



## Factors associated with depression in the patients with diabetes mellitus type 2

Faktori povezani sa depresijom kod bolesnika sa dijabetesom melitusom tip II

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### Abstract

**Background/Aim.** The assessment of association of depression and diabetes mellitus type 2 using the Patient Health Questionnaire (PHQ-9) has not been done in Montenegro. The aim of this study was to assess the prevalence of depression in the patients with type 2 diabetes mellitus, and to identify the risk factors associated with the presence of depression. **Methods.** A cross-sectional study was conducted at the General Hospital in Bijelo Polje, from July to September, 2015. It included 70 patients over 35 years of age with the diagnosis of diabetes for at least six months. For the assessment of depression presence and intensity PHQ-9 was used. All variables associated with the presence of depression at a significance level of  $p < 0.05$  were included into the final method of the multivariate logistic regression analysis. **Results.** Comorbidities were statistically significant more frequent among patients with depression ( $\chi^2 = 5.40$ ;  $p = 0.020$ ). Duration of diabetes over five years was significantly associated with depression ( $\chi^2 = 12.48$ ;  $p < 0.001$ ). Depression occurred more frequently among physically inactive subjects ( $\chi^2 = 10.74$ ;  $p = 0.005$ ). The presence of diabetic polyneuropathy ( $\chi^2 = 6.04$ ;  $p = 0.014$ ) and cataract ( $\chi^2 = 5.351$ ;  $p = 0.021$ ) were also significantly associated with depression. A multivariate logistic regression analysis showed that the duration of diabetes over five years and presence of cataract were independently associated with depression. **Conclusion.** The risk factors for depression among the subjects with diabetes were disease duration more than five years and the presence of cataract. Since depression is a serious disease and can be a risk factor for many chronic diseases, the best way of prevention is its early detection and treatment.

**Key words:**  
depression; diabetes mellitus, type 2; patient health questionnaire; montenegro.

### Apstrakt

**Uvod/Cilj.** Merenje povezanosti depresije i dijabetesa melitusa tip 2, primenom *Patient Health Questionnaire 9* (PHQ-9) upitnika, nije do sada rađeno u Crnoj Gori. Cilj ovog rada je bio da se proceni prevalencija depresije kod bolesnika sa dijabetesom tip 2 i da se identifikuju faktori rizika povezani sa prisustvom depresije. **Metode.** Studija preseka sprovedena je u Opštoj bolnici Bijelo Polje, u periodu od jula do septembra 2015. godine. Studijom je bio obuhvaćeno 70 osoba starijih od 35 godina sa dijagnozom dijabetesa od najmanje šest meseci. Za procenu prisustva depresije korišćen je upitnik PHQ-9. Sve varijable koje su bile značajno povezane sa prisustvom depresije ( $p < 0,05$ ) ušle su u model multivarijantne logističke regresije. **Rezultati.** Komorbiditeti su se značajno češće javljali kod osoba sa depresijom ( $\chi^2 = 5,40$ ;  $p = 0,020$ ). Trajanje dijabetesa više od pet godina bilo je značajno povezano sa prisustvom depresije ( $\chi^2 = 12,48$ ;  $p < 0,001$ ). Depresija je bila značajno češća kod fizički neaktivnih osoba ( $\chi^2 = 10,74$ ;  $p = 0,005$ ). Prisustvo komplikacija dijabetesa u vidu dijabetične polineuropatija ( $\chi^2 = 6,04$ ;  $p = 0,014$ ) i katarakte ( $\chi^2 = 5,351$ ;  $p = 0,021$ ) je takođe bilo statistički značajno povezano sa prisustvom depresije. Multivarijantna logistička regresija je pokazala da su trajanje bolesti preko pet godina i katarakta nezavisni prediktori depresije. **Zaključak.** Istraživanjem je ustanovljeno da su faktori rizika od pojave depresije bili trajanje dijabetesa preko pet godina i prisustvo katarakte. Kako je depresija ozbiljno oboljenje i faktor rizika od pojave mnogih hroničnih bolesti, najbolja prevencija su njena rana detekcija i lečenje.

**Ključne reči:**  
depresija; dijabetes melitus, tip 2; upitnik o zdravstvenom stanju bolesnika; crna gora.

## Introduction

Depression is the most common psychiatric disorder and one of the most common diseases in general<sup>1</sup>. It is estimated that about 350 million people suffer from depression worldwide<sup>2</sup>. According to the forecasts of the World Health Organization (WHO) experts, in 2030, depression would be the most common cause of morbidity in the world, indicating the increasing importance of investing efforts in the promotion and preservation of mental health<sup>3</sup>.

