

# DIABETES MELLITUS I ORALNA KANDIDOZA

## DIABETES MELLITUS AND ORAL CANDIDIASIS

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### Kratak sadržaj

**Uvod.** Diabetes mellitus je hronično oboljenje povezano sa mnogobrojnim faktorima rizika. Zbog povećanja dugovečnosti stanovništva i sve veće prevalence oboljenja stomatolozi u okviru svakodnevnog prakse sve češće leče dijabetesne pacijente. Diabetes mellitus se povezuje sa mnogobrojnim oralnim komplikacijama kao što je infekcija *Candida albicans* koja je i najčešća vrsta gljivica koja naseljava sluzokožu usne duplje u dijabetesnih bolesnika.

**Cilj** istraživanja bio je ispitati učestalost oralne kandidoze u dijabetesnih i nedijabetesnih ispitanika.

**Materijal i metode.** 150 ispitanika uključenih u istraživanje podeljeno je u tri grupe: 50 ispitanika sa diabetes mellitusom tip 1 bili su prva grupa, 50 ispitanika sa diabetes mellitusom tip 2 bili su druga grupa, a 50 ispitanika koji nisu bolovali od diabetes mellitusa činili su treću grupu. Stomatološkim pregledom procenjeno je stanje oralne higijene, parodonticijuma, prisustvo/odsustvo zuba i zubnih proteza u svakog pacijenta. Za vreme pregleda dobijeni su podaci iz anamneze o bolovanju od oralne kandidoze u prethodnih pet godina. Dijagnoza oralne kandidoze u vreme istraživanja postavljena je na osnovu kliničkog nalaza i laboratorijske identifikacije gljivica iz roda *Candida*.

**Rezultati.** Utvrđeno je statistički značajno manje prisustvo kandidoze i subjektivnog osećaja oralne suvoće u kontrolnoj grupi ( $p < 0.001$ ).

**Zaključak.** Učestalost kandidoze u usnoj duplji statistički je značajno veća u dijabetesnih bolesnika u odnosu na osobe koje ne boluju od diabetes mellitusa. Neophodna su dalja istraživanja i praćenje dijabetesnih bolesnika, kako bi se razjasnila uloga gljivica roda *Candida* kao dijagnostičkog faktora za diabetes mellitus i značajnog uzroka oboljenja u ovih pacijenata.

**Ključne reči:** diabetes mellitus, oralna kandidoza, oralna suvoća

### Abstract

**Background.** Owing to the increasing longevity of the population and the growing prevalence of diabetes dental practitioners treat frequently patients with this disease. Diabetes mellitus has been related to numerous oral complications such as *Candida albicans* which is the commonest species that harbor in the oral mucosa of diabetic patients. The highest rate of colonization occurs in diabetic patients with poor glycemic control.

**The aim of the study** was to examine the frequency of oral candidiasis.

**Material and Methods.** 150 patients participated in the study: 50 patients with diabetes mellitus type 1 were the first, 50 patients with diabetes mellitus type 2 were the second and 50 non-diabetic patients were the third group. Status of oral hygiene, periodontal condition, the presence/absence of teeth and dentures were recorded for each individual participating in the study. During dental check up, information about oral candidiasis during previous five years were collected. Oral candidiasis had been diagnosed on the basis of both clinical assessment and laboratory identification of *Candida* species.

**Results.** Analysis showed that the oral candidiasis presence and dry mouth sensation were significantly smaller in the control group ( $p < 0.001$ ).

**Conclusion.** The oral candidiasis is significantly more frequent in diabetic patients compared to the non-diabetic subjects. Further investigation and follow-up of the diabetic patients is necessary, in order to clarify the role of *Candida* species as a diagnostic factor for diabetes mellitus and a significant cause of illness among these sensitive group of individuals.

**Key words:** diabetes mellitus, oral candidiasis, dry mouth

### Uvod

Diabetes mellitus je hronično oboljenje povezano sa mnogobrojnim faktorima rizika.<sup>1-3</sup> Prisutan je poremećaj metabolizma ugljenih hidrata, masti i proteina izazvan smanjenom sekrecijom i/ili poremećenom aktivnošću insulina.

### Introduction

Diabetes mellitus is a chronic disease frequently associated with many risk factors.<sup>1-3</sup> It is a syndrome of abnormal carbohydrate, fat and protein metabolism due to the decreased insulin secretion or/and disturbed insulin activity.

Postoje četiri osnovna klinička tipa diabetes mellitusa: tip 1 koji je posledica nedostatka insulina; tip 2 koji nastaje usled rezistencije ciljnih tkiva na dejstvo insulina i smanjene sekrecije insulina; gestacioni diabetes mellitus koji predstavlja poremećaj glikemije u toku trudnoće; i posebne specifične forme diabetes mellitusa. Diabetes mellitus se javlja kod ljudi svih rasa i starosti, iako mu je učestalost veća u Afro-Amerikanaca i latino-Amerikanaca. Prevalenca oboljenja je dramatično povećana poslednjih nekoliko decenija. Predviđa se da će do 2030 godine broj obolelih u Svetu dostići 439 miliona.<sup>4</sup>

