

# The influence of number of comorbidities on the quality of life of diabetic patients

## Utjecaj većeg broja komorbiditeta kod oboljelih od dijabetesa na kvalitetu života

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### Abstract

**Introduction:** With the continuous aging of the population of Western societies, an increase is expected not only in the number of patients with diabetes but also in the number of patients with comorbidities. Population studies suggest that most patients with diabetes have at least one comorbidity. Comorbidities can profoundly impact a person's ability to care for himself/herself and can present barriers to adherence to lifestyle changes and compliance with therapy.

**Methods:** The research was conducted in the Public Institution Health Centre of Sarajevo Canton - Health Center Hadžići and Health Center Novi Grad. It included 161 patients diagnosed with diabetes; 96 women and 65 men. The respondents were between 18 and 65 years old (the upper age limit for the working population for both genders). The instruments for conducting the research were a questionnaire on the socio-demographic characteristics of the respondents and Ferrans and Powers index of quality of life, a version for diabetes.

**Results:** The research included 43.48% of respondents with diabetes mellitus (DM) Type II, 31.06% with DM Type I, while even 25.46% of respondents did not know which type of diabetes they suffered from. There were no statistically significant differences in the Total Quality of Life Index (TQLI) ( $p=0.328$ ) between respondents with different types of diabetes. The average TQLI value in the group with diabetes duration from 1 to 5 years was 22.07 +/- 5.10; in the group from 6 to 10 years was 21.23 +/- 6.0; in the group from 11 to 20 years was 21.86 +/- 4.82; in the group from 21 to 30 years was 19.20 +/- 6.81; and in the group with diabetes duration >30 years, was 23.36 +/- 5.46. High blood pressure was present in 60.24% of respondents, followed by elevated blood fats in 51.55% of respondents, and heart/brain blood vessel diseases, in 43.48% of respondents. Neuropathies were present in 38.5%, visual impairment in 26.08%, and malignant diseases were present in a total of 14.28% of respondents.

**Conclusion:** The average value of the quality of life of respondents with 1 comorbidity was 21.30; with 2 comorbidities 20.91; and with 3 comorbidities was 21.94. There was no statistically significant difference in the quality of life of diabetes patients about the presence of one, two, or more comorbidities ( $p=0.537$ ). The presence of a greater number of comorbidities in patients with diabetes does not contribute to poor quality of life.

**Keywords:** comorbidities, diabetes mellitus, Total Quality of Life Index

**Short title:** Life quality with diabetes

### Sažetak

**Uvod:** Uz kontinuirano starenje stanovništva zapadnih društava, očekuje se porast ne samo broja oboljelih od šećerne bolesti već i broja bolesnika s komorbiditetima. Populacijske studije pokazuju da većina bolesnika s dijabetesom ima barem jedan komorbiditet. Komorbiditeti mogu duboko utjecati na sposobnost osobe da se brine o sebi i mogu predstavljati prepreke za pridržavanje promjena načina života i pridržavanje terapije.

**Metode:** Istraživanje je provedeno u JU Dom zdravlja Kantona Sarajevo – Dom zdravlja Hadžići i Dom zdravlja Novi Grad. Uključen je 161 pacijent s dijagnostičnom šećernom bolešću; 96 žena i 65 muškaraca. Ispitanici su imali između 18 i 65 godina (gornja dobna granica za radno aktivno stanovništvo za oba spola). Instrumenti za provođenje istraživanja bili su upitnik o sociodemografskim karakteristikama ispitanika te Ferransov i Powersov indeks kvalitete života, verzija za dijabetes.