Depression is a common comorbidity among patients with diagnosis of chronic somatic diseases<sup>3</sup>. Reasons are complex and usually depend on the nature of disease, complications, length of survival, and partially, on the patient's perception of the disease<sup>4</sup>. Depression has been shown to be a common co-morbidity in diabetes, affecting 10% to 30% of the diabetic population<sup>4,5</sup>. In the patients with diabetes, depression may worsen the overall situation, accelerate the development of complications and increased mortality<sup>4</sup>. A course of depression in the patients with type 2 diabetes is a chronic and a large number of them (80%) lead to exacerbation of depression for a period of five years<sup>4</sup>. The patients with diabetes who have developed major depression are 1.5 to twofold in a higher risk of developing the cardiovascular complications than those who do not have major depression<sup>4,5</sup>. Depression can also be a risk factor for degenerative changes in the small blood vessels if not adequately treated<sup>6</sup>. In the patients with cerebrovascular complications, depression is associated with the permanent ischemic changes in subcortical brain mass (vascular depression)<sup>7</sup>.

Depression remains unrecognized and untreated in about the two-thirds of patients with the type 2 diabetes<sup>8,9</sup>. Women are at higher risk than men<sup>10</sup>. The results of the impact of psychological factors on glycemic control in men and women research showed that the main predictors of poor glycemic control in women are depressed mood, low sexual desire and poorer quality of life, and in men, the way they perceive their illness ("emotional experiences" of hyperglycemia)<sup>10</sup>. The pathophysiological mechanisms that link depression and diabetes are still not completely understood. Some studies have shown that in the depressed patients with and without diabetes, there is an increase of blood glucose level and insulin resistance on the oral glucose tolerance test (OGTT)<sup>10</sup>.

Connection between depression and chronic diseases, including type 2 diabetes mellitus, using the Patient Health Questionnaire (PHQ-9) was tested around the world<sup>11,12</sup>, but similar study has not been done in Montenegro. These studies are important because the chronic patients are at the increased risk of developing depression. PHQ-9 is a brief, standardized questionnaire for the rapid screening, diagnosing, monitoring and measuring the severity of depression in primary health care<sup>11</sup>.

The aim of this study was to assess the prevalence of depression in the patients with type 2 diabetes mellitus as well as to identify the risk factors associated with the presence of depression in the patients with type 2 diabetes.

## Methods

In order to investigate the potential risk factors for depression in the patients with type 2 diabetes mellitus, a cross-sectional study was conducted at the General Hospital in Bijelo Polje, Montenegro, from July 1st until September 1st, 2015. The study included 70 patients older than 35 years of age who were treated in the Department of Endocrinology in the General Hospital in Bijelo Polje, with at least a six-months diagnosis of diabetes. Exclusion criteria were: suffering from malignant disease, severe neurological disorders (dementia, epilepsy, muscular dystrophy) and psychosis.

All participants were interviewed using an epidemiological questionnaire made for the study purposes. The questionnaire consisted of several parts: patients' sociodemographic characteristics (age, gender, place of residence, dwelling place, occupation, marital status), physical activity (physically inactive – less than 30 minutes per day; moderate physically active – 30 minutes per day; intensive physically active – more than 30 minutes per day), body mass index (BMI), data related to the diabetes type 2: duration of disease, complications (diabetic ketoacidosis, ketogenic coma, diabetic polyneuropathy, diabetic nephropathy, diabetic retinopathy, cerebrovascular disease, cataract, diabetic foot), and comorbidities (hypertension, osteoarthritis, heart failure, chronic obstructive pulmonary disease, benign prostatic hyperplasia, osteoporosis and cholelithiasis). The data related to the complications of diabetes and comorbidities were obtained from the medical records.

For the assessment of presence and intensity of depression, we used the PHQ-9. The PHQ-9 is a standardized questionnaire which consists of 9 questions. Each question has four response categories ("not at all", "several days", "more than half the days" and "nearly every day") corresponding to scores of 0, 1, 2 and 3, respectively. As a severity measure, the PHQ-9 score ranges from 0 to 27 and a score greater than 4 indicates the existence of depression. Based on the total score of the PHQ-9, the values from 0 to 4 indicate the absence of depression; from 5 to 9 mild depression; from 10 to 14 moderate depression; from 15 to 19 moderately severe depression and over 20 severe depression. Only those patients who gave their written consent were included in the study. The Institutional Review Board for Human Subject Investigations reviewed and approved the study.

