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PARODONTOPATIJA KOD PACIJENATA SA DIJABETES MELLITUSOM TIPA 2

PERIODONTAL DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Sažetak

Uvod: Dijabetes (DM; diabetes mellitus) je jedan od najzastupljenijih endokrinih metaboličkih poremećaja. Dijabetes izaziva oštećenje usne duplje i predstavlja faktor rizika za razvoj parodontopatije. **Cilj** istraživanja je opisati parodontalni status kod pacijenata sa dijabetesom tipa 2 i proceniti demografske, socijalne, medicinske i stomatološke faktore rizika povezane sa parodontopatijom i dijabetesom.

Materijal i Metode: Analizirani su demografski podaci, medicinska i stomatološka istorija bolesti, urađen pregled parodonta (određen nivo pripojnog epitela, krvarenje pri sondiranju i prisustvo zubnog kamenca) i citomorfometrijska analiza.

Rezultati: 160 ispitanika je učestvovalo u istraživanju, starosti 64,2 (±0,2) godina, prosečne dužine trajanja DM 23,6 (±0,39) godina i srednje vrednosti HbA1c 8,70% (±0,45). Visoke vrednosti nivoa epitelnog pripoja i kamenac bili su zastupljeniji kod starijih pacijenata. Krvarenje pri sondiranju je bio istih vrednosti nezavisno od starosti pacijenata. Citomorfometrijska analiza je pokazala prisustvo većih jedara kod starijih pacijenata. Prema regresionoj analizi faktori povezani sa uznapredovalom parodontopatijom su: starost (P<0,001), pušenje cigareta (p<0,001), bivši pušači (p<0,001), pranje zuba (p=0,017), posete stomatologu (p=0,068), dužina trajanja DM (p=0,034), kserostomija (p=0,500), povećanje vrednosti HbA1c (p=0,119), neuropatija (p=0,017), nefropatija (p=0,389), retinopatija (p=0,550) i periferna vaskularna kardiomiopatija (p=0,060).

Zaključak: Parodontopatija je često oboljenje kod starijih dijabetesnih bolesnika. Pušenje cigareta u starijoj životnoj dobi je povezano sa visokom učestalošću uznapredovale parodontopatije. Pušači dijabetičari imaju visok rizik za lošu prognozu parodontopatije i moraju dolaziti na redovne parodontološke kontrolne preglede i terapiju.

Cljučne reči: parodontopatija, dijabetes, eksfolijativna citologija, oralno zdravlje

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Abstract

Background: Diabetes mellitus (DM) is one of the most prevalent endocrine metabolic disorders. It has damaging effects on the oral cavity and is reported to be a risk factor for periodontal disease. **The aim** of the study was to describe the periodontal status of patients with type 2 DM and to evaluate the multiple demographic, behavioral, medical and dental factors that may be associated with periodontal disease and DM.

Material and Methods: Demographic data and medical and dental histories were reviewed, periodontal assessments (loss of attachment, bleeding on probing, presence of supragingival calculus) and cytomorphometric analysis were made.

Results: 160 subjects participated in the study, age of 64.2 (±0.2) years, duration of DM 23.6 (±0.39) years and HbA1c 8.70% (±0.45). Severe loss of attachment and calculus were more present in older patients. Bleeding on probing was consistent among subjects in each age group. Cytomorphometric analysis revealed larger nuclear area values in older subjects. Factors possibly associated with advanced periodontal disease included in the regression analysis were: age (P<0.001), current smoking cigarettes (p<0.001), having ever smoked cigarettes (p<0.001), tooth brushing (p=0.017), visits to the dentist (p=0.068), duration of disease (p=0.034), xerostomia (p=0.500), HbA1c(p=0.119), neuropathy (p=0.017), nephropathy (p=0.389), retinopathy (p=0.550) and peripheral vascular disease (p=0.060).

Conclusion: Periodontal disease was common in adult diabetic population. Cigarette smoking and older age were associated with a higher prevalence of advanced periodontal disease. Smoker-diabetic patients are at high risk for poor periodontal prognosis, and they should be included in regular periodontal control check up and treatment.

Key words: periodontal disease, diabetes, exfoliative cytology, oral health

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Uvod

Dijabetes (diabetes mellitus; DM) predstavlja jedan od najčešćih metaboličkih endokrinih poremećaja i od njega boluje oko 100 miliona ljudi u celom svetu¹. Kod obolelih od dijabetesa javlja se poremećaj metabolizma ugljenih hidrata, masti i proteina koji sledstveno izaziva dijabetesne komplikacije poput oboljenja bubrega, očiju, nerava, perifernog vaskularnog sistema i koronarnu bolest srca². Danas, tip 2 DM čini oko 95% svih slučajeva DM i peto je po učestalosti hronično oboljenje čoveka^{3,4}. Njegova učestalost stalno raste (sada je 1% - 6%) i po uzroku smrtnosti starijih osoba nalazi se na šestom mestu u svetu⁵⁻⁸. Tip 2 DM javlja se kod osoba starijih od 40 godina, karakteriše se postepenom pojavom simptoma i konstantnim napredovanjem bolesti. Ostali oblici DM su tip 1 DM, gestacioni DM (prisutan u trudnoći) i DM u sklopu sindroma⁹.

