DEPRESSION IN ROMANIAN PATIENTS WITH TYPE 2 DIABETES: PREVALENCE AND RISK FACTORS

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Abstract

Background and aims. Co-existing major depression was found to have a negative impact on the diabetes outcome and the quality of life. The aim of the present study was to assess the prevalence of depressive symptoms in Romanian diabetes patients and to identify the risk factors associated with depression.

Methods. A total of 144 type 2 diabetes patients were included in the study. Five models of presumed predictors were used to assess the risk factors for depressive symptoms, using hierarchical regression analysis. Together with demographics, disease, lifestyle predictors, previous depressive symptoms and diabetes distress were taken into account.

Results. In our sample the prevalence of depression was 12.6%. Main risk factors for depressive symptoms were previous depressive symptoms which were associated with depression in both Model 4 (β =0.297, p=0.013) and Model 5 (β =0.239, p=0.017) and diabetes distress in Model 5 (β =0.540, p≤0.001). Employment (β =-0.276, p=0.029) and increased number of diabetes complications (β =0.236, p=0.017) became significant when diabetes distress was added to the analysis.

Conclusions. The overall prevalence of depressive symptoms was found to be in range with the prevalence identified in the literature. Previous depression and diabetes distress were both independently associated with depression, confirming the bidirectional relationship between depression and diabetes distress. Due to the consequences for daily living, screening for diabetes distress and depression should be done in primary care units both by physicians and trained nurses.

Keywords: type 2 diabetes, depression, diabetes distress

Background and aims

The prevalence of depression in people with diabetes, like in other chronic diseases [1,2], is higher than in people without this disease [3], affecting approximately one in every 6 people with type 2 diabetes [4]. Depression was found to decrease the quality of life [5-7], to increase mortality rates [8,9] and health care related costs in individuals with

diabetes [10,11]. Co-existing major depression was found to be associated with poor self-care behavior expressed by lack of physical exercise, unhealthy diet, smoking, adherence to oral diabetes treatment and poorer physical functioning [12]. Furthermore, depression is associated with a variety of diabetic complications such as diabetic neuropathy, retinopathy, nephropathy, macro-vascular complications and sexual dysfunction [13]. The pain and unsteadiness felt by the patients with neuropathy increase the risk of depression due to the diminished perception of self-worth caused by decreased social roles [14].

In order to explain the increased risk of depressive symptoms in diabetes, both physiological mechanisms, such as inflammatory processes [15] or increased glucose level [16] and "psychological burden of diabetes" hypothesis have been proposed [17]. In support of the "psychological burden" hypothesis, a recent meta-analysis [18] showed that people with previously diagnosed type 2 diabetes are at higher risk of developing depression compared with those with impaired glucose metabolism or undiagnosed diabetes, underlining the demands of daily living with the illness.

Diabetes burden involves difficulties in the daily regimen and diabetes management, fear of complications, feeling of being overwhelmed by diabetes, poorly perceived social support. Diabetes distress and depressive symptoms were found to be highly associated with a cyclical relationship between them [19]. Nevertheless, diabetes distress and not depressive symptoms were found to be associated with glycemic control [20]. These arguments show that diabetes has a negative impact on the individuals' emotional wellbeing and on diabetes outcome.

The aim of the present study was to determine the prevalence of depressive symptoms in a sample of Romanian diabetes patients and to identify the risk factors associated with these symptoms. We hypothesized that a lower level of education, intensified treatment, increased number of complication and comorbidities, previous major depression symptoms and diabetes distress are positively associated with increased depressive symptoms.

Methods

Participants

A total number of 150 outpatients from Center for Diabetes, Nutrition and Metabolic Diseases – Emergency Clinical County Hospital Cluj were recruited in the study at baseline. Of these, four patients failed to complete all the questionnaires and two refused to consent the access to their medical data. In the end, 144 patients were included in the study. Type 2 diabetes, age 18 or older, fluently speaking Romanian patients were included. Active anxiety, dementia, substance use or psychotic diseases represented exclusion criteria. Patients were informed of the aim of the study and the possibility to withdraw at any time. They gave written consent before filling in the questionnaire. If they could not complete the questionnaire by themselves, a trained person was provided for them.

