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REVIEW ARTICLE

Evaluation of the periodontal disease on oral microorganisms during pregnancy: A systematic review and meta-analysis

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Abstract

Background and Aim: In the present study, the potential changes of oral microbes during pregnancy were investigated by examining the findings of the previous studies and comprehensively examining their results. The relationship between oral microorganisms and birth outcomes and adverse labor outcomes was investigated; to provide sufficient evidence. The purpose of the present study was to evaluate periodontal disease in oral microorganisms during pregnancy.
Materials and Methods: All articles were published between January 2011 and January 2023 in international databases, including PubMed, Scopus, Science Direct, and Embase. To answer the research questions, the Google Scholar search engine employed the PECO strategy. STATA.V17 software was used to analyze the data.
Results: Two hundred and eighteen studies were found in the initial search; 63 full texts were reviewed; and finally, 14 articles were included in the analysis. The mean differences in salivary S. mutans carriage before and after prenatal dental treatment were 0.92 (MD; 95 CI [0.57, 1.27], $P > 0.05$). The odds ratio of association between perinatal mortality and periodontal treatment was −0.88 (OR; 95 CI [−2.53, 0.76], $P > 0.05$) and the odds ratio of association between pre-term birth and periodontal treatment was −0.31 (OR; 95 CI [−0.70, 0.09], $P > 0.05$). There was a statistically significant relationship between birth weight and periodontal treatment during pregnancy.
Conclusion: According to the present meta-analysis, periodontal treatment can reduce the odds ratio of perinatal mortality and pre-term birth by 88% and 31%, respectively. High association of microorganisms between pregnancy and postpartum requires further study.
Relevance for Patients: In the findings of the present study, it is observed that during pregnancy, there is a direct relationship between periodontal disease with low birth weight, perinatal mortality, and pre-term delivery; however, the high association of microorganisms between pregnancy and postpartum requires further study. Oral microforms are reported to be affected in pregnant women, and they should take extra care of their mouth and teeth. Sufficient and strong evidence can help to improve the health outcomes of mothers and children.

1. Introduction

During pregnancy, physiological changes occur in the body of women. In general, these changes maintain stable conditions for the mother and fetus; hormonal changes and dietary changes in pregnant women increase the risk of oral diseases such as periodontal disease and tooth decay [1]. In pregnant women, studies have shown that these changes

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affect the microbial composition of the body [2]. The human oral microbiome database has identified over 700 commensals that are present in the oral cavity, creating a complex and diverse microbiome [3]. Microbial changes in the mouth can affect both mother and baby. It is essential to study the relationship between oral microbial changes and birth outcomes [4]. Changes in the oral microbiota during pregnancy and the increased risk of oral diseases in pregnant women should be studied to take appropriate measures by examining the diversity of components of the oral microbiome and their relationship to birth outcomes [5]. According to studies on pregnant women, tooth decay is associated with an increased risk of *Streptococcus mutans* [6,7].

Other studies have shown that increased levels of periodontal pathogens are more common in pregnant women. However, there needs to be stronger and more sufficient evidence. Further studies should examine these findings to reach a definite consensus by comprehensively evaluating the available evidence. In a recent systematic review, it was reported that there was a positive association between adverse pregnancy outcomes and periodontal disease [8-10]. Studies also show that periodontal disease is likely to have an effect on birth outcomes, including the delivery of premature and low birth weight babies. However, there are contradictions between the findings of the studies [11-15]. In a narrative review by Tettamanti *et al.* (2017), observed that there was no relationship between periodontal disease and adverse pregnancy outcomes, and periodontal disease treatment during pregnancy does not provide overall protection against adverse pregnancy outcomes [16]. According to research, *Porphyromonas gingivalis* has a higher prevalence of oral microorganisms in women with pre-term labor [17].

On the other hand, studies have shown that diagnosing periodontal anaerobes in subgingival plaque can reduce the risk of preterm delivery [18]. However, studies have reported conflicting results that there is no direct link between increased periodontal bacteria and preterm labor [19]. Therefore, reviewing the results of various studies related to oral microorganisms and birth outcomes is important. Because maternal oral health is directly related to infant health, the vertical transmission of oral pathogens from mother to infant should be carefully considered. According to the findings of studies, reducing maternal oral pathogens during pregnancy is very important and, on the other hand, can reduce oral pathogens in the baby's oral cavity. Therefore, in the present study, the potential changes of oral microbes during pregnancy were investigated by examining the findings of the previous studies and comprehensively examining their results. The relationship between oral microorganisms and birth outcomes and adverse labor outcomes was investigated; to provide sufficient evidence.

