

# Effect of Periodontal Treatment on Preterm Birth Rate: Meta-analysis

Adel S Alobaid

## ABSTRACT

**Introduction:** During pregnancy, the prevalence and severity of gingivitis have been reported to be elevated. Studies suggest that periodontitis is associated with an increased risk of preterm birth (PTB), as well as low birth weight (LBW) and pre-eclampsia. The purpose of this meta-analysis is to determine whether the treatment of periodontal disease by mechanical debridement and oral hygiene instructions during pregnancy will reduce the incidence of PTB < 37 weeks.

**Materials and methods:** Literature search was conducted for all clinical trials that related to periodontal disease and PTB from 2005 to 2012. Five were selected based on randomization technique, sample size and treatment approach. There were 2,767 patients randomly assigned to treatment group, in these trials, and 2,592 subjects randomly assigned to control group.

**Results:** There were 276 (9.98%) PTBs in treatment group vs 270 (10.42%) in control group. A total of 216 (8%) LBW were seen in experimental groups and 193 (7.5%) in control group. Our results showed no significant difference in the incidence of PTB with or without received periodontal treatment during pregnancy. Risk ratio (RR) was 0.99 (95% CI: 0.74-1.33) ( $p = 0.97$ ) with moderate heterogeneity  $I^2 = 12.33$ ,  $df = 4$  ( $p = 0.02$ ) with  $I^2 = 68\%$ . Experimental groups showed better periodontal health after delivery.

**Conclusion:** Periodontal treatment may improve the oral health during pregnancy without affecting the pregnancy outcome however; it did not reduce the incidence of PTB and LBW. Larger meta-analysis with less heterogeneity is needed.

**Keywords:** Periodontal disease, Pregnancy, Low birth weight, Preterm birth, Meta-analysis.

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## INTRODUCTION

Preterm birth (PTB, which remains a major public health issue in the United States) accounts for substantial morbidity and death. Unfortunately, the incidence of PTB has been largely unchanged in recent years, hovering at 12%.<sup>1</sup> About half of mothers delivering preterm infants have no known risk factors.<sup>2</sup> There is substantial observational evidence from a variety of populations that links maternal periodontal disease to PTB, possibly because of the maternal inflammatory response to periodontal disease.<sup>3-7</sup>

Destructive periodontal disease (periodontitis) is common, with a reported prevalence of 30% in some

populations.<sup>8</sup> Plaque-induced gingivitis is an inflammation of the gingiva resulting from bacterial infection, and this disease is the most common periodontal disease in pregnant women.<sup>9</sup> During pregnancy, the prevalence and severity of gingivitis have been reported to be elevated yet unrelated to the amount of plaque present.<sup>11,12</sup> However, the severity of gingivitis is correlated with sex steroid hormone levels during pregnancy.<sup>13</sup>

One of the hypotheses to explain the relation between periodontal disease and PTB is that periodontal infection is a source of bacteria and bacterial products that may spread from the infected periodontium to the amniotic cavity, as when transient bacteremia occurs in patients with periodontitis.<sup>6,14,17,18</sup> It has been demonstrated that transient bacteremia commonly occurs in subjects with periodontitis<sup>19</sup> as well as in those with gingival inflammation,<sup>20</sup> and bacteria or their products may conceivably reach the placental tissue providing the inflammatory effect for labor induction.<sup>9</sup> Recent studies suggest that periodontitis, an inflammatory disease caused primarily by Gram-negative bacteria that destroy tooth supporting connective tissue and bone, is associated with an increased risk of PTB, as well as low birth weight (LBW) and pre-eclampsia.<sup>7,21</sup>

Studies have suggested that maternal periodontal disease is associated with an increased risk for preterm delivery.<sup>2,22-30</sup> Many case series and cohort studies have shown significant associations between periodontal disease and PTB,<sup>6</sup> fetal growth restriction<sup>31</sup> and pre-eclampsia.<sup>21</sup> The mechanisms by which an inflamed and infected periodontium could adversely affect the pregnant uterus and developing fetus are uncertain, although evidence suggests roles for translocation of periodontopathic organisms, and stimulation and release of inflammatory mediators and prostaglandins into the maternal circulation.<sup>9</sup>

