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Original scientific paper

Depression, Anxiety and Cognitive Dysfunction in Patients with Type 2 Diabetes Mellitus – A Study of Adult Patients with Type 2 Diabetes Mellitus in Osijek, Croatia

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A B S T R A C T

Aim of the study was to determine the rate of depression and anxiety in the patients with diagnosed Type 2 Diabetes mellitus (DM), and also to determine the state of the congnitive functions in patients with Type 2 Diabetes mellitus compared with the control group. Study was designed as a epidemiological cross sectional study, sample consisted of 108 patients, 66 of the patients were diagnosed with Type 2 Diabetes mellitus, and 42 were control group. All of them were interviwed by psychiatrist and tested through clinical interview with Hamilton depression rating scale, Hamilton Anxiety rating scale, Mini mental state examination and questionnaire about sociodemografic data. Results show that group of patients with DM were statistically significat more depressed than the control group of the patients (p=0.035). Pathological anxiety measured by Hamilton Anxiety Rating Scale (HAM-A) appeared in 34 DM patients and 7 of the patients in control group, which is also statistically significant difference (p=0.002). Evaluation of the congnitive status done with Mini Mental State Examination (MMSE showed us tha patients with DM presented more cognitive dysfunctions compared with the control group. We can conclude that the high prevalence of psychiatric disorders in diabetic patients points to the need for greater investment in appropriate diagnostic evaluation of patients that consider mental issues.

Key words: *depression, anxiety, cognitive dysfunction, Type 2 Diabetes mellitus*

Introduction

The interface of diabetes and psychiatry has fascinated both endocrinologists and mental health professionals for years. Thomas Willis in the seventeenth century stated that »diabetes is caused by sadness or long sorrow«[1]. In »The Pathology of Mind« published in 1879. Sir Henry Maudsley commented that »Diabetes is a disease which often shows itself in families in which insanity prevails«. Insulin coma therapy was used as a psychiatric treatment within a decade of isolation of insulin[2]. Healthcare providers should be aware of the frequent coexistence of psychiatric conditions in patients with diabetes mellitus. Dementia, depression and anxiety are commonly seen in adition to other psychiatric conditions. The relationship between diabetes and psychiatric disorders is complex. Evidence suggests that common mechanisms may play a role in both the pathogenesis of diabetes mellitus and several psychiatric illnesess[3]. Diabetes and psychiatric disorders share a bidirectional association – both influencing each other in multiple ways[2]. Current epidemiological evidence suggests that at least one third of patients with diabetes suffer from clinically relevant depressive disorders[4–6]. Also, people with depressive disorders have an increased risk of developing diabetes[1]. A report from the World Health Survey estimated the prevalence of depression from 60 countries around the world, the overall one-year prevalence of

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self-reported symptoms of depression in individuals with diabetes was 9.3%[1]. Some other studies have reported prevalence rates of depression of 24–30%[4,5,8,9]. In a study done in Croatia by Filipčić et al.(2007.) 32.2% of patients with diabetes were depressed[10]. The prevalence of anxiety disorders among patients with diabetes is considerably higher compared to the general population. Anxiety symptoms have been found to be significant risk factors for development of diabetes. Negative correlations have been observed between prevalence of anxiety disorders and levels of HbA1c[2]. Patients with diabetes are at increased risk of developing cognitive impairment in comparison with the general population. Diabetes mellitus increases the risk of dementia (vascular and/or neurodegenerative). Diabetes accelerates the progression from mild cognitive impairment to dementia. It has been estimated that Type 2 Diabetes or impairment of glucose metabolism might be present in up to 80% of patients with Alzheimer disease. The cognitive dysfunction is associated with poorer ability in diabetes self-care and decreased adherence to antidiabetic treatment[11]. Studies shows that newly diagnosed Type 2 Diabetes is associated with a 63% higher future risk of dementia during the 7-year follow up period. The high dementia and ischemic stroke overlap rate in the diabetic study group suggests that vascular events play an important role in the pathogenesis of developing dementia[12].

Aim of the study was to determine the rate of depression and anxiety in the patients with diagnosed Type 2 Diabetes mellitus, and also to determine the state of the congnitive functions in patients with Type 2 Diabetes mellitus compared with the control group.

