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Impact of treatment modalities on quality of life and depression in type 2 diabetes

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Abstract. – OBJECTIVE: Type 2 diabetes mellitus (T2DM) is a chronic disease with numerous complications that increase mortality and reduce the quality of life (QoL). The current study compares QoL in T2DM patients treated with insulin to those treated with oral antihyperglycemics (OAHs), as well as the frequency and severity of depression in patients.

SUBJECTS AND METHODS: This prospective cross-sectional study included 200 patients with insulin or OAHs. Triglycerides, total cholesterol, low-density lipoprotein, and high-density lipoprotein cholesterol levels were measured. The Beck Depression Inventory and the SF-36 Quality of Life Questionnaire were used to assess depression symptoms and QoL in response to different treatment modalities.

RESULTS: Insulin-treated patients have a longer duration of illness, higher preprandial glycemic levels, lower scores in three of four dimensions of the SF-36 physical component, and a lower score in the SF-36 psychological component's emotional role dimension. Patients on insulin have milder depression symptoms than those with OAHs. Depression symptoms, according to the findings, worsen QoL and glycemic control in insulin-treated patients.

CONCLUSIONS: According to these findings, any treatment modality's success in T2DM patients primarily depends on psychological support and preventive measures that promote and maintain mental health.

Key Words:
Depression, Insulin, Oral antihyperglycemics, Quality of life, Type 2 diabetes mellitus.

Introduction

Type 2 diabetes mellitus (T2DM) is one of the most common non-communicable chronic diseases, with numerous associated complications that frequently result in increased mortality and decreased quality of life (QoL). Diabetes currently affects an estimated 537 million adults, which is expected to rise to 643 million by 2030. Diabetes affects one out of every five people over 65, with the majority living in low- and middle-income countries[1]. T2DM necessitates self-management, strict adherence to treatment recommendations, and numerous lifestyle changes, all of which can cause stress, culminating in depression and cognitive impairments in T2DM[2-7]. T2DM negatively affects the individual, the patient's family, and society as a whole[8]. As a result, various factors influencing patients' overall well-being and treatment adherence contribute to QoL in T2DM patients and are critical in disease management. QoL is a multidimensional, subjective concept that evaluates a person's life's positive and negative aspects. Health-related quality of life (HRQoL) is an important component of QoL because it includes physical and mental health factors such as specific health conditions, social and socioeconomic status, and practices that influence health perceptions and functional status[9-11]. HRQoL questionnaires, such as the 36-Item Short-Form Health Survey (SF-36), are valid and reliable intervention outcome indicators[12-15]. The SF-36 also assesses physical and mental dimensions[16].

The patient's age, disease duration, complications that appear during illness, and different treatment modalities, in addition to specific demographic characteristics, are the most important factors that influence the worsening of multiple dimensions of HRQoL in T2DM patients[17-21]. Among demographic and clinical factors, age is

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the strongest predictor of decreased HRQoL[20-22]. Most commonly, hypertension and dyslipidemia are comorbidities common among T2DM patients, and people with diabetes complications have a lower HRQoL[20,23,24]. Numerous studies[25,26] showed that individuals treated with insulin have a lower HRQoL score than those treated with OAHs, which may be explained by the pain caused by daily injections and the associated fear of insulin dependence, which may lead to depression.

Depression as a comorbidity is a significant factor associated with decreased QoL in patients with T2DM[27,28]. Existing evidence[29] suggests that depression is twice as prevalent in people with T2DM as in the general global population. Depression is moderately higher in pre-diabetes and undiagnosed diabetes patients than in individuals with normal glucose metabolism and significantly higher in diabetes patients who have already been diagnosed[30]. Depression worsens the prognosis of T2DM patients, decreases compliance with medical treatment[31], reduces QoL[32], and increases mortality[33].

The current study compares QoL in T2DM patients treated with insulin or OAHs in Serbia. The study aimed to determine the prevalence and severity of depression in T2DM patients receiving various treatment modalities.

Subjects and Methods

Study Participants

A prospective cross-sectional study was conducted at the Clinical Hospital Center "Zemun" at the Endocrinology, Diabetes, and Metabolic Disease Clinic. The study included 200 T2DM patients treated by insulin or OHAs who voluntarily signed an informed consent form. Fifty patients underwent insulin treatment, while 150 were treated by OAHs. The research was approved by the Ethical Committee of the School of Medicine at the University of Belgrade (No. 29/II-10) and carried out following the Helsinki Declaration on patient safety[34]. Three different questionnaires are used for this study: a structured, general questionnaire, Beck's Depression Inventory (BDI), and the SF-36 QoL questionnaire, all in culturally and linguistically adapted versions for populations residing in the Republic of Serbia territory. The BDI and SF-36 questionnaires have been psychometrically validated in the Serbian population.