DM oštećuje usnu duplju i smatra se faktorom rizika za parodontopatiju^{10,11}. Kod odraslih osoba sa DM tip 2 inflamacija gingive se češće javlja i predstavlja veoma značajan znak aktivnosti i progresije dijabetesa¹²⁻¹⁴. Prevencija i terapija parodontopatije kod pacijenata sa DM je od velikog značaja jer posledice parodontopatije i gubitak zuba značajno utiču na kvalitet života i na celokupno zdravlje dijabetesnih bolesnika tako što otežavaju zdravu ishranu a samim tim i adekvatnu kontrolu glikemije. Takođe, dokazano je da parodontopatija negativnim uticajem na glikemijsku kontrolu izaziva češće komplikacije DM¹⁵.

Parodontopatija započinje kao inflamacija gingive koja se razlikuje po intenzitetu i brzini napredovanja u dublja parodontalna tkiva, izaziva razaranje pripojnog epitela i na kraju gubitak zuba. Njeni znaci i simptomi obuhvataju crvenilo, otok i osetljivost gingive. Klinička dijagnoza parodontopatije se postavlja najčešće na osnovu kliničkog pregleda koji obuhvata i određivanje gubitka pripojnog epitela (clinical attachment loss - CAL). Ovakav način tradicionalnog merenja ima ograničenja jer se samo evidentiraju prethodno već nastala oštećenja, a ne otkrivaju mesta koja se trenutno razaraju u vreme ispitivanja¹⁶. Takođe, kod nekih dijabetesnih pacijenata ova merenja se ne mogu izvršiti zbog prisutnih varijacija u nivou glikemije. U ovako specifičnim slučajevima eksfolijativna citologija predstavlja praktičniju dijagnostičku metodu koja se može izvoditi čak i na inflamiranom tkivu i kod osoba sa hemoragijskim poremećajima.

Introduction

Diabetes mellitus (DM) is one of the most prevalent endocrine metabolic disorders and affects over 100 million people worldwide¹. During DM carbohydrates, fat and protein metabolism disorders may be present causing DM complications like renal disease, retinopathy, neuropathy, peripheral vascular disease and coronary heart disease². Type 2 DM accounts for approximately 95% of DM cases and is the fifth most common chronic condition nowadays^{3,4}. Its frequency has been increasing (1% - 6%) and it is the sixth leading cause of mortality among the elderly in the world⁵⁻⁸. Type 2 DM is characterized by slow onset of symptoms, usually after 40 years of age and continuous progression. Other forms of DM include type 1 DM, gestational DM (seen during pregnancy) and DM secondary to other medical conditions⁹.

DM has damaging effects on the oral cavity and is reported to be a risk factor for periodontal disease^{10,11}. In adults with type 2 DM, gingival inflammation occurs at higher rates and it is a very important sign of disease's activity and development¹²⁻¹⁴. Prevention and therapy of periodontal disease in patients with DM is very important because the consequences of periodontal disease and subsequent tooth loss influence the quality of life of a diabetic patient and significantly impact an overall health by compromising a patient's ability to maintain a healthy diet and proper glycemic control. Also, periodontal disease is shown to have potential negative effect on glycemic control and diabetic complications¹⁵.

Periodontal disease begins as gingival inflammation which can vary in intensity and progression speed into deeper periodontal tissues, resulting in the destruction of the dental attachment apparatus and consequent tooth loss. Its signs and symptoms include redness, swelling and tenderness. The clinical diagnosis of periodontal disease is usually made on the basis of clinical examination which includes measuring clinical attachment loss (CAL). This is complicated by the fact that this traditional measure of periodontal damage only measures past destruction and does not detect sites that are currently breaking down¹⁶. Also, in some diabetic cases it cannot be performed due to glycemic variations.

For such specific situations exfoliative cytology is more practical technique which can

Ona je jednostavna i neinvazivna dijagnostička procedura kojom se uzorkuju površinske deskvamirane ćelije i zatim mikroskopski analiziraju, a može se često ponavljati bez narušavanja komfora pacijenta^{12,17}.

Cilj istraživanja

Cilj istraživanja je odrediti parodontalni status kod osoba sa dijabetesom tipa 2 uz pomoć parodontalnih indeksa i eksfolijativne citologije i proceniti uticaj demografskih, medicinskih i stomatoloških faktora rizika koji mogu biti povezani sa parodontopatijom osoba sa dijabetesom.

Pacijenti i metode

U ovom istraživanju je učestvovalo 160 pacijenata, koji su dolazili na svoje redovne kontrolne preglede na Odeljenje za endokrinologiju Kliničkog centra u Nišu, koji su obuhvatali: fizički pregled pacijenta, EKG, uzorkovanje urina, procenu bubrežnih, neuroloških i kardioloških funkcija. Pacijenti koji su imali rizik od bakterijskog endokarditisa ili neke druge bakterijemije nisu uključeni u istraživanje.

Kako bi se procenilo oralno zdravlje ispitanika isti su upućivani na Odeljenje za Oralnu medicinu i parodontologiju Klinike za stomatologiju Medicinskog fakulteta Univerziteta u Nišu. Svaki ispitanik je potpisao obrazac o saglasnosti za ispitivanje i popunio upitnik. Etički komitet Medicinskog fakulteta u Nišu je odobrio istraživanje (evidencioni broj 01-2800-7).