Subjects and Methods

Study was designed as a epidemiological cross sectional, sample consisted of 108 patients, 66 of the patients were diagnosed with Type 2 Diabetes mellitus, and 42 were control group. The patients were recruited as they come to the out-treatment control, nobody rejected the inclusion in the study, all patients agreed to be a part of the study and all of them signed informed consent. Inclusion criterions were persistance of Type 2 Diabetes mellitus at least one year, also allof the DM patients were on the hypoglicemic medication longer than 6 months, also all of the DM patients were without chronic DM complications. Study group and control group were comparable by age, gender and educational background. Overall, study included 66 male subjects (38 with DM and 25 without DM) and 42 female subjects (28 with DM and 17 without DM). In the group of DM patients 40 were retired, 17 still working and 9 of the patients were unemployed, while in the control group of the patients 27 were retired, 11 still working and 4 of them unemployed. Considering the education groups were also comparable (group of DM patients 9 with finished college, 26 finished high school, 31 elementary school, and control group 5 finished college, 18 high school and 19 elementary school). Considering the marital status 50 of patients with DM were married, 4 unmarried, 7 divorced, and 5 widowed, while in the control group 29 were married, 6 unmarried, 6 divorced and 1 widowed. All of them were interwied by psychiatrist and tested through clinical interview with Hamilton depression rating scale, Hamilton Anxiety rating scale, Mini mental state examination and questionnaire about sociodemografic data.

Hamilton Depression Rating Scale (HAM-D) is a multiple item questionnaire used to provide an indication of depression. The questionnaire is designed for adults and is used to rate the severity of their depression. Each item on the questionnaire is scored on a 3 or 5 point scale, depending on the item, and the total score is compared to the corresponding descriptor. A score of 0–7 is considered to be normal, 8–13 indicate mild depressive episode, 14–18 indicate moderate depressive episode and score 19 and higher indicate severe or very severe depression[13].

Hamilton Anxiety Rating Scale (HAM-A) is used by clinicians to rate the severity of a patient's anxiety, it contains 14 symptom-oriented questions. Each of these symptoms is given a severity rating, from not present (scored as 0) to very severe (scored as 4). The clinician must choose the possible responses to each question by interviewing the patient and by observing the patient's symptoms. A total score of 0–13 is considered to be normal and score of 14 and higher indicate presence of pathological anxiety[14].

The mini-mental state examination (MMSE) or Folstein test is a brief 30-point questionnaire test that is used to screen for cognitive impairment. It is commonly used in medicine to screen for dementia. It is also used to estimate the severity of cognitive impairment and to follow the course of cognitive changes in an individual over time. It samples functions including arithmetic, memory and orientation. The MMSE test includes simple questions and problems in a number of areas: the time and place of the test, repeating lists of words, arithmetic such as the serial sevens, language use and comprehension, and basic motor skills. A total score lower than 24 indicates cognitive impairment[15].

Subjects were aged between 44 and 78 years (mean 61,11 year), and all of them were from the city of Osijek in Croatia. SPSS Statistics version 20 statistical program has been used for the statistical analysis.

Results

The data of the rates of depression and anxiety in the patients with diagnosed Type 2 Diabetes mellitus (DM), and the data about the state of the cognitive functions in patients with Type 2 Diabetes mellitus compared with the control group are presented in Tables 1, 2, and 3

Patients with diagnosed Type 2 Diabetes mellitus (DM) were more depressed than the control group, 22 of the DM patients fullfilled criteria for moderate depressive episode, 7 of DM patients fullfilled criteria for severe and very severe depressive episode. Also group of patients with DM were statistically significat more de-

TABLE 1
RESULTS OF THE HAMILTON DEPRESSION RATING SCALE (HAM-D)

	Without DM	With DM	Total
Scores on HAM-D	N (%)	N (%)	N (%)
0–7 (without symptoms)	19 (42.5)	14 (21.2)	33 (30.6)
8–13 (mild depressive episode)	13 (31.0)	23 (34.8)	36 (33.3)
14–18 (moderate depressive episode)	9 (21.4)	22 (33.3)	31 (28.7)
19 and higher (severe and very severe depressive episode)	1 (2.4)	7 (10.6)	8 (7.4)
Total	42 (100)	66 (100)	108 (100)

DM – Diabetes mellitus type 2, Pearsons χ^2=8.577, df=3, p=0.035.

TABLE 2
RESULTS OF THE HAMILTON ANXIETY RATING SCALE (HAM-A)

	Without DM	With DM	Total
Scores on HAM-D	N (%)	N (%)	N (%)
0–13 (normal anxiety)	33 (78.6)	32 (48.5)	65 (60.2)
14 and higher (pathological anxiety)	9 (21.4)	34 (51.5)	43 (39.8)
Total	42 (100)	66 (100)	108 (100)

DM – Diabetes mellitus type 2, Pearsons χ^2=9.696, df=2, p=0.002.

