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Povezanost između parodontne bolesti i prijevremenog porođaja i niske porođajne težine djeteta na Kosovu

The Association between Periodontal Disease and Preterm Low Birthweight in Kosovo

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Sažetak

Svrha: U svijetu je visoka prevalencija parodontne bolesti. Dosadašnji dokazi podupiru stajalište da su gingivitis i parodontitis potencijalno infektivne bolesti i izvori upale koji mogu ugroziti fetoplacentarnu jedinicu. Cilj ovog istraživanja bio je usporediti parodontni status žena s normalnom i niskom porođajnom težinom djeteta. **Ispitanici i metode:** U istraživanje je bilo uključeno 200 roditelja te su analizirani njihovi parodontni i opstetrijski parametri. Parodontno stanje procjenjivano je u krevetu prema prilagođenim kriterijima Machteia, a tjelesna težina i gestacijska dob prema kriterijima Svjetske zdravstvene organizacije. **Rezultati:** Žene s parodontitisom statistički su 3,2 puta u većoj opasnosti da će roditi dijete niske porođajne težine i 3,4 puta da će roditi prije termina negoli žene bez te bolesti. Naime, takve žene imale su dublje parodontne džepove ($2,49 \text{ mm} \pm 0,49 \text{ mm}$) od onih koje su rodile u terminu ($2,26 \text{ mm} \pm 0,49 \text{ mm}$). **Zaključak:** Parodontološke bolesti kod trudnih žena, zato što su žarište mikroorganizama i njihovih produkata, mogu se smatrati rizičnim čimbenikom kad je riječ o neželjenom ishodu trudnoće.

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Ključne riječi

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Uvod

Gestacija uobičajeno traje 40 tjedana. Prema definiciji Svjetske zdravstvene organizacije (SZO-a), porođaj prije 37. gestacijskog tjedna smatra se prijevremenim (PVP), a niska porođajna težina djeteta (NPT) jest ona manja od 2500 grama (1). Prijevremena porođajna težina (PVPT) najčešći je uzrok novorođenačkog mortaliteta i gotovo polovine teških dugoročnih neuroloških bolesti (2, 3). Takvi porođaji i medicinski troškovi za njihovo liječenje postali su financijski teret ne samo za pogođene obitelji, nego i za cjelokupno društvo (4).

Unatoč napretku u razumijevanju reproduktivne fiziologije, prevalencija PNPT-a nije se promijenila, nego se u nekim populacijskim skupinama čak povećala (5, 6).

Danas se zna da mnogobrojni čimbenici potiču PNPT, poput majčine dobi (manja od 17 godina i veća od 35 godina) (7), nizak socijalno-ekonomski status, alkohol, droga, afroamerička rasa, loša prenatalna skrb (8), pušenje, višestruka trudnoća, infekcija genitalno-urinarnog trakta, te sistemske bolesti majke (hipertenzija, eklampsija, preeklampsija, gestacijski dijabetes) (9). U 25 posto slučajeva, PNPT nije identificiran kao rizičan faktor (10).

Temeljni klinički parametri za mjerenje stupnja parodontne bolesti (PB) su klinička razina pričvrstka (KRP) i dubina

Introduction

The normal gestation period lasts forty weeks. According to the World Health Organization (WHO), the birth given before thirty-seventh week of gestation is defined as a preterm birth (PB) and low birthweight (LBW) represents a newborn weighing less than 2500 grams (1). Preterm low birth weight (PLBW) is the most frequent cause of infant mortality and nearly half of serious long-term neurological diseases (2, 3). These deliveries and medical expenses for their treatment have become an economic burden, not only for the affected family but also for the society as a whole (4). Despite the progress in the understanding of reproductive physiology, the prevalence of PLBW has not changed. In some population groups, the prevalence of PLBW has increased (5, 6).

Numerous studies have identified the following risk factors for PLBW: mother's age (under 17 and over 35 years) (7), low socioeconomic level, alcohol, drugs, African-American race, low prenatal care (8), smoking, multiple pregnancy, genitourinary tract infections, mother's systemic diseases (hypertension, eclampsia, preeclampsia, gestational diabetes) (9). However, those risk factors were not present in 25% of the cases with PLBW (10).

The basic clinical parameters for measuring the severity of periodontal disease (PD) are clinical attachment level

sondiranog džepa (DSD), ali i krvarenje desni te radiološka procjena koštane resorpcije. Današnji standardizirani protokol za mjerenje KRP-a i DSD-a ručnom sondom prvi je put opisan prije više od 50 godina i od tada se nije mijenjao.

Problemi s kojima su se suočili istraživači u vezi s pouzdanošću mjerenja parodontnom sondom primorali su ih na potragu za pouzdanijim markerima koji bi točnije označavali aktivnost parodontnih bolesti. Kronična i ciklička priroda PB-a povećava vjerojatnost od ponovljene hematogene diseminacije periopatogena i izravnog dotoka mikroorganizama u krvne žile i jetru, uključujući i fetalno-placentarnu jedinicu trudnica. Povišeni C-reaktivni protein biljeg je jetrene aktivacije akutnoga odgovora koji je povišen kod trudnica s rizikom od prijevremenog porođaja (12).

Istraživanja na modelima skotnih glodavaca pokazala su da izlaganja oralnim organizmima niskog stupnja mogu poremetiti fetalni rast. To je demonstrirano na životinjskom modelu kod kojega su se znanstvenici koristili potkožnim unošenjem *Porphyromonas gingivalis* (13,14), ali i na humanom modelu eksperimentalne parodontnih bolesti (15).