Zbog povećanja dugovečnosti stanovništva i sve veće prevalencije diabetes mellitusa, kao i povećane efikasnosti dijagnostičkih i terapijskih procedura, stomatolozi u okviru svakodnevne prakse sve češće leče pacijente sa ovom bolešću. Takođe, stomatolozi mogu igrati značajnu ulogu i u dijagnostici diabetes mellitusa.<sup>2</sup> Pojava simptoma u toku diabetes mellitusa tip 1 je brza i i obuhvata klasičnu trijadu: polifagiju, polidipsiju i poliuriju, kao i gubitak na telesnoj težini, razdražljivost, pospanost i umor. Simptomi diabetes mellitusa tip 2 se razvijaju sporije, a ovi pacijenti mogu biti gojazni i imati zamućen vid. Osobe sa diabetes mellitusom imaju kraći životni vek i mogu razviti mikrovaskularne i makrovaskularne komplikacije koje izazivaju nepovratna oštećenja očiju (retinopatija), bubrega (nefropatija), nervnog sistema (neuropatije) i srca (ubrzana ateroskleroza), kao i češću pojavu rekurentnih infekcija i usporeno zarastanje rana.<sup>6</sup>

Diabetes mellitus se povezuje sa mnogobrojnim oralnim komplikacijama, kao što su parodontopatija, smanjena sekrecija pljuvačnih žlezdi (kserostomija), sindrom pečenja i žarenja usta, i dr.<sup>7</sup> Takođe, dijabetesni bolesnici se češće žale na osećaj oralne suvoće.<sup>8,9</sup> Oportunističke infekcije poput oralne kandidoze predstavljaju još jedan znak sistemske imunopresije u toku ovog oboljenja.<sup>10-12</sup> Veliki broj navoda iz literature sugerira da je *Candida albicans* najčešća vrsta gljivica koja naseljava sluzokožu usne duplje u dijabetesnih bolesnika, a najviša stopa kolonizacije se javlja u slučaju loše glikoregulacije.<sup>10-15</sup> Takođe, oralna kandidoza je češća u dijabetesnih bolesnika koji puše i/ili nose zubne proteze, a smanjeno lučenje pljuvačke u ovih pacijenata doprinosi njenoj većoj učestalosti.<sup>12,16</sup> Dijagnoza i terapija oralne kandidoze nije kom-

There are four general categories of diabetes mellitus: type 1, which results from an insulin deficiency; type 2, which is the result of insulin resistance and an insulin secretory defect; gestational, a condition of abnormal glucose tolerance during pregnancy; and some specific forms of diabetes mellitus. Diabetes mellitus develops in people of all ages and races, although in greater frequency in African-Americans and Hispanics, and prevalence has increased dramatically over the past several decades. By the year 2030, the number of people with diabetes mellitus worldwide is projected to reach 439 million.<sup>4</sup>

Owing to the increasing longevity of the population and the growing prevalence of diabetes, as well as the increased effectiveness of diagnostic and therapeutic protocols, dental practitioners treat frequently patients with this disease. Also, dental professionals can play an important role in diagnosing diabetes mellitus.<sup>2</sup> The onset of symptoms is rapid in type 1 diabetes mellitus, and includes the classic triad of polyphagia, polydipsia and polyuria, as well as weight loss, irritability, drowsiness and fatigue. Symptoms of type 2 diabetes mellitus develop more slowly and these patients may be obese and may have blurred vision. People with diabetes mellitus have shorter life expectancy and may develop microvascular and macrovascular complications that can produce irreversible damage to the eyes (retinopathy), kidneys (nephropathy), nervous system (neuropathy), and heart (accelerated atherosclerosis), as well as recurrent infections and impaired wound healing.<sup>6</sup>

Diabetes mellitus has been related to numerous oral complications, such as periodontal disease, decreased function of salivary glands (xerostomia), burning mouth sensation.<sup>7</sup> Subjective oral dryness is a more frequent complaint among diabetic patients than among healthy subjects.<sup>8,9</sup> Another manifestation of diabetes and an oral sign of systemic immunosuppression is the presence of opportunistic infections, such as oral candidiasis.<sup>10-12</sup> A great number of reports suggest that *Candida albicans* is the commonest species that harbor in the oral mucosa of diabetic patients, and the highest rate of colonization occurs in diabetic patients with poor glycemic control.<sup>13-15</sup> Oral candidal infection has been associated significantly with cigarette smoking and use of dentures in adults with diabetes mellitus and reduction in salivary flow in these patients increases the incidence of oral candidiasis.<sup>12,16</sup> The oral health care professionals can readily make the diagnosis of oral candidiasis and provide therapy, but most

plikovana, ali najvažnije, potrebno je otkriti pravi uzrok nastanka infekcije, što može biti i nedijagnostikovani diabetes mellitus.<sup>17</sup>

### ***Cilj istraživanja***

Cilj istraživanja je ispitati učestalost oralne kandidoze u dijabetičkih i nedijabetičkih ispitanika.

### ***Materijal i metod rada***

U istraživanju je učestvovalo 150 ispitanika. Prvu grupu činilo je 50 ispitanika sa diabetes mellitusom tip 1, drugu 50 ispitanika sa diabetes mellitusom tip 2, a 50 ispitanika koji nisu bolovali od diabetes mellitusa bili su treća (kontrolna) grupa.