Procena oralnog zdravlja

Za vreme prve posete anamnezom su prikupljeni demografski i medicinski podaci ispitanika. Demografski podaci su podrazumevali starost i pol ispitanika, a analiza medicinske istorije bolesti je dala uvid u trenutno lečenje pacijenta, upotrebu lekova, hospitalizaciju i bolovanje od značajnijih opštih oboljenja (hepatitis, epilepsija, alergije, prethodne operacije, trudnoća). Stomatološka istorija bolesti je dala uvid u pružene stomatološke usluge i oralno higijenske navike. Ispitanici su odgovarali na pitanja u vezi sadašnjeg i prethodnog pušenja cigareta ili proizvoda od duvana. Konzumacija alkohola je procenjena na osnovu popunjavanja upitnika vezanog za konzumiranje piva, vina i mešovitih alkoholnih pića.

Procena stanja parodonta

Procena stanja parodonta je vršena na tri mesta sa vestibularne strane svakog zuba (mezijalno, srednje i distalno). Treći molari nisu uzimani u obzir¹⁸. Gubitak nivoa pripojnog epitela (loss of attachment - LOA) je određivan

be applied even during inflammation and hemorrhagic disorders. It is simple and noninvasive diagnostic method that picks superficial desquamated cells and analyzes them microscopically and can be repeated frequently with little discomfort to the patient^{12,17}.

The aim of the study

The aim of the study was to describe the periodontal status of patients with type 2 DM using periodontal indices and gingival exfoliative cytology and to evaluate the multiple demographic, behavioral, medical and dental factors that may be associated with periodontal disease and DM.

Subjects and methods

The 160 diabetic subjects recruited into this oral health study were ongoing participants of the Department of Endocrinology who came for their regular checkup visit which included physical exam, ECG, urine sample, evaluation of renal, neural and cardiological functions. Subjects at risk for bacterial endocarditis or other bacteriemia were excused.

For the oral health evaluation, subjects were referred to the Department for Oral medicine and Periodontology Dental Clinic, Niš University Faculty of Medicine. Approved consent form was presented and signed, and questionnaires filled. The Ethics Committee of the Faculty of Medicine in Niš approved the study protocol (evidential number 01-2800-7).

Oral Health Assessment Methodology

During the initial interview, demographic data and medical and dental histories were reviewed. Demographic data included age and gender. The medical history solicited information regarding current medical care, medications, hospitalizations, significant medical histories (hepatitis, epilepsy, allergies, surgery, pregnancy). The dental history solicited information regarding dental care and oral hygiene habits. Subjects were questioned regarding their current and lifetime history of cigarette and tobacco products use. Alcohol consumption was determined from a questionnaire that elicited consumption estimates for beer, wine and mixed drinks.

Periodontal assessments

Periodontal assessments were made on 3 sites on vestibular surface of each tooth (mesial, mid and distal). Third molars were excluded¹⁸.

Measurements from the cementenamel junction to the base of the pockets were made

merenjem rastojanja od gleđno-cementne granice do dna parodontalnog džepa uz pomoć standardne parodontološke sonde. Procena krvarenja pri sondiranju (bleeding on probing - BOP) vršena je inseriranjem parodontološke sonde u gingivalni sulkus ili parodontalni džep. BOP je evidentirano kao: prisutno ili nije prisutno. Prisustvo zubnog kamenca je određeno vizuelnim pregledom i evidentirano kao: prisutno ili nije prisutno.

Citomorfometrijska analiza

Pacijenti su prvo isiprali usta fiziološkim rastvorom u trajanju od 5 minuta, a zatim je bris uzet uz pomoć smotuljka vatiće sa vestibularne površine gingive celih usta. Zatim su brisevi prenešeni na suvo, čisto predmetno stakalce i fiksirani 95% etil alkoholom i bojani po Papanicolaou za citomorfometrijsku analizu koja je izvršena uz pomoć Image programa, NU2 mikroskop (Carl Zeiss, Nemačka) objektiv x 63 (NA 0,8)¹⁹.

Obrada i analiza podataka

Na početku analize svi podaci su detaljno pregledani u smislu njihove kompletnosti i tačnosti. SPSS softverski program je korišćen za statističku analizu. Razlike indeksa za svaku ispitivanu starosnu grupu su analizirane uz pomoć ANOVA analize za kontinuirane varijable i chi square analize za nekontinuirane varijable. Kako bi definisali parodontološke zavisne faktore, definisano je prisustvo "uznapredovale parodontopatije" kod svih ispitanika koji su imali LOA ≥ 6 mm u više od 10% pregledanih mesta. Rezultanta binarne varijable (prisutan / odsutan) za uznapredovalu parodontopatiju je korišćena kao zavisna varijabla u nominalnom logističkom regresionom modelu analize. Takođe, kao dopunske varijable korišćeni su: starost, pol, trenutno pušenje cigareta, bivši pušači, konzumiranje alkohola (više od 2 decilitra nedeljno), pranje zuba (jednom ili više puta u toku dana), da li su posetili stomatologa u prethodnih godinu dana, kserostomija, trajanje DM, HbA1c, nefropatija (da-insuficijencija bubrega, ne-početna nefropatija), neuropatija (da-uznapredovala, ne-početna neuropatija), retinopatija (da-uznapredovala, ne-početna retinopatija) i oboljenja perifernih krvnih sudova (da-uznapredovala, ne-početna).

in order to establish loss of attachment (LOA) using a standard CPITN pressure controlled probe. For bleeding on probing (BOP) measurements the periodontal probe was gently inserted into the gingival sulcus or periodontal pocket. BOP was assessed as present or absent. Visual assessments of supragingival calculus were rated as present or absent.