Measurements

Sex, age, education, social-status, previous depressive symptoms and treatment for depression were self-reported. Medical characteristics were collected from the medical charts of the patients and included type and duration of diabetes, treatment and complications, most recent glycated hemoglobin (HbA1c). The number of complication and comorbidities were expressed by the sum of the three main diabetes complications (retinopathy, neuropathy and nephropathy) and of the illnesses that were present. Number of cigarettes/day and alcohol consumptions were assessed. Alcohol consumption was classified as rare consumption, for those who occasionally drink alcohol and daily consumption, for those who daily drink more than one glass of alcohol.

To assess the depressive symptoms of the patients, Beck Depression Inventory Second Edition (BDI-II) was used [21]. The questionnaire consists of 21 items rated on an intensity scale from 0 (low intensity) to 3 (highest intensity) with a maximum score of 63, the highest the score being equivalent to most severe depressive symptoms. Four groups of scores were established for BDI-II as the following: minimal: 0-13; mild: 14-19; moderate: 20-28 and severe: 29-63. To identify the symptoms of depression, the cutoff score of \geq 14 was used [22]. It should be emphasized that the scores of BDI-II present in this study do not represent diagnosis criteria for depression, they were only screening for depressive symptoms and for diagnosis criteria further consultation is needed.

Diabetes Distress Scale [23] was used to asees the emotional burden of the illness. The Romanian version of the scale [24], Diabetes Distress Scale-Ro (DDS-Ro), is a 17-item questionnaire that has good psychometric properties (DDS-Ro Cronbach's alpha = 0.824). A six point Likert scale is used to calculate the total score, starting from 1(no problem) to 6 (serious problem). The score can be calculated for the entire scale or for the four subdimensional scale: physician related ditress, regimen distress, interpersonal distress and distress due to the emotional burden of the disease.

Statistical analysis

Mean, standard deviation and frequency were used for descriptive statistics of the general sample. Independent t-test and χ^2 were used to compare characteristics for females and males. Predictors of depression were determined by using hierarchical multiple linear regression analysis with total score of BDI -II as dependent variable. To obtain significant factor associated with depression, the level of significance was set at p<0.05. Five subsequent models of presumed predictors for depression were tested: Model 1 included demographic variables like age and education; Model 2 contained variables in Model 1 along with diabetes characteristics; Model 3 consisted of previous two models together with lifestyle characteristics such as smoking or alcohol consumption; in Model 4, along with the other three models included previous depression; Model 5, beside the first four models, also included diabetes distress. The underlying motivation for using five different models was to a) determine the predictive value of demographic and diabetes related characteristics (Model 1 and 2); b) to test the possible contribution of lifestyle to depressive symptoms (Model 3) and c) to investigate the individual influence of previous depression and diabetes distress (Model 4 and 5) to elevated present symptoms of depression.

Results

Demographic and clinical data

In the present study the majority of the participants were women (59.7%), aged between 35 to 70 years old, with high school education (84%), diabetes duration ranged from 1 to 50 years, treated mostly with oral anti-diabetic agents, with neuropathy being the most frequent diabetes complication (12.5%), 66% having another co-morbidity,

most frequent being cardiovascular disease (52.8%). From the total sample, 18 participants (12.6%) were experiencing depressive symptoms while 35 patients (24.3%) had a previous depressive episode. When compared with men, women were less educated, less employed, were smoking and drinking alcohol less than men and were experiencing more present and past depressive symptoms. Sample characteristics are displayed in Table I.