TABLE 3
RESULTS OF THE MINI MENTAL STATE EXAMINATION (MMSE)

	Without DM	With DM	Total
Scores on MMSE	N (%)	N (%)	N (%)
24–30 (normal cognition)	41 (97.6)	49 (74.2)	90 (83.3)
Lower than 24 (cognitive impairment)	1 (2.4)	17 (25.8)	18 (16.7)
Total	42 (100)	66 (100)	108 (100)

DM – Diabetes mellitus type 2, Pearsons χ^2=10.0999, df=1, p=0.001.

pressed than the control group of the patients (p=0.035, Table 1). Pathological anxiety measured by Hamilton Anxiety Rating Scale (HAM-A) appeared in 34 DM patients and 7 of the patients in control group, which is also statistically significant difference (p=0.002, Table 2). Evaluation of the congnitive status done with Mini Mental State Examination (MMSE) showed us that patients with DM presented more cognitive dysfunctions compared with the control group. 17 of the DM patients had MMSE score lower than 24. Comparation of the study groups showed us statistically significant difference (p= 0.001, Table 3).

Discussion

In a chronic disorder like diabetes mellitus coexistent psychiatric illness leads to impaired quality of life, increased cost of care, poor treatment adherence, poor glycemic control with increased admissions due to hyperglycemic emergencies and other complications, altered pharmacokinetics of antidiabetic agents due to substance abuse involving tobacco and alcohol, higher absenteeism and overlaping clinical presentation. It is common for patients to experience emotional distress from living with diabetes and the effect of its complications. »Diabetes burnout« and »Diabetes overwhelmus« are the terms that have been used to display the distress of diabetes[16]. For example in the Survey Croatian-Dutsch-English from the European Depression in Diabetes (EDID) Research Consortium aim was to determine the levels of diabetes specific emotional problems in diabetic individuals with high versus low levels of depression. Percentages of patients with high depression scores were 39% and 34% (Croatian men and women), 19% and 21% (Dutch men and women), 19% and 39% (English men and women). Moreover, 79% (Croatian), 47% (Dutch) and 41% (English) of the patients with a severe depression score reported to have four or more serious diabetes-specific emotional problems. For patients with low depression scores, these percentages were 29% (Croatian), 11% (Dutch) and 1% (English). Serious diabetes-specific emotional problems are particularly prevalent in depressed diabetes patients[17].

Depression occurs in aproximately 30% of patients with type 1 and Type 2 Diabetes[18]. Both diabetes and de-

pression belong to so called »life style« or »civilisation diseases«[19] and their development may depend on life-style in the case of Type 2 Diabetes[20,21]. Rates of depression in people with diabetes are significantly increased and are thought to be at least doubled for those with diabetes compared to those without any chronic disease[4]. Different studies have reported prevalence rates of depression of 24–30%[4,5,8,9]. The published studies differ widely in terms of the methods used to measure depression. Research has shown that the prevalence of clinical depression in diabetic patients is approximately twice as high as in the general population[22].

Results in our study show that prevalence of depression in patients with DM is 36.1% (moderate, severe and very severe depression) in our sample. Severe and very severe depression appeared in 7.4%. The obtained dana indicate that the prevalence rate of depression in Type 2 diabetic patients in our sample is comparable to findings from other cultural settings. Also we observed that depression appeared with statistically significant diference between two study groups, group of patients with DM and the control group.

According to the studies prevalence of depression does not appear to differ according to type of diabetes[4,23,24]. Alagiakrishnan et al. (2012.) in their study showed that compared with the general population patients with major depressive disorder had a higher prevalence of diabetes, which was associated with increased age, use of antipsychotic agents, use of mood stabilisers and residence in suburban areas[25]. Huang CJ et al. (2012) showed in their study that the prevalence of diagnosed depressive disorder among patients with diabetes in Taiwan was lower than the rate in Western countries[26], which indicates influence of the different habbits and cultural settings. In a study done by Pibernik-Okanović et al.(2005) 33% of the sample had clinical depression which was confirmed by the psychiatric interview. Depressed patients compared with non-depressed ones reported more diabetes-related problems and poorer well-being. Female gender, experienced support and the level of emotional well-being were factors to predict depression[27]. Jurisić-Erzen D et al. (2011) done the study of the prevalence of depression and anxiety in seafarers type 2 diabetic patients and showed that depression and anxiety was significantly higher in the group of diabetic seafarers than in control group (more than 30%). Significant correlation was noted between depression and duration of diabetes mellitus, degree of obesity and poor glycaemic control and longer duration of shipping routes (over 6 months)[28].

Despite the clear evidence of an undesirable interaction between depression and diabetes, depression remains unrecognised in approximately one half of diabetic patients, and is consequently not treated properly[29].

Considering the anxiety in our sample pathological anxiety appeared in 39.8 %, with statistically significant difference among two study groups. According to the other studies from the literature anxiety symptoms are considered to be significant risk factors for diabetes[30]. Diabetes too is associated with three times higher prevalence of anxiety disorders, with anxiety accounting for poor glycemic control. Phobia to needles and hypoglycemic episodes further worsen glycemic control. Clinical features such as anxiety, sweating, tremor, tachycardia, and confusion are present in both anxiety and hypoglycemic episodes.