Offenbacher i suradnici (16) prvi su 1996. godine klinički pokazali da su parodontne bolesti statistički značajan rizični čimbenik kad je riječ o prijevremenoj porođajnoj težini, s omjerima vjerojatnosti (OV) od 7,9 za sve slučajeve prijevremene porođajne težine i 7,5 za slučajeve prijevremene porođajne težine kod prvorođkinja, a nakon prilagodbe za poznate rizične čimbenike.

Davenport i suradnici nisu našli dovoljno dokaza za povezivanje PB-a s PPNT-om. Nakon analize 236 slučajeva s PPNT-om i 507 kontrola žena koje su normalno rodile, rezultati su pokazali da se s povećanjem dubine parodontnih džepova smanjuje rizik od PPNT-a (OV = 0,83). Nakon što je prilagođen dobi, etničkoj skupini, pušenju i infekcijama, ovaj se rizik još više smanjio (OV = 0,78) (17, 18).

U metaanalizi više od 40 članaka (8 je bilo visokorelevantnih) o utjecaju PB-a na PPNT, zaključili su da bolest značajno povećava opasnost od prijevremenog porođaja i/ili niske porođajne težine te, unatoč važnosti promicanja oralnoga zdravlja, kod trudnica još nema jasnog dokaza da bi liječenje bolesnoga parodonta smanjilo rizik od prijevremenog porođaja (19).

Cilj ovog istraživanja bio je usporediti parodontne parametre majki koje su rodile prije vremena i/ili su djeca imala nisku porođajnu težinu, s majkama čija su djeca bila normalne porođajne težine i gestacije te istražiti povezanost između PB-a i PPNT-a.

(CAL) and pocket probing depth (PPD) together with gingival bleeding and radiological evaluation of osseous resorption. The standardized protocol which is used today for measuring both the clinical attachment level and pocket probing depth with the manual probe was described for the first time more than 50 years ago (11), and has not changed much since then.

Problems for researchers that have emerged from a low reliability of the measurements with the periodontal probe have prompted them to seek more reliable markers that, which would result in a more precise periodontal diagnosis and subsequent treatment planning. Chronic and cyclic nature of the PD increases the likelihood of repeated hematogenous dissemination of periopathogens and of direct microbial exposure of the blood vessels, liver, including a fetal-placental unit of pregnant women. An increased C-reactive protein is a marker of liver activation as the acute phase response, and this increase in pregnant women is associated with premature delivery (12).

Investigations in pregnant rodent models have demonstrated that even low-level exposure to oral microorganisms may result in fetal growth disorders. This is demonstrated in an animal model that used a subcutaneous injection of *Porphyromonas gingivalis* (13, 14), but also in a human model of experimental periodontal disease (15).

In 1996, Offenbacher et al. (16) were the first researchers to clinically demonstrate that PD is a statistically significant risk factor for PLBW, with the odds ratio (OR) of 7.9 for all PLBW cases, and 7.5 for primiparous PLBW cases, after adjustment for known risk factors.

Davenport et al. failed to find sufficient evidence to link PD with PLBW. After analyzing 236 cases with PLBW and 507 controls with normal delivery, the results showed that with increasing depth of periodontal pockets, the risk for PLBW reduced (OR = 0.83). After the age adjustments had been made, and also, adjustments related to ethnicity, smoking, and infections, this risk was even more reduced (OR = 0.78) (17, 18).

In a meta-analysis of over forty articles (of which eight are highly relevant) on the impact of the PD on PLBW, it has been concluded that the disease significantly increases the risk of PB and/or LBW, and that despite the importance of promoting the oral health in pregnant women, there is still no strong evidence that treatment of diseased periodontium would reduce the risk of PB (19).

The objective of this study was to compare periodontal parameters of mothers who had a preterm delivery and/or a low-birth-weight infant with those who had a normal delivery and a normal birth weight infant and gestation and, subsequently, to investigate the relationship between PD and PLBW.

Materijali i metode

Korišteni su podaci dobiveni tijekom parodontnih pregleda i iz trudničkih kartona 200 roditelja, bez obzira na njihovu dob, koje su rodile u Sveučilišnom kliničkom centru Kosovo u Klinici za opstetriciju i ginekologiju.

Material and Methods

Data from periodontal examination and obstetric records of 200 nursing mothers, regardless of their age, who gave birth at the University Clinical Center of Kosovo's Obstetrics and Gynecology Clinic, were used. The approval of the

Prije početka istraživanja dobiveno je odobrenje Etičkoga povjerenstva Medicinskog fakulteta u Prištini. Ispitanice su nasumce odabrane i, nakon što su potpisale informirani pristanak, bile su podvrgnute parodontnom pregledu i uzeti su im opstetrijski podatci.

Parodontni pregled obavljen je u krevetu pod prirodnim svjetlom i to stomatološkim zrcalom i parodontnom sondom oznaka 1-2-3-5-7-8-9-10 (3N Nabers P3N probe; Hu-Friedy Manufacturing, Inc., Chicago, Illinois, SAD). Parodontološki podatci uključivali su zubni plak (Sillness-Löe) (20) i gingivalni indeks (Löe-Sillness) (21), a procjenjivani su na četirima zubnim površinama – bukalnoj, lingvalnoj, mezijalnoj i distalnoj; krvarenje nakon sondiranja (u postotcima) procjenjivalo se na sličnim mjestima kao i zubni plak i gingivni indeks koji je bio pozitivan ako se krvarenje pojavilo tijekom 15 sekunda nakon sondiranja; PPD, CAL i gingivna recesija (GR) (sve u milimetrima) procjenjivani su na šest pozicija zubnih površina – mezioingvalnoj, središnjoj lingvalnoj, distolingvalnoj, meziobukalnoj, središnjoj bukalnoj i distobukalnoj. PD je označavao udaljenost od gingivnoga ruba do baze džepa; GR je bio udaljenost između cementno-caklinskoga spoja i gingivnoga ruba; CAL je izračunat iz dubine sondiranja i gingivne recesije i označavao je udaljenost između cementno-caklinskoga spoja i baze džepa. Treći kutnjaci i zubi indicirani za vađenje bili su isključeni iz procjene.