U istraživanje su uključeni dijabetički bolesnici Klinike za endokrinologiju Medicinskog fakulteta u Nišu, koji su dolazili na redovne ambulantne kontrolne preglede. Za procenu glikoregulacije određivane su vrednosti glikoliziranog hemoglobina (HbA<sub>1c</sub>) i glikemija natašte. Pacijenti su zatim upućeni u Kliniku za stomatologiju Medicinskog fakulteta u Nišu. Kontrolnu grupu ispitanika predstavljali su pacijenti Odeljenja za oralnu medicinu i parodontologiju Klinike za stomatologiju Medicinskog fakulteta u Nišu koji su dolazili na redovne kontrolne preglede.

Svi učesnici su bili potpuno obavješteni pre uključivanja u ispitivanje. Specijalista Oralne medicine i parodontologije uradio je stomatološki pregled i procenu stanja oralne higijene, parodonticijuma, prisustvo/odsustvo zuba i zubnih proteza u svakog pacijenta. Za vreme pregleda dobijeni su podaci iz anamneze o bolovanju od oralne kandidoze u prethodnih pet godina. Dijagnoza oralne kandidoze u vreme istraživanja postavljena je na osnovu kliničkog nalaza i laboratorijske identifikacije gljivica iz roda *Candida*.

Pacijenti kod kojih je u vreme istraživanja klinički i laboratorijski dokazana gljivična infekcija lečeni su (Sol. Nystatin® 200ml/3 puta dnevno ili Dactanol oral gel® 150ml/4 puta dnevno) u trajanju od dve nedelje. Kliničko poboljšanje zdravlja i prateći negativni nalazi briseva na rod *Candida* bili su kriterijumi za procenu uspešnosti antigljivične terapije.

importantly, the infection's etiology should be pursued, which could include a diagnosis of diabetes mellitus.<sup>17</sup>

### ***Aim of the study***

To examine the frequency of oral candidiasis in diabetic and non-diabetic patients.

### ***Material and Methods***

A cohort of 150 patients participated in the study. 50 patients with diabetes mellitus type 1 were the first group, 50 patients with diabetes mellitus type 2 were the second group, and 50 non-diabetic patients were the third (control) group.

The diabetic patients were attended in the Endocrine Clinic of Medical faculty Niš, as outpatients during their routine diabetic review appointments. Glycosylated hemoglobin (HbA<sub>1c</sub>) and fasting blood glucose level were measured to assess glycemic control. Patients were referred to Dental clinic of Medical faculty Niš. The control group was recruited from outpatients attending the Department of Oral Medicine and Periodontology in Dental clinic of Medical faculty Niš for their routine dental appointment.

All participants were fully informed before completing their written consent document. They were evaluated intraorally by a periodontologist in the Department of Oral Medicine and Periodontology, and status of oral hygiene, periodontal condition, the presence/absence of teeth and dentures were recorded for each individual participating in the study. During dental check up, information about oral candidiasis during previous five years were collected. Oral candidiasis had been diagnosed on the basis of both clinical assessment and laboratory identification of *Candida* species.

Patients with clinically and laboratory confirmed oral yeast infection at the time of the investigation, were treated (with either Sol. Nystatin® 200ml/3 times per day or Dactanol oral gel® 150ml/4 times per day) for two weeks. Clinical improvement and the concomitant negative *Candida* cultures (mycological cure) were the criteria for response to antifungal treatment.

Entry and tabulation of results were performed using MS Excel program, and cal-

Unos i tabelarno prikazivanje rezultata obavljeno je korišćenjem MS Office Excel programa, a proračuni su vršeni programom SPSS, verzija 15.0. Personov  $\chi^2$  test korišten je kao neparametrijski test za poređenje učestalosti pojedinih atributivnih numeričkih parametara. Student-ovim t-testom nezavisnih uzoraka vršeno je testiranje statističke značajne razlike srednjih vrednosti dveju grupa. Rezultati statističke analize prikazani su tabelarno.

## Rezultati

Prosečna starost ispitanika prve grupe bila je  $25.54 \pm 3.65$  godina, druge  $62.57 \pm 8.57$  godina, a treće  $45.68 \pm 8.91$  godina. U prvoj grupi bilo je 23 muškaraca (46%), u drugoj 26 (52%), a u trećoj 25 (50%). Trajanje diabetes mellitusa u prvoj grupi bilo je  $9.01 \pm 1.22$  godina, a u drugoj  $14.68 \pm 3.43$  godina. Srednja vrednost HbA<sub>1C</sub> izmerena u prvoj grupi je  $9.87 \pm 0.32\%$ , a u drugoj  $8.70 \pm 0.45\%$ . Vrednosti HbA<sub>1C</sub> u osoba koje nisu bolovala od diabetes mellitusa bile su u okviru referentnih vrednosti od 3.3% do 5.2% (Tabela 1).

Prikupljanjem anamnestičkih podataka ustanovljeno je da su 28 pacijenata (56%) prve grupe i 31 pacijent (62%) druge grupe bolovali

culations were carried using SPSS, version 15.0. Person  $\chi^2$  test was a nonparametric test for attribute comparison of numerical parameters frequency. Student t-test for independent samples was performed to test statistically significant differences in the mean values of two groups. Results of statistical analysis are presented in tables.

