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COGNITIVE DISORDERS, DEPRESSIVE STATUS AND CHRONIC COMPLICATIONS OF TYPE 2 DIABETES MELLITUS

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Abstract

Background and aims: *Depression and cognitive disorders were reported more frequently in patients with diabetes mellitus (DM). Our aim was to analyze the association of cognitive disorders and depression association with chronic complications of DM in a group of Romanian patients.* ***Materials and methods:*** *The data was analyzed from 181 patients, with a mean age of 58,3 years to whom we applied the MMSE (Mini-Mental State Examination) and MADRS (Montgomery-Asberg Depression Rating Scale) questionnaires. We also analyzed the presence of chronic DM complications, HbA1c and lipid profile.* ***Results****: Most patients with type 2 diabetes mellitus (T2DM) had mild cognitive impairment (92%), more common in the age group 50-59 years. Chronic macrovascular complications were present in 74.58%, while chronic microvascular complications were present in 61.87% of patients with T2DM who associated mild and moderate cognitive impairment (p = 0.013). The most common form of depression was mild depression (90.2%), present in most patients with DM, regardless of progression and type of treatment. MADRS depression test scores were statistically significant correlated with the presence of peripheral artery disease - PAD (p <0.001), ischemic heart disease – IHD (p <0.001) and chronic kidney disease - CKD (p =0.05). We did not find a statistically significant correlation with HbA1c and serum lipid values (p>0,05).*
Conclusion: *Chronic diabetes macrovascular complications (PAD, IHD) and CKD were more frequently associated with cognitive disorders and depression in patients with T2DM independent of the degree of metabolic control.*

key words: *diabetes mellitus, depression, cognitive impairment, chronic complications.*

Background and Aims

Diabetes mellitus (DM) is a chronic illness that requires continuing medical care, rigorous programs of self-control and effective disease monitoring in order to prevent acute complications and decrease the risk of chronic complications. Type 2 diabetes (T2DM) is a major risk factor associated with cognitive decline and is associated with major complications that shorten life expectancy. Cognitive impairment in elderly patients with DM is associated with functional disability, impaired self-care, poor control of DM and a higher risk of mortality. The etiology of cognitive impairment and dementia in people

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with T2DM is multifactorial, but the pathophysiological mechanism remains unknown.

Multiple epidemiological studies have shown a correlation between DM and an increased risk for cognitive dysfunction [1]. DM is associated specifically with a moderate cognitive decline (MCD) in middle-aged groups and progression towards dementia in elderly patients. In the last 3 decades, the Mini-Mental State Examination (MMSE) questionnaire has been used internationally as a screening method to evaluate cognitive decline. Applying the MMSE questionnaire is considered a good tool for the screening and evaluation of cognitive decline in elderly patients with DM [2]. The prevalence of depression in patients with DM is 2 times higher than in the general population. Depression in DM is often associated with a low compliance to healthy diet, exercise and self-control, leading to metabolic imbalance evidenced by elevated HbA1c, micro-and macrovascular complications and increased mortality [3].

Material and methods

We analyzed data from181 adult patients with DM to whom we applied the MMSE and MADRS (Montgomery-Åsberg Depression Rating Scale) questionnaires. All patients signed and informed consent prior to inclusion in the study.

MMSE may reveal disorders of cognitive functions in the elderly without dementia and identify individuals in the prodromal phase of dementia. The score ranges from 0 to 30 points. A high score indicates better performance. Cut-offs for the MADRS score are: 0 points - no depression; 2-30 points - mild depression; >30 points - severe depression.

We also recorded HbA1c, lipid profile, weight, height, body mass index (BMI) and the presence of hypertension, chronic microvascular (neuropathy, retinopathy, diabetic renal disease) and macrovascular (ischaemic heart disease - IHD, peripheral artery disease - PAD) diabetes complications as reported in the medical records. We have excluded patients with previous stroke.