Opstetrijski podatci sastojali su se od dvaju dijelova – demografskih i onih o porođaju, djetetovoj porođajnoj težini i gestacijskoj dobi. Prvi dio dobiven je iz trudničkih kartona nakon parodontnog pregleda, a za drugi dio upotrijebljeni su kartoni novorođenčadi. Isključni kriterij bili su višestruki porođaji (blizanci, trojci), majčina sistemska bolest (hipertenzija, dijabetes itd.) i infekcije genitourinarnog trakta.

Za određivanje parodontitisa korišten je modificirani kriterij prema Machteiu (22). U skupini s parodontitisom bile su žene s parodontnim džepovima od 5 milimetara i dubljima na jednom ili više pozitivnih mjesta te s krvarenjem i kliničkim pričvrstkom od 6 milimetara ili više njih na dva ili više mjernih mjesta. Ispitanice koje nisu zadovoljile ove kriterije bile su svrstane u skupinu bez parodontitisa.

Parodontne parametre bilježio je naslijepo jedan parodontolog (KM), kao kontrolu statusa ispitanica. Unutarispitivna pouzdanost određena je kappa koeficijentom za mjerenja unutar ± 1 milimetar i iznosila je od 0,80 do 0,90.

Prema kriterijima SZO-a (1), rodilje koje su rodile prije 37. tjedna gestacije i djeca s težinom manjom od 2500 grama uvrštena su u skupinu prijevremenog porođaja (PVP) i niske porođajne težine (NPT), a žene koje su rodile nakon 37. tjedna gestacije i djeca s 2500 grama težine uvrštena u kontrolnu skupinu normalnog porođaja.

Statistička analiza provedena je korištenjem indeksa strukture, aritmetičke sredine i standardne devijacije. Za određivanje razlike između aritmetičkih prosjeka korišten je t-test, a za razliku neparametričkih podataka test χ^2 (Hi-kvadrat).

University of Pristina Medical School Ethics Committee was obtained prior to the commencement of the study. Subjects were randomly selected, and after they had given an oral informed consent, they initially underwent a periodontal examination. Subsequently, their obstetric records were taken.

In addition, the periodontal examination was performed under natural light, using dental mirror and periodontal probe with 1-2-3-5-7-8-9-10 increments (3N Nabers P3N probe; Hu-Friedy Manufacturing, Inc., Chicago, Illinois). Periodontal data included: dental plaque (by Sillness-Löe) (20) and gingival index (by Löe-Sillness) (21) was assessed in the following four tooth surfaces: buccal, lingual, mesial and distal; bleeding on probing (in percentage) was assessed in similar sites as dental plaque and gingival index, which was positive if hemorrhage occurred within 15 seconds after probing; PPD, CAL and gingival recession (GR) (all in millimeters) were assessed on the following six tooth surfaces: mesioingual, mid-lingual, distolingual, mesiobuccal, mid-buccal and distobuccal. PPD represented the distance from the gingival margin to the base of the pocket; GR represented the distance from the cemento-enamel junction to the gingival margin; CAL was calculated from probing depth and gingival recession, representing the distance from the cement-enamel junction to the base of the pocket. The third molars and teeth indicated for extraction were excluded from the evaluation.

Obstetric data were composed of two parts: demographic and actual birth - date of delivery, weight at birth and gestation age. Data from the first part were obtained from the subjects' obstetric records after the periodontal examination, and from the second part they were obtained from the newborn's history. Obstetric exclusion criteria were: multiple births (twins, triplets), maternal systemic disease (hypertension, diabetes, etc.), and genitourinary tract infections.

The modified Machtei's criteria were used for determining whether the subjects had periodontitis or not (22). The periodontitis group included subjects with periodontal pocket depth 5 mm or more in one or more bleeding-positive sites and with clinical attachment level amounting to 6 mm or more in two or more sites. The subjects who did not meet the abovementioned criteria formed the group without periodontitis.

Periodontal parameters were recorded by one blinded periodontist (KM) to case-control status of the subjects. The intra-examiner reliability weighted with kappa coefficients for measurements within ± 1 mm ranged from 0.80 to 0.90.

Based on the WHO criteria (1), nursing mothers who gave birth before the 37th week of gestation and infants weighing less than 2500 grams formed case groups with PB and LBW, while others who gave birth after the 37th week of gestation and infants weighing more than 2500 grams formed the control group with normal deliveries.

A statistical analysis was performed using the index of structure, arithmetic mean, and standard deviation. The Student's t-test was used to determine the difference between the arithmetic averages, and the chi square test (χ^2) was used to determine the differences between non-parametric data.

Rezultati

Podatci iz ovog istraživanja analizirani su na temelju razlikovanja subjekata prema njihovoj dobi, a od dvije stotine roditelja trinaest (6,5 %) je bilo starije od 35 godina. Srednja vrijednost dobi svih ispitanica bila je 26,9, a nakon isključivanja starijih od 35 godina, prosjek je pao na 26.

Rezultati su prikazani za trajanje gestacije i porođajnih težina djeteta te *en bloc*.