2. Materials and Methods

Databases of PubMed, Scopus, Science Direct, ISI, Web of Knowledge, and Embase were searched for systematic literature between January 2011 and January 2023. A review of the results of studies from the past 10 years can provide newer results. Use the MeSH Database to build searches in PubMed:

("Pregnancy"[Mesh]) OR ("Pregnancy Trimesters"[Mesh] OR "Pregnancy Trimester, Third"[Mesh] OR "Pregnancy Trimester, Second"[Mesh] OR "Pregnancy Trimester, First"[Mesh])) OR "Postpartum Period"[Mesh]) AND "Oral Health"[Mesh] AND "Mouth"[Mesh]) AND "Microbiota"[Mesh]) AND "Dental Care"[Mesh]) AND "Microorganisms, Genetically-Modified"[Mesh]) AND "Pregnancy Complications"[Mesh]) AND ("Premature Birth"[Mesh] OR "Term Birth"[Mesh] OR "Live Birth"[Mesh])) AND "Periodontal Index"[Mesh].

Key considerations PRISMA was the basis of the present study [20] and PECO strategy to answer the research questions as shown in Table 1.

2.1. Eligibility criteria

Inclusion criteria: Only articles published in English, randomized clinical trials, prospective and retrospective studies, sample size above 10, and complete data were included in the study.

Exclusion criteria: Case studies, case reports and reviews papers; studies without full text access were excluded from the study.

2.2. Selection of the study, data extraction, and analysis methods

Data from studies were reported according to the study, year, design, age, patient number, group, sample source, and microorganisms. The quality of randomized control clinical trial studies was evaluated using the Cochrane Collaboration's tool [21]. High and unclear risk received a scale score of 0, while the low risk scored 1. The scores on the scale range from 0 to 6. High quality means a higher score. The quality of studies was measured using Risk of Bias in Non-Random Studies of Interventions (ROBINS-I) [22]. The categories for risk of bias judgements are "Low risk", "Moderate risk", "Serious risk", and "Critical risk" of bias. Importantly, "Low risk" corresponds to the risk of bias in a high-quality randomized trial. The response options are: "Yes", "Probably yes", "Probably no", "No, and "No information". Responses of "Yes" are intended to have similar implications to responses of "Probably yes" (and similarly for "No" and "Probably no").

The full texts and abstracts of the included articles were reviewed by two blinded reviewers who independently extracted data. Before the screening, the level of agreement between the reviewers was evaluated using kappa statistics. The 95% confidence interval for mean differences and the risk ratio with invariance or Mantel-Haenszel was calculated because the kappa

Table 1. PECO strategy

PECO strategy	Description
P	Population: Pregnant women
E	Exposure: Oral microorganisms
C	Comparison: Pregnancy stages, during pregnancy, pregnant and non-pregnant women
O	Outcome: Oral microbial, periodontal disease, and birth outcome

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values were higher than 0.80. Random effects were utilized to address potential heterogeneity, and I^2 showed heterogeneity. The level of heterogeneity was evaluated using the I^2 index test ($I^2 < 50\%$ = Low levels, $50 < I^2 < 75\%$ = Moderate and $I^2 > 75\%$ = High levels). STATA.V17 software was used for the data analysis.

3. Results

After the initial search for articles in databases, 282 articles were identified. Duplicate articles were removed (n = 80) after all articles were imported into the EndNote.X8 software. In the second step, 202 articles were entered and examined. After being reviewed for titles and abstracts, 139 unrelated articles were excluded from the study. The full text of 63 articles was reviewed in the third stage. Finally, 15 articles that met the inclusion criteria and were published between January 2011 and January 2023 entered the analysis (Figure 1).

3.1. Characteristics

The present article includes one retrospective study, five cross-sectional studies, six RCT studies, and three prospective cohorts. The sample size was 1,388,272 (Table 2). The sample source and microorganisms evaluated are reported in Table 2.

3.2. Risk assessment

According to Cochrane Collaboration's tool, six randomized clinical trial study had high quality (low risk of bias) and according to ROBINS-I tool, six studies had low risk of bias and three studies had Middle risk of bias (Tables 3 and 4).