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l able I.	Baseline	sample	characteristics	for the	overall	sample,	for males	s and	temales.
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	N=144 (100%)	Female N= 86 (59.7%)	Male N= 58 (40.3%)	р
Age, mean(SD)	59.31 (8.37)	60.46 (8.30)	57.60 (8.25)	p=0.044
Education (%) Elementary Secondary High School University	3 (2.10%) 29 (20.13%) 89 (59.8%) 23 (16.0%)	3 (2.10%) 20 (13.88%) 57 (39.58%) 6 (4.16%)	0 9 (6.25%) 32 (20.22%) 17 (11.80%)	p=0.002
Employment status Unemployed or retired Employed	99 (68.80%) 45 (31.20%)	65 (45.13%) 21 (14.58%)	34 (23.61%) 24 (16.66%)	p=0.031
Cigarettes No consumption Daily consumption	128 (88.9%) 15 (10.4%)	81(56.25%) 4 (2.77%)	47 (32.63%) 11 (7.63%)	p=0.017
Alcohol consumption Rarely consumption Daily consumption	135 (93.8%) 9 (6.3%)	86 (59.72%) 0	49 (34.08%) 9 (6.3%)	p<0.01
BMI	30.84 (4.49)	30.98 (4.45)	30.65 (4.57)	p=0.692
Diabetes years, mean (SD)	9.58 (6.94)	10.15 (7.42)	8.75 (6.14)	p=0.237
Treatment (%) Medication Insulin + Medication Insulin only	80 (55.6%) 28 (19.4%) 36 (25.0%)	29 (20.13%) 11 (7.63%) 18 (12.50%)	51 (35.47) 17 (11.77%) 18 (12.5%)	p=0.472
Insulin years, mean (SD)	2.94 (4.79)	2.81 (4.91)	3.13 (4.65)	p=0.703
Diabetes complication no. (%) No complications Retinopathy Nephropathy Neuropathy	113 (78.4%) 12 (8.3 %) 1 (0.7%) 18 (12.5%)	68 (47.22%) 7 (4.86%) 0 13 (9.02%)	45 (31.18%) 5 (3.44%) 1 (0.7%) 5 (3.44%)	p=0.572
No. of diabetes complications, mean (SD)	0.25 (0.52)	0.25 (0.53)	0.25 (0.51)	p=0.975
Comorbidities, mean (SD)	1.08 (0.98)	1.24 (1.07)	0.84 (0.79)	p=0.017
HbA1c, mean % (SD) BDI-II, mean (SD) DDS-Ro, mean (SD)	7.54 (1.57) 7.50 (7.40) 2.10 (0.79)	7.41 (1.47) 8.44 (8.47) 2.19 (0.79)	7.77 (1.71) 6.12 (5.24) 1.96 (0.76)	p=0.235 p=0.045 p=0.095
BDI –II 0-13 (no symptoms) 14-19 (mild symptoms) 20-28 (moderate symptoms) 29-63 (severe symptoms)	126 (87.5%) 9 (6.3%) 7 (4.9%) 2 (1.4%)	73 (50.69%) 5 (3.44%) 7 (4.86%) 2 (1.38%)	53 (36.8%) 4 (2.77%) 0 0	p=0.068
No previous Depressive Symptoms Previous Depressive Symptoms	109 (75.69%) 35 (24.3%)	54 (37.5%) 31(21.52%)	55 (38.19%) 4 (2.78%)	p< 0.01

Values represent frequencies (%), mean and standard deviation (SD)

Table II shows the factors associated with present depressive symptoms among patients with diabetes. Previous depressive symptoms was independently associated with present depression both in Model 4 (β =0.297, p=0.013) and Model 5 (β =0.239, p=0.017). Model 5 shows the contribution of diabetes distress which was found to be an

independent risk factor for present depressive symptoms (β =0.540, p≤0.001). When diabetes distress was added to the analysis, Model 5, both employment (β =-0.276, p=0.029) and increased number of diabetes complications (β =0.236, p=0.017) became significant.