## Results

The mean age of patients in the first group was  $25.54 \pm 3.65$  years, in the second  $62.57 \pm 8.57$  years, and in the third group  $45.68 \pm 8.91$  years. In the first group there were 23 males (46%), in the second 26 males (52%), and in the third 25 males (50%). The mean duration of diabetes mellitus in the first group was  $9.01 \pm 1.22$  years, and in the second group  $14.68 \pm 3.43$  years. The mean HbA<sub>1C</sub> measured in the first group was  $9.87 \pm 0.32\%$ , and in the second group  $8.70 \pm 0.45\%$ . The normal level for HbA<sub>1C</sub> in healthy subjects ranged between 3.3% and 5.2% (Table 1).

28 patients (56%) in the first group and 31 patients (62%) in the second group had positive anamnesis for oral candidiasis. In the control group, *Candida albicans* was the species which

Tabela 1: Vrednosti laboratorijskih i anamnestičkih podataka ispitanika (pol, starost, dužina trajanja diabetes mellitusa, vrednosti glikemije i HbA<sub>1C</sub>)

Table 1: The data obtained of all participants files (gender, age, diabetes mellitus duration, levels of glucose and HbA<sub>1C</sub>)

Grupe Groups		Grupa I diabetes mellitus tip 1 Group I diabetes mellitus type 1	Grupa II diabetes mellitus tip 2 Group II diabetes mellitus type 2	Grupa III (kontrola) Group III (control)
Pol Gender	muški male	23 (46%)	26(52%)	25(50%)
	ženski female	27(54%)	24(48%)	25(50%)
Starost (godine) Age (years)		25.54±3.65	62.57±8.57	45.68±8.91
Dužina trajanja diabetes mellitusa (godine) Diabetes mellitus duration (years)		9.01±1.22	14.68±3.43	/
HbA <sub>1C</sub> (%)		9.87±0.32	8.70±0.45	/
Glikemija (mmol/l) Levels of glucose (mmol/l)		10.43±0.37	10.37±0.26	/

od oralne kandidoze. U kontrolnoj grupi infekcija oralne mukoze izazvana *Candidom albicans* bila je prisutna kod 2 (4%) pacijenta (Tabela 2).

Iz tabele kontigencije 3×2 Personovim  $\chi^2$  testom utvrđeno je postojanje statistički značajne razlike prisustva kandidoze u ispitivanim grupama  $\chi^2=42.16$ ,  $p<0.001$ . Raščlanjivanjem na tabele kontigencije 2×2, utvrđeno je statistički značajno manje prisustvo kandidoze u kontrolnoj grupi ( $p<0.001$ ) (a ns, b  $\chi^2=29.76$ ,  $p<0.001$ , c  $\chi^2=35.46$ ,  $p<0.001$ , I+II vs kontrola,  $\chi^2=39.54$ ,  $p<0.001$ ). Nije postojala statistička značajnost u prisustvu oralne kandidoze između dijabetesnih grupa ispitanika (grupa I i II).

U grupama dijabetesnih ispitanika, 26 ispitanika (52%) u prvoj i 25 ispitanika (50%) u drugoj, imalo je subjektivni osećaj oralne suvoće. Nije postojala razlika u zastupljenosti ovog osećaja između dve grupe dijabetesnih ispitanika. U kontrolnoj grupi, statistički značajno manji broj osoba (2 ispitanika; 4%) imao je subjektivni osećaj oralne suvoće. 15 ispitanika (58%) prve i 13 ispitanika (52%) druge grupe imali su subjektivni osećaj oralne suvoće i pozitivni anamnestički podatak o bolovanju od oralne kandidoze.

Pacijenti koji su болоvali od oralne kandidoze u vreme ispitivanja imali su osećaj oralne suvoće i pečenja usta. Neki od ovih pacijenata imali su eritemne promene ispod gornje protezne ploče. Terapijski protokol u ovih pacijenata obuhvatao je lokalnu primenu antimikotika.

caused oral candidiasis in 2 (4%) patients (Table 2).

Person  $\chi^2$  test revealed a significant difference for oral candidiasis presence between investigated groups  $\chi^2=42.16$ ,  $p<0.001$ . Analysis showed that the oral candidiasis presence was significantly smaller in the control group ( $p<0.001$ ) (a ns, b  $\chi^2=29.76$ ,  $p<0.001$ , c  $\chi^2=35.46$ ,  $p<0.001$ , I+II vs control,  $\chi^2=39.54$ ,  $p<0.001$ ). There was no significant difference for candidiasis presence between diabetic groups (group I and II).

In the diabetic groups, 26 patients (52%) in the first and 25 patients (50%) in the second group, reported dry mouth sensation. Presence of dry mouth sensation showed no significant difference between diabetic groups. In the control group, significantly smaller number of patients (2 patients; 4%) reported dry mouth sensation. 15 patients (58%) in the first group and 13 patients (52%) in the second group with positive anamnesis for candidiasis reported that they had dry mouth sensation.

