Is Periodontal Disease a Risk Factor for Preterm Low Birth Weight Infants? A Systematic Review.

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Is Periodontal Disease a Risk Factor for Preterm Low Birth Weight Infants? A Systematic Review.

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Summary Introduction

Over the last 20 years, a body of knowledge has accumulated relating periodontal disease (PDD) with a number of systemic conditions, including diabetes, coronary heart disease and stroke.[1] Among these relationships is the association between PDD and the incidence of preterm low birth weight (P/LBW) infants.[2] Starting with Offenbacher et al,[3] this area has attracted researchers hoping to establish PDD as a risk *marker* (an attribute or event that is associated with increased probability of disease, but is not necessarily a causal factor) and, possibly, as a risk *factor* for P/LBW (an action or event that is statistically related in some way to an outcome). Since P/LBW continues to be a major health and financial problem, with a significant percentage of cases having no identifiable cause, and since PDD is, by and large, both treatable and preventable, the potential for improvement of pregnancy outcome through periodontal intervention is clearly appealing. In this regard, perhaps, PDD is a previously unrecognized factor relating to the development of P/LBW. However, recent studies[4,5] cast doubt on the validity of a direct causal link between PDD and systemic conditions, while implicating smoking (and, by inference, inadequate control for smoking) as the major confounding variable behind the apparent associations.

Our systematic review of available literature was conducted to determine if PDD is a causal risk factor for P/LBW and if periodontal intervention is a valid preventive strategy for P/LBW. We identified two systematic reviews, four intervention studies, four cohort studies, and nine case-control studies.

Case-Control Studies

TABLE ABBREVIATIONS

BOP = Bleeding on probing
CAL = Clinical attachment loss
CI = Confidence interval
CPITN = Community periodontal index and treatment needs
LBW = Low birth weight
OH = Oral hygiene
OR = Odds ratio
PD = Probing depth
P/LBW = Preterm low birth weight
PSR = Periodontal screening and recording
PTB = Preterm birth
RCT = Randomized controlled trial
SC/RP = Scaling and root planning
SES = Socio-economic status
SSD = Significant statistical difference

Table 1: Case-Control Studies (9)