**Rezultati:** Istraživanjem je obuhvaćeno 43,48 % ispitanika s dijabetesom mellitusom (DM) tip II, 31,06 % s DM-om tip I, dok čak 25,46 % ispitanika nije znalo od kojeg tipa dijabetesa boluje. Nije bilo statistički značajnih razlika u ukupnom indeksu kvalitete života (TQLI) ( $p = 0,328$ ) između ispitanika s različitim tipovima dijabetesa. Prosječna vrijednost TQLI u skupini s trajanjem dijabetesa od 1 godine do 5 godina iznosila je 22,07 +/- 5,10, u skupini od 6 do 10 godina bila je 21,23 +/- 6,0, u skupini od 11 do 20 godina bila je 21,86 +/- 4,82. U skupini od 21 do 30 godina indeks je iznosio 19,20 +/- 6,81, a u skupini s trajanjem dijabetesa > 30 godina iznosio je 23,36 +/- 5,46. Povišen krvni tlak imalo je 60,24 % ispitanika, zatim povišene masnoće u krvi uočene su kod 51,55% ispitanika, a bolesti krvnih žila srca/mozga kod 43,48% ispitanika. Neuropatije su bile prisutne kod 38,5 % ispitanika, oštećenje vida kod 26,08 %, a maligne bolesti kod ukupno 14,28 % ispitanika.

**Zaključak:** Prosječna vrijednost kvalitete života ispitanika s 1 komorbiditetom iznosila je 21,30, s 2 komorbiditeta 20,91, a s 3 komorbiditeta 21,94. Nije bilo statistički značajne razlike u kvaliteti života bolesnika sa šećernom bolešću u prisutnosti jednog, dva ili više komorbiditeta ( $p = 0,537$ ). Prisutnost većeg broja komorbiditeta kod bolesnika sa šećernom bolešću ne doprinosi lošijoj kvaliteti života.

**Ključne riječi:** komorbiditeti, dijabetes melitus, ukupni indeks kvalitete života

**Kratak naslov:** Kvaliteta života s dijabetesom

## Introduction

Nowadays, non-communicable diseases represent a dominant global public health challenge. Based on the World Health Organization (WHO) data, non-communicable diseases with dominant heart and blood vessel diseases, malignant neoplasms, diabetes, and chronic respiratory diseases, cause 63% of the total number of deaths in the world, of which more than 14 million people die prematurely, between the age of 30 and 70 [1]. The largest share of premature deaths was reported in countries with a low and medium level of development, which further contributes to the costs of health care and poverty in these countries. Assessment of quality of life is a common part of the evaluation of various rehabilitation and therapy procedures and is used for health care for chronic patients and the general population. [2]. Chronic diseases such as diabetes affect a significant part of the population due to their frequency and complexity, and therefore, the self-assessment of the quality of life of the patient and his/her family is increasingly used as a measure of their treatment success. Maintaining the best possible quality of life for diabetic patients is a significant task of the healthcare system [3]. Despite the impressive advances in diabetes pharmacotherapy, concrete results of success in the treatment of diabetes at the global level do not yet have a tangible outline. Although significantly less prevalent, Type 1 diabetes is a significant public health problem on a global scale, mostly due to the average onset at a younger age and the chronic complications that must occur over time [4]. With the continuous aging of the population of Western societies, an increase is expected not only in the number of patients with diabetes but also in the number of patients with comorbidities. Therapies to treat comorbidities can hurt a person's diabetes. Population studies suggest that most patients with diabetes have at least one comorbidity. Comorbidities can profoundly impact a person's ability to care for himself/herself and can present barriers to adherence to lifestyle changes and compliance with therapy [5-8]. In addition, serious conditions such as cardiovascular diseases, diabetic retinopathy, or malignancies can limit a person's ability to manage diabetes independently. Comorbidities often require multiple pharmacological interventions, some of which may harm diabetes treatment [9].

Numerous studies have shown that lowering blood pressure has a major role in reducing death caused by diabetes, the incidence of stroke, and the progression of retinopathy or nephropathy (Medical Education, OGTT, and HbA1c) [10-13].

