated hemoglobin levels greater than 8% was higher among the depressed. Depression is associated with hyperglycemia in patients with diabetes, with a still unclear mechanism and uncertain direction.[20]

Other authors also reported that patients with T2DM and depression have higher glycated hemoglobin levels compared to people without depression.[18] However, in this study, glycated hemoglobin levels were not associated with the presence of depression, in contrast to most of the evidence from the literature. Another study also previously suggested that blood glucose levels tend to be higher in depressed individuals, despite the lack of significant differences according to the presence of depression.[21] The existing literature data are still inconsistent with respect to the relationship of depressive symptoms and poor glycemic control.

Researchers have also shown that depression can be associated with an increased risk of complications from diabetes. A meta-analysis, including 27 studies, found a positive association between depression and diabetes complications, both macrovascular and microvascular.[22] Another review, longitudinal-based, revealed that, over a period of five years, patients with major depression and diabetes mellitus had a risk 36% higher of developing advanced microvascular complications such as nephropathy or blindness, and a risk 25% higher of developing advances macrovascular complications, such as myocardial infarction and stroke.[5] In this study, the presence of macrovascular and microvascular complications was not associated with the presence of depressive disorder.

The presence of symptoms of diabetic neuropathy, in this case, was significantly higher in subjects with depression. In the past, some authors have already observed that neuropathy symptoms (pain, instability, decreased sensation in the feet) are associated with depressive symptoms.[23] Additionally, this same study provided evidence that the presence of depression is associated with the severity of diabetic neuropathy. Individuals with diabetic neuropathy symptoms present worse quality of life, possibly due to more depressive symptoms and greater severity of pain.[24] Another important correlation found by some authors is the presence of foot ulcers and depressive symptoms – people with these symptoms showed a 2-fold higher risk of diabetic foot ulceration.[25] In this study, there was no significant association between these conditions. This was due to the fact that the number of individuals with diabetic ulcers was very small, making it impossible to compare.

Conclusion

The presence of T2DM was associated with an increased risk of depression and depressive symptoms. Furthermore, these patients had more symptoms of diabetic neuropathy. The significant risk of depression among indi-

viduals with T2DM in this study population is an important finding, given the increasing rates of T2DM and its clinical and public health implications. The authors believe, therefore, that the assessment of depressive symptoms should be part of the overall control of the patient with T2DM, aimed at comprehensive treatment in order to reduce any consequences.

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Resumo

Características clínicas associadas à depressão em pacientes com diabetes tipo 2

Objetivo: avaliar a relação entre *diabetes mellitus* tipo 2 (DM2), depressão e sintomas depressivos e seu impacto no controle clínico do DM2.
Métodos: foram avaliados 214 pacientes ambulatoriais, 105 com DM2 e 109 não diabéticos, com idade entre 55 e 75 anos (grupo DM2 65,1±5,6 anos e grupo controle 63,4±5,8 anos). Considerou-se depressão o uso de tratamento antidepressivo ou escore ≥16 no inventário de Beck (BDI). Complicações do DM2 e escore total de sintomas (TSS) para neuropatia periférica foram questionados aos pacientes.
Resultados: o grupo DM2 apresentou maior frequência de depressão (35,2%) em relação aos controles (21,1%) (p=0,021), com um risco 2,4 vezes maior de apresentar depressão. A presença de sintomas depressivos também foi superior no grupo DM2 (média BDI 9,5±8,8 *versus* 6,9±6,2; p=0,039). Os sintomas de neuropatia diabética foram superiores nos depressivos. O controle metabólico e a presença de complicações no grupo DM2 não foram associados à depressão.
Conclusão: o DM2 determinou um maior risco de depressão; porém, essa associação não influenciou o controle metabólico e a presença de outras complicações da doença.

Palavras-chave: *diabetes mellitus*, depressão, complicações do diabetes, neuropatias diabéticas.

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