Study	Population	Sample size	Outcomes: Periodontal (P) and Obstetrical (O) Parameters	Results
Moore et al[1]	a. Recruited within 5 days of delivery from Guy's/St. Thomas' Hospital, London, UK	1. Cases (n = 61) 2. Controls (n = 93)	**P:** Blinded, whole mouth, PD, CAL, BOP Severe PDD: >5% of sites with PD 5+mm & >5% of sites with CAL 3+mm **O:** PTB	a. No SSD in any of the periodontal variables between cases and controls
Mokeem et al[6]	a. High SES, healthy Saudi Arabian women, all non smokers	1. Cases (n = 30) 2. Controls (n = 60)	**P:** Blinded, calibrated, whole mouth, PD, BOP, CPITN index used **O:** P/LBW	a. Adjusted OR for P/LBW in the presence of PDD is 4.21 (95% CI=1.9-8.9)
Randal et al[7]	a. Healthy, Hungarian women (16-42 year olds) enrolled in the national prenatal care program	1. Cases (n = 41) 2. Controls (n = 44)	**P:** Blinded, whole mouth PD, BOP, mobility, plaque, calculus Early localized PDD: 4+mm PD 1+site & BOP >50% of teeth **O:** P/LBW	a. Adjusted OR for P/LBW in the presence of early localized PDD is 5.46 b. Average weight of newborn in women with PDD (n=24) is lower than in women without PDD (n=61)
Davenport et al[8]	a. Low SES, multi-ethnic, inner-city population in London, UK b. 50% Bengali, 10% Black	1. Cases (n = 236) 2. Controls (n = 507)	**P:** Calibrated, blinded, whole mouth, PD, BOP, CAL CPITN index used **O:** P+LBW	a. No SSD in CPITN index between P+LBW and PDD
Goepfert et al[9]	a. Low SES women enrolled in study at the Perinatal Emphasis Center at University of Alabama, Birmingham and maternal transfers from across the state with an expectant preterm delivery b. 60% black	1. Cases (n = 59) (spontaneous PTB <32 weeks) 2. Controls (n = 36) (indicated PTB <32 weeks) 3. Controls (n= 44) (term birth >37w)	**P:** Blinded, Extent 3 Index (the proportion of sextants with CAL of 3+mm in the worst site) Gingivitis: no CAL Mild periodontitis: 3 to 5 mm CAL in the worst site in any one sextant Severe periodontitis: 5+mm CAL in the worst site in any one sextant **O:** Spontaneous PTB, Indicated PTB	a. Adjusted OR for spontaneous PTB in the presence of severe PDD is 3.4 (95% CI=1.5-7.7)
Dasanayake et al[10]	a. Low SES women enrolled in study at the University of Alabama, Birmingham and Medical College in Nashville, Tennessee; first pregnancy for all women b. 80% black	1. Cases (n = 17) 2. Controls (n = 63)	**P:** Calibrated, blinded (by default, since PSR values obtained before pregnancy outcome in 2nd trimester) PSR index used **O:** LBW	a. No SSD in PSR values between LBW and non-LBW
Offenbacher et al[11]	a. Women enrolled from Department of Obstetrics and Gynecology at UNC Hospitals either immediately before delivery or within 3 days post-partum	1. Cases (n = 25) 2. Controls (n = 15)	**P:** Calibrated, whole mouth Extent scores: (% of sites with >=4 mm attachment level loss) **O:** PLBW	a. No SSD in Extent scores between PLBW mothers and normal birth weight mothers
Dasanayake[12]	a. Healthy, married Thai women enrolled in study who delivered at Mother and Child Hospital in Chiang Mai, Thailand	1. Matched pairs (n = 55)	**P:** Blinded, calibrated CPITN **O:** LBW	a. Mothers with more healthy sextants had a lower risk of LBW infant OR=0.3 (95% CI=0.12-0.72)
Offenbacher et al[13]	a. Women enrolled while seen for routine prenatal care (<10%) or within 3 days postpartum (>90%) at the University of North Carolina Hospitals b. 60% black	**All Women** 1. Cases (n = 93) 2. Controls (31) **Primiparous women** 1. Cases (n = 46) 2. Controls (n = 20)	**P:** Blinded, calibrated, whole mouth, PD, CAL, BOP Extent 3 Index (proportion of sites with CAL >3mm) Extent 3:60 (subjects where more than 60% of sites have CAL >3mm) **O:** P/LBW in all women; P/LBW in primiparous women	a. Adjusted OR for P/LBW among all women was 7.5 (95% CI=1.95-28.8) b. Adjusted OR for P/LBW among primiparous women 7.9 (95% CI=1.52-41.4)

We identified nine case-control studies (an observational design where patients are selected on the basis of an outcome variable) that met our selection criteria. Case-control studies constituted the largest single group of studies on this topic. Five found a relationship between PDD and P/LBW with the odds ratio (OR) ranging from 3.4 to 7.9, while four studies found no relationship between these two parameters. Seven studies dealt with low socio-economic status (SES) populations and two studies focused on healthy, middle class women. Mokeem et al[6] examined 90 Saudi Arabian women and found OR of 4.1. Randai et al[7] looked at 85 Hungarian women and found OR of 5.46. Mokeem et al[6] is the only study to date to examine the relationship between PDD and P/LBW in non-smokers. The findings of Randai et al,[7] on the other hand, appear to be inadequately adjusted for smoking. Davenport et al[8] is the only study to validate self-reported history of smoking with an objective test (cotinine) and it found no relationship between PDD and P/LBW. It is by far the largest case-control study to date with a sample size (236 cases and 507 controls) nearly equal to the sum total of sample sizes of the other eight studies.