Most guidelines currently recommend a target blood pressure to be <140/80 mmHg in patients with Type II diabetes mellitus, which is reduced to <130/80 mmHg in patients with concomitant renal, retinal, or cerebrovascular disease, with angiotensin-converting enzyme (ACE) inhibitors, which play an important role in blood pressure and electrolyte regulation and are recommended as first-line therapy for most patients [14, 15]. Also, several large randomized controlled studies have shown that keeping fat under control is crucial in the primary prevention of cardiovascular diseases in people with diabetes [16-18]. Ma-

lignant diseases and diabetes occur jointly in more cases than expected, and it is now generally recognized that people with diabetes mellitus Type II have a higher risk of several cancers. That primarily relates to colon cancers and cancers of the liver, pancreas, breast, endometrium, kidney, and esophagus. It seems that many malignancy therapies increase the risk of developing Type II diabetes, including glucocorticoids, which can cause the new onset of diabetes or worsen preexisting diabetes [19]. Microvascular complications (retinopathy, nephropathy, neuropathy) cause a significant decrease in the quality of life of diabetic patients, loss of vision, loss of kidney function requiring dialysis, loss of walking function, and chronic pain [20]. Macrovascular (coronary, cerebrovascular, and peripheral arterial) diseases are the main cause of death; 75% of patients with macrovascular complications die from coronary disease, 25% and from cerebrovascular insult or peripheral vascular disease and amputation complications [21]. Diabetic autonomic neuropathy is a complication not well known among patients, which leads to various clinical changes related to the sympathetic and parasympathetic parts of the autonomic nervous system, manifesting in several organ systems, including cardiovascular, gastrointestinal, genitourinary, and circulation systems. The most well-known symptoms of cardiovascular diabetic neuropathy are tachycardia, hypotension, and silent ischemia [22]. Patients with diabetes have an increased risk of developing cardiovascular diseases, depression, and infections. A high level of glucose in the plasma modifies the immune response. In patients with Type 2 diabetes, there is constant chronic inflammation, which causes a slower and inadequate response in the case of infection [23]. Vaccination against influenza, pneumococcus, and SARS-COV-2 is recommended, as well as adherence to basic epidemiological measures, frequent hand washing, wearing a protective mask, and maintaining social distancing during an epidemic [24]. Assessment of psychological problems is necessary for every patient with diabetes, and it is especially important in patients whose treatment outcomes are not satisfactory and in those who develop complications or need to introduce a more intensive regimen. In such cases, it is necessary to pay attention to possible depression, anxiety, eating disorders, and cognitive disorders [25].

## Methods

The research was conducted in the Public Institution Health Centre of Sarajevo Canton - Health Center Hadžići and Health Center Novi Grad. The study included 161 patients diagnosed with diabetes; 96 women and a slightly smaller number of men [65]. The respondents were between 18 and 65 years of age, given that according to the legal regulations in our country, the upper age limit for the working population is 65 for both genders.

The research inclusion criteria included respondents of the working-age population over 18 and younger than 65 who suffered from diabetes. The exclusion criteria included retired and non-working age population respondents under 18 and over 65 who did not suffer from diabetes.

The instruments for conducting the research were as follows:

- Questionnaire on the socio-demographic characteristics of the respondents;
- Ferrans and Powers index of quality of life, version for diabetes.

A general survey questionnaire on the socio-demographic characteristics of the respondents was used for basic data collection. Upon completion of the research, statistical data processing was performed. The software packages SPSS for Windows (version 21.0, SPSS Inc, Chicago, Illinois, USA) and Microsoft Excell 2016 (Microsoft Corporation, Redmond, WA, USA) were used for statistical analysis of the obtained data. The results were thoroughly elaborated and documented, presented in absolute numbers, relative numbers, and statistical values using the statistical indicators, and presented in simple and comprehensible tables.

Descriptive statistics and parametric and non-parametric significance tests were used in the data processing. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to examine the data distribution. Differences in frequencies between groups were tested with the X2 test. Differences in the values of the tested parameters between the groups were tested with the Mann-Whitney U test and the Kruskal-Wallis H test. A statistically significant value for all tests was  $p < 0.05$ .

## Results

Out of the total number of respondents,  $n=161$  (100%), the research included 96 (59.63%) women and a slightly smaller number of men, 65 (40.37%). There was an even number of respondents, 66 (40.99%) in the 35-54 age group and 64 (39.76%) in the 55-65 age group, whereas the smallest number of respondents, 31 (19.25%), was recorded in the 18-34 age group. It is also evident that the largest number of men, 27 (41.53%), was in the 35-54 age group, while the largest number of women, 40 (41.66%), was in the 55-65 age group.