The data analysis was performed using the descriptive statistics, that is, the Pearson's  $\chi^2$  test and Student *t*-test. All variables associated with the presence of depression at a significance level of  $p < 0.05$  were included into the final method of the multivariate logistic regression analysis to assess the independent association of these variables with the presence of depression. The statistical analysis was done in the SPSS 21.0 software package.

## Results

The study included 70 patients with type 2 diabetes, 39 men and 31 women. The basic demographic characteristics of the respondents in relation to the presence of depression,

including the physical activity, body mass index, duration of disease and comorbidities are shown in Table 1. Forty-four (62.9%) patients had the symptoms of depression, of which the largest percentage of respondents manifested the symptoms of mild depression (38.6%). By analyzing the depression patients in relation to sex, age, place of residence, dwelling place, level of education, marital status and occupation, no significant differences were found among the studied groups. The presence of comorbidities was a statistically significant more frequent among those with depression compared with those without it ( $\chi^2 = 5.40$ ;  $p = 0.020$ ). However, this variable in the multivariate logistic analysis did not occur as an independent risk factor for depression. By analyzing depression in relation to the duration of the disease, duration more than five years was a statistically significantly associated with depression ( $\chi^2 = 12.48$ ;  $p < 0.001$ ). Regarding

physical activity, depression occurred more frequently among physically inactive subjects ( $\chi^2 = 10.74$ ;  $p = 0.005$ ). There was no statistically significant difference in the presence of depression depending on the body mass index. By analyzing depression in relation to the presence of complications of diabetes statistically significant differences between the studied groups were found in relation to the presence of diabetic polyneuropathy ( $\chi^2 = 6.04$ ;  $p = 0.014$ ) and cataract ( $\chi^2 = 5.351$ ;  $p = 0.021$ ) (Table 2).

To examine the independent impact of potential risk factors for depression, the multivariate logistic regression analysis was performed (Table 3). By performing the multivariate logistic regression analysis, we found that the duration of disease over five years and the presence of cataract as complications of diabetes were significantly independently associated with depression.

**Table 1****Characteristics of patients according to the presence of depression**

| Characteristics of patients                                    | With depression | No depression | $p$<br>( $\chi^2$ test) |
|--|-----------------|---------------|-------------------------|
|  | n (%)           | n (%)         |                         |
| Sex  |                 |               |                         |
| male   | 23 (59.0)       | 16 (41.0)     | 0.451                   |
| female   | 21 (67.7)       | 10 (32.3)     |                         |
| Age (years)  |                 |               |                         |
| < 60   | 20 (55.6)       | 16 (44.4)     | 0.193                   |
| ≥ 60   | 24 (70.6)       | 10 (29.4)     |                         |
| Place of residence   |                 |               |                         |
| apartment  | 10 (71.4)       | 4 (28.6)      | 0.458                   |
| house  | 34 (60.7)       | 22 (39.3)     |                         |
| Dwelling place   |                 |               |                         |
| rural  | 8 (66.7)        | 4 (33.3)      | 0.936                   |
| urban  | 19 (63.3)       | 11 (36.7)     |                         |
| semi urban   | 17 (60.7)       | 11 (39.3)     |                         |
| Level of education   |                 |               |                         |
| incomplete primary school, primary school and secondary school | 39 (63.9)       | 22 (36.1)     | 0.627                   |
| college and university degree                                  | 5 (55.6)        | 4 (44.4)      |                         |
| Employment   |                 |               |                         |
| employed   | 23 (67.6)       | 11 (32.4)     | 0.420                   |
| unemployed   | 21 (58.3)       | 15 (41.7)     |                         |
| Marital status   |                 |               |                         |
| married  | 28 (56.0)       | 22 (44.0)     | 0.060                   |
| widows/widowers, unmarried/single; divorced                    | 16 (80.0)       | 4 (20.0)      |                         |
| Physical activity  |                 |               |                         |
| inactivity   | 16 (80.0)       | 4 (20.0)      | 0.005                   |
| moderate activity  | 26 (60.4)       | 20 (39.6)     |                         |
| intensive activity   | 2 (28.6)        | 5 (71.4)      |                         |
| Duration of the disease (years)                                |                 |               |                         |
| < 5  | 13 (40.6)       | 19 (59.4)     | < 0.001                 |
| ≥ 5  | 31 (81.6)       | 7 (18.4)      |                         |
| Body mass index (kg/m <sup>2</sup> )                           |                 |               |                         |
| < 25   | 9 (75.0)        | 3 (25.0)      | 0.299                   |
| ≥ 25   | 33 (58.9)       | 23 (41.1)     |                         |
| Comorbidity  |                 |               |                         |
| with comorbidity   | 40 (69.0)       | 18 (31.0)     | 0.020                   |
| no comorbidity   | 4 (33.3)        | 8 (66.7)      |                         |