Kad se usporedilo parodontne parametre svih ispitanica s normalnom gestacijom, u odnosu na PVP, PPD i CAL, bili su znatno viši kod onih s prijevremenim porođajem ($p = 0,009$ i $p = 0,037$). Nakon uključivanja sudionica starijih od 35 godina, GR je bio dodatno viši kod PVP ispitanica (tablica 1.).

Results

The data of this study were analyzed in the sense of differentiating the subjects by their age. Out of two-hundred parturients, thirteen (6.5%) were aged 35 years or older. The mean age of all subjects was 26.9. After the women older than 35 had been excluded, the average dropped to 26.

The results are presented for the duration of gestation and birth weight separately and *en bloc*.

When comparing periodontal parameters of all subjects with normal gestation vs. PB, PPD and CAL were significantly higher in preterm birth subjects ($p=0.009$ and $p=0.037$, respectively). After the subjects who were aged 35 years or older had been excluded, GR was additionally higher in PB subjects (Table 1).

Tablica 1. Uspoređeni parodontni parametri svih ispitanica u dobi od 17 do 35 godina koje su prijevremeno i normalno rodile
Table 1 Periodontal parameters compared between all subjects and subjects aged 17-35 in normal and preterm birth.

Parodontna obilježja • Periodontal parameters	Sve • All (n=200)			Dob • Age 17-35 (n=187)		
	Normalna gestacija > 37 tj. • Normal gestation >37w (n=160)	Prijevremeni porođaj < 37 tj. • Preterm birth <37w (n=40)	P	Normalna gestacija > 37 tj. • Normal gestation >37w (n=152)	Prijevremeni porođaj < 37 tj. • Preterm birth <37w (n=35)	P
Indeks zubnog plaka (ar. sredina ± SD) • Dental plaque index (mean ± SD)	2.26 ± 0.58	2.44 ± 0.55	0.083	2.25 ± 0.59	2.45 ± 0.53	0.08
Gingivni indeks (ar. sredina ± SD) • Gingival index (mean ± SD)	1.71 ± 0.27	1.78 ± 0.16	0.096	1.70 ± 0.27	1.77 ± 0.16	0.14
Krvarenje poslije sondiranja (% ± SD) • Bleeding on probing (% ± SD)	71.30 ± 23.00	76.50 ± 19.30	0.19	70.83 ± 23.11	75.11 ± 19.54	0.31
Dubina parodontnog džepa (ar. sredina ± SD) • Periodontal pocket depth (mean ± SD)	2.26 ± 0.49	2.49 ± 0.49	0.009*	2.24 ± 0.47	2.47 ± 0.50	0.0098*
Klinička razina pričvrstka (ar. sredina ± SD) • Clinical attachment level (mean ± SD)	2.32 ± 0.63	2.55 ± 0.53	0.037*	2.26 ± 0.48	2.52 ± 0.54	0.0046*
Gingivna recesija (ar. sredina ± SD) • Gingival recession (mean ± SD)	0.07 ± 0.27	0.07 ± 0.09	0.97	0.03 ± 0.07	0.07 ± 0.09	0.0134*

* značajna razlika • significant difference

Tablica 2. Parodontna obilježja uspoređena između svih roditelja i roditelja od 17 do 35 godina s normalnim i prijevremenim porođajem djeteta niske porodajne težine
Table 2 Periodontal parameters compared between all subjects and subjects aged 17-35 in normal and low birth-weight.

Parodontna obilježja • Periodontal parameters	Svi • All (n=200)			Starost • Age 17-35 (n=187)		
	Normalna porodajna težina > 2500 gr • Normal birth-weight >2500gr (n=159)	Niska porodajna težina < 2500 gr • Low birth-weight <2500gr (n=41)	P	Normalna porodajna težina > 2500 gr • Normal birth-weight >2500gr (n=151)	Niska porodajna težina < 2500 gr • Low birth-weight <2500gr (n=36)	P
Indeks zubnog plaka (ar. sredina ± SD) • Dental plaque index (mean ± SD)	2.25 ± 0.58	2.48 ± 0.54	0.03*	2.24 ± 0.59	2.48 ± 0.52	0.027*
Gingivni indeks (ar. sredina ± SD) • Gingival index (mean ± SD)	1.70 ± 0.27	1.79 ± 0.17	0.063	1.70 ± 0.27	1.78 ± 0.17	0.095
Krvarenje nakon sondiranja (% ± SD) • Bleeding on probing (% ± SD)	71.00 ± 22.80	77.30 ± 20.10	0.11	70.57 ± 22.90	76.08 ± 20.42	0.187
Dubina parodontnog džepa (ar. sredina ± SD) • Periodontal pocket depth (mean ± SD)	2.27 ± 0.50	2.46 ± 0.47	0.028*	2.24 ± 0.47	2.43 ± 0.48	0.032*
Razina klin.pričvrstka (ar. sredina ± SD) • Clinical attachment level (mean ± SD)	2.33 ± 0.65	2.51 ± 0.50	0.1	2.27 ± 0.49	2.47 ± 0.49	0.025*
Gingivna recesija (ar. sredina ± SD) • Gingival recession (mean ± SD)	0.07 ± 0.27	0.06 ± 0.07	0.85	0.04 ± 0.08	0.06 ± 0.07	0.093

* značajna razlika • significant difference

Ispitanice koje su rodile djecu niske porođajne težine imale su značajno viši indeks zubnog plaka ($p = 0,03$) i dublje parodontne džepove ($p = 0,028$). Nakon prilagodbe za dob veću od 35 godina, osim indeksa zubnog plaka ($p = 0,027$) i PPD-a ($p = 0,032$), i CAL je bio značajno viši ($p = 0,025$) (tablica 2.).