**TABLE 1.** Gender structure of respondents

Gender	NO,	%
Men	65	40.37
Women	96	59.63

**TABLE 2.** The age structure of the respondents

Age	Total 100 % (161)		Gender		
			Men 100 % (65)	Women 100 % (96)	
18 - 34	19.25 %	31	21.55 %	14	17.72 %
35 - 54	40.99 %	66	41.53 %	27	40.62 %
55 - 65	39.76 %	64	36.92 %	24	41.66 %

The majority of respondents, 70 (43.48%), suffered from diabetes mellitus Type II, 50 (31.06%) from diabetes mellitus Type I, while even 41 (25.46%) respondents did not know which type of diabetes they suffered from.

In our research, 51 (31.68%) respondents suffered from diabetes from 11 to 20 years, while 49 (30.43%) suffered from diabetes from 6 to 10 years.

Most respondents, 58 (36.02%), were on oral antidiabetic therapy, while the smallest number of them, 25 (15.53%), was on GLP-1 therapy.

Based on the Kruskal Wallis test, there were no statistically significant differences in the Total Quality of Life Index (TQLI) ( $p=0.328$ ) between respondents with different types of diabetes.

The average TQLI value in the group with diabetes duration from 1 to 5 years was  $22.07 \pm 5.10$ ; in the group with diabetes duration from 6 to 10 years it was  $21.23 \pm 6.0$ ; in the group with diabetes duration from 11 to 20 years it was  $21.86 \pm 4.82$ ; in the group with diabetes duration from 21 to 30 years it was  $19.20 \pm 6.81$ ; and in the group with diabetes duration  $>30$  years, it was  $23.36 \pm 5.46$ .

High blood pressure was present in 97 (60.24%) respondents, specifically in 52 (53.5%) women and 45 (46.4%) men, followed by elevated blood fats in 83 (51.55%) respondents, specifically in 47 (56.6%) women and 36 (43.4%) men. The third position in the overall sample of respondents was allocated to heart and brain blood vessel diseases, with 70 respondents (43.48%) affected, comprising 36 men (51.4%) and 34 women (48.6%). Neuropathies as a comorbidity were present in 62 (38.5%) respondents, specifically in 42 (67.8%) women and 20 (32.2%) men.

Visual impairment was present in 42 (26.08%) respondents, specifically in 23 (54.7%) women and 19 (45.3%) men, whereas with the third place malignant diseases, which were present in a total of 23 (14.28%) respondents, 15 (65.2%) related to women and 8 (34.8%) to men. Respondents could circle several answers.

Based on the Kruskal-Wallis test, there were no statistically significant differences in TQLI between patients with one, two, or three comorbidities,  $p=0.537$ .

The average TQLI value in the group of patients with 1 comorbidity was  $21.30 \pm 3.96$ ; in patients with 2 comorbidities, it was  $20.91 \pm 5.93$ ; and in patients with 3 comorbidities  $21.94 \pm 5.39$ .

**TABLE 3.** Type of diabetes by gender

Type of diabetes	Total 100 % (161)		Gender			
			Men 100 % (65)		Women 100 % (96)	
Type I (insulin dependant)	31.06 %	50	30.77 %	20	31.25 %	30
Type II (insulin dependant)	43.48 %	70	40 %	26	45.83 %	44
Not known	25.46 %	41	29.23 %	19	22.92 %	22

**TABLE 4.** Duration of diabetes by gender

Age	Total 100 % (161)		Gender			
			Men 100 % (65)		Women 100 % (96)	
1 - 5 years	13.04 %	21	10.77 %	7	14.58 %	14
6 - 10 years	30.43 %	49	32.31 %	21	29.17 %	28
11 - 20 years	31.68 %	51	30.77 %	20	32.29 %	31
21 -30 years	19.25 %	31	21.54 %	14	17.71 %	17
Over 30 years	5.59 %	9	4.61 %	3	6.25 %	6