**Table 2****Complication of the diseases in subjects in relation to the presence of depression**

| Complication of the disease | With depression | No depression | <i>p</i><br>( $\chi^2$ test) |
|-----------------------------|-----------------|---------------|------------------------------|
|                             | n (%)           | n (%)         |                              |
| Diabetic ketoacidosis       |                 |               |                              |
| yes                         | 2 (100.0)       | 0 (0.0)       | 0.264                        |
| no                          | 41 (61.2)       | 26 (38.8)     |                              |
| Ketogenic coma              |                 |               |                              |
| yes                         | 4 (100.0)       | 0 (0.0)       | 0.109                        |
| no                          | 39 (60.0)       | 26 (40.0)     |                              |
| Diabetic polyneuropathy     |                 |               |                              |
| yes                         | 19 (82.6)       | 4 (17.4)      | 0.014                        |
| no                          | 24 (52.2)       | 22 (47.8)     |                              |
| Diabetic nephropathy        |                 |               |                              |
| yes                         | 4 (80.0)        | 1 (20.0)      | 0.397                        |
| no                          | 39 (60.9)       | 25 (39.1)     |                              |
| Diabetic retinopathy        |                 |               |                              |
| yes                         | 21 (75.0)       | 7 (25.0)      | 0.072                        |
| no                          | 22 (53.7)       | 19 (46.3)     |                              |
| Cerebrovascular disease     |                 |               |                              |
| yes                         | 5 (100.0)       | 0 (0.0)       | 0.071                        |
| no                          | 38 (59.4)       | 26 (40.6)     |                              |
| Cataract                    |                 |               |                              |
| yes                         | 16 (84.2)       | 3 (15.8)      | 0.021                        |
| no                          | 27 (54.0)       | 23 (46.0)     |                              |
| Diabetic foot               |                 |               |                              |
| yes                         | 4 (66.7)        | 2 (33.3)      | 0.818                        |
| no                          | 39 (61.9)       | 24 (38.9)     |                              |

**Table 3**  
**Factors related to the presence of depression according to the multivariate logistic regression analysis**

| Variable                          | OR   | 95% CI     | <i>p</i> |
|-----------------------------------|------|------------|----------|
| Duration of the disease > 5 years | 7.27 | 2.37–22.84 | 0.001    |
| Cataract                          | 4.84 | 1.11–20.99 | 0.036    |

**OR – odds ratio; CI – confidence interval.**

### Discussion

In our survey, 62.9% of respondents, according to the PHQ-9 questionnaire, had depression and most of them met criteria for mild depression (38.6%), while the criteria for severe depression had 11.4% of respondents. According to the results of a study made by Raval et al.<sup>13</sup>, in which 300 subjects with type 2 diabetes were included, depression was present in 41% of respondents, while 23% of them met criteria for severe depression. In a study conducted in Canada, 19.6% of subjects showed the symptoms and signs of depression and 8.7% among them were severe depressed<sup>14</sup>. According to the results of our study, there was no significant difference in the presence of depression between males and females. Also, no statistically significant difference was found in the presence of depression in relation to age. Roy et al.<sup>15</sup>, in the cross-sectional study in Bangladesh, found a significantly higher prevalence of depression in older age groups (over 50 years). However, in the studies by Das Mun-

shi et al.<sup>16</sup> and Miyaoka et al.<sup>17</sup> it was not found that age can be a risk factor for depression in the patients with type 2 diabetes.

By examining the levels of education, we found no significant difference between the examined groups. In a prospective cohort study Mezuk et al.<sup>18</sup>, which aims were to determine the association between depression and type 2 diabetes, it was observed that the people with lower education have a higher risk of developing depression compared to the people with higher level of education. The analysis of marital status in relation to the presence of depression showed no significant difference among the studied groups, which is in agreement with other studies.

By analyzing depression in relation to the presence of comorbidity, we found a statistically significant difference between the treated groups. Depression was more common among the respondents who had comorbidities compared to those who did not have them. The most common reported comorbidity among the subjects with type 2 diabetes was hypertension (41.7%). The heart failure and disorders of joint function was reported by 8.3% of respondents, and 6.9% of them reported benign prostatic hyperplasia. Shmitz et al.<sup>14</sup> found a significantly higher percentage of patients with type 2 diabetes who developed the major depressive episode among the respondents who had two or more comorbidities compared to those who had no comorbidities, or those who had only one comorbidity. However, comorbidity, in our study, in the multivariate logistic analysis, did not appear as an independent risk factor for depression.