Table II. Models of pre-	dictors in	Itroduced	in regres	sion anal	ysis to a:	ssess dep.	ressive sy	mptoms.							
	Model] R²= 0.0? Demogr	l 57 raphic		Model 2 R ² =0.14 Diabetes	0 s related		Model 3 R²=0.160 Lifestyle	related		Model 4 R ² =0.22 Previous Symptor	6 6 ns De	pressive	Model 5 R ² =0.485 Diabetes	Distress	
	β	t	b	β	t	d	β	t	d	β	t	d	β	t	p
Age	-0.149	-1.058	0.293	-1.073	0.286	-1.073	-0.159	-1.052	0.296	-0.127	-0.868	0.388	-0.103	-0.840	0.403
Sex	0.163	1.514	0.133	1.808	0.074	1.808	0.218	1.849	0.068	0.101	0.823	0.413	0.041	0.403	0.688
Employment stats no vs yes	-0.157	-1.111	0.269	-1.373	0.173	-1.373	-0.185	-1.216	0.227	-0.176	-1.190	0.237	-0.276	-2.227	0.029
Education	0.032	0.292	0.771	0.645	0.521	0.645	0.058	0.503	0.616	0.026	0.235	0.815	0.048	0.516	0.607
Diabetes Duration (years)				-1.362	0.177	-1.362	-0.167	-1.160	0.249	-0.182	-1.304	0.196	-0.233	-1.992	0.060
Number of Insulin Years				0.602	0.548	0.602	0.089	0.539	0.591	0.085	0.534	0.595	0.105	0.791	0.432
Treatment				0.569	0.571	0.569	0.055	0.372	0.711	0.014	0.099	0.922	-0.054	-0.448	0.655
Number of Diabetes Complications				1.613	0.110	1.613	0.154	1.301	0.197	0.168	1.461	0.148	0.236	2.447	0.017
HbAlc				0.411	0.682	0.411	0.097	0.795	0.429	0.043	0.358	0.721	0.018	0.182	0.856
BMI							-0.091	-0.805	0.423	-0.054	-0.487	0.627	-0.052	-0.571	0.569
Cigarette number/day							0.052	0.453	0.652	0.042	0.381	0.704	0.078	0.851	0.397
Alcohol consumption no vs yes							0.095	0.820	0.415	0.073	0.644	0.521	0.090	0.953	0.344
Number of Comorbidities							0.160	1.345	0.182	0.069	0.577	0.566	-0.038	-0.378	0.706
Previous Depressive Symptoms										0.297	2.551	0.013	0.239	2.448	0.017
Diabetes Distress													0.540	6.085	0.000

Discussion

The overall prevalence of depressive symptoms in patients with diabetes was 12.6%, in concordance with other studies that reported a prevalence of 9.8% [25], 15.8 % [26] or higher [27]. In literature, the prevalence of depression was found to range from 8% [28] to 44.66% [29,30]. In accordance with published data [31], the majority of our participants with depression were experiencing mild to moderate depressive symptoms (11.2%). One possible explanation for these findings might be the fact that when depression is screened, different measurement instruments with different cutoff points are used. Most frequent questionnaires for screening for depression are PHO9. CES-D, BDI and HDRS. Lloyd and colleagues suggested that differences in reporting the prevalence of depression in diabetes patients might be a consequence of the fact that people might experience differently their health status according to their present stressors, their culture and social dynamics [32].

When depression was analyzed from the risk factor point of view, demographic, life style or diabetes characteristics were not making any contribution to the depressive symptoms. This is in contrast with the literature where lower age and lower education [33], intensified treatment and increased number of comorbidities [34] were found to be associated with depression. One possible explanation for the lack of evidence might be the fact that our sample was homogeneous regarding age, education, treatment or comorbidities, the majority of our sample being in the late fifties, undergraduate and unemployed, having oral anti-diabetic treatment and disease, cardiovascular disease as comorbidity in general.

Self-reported history of depression was one of the two factors that increased the risk of depressive symptoms. In a longitudinal study, after controlling for demographics, medical co-morbidities and stressful life events, past depressive symptoms were the only factor that recognized the individuals with increased chances in experiencing depression in a period of 2.5 years [35]. In another study, prior depressive symptoms independently predicted depressive symptoms at 9 or 18 months. The authors showed that current negative effect partially mediated the relationship between prior and future depression. Also, negative life events and prior depressive symptoms influenced future depressive symptoms and negative effect [36]. Depression involves a series of cognitive patterns and physiological mechanisms that can be learned and reproduced over time, even if the symptoms diminished or disappeared for a period of time.