Statistical analysis: Values are expressed as mean ± standard deviation (SD) for normally distributed data. Comparisons between groups were made using ANOVA for quantitative variables and $\chi 2$ test for categorical variables. $P< 0.05$ was regarded as statistically significant.

Results

The group of patients was composed of 153 patients with T2DM (84.3%) and 28 patients with type 1 diabetes - T1DM (15.7%), with a mean age of 54.93 years. There were 54% women and 46% men. The main anthropometric and biochemical characteristics of the patients as well as prevalence of chronic complications and the mean MMSE and MADRS scores are shown in Table 1.

Most T2DM patients were overweight or obese (74%) and the most representative age group was 50-59 years. 15% of patients with T2DM were treated with oral anti diabetic agents (OADs), 16% with OADs and insulin treatment and 69% of patients were treated with insulin.

Chronic macrovascular complications were more frequent in patients with T2DM (Table 1) with the exception of PAD which, unexpectedly, was significantly more frequent in T1DM patients (28.57%) compared to T2DM patients (13.73%).

Patients with T2DM associated mostly mild cognitive impairment 92% (MMSE $\geq$ 21), 8% associated moderate cognitive impairment (MMSE 10-20) and 0% associated severe impairment (MMSE $\leq$ 9), without a statistically significant difference in relation with the duration of DM ($p > 0.05$) as shown in Figure 1.

Table 1. Anthropometric and biochemical features of patients with T1DM/T2DM, prevalence of chronic complications and the mean scores of the MMSE and MADRAS questionnaires.

Parameter	T2DM(n=153)	T1DM (n= 28)
Age (years)	58.37±13.40	62.32±10.13
BMI (kg/m²)	32.00±5.24	22.00±3.52
HbA1c(%)	9.88±2.34	9.29±2
Cholesterol(mg/dl)	215.61±60.16	189.71±45.91
Triglycerides(mg/dl)	175.31±97.74	132.36±54.54
Diabetes duration(years)	8.69± 5.88	25.29±5.43
IHD	61.44%	32.14%
Previous hypertension or use of anthypertensive drugs	74.51%	67.86%
PAD	13.73%	28.57%
Diabetic retinopathy	41.18%	67.86%
Diabetic neuropathy	63.40%	57.14%
Chronic renal disease	18.30%	7.14%
MMSE mean score	25.49±3.52	25.39±3.17
MADRS mean score	14.05±9.72	14.14±9.93