Cytomorphometric analysis

Patients washed mouths with normal saline for about 5 minutes and then the surface smear was taken with cotton wadding from vestibular gingival surface in whole mouth. The smears were transformed to a clean dry glass slide and fixed with 95% ethyl alcohol and prepared with Papanicolaou staining for cytomorphometric analysis. The morphometric analysis was done using Image program, NU2 microscope (Carl Zeiss, Germany) objective x 63 (NA 0.8)¹⁹.

Data management and analyses

All data were initially screened for accuracy and completeness. SPSS software program was used for the statistical analysis.

Differences in the prevalence rates of indices for each of the age categories were compared using ANOVA for continuous variables and chi square analyses for categorical variables. To address dependent factors possibly associated with periodontal disease, a classification of "advanced periodontal disease" was created. Subjects with LOA ≥ 6 mm in more than 10% of periodontal sites examined were so defined. The resultant binary variable (presence / absence) of advanced periodontal disease was used as the dependent variable in a nominal logistic regression model.

Potential explanatory variable were: age, gender, currently smoking cigarettes, having ever smoked cigarettes, alcohol consumption (greater than 2 deciliters per week), tooth brushing (one or fewer times per day), having visited a dentist in the last year, presence of xerostomia, duration of DM, HbA1c, nephropathy (yes-renal failure or no), neuropathy (yes-definite and no-early), retinopathy (yes-advanced or no-early) and peripheral vascular disease (yes-advanced and no-early).

Rezultati

160 ispitanika je učestvovalo u istraživanju, starosti 64,2 ($\pm 0,2$) godina, a srednje starost u vreme postavljanja dijagnoze DM bila je 48,4 ($\pm 0,2$) godina. Od dijabetičkih ispitanika 89 je bilo muškog, a 71 ženskog pola.

Prosečna dužina trajanja DM je bila 23,6 ($\pm 0,39$) godina, a srednja vrednost HbA1c 8,70% ($\pm 0,45$). U toku kliničkog pregleda zabeleženo je i prisustvo komplikacija dijabetesa i to: 46,88% ispitanika je imalo uznapredovalu ili proliferativnu retinopatiju, 23,75% je imalo nefropatiju ili insuficijenciju bubrega, 31,88% perifernu neuropatiju, i 10% perifernu vaskularnu bolest (Tabela 1).

Razlike u parodontalnim indeksima u zavisnosti od starosti ispitanika su prikazane u tabeli 2. Vrednosti LOA su se povećavale sa povećanjem starosti ispitanika. Veći LOA (≥ 6 mm) je zastupljeniji kod starijih ispitanika. BOP je imao iste vrednosti kod svih starosnih grupa. Veće količine zubnog kamenca bile su prisutne kod starijih ispitanika. Citomorfometrijska analiza je pokazala veće vrednosti jedara (NA) kod starijih ispitanika.

Results

160 subjects aged 64.2 (± 0.2) years participated in the study, and a mean age at the onset of DM 48.4 (± 0.2) years. This diabetic population study comprised 89 males and 71 females.

The mean duration of the disease for these diabetic subjects was 23.6 (± 0.39) years while the mean HbA1c level was 8.70% (± 0.45). Assessments of diabetic complications at the time of oral examination found 46.88% to have advanced or proliferative retinopathy, 23.75% to have overt nephropathy or renal failure, 31.88% to have definite peripheral neuropathy, and 10% to have definite peripheral vascular disease (Table 1).

Variation in periodontal disease indices with age is shown in Table 2. Measures of LOA generally increase with age. Severe LOA (≥ 6 mm) was more present in older patients. BOP was consistent among subjects in each age group. Supragingival calculus was more prevalent in the older subjects. Cytomorphometric analysis revealed larger nuclear area (NA) values in older subjects.