The second factor that independently predicted depression was diabetes distress. Ehrmann [37] showed a bi-directional relation between diabetes distress and depression. Diabetes distress increased 2.56 times the risk for developing depression and doubled the risk for its persistence, while depression at baseline increased by 5.94

the risk of the persistency of diabetes distress. Moreover, changes in diabetes regimen, distress and depressive symptoms occurred in tandem over a period of time [38]. When diabetes distress was introduced into the analysis, employment status and increasing number of diabetes complication became significant for future depression. Diabetes distress refers to the emotional impact that the chronic illness has on the individual. Sadness and anger regarding diabetes, low perceived social support from family and friends, poor relationship with the physician, fear of complications manifest in the daily living. These results might be due to the fact that there is a significant difference between men and women with respect to employment status, favoring men. Moreover, we know from literature [39] that women have a higher risk for depression than men, a result not confirmed by our study, but suggested. On the other hand, having to go to work can have a protective role against depression due to social support received from the co-workers and decrease in the negative rumination. The increased number of diabetes complication can have a negative effect on depression due to both inflammatory reactions and negative cognitive pattern experienced in depression.

Fisher [40] has shown that not all the patients with diabetes and high levels of depression are really depressed. Also, depression was found to be associated with HbA1c, kilocalories and saturated fat calories, but when diabetes distress was added to the analysis, depression was no longer significant. Moreover, when related to diabetes outcome and management, intervention that focus only on depression have no results on glycemic control and diabetes management [41], suggesting that improvement in depressive symptoms is not sufficient to enhance glycemic control or diabetes management.

In order to improve glycemic control and diabetes management and in respect to these findings we need to understand the relationship between diabetes distress and depression. Beside physiological mechanisms involved in depression, the "psychological burden of diabetes" hypothesis should be investigated. Other psychological constructs, like illness perception, self-efficacy, coping mechanism might be implicated in influencing both depression and diabetes distress and the development and persistency of their relationship.

Several limits to the study should be reminded. First, because previous depressive symptoms were self-reported, the patients could not specify the type of depression they had, such as dysthymia, depressive episode, or recurrent depression. As a consequence, all symptoms were introduced in only one large category of previous depressive symptoms. Second, there was no time limit regarding previous depressive symptoms and therefore, the period of previous depression range from a few years ago to a few months ago. Third, the large number of unemployed participants compared with the ones who had a working place should also be mentioned. Regardless of age, the unemployed participants were either retired due to illness or unemployed due to social-economic status. Further analysis should focus on the relationship between depression and working category, as employed, never employed, retired, in order to assess both the behavioral activation, social support and cognitive ruminations. Fourth, although the sample size was sufficient to reach statistical significance for the purpose of the study, larger stratified samples might give the opportunity to have more comprehensive analysis. Further research is necessary to explore in depth the risk factors associated with depression and to assess the effects of diabetes distress on diabetes outcome and depression.

Early screening for diabetes distress and depression by medical doctors or nurses can help increase treatment adherence and quality of life in diabetes patients. Also, specific designed interventions that target diabetes distress, depressive symptoms and diabetes education can improve illness perception and self-efficacy which in turn can improve self-care activities and diabetes outcome.

Conclusion

The prevalence of depressive symptoms in our study was 12.6%, lower than in other studies but within the range specified by literature. Previous depression and diabetes distress were the two risk factors that significantly and independently predicted present depressive symptoms. Screening for diabetes distress and depression should be done in primary care units by medical doctors or trained nurses.

References

1. Lesperance F, Frasure-Smith N. Depression in patients with cardiac disease: a practical review. J Psychosom Res. 2000;48(4-5):379-391.

2. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care. 2001;24:1069-1078.

3. Pouwer F, Geelhoed-Duijvestijn PH, Tack CJ, Bazelmans E, Beekman AJ, Heine RJ, et al. Prevalence of comorbid depression is high in out-patients with Type 1 and Type 2 diabetes mellitus. Results from three out-patient clinics in the Netherlands. Diabet Med. 2010;27(2):217-224.

4. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K. The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. Diabet Med. 2006;23:1165-1173.

5. Schram MT, Baan CA, Pouwer F. Depression and quality of life in patients with diabetes: a systematic review from the European depression in diabetes (EDID) research consortium. Curr Diabetes Rev. 2009;5:112-119.