**TABLE 5.** Therapy by gender

Type of therapy	Total 100 % (161)		Gender			
			Men 100 % (65)		Women 100 % (96)	
Oral antidiabetics	36.02 %	58	41.54 %	27	32.29 %	31
Insulin	26.09 %	42	24.62 %	16	27.08 %	26
GLP-1 (Victoza, Bydureon, Byetta, Lyxumia)	15.53 %	25	12.31 %	8	17.72 %	17
Not known	22.36 %	36	21.54 %	14	22.91 %	22

**TABLE 6.** Differences in the values of the total quality of life index based on the type of diabetes

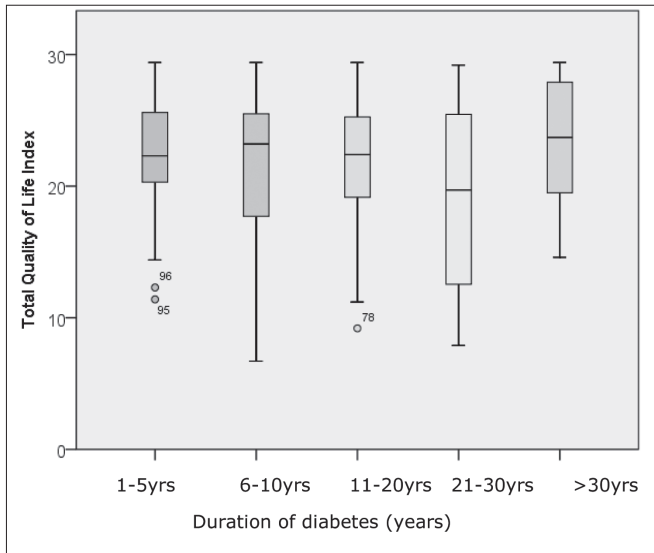
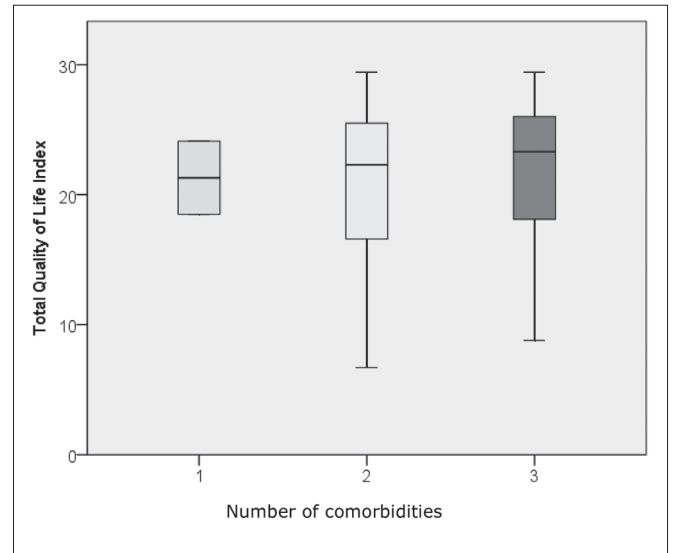
	Type of diabetes	N	Mean	Mean Rank	Chi-Square	p-value
Total Quality of Life Index	Type I	50	20.62	75.99	2.228	0.328
	Type II	70	21.11	79.26		
	Unknown	41	22.33	90.07		

**TABLE 7.** Comorbidity by gender of respondents

Comorbidity	Total		Gender			
			Men		Women	
High blood pressure	60.24 %	97	46.4%	45	53.6%	52
High levels of fat in the blood	51.55 %	83	43.4%	36	56.6%	47
Visual impairment	26.08 %	42	45.3%	19	54.7%	23
Neuropathies	38.50 %	62	32.2%	20	67.8%	42
Heart/brain blood vessel diseases	43.48 %	70	51.4%	36	48.6%	34
Malignant diseases	14.28 %	23	34.8%	8	65.2%	15

**TABLE 8.** Differences in the values of the quality of life index (total and in parts) based on the number of comorbidities

	Number of comorbidities	N	Mean	Mean Rank	Chi-Square	p-value
Total Quality of Life Index	1	2	21.30	75.50	1.243	0.537
	2	104	20.91	78.11		
	3	55	21.94	86.67		

**GRAPH 1.** Statistical values for the Total Quality of Life Index (TQLI) based on the diabetes duration**GRAPH 2.** Statistical values for the Total Quality of Life Index (TQLI) based on the number of present comorbidities

## Discussion

The main goal of this research was to examine the quality of life of diabetic patients in with comorbidities.