Tabela 1. Demografski podaci
Table 1. Data demographic

	Muškarci	Žene	Ukupno
	Males	Females	Total
Starosna grupa			
Age category			
≤ 40 godina	14	16	30
41-50 godina	20	14	34
51-60 godina	23	16	39
61-70 godina	18	15	32
71-80 godina	10	8	18
>80 godina	3	4	7
Ukupno	89	71	160
Starost (god.)	64.6 \pm 0.57	64.0 \pm 0.64	64.2 \pm 0.43
Age (year)			
Starost u vreme otkrivanja DM (god.)	48.2 \pm 0.31	48.6 \pm 0.35	48.4 \pm 0.23
Age at onset (year)			
Dužina trajanja DM (god.)	24.0 \pm 0.36	23.5 \pm 0.32	23.6 \pm 0.39
Duration of disease (year)			

Tabela 2: Vrednosti parodontalnih indeksa i citomorfometrijskih parametara u zavisnosti od starosti ispitanika**Table 2:** Variations in periodontal indices and cytomorphometric values with age

	Starost (godine) Age Category (years)						Ukupno Overall
	≤ 40	41-50	51-60	61-70	71-80	>80	
LOA* (mm)	0.75±0.08	1.00±0.08	1.33±0.07	1.83±0.09	2.89±0.13	3.63 ±0.17	1.53± 0.04
Ispitanici sa Subjects with any LOA≥4mm^a (%)	30.0	58.8	61.5	65.6	66.7	85.7	52.34
Ispitanici sa Subjects with any LOA≥6mm* (%)	10.0	14.7	23.1	25.0	27.8	42.6	20.62
Najveći LOA Deepest (mm) svakog ispitanika for each subject*	2.69 ±1.9	3.82±0.19	4.31±0.16	4.38±0.16	4.84±0.25	5.03 ±0.35	4.01±0.08
Ispitanici sa Subjects with any (%)	80.0	70.6	71.8	81.2	66.7	71.4	74.4
Ispitanici sa Subjects with any kamencem calculus (%)	20.0	29.4	25.6	31.3	33.3	42.9	28.1
NA	78.81±8.5	78.93±9.2	82.03±8.5	89.44±3.2	92.46±3.4	99.48±11.69	83.69±8.5

*p<0.05.

Tabela 3. Faktori povezani sa uznapredovalom parodontopatijom
Table 3. Factors possibly associated with advanced periodontal disease

Faktor	Broj Number	ZastupljenostEPD	Odnos Odds ratio	95% C.I.	p vrednost value
Demografske karakteristike Demographics prevalence					
Starost Age					
≤ 50 godina years	103	16.9%	39.7	1.82-9.63	<0.001
> 50 godina years	57	4.8%			
Pol Gender					
Muškarci Males	89	12.5%	1.52	0.73-3.20	0.261
Žene Females	71	8.4%			
Konzumiranje cigareta i alkohola Tobacco and alcohol consumption					
Trenutno pušenje cigareta Current cigarette smoking					
Da Yes	31	35.6%	9.98	4.87-20.9	<0.001
Ne No	129	4.9%			
Prethodno pušenje cigareta Cigarette smoking					

history					
Bivši pušači	56	21.9%	6.24	2.88-14.47	<0.001
Previously smoked					
Nikad nisu pušili	103	4.3%			
Never smoked					
Konzumiranje alkohola Alcohol consumption					
≥2dcl/nedeljno deciliter/week	48	13.4%	1.55	0.72-3.28	0.242
<2dcl/nedeljno deciliter/week	109	9.0%			
Oralno zdravlje Oral health					
Pranje zuba					
Tooth brushing					
≤ jednom dnevno	42	17.5%	2.43	1.16-5.04	0.017
> jednom dnevno	118	8.2%			
≤ once a day					
> once a day					
Posetili stomatologa prošle godine					
Visited dentist in a last year					
Ne No	114	15.4%	1.94	0.92-4.01	0.067
Da Yes	46	8.6%			
Simptomi vezani za kserostomiju					
Xerostomia symptoms					
Ne No	40	19.9%	1.30	0.56-2.81	0.500
Da Yes	120	10.1%			
Starost u vreme postavljanja dijagnoze DM					
Age at DM onset					
≤ 50 godina years	80	4.6%	4.36	1.90-11.17	<0.001
> 50 godina years	80	16.1%			
Trajanje DM					
Duration of DM					
> 24 godina years	71	14.7%	2.24	1.06-4.64	0.034
≤ 24 godina years	89	7.8%			
HbA1C					
Loša glikemija Poor (>10.1%)	113	12.6%	2.08	0.86-5.68	0.119
Dobra glikemija Good (≤10.1%)	48	6.3%			
Nefropatija Nephropathy					
Da (insuf. bubrega)	29	13.7%	1.46	0.58-3.19	0.389
Yes (renal failure)					
Ne No	131	9.7%			
Neuropatija Neuropathy					
Da (uznapredovala)	35	18.7%	2.48	1.14-5.19	0.017
Yes (definite)					
Ne (početna)	125	8.3%			
No (early)					
Retinopatija Retinopathy					
Da (uznapredovala)	64	11.9%	1.27	0.61-2.64	0.550
Yes (advanced)					
Ne (početna) No (early)	96	9.5%			
Periferna vaskularna oboljenja					
Peripheral vascular disease					
Da (uznapredovala) Yes (advanced)	15	21.9%	2.59	0.91-6.54	0.060
Ne (početna) No (early)	145	9.4%			

Prema regresionoj analizi, faktori povezani sa uznapredovalom parodontopatijom su: starost ($P < 0,001$), trenutno pušenje cigareta ($p < 0,001$), bivši pušači ($p < 0,001$), pranje zuba ($p = 0,017$), redovne posete stomatologu ($p = 0,068$), trajanje DM ($p = 0,034$), kserostomija ($p = 0,500$), vrednost HbA1c ($p = 0,119$), neuropatija ($p = 0,017$), nefropatija ($p = 0,389$), retinopatija ($p = 0,550$) i periferna vaskularna oboljenja ($p = 0,060$) (Tabela 3).