Results from four randomized, single-center clinical trials suggest that periodontal treatment during pregnancy may reduce PTBs.<sup>15-17,32,33</sup> However, results of a randomized, multicenter clinical trial show no difference between treatment and control groups for mean gestational age and for PTB at less than 37 weeks.<sup>34</sup> A recent meta-analysis of 17 observational studies indicated the association between periodontal disease and PTB or LBW infants.<sup>35</sup>

The purpose of this meta-analysis is to determine whether the treatment of periodontal disease by mechanical debridement and oral hygiene instructions during pregnancy

will reduce the incidence of PTB < 37 weeks. This is a meta-analysis of the largest, based on sample size; up to date five randomized controlled clinical trials.

**MATERIALS AND METHODS**

**Identification of Randomized Trials**

One independent investigator (AA) searched the clinical trials website, Medline, Google scholars, and PubMed with English language, clinical trials and 2005 up restrictions. We used the following researching algorithms (periodontal therapy, treatment, diseases, periodontitis or gingivitis) and (PTB, preterm labor, LBW or PTB < 37 weeks).

**Eligibility Criteria**

At the very beginning of the searching method we decided to select the best five randomized control trials based on the sample size effect and the strength of the study methodology. We selected all studies that compare periodontal therapy including mechanical removal of plaque and calculus (scaling and root planning) vs no treatment placebo or prophylaxis and OHI. The study also included if it included pregnant women with periodontal problem.<sup>10</sup> All single armed, nonrandomized, pure observational studies were excluded. Also, all studies accepting subjects with antibiotic use were excluded.

The electronic search found 353 articles talk about periodontal disease and PTB, 343 at Medline and 10 at clinical trials. After limiting the research to randomized

clinical trials we found 46 articles of all kinds. In addition, after more specific research selection we end up with 12 articles. All 12 clinical trials that we found from these searching methods were retrieved from NYU College of Dentistry Library at VA Hospital and examined for eligibility criteria. After going through all these articles we considered two were ineligible and 10 were recorded as eligible trials. We selected the most up to date articles with the largest sample size and best methodology. We finally end up with five items to be in our meta-analysis.

**Data Extraction**

Data were extracted by (AA) from all five eligible trials. Multiple factors were taken in consideration like author’s name, journal’s name, publication year, gestational age at enrollment, and number of subjects in the trial and in each arm. Furthermore, baseline characteristic that can affect the PTB were taken in consideration like mean age of the subjects, smoking history, history of PTB (Table 1). Periodontal status was checked at baseline by determining the probing depth and bleeding with probing (Table 2). Birth related events were recorded at baseline for each subject in both arms of all studies: stillbirth, spontaneous abortion, number of PTB (<37 weeks), LBW infants (<2,500 gm) in (Table 3).

**STATISTICAL ANALYSIS**

The risk ratio (RR) was calculated for each study to estimate the relative risk of abortion/stillbirth, PTB, and LBW infants

**Table 1:** Baseline characteristics

ID	Study	Tx	Total patient number	Patient followed up	Live birth	Gestation age (wks)	Age mean (Y)	Previous PTB/LBW (%)	<12 Education (%)	Smoke (%)
1	Lopez et al <sup>38</sup> 2005	Yes	580	570	563	<22	25.54	3.44	77.76	14.47
		No	290	286	282		24.98	7.47	80.78	17.44
2	Michalowicz et al <sup>34</sup> 2006	Yes	413	407	402	<21	26.1	12.5	76.3	13
		No	410	405	391		25.9	16.5	77.6	13
3	Offenbacher et al <sup>36</sup> 2009	Yes	903	880	871	<23	25.4	10.6	75.4	NA
		No	903	881	874		25.3	9.0	76.5	NA
4	Newnham et al <sup>37</sup> 2009	Yes	546	538	538	<20	30.5	13.2	48.2	17.7
		No	541	540	535		30.5	11.1	53.7	17.7
5	Macones et al <sup>8</sup> 2010	Yes	376	359	351	<20	24.1	11.7	71.5	NA
		No	380	361	352		24.4	12.9	64.7	NA