The General Questionnaire

The general questionnaire contained the following information: 1. demographic data (gender, age, profession, education level, marital and socioeconomic status); 2. personal habits information (alcohol and tobacco use and physical activity level); 3. comorbidities information; 4. laboratory parameters (preprandial blood glucose level, hemoglobin A1c, lipid status); 5. information about T2DM treatment modalities. The patient completed paragraphs 1, 2, and 3, while the medical staff completed paragraphs 4 and 5.

The SF-36 Questionnaire

The HRQoL of T2DM patients undergoing treatment was assessed using the SF-36 questionnaire. The questions concern the four weeks preceding the assessment[16]. Patients answered 36 questions that measured eight scales: physical functioning (PF), role limitation due to physical health problems [role physical, (RP)], bodily pain (BP), general health perception (GH), vitality (VT), social functioning (SF), limitations due to emotional health problems [role emotional, (RE)], and mental health (MH)[16]. PF is a dimension comprised of ten questions that assess the ability to perform various activities during a typical day and the level of limitations imposed by the disease. Sports, running, and lifting heavy objects are classified as high-intensity activities, moderate-intensity activities (riding a bicycle, gardening, vacuuming, and moving the table), and low-intensity activities (walking, bathing, dressing, climbing the stairs, squatting, bending, lifting, and carrying light objects). BP is a dimension that includes two questions that assess the presence, intensity, and impact of pain on various activities. RP is a dimension comprised of four questions that assess limitations in performing work-related and daily duties due to poor physical health. GH is a dimension that includes five questions about current health, personal opinion, current health prognosis, and comparisons to the health of others. VT is a dimension with four questions assessing how the patients felt during the previous four weeks: if they felt with sufficient energy, felt tired and/or exhausted, and how frequently they felt "full of life". SF is a dimension that includes two questions that assess how much emotional and physical health problems interfere with the ability to perform daily social activities with friends and family and how frequently physical and emotional problems interfere with performing social activities such as

visiting friends or other family members. RE is a dimension comprised of three questions that assess problems at work or daily activities that are directly related to depression or anxiety, i.e., poor emotional health. MH is a five-question scale that assesses the presence and duration of sadness, nervousness, depression, or peace and happiness in patients. Two summary components/measures can be constructed based on the eight dimensions mentioned above: physical component summary (PCS) scores, mental component summary (MCS) scores, and the total score of QoL. A low MCS or PCS (50) reflects poor HRQoL[35,36]. PCS dimensions include PF, RP, BP, and GH, whereas MCS dimensions include MH, SF, RE, and VT. The linear transformation was performed on a scale of 0 to 100 points, with 0 representing the worst possible health and 100 representing the best possible health, after the given scores on a summary and individual scale were calculated using appropriate algorithms.

Beck Depression Inventory

The Beck Depression Inventory (BDI) is a rating inventory used to assess the presence and severity of depression symptoms in a healthy and diseased adult population. The questionnaire is comprised of twenty-one multiple-choice questions, each with four answers corresponding to the severity of symptoms being assessed. The answers to each question are graded with scores ranging from 0 to 3, then totaled and represented by a sum ranging from 0 to 63[37].

Scores 0-9 indicate no or minimal depression; 10-16 indicate mild depression; 17-29 indicate moderate depression; and 30-63 indicate severe depression.

Statistical Analysis

Descriptive and analytical statistics were used to interpret data using the statistical software SPSS vers. 22.0 for Windows (IBM Corp., Armonk, NY, USA). Descriptive statistics methods included relative numbers, measures of central tendency, and variability measures. Analytical statistics methods included tests for determining the significance of differences and correlations. Statistical significance was recorded if the *p*-value was lower than 0.05.

Results

Table I display the basic sociodemographic information of patients. The average age of insulin-treated patients is significantly higher than

Table I. Sociodemographic characteristics of patients concerning the treatment regimen.