All values have been expressed as mean ± SD or %

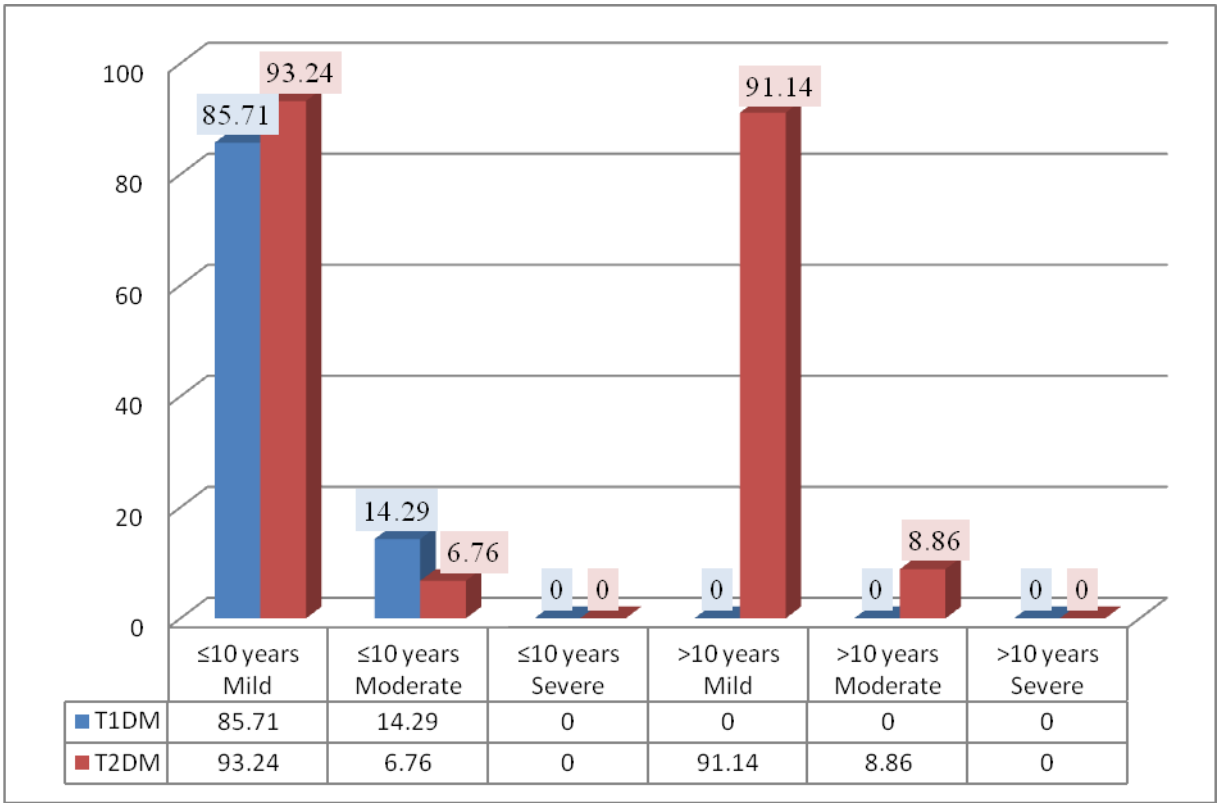

Figure 1. *Prevalence of cognitive disorders in T1DM compared to T2DM in relation with duration of diabetes.*

Mild and moderate cognitive impairment were more frequent in the age group 50-59 years. The mean value of HbA1c and serum lipids did not correlate with the MMSE score.

Chronic macrovascular complications were present in 74.58% of patients, while 61.87% of chronic microvascular complications were present in patients with T2DM who associated mild and moderate cognitive impairment (p =0.013).

After applying the MADRS questionnaire to assess depression, we found that 90.20% of

patients with T2DM had mild depression, and 5.88% severe depression, without statistically significant difference according to DM duration. The most affected age group was 50-59 years. The mean value of HbA1c and serum lipids was not different statistically significant in relation with the MADRS score ($p > 0.05$).

Patients with T2DM and mild or moderate depression had chronic macrovascular complications in 74.13% of patients, and chronic microvascular complications in 62.06% of patients ($p = 0.015$). Among patients diagnosed with severe depression (MADRS >30), 50% associated two macrovascular complications (IHD and PAD) and hypertension, 37.5% associated two macrovascular complications and only 12.5% associated one macrovascular complication.

PAD and IHD were significantly associated with depressive disorders ($p <0.001$) as shown in Figures 2 and 3.