Diskusija

Dijabetes predstavlja značajno globalno hronično oboljenje ljudi koje je Svetska Zdravstvena Organizacija (World Health Organization - WHO) zbog velike učestalosti proglasila epidemijom. Ovaj izražen porast učestalosti, pre svega na osnovu povećanja broja obolelih od DM tipa 2, javlja se i u zemljama u razvoju i u razvijenim zemljama. Takođe, kao dodatak mnogobrojnim nalazima koji potvrđuju da je dijabetes rizik faktor za loše parodontalno zdravlje, postoji sve više naučnih dokaza koji ističu da parodontalna infekcija loše utiče na glikemijsku kontrolu i pojavu dijabetesnih komplikacija^{1,4}. Ipak, navedene podatke treba uzeti obazrivo u obzir, jer sami dobijeni rezultati istraživanja zavise od godine kada je rađeno istraživanje, kriterijuma procenjivanja, interpretacije dobijenih rezultata i specifičnih populacionih karakteristika⁸. U ovom istraživanju LOA je pokazao veće vrednosti sa povećanjem starosti ispitanika što je u saglasnosti sa drugim istraživanjima koja ističu da stariji ispitanici imaju uznapredovali oblik parodontalne bolesti i veći rizik za napredovanje bolesti nego mlađe osobe^{20,21}. U ovom istraživanju, za razliku od literaturnih podataka nije uočena povezanost BOP sa starošću ispitanika što nam sugerise da inflamacija gingive i BOP zavise od akumulacije oralnog biofilma i oralne higijene²⁰. Može se reći da je BOP značajan pokazatelj održavanja parodontalnog zdravlja^{22,23}. Mnogobrojna istraživanja ističu da je pušenje cigareta značajan etiološki faktor za pojavu LOA^{24,25}. Hyman i sar.²⁶ su sproveli ispitivanje kod 12,325 odraslih osoba u SAD-u i uočili, kao i mi u ovom istraživanju, da su veće vrednosti LOA povezane sa pušenjem cigareta. Ovo je posebno uočljivo kod osoba starijih od 50 godina. U našem istraživanju, prisustvo zubnog kamenca se povećavalo sa porastom starosti ispitanika (20,0% do 42,9%), kao što je uočeno i u istraživanjima drugih autora^{21,22,27}.

Factors possibly associated with advanced periodontal disease included in the regression analysis were: age ($P < 0.001$), current smoking cigarettes ($p < 0.001$), having ever smoked cigarettes ($p < 0.001$), tooth brushing ($p = 0.017$), visits to the dentist ($p = 0.068$), duration of disease ($p = 0.034$), xerostomia ($p = 0.500$), HbA1c ($p = 0.119$), neuropathy ($p = 0.017$), nephropathy ($p = 0.389$), retinopathy ($p = 0.550$) and peripheral vascular disease ($p = 0.060$) (Table 3).

Discussion

Diabetes is an important chronic disease globally as reflected in the World Health Organization (WHO) declaring the rate of increase in diabetes prevalence is an epidemic. This growth in diabetes prevalence, driven principally by increasing prevalence of type 2 diabetes, is occurring in both developing and developed countries. In addition to the substantial evidence demonstrating diabetes as a risk factor for poor periodontal health, there is a growing body of evidence supporting periodontal infection adversely affecting glycemic control and diabetes complications^{1,4}. However, the specific values should be compared to published surveys with caution because the actual values vary depending on the year when the study was performed, assessment criteria, examiner interpretations and specific population characteristics⁸. In our study LOA shows enlargement trends with age as noticed in other studies which emphasize that older subjects have more advanced form of periodontal disease and a greater risk of disease progression than younger subjects^{20,21}. Trends in BOP with age are essentially nonexistent in our study as noticed in literature data which point out that gingival inflammation and BOP are related with plaque accumulation and oral hygiene²⁰. It is thought that BOP is a reliable predictor for the maintenance of periodontal health^{22,23}. Many studies emphasize the role of cigarette smoking in the etiology of LOA^{24,25}. Hyman²⁶ conducted the study of 12,325 US adults and noticed, as we did in our study, that higher LOA was associated with current smoking. This was especially noticeable among those aged 50 years or more. In our study, the prevalence of supragingival calculus seems to increase with age (20.0% to 42.9%) as seen in studies conducted by other authors^{21,22,27}.