Cohort Studies

Table 2: Cohort Studies (4)

Study	Population	Sample size	Outcomes: Periodontal (P) and Obstetrical (O) Parameters	Results
Moore et al[14]	a. Recruited when attending Guy's Hospital in London, UK for a nuchal translucency scan between 10-15 weeks of pregnancy b. Multi-ethnic	Prospective (n = 3738)	**P:** Whole mouth - PD, CAL, BOP Periodontal Health: <10% sites with PD 3+ mm and <5% sites with CAL 2+mm Comparison made of clinical periodontal parameters **O:** PTB, extreme PTB (<32w), LBW	a. No SSD in any periodontal variables: - when comparing no-preterm group to either PTB group or extreme PTB group; - when comparing LBW group to non-LBW group. b. No SSD between the Periodontally Healthy group and Severe PDD group in the incidence of *previous* adverse pregnancy outcome.
Holbrook et al[15]	a. High SES, healthy Nordic Caucasian (Icelandic) women enrolled in study with low incidence and severity of periodontal disease	Prospective (n = 96)	**P:** Ramfjord teeth, PD Comparison made of clinical periodontal parameter (PD) **O:** PTB	a. None of the women with pockets of 4+mm delivered preterm.
Riche et al[16]	a. Women enrolled at the University of North Carolina, Chapel Hill b. Oral exam completed at enrollment and within 2 days postpartum c. 47 % Black	Prospective (n = 1020) (47 of which were preeclampic)	**P:** Whole mouth, PD, CAL, BOP Health: PD 3 mm or less and no 3 mm pockets with BOP Mild PDD: BOP at 1+ site with PD 3+ mm, but less than 15 sites with PD 4+ mm Moderate to Severe PDD: 15+ sites with PD 4+ mm Worsening PDD: 4+ sites that increased PD by 2+ mm **O:** PTB	a. In general, the rate of PTB was significantly greater among preeclampic women and increased with increased severity of PDD and with worsening PDD. b. The trend was observed for both non-eclampic and preeclampic females, although the results were not always statistically significant for non-eclampic females. c. Overall rate of prematurity in this sample is 18%.
Jeffcoat et al[17]	a. Recruited from Perinatal Research Center at Univeristy of Alabama, Birmingham between 21 and 24 weeks' gestation b. 82% black	Prospective (n = 1313)	**P:** Calibrated, whole mouth, PD, CAL Health: < 3 sites with 3mm CAL PDD: 3+ sites with 3+mm CAL Generalized PDD: 90+% sites with 3+mm CAL **O:** PTB	a. Adjusted OR for preterm delivery in patients with severe PDD is 4.45 (95% CI=2.16-9.18) b. Adjusted OR increased with increasing prematurity (before 37 weeks' gestational age vs. 35 weeks' Vs. 32 weeks') | | <37 | <35 | <32 | | adjusted OR | 4.45 | 5.28 | 7.07 |

Four cohort studies (an observational design where patients are selected on the basis of an exposure variable) were included in our analysis. Two supported the association between PDD and P/LBW and two did not. Moore et al[14] has by far the largest sample size (roughly the same as the sum total of sample sizes of all other cohort and case-control studies) and enrolled women at the earliest stages of pregnancy (between 10 and 15 weeks) compared to all other studies (including intervention and case-control studies). It found no association between PDD and any of the three pregnancy

outcomes – PTB, extreme PTB (<32 weeks), and LBW. By contrast, Jeffcoat et al[17] not only found a relationship between PDD and PTB, but also found that adjusted OR for PTB increased with increasing prematurity. Holbrook et al[15] examined a healthy, high SES population with low incidence and severity of PDD and found no association between PTB and PDD.

A potential threat to the validity of all prospective investigations is that the women were either informed of the periodontal findings and encouraged to see their dentist,[14] or the studies did not specify if the women were informed or not, as is the case with the other three prospective studies. Thus, following the periodontal exam as part of the study, women in these studies could have gone to see their private dentist and may have had dental treatment, which was unaccounted for in the analysis of the study. Since the objective of these four investigations was to examine the natural course of PDD and its possible effect on pregnancy outcome, not accounting for potential uncontrolled co-intervention from private dentists introduces the potential for inaccurate measurement of exposure.