Characteristics	OAHs		Insulin		*p*
	N	(%)	N	(%)	
Age[a]	59.00 ± 10.27		61.83 ± 7.81		0.042*
Sex					< 0.001*
Male	35	(70.0)	60	(40.0)	
Female	15	(30.0)	90	(60.0)	
Education level					0.047*
No formal education	0	(0.0)	1	(0.7)	
Primary education (elementary school)	2	(4.0)	23	(15.8)	
Secondary education (high school)	36	(72.0)	88	(60.3)	
Tertiary education (university-level education)	12	(24.0)	34	(23.3)	
Marital status					0.570
Single	2	(4.0)	9	(6.2)	
Married	33	(66.0)	96	(66.2)	
Divorced	4	(8.0)	16	(11.0)	
Widowed	6	(12.0)	18	(12.4)	
Extramarital partnership	5	(10.0)	6	(4.1)	
Socioeconomic status					0.722
Good	15	(31.2)	34	(25.4)	
Average	29	(60.4)	89	(66.4)	
Bad	4	(8.3)	11	(8.2)	
Sport activities	15	(32.6)	30	(25.4)	0.354
Smoking	17	(35.4)	47	(35.4)	0.058
Duration of disease[a]	8.97 ± 9.41		12.43 ± 7.03		0.023*

[a]Values are shown as arithmetic mean ± standard deviation; OAHs- oral antihyperglycemics. *Statistically significant difference.

Table II. Patients' comorbidities and Laboratory parameters concerning the treatment regimen.

Comorbidity	OAHs		Insulin		p
	N	(%)	N	(%)	
Injuries	14	(31.8)	54	(38.6)	0.418
Surgeries	27	(56.2)	85	(61.6)	0.515
Chronic diseases	27	(55.1)	83	(55.3)	0.977
Malignant diseases	1	(2.0)	7	(4.9)	0.384
Parameter	$\bar{X}$	**SD**	$\bar{X}$	**SD**	
Preprandial glycemia	11.01	3.48	12.40	4.06	0.033*
HbA1c	9.7	6.0	9.4	1.9	0.607
Triglycerides	2.42	1.21	2.46	1.61	0.890
Total cholesterol	5.03	1.43	5.60	3.11	0.212
HDL cholesterol	1.22	0.25	1.27	0.35	0.323
LDL cholesterol	3.05	0.95	3.19	0.91	0.364

*Statistically significant difference. OAHs- oral antihyperglycemics; HbA1c- hemoglobin A1c- glycated hemoglobin; HDL- high-density lipoprotein; LDL- low-density lipoprotein.

that of OAH patients. The gender distribution of patients undergoing various treatment modalities differs significantly, in addition to a statistically significant difference in education (Table I). Patients on OAHs had a significantly shorter mean disease duration.

Injuries, surgery, and other comorbidities such as malignant diseases, chronic cardiovascular, respiratory, and other diseases were investigated in T2DM patients (Table II). There was no statistically significant difference between the studied groups in terms of the presence of any particular comorbidity. The mean preprandial blood glucose levels in insulin-treated patients were significantly higher than in OAH-treated patients, and HbA1c mean values did not differ between groups. Furthermore, there were no significant differences between the two groups of patients in the mean values of the lipid status indicators [triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol] (Table II). According to a statistical analysis of SF-36 questionnaire results, patients who receive OAHs have significantly higher PF, RP, BP, and RE scores (Table III). The insulin-treated group's mean BDI score indicates mild depression, which is significantly higher

Table III. Patients' SF-36 and Beck's Depression Inventory scores concerning the therapy regimen.

Comorbidity	OAHs		Insulin		p
	N	(%)	N	(%)	
Injuries	14	(31.8)	54	(38.6)	0.418
Surgeries	27	(56.2)	85	(61.6)	0.515
Chronic diseases	27	(55.1)	83	(55.3)	0.977
Malignant diseases	1	(2.0)	7	(4.9)	0.384
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than the OAHs-treated group's mean total score, which indicates the absence of depression (Table III). In patients with T2DM, regardless of treatment modality, there was a significantly higher negative correlation between the total score of the BDI and the scores of each dimension of the SF-36 questionnaire (Table IV). There is no significant correlation between SF-36 and BDI questionnaire dimensions scores and diabetes duration in T2DM patients (Table V).

Discussion

T2DM is a complex, chronic disease with numerous complications that increase mortality and lower QoL. The most important factors influencing the deterioration of multiple aspects of QoL related to health are the duration of the disease, complications that occur during the progression of illness, treatment modalities, and specific demographic characteristics of patients[17,18]. The high prevalence of depression as a comorbidity in T2DM patients is one of the important additional factors responsible for decreased QoL[27,28].