Usporedba porođajne težine djece žena s parodontnom bolešću i onih bez nje, pokazala je da je srednja vrijednost PT-a novorođenčadi znatno niža u skupini s parodontnom bolešću negoli u onoj zdravih ispitanica ($p = 0,0003$). Nakon isključivanja 13 ispitanica starijih od 35 godina, ova razlika postala je još veća ($p = 0,0002$), što upućuje na to da, u ovom istraživanju, na srednju vrijednost porođajne težine djece ne utječe majčina dob (tablica 3.).

Uspoređivana je i duljina gestacije u skupini zdravih žena i u onoj s parodontitisom. Gestacijsko razdoblje za skupinu s parodontitisom bilo je značajno kraće u usporedbi sa skupinom bez parodontitisa ($p < 0,0001$). Značajnost kraće gestacije u skupini s parodontitisom nije se promijenila čak ni nakon prilagodbe prema dobi roditelja starijih od 35 godina ($p = 0,0001$) (tablica 4.).

The subjects who gave birth to low-weighted babies had significantly higher dental plaque index ($p=0.03$) as well as deeper periodontal pockets ($p=0.028$). After adjustment for age older than 35, apart from the dental plaque index and PPD ($p=0.027$ and $p=0.032$, respectively), the CAL was also significantly higher ($p=0.025$) (Table 2).

The comparison of the birth-weight of women with PD and those without PD has shown that mean weight of the newborn is significantly lower in PD group than in healthy subjects ($p=0.0003$). After excluding thirteen subjects older than 35 years, this difference became more significant ($p=0.0002$), which indicates that, in this study, the mean birth-weight was not influenced by mothers' age (Table 3).

Also, the duration of gestation was compared for healthy vs. periodontitis groups. The gestation period of the periodontitis group was significantly shorter compared to the non-periodontitis group ($p<0.0001$). The significance of shorter gestation in periodontitis group did not change even after the age adjustment for parturients older than 35 years old ($p=0.0001$) had been made (Table 4).

Tablica 3. Prosječne vrijednosti porođajnih težina djece kod zdravih roditelja i roditelja s parodontitisom
Table 3 Mean birth weight of healthy and periodontitis subjects.

Prosječna porođajna težina • Mean birth weight (gr ± SD)	Zdrave • Healthy	S parodontitisom • Periodontitis	p
Sve ispitanice • All subjects (n=200)	3208 ± 682.3	2751.4 ± 1008.5	0.0003
Ispitanice starije od 35 godina • Subjects older than 35 (n=13)	2661.7 ± 962.0	2728.6 ± 1380.2	0.92
Ispitanice od 17 do 35 godina • Subjects 17-35 years old (n=187)	3232.2 ± 662.0	2754.6 ± 963.9	0.0002

Tablica 4. Prosjek gestacije kod zdravih roditelja i roditelja s parodontitisom
Table 4 Mean gestation of healthy and periodontitis subjects.

Prosječna gestacija (tjedni ± SD) • Mean gestation (weeks ± SD)	Zdrave • Healthy	S parodontitisom • Periodontitis	p
Sve ispitanice • All subjects (n=200)	38.6 ± 2.7	36.4 ± 4.8	<0.0001
Ispitanice starije od 35 godina • Subjects older than 35 (n=13)	37.3 ± 3.01	36.0 ± 5.20	0.59
Ispitanice od 17 do 35 godina • Subjects 17-35 years old (n=187)	38.6 ± 2.68	36.5 ± 4.77	0.0001

Tablica 5. Korelacija i omjeri vjerojatnosti za nisku porođajnu težinu djece kod zdravih roditelja i roditelja s parodontitisom
Table 5 Correlation and the odds ratio of low birth-weight in healthy and periodontitis groups.

Porođajna težina • Birth weight (g)	Zdrave • Healthy	S parodontitisom • Periodontitis	χ^2	OR (95 % CI) - omjer vjerojatnosti
<2500	19	17	9.55 $p<0.01$	3.2 (1.5 – 6.8)
>2500	118	33		
Ukupno • Total	137	50		

Tablica 6. Korelacija i omjeri vjerojatnosti za prijevremeni porođaj kod zdravih roditelja i roditelja s parodontitisom
Table 6 Correlation and the odds ratio of preterm birth in healthy and periodontitis groups.

Gestacija • Gestation	Zdrave • Healthy	S parodontitisom • Periodontitis	χ^2	OR (95 % CI) - omjer vjerojatnosti
< 37 tjedana • <37 weeks	18	17	10.48 $p<0.01$	3.4 (1.6 – 7.3)
> 37 tjedana • >37 weeks	119	33		
Ukupno • Total	137	50		

Nakon prilagodbe prema dobi majki, Hi-kvadrat test za porođajnu težinu i parodontitis pokazao je značajnu korelaciju (Hi-kvadrat 9,55, $p < 0,01$), dok su godinama prilagođene vjerojatnosti za ispitanice s parodontnim bolestima da rode novorođenčad niske porođajne težine bile 3,2 puta više negoli za one bez te bolesti (tablica 5.).

Osim toga, prijevremeni porodaj i parodontitis pokazali su značajnu korelaciju kad su se procjenjivali Hi-kvadrat testom (10,48, $p < 0,01$). Vjerojatnost za žene s PB-om da rode prije 37. tjedna gestacije bila je tri puta veća negoli kod žena bez PB-a (tablica 6.).