Our research showed that elevated blood pressure as a comorbidity was present in 60.24% of the respondents, specifically in 53.5% of women and 46.6% of men. That is followed by elevated blood fats that were reported in 51.55% of the respondents, heart/brain blood vessel diseases in 43.48%, neuropathy in 38.5%, visual impairment in 26.08% of the respondents, and finally, malignant diseases present in a total of 14.28% of the respondents. Percentage-wise, the presence of comorbidities was equal in both employed and unemployed respondents.

Similar results were found in research by Krstović Spremo, where 65% of employed respondents had hypertension [9].

In their study from 2005, Jovanović et al. stated that in people with Type II diabetes, the prevalence was over 50%, which increased with age, while in people with Type I diabetes, the prevalence was around 25% [26].

In 2012, Bosić-Živanović et al. stated that 83% of the respondents had comorbidities and a lower quality of life than respondents without comorbidities. The most common comorbidities were arterial hypertension (63%), chronic cardiovascular diseases (46%), neuropathies (23%), visual impa-

irment (24%), elevated blood fats (39%), and finger or foot amputations (2.2%) [27].

In their meta-analysis of a large number of prospective observational studies in 1998, Gaster and Hirsch showed the association between hyperglycemia and neuropathy, retinopathy and nephropathy, and they also showed that the treatment of hyperglycemia delayed the onset and slowed down the progression of these complications [28].

A descriptive, observational study conducted in 2021 at the San Rogue Health Center by Galvez G. et al. showed different results compared to those obtained in our research. The authors proved an inverse relationship between the quality of life and diabetes mellitus chronic comorbidities (more than half of the subjects had hypertension, dyslipidemia, or obesity) [29].

## Conclusion

The average value of the quality of life of respondents with 1 comorbidity was 21.30; with 2 comorbidities, it was 20.91; and in respondents with 3 comorbidities, it was 21.94. In our research, there was no statistically significant difference in the quality of life of diabetes patients about the presence of one, two, or more comorbidities ( $p=0.537$ ).



There is no statistically significant difference in the quality of life of diabetes patients about the presence of one, two, or more comorbidities ( $p=0.537$ ). The presence of a greater number of comorbidities in patients with diabetes does not contribute to poor quality of life.