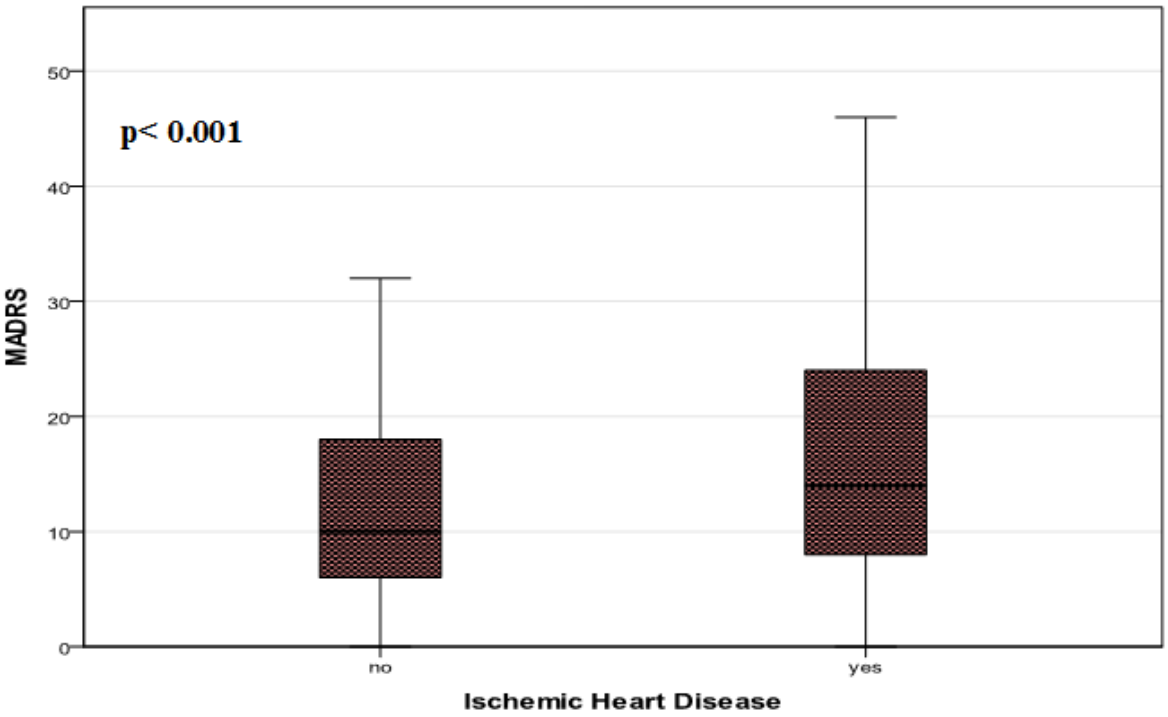

Figure 2. *Correlation between MADRS score and the presence of IHD.*

Depression and cognitive tests were correlated statistically significant with the presence of PAD ($p < 0.001$), chronic renal disease ($p = 0.05$) and IHD ($p < 0.001$).

Discussions

DM is associated specifically with MCD in middle and older age groups [4], a feature observed also in this study. A number of studies have found significant correlations between the value of Hb1Ac and cognitive disorders [5]. In the ACCORD- MIND study an increase with 1% of HbA1c was significantly correlated with a lower score on the MMSE questionnaire [6].

The mean values of HbA1c and serum lipids were not significantly correlated with the MMSE score in our study, possibly due to the small number of patients. Cognitive decline was particularly associated with the presence of chronic macrovascular complications. Prevalence of cardiovascular complications was high in this study, considering that the group of patients included only hospitalized patients who have presented a large number of complications and comorbidities.