Intervention Studies

Table 3: Intervention Studies (4)

Study	Population	Study Groups	Outcomes: Periodontal (P) and Obstetrical (O) Parameters	Results
Jeffcoat et al[18]	a. Enrolled in the study if greater than 3 sites of CAL (3+mm) to the Periodontal clinic at Univ. of Alabama, Birmingham b. 85% black; 86% single mothers	**RCT** (n = 1089) **1. Treatment groups** (n = 366): a. supraging. scaling and polish + placebo b. SC/RP + placebo c. SC/RP + Metronidazole 250mg tid x7d **2. Control group** (n = 723)	**P:** Calibrated No other information provided Average number of sites with CAL 3+mm was 69 sites per pa tient in all three groups **O:** PTB	a. No SSD among all the treatment groups and the control group at both definitions of PTB: <37 weeks and <35 weeks
Lopez et al[19]	a. Low SES women receiving prenatal care in a public health clinic in Santiago, Chile who delivered at El Salvador Hospital b. Women enrolled with gingivitis (n=618) and periodontitis (n=263) c. Women with gingivitis received treatment (n=459) and women with periodontitis received no treatment	**Cohort study with inter-vention** (n = 722) **1. Treatment Group 1** (n = 459) a. OHI, SC/RP +/- LA b. 0.12% CHX daily c. maintenance q 2-3 w d. completed before 28w **2. No Treatment Group 2** (n = 263)	**P:** Calibrated, whole mouth PD, CAL, inflammation, OH Periodontitis: 4+ teeth with PD 4+mm **and** CAL 3+ mm Gingivitis/ Mild Periodontitis: -- gingival erythema and BOP at >25% of sites **O:** PTB, LBW, P/LBW	a. Adjusted relative risk for woman with periodontal disease having: - a low birth weight infant was 3.6 (95% CI=1.06-12.2); - a preterm or low birth weight infant was 3.5 (95% CI=1.5-7.9); - a preterm infant was 2.9 (95% CI=1.0-8.1) b. None of the women with the PDD showed a clinical worsening of PDD during the gestation period.
Lopez et al[20]	a. Low SES women with periodontal disease be-tween 9-21 weeks of gestation receiving prenatal care in Santiago, Chile b. Patients matched on the basis of mean pocket depth (>2.5mm or <2.5mm) and randomized to treatment or control group by a coin toss	**RCT** (n = 400) **1. Treatment Group 1** (n = 200): a. 0.12% CHX daily b. OHI, SC/RP with LA c. Metronidazole 250 mg + Amox 500mg tid for 7d for 29 women with se vere PDD; d. completed before 28w e. maintenance q 2-3 w **2. Control group (n=200)** a. no treatment	**P:** Calibrated, whole mouth PD, CAL, BOP, OH, gingival inflammation Periodontal disease: 4+ teeth with 1+ sites of PD 4+mm and with CAL 3+mm at the same sites **O:** P/LBW	a. After periodontal therapy, women in Treatment Group 1 showed significant improvement in perio parameters. b. Women in Group 2 showed no change in periodontal parameters. c. Adjusted OR for women with PDD having a P/LBW is 4.7 (95% CI=1.3-17.1)
Mitchell-Lewis et al[21]	a. Low SES, pregnant or postpartum young women (12-19 years old) recruited among consecutively enrolled women attending the School for Pregnant and Parenting Teens in Central Harlem b. 60% black; 39% Hispanic c. Enrollment in study varied between 2nd and 3rd trimester	**Cohort study with inter-vention** (n = 164) **1. Intervention Group:** a. OHI, SC/RP b. decay treated	**P:** Calibrated, whole mouth PD, BOP, plaque, calculus Comparisons made of clinical periodontal parameters **O:** P/LBW	a. No SSD in P/LBW frequency among women with perio intervention and with-out b. Women with P/LBW infants and women with normal birth outcomes had similar levels of periodontal parameters.