6. Jacobson AM, de Groot M, Samson JA. The effects of psychiatric disorders and symptoms on quality of life in patients with type I and type II diabetes mellitus. Qual Life Res. 1997;6:11-20.

7. Egede LE, Hernandez-Tejada MA. Effect of comorbid depression on quality of life in adults with Type 2 diabetes. Expert

Rev Pharmacoecon Outcomes Res. 2013;13(1):83-91.

8. van Dooren FE, Nefs G, Schram MT, Verhey FR, Denollet J, Pouwer F. Depression and risk of mortality in people with diabetes mellitus: a systematic review and meta-analysis. PLoS One. 2013;8(3):e57058.

9. Katon WJ, Rutter C, Simon G, Lin EH, Ludman E, Ciechanowski P, et al. The association of comorbid depression with mortality in patients with type 2 diabetes. Diabetes Care. 2005;28(11):2668-2672.

10. Subramaniam M, Sum CF, Pek E, Stahl D, Verma S, Liow PH, et al. Comorbid depression and increased health care utilisation in individuals with diabetes. Gen Hosp Psychiatry. 2009;31(3):220-224.

11. Egede LE, Zheng D, Simpson K. Comorbid depression is associated with increased health care use and ecpenditures in individuals with diabetes. Diabetes Care. 2002;25(3):464-470.

12. Lin EH, Katon W, Von Korff M, Rutter C, Simon EG, Oliver M, et al. Relationship of depression and diabetes slefcare, medication adherence, and preventive care. Diabetes Care. 2004;27:2154-2160.

13. De Groot M, Andreson M, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complication: a metaanalysis. Psychosom Med. 2001;63:619-630.

14. Vileikyte L, Peyrot M, Gonzalez J S, Rubin RR, Garrow AP, Stickings D, et al. Predictors of depressive symptoms in persons with diabetic peripheral neuropathy: a longitudinal study. Diabetologia. 2009;52:1265-1273.

15. Laake JS, Stahl D, Amiel SA, Petrak F, Sherwood RA, Pickup JC, et al. The association between depressive symptoms and systemic inflammation in people with type 2 diabetes. Findings from the South London Diabetes Study. Diabetes Care. 2014;37:2186-2192.

16. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control: a meta-analytic review of the literature. Diabetes Care. 2000;23:934-942.
17. Talbot F, Nouwen A. A review of the relationship between depression and diabetes in adults: is there a link? Diabetes Care. 2000;23:1556-1562.

18. Nouwen A, Nefs G, Caramlau I, Connock M, Winkley K, Lloyd CE, et al. Prevalence of depression in individuals with impaired glucose metabolism or undiagnosed diabetes: a systematic review and meta-analysis of the European Depression in Diabetes (EDID) Research Consortium. Diabetes Care. 2011;34(3):752-762.

19. Burns RJ, Deschenes SS, Schmitz N. Cyclical relationship between depressive symptoms and diabetes distress in people with Type 2 diabetes mellitus: results from the Montreal Evaluation of Diabetes Treatment Cohort Study. Diabet Med. 2015;32(10):1272-1278.

20. Fisher L, Mullan JT, Arean P, Glasgow RE, Hessler D, Masharani U. Diabetes distress but not clinical depression or depressive symptoms is associated with glycemic control in both cross-sectional and longitudinal analyses. Diabetes Care. 2010;33:23-28.

21. Beck AT, Steer RA, Brown GK. Manual for the Beck Depression Inventory-II. San Antonio, TX: Psychological Corporation; 1996.

22. David D, Dobrean A, Sucala M. BDI II - Inventarul de depresie BECK: Manual.[Beck's depression inventory] Cluj-Napoca: RTS; 2012.

23. Polonsky WH, Fisher L, Earles J, Dudl RJ, Lees J, Mullan J, et al. Assessing psychosocial distress in diabetes: development of

the diabetes distress scale. Diabetes Care. 2005;28:626-631.

24. Mocan AS, Baban A. An useful tool for diabetes emotional distress assessment: validation of the Romanian version of Diabetes Distress Scale. Rom J Diabetes Nutr Metab Dis. 2015;22(4):425-431.