Poslednjih godina, raste interesovanje za primenu eksfolijativne citologije kao standardne tehnike za otkrivanje patoloških promena u usnoj duplji. Citomorfometrijska analiza eksfolijativnih ćelija se preporučuje kao ključna tehnika za identifikaciju ćelijskih promena i mnogi istraživači su vršili ispitivanja različitih delova usne duplje kod dijabetesnih ispitanika. Ipak, podaci vezani za uzorkovanje gingivalnog tkiva su oskudni^{28,29}. Smatra se da su veće vrednosti NA dobijenih citomorfometrijskom analizom oralne mukoze povezane sa većom starosti ćelija kod dijabetesnih bolesnika³⁰⁻³³. Hiperglikemija kod pacijenata sa DM izaziva nakupljanje produkata glikolizacije na nivou bazalne membrane malih krvnih sudova, čime se sužava lumen krvnih sudova, smanjuje perfuzija i razmena hranjivih materija. Na ovaj način dolazi do usporene keratinizacije i usporenog procesa diferencijacije epitelnih ćelija što vodi povećanju broja zrelih ćelija. Zrele ćelije imaju veliko jedro kao svoju osnovnu karakteristiku što može biti razlog većih vrednosti NA uočenih kod dijabetesnih bolesnika³¹.

U ovom istraživanju 120 (75%) ispitanika je imalo simptome kserostomije. Smanjeno lučenje pljuvačke kod dijabetesnih bolesnika može dovesti do dehidracije usne duplje i atrofije oralne mukoze. Brisevi sa atrofične mukoze obično imaju ćelije koje su manje po veličini ali imaju veliko jedro pa daju utisak da su vrednosti NA veće, kao što je uočeno u istraživanju. Uprkos tome što je istraživanje pokazalo da DM tip 2 izaziva ćelijske promene u gingivalnom epitelu, ove promene nisu specifične za DM. Ovakva ćelijska oštećenja se takođe javljaju kod pacijenata sa endokrinim i respiratornim oboljenjima, povezanim sa smanjenom keratinizacijom koja je i razlog povećanja veličine jedra. Patel i sar.²⁸ su pokušali da postave osnove u načinu prepoznavanja patoloških briseva gingive i sugerisali su da je inflamacija jedan od faktora koji može povećati veličinu NA i dovesti do lošeg očuvanja citoplazme. Istraživači su uočili slične promene u toku poremećaja keratinizacije kod osoba koje su pušači^{34,35}. Naši nalazi potvrđuju značajnu ulogu duvana u povećanoj učestalosti i težini parodontopatije.

Odnos od 9,98 u povezanosti pušenja i parodontopatije koje smo pronašli u našem sprovedenom istraživanju je u skladu sa navodima iz literature²⁶.

In recent years, there has been increasing interest in the role of exfoliative cytology as a standard technique in screening of oral pathologies. Cytomorphometric analysis of exfoliated cells has been suggested as a key approach to identify the cellular changes and many investigators have evaluated different sites in oral cavity of diabetic patients. However, data on gingival tissue is scarce^{28,29}. It is suggested that higher NA values in cytomorphometric analysis of oral mucosa could be related to increased cellular age in patients with DM³⁰⁻³³. Hyperglycemia in patients with DM causes agglomeration of advanced glycation end products in the basement membrane of the small blood vessels narrowing of the vessel lumen and decreasing perfusion and cell turnover. This can explain slow keratinization and epithelial differentiation processes which lead to an increase in the number of mature cells. Mature cells have large nucleus as a primary characteristic and can be related to higher NA values noticed in diabetic patients³¹.

In our study 120 (75%) of patients had xerostomia symptoms. Decreased salivation in diabetic patients may lead to dehydration which causes mucosal atrophy. Smears from atrophic mucosa usually have cells that are smaller in cell size, but have larger nuclei and give an impression of higher NA values as noticed in our study. Although our study showed that DM type 2 produces cellular changes in the gingival epithelium, these changes are not specific to DM. Cellular alterations are also present in patients with endocrine and respiratory diseases, associated with a decreased rate of keratinization which is the reason for the increase in the nuclear size. Patel et al.²⁸ attempted to define a baseline for pathological smears obtained from gingival tissue and suggested that inflammation is one of the factors that can increase NA and lead to a poorly preserved cytoplasm. Investigators noticed similar changes during keratinization alteration in smoking subjects^{34,35}. Our results confirm the important role of tobacco in the prevalence and severity of periodontal disease. The odds ratio of 9.98 for the association with smoking found in the current study agrees with the literature data²⁶.

Epidemiological studies have shown that DM is a risk factor for periodontal disease and

Epidemiološka istraživanja su pokazala da je DM rizik faktor za parodontopatiju i smatra se da će osobe sa DM tri puta verovatnije imati parodontopatiju u odnosu na zdrave osobe^{36,37}. Ako se sagleda pušenje cigareta kao faktor rizika, rizik za razvitak parodontopatije je 20 puta veći. Prema literaturnim podacima, dijabetesni bolesnici koji su pušači imaju dublje parodontalne džepove i veće vrednosti LOA u odnosu na nepušače^{38,39}. Pušenje negativno utiče na tok parodontopatije kod dijabetesnih bolesnika i povećava rizik za gubitak nivoa epitelnog pripoja⁴⁰.