Patients with oral candidiasis at the time of investigation had symptomatology which included dry and burning mouth sensation. Many of these patients had erythematous mucosa under the upper denture. Management of these patients included use of antifungal drugs.

Tabela 2: Prisustvo oralne kandidoze u ispitivanim grupama.  
Table 2: Oral candidiasis presence in the investigated groups.

Grupe Groups	Bez kandidoze No candidiasis	Sa kandidozom Candidiasis
<b>Grupa I</b> (diabetes mellitus tip 1) Group I (diabetes mellitus type 1)	22±0.22	28±0.27
<b>Grupa II</b> (diabetes mellitus tip 2) Group II (diabetes mellitus type 2)	19±0.32	31±0.41
<b>Grupa III</b> (kontrola) Group III (control)	48±0.43 <sup>b,c***</sup>	2±0.28

<sup>a</sup>- I vs II, <sup>b</sup> - I vs III, <sup>c</sup> - II vs III, \*\*\* -  $p<0.001$   
<sup>a</sup>- I vs II, <sup>b</sup> - I vs III, <sup>c</sup> - II vs III, \*\*\* -  $p<0.001$

## Diskusija

Infekcije kandidom predstavljaju veliki problem, pogotovo u imunokompromitovanih osoba. Smatra se da su oralne gljivične infekcije češće u dijabetesnih bolesnika, ali postoje kontraverzni i kontradiktorni rezultati.<sup>9,11,13</sup> Smatra se da gljivice iz roda *Candida* naseljavaju oralnu mukozu čak u 80% dijabetesnih bolesnika.<sup>18</sup> Slični rezultati su uočeni i u ovom istraživanju, 28 pacijenata (56%) prve grupe i 31 pacijent (62%) druge grupe bolovali su od oralne kandidoze u prethodnih pet godina. Uočena je statistički veća učestalost oralne kandidoze u dijabetesnih bolesnika u odnosu na kontrolnu grupu.

Epidemiologija oralne kandidoze u dijabetesnih bolesnika je složena, zbog mnogobrojnih predisponirajućih faktora. Smatra se da je rast gljivica olakšan zbog povećanih vrednosti šećera u tkivnim tečnostima.<sup>7</sup> U ovom istraživanju vrednosti glikemije u prvoj grupi bili su  $10.43 \pm 0.37$  mmol/l, a u drugoj  $10.37 \pm 0.26$  mmol/l. Povećana glikosilacija promovira pojačanu adheziju gljivica za epitelne ćelije pa se prisustvo gljivica povezuje sa kvantitativnim (kserostomija) i kvalitativnim poremećajem pljuvačne sekrecije i oslabljenim ćelijskim imunitetom.<sup>7-9</sup> U ovom istraživanju uočena je povećana prevalencija oralne kandidoze u dijabetesnih bolesnika u odnosu na ispitanike kontrolne grupe. Kandidoza u dijabetesnih bolesnika koji nose zubnu protezu povezuje se sa lošim održavanjem oralne higijene i dugotrajnim nošenjem proteze.<sup>19-21</sup> Pošto je diabetes mellitus posledica genetski i klinički različitih uzroka čija je zajednička osobina poremećaj glikemije, može se pretpostaviti da postoji povezanost između diabetes mellitusa i Stomatitisa protetica.

Belazi i sar.<sup>22</sup> uočili su da ne postoji statistički značajna veza između učestalosti oralne kandidoze i starosti ispitanika. Drugi istraživači su uočili intenzivan rast gljivica iz roda *Candida* u dijabetesnih bolesnika starijih od 60 godina.<sup>23,24</sup> Potencijalni faktori rizika koji ga promoviraju su: prisutna druga oboljenja, povećano propisivanje i prekomeran unos lekova, loša oralna higijena, poremećena ishrana i češći stomatološki problemi.<sup>11,23,24</sup> Istraživači su uočili da je oralna kandidoza zastupljenija u dijabetesnih bolesnika koji nose proteze, jer se *Candida albicans* vezuje za akrilat pa zubne

## Discussion

Candidal infections are a major problem, especially among the immunosuppressed people. Oral infections with yeasts are more frequent in diabetic patients, but some results remain controversial and contradictory.<sup>9,11,13</sup> The oral candidal carriage rate has been estimated to be as high as 80% in diabetic patients.<sup>18</sup> In this investigation similar results were noticed; 28 patients (56%) in the first group and 31 patients (62%) in the second group had oral candidiasis during last five years. This finding showed a statistically higher frequency of oral candidal infection compared to the control group.

The epidemiology of oral candidal infection in diabetic patients seems to be complex, resulting from a combination of many predisposition factors. Yeast growth is promoted by elevated tissue fluid glucose levels.<sup>7</sup> In this investigation glucose level in first group was  $10.43 \pm 0.37$  mmol/l and in the second  $10.37 \pm 0.26$  mmol/l. Moreover, besides the presence of a high concentration of salivary glucose combined, low salivary secretion may enhance growth of yeasts and their adherence in epithelial oral cells.<sup>7-9</sup> In this investigation an increased prevalence of oral candida infections in diabetic patients compared with control subjects has been noticed. Candidal infection associated with dentures is related to the poor hygienic condition and to the long time of prostheses usage.<sup>19-21</sup> As diabetes mellitus is a result of genetically and clinically heterogeneous causes that share glycemic disturbance as a common feature, it can be hypothesized that there is a connection between diabetes mellitus and Candida-associated denture stomatitis.