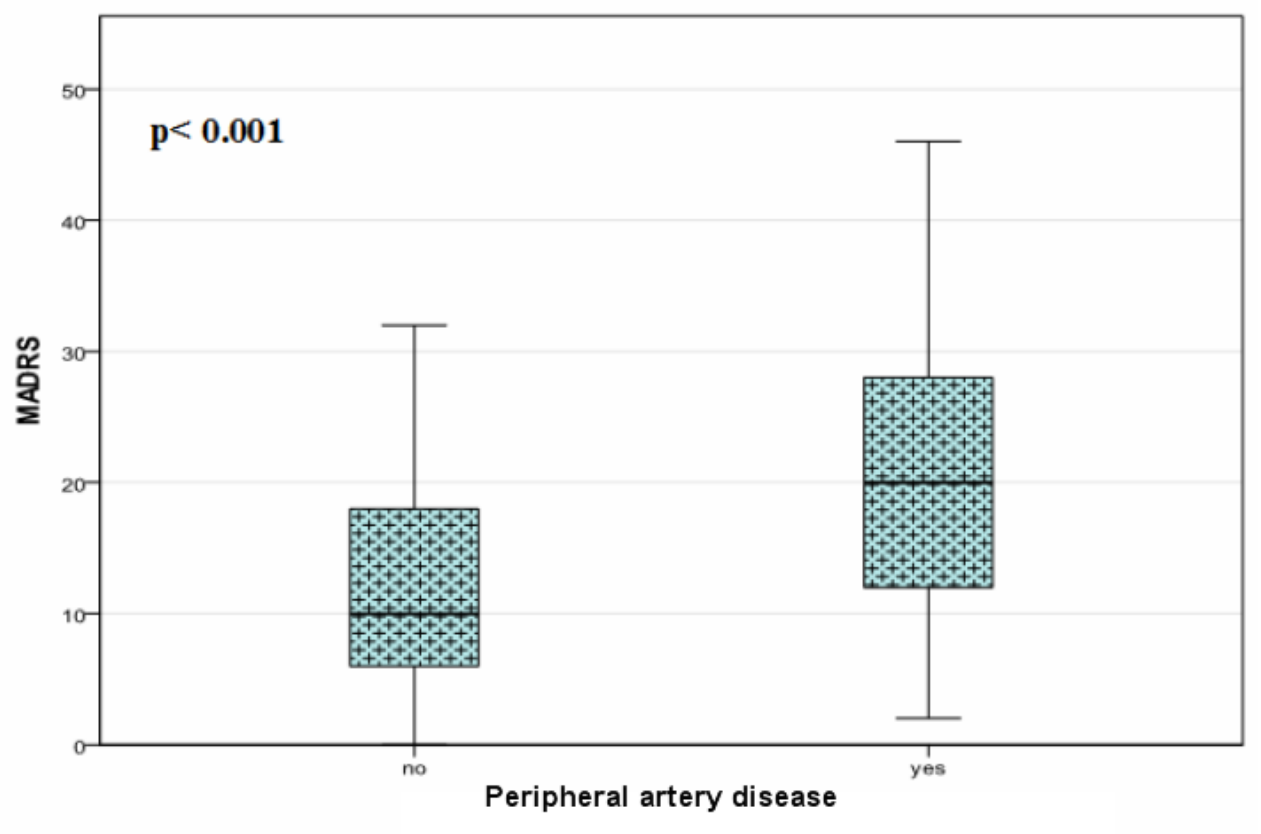

Figure 3. *Correlation between MADRS score and the presence of PAD.*

Depression is one of the most common disorders encountered in the general population [7]. Prevalence of depression in patients with DM is much higher than in the general population [3,8]. This was observed also in our study in both patients with T1DM and T2DM. Major depression was not a common form of presentation. Most cases were being noted as mild depression. Depression prevalence was not significantly correlated with the duration of DM. Depression is also considered a risk factor for coronary heart disease and stroke through multiple mechanisms, involving psyho-stress and dysmetabolic factors, neurochemical, oxidative stress and decreased levels of dopamine, favoring spasms of small vessels [9,10].

Our study confirmed an association between depression and chronic macrovascular complications, regardless of HbA1c and serum lipids values, suggesting the involvement of other mechanisms than chronic hyperglycemia in the development of depression. PAD and IHD which are frequently associated with depressive disorders were found to be significantly associated with the MADRS score in our study.

In 2006 a study by Slovacek et al. reported a direct correlation between the presence of PAD and depression in patients with DM, with subsequent decrease in the quality of life [11].

Two different studies carried out in India highlighted a high prevalence of depression in patients with T2DM who had retinopathy, neuropathy, renal disease and diabetic peripheral arterial disease. Depression correlated with the presence of diabetes complications in patients with newly diagnosed diabetes, and the likelihood of developing depression increased in parallel with the worsening of diabetic complications [12,13]. Our study found an association between severe depression and higher number of chronic complications.

Conclusion

We found a correlation between chronic macrovascular diabetes complications, cognitive disorders and depression, mostly in T2DM patients, independently of the degree of metabolic control, suggesting involvement of other mechanisms than chronic hyperglycemia. Quality of life of subjects with PAD and depressive disorders is poor and its improvement requires a multidisciplinary approach.

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