Glikolizirani hemoglobin (HbA1c) se kontinuirano formira u eritrocitima kao produkt neenzimske reakcije između proteina hemoglobina, koji nosi molekule kiseonika i glukoze. Ova veza je visoko stabilna i hemoglobin ostaje u glikoliziranom stanju za vreme života eritrocita⁴¹. Određivanje nivoa HbA1c daje predstavu o nivou glukoze u krvi kroz duži vremenski period (1-3 meseca), pri čemu se više vrednosti glukoze u krvi pokazuju kao više vrednosti HbA1c⁴². Takođe, vrednosti HbA1c su u pozitivnoj vezi sa prisustvom dijabetesnih komplikacija. Preporučene ciljne vrednosti HbA1c kod dijabetesnih bolesnika su <7,0%. Postizanje ovog cilja je teško, i novija istraživanja su pokazala da samo 36% osoba sa DM tipa 2 postiže ciljnu vrednost HbA1c manju od 7,0%⁴³. U našem istraživanju kontrola glikemije je bila loša, ali nije pokazala povezanost sa parodontopatijom u regresionoj analizi. Slično, mnoga istraživanja nisu uspela da objasne jasnu vezu između metaboličke kontrole i težine parodontopatije. Ono što je istaknuto u literaturi je pozitivna veza između visokih vrednosti HbA1c i medicinskih komplikacija dijabetesa koje su znak lošeg zdravstvenog ponašanja i zainteresovanosti bolesnika.

Značajan rizik faktor parodontopatije kod dijabetesnih bolesnika su starost i trajanje dijabetesne bolesti. Ispitanici u ovom istraživanju bili su starosti 48,4 ($\pm 0,2$) godina u vreme postavljanja dijagnoze dijabetesa tipa 2, a bolest je trajala u proseku 23,6 ($\pm 0,39$) godina. Krajnji, regresioni model (tabela 3) je pokazao da su starost, pušačke navike, trajanje DM i prisutne dijabetesne komplikacije povezani sa uznapređovalom parodontopatijom. Klinički i epidemiološki dokazi prisutni u mnogobrojnim istraživanjima podržavaju koncept da parodontalna infekcija doprinosi dijabetesnim komplikacijama.

it is believed that people with type 2 DM are three times more likely to have periodontal disease compared to healthy controls^{36,37}. If smoking as a risk factor is considered, the risk for developing periodontal disease is 20 times higher. According to the literature, smoker-diabetic patients have deeper periodontal pockets and greater LOA compared to non-smokers^{38,39}. Smoking negatively influences the course of diabetic periodontal disease and increases the risk of attachment loss⁴⁰.

Glycohemoglobin is formed continuously in erythrocytes as a product of the non-enzymatic reaction between the hemoglobin protein, which carries oxygen molecules, and glucose. This link is highly stable and hemoglobin remains glycosylated for the life span of the erythrocyte⁴¹. Determination of HbA1c levels provides an estimate of the average blood glucose level over time (the preceding 1–3 months), with higher average blood glucose levels reflected in higher HbA1c values⁴². Also, HbA1c levels correlate well with the development of diabetic complications. The recommended HbA1c target value for people with diabetes is <7.0%. Achieving this goal is difficult, and recent population studies showed that only 36% of people with type 2 diabetes achieved a target HbA1c of <7.0%⁴³. In our investigation glycemic control was poor but not associated with periodontal disease in the final regression model. Similarly, many studies have failed to reveal any conclusive association between metabolic control and the severity of periodontal disease. They noticed positive correlation of high HbA1c values with medical complications of DM and may be possibly be viewed as poor health behavior.

Significant risk factors associated with periodontal disease in diabetic populations include both age and duration of the disease. The current population had a mean onset age of 48.4 (± 0.2) years and duration of disease of 23.6 (± 0.39) years. The final regression model (Table 3) showed age, smoking habits, duration of DM and diabetic complications to be related to advanced periodontal disease. The clinical and epidemiological evidence noted in numerous studies provides support for the concept that periodontal infection contributes to DM complications. On the other hand DM complications negatively influence

Sa druge strane, dijabetesne komplikacije negativno utiču na aktivnost i prognozu parodontalne bolesti^{15,16,26,36}. Ipak, neophodna su dalja rigorozna, kontrolisana istraživanja kako bi se čvrsto ustanovilo da li terapija parodontalne infekcije može uticati na smanjenje komplikacija dijabetesa.

Zaključak

Parodontopatija je česta i uznapredovala kod odraslih dijabetesnih bolesnika. Pušenje cigareta i starija životna dob su povezani sa većom učestalošću uznapredovale parodontopatije. Dijabetesni bolesnici koji su pušači imaju povećani rizik za loše parodontalno zdravlje i lošu prognozu parodontopatije, i moraju biti uključeni u redovne parodontološke kontrolne preglede i terapiju. Lečenje i prevencija uznapredovale parodontopatije kod dijabetesnih bolesnika mora obuhvatiti stroge preporuke za prekid pušenja, redovne stomatološke preglede i striktno održavanje oralne higijene.

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the activity and prognosis of periodontal disease^{15,16,26,36}. However, further rigorous, controlled trials are warranted to firmly establish that treating periodontal infections can be influential in the reduction of the burden of complications of diabetes mellitus.

Conclusion

Periodontal disease is common and advanced in adult diabetic population. Cigarette smoking and older age are associated with a higher prevalence of advanced periodontal disease. Smokerdiabetic patients are at high risk for poor periodontal health and prognosis, and they should be included in regular periodontal assessment and treatment. Management and prevention of advanced periodontal disease in diabetics should include strong recommendations to discontinue cigarette smoking, regular dental visits and oral hygiene.

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