Belazi et al.<sup>22</sup> noticed that there was no statistical association between oral candidal infection and age. Other investigators revealed intensive candidal growth in diabetics older than 60 years.<sup>23,24</sup> There could be several etiologies for such an association: other disease presence, increased prescription and over-the-counter medication intake, poor oral hygiene, dietary selections and increased dental problems.<sup>11,23,24</sup> Some investigators have demonstrated that candidal carriage is higher among diabetics wearing dentures because *Candida albicans* adheres to acrylic and dentures behave as a reservoir for these yeasts.<sup>25,26</sup> Correlation between Candida-associated denture stomatitis and diabetes mel-

proteze mogu služiti kao rezervoar gljivica.<sup>25,26</sup> Povezanost između Stomatitis protetica izazvanog *Candida albicans* i diabetes mellitusa može olakšati rano dijagnostikovanje diabetes mellitusa.<sup>16,27</sup> Ali, takođe postoje i kontradiktorni nalazi.<sup>22,28</sup> Belazi i sar.<sup>22</sup> nisu pokazali statistički značajnu povezanost između prevalence oralne kandidoze i nošenja proteza, ali su uočili da dijabetesni bolesnici stariji od 60 godina koji nose proteze češće pate od oralne kandidoze u odnosu na osobe koje ne boluju od diabetes mellitusa.

Smatra se da pojava infekcije gljivicama iz roda *Candida* nije različita među polovima.<sup>22</sup> Takođe, ovom istraživanju distribucija oboljenja među polovima nije pokazala značajnu razliku. Dijabetesni bolesnici se većinom žale na subjektivni osećaj oralne suvoće, poremećaj ukusa i osećaj pečenja u ustima. Ovi simptomi mogu nastati usled poremećaja funkcije pljuvačnih žlezda i dehidracije organizma izazvane hiperglikemijom.<sup>1,28</sup> U dijabetesnih bolesnika sa lošom kontrolom glikemije, prisutna je poliurija koja izaziva dehidraciju i gubitak urinarnih elektrolita, smanjuje sekreciju pljuvačke i javlja se subjektivni osećaj oralne suvoće.<sup>19,29</sup> U ovom istraživanju u dijabetesnim grupama ispitanika, 26 pacijenata (52%) u prvoj i 25 pacijenata (50%) u drugoj grupi, žalili su se na osećaj oralne suvoće. Pregled literature otkriva da se više od trećine dijabetesnih bolesnika žali na osećaj oralne suvoće u prisustvu normalne količine pljuvačke u ustima.<sup>19,23</sup> Rezultati ovog istraživanja potvrdili su značajnije prisustvo osećaja oralne suvoće u dijabetesnih bolesnika. Nije bila prisutna statistička razlika u prisustvu osećaja oralne suvoće između dve grupe dijabetesnih ispitanika. Uočeno je da prevalenca kandidoze u dijabetesnih bolesnika ne zavisi od osećaja oralne suvoće pošto je 15 pacijenata prve (58%) i 13 pacijenata druge (52%) grupe koji su bolovali od oralne kandidoze istaklo da nisu imali osećaj oralne suvoće.

Poznavanje diabetes mellitusa i njegovih oralnih manifestacija su preduslov sigurne i efikasne medicinske nege. Stomatolozi moraju biti upoznati sa različitim metodama efikasne terapije oralne kandidoze i drugih oralnih komplikacija diabetes mellitusa.<sup>30,31</sup> U ovom istraživanju bolesnici sa oralnom kandidozom u vreme istraživanja, lečeni su (sa Sol. Nystatin® 200ml/3 puta dnevno ili sa Dactanol oral gel® 150ml/4 puta dnevno) u trajanju od dve nedelje.

litus indicates a mean for the early diagnosis of the diabetes mellitus.<sup>16,27</sup> But, also there are some contradictory findings.<sup>22,28</sup> Belazi et al.<sup>22</sup> showed no significant relationship between the prevalence of candidal infection and denture wearers, but that diabetics who wore dentures and were older than 60 years suffer more from oral candidiasis than healthy persons.

It is thought that the occurrence of *Candida* species infections is not different between gender.<sup>22</sup> Similar, in this investigation distribution of disease showed no significant difference between gender. It is known that the most common complaints among diabetics include dry mouth sensation, alteration of taste, and burning mouth sensation. These symptoms may result from impaired salivary gland function and dehydration secondary to hyperglycemia.<sup>1,28</sup> In poorly controlled glycaemic diabetics, polyuria reduces the salivary secretion with the subsequent clinical complaint of xerostomia by causing dehydration and loss of urinary electrolytes.<sup>19,29</sup> In this investigation, in the diabetic groups 26 patients (52%) in the first and 25 patients (50%) in the second group, reported dry mouth sensation. Review of the literature reveals that more than third of diabetic patients reported dry mouth sensation in the presence of a normal rate of salivary production.<sup>19,23</sup> The results of the present study verified significantly higher presence of dry mouth sensation in diabetic patients. Dry mouth sensation is a parameter that showed no significant difference between the two diabetic groups. It was noticed that candidal prevalence of diabetics is independent of dry mouth sensation as 15 patients in the first group (58%) and 13 patients in the second group (52%) with positive anamnesis for oral candidiasis reported that they did not suffer from dry mouth sensation.