3.3. Effect of pregnancy status on Candida carriage in saliva

The mean difference of oral *Candida* during pregnancy between pregnant and non-pregnant women was 0.05 (MD; 95 CI (0.03 – 0.08), $P > 0.05$) ($I^2 = 0.00\%$; $P = 0.45$). According to Figure 2, no difference was observed between groups (Figure 2).

The mean difference of *Candida* carriage between non-pregnancy and first trimester was 0.31 (MD; 95 CI (0.15 – 0.47), $P > 0.05$) ($I^2 = 0.00\%$; $P = 0.33$). According to Figure 2, no difference was observed between groups (Figure 2).

The mean difference of *Candida* carriage between non-pregnancy and third trimester was 0.69 (MD; 95 CI (0.31 – 1.08), $P > 0.05$)

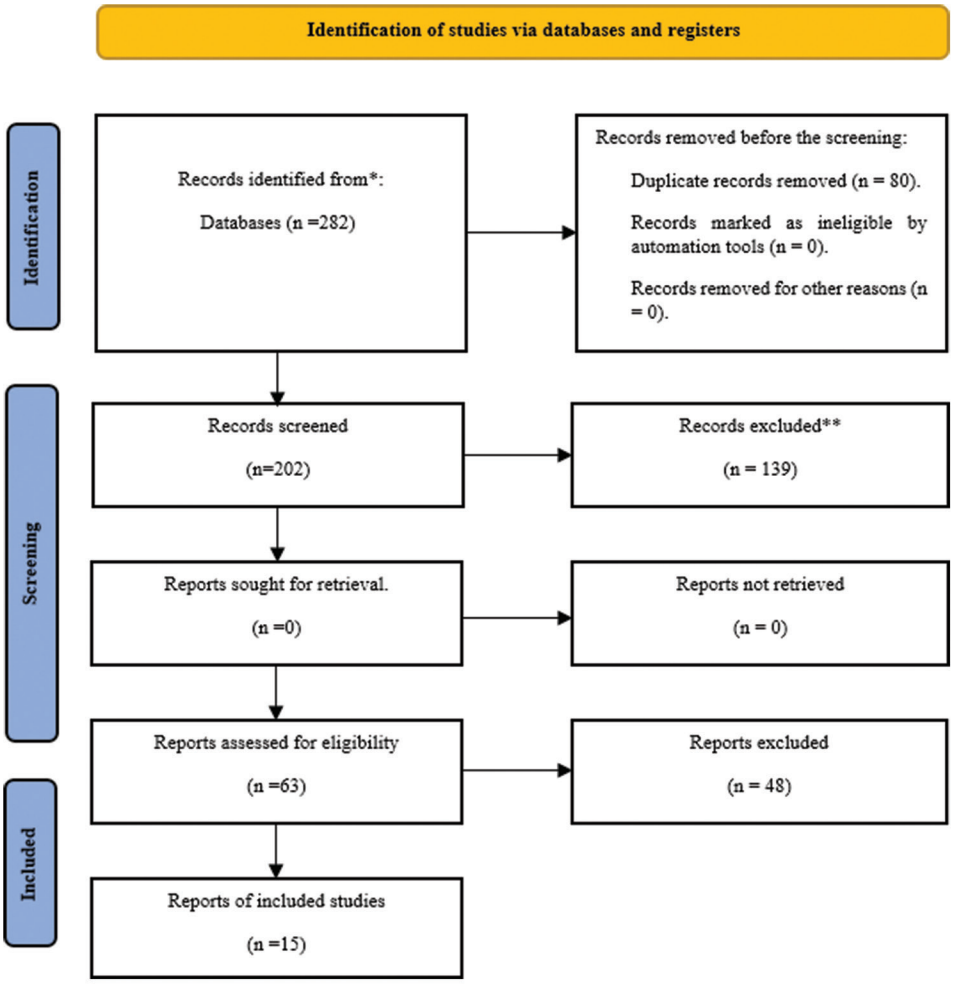

Figure 1. PRISMA 2020 checklist.