25. Alonso-Moran E, Satylganova A, Orueta JF, Nuno-Solinis R. Prevalence of depression in adults with type 2 diabetes in the Basque Country: relationship with glycemic control and health care costs. BMC Public Health. 2014;14:769.

26. Bell RA, Smith SL, Arcury TA, Snively BM, Stafford JM, Quandt SA. Prevalence and correlates of depressive symptoms amoung rural African Americans, Native Americans, and whites with diabetes. Diabetes Care. 2005;28(4):823-829.

27. Ganasegeran K, Renganathan P, Manaf RA, Al-Dubai SA. Factors associated with anxiety and depression among type 2 diabetes outpatients in Malaysia: a descriptive cross-sectional single-center study. BJM Open. 2014;4(4.

28. Lloyd CE, Dyer PH, Barnett AH. Prevalence of symptoms of depression and anxiety in diabetic clinic population. Diabet Med. 2000;17(3):198-202.

29. Sweileh WM, Abu-Hadeed HM, Al-Jabi SW, Zyoud SH. Prevalence of depression amoung people with type 2 diabetes mellitus: a cross sectional study in Palestine. BMC Public Health. 2014;14:163.

30. Mocan AS, Dumitras DE, Iancu SS, Băban AS. Depressive symptoms in obese diabetes patients. Pilot study. in Proceedings of EAPM 2014. Care and cure. An integrative approach to psychosomatic medicine. Ed. Medimond 2014;188-191.

31. Tace M, Tocu SM, Dobjanschi S. Cognitive disorder, depressive status and chronic complication of type 2 diabetes. Rom J Diabetes Nutr Metab Dis 2014;21(4):313-318.

32. Lloyd CE, Roy T, Nouwen A, Chauhan AM. Epidemiology of depression in diabetes: International and cross-cultural issues. J Affect Disord. 2012;142 Suppl:S22-S29.

33. Egede LE, Grubaugh AL, Ellis C. The effect of major depression on preventive care and quality of life among adults with diabetes. Gen Hosp Psychiatry. 2010;32:563-569.

34. Gorska-Ciebiada M, Saryusz-Wolska M, Ciebiada M, Loba J. Mild cognitive impairment and depressive symptoms in eldery patients with diabetes: prevalence, risk factors and comorbidity. J Diabetes Res. 2014;2014:179648. DOI: 10.1155/2014/179648

35. Nefs G, Pouwer F, Denollet J, Pop V. The course of depressive symptoms in primary care patients with type 2 diabetes: results from the Diabetes, Depression, Type D Personality Zuidoost-Brabant (DiaDDZoB) Study. Diabetologia. 2012;55:608-616.

36. Naranjo DM, Fisher L, Arean PA, Hessler D, Mullan J. Patients with type 2 diabetes at risk for major depressive disorder over time. Ann Fam Med. 2011;9(2):115-120.

37. Ehrmann D, Kulzer B, Haak T, Hermanns N. Longitudinal relationship of diabetes-related distress and depressive symptoms: analysing incidence and persistence. Diabet Med. 2015;32(10):1264-1271.

38. Hessler D, Fisher L, Strycker LA, Arean PA, Bowyer V. Causal and bidirectional linkages over time between depression and diabetes regimen distress in adults with type 2 diabetes. Diabetes Res Clin Pract. 2015;108:360-366.

39. Pibernik-Okanovic M, Peros K, Szabo S, Begic D, Metelko Z. Depression in Croatian Type 2 diabetes patients: prevalence and risk factor. A Croatian survey from the European Depression in Diabetes (EDID) Research Consortium. Diabet Med. 2005;22(7):942-945.

40. Fisher L, Skaff MM, Mullan JT, Arean P, Mohr D, Masharani U, et al. Clinical depression versus distress among patients with type 2 diabetes: not just a question of semantics. Diabetes Care. 2007;30:542-548.

41. Markowitz S, Gonzales J, Wilkinson J, Safren S. A review of treating depression in diabetes: emerging findings. Psychosomatics 2011;52(1):1-18.