Providing safe and effective oral medical care for patients with diabetes mellitus requires an understanding of the disease and familiarity with its oral manifestations. Dentists must be cognizant of the various methods of treating effectively the oral candidiasis and other oral complications of diabetes mellitus.<sup>30,31</sup> In this investigation patients with oral candidal infection at the time of investigation were treated (with either Sol. Nystatin® 200ml/3 times per day or Dactanol oral gel® 150ml/4 times per day) for two weeks. Also, managing patients with diabe-

Takođe, stomatološka terapija u bolesnika sa diabetes mellitusom zahteva detaljno praćenje, upornu terapiju i saradnju sa lekarom koji leči osnovno oboljenje u odnosu na lečenje pacijenata koji ne boluju od diabetes mellitusa. Dijabetični bolesnici, posebno oni sa lošom kontrolom glikemije i oralnim infekcijama, moraju dolaziti na češće kontrolne preglede, održavati najviši nivo oralne higijene i noću skidati proteze, kako bi smanjili učestalost oralne kandidoze. Prevencija i terapija oralnih komplikacija diabetes mellitusa poboljšava kvalitet života u osoba obolelih od ove neizlečive bolesti.

### **Zaključak**

Učestalost kandidoze u usnoj duplji statistički je značajno veća u dijabetičnih bolesnika u odnosu na osobe koje ne boluju od diabetes mellitusa. Nema razlike u zastupljenosti oralne kandidoze između osoba koje boluju od diabetes mellitusa tip 1 i tip 2. Subjektivni osećaj oralne suvoće je zastupljeniji u dijabetičnih bolesnika u odnosu na osobe koje ne boluju od diabetes mellitusa. Nema razlike u zastupljenosti subjektivnog osećaja oralne suvoće između osoba koje boluju od diabetes mellitusa tip 1 i tip 2.

Neophodna su dalja istraživanja i praćenje dijabetičnih bolesnika, kako bi se razjasnila uloga gljivica roda *Candida* kao dijagnostičkog faktora za diabetes mellitus i značajnog uzroka oboljenja u ovih pacijenata.

tes mellitus requires more rigorous follow-up, more persistent therapy and cooperation with physicians than in non-diabetic patients. Patients with diabetes mellitus, particularly those with a history of poor glycemic control and oral infections, require more frequent recall visits. They need to maintain the highest level of oral hygiene and remove their dentures overnight, in order to reduce the frequency of oral candidiasis. Prevention and therapy of diabetes mellitus oral complications enhance the quality of life for patients with this incurable disease.

### **Conclusion**

The frequency of oral candidal infections is significantly higher in diabetic patients compared to non-diabetic subjects. There is no difference in the prevalence of oral candidiasis among patients who suffer from diabetes mellitus type 1 and type 2. Subjective feeling of oral dryness is more frequent in diabetic patients compared to subjects who do not suffer from diabetes mellitus. There was no difference in subjective feeling of oral dryness between patients with diabetes mellitus type 1 and type 2.

Further investigation and follow-up of the diabetic patients is necessary, in order to clarify the role of *Candida* species as a diagnostic factor for diabetes mellitus and a significant cause of illness among these sensitive group of individuals.