**Authors declare no conflict of interest.**

**Nema sukoba interesa.**

## Literatura / References

- [1] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med.* 2006; 3 (11): 442.
- [2] Meeberg GA. Quality of life: a concept analysis. *J Adv Nurs.* 1993; 18 (1): 32–8.
- [3] Solli O, Stavem K, Kristiansen I. Health-related quality of life in diabetes: the associations of complications with EQ-5D scores. *Health Qual Life Outcomes.* 2010; 8 (1): 1–8.
- [4] Skyler JS, Bakris GL, Bonifacio E, Darsow T, Eckel RH, Groop L et al. Differentiation of diabetes by pathophysiology, natural history, and prognosis. *Diabetes.* 2017; 66 (2): 241–55.
- [5] Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Arch Intern Med.* 2002; 162 (20): 2269–76.
- [6] Russell LB, Suh DC, Safford MA. Time requirements for diabetes self-management: too much for many? *J Fam Pract.* 2005; 54 (1): 52–6.
- [7] Boyd CM, Darer J, Boulton C, Fried LP, Boulton L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA.* 2005; 294 (6): 716–24.
- [8] Heisler M, Smith DM, Hayward RA, Krein SL, Kerr EA. How well do patients' assessments of their diabetes self-management correlate with actual glycemic control and receipt of recommended diabetes services? *Diabetes Care.* 2003; 26 (3): 738–43.
- [9] Krstović Spremo V. Radna invalidnost oboljelih od dijabetesa i hipertenzije. *Biomedicinska istraživanja.* 2012; 3 (2): 34–42.
- [10] Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of Diabetes 2017. *J Diabetes Res.* 2018; 30 (8): 61–67.
- [11] Boren SA, Gunlock TL, Schaefer J, Albright A. Reducing risks in diabetes self-management: a systematic review of the literature. *Diabetes Educ.* 2007; 33 (6): 1053–77.
- [12] Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R et al. American Diabetes Association. Diabetic neuropathies: a statement by the American Diabetes Association. *Diabetes Care.* 2005; 28 (4): 956–62.
- [13] Fong DS, Aiello LP, Ferris FL 3rd, Klein R. Diabetic retinopathy. *Diabetes Care.* 2004; 27 (10): 2540–53.
- [14] James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA.* 2014; 311 (5): 507–20.
- [15] Weber MA, Schiffrin EL, White WB, Mann S, Lindholm LH, Kenerson JG et al. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. *J Clin Hypertens (Greenwich).* 2014; 16 (1): 14–26.
- [16] Katz ML, Mehta S, Nansel T, Quinn H, Lipsky LM, Laffel LM. Associations of nutrient intake with glycemic control in youth with type 1 diabetes: differences by insulin regimen. *Diabetes Technol Ther.* 2014; 16 (8): 512–8.
- [17] Maffei C, Morandi A, Ventura E, Sabbion A, Contreas G, Tomasselli F et al. Diet, physical, and biochemical characteristics of children and adolescents with type 1 diabetes: the relationship between dietary fat and glucose control. *Pediatr Diabetes.* 2012; 13 (2): 137–46.
- [18] Ayano-Takahara S, Ikeda K, Fujimoto S, Asai K, Oguri Y, Harashima S et al. Carbohydrate intake is associated with time spent in the euglycemic range in patients with type 1 diabetes. *J Diabetes Investig.* 2015; 6 (6): 678–86.
- [19] Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet.* 2006; 367 (9524): 1747–57.
- [20] Gross JL, de Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: diagnosis, prevention, and treatment. *Diabetes Care.* 2005; 28 (1): 164–76.
- [21] Laakso M. Hyperglycemia and cardiovascular disease in type 2 diabetes. *Diabetes.* 1999; 48 (5): 937–42.
- [22] Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, Wilson DM, O'Brien PC, Melton LJ 3rd, Service FJ. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. *Neurology.* 1993; 43 (4): 817–24.
- [23] Suaya JA, Eisenberg DF, Fang C, Miller LG. Skin and soft tissue infections and associated complications among commercially insured patients aged 0–64 years with and without diabetes in the U.S. *PLoS One.* 2013; 8 (4): 65–7.
- [24] Heymann AD, Shapiro Y, Chodick G, Shalev V, Kokia E, Kramer E, Shemer J. Reduced hospitalizations and death associated with influenza vaccination among patients with and without diabetes. *Diabetes Care.* 2004; 27 (11): 2581–4.
- [25] Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care.* 2001; 24 (6): 1069–78.
- [26] Jovanović J, Manić S, Jeftić I, Đorđević D, Mitić D. Ocenjivanje radne sposobnosti radnika sa arterijskom hipertenzijom. *Svet rada.* 2005; 4: 736–37.
- [27] Bosić-Živanović D, Medić-Stojanovska M, Kovačev-Zavišić B. Kvalitet života obolelih od dijabetesa melitusa tipa II, Vojno sanitetski pregljed. 2012; 69 (10): 858–863.
- [28] Gaster B, Hirsch IB. The effects of improved glycemic control on complications in type 2 diabetes. *Arch Intern Med.* 1998; 158: 134–40.
- [29] Gálvez Galán I, Cáceres León M, Guerrero-Martín J, López Jurado C, Durán-Gómez N. Health-related quality of life in diabetes mellitus patients in primary health care. *Enfermería Clínica (English Edition),* 2021; 31 (5): 313–22.