Because different medications and administration regimens can be complicated for T2DM patients, treatment modalities have a distinct impact on their QoL. This is especially the case for patients with dopamine receptor 2 gene variants predisposing them to T2DM and depression comorbidity[38]. T2DM patients can be treated with OAHs, injectable insulin, or a combination of the two. The current study compares the quality of life of T2DM patients in Serbia who are treated with insulin or OAHs. The study aimed to determine the prevalence and severity of depression in T2DM patients undergoing various treatment options. According to our findings, patients with T2DM treated with insulin have lower scores on QoL in three of the four dimensions of the SF-36 questionnaire's physical component, including PF, RP, and BP, and one dimension of the SF-36 questionnaire's mental component, RE. These findings are consistent with Schunk et al[39] findings that participants treated with insulin have a lower total score on the physical component of QoL as measured by the SF-36 than people treated OAHs or combined therapy. These findings imply that a significant effect of insulin therapy or combined therapy on deteriorated QoL is related to patients' health[40,41].

According to Pichon-Riviere et al[42], insulin therapy has a negative effect on certain QoL domains, with the most noticeable negative effect observed for the following domains: "worry about the future", "freedom to choose diet", "life conditions", "sexual life", and "family life". Patients who received oral OAH metformin reported the highest level of treatment satisfaction, which is consistent with recent data indicating that metformin is associated with a lower risk of depression when compared to other oral hypoglycemic therapeutics[43]. Using fewer medications in combination therapy is linked to improved treatment satisfaction and QoL[43]. Poor glycemic and metabolic control[44,45], together with the potential occurrence of diabetes-related complications such as insulin resistance (IR), which has been shown to severely deteriorate HRQoL[46] and double the risk of occurrence of major depressive disorder, are one possible explanation for lower QoL in T2DM patients treated with insulin[47]. According to Azami et al[48], subjects with clinical signs of depression have

Table IV. Correlation between SF-36 and Beck's Depression inventory scores.

SF-36	Beck's Depression Inventory scale
Physical functioning	-0.345; $p < 0.001$*
Physical role	-0.428; $p < 0.001$*
Pain	-0.492; $p < 0.001$*
General Health	-0.430; $p < 0.001$*
Vitality	-0.446; $p < 0.001$*
Social functioning	-0.611; $p < 0.001$*
Emotional role	-0.589; $p < 0.001$*
Mental health	-0.226; $p = 0.002$*

*Statistically significant difference.

Table V. Correlation between SF-36. Beck's Depression Inventory and the length of duration of type 2 diabetes mellitus.

Scale	Length of the duration of type 2 diabetes
SF-36	
Physical functioning	-0.031; $p = 0.716$
Physical role	-0.125; $p = 0.152$
Pain	-0.056; $p = 0.516$
General Health	-0.108; $p = 0.207$
Vitality	0.036; $p = 0.681$
Social functioning	-0.057; $p = 0.508$
Emotional role	-0.038; $p = 0.666$
Mental Health	0.053; $p = 0.546$
Beck's Depression Inventory	
Total score	0.047; $p = 0.579$

low self-efficacy and self-management, which is negatively related to glycemic control and HbA1c. In our study, we observed that patients on insulin therapy had higher preprandial glycemic levels, whereas HbA1c levels did not differ between groups. These findings support those of Cepeda Marte et al[49], who found a significant negative correlation between QoL and HbA1c and preprandial blood glucose levels. In another study[50], patients who reported a negative effect of T2DM on QoL had higher HbA1c levels five years after the initial diagnosis of illness compared to patients who did not report any effect of illness on QoL. However, the multivariate regression analysis in this study did not show an effect of HbA1c levels in patients' blood on total scores of the physical and emotional components of the SF-36 questionnaire[50]. Thus, our findings are consistent with a recent report by Langberg et al[51] that also found no evidence of a link between HbA1c levels as a measure of adequate glycemic control and depression. Insulin therapy is associated with an increased risk of hypoglycemia[52]. According to recent research[53], up to 25% of T2DM patients on insulin therapy experience severe hypoglycemic events. During three days of continuous glucose monitoring in a trial of T2DM patients treated with the long-acting insulin analogue glargine, hypoglycemia, defined as a blood glucose level of 3.3 mmol/L (60 mg/dL), was detected in 56.9% of the subjects during three-days continuous glucose monitoring (CGM)[54]. According to Kent and Quinn[55], fear of hypoglycemic episodes and chronic complications affects QoL in younger adults treated with insulin.