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Table 2. Summary of studies characteristics

Study. years	Study design	Sample size		Source	Microorganisms
		Experimental group	Control group		
Chen *et al*., 2022 [23]	Retrospective	1,386,887		Periodontal emergency treatment	NR
Aikulola *et al*., 2020 [24]	Cross-sectional	26	32	Oral swab	*S. aureus, N. catarrhalis, K. pneumonia, E. coli, P. melaninogenicus, P. propionicum, V. pervula, S. viridans, Coagulase negative Staphylococcus*
Huang *et al*., 2020 [25]	Cross-sectional	84	33	Saliva	*P. gingivalis, P. intermedia, P. nigrescens*
Sparvoli *et al*., 2020 [26]	Cross-sectional	42	18	Oral swab	NR
Wagle *et al*., 2020 [27]	Cross-sectional	38	50	Saliva	*S. mutans, Lactobacillus*
Escalante-Medina *et al*., 2019 [28]	RCT	23	22	Saliva	*S. mutans*
Xiao *et al*., 2019 [29]	Cross-sectional	48	34	Saliva, mucosal swabs	*C. albicans, C. glabrata, C. tropicalis, C. krusei, C. dubliniensis, S. mutans*
Asad *et al*., 2018 [30]	RCT	32	32	Saliva	*S. mutans*
Fujiwara *et al*., 2017 [31]	Prospective cohort	26	32	Subgingival plaque, saliva	Subgingival *A. actinomycetemcomitans, P. gingivalis, P. intermedia, F. nucleatum Saliva Above 4+Streptococci, Staphylococci, Candida spp.*
Rio *et al*., 2017 [32]	Prospective cohort	30	30	Saliva	Yeast
Khairnar *et al*., 2015 [33]	RCT	100		NR	Periodontal disease
Pirie *et al*., 2013 [34]	RCT	99		NR	Periodontal disease
Weidlich *et al*., 2013 [35]	RCT	299		NR	Periodontal disease
Oliveira *et al*., 2011 [36]	RCT	225		NR	Periodontal disease
Volpato *et al*., 2011 [37]	Prospective cohort	30		Saliva	*S. mutans*

S. aureus: Staphylococcus aureus, N. catarrhalis: Moraxella catarrhalis, K. pneumonia: Klebsiella pneumonia, E. coli: Escherichia coli, P. melaninogenicus: Prevotella melaninogenica, P. propionicum: Propionibacterium propionicum, V. pervula: Veillonella parvula, S. viridans: Streptococcus viridans, P. gingivalis: Porphyromonas gingivalis, P. intermedia: Prevotella intermedia, P. nigrscens: Prevotella nigrescens, S. mutans: Streptococcus mutans, C. albicans: Candida albicans, C. glabrata: Candida glabrata, C. tropicalis: Candida tropicalis, C. krusei: Candida krusei, C. dubliniensis: Candida dubliniensis, A. actinomycetemcomitans: Aggregatibacter actinomycetemcomitans

Table 3. Risk of bias assessment (Cochrane Collaboration's tool)

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Total score
Escalante-Medina *et al*., 2019 [28]	+	+	?	+	+	+	5
Asad *et al*., 2018 [30]	+	+	?	+	+	+	5
Khairnar *et al*., 2015 [33]	+	+	?	+	+	+	5
Pirie *et al*., 2013 [34]	+	+	?	+	?	+	4
Weidlich *et al*., 2013 [35]	+	+	?	+	+	+	5
Oliveira *et al*., 2011 [36]	+	+	?	+	?	+	4

($I^2 = 0.00\%$; $P = 0.78$). According to Figure 2, no difference was observed between groups (Figure 2).

3.4. Salivary S. mutans carriage

The mean differences in salivary *S. mutans* carriage before and after prenatal dental treatment was 0.92 (MD; 95 CI (0.57 – 1.27), $P > 0.05$) ($I^2 = 56.33\%$; $P = 0.13$). Figure 3 shows no difference between before and after prenatal dental treatment on salivary *S. mutans* reduction (Figure 3).

3.5. Perinatal mortality

The odds ratio of association between perinatal mortality and periodontal treatment was −0.88 (OR; 95 CI (−2.53, 0.76), $P > 0.05$) ($I^2 < 0\%$; $P = 0.97$). A statistically significant relationship

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Table 4. Bias assessment (ROBINS-I)