Four intervention studies (a research design where the researchers control the allocation of a treatment to the research subjects) were identified. Two studies[19,20] found a reduction in the incidence of P/LBW in their examination of a population of Chilean women. Two studies[18,21] found no statistically significant effect of an

intervention in two separate centers in the US with a significant minority representation. All these studies examined women from low SES. Mitchell-Lewis et al[21] is unique among studies examined in this systematic review in their focus on young disadvantaged women between 12 and 19 years of age. All other studies limited their investigation to women over the age of 18 (or 16, in Randai et al[7]).

Jeffcoat et al[18] and Lopez et al[20] examined women with PDD, while the other two studies examined a sample of general populations. However, Lopez et al[19] found that none of the women in their general population were free of mild PDD (according to their definition of mild PDD). The intervention typically involved multiple visits for scaling and root planning (with or without local anaesthesia) and oral hygiene instructions. These were supplemented with daily 0.12% chlorhexidine rinses[19,20] or with short courses of antibiotics (Metronidazole in Jeffcoat et al[18]; and Metronidazole with Amoxicillin in Lopez et al[20]) for all or some women.

Studies differed significantly in who was used as a control group. Lopez et al[20] was the only trial where subjects were truly randomized between the intervention and control groups. In Lopez et al,[19] intervention group consisted of subjects with gingivitis, while control group consisted of subjects with PDD. In Mitchell-Lewis et al,[21] the control group consisted of women who had already given birth within three months of the start of the trial. Jeffcoat et al,[18] randomized subjects among the three intervention groups and ensured that the intervention groups demonstrated relatively equal distribution of other relevant risk factors, but subjects were not randomized between the treatment groups and the control group and there is no discussion that the intervention and control groups were compared to ensure relatively equal distribution of other relevant risk factors.

Systematic Reviews

Table 4: Systematic Reviews (2)

Study	*Exclusion/Inclusion criteria*	*Studies*	*Study selection relative to our study selection*	*Conclusions*
Scannapieco et al[22]	Exclusion criteria: 1) Limited to human studies 2) Up to October 2002	6 case-control 3 cohort 3 intervention	We excluded 3 studies included in this review: • Madianos et al[26] • Offenbacker et al[24] • Romero et al[25]	a. Periodontal disease may be a risk factor for P/LBW. b. Some studies do not support the association between PDD and P/LBW. c. It is not yet clear if the relationship is causal in nature. d. Some evidence suggests that periodontal intervention may reduce adverse pregnancy outcome. e. Additional longitudinal, epidemiologic and interven tion studies are needed to validate the association and to determine if it is causal.
Madianos et al[23]	Inclusion criteria: 1) Study examines clinical, microbial or host response aspect of PDD; 2) Study reports on gestational age or birth weight of the newborn. Exclusion criteria: 1) Limited to human studies 2) Limited to English language	3 case-control 1 cohort 1 intervention	We included all studies included in this review but in 2 studies[11,21] we base our analysis on a different subset of data (measurements related to clini-cally relevant parameters) vs. the subset of data (bacterial types and count determination) analyzed by this review.	a. The evidence linking PDD and P/LBW is limited. b. Some multivariable models are not adequately ad justed for confounding variables. c. There is need for well designed studies to confirm observations, to validate them in different populations, establish whether they are causal in nature and deter-mine potential benefits of the intervention.

The systematic reviews by Scannapieco et al[22] and Madianos et al[23] were cautious in their assessment and reached similar conclusions: 1) periodontal disease may be a risk factor for P/LBW, but the evidence is limited; 2) several studies do not support

periodontal disease as a risk factor for P/LBW; 3) it is not clear whether the link is causal in nature; 4) the studies on the impact of treatment and prevention of PDD on adverse pregnancy outcomes are few, limited in population focus and conflicting in terms of their results; 5) in a number of studies, the multivariable model was not adequately adjusted for the confounding variables.