Rasprava

Istraživanja posljednjih godina upućuju na to da infekcije parodontnih tkiva mogu pridonijeti morbiditetu i mortalitetu pojedinaca s pojedinim sistemskim stanjima, poput arterioskleroze, infarkta miokarda, moždanog udara i prijevremenog porođaja. Jeffcoat i suradnici (23) ustanovili su da su žene s generaliziranim parodontitisom četiri do sedam puta ugroženije od prijevremenog porođaja negoli zdrave. Naše istraživanje, u kojem je sudjelovalo manje ispitanica, pokazalo je da žene s parodontnom bolešću 3,2 puta češće rađaju djecu s niskom porođajnom težinom i 3,4 puta vjerojatno će prijevremeno roditi negoli žene bez PB-a. Naše istraživanje uključivalo je ispitanice bijele rase, pa zbog demografskih ograničenja nismo mogli odrediti razlike ovisne o rasi. U istraživanju u kojem je sudjelovalo 327 Brazilki niskoga trudničkoga rizika s PB-om ili bez njega, zaključeno je da je PB rizičan čimbenik za PPNT i prijevremeno pucanje membrane (24).

U istraživanju Dasanayake (25) i Dempseyja i suradnika (26), majke s PPNT-om imale su značajno više krvarećih sekstanata negoli one u kontrolnim skupinama. No, suprotno tomu, istraživanja Offenbachera i suradnika (16) te Mitchell-Lewisa i njegovih kolega (27) nisu dokazala povezanost između indeksa krvarenja i PPNT-a, a to je nalaz sličan kao u ovom istraživanju.

Istaknuto je da PB možda nije uzrok PVP-a, ali možda dijeli zajednički etiološki mehanizam, poput genske predispozicije za hiperimunosti odgovor (28).

Različite povezanosti između parodontnog statusa i PVP-a, niske porođajne težine, ili prijevremenog porođaja povezanog s niskom porođajnom težinom, opisane su u presječnim istraživanjima (29 – 36) te u istraživanjima kontroliranih slučajeva (37, 38). Ipak, u drugim istraživanjima (36, 39 – 41) i istraživanjima kontroliranih slučajeva nije pronađena značajna povezanost.

U našem istraživanju pronađena je značajna povezanost između parodontitisa i niske porođajne težine ($\chi^2 = 9,55$), te korelacija između parodontitisa i prijevremenog porođaja ($\chi^2 = 10,48$). Prilagođena vjerojatnost za žene s parodontitisom da imaju potomstvo niske porođajne težine veća je 3,2 puta negoli kod žena bez parodontitisa. Iste prilagođene vrijednosti za žene s parodontitisom da prijevremeno rode bile su 3,4 puta više negoli za žene bez te bolesti.

Premda su u istraživanje bile uključene roditelje bez obzira na dob, pronađeno je da žene s parodontitisom imaju nižu srednju vrijednost porođajne težine djece i nižu srednju vri-

After the adjustment for the mothers' age, the Chi-square test for birth-weight and PD resulted in significant correlation (Chi-square 9.55, $p < 0.01$), while the age-adjusted odds for subjects with PD to give birth to low-weighted babies were 3.2 fold higher than for non-PD subjects (Table 5).

Also, PB and periodontitis showed highly significant correlation when assessed with the Chi-square test (10.48, $p < 0.01$). The odds for women with PD to have a child born before the 37th week of gestation were more than 3 times higher than for women without PD (Table 6).

Discussion

Some recent studies indicate that infections of periodontal tissues may contribute to morbidity and mortality of individuals with some systemic diseases such as atherosclerosis, myocardial infarction, stroke and premature delivery. Jeffcoat et al. (23) found that women with generalized periodontitis are at risk of preterm delivery 4 to 7 times more frequently than healthy subjects. Our study, although with fewer subjects, showed that women with PD were at risk 3.2 times more frequently for delivering a low birth-weighted offspring and were at risk 3.4 times more frequently for delivering prematurely than women without PD. Our population consisted of subjects of Caucasian race, and due to demographic limitations, we could not find any differences based on the race of the subjects.

In a cohort study of 327 Brazilian low-risk pregnant women with or without PD, it was concluded that it was a risk factor for PLBW and premature rupture of membranes (24).

In the studies of Dasanayake (25) and Dempsey et al. (26), mothers with PLBW had significantly more bleeding sextants than controls. In contrast, finding from previous research by Offenbacher et al. (16) and Mitchell-Lewis et al. (27) did not show an association between the bleeding index and PLBW, which is a finding similar to that of the present study.

It has been pointed out that PD may not be the cause of PB, but may share a combined etiologic mechanism, such as a genetic predisposition for a hyper-inflammatory response (28).

Different associations between periodontal status and preterm birth alone (PB), low birth weight (LBW), or preterm birth associated to low birth weight (PLBW) have been shown in cross-sectional studies (29-36), as well as in case-control studies (37, 38). However, other cohort studies (36, 39-41), as well as case-control studies (17, 42-45), did not find a significant association.

Our investigation has found a significant correlation between periodontitis and low birth-weight ($\chi^2=9.55$), as well as between periodontitis and preterm birth ($\chi^2=10.48$). The adjusted odds for women with periodontitis to have low-weighted offspring were 3.2 times higher than for women without periodontitis. Also, the same adjusted odds for women with periodontitis to give birth prematurely were 3.4 times higher than for women without periodontitis.

jednost trajanja gestacije, negoli one bez parodontitisa, čak i nakon isključivanja starijih od 35 godina.

Zaključak

U prikupljenim podacima kojima se želio otkriti odnos između parodontnih bolesti i niske porođajne težine djece, naše istraživanje sugerira da je kod žena s parodontitisom vjerojatniji prijevremeni porođaj. Osim ograničenja ovog istraživanja, možda je i definicija parodontne bolesti utjecala na kvalitetu dokaza. Vremensko određivanje neposrednog utjecaja parodontne bolesti na tijek trudnoće moglo bi poboljšati metodologiju budućih istraživanja.