Tx: Treatment; PTB: Preterm birth; LBW: Low birth weight; Smoke: Smoking status

**Table 2:** Periodontal status baseline characteristics

ID	Study	Tx	Disease type	Definition of periodontal disease	Natural teeth (N)	BOP (%)	PD > 4 mm (%)
1	Lopez et al <sup>38</sup> 2005	Yes	Gingivitis	BOP > 25% of sites with CAL > 2 mm	25	55.09	9.24
		No			24.8	51.42	12.23
2	Michalowicz et al <sup>34</sup> 2006	Yes	Mild-moderate	>4 teeth with CAL > 2 mm	26.7	69.6	26.5
		No			26.8	69.0	24.8
3	Offenbacher et al <sup>36</sup> 2009	Yes	Not specified	>3 teeth with CAL > 3 mm	>20	45.2	26.1
		No			>20	47.1	26.6
4	Newnham et al <sup>37</sup> 2009	Yes	Moderate-severe	PD > 4 mm at 12 sites	28.8	71.29	14.8
		No			28.7	77.7	14.9
5	Macones et al <sup>8</sup> 2010	Yes	Moderate-severe	>3 teeth with CAL > 3 mm	NA	NA	NA
		No			NA	NA	NA

Tx: Treatment; BOP: Bleeding on probing; PD: Probing depth

**Table 3:** Pregnancy and periodontal-related parameters after treatment

ID	Study	Tx	PTB (N)	Stillbirth abortion (N)	LBW (N)	BOP (%)	PD > 4 mm (%)
1	Lopez et al <sup>38</sup> 2005	Yes	18	7	4	15.09	1.8
		No	17	4	3	56.6	14.5
2	Michalowicz et al <sup>34</sup> 2006	Yes	44	5	40	3.8	NA
		No	38	14	43	22.7	NA
3	Offenbacher et al <sup>36</sup> 2009	Yes	104	NA	71	17.7	13.2
		No	118	NA	72	12.2	9.3
4	Newnham et al <sup>37</sup> 2009	Yes	52	0	52	28.7	3.3
		No	50	4	39	70.2	13.8
5	Macones et al <sup>8</sup> 2010	Yes	58	8	49	NA	NA
		No	47	9	36	NA	NA

Tx: Treatment; PTB: Preterm birth; LBW: Low birth weight; BOP: Bleeding on probing; PD: Probing depth

among treatment group compared with control group. Analysis of abortion, stillbirth, PTB and LBW were based on all randomized subjects except for those who lost the follow-up. Statistical significant was defined as  $p < 0.05$ .

The  $\chi^2$  statistical test was used to test the homogeneity of the estimates of RR between studies. Analysis was performed to explain the possible source of heterogeneity between studies on the bases of some

baseline characteristics of the trials regarding potential risk factors for PTB and LBW infants.

Previous history of PTB and LBW was taken in consideration. We also, considered the level of education (<12 years) effects on the studies' population. We considered the severity of periodontal disease before randomization in each study and its effect and progression during the course of pregnancy. The data were analyzed using review manager 5 software.

**RESULTS**

**Design and Quality of Characteristics**

Lopez et al<sup>38</sup> trial in 2005 was 2:1 ratio in favor of experimental group; however all other four trials<sup>8,34,36,37</sup> were in adequate random mode. All studies' primary outcome was the PTB incidence. Two studies<sup>8,37</sup> estimated <35 weeks gestation as primary end point however three studies<sup>34,36,38</sup> estimated <37 weeks.