Our review differed from the other two systemic reviews in two parameters:

1) we examined more current literature; and

2) our selection (inclusion/exclusion) criteria were different.

Studies that have been released after the publication of these two systematic reviews include one intervention, three prospective, and five case-control studies, and this almost doubles the number of studies available on this topic. The difference in selection criteria compared to previous systematic reviews led to elimination of some studies from the consideration. In particular, we excluded from analysis three studies (Offenbacher et al,[24] Romero et al,[25] and Madianos et al[26]) that had been included in the systematic review by Scannapieco et al.[22] Offenbacher et al[24] and Romero et al[25] were excluded because they did not control for confounding variables and did not utilize regression analysis. Madianos et al[26] was excluded from consideration because it did not use clinically relevant parameters in the investigation.

Our systematic review examined all the studies included in the systematic review by Madianos et al,[23] but in two studies (Offenbacher et al;[11] Mitchell-Lewis et al[21]) we based our analysis on a different subset of data (measurements related to clinically relevant parameters) vs. the subset of data (bacterial types and count determination) analyzed by Madianos et al.[23] This is important because examining clinically relevant parameters, as opposed to identifying levels of bacteria or their type, actually leads to a complete reversal of the conclusions reached by Offenbacher et al[11] and Mitchell-Lewis et al.[21]

Conclusions

Overall, the evidence is best described as conflicting. Our review of this topic agrees generally with the other two systematic reviews. We conclude that:

1. the available evidence is contradictory; with few exceptions, the studies in this area share several methodological shortcomings. The inadequate control of other risk factors and the difficulty in utilizing a valid measure of *currently active* PDD and distinguishing it from gingivitis are the main culprits casting doubt on the research done thus far;
2. P/LBW and PDD are both widely encompassing entities with numerous smaller sub-classifications and conditions; it is possible that a relationship may exist among certain subgroups of patients within either condition;
3. the evidence does **not** allow one to draw a definitive conclusion that PDD is a causal risk *factor* for P/LBW or that it is even a risk *marker* for P/LBW;
4. on balance, the utility of periodontal intervention as a preventive strategy for P/LBW has **not** been established;
5. the existing evidence certainly indicates that this topic deserves further investigation utilizing strong research designs and good control of confounding variables.

References

Scannapieco FA. Position paper of The American Academy of Periodontology: periodontal disease as a potential risk factor for systemic diseases. *J Periodontol* 1998; 69(7):841-50.

McGaw, T. Periodontal disease and preterm delivery of low birth-weight infants. *JCDA* 2002;68(3):165-169.

Offenbacher S, Katz V, Fertik G, Collins J, Boyd D, Maynor G, McKaig R, & Beck J. Periodontal infection as a possible risk factor for preterm low birth weight. *J Periodontol* 1996;67:1103-13.

Hujoel PP, Drangsholt M, Spiekerman C, & DeRouen TA. Periodontitis-systemic disease associations in the presence of smoking – causal or coincidental? *Periodontology 2000* 2002;30:51-60.

Moore S, Randhawa M, Ide M. A case-control study to investigate an association between adverse pregnancy outcome and periodontal disease. *J Clin Periodontol* 2005;32:1-5.

Mokeem SA, Molla GN, Al-AJewair TS. The prevalence and relationship between periodontal disease and preterm low birth weight infants at King Khalid University Hospital in Riyadh, Saudi Arabia. *J Cont Den Prac* 2004;5:40-56.

Randai M, Gorzo I, Nagy E, Urban E, Novak T, Pal A. A possible association between preterm birth and early periodontitis. Pilot study. *J Clin Periodontol* 2004;31:736-41.

Davenport ES, Williams CECS, Sterne JAC, Murad S, Sivapathasundram V, Curtis MA. Maternal periodontal disease and preterm low birthweight: Case-control study. *J Dent Res* 2002;81(5):313-8.