On the other hand, fear of insulin use is one of the significant impediments to diabetes-related QoL[56-58]. In contrast to patients treated with OAHs, patients on insulin therapy have an increased risk of developing depressive symptoms, according to Bai et al[59]. Our findings are consistent with the literature[17-21], which suggests that differences in QoL between patients receiving different treatment modalities may be caused by medication regimen characteristics such as dosage frequency and route of administration, i.e., oral *vs.* subcutaneous administration. Furthermore, our findings show that QoL deteriorates primarily in physical health domains, implying that other possible explanations for the observed effects of insulin therapy on QoL in T2DM patients exist. The duration of the illness is another factor that may influence patients' QoL[60]. Diabetes is associated with lower QoL over time, particularly in physical functioning, emotional role, and mental health[61]. Similarly, Mikailiukstiene et al[62] observed a moderate negative correlation between illness duration and QoL scores in the surveyed population. Our results demonstrate that patients with T2DM on insulin therapy have a more prolonged illness duration than those on

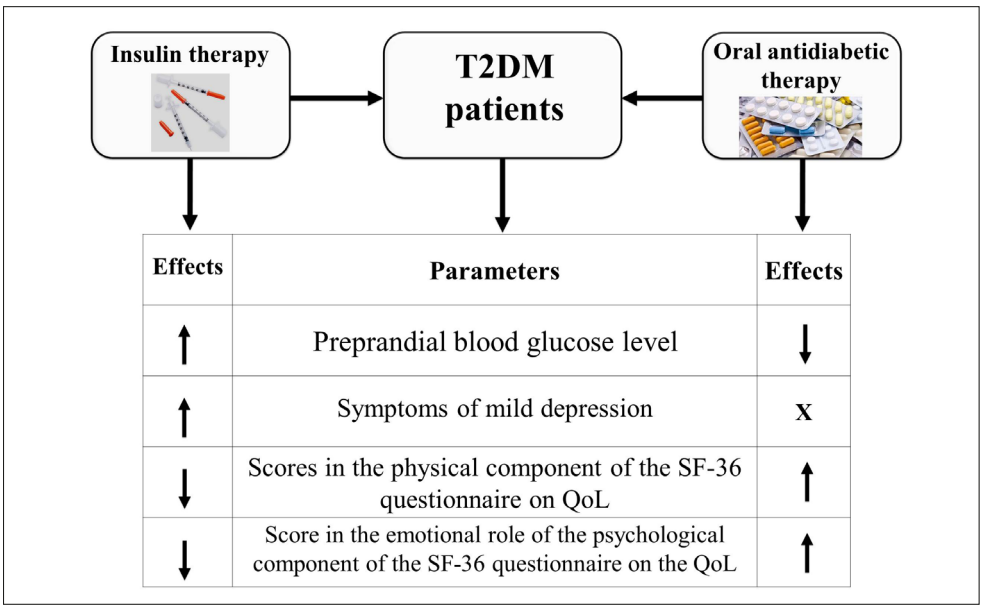

Figure 1. Schematic representation of effects of treatment modalities (insulin therapy or oral anti-diabetic therapy) on glucose level, quality of life (QoL) and occurrence of depression in type 2 diabetes (T2DM). X: no effect; ↑: indicates increment; ↓: indicates decrement.

OAHs, and there is a non-significant correlation between individual SF-36 domains and the duration of T2DM in both patient groups. This finding is partially consistent with the findings of Tonetto et al[63], who noticed that patients' QoL deteriorates as the illness progresses, with a tendency for a further decline as a patient progresses from primary to higher levels of medical care. Because T2DM patients have a high rate of depression, timely diagnosis of depressive disorder is critical in T2DM management[28,64-66]. Our study aimed to identify and compare potential differences in depression symptoms between subjects receiving insulin and those receiving OAHs. The findings suggest that the treatment modality may influence the occurrence of depression. BDI scores in patients with T2DM treated with insulin indicate the presence of mild depression, whereas depression is not observed in the group of patients on OAHs. We also observed a negative link between BDI scores and depression severity. Goldney et al[67] states that comorbid T2DM and depression are associated with worse physical and mental health than patients with only T2DM. Females, the elderly, patients with T2DM for a more extended period of time with two or more accompanying complications, and patients on insulin treatment have lower QoL and depressive symptoms[68].

Conclusions

In conjunction with the literature, our study's findings indicate that the QoL of people with T2DM has deteriorated, particularly in insulin-treated patients (see Figure 1). The onset of depression symptoms reduces QoL and accelerates the progression of T2DM. As a result, the presence of a psychological support system and preventive measures that promote and maintain mental health is critical to the success of any treatment modality in T2DM patients.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

Milena Lackovic – recruited the patients and collected the data, performed the research and wrote the paper, Mirjana Macvanin, Milan Obradovic, and Emina Sudar-Milovanovic – analyzed the data and wrote the paper, Zoran Gluvic – performed the research, collected and analyzed the data and wrote the paper, Sandra Sipetic Grujicic-critically reviewed the paper and E. R. Isenovic – wrote and critically reviewed the article.

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Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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