**Outcome Measures**

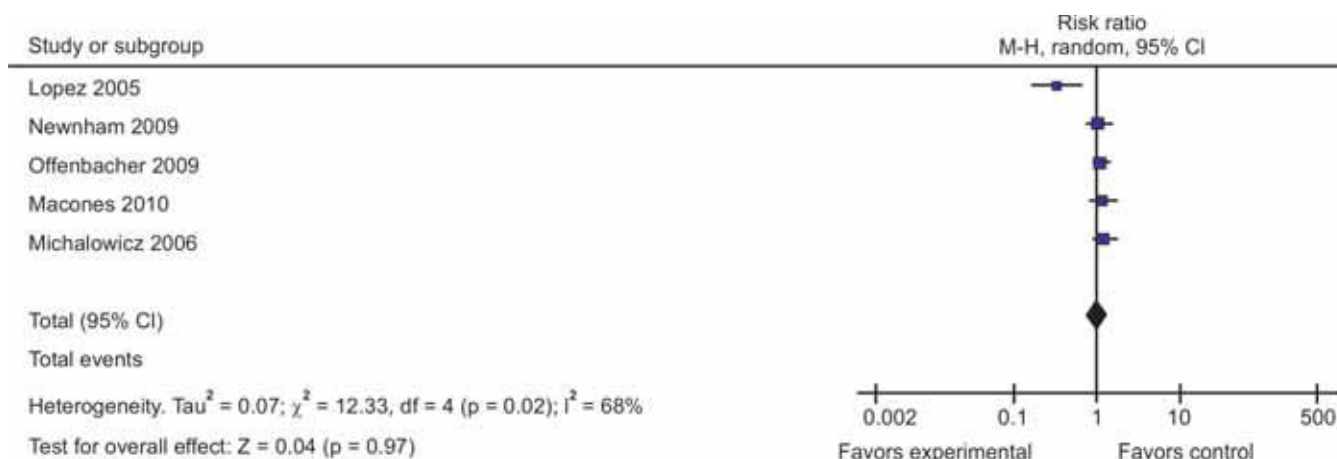
There were 2,767 patients randomly assigned to treatment group in these trials. On the other hand, there were 2,592 subjects randomly assigned to control group as in (Table 1). We found reported PTB in all trials in both groups except for treatment group of Newham et al,<sup>37</sup> 2010. Cumulatively,

there were 276 (9.98%) observed PTB in women received periodontal treatment during pregnancy. Three studies<sup>8,34,36</sup> were multicenter studies whereas two studies<sup>37,38</sup> were single center studies. On the other side, we cumulatively observed that 270 (10.42%) PTBs in women did not receive periodontal treatment during pregnancy. The number of PTBs was higher in treatment groups in four studies.<sup>8,34,37,38</sup> The reason for Lopez et al study<sup>38</sup> was because the randomization ratio of groups was 2:1 favoring treatment group. The number of PTB event was higher in control group in Offenbacher et al study.<sup>36</sup> Only Lopez et al study<sup>38</sup> showed statistically significant difference between groups favoring the treatment group whereas all other four<sup>8,34,36,37</sup> showed no difference regardless single or multicenter type. Meta-analysis regarding PTB incidence revealed no significant difference between compared groups. RR was 0.99 (95% CI:

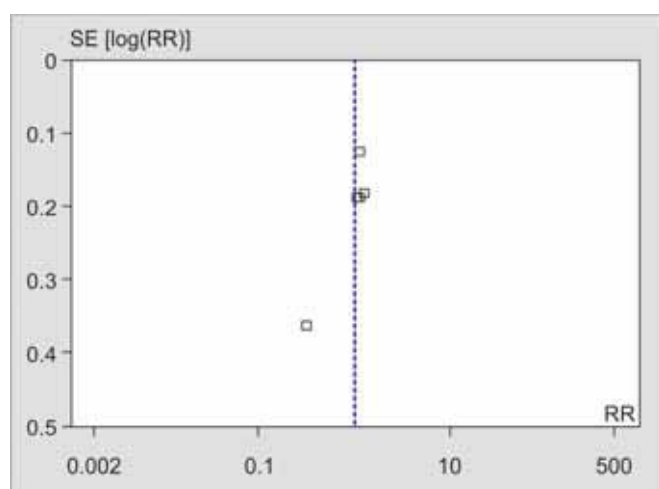
**Table 4: Studies outcome risk ratios**