## LITERATURA / REFERENCES

1. Lorenzo C, Haffner SM. Performance characteristics of the new definition of diabetes. *Diabetes Care* 2010; 33(2): 335-337.
2. Craig ME, Hattersley A, Donaghue KC. Definition, epidemiology and classification of diabetes in children and adolescents. *Pediatric Diabetes* 2009; 10 Suppl 12: 3-12.
3. Dodds MW, Yeh C-K, Johnson DA. Salivary alterations in type 2 (non-insulin-dependent) diabetes mellitus and hypertension. *Comm Dent Oral Epidemiol* 2000; 28: 373-381.
1. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes research and clinical practice* 2010; 87: 4-14.
2. Lalla RV, D'Ambrosio JA. Dental management considerations for the patient with diabetes mellitus. *JADA* 2001; 132: 1425-1432.
3. Franco OH, Steyerberg EW, Hu FB, Mackenbach J, Nusselder W. Associations of diabetes mellitus with total life expectancy and life expectancy with and without cardiovascular disease. *Arch Intern Med* 2007; 167(11): 1145-1151.
4. Lamster IB, Lalla E, Borgnakke WS, Taylor GW. The relationship between oral health and diabetes mellitus. *J Am Dent Assoc* 2008; 139 Suppl 5: 19-24.
8. Kesić Lj, Petrović D, Obradović R, Gašić J. Diabetes mellitus i parodontopatija. *Medicinski pregled* 2009; 11-12: 596-600.
9. Khovidhunkit SP, Suwantuntula T, Thaweboon S et al. Xerostomia, hyposalivation, and oral microbiota in type 2 diabetic patients: A preliminary study. *J Med Assoc Thai* 2009; 92(9): 1220-1228.
10. Samaranayake LP, Leung WK, Jin L. Oral mucosal fungal infections. *Periodontology* 2000 2009; 49(1): 39-59.
11. Muzyka BC, Glick M. A review of oral fungal infections and appropriate therapy. *J Am Dent Assoc* 1995; 126: 63-72.
12. Guggenheimer J, Moore PA, Rossie K et al. Insulin-dependent diabetes mellitus and oral soft tissue pathologies. II: prevalence and characteristics of Candida and Candidal lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000; 89(5): 570-576.
13. Gupta S, Koirala J, Khardori R, Khardori N. Infections in diabetes mellitus and hyperglycemia. *Infectious Disease Clinics of North America* 2007; 21(3): 617-638.
14. Daniluk T, Tokajuk G, Stokowska W et al. Occurrence rate of oral *Candida albicans* in denture wearer patients. *Adv Med Sci.* 2006; 51 Suppl 1: 77-80.
15. Javed F, Klingspor L, Sundin U, Altamash M, Klinge B, Engström PE. Periodontal conditions, oral *Candida albicans* and salivary proteins in type 2 diabetic subjects with emphasis on gender. *BMC Oral Health* 2009; 9(12): 1-8.
16. Kadir T, Pisiriciler R, Akyuz S, Yarat A, Emekli N, Ipbuker A. Mycological and cytological examination of oral candidal carriage in diabetic patients and non-diabetic control subjects: thorough analysis of local aetiologic and systemic factors. *J Oral Rehabil* 2002; 29: 452-457.
17. Willis AM, Coulter WA, Fulton CR, Hayes JR, Bell PM, Lamey PJ. The influence of antifungal drugs on virulence properties of *Candida albicans* in patients with diabetes mellitus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; 91: 317-321.
18. Sashikumar R, Kannan R. Salivary glucose levels and oral candidal carriage in type II diabetics. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology* 2010; 109(5): 706-711.
19. Motta-Silva AC, Aleva NA, Chavasco JK, Armond MC, França JP, Pereira. LJ. Erythematous oral candidiasis in patients with controlled type II diabetes mellitus and complete dentures. *Mycopathologia* 2010; 169(3): 215-223.
20. Borgnakke WS. Salivary glucose levels are unable to predict oral candidiasis or monitor diabetes. *The Journal of Evidence – Based Dental Practice* 2010; 10(4): 237-240.
21. Lotfi-Kamran MH, Jafari AA, Falah-Tafti A, Tavakoli E, Falahzadeh MH. *Candida* colonization on the denture of diabetic and non-diabetic patients. *Dent Res J* 2009; 6(1): 23-27.
22. Belazi M, Velegraki A, Fleva A et al. Candidal overgrowth in diabetic patients: potential predisposing factors. *Mycoses* 2005; 48: 192-196.
23. Hof H. Mycoses in the elderly. *Eur J Clin Microbiol Infect Dis* 2010; 29: 5-13.
24. Kadir T, Pisiriciler R, Akyüz S, Yarat A, Emekli N, Ipbüker A. Mycological and cytological examination of oral candidal carriage in diabetic patients and non-diabetic control subjects: thorough analysis of local aetiologic and systemic factors. *J Oral Rehabil* 2002; 29: 452-461.
25. Manfredi M, Al-Karaawi Z, McCullough MJ, Hurei S, Porter SR. The isolation, identification and molecular analysis of *Candida* spp. isolated from the oral cavities of patients with diabetes mellitus. *Oral Microbiol Immunol* 2002; 17: 181-185.
26. Abaci O, Haliki-Uztan A, Ozturk B, Toksavul S, Ulusoy M, Boyacioglu H. Determining *Candida* spp. incidence in denture wearers. *Mycopathologia* 2010; 169(5): 365-37.
27. Dorocka-Bobkowska B, Zozulinska-Ziolkiewicz D, Wierusz-Wysocka B, Hedzelek W, Szumala-Kakol A, Budtz-Jørgensen E. *Candida*-associated denture stomatitis in type 2 diabetes mellitus. *Diabetes Research and Clinical Practice* 2010; 90(1): 81-86.
28. Lyon JP, da Costa SC, Totti VMG, Munhoz MFV, de Resende MA. Predisposing conditions for *Candida* spp. carriage in the oral cavity of denture wearers and

individuals with natural teeth. *Can. J. Microbiol.* 2006; 52(5): 462-467.

29. Klasser G, Fischer D, Epstein J. Burning mouth syndrome: recognition, understanding, and management. *Oral and Maxillofacial Surgery Clinics of North America* 2008; 20(2): 255-271.

30. Bernardi MJ, Reis A, Loguercio AD, Kehrig R, Leite MF, Nicolau J. Study of the buffering capacity, pH and salivary flow rate in type 2 well-controlled and poorly controlled diabetic patients. *Oral Health Prev Dent.* 2007; 5(1): 73-78.

31. Little JW, Falace DA, Miller CS, Rhodus NL. Diabetes. In: Little JW, ed. *Dental management of the medically compromised patient.* 6<sup>th</sup> ed. St. Louis: The Mosby Company; 2002: 248-270.

32. Vernillo AT. Dental considerations for the treatment of patients with diabetes mellitus. *JADA* 2003; 134 Suppl: 24-33.

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