By analyzing depression in relation to the duration of the diabetes we found statistically significant difference between the treated groups. Depression was more common among subjects whose illness lasted longer than 5 years. One Australian survey corroborated this association<sup>19</sup>. By analyzing depression in relation to physical activity, there was a statistically significant difference between the observed groups. Depression was significantly more common among the physically inactive subjects (72.7%), or moderately active (52.4%), while much less intensively occurs among the physically active subjects (28.6%). Physical inactivity appeared in other studies as a predictor of depression among the people with type 2 diabetes and other chronic diseases. Von Korff et al.<sup>20</sup> concluded that depression was significantly more common among the respondents who were physically inactive (40.7%) compared to those who were moderately physically active (2–3 times per week, 25.7%), and among the respondents who were physically active more than 4 times per week (33.7%). There were studies in which physical activity did not appear as a significant risk factor for depression in the patients with type 2 diabetes<sup>21</sup>.

By analyzing depression in relation to the body mass index, in the patients with type 2 diabetes, we found no significant difference between the observed groups ( $p = 0.299$ ). The body mass index  $\geq 30$  kg/m<sup>2</sup> in the study of Nasser et al.<sup>21</sup> was a significant predictor of depression in the patients with type 2 diabetes, as so in a study of Reddy et al.<sup>19</sup>. But, in the study of Roy et al.<sup>15</sup> the body mass index was not found as a risk factor for depression in the patients with type 2 diabetes.

When it comes to the complications of diabetes mellitus, according to our research, the univariate analysis showed that the diabetic polyneuropathy and cataract were associated with depression. The presence of cataract was significantly and independently associated with depression. The significant number of studies indicated that the presence of diabetes complications acted as a risk factor for depression. According to the study developed in Bahrain, complications of diabetes associated with depression were nephropathy and ischemic heart disease<sup>21</sup>. According to the results of Schmitz et al.<sup>14</sup> a number of present complications was significantly associated with severe depression. Major depression was more frequent among the subjects who developed two or more complications than those with one, or without any complication.

Beside that depression often occurred as a comorbidity in the people with chronic illnesses, depression was often mentioned as a possible risk factor for chronic diseases, including type 2 diabetes. The conclusions of a prospective study conducted at several thousand people pointed to two-fold higher incidence of type 2 diabetes in the people with depression, independent of other risk factors (obesity, age, physical inactivity, chronic somatic diseases and family history of diabetes)<sup>22</sup>. According to the results of a meta-analysis of nine longitudinal studies, the depressed, adult pa-

tients had a 37% higher risk of developing diabetes<sup>23</sup>. With the results of meta-analysis, Cosgrove et al.<sup>24</sup> confirmed that depression was accompanied by the subsequent development of type 2 DM. According to the results of Brown et al.<sup>25</sup>, the presence of depression increased the risk for diabetes for about 23%, but only in the younger patients (from 20–50 years of age).

Our study has several limitations. Firstly, it was the absence of a control group which in this case entailed the persons who were not suffering from chronic diseases. Secondly, the selected sample of respondents was not large (70 patients), which could have reduce the accuracy of the estimates of the association of independent variables with the outcome variable, and thus affected the validity of the findings and the generalization of results. Thirdly, in our study there was not the “gold standard”, so there was no comparison of the results obtained by the PHQ-9 questionnaire with a specific relevant psychiatric approach to prove, or refute the existence of depression in the patients, because the PHQ-9 questionnaire contains questions about specific symptoms that might be part of the clinical picture of certain somatic diseases. And finally, certain biochemical tests, such as the testing blood glucose or glycosylated hemoglobin in the patients with type 2 diabetes were not included in this study. Such tests would require significantly greater financial resources and participation of doctors of other specialties. Despite the above mentioned shortcomings, the significance of our study is that this is the first study that examines the connection between depression and type 2 diabetes in the population of Montenegro, where the PHQ-9 questionnaire to assess depression of respondents was used.

## Conclusion

In our study, we found that the risk factors for depression among the subjects with type 2 diabetes were duration of disease more than 5 years and the presence of cataract as a complication of diabetes. In this regard, it is necessary to treat the underlying disease and prevent the occurrence of complications because the presence of complications is a predictor of poor disease control. Since the depression can be a high risk factor for many chronic and serious diseases, as well as for suicide, the most effective way of prevention is its early detection and adequate treatment.

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## Disclosure statement

No potential conflicts of interest were disclosed.

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