Patients with diabetes are approximately 1.5 times more likely to experience cognitive decline than individuals without diabetes mellitus[31]. Most of the data suggests that patients with diabetes have reduced performance in numerous domains of cognitive functioning. In patients with type 1 diabetes, specific and global deficits involving speed of psychomotor efficiency, information processing, mental flexibility, attention, and visual perception seem to be present, while in patients with Type 2 Diabetes an increase in memory deficits, a reduction in psychomotor speed, and reduced frontal lobe (executive) functions have been found[31,32]. The complex pathophysiology of changes in the central nervous system in diabetes has not yet been fully elucidated. It is important to consider the patients age at the onset of diabetes, the glycemic control status, and the presence of diabetic complications[31,32]. Neurological consequences of diabetes appear parallel to those observed in the aging brain. Neuroimaging studies highlight several structural cerebral changes, cortical and subcortical atrophy, beside increased leukoaraiosis that occurs in association with diabetes. There is supporting evidence from many hypotheses to explain the pathophysiology of cognitive decline associated with diabetes. The main hypotheses pointing to the potential, implied mechanisms involve hyperglycemia, hypoglycemia, microvascular disease, insulin resistance, hyperinsulinism, hyperphorylation of tau protein and amyloid beta deposition[31,32]. Elderly patients with diabetes have an increased risk of developing cognitive problems. One-third of the elderly diabetics have a cognitive dysfunction and its presence is associated with poor diabetes control[33]. Cognitive dysfunction in our sample appeared with statistically significant difference between study groups, 25.8% of the DM patients had cognitive impairment. It is important to point out that cognitive functions that enable complex behaviours are particularly important for patients with diabetes and their capacity for self-care. Recent systematic reviews have found that both depression and diabetes independently increase the risk of dementia. Persons with diabetes compared to those without had a 47% increased risk of all-cause dementia, a 39% increased risk of Alzheimers disease (AD) and over a two fold increased risk of vascular dementia[34]. Two recent systematic reviews found that depression doubled the risk of subsequent AD and all-cause dementia[35,36].

Conclusions

Interaction of diabetes and psychiatric disorders is multifaceted and an increase in understanding of the same would help endocrinologist and psychiatrists alike

to serve this cohort effectively and comprehensively[2]. The high prevalence of psychiatric disorders in diabetic patients points to the need for greater investment in appropriate diagnostic evaluation of patients that considers mental issues[37]. We can conclude that multipronged interaction between psychiatric illnesses and diabetes makes the management of diabetes more challenging. Increased awareness about these comorbidities and timely psychiatric consultation would help in better care in this group of patients[33]. Collaboration among primary care and specialist clinicians as well as program and public health managers should reflect the commonalities among diabetes, depression and other chronic mental and physical disorders. Interventions should include integrated clinical care and self-management programs along with population approaches to prevention and management[38].

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DEPRESIJA, ANKSIOZNOST I KOGNITIVNA DISFUNKCIJA U BOLESNIKA SA TIPOM 2 DIABETES MELLITUSA – STUDIJA NA ODRASLIM BOLESNICIMA SA TIPOM 2 DIABETES MELLITUSA U OSIJEKU, HRVATSKA

SAŽETAK

Cilj studije je bio odrediti pojavnost depresije i anksioznosti u bolesnika sa tipom 2 diabetes mellitusom, te također odrediti stanje kognitivnih funkcija u bolesnika sa tipom 2 diabetes mellitusom te načiniti usporedbu sa kontrolnom skupinom. Studija je dizajnirana kao prospektivna, uzorak je sačinjavalo 108 bolesnika od kojih je 66 oboljelo od tip 2 diabetes mellitusa, a 42 su sačinjavali kontrolnu skupinu. Svi su bili intervjuirani od strane psihijatra te su testirani sa

ocjenskim ljestvicama Hamilton skala za procjenu depresije (HAM-D), Hamilton skala za procjenu anksioznosti (HAM-A), te sa Mini Mental State Examination (MMSE) skalom za procjenu kognitivnih funkcija, kao i upitnikom o sociodemografskim podacima. Rezultati pokazuju da su bolesnici sa tip 2 diabetes mellitusom bili depresivniji od kontrolne skupine sa statistički značajnom razlikom ($p=0,035$). Patološka anksioznost je zabilježena u 34 bolesnika sa diabetesom te u 7 ispitanika kontrolne skupine, što je također statistički značajna razlika ($p=0,002$). Bolesnici sa diabetesom tip 2 su imali više kognitivnih disfunkcija u usporedbi sa kontrolnom skupinom. Dakle, visoka prevalencija psihijatrijskih poremećaja u diabetičkih bolesnika ukazuje na potrebu i važnost pravilne dijagnostičke procjene psihičkih poremećaja u inih bolesnika.