ID	Study	Tx	Event	Total	Weight (%)	Risk ratio M-H random CI (95%)
1	Lopez et al <sup>38</sup> 2005	Yes	12	560	11.1	0.32 (0.16-0.65)
		No	19	283		
2	Michalowicz et al <sup>34</sup> 2006	Yes	58	359	21.4	1.24 (0.87-1.77)
		No	47	361		
3	Offenbacher et al <sup>36</sup> 2009	Yes	118	903	25.6	1.13 (0.89-1.45)
		No	104	903		
4	Newnham et al <sup>37</sup> 2009	Yes	52	538	20.9	1.04 (0.72-1.51)
		No	50	540		
5	Macones et al <sup>8</sup> 2010	Yes	49	407	21.0	1.17 (0.81-1.89)
		No	52	405		

Heterogeneity: 0.07; Chi: 12.33; df: 4; p: 0.02; I: 68; Total for overall effect (Z): 0.04 (p = 0.97)



**Graph 1: Forest plot**



Graph 2: Funnel plot

0.74-1.33) ( $p=0.97$ ) with moderate heterogeneity 12.33.  $df=4$  ( $P=0.02$ )  $I^2$  (variation in RR attributable to heterogeneity) = 68% (Table 4). It suggested that periodontal treatment, including scaling and root planning; during pregnancy did not reduce the incidence of PTB among pregnant women diagnosed with periodontal disease.

Forest plot showed the distribution of the selected studies and compared them together based on RR effect with left side favoring the experimental group (Graph 1). It showed no significant difference for total events weight. In addition, (Graph 2) funnel plot showed the distribution of all studies around the RR point with no significant difference.

LBW infants were reported in all five trials. A total of 216 (8.0 %) LBW infants were observed in periodontal treatment group. On the other hand, a total of 193 (7.5%) were seen in control groups. Studies<sup>34,36</sup> showed less LBW in control group when compared with other studies.<sup>8,37,38</sup> Regarding abortions and stillbirths, Offenbranch et al study<sup>36</sup> did not mention anything about it. However, all other four studies<sup>8,34,37,38</sup> had a total of 20 (1.1%) stillbirths in experimental groups and 31 (1.8%) stillbirths in control groups.

All studies, regarding periodontal treatment, showed a significant improvement in periodontal condition in treatment groups after delivery except for two. Offenbacher et al study<sup>36</sup> showed no difference. However, it showed slight improvement in control group whereas Macones et al study<sup>8</sup> did not mention anything about periodontal probing depth and bleeding index.

## DISCUSSION

Our findings came along with several meta-analyses and randomized clinical trials. It showed no statistically significant difference whether or not we performed periodontal treatment including routine scaling and root planning during pregnancy regarding the final results of

pregnancy including PTB, LBW infants and abortion and stillbirths despite the rate of heterogeneity between studies.

The presence or absence of high risk factors is the most important in all studies. We considered previous history of PTB or LBW infants, level of education and smoking status of the mother during pregnancy as the most relevant risk factors in the study. These factors were related to the outcome of delivery more than the periodontal condition. After controlling these factors by randomization we found no significant effect of periodontal condition therefore, the hypothesis of relating periodontal infections to PTB and LBW seemed to be nonvalid.

History of previous PTB or LBW infants is strongly associated with a subsequent PTB.<sup>39</sup> Thus, the potential of experiencing a second PTB in this subgroup of women is higher than for general population and may be irrelevant from coexisting conditions, such as periodontal disease or smoking.<sup>40</sup>

Lopez et al,<sup>38</sup> was different than other studies in this analysis. All subjects in Lopez et al<sup>38</sup> were restricted to gingivitis cases only however; other studies selected more advanced periodontal disease, which may be more valid. Also, Lopez et al<sup>38</sup> randomization was based on 2:1 ratio favoring experimental group. That added to moderate heterogeneity between studies and difficult compression and interpretation of the results.

## CONCLUSION

Since, the periodontal treatment did not influence the outcome of pregnancy regarding PTB and LBW infants and improved the postdelivery periodontal condition; it may be advisable to perform routine scaling and root planning for pregnant woman with no history of PTB. More studies are needed to insure accurate analysis.

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## ABOUT THE AUTHOR

### Adel S Alobaid

Department of Restorative Dentistry, College of Dentistry King Khalid University, PO Box 3263 Zip 61471, Abha, Saudi Arabia, Phone: 00966172418014, Fax: 00966172418197 e-mail: aalobaid@kku.edu.sa