Goepfert AR, Jeffcoat MK, Andrews WW, Faye-Petersen O, Cliver SP, Goldenberg RL, Hauth JC. Periodontal disease and upper genital tract inflammation in early spontaneous preterm birth. *Obstet Gynecol* 2004;104:777-83.

Dasanayake AP, Boyd D, Madianos PN, Offenbacher S, Hills E. The association between Porphyromonas gingivalis-specific maternal serum IgG and low birth weight. *J Periodontol* 2001;72:1491-7.

Offenbacher S, Jared HL, O'Reilly PG, Wells SR, Salvi GE, Lawrence HP, Socransky SS, Beck JD. Potential pathogenic mechanisms of periodontitis associated pregnancy complications. *Ann Periodontol* 1998;3:233-50.

Dasanayake AP. Poor periodontal health of the pregnant woman as a risk factor for low birth weight. *Ann Periodontol* 1998;3:206-12.

Offenbacher S. Periodontal diseases: pathogenesis. *Ann Periodontol* 1996;1(1):821-78.

Moore S, Ide M, Coward PY, Randhawa M, Borkowska E, Baylis R, Wilson R. A prospective study to investigate the relationship between periodontal disease and adverse pregnancy outcome. *British Dental J* 2004;197:251-8.

Holbrook WP, Oskarsdottir A, Fridjonsson T, Einarsson H, Hauksson A, Geirsson RT. No link between low-grade periodontal disease and preterm birth: a pilot study in a healthy Caucasian population. *Acta Odontol Scand* 2004;62:177-9.

Riche EL, Bogess KA, Lieff S, Murtha AP, Auten RL, Beck JD, Offenbacher S. Periodontal disease increases the risk of preterm delivery among preeclampic women. *Ann Periodontol* 2002;7:95-101.

Jeffcoat MK, Geurs NC, Reddy MS, Cliver SP, Goldenberg RL, Hauth JC. Periodontal infection and preterm birth. *JADA* 2001;132:875-80.

Jeffcoat MK, Hauth JC, Geurs NC, Reddy MS, Cliver SP, Hodgkins PM, Goldenberg RL. Periodontal disease and preterm birth: results of a pilot intervention study. *J Periodontol* 2003;74:1214-8.

Lopez NJ, Smith PC, Gutierrez J. Higher risk of preterm birth and low birth weight in women with periodontal disease. *J Dent Res* 2002;81(1):58-63.

Lopez 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;73:911-24.

Mitchell-Lewis D, Engebretson SP, Chen J, Lamster IB, Papapanou PN. Periodontal infections and pre-term birth: early findings from a cohort of young minority women in New York. *Eur J Oral Sci* 2001;109:34-9.

Scannapieco FA, Bush RB, Paju S. Periodontal disease as a risk factor for adverse pregnancy outcomes. A systematic review. *Ann Periodontol* 2003;8:70-8.

Madianos PN, Bobetsis GA, Kinane DF. Is Periodontitis associated with an increased risk of coronary heart disease and preterm and/or low birth weight births? *J Clin Periodontol* 2002;29(s3):22-36.

Offenbacher S, Lieff S, Boggess KA, Murtha AP, Madianos PN, Champagne CM, McKaig RG, Jared HL, Mauriello SM, Auten RL Jr, Herbert WN, Beck JD. Maternal periodontitis and prematurity. Part I: Obstetric outcome of prematurity and growth restriction. *Ann Periodontol* 2001;6(1):164-74.

Romero BC, Chiquito CS, Elejalde LE, & Bernardoni CB. Relationship between periodontoal disease in pregnant women and the nutritional condition of their newborns. *J Periodontol* 2002;73:1177-83.

Madianos PN, Lieff S, Murtha AP, Boggess KA, Auten RL, Beck JD, et al. Maternal periodontitis and prematurity. Part II: Maternal infection and fetal exposure. *Ann Periodontol* 2001; 6(1):175-82.

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