Sukob interesa

Autori nisu bili u sukobu interesa.

Although this study included parturients regardless of their age, it was found that women with periodontitis had mean birth weight and mean gestation significantly lower than women without periodontitis, even after excluding women older than 35 years.

Conclusion

In the pool of data that try to detect the relationship between periodontal disease and preterm low birth weight, our study suggests that women are likely to give birth prematurely if they have periodontal disease. Within the limitations of this investigation, a definition of periodontal disease might have affected the quality of evidence. The timing of possible direct influence of periodontal disease on the course of pregnancy may improve the methodology of future investigations.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this article.

Abstract

Objective: Periodontal diseases have a high prevalence worldwide. Existing evidence support the concept that gingivitis and periodontitis are potentially infectious and they present inflammatory reservoirs that can be threatening to the fetoplacental unit. The objective of this study was to compare the periodontal status between women with normal delivery and those with preterm low-birthweight delivery. **Materials and Methods:** This study included 200 postpartum women whose periodontal and obstetrical parameters were taken. The periodontal condition was assessed bedside according to the modified criteria established by Machtei, while the birthweight and gestational age were assessed according to the World Health Organization criteria. **Results:** Women with periodontitis are statistically at 3.2 times higher risk to deliver a child with low weight, and at 3.4 times higher risk to deliver preterm, compared to women without periodontitis. The women with preterm low-birthweight babies had deeper periodontal pockets ($2.49\text{mm} \pm 0.49\text{mm}$) than women with normal delivery ($2.26\text{mm} \pm 0.49\text{mm}$). **Conclusions:** Periodontal disease in pregnant women with a reservoir of organisms and their products can be considered a risk factor for adverse pregnancy outcome.

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Key words

Periodontitis; Gingivitis; Pregnant Women; Premature Birth; Infant, low birth weight, risk factor

References

- World Health Organization. The incidence of low birth weight - an update. *Weekly Epidemiology Records*. 1984; 59(27):205–11.
- McCormick MC. The contribution of low birth weight to infant mortality and childhood morbidity. *N Engl J Med*. 1985 Jan 10;312(2):82-90.
- McParland P, Jones G, Taylor D. Preterm labour and prematurity. *Curr Obstet Gynaecol*. 2004; 14(5):309–19.
- Mozurkewich EL, Naglie G, Krahn MD, Hayashi RH. Predicting preterm birth: A cost-effectiveness analysis. *Am J Obstet Gynecol*. 2000 Jun;182(6):1589-98.
- Office for National Statistics. Mortality statistics. Childhood, infant and perinatal. Review of the National Statistician on deaths in England and Wales, Series DH3: No. 40; 2007.
- National Center for Health Statistics. Report of final natality statistics. Washington, DC, MVSr Vol. 45, No. 11 (S); 1995.
- de Sanjose S, Roman E. Low birth weight, preterm and small for gestational age babies in Scotland, 1981-1984. *J Epidemiol Community Health*. 1991 Sep;45(3):207-10.
- Committee to Study the Prevention of Low Birth weight, Division of Health Promotion and Disease Prevention, Institute of Medicine. Preventing Low Birth weight. Washington, DC: National Academy Press, 1985.
- Cohen W, Rose LF, Minsk L. The periodontal-medical risk relationship. *Compend Contin Educ Dent*. 2001;22(2 Spec No):7-11.
- Gibbs RS, Romero R, Hillier SL, Eschenbach DA, Sweet RL. A review of premature birth and sub clinical infections. *Am J Obstet Gynecol*. 1992 May;166(5):1515-28.
- Ramfjord SP. Indices for prevalence and incidence of periodontal disease. *J Periodontol*. 1959; 30(1):51–9.
- Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med*. 2000 May 18;342(20):1500-7.
- Lin D, Smith MA, Champagne C, Elter J, Beck J, Offenbacher S. Porphyromonas gingivalis infection during pregnancy increases maternal tumor necrosis factor alpha, suppresses maternal interleukin-10, and enhances fetal growth restriction and resorption in mice. *Infect Immun*. 2003 Sep;71(9):5156-62.
- Lin D, Smith MA, Elter J, Champagne C, Downey CL, Beck J, et al. Porphyromonas gingivalis infection in pregnant mice is associated with placental dissemination, an increase in the placental Th1/Th2 cytokine ratio, and fetal growth restriction. *Infect Immun*. 2003 Sep;71(9):5163-8.
- Loesche WJ. Association of the oral flora with important medical diseases. *Curr Opin Periodontol*. 1997;4:21-8.
- Offenbacher S, Katz V, Fertik G, Collins J, Boyd D, Maynor G, et al. Periodontal infection as a possible risk factor for preterm low birth weight. *J Periodontol*. 1996 Oct;67(10 Suppl):1103-13.
- Davenport ES, Williams CE, Sterne JA, Murad S, Sivapathasundram V, Curtis MA. Maternal periodontal disease and preterm low birth weight: Case-control study. *J Dent Res*. 2002 May;81(5):313-8.
- Davenport ES, Williams CE, Sterne JA, Sivapathasundram V, Fearne JM, Curtis MA. The East London study of maternal chronic periodontal disease and preterm low birth weight infants: study design and prevalence data. *Ann Periodontol*. 1998 Jul;3(1):213-21.

19. Khader YS, Ta'ani Q. Periodontal diseases and the risk of preterm birth and low birth weight: A meta-analysis. *J Periodontol.* 2005 Feb;76(2):161-5.
20. Silness J, Løe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *J Periodontol.* 2005 Feb;76(2):161-5.
21. Løe H, Silness J. Periodontal disease in pregnancy I. Prevalence and severity. *Acta Odontol Scand.* 1963 Dec;21:533-51.
22. Machtei EE, Christersson LA, Grossi SG, Dunford R, Zambon JJ, Genco RJ. Clinical criteria for the definition of established periodontitis. *J Periodontol.* 1992 Mar;63(3):206-14.
23. Jeffcoat MK, Hauth JC, Geurs NC, Reddy MS, Cliver SP, Hodgkins PM, et al. Periodontal disease and preterm birth: results of a pilot intervention study. *J Periodontol.* 2003 Aug;74(8):1214-8.
24. Vogt M, Sallum A, Cecatti JG, Morais SS. Periodontal disease and some adverse perinatal outcomes in a cohort of low risk pregnant women. *Reprod Health.* 2010 Nov 3;7:29
25. Dasanayake A. Poor periodontal health of the pregnant woman as a risk factor for low birth weight. *Ann Periodontol.* 1998 Jul;3(1):206-12.
26. Dempsey R, Bissada N, Ashmead G, Clapp J, Amini S. Is periodontitis a risk factor for preterm labour and/or low birth weight? *J Dent Res.* 2000(1s); 79:400.
27. Mitchell-Lewis DA, Papapanou PN, Engebretson S, Grbic J, Herrera Abreu M, Celenti R. Periodontal intervention decreases the risk of preterm low birth weight. *J Dent Res.* 2000(1s); 79:607.
28. Vergnes J-N, Sixou M. Preterm low birth weight and maternal periodontal status: A meta-analysis. *Am J Obstet Gynecol.* 2007; 196(2):135.e1-e7.
29. Lunardelli N, Peres MA. Is there an association between periodontal disease, prematurity and low birth weight? A population-based study. *J Clin Periodontol.* 2005 Sep;32(9):938-46.
30. Offenbacher S, Lief S, Boggess KA, Murtha AP, Madianos PN, Champagne CM, et al. Maternal periodontitis and prematurity. Part I: obstetric outcome of prematurity and growth restriction. *Ann Periodontol.* 2001 Dec;6(1):164-74.
31. López NJ, Smith PC, Gutierrez J. Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: A randomized controlled trial. *J Periodontol.* 2002 Aug;73(8):911-24.
32. Siqueira FM, Cota LOM, Costa JE, Haddad JPA, Lana ÂMQ, Costa FO. Intrauterine growth restriction, low birth weight, and preterm birth: adverse pregnancy outcomes and their association with maternal periodontitis. *J Periodontol.* 2007 Dec;78(12):2266-76.
33. Rajapakse PS, Nagarathne M, Chandrasekara KB, Dasanayake AP. Periodontal disease and prematurity among non-smoking Sri Lankan women. *J Dent Res.* 2005 Mar;84(3):274-7.
34. Toygar HU, Seydaoglu G, Kurklu S, Guzeldemir E, Arpak N. Periodontal health and adverse pregnancy outcome in 3,576 Turkish women. *J Periodontol.* 2007 Nov;78(11):2081-94.
35. Agueda A, Ramón JM, Manau C, Guerrero A, Echeverría JJ. Periodontal disease as a risk factor for adverse pregnancy outcomes: a prospective cohort study. *J Clin Periodontol.* 2008 Jan;35(1):16-22.
36. Heimonen A, Janket SJ, Kaaja R, Ackerson LK, Muthukrishnan P, Meurman JH. Oral inflammatory burden and preterm birth. *J Periodontol.* 2009; 80(6):884-91.
37. Gomes-Filho IS, Cruz SS, Rezende EJC, Dos Santos CAST, Sole-dade KR, Magalhães MA, et al. Exposure measurement in the association between periodontal disease and prematurity/low birth weight. *J Clin Periodontol.* 2007 Nov;34(11):957-63.
38. Khader Y, Al-shishani L, Obeidat B, Khassawneh M, Burgan S, Amarin ZO, et al. Maternal periodontal status and preterm low birth weight delivery: a case-control study. *Arch Gynecol Obstet.* 2009 Feb;279(2):165-9.
39. Moore S, Ide M, Coward PY, Randhawa M, Borkowska, E, Baylis R, et al. A prospective study to investigate the relationship between periodontal disease and adverse pregnancy outcome. *Br Dent J.* 2004 Sep 11;197(5):251-8; discussion 24
40. Noack B, Klingenberg J, Weigelt J, Hoffmann T. Periodontal status and preterm low birth weight: a case control study. *J Periodontol Res.* 2005 Aug;40(4):339-45.
41. Nabet C, Lelong N, Colombier ML, Sixou M, Musset AM, Goffinet F, et al. Maternal periodontitis and the causes of preterm birth: the case-control Epipap study. *J Clin Periodontol.* 2010 Jan;37(1):37-45.
42. Bassani G, Olinto MTA, Kreiger N. Periodontal disease and perinatal outcomes: a case-control study. *J Clin Periodontol.* 2007 Jan;34(1):31-9.
43. Vettore MV, Leal MC, Leão AT, da Silva AMM, Lamarca GA, Sheiham A. The relationship between periodontitis and preterm low birthweight. *J Dent Res.* 2008 Jan;87(1):73-8.
44. Xiong X, Buekens P, Fraser WD, Beck J, Offenbacher S. Periodontal disease and adverse pregnancy outcomes: a systematic review. *BJOG.* 2006 Feb;113(2):135-43.
45. Manau C, Echeverría A, Agueda A, Guerrero A, Echeverría JJ. Periodontal disease definition may determine the association between periodontitis and pregnancy outcomes. *J Clin Periodontol.* 2008 May;35(5):385-97.