Study, years	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall
Chen *et al*., 2022 [23]	Low	Low	Low	Low	Low	Low	Low	Low
Aikulola *et al*., 2020 [24]	Low	Low	Low	Low	Low	Low	Low	Low
Huang *et al*., 2020 [25]	Low	Low	Low	Low	Low	Low	Low	Low
Sparvoli *et al*., 2020 [26]	Low	Low	Low	Low	Low	Low	Low	Low
Wagle *et al*., 2020 [27]	Low	Low	Low	Low	Low	Low	Low	Low
Xiao *et al*., 2019 [29]	Low	Low	Low	Low	Low	Middle	Low	Middle
Fujiwara *et al*., 2017 [31]	Low	Low	Low	Low	Low	Low	Middle	Middle
Rio *et al*., 2017 [32]	Low	Low	Low	Low	Low	Low	Low	Low
Volpato *et al*., 2011 [37]	Low	Low	Low	Low	Low	Middle	Low	Middle

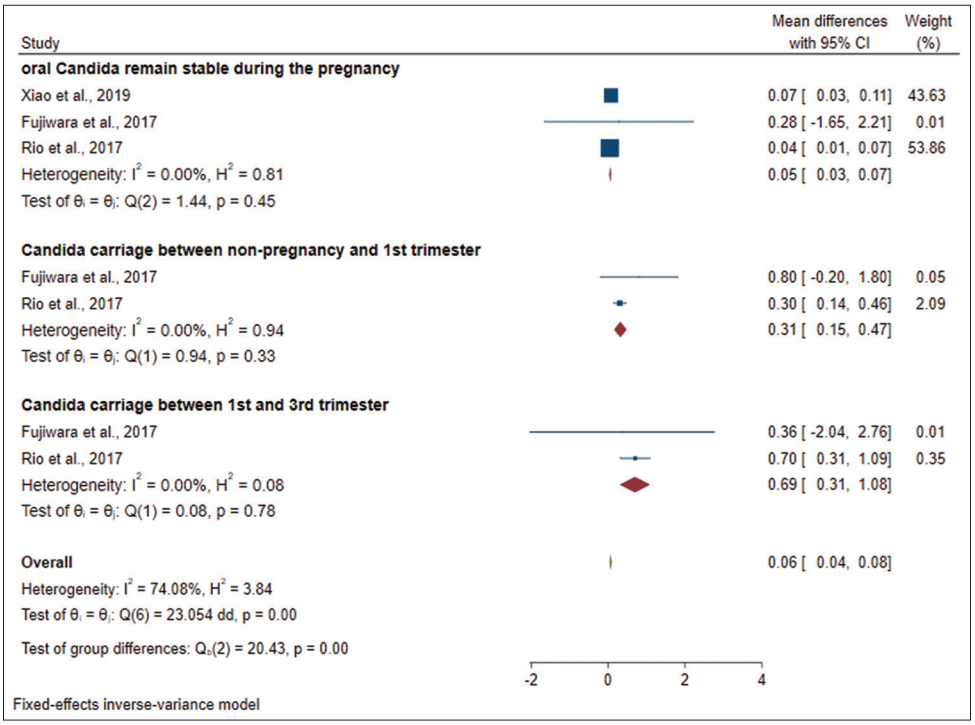

Figure 2. The forest plot showed oral Candida carriage in pregnant women.

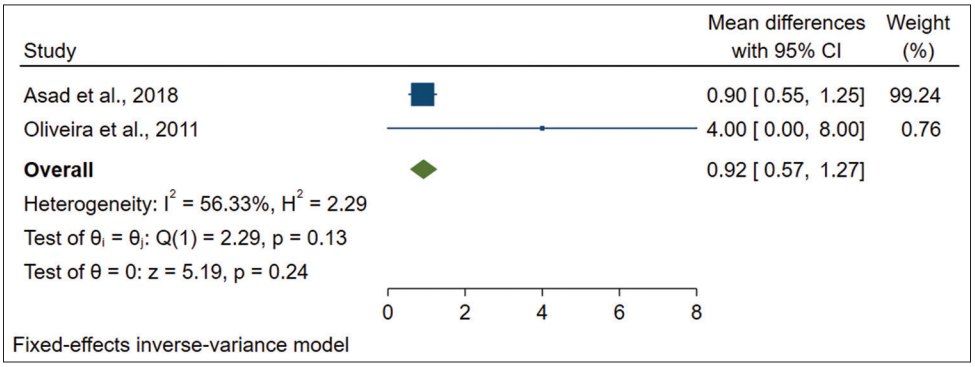

Figure 3. The forest plot showed salivary *Streptococcus mutans* carriage.

was observed between perinatal mortality and periodontal treatment during pregnancy (P = 0.02), so that periodontal treatment can reduce the odds ratio of perinatal mortality by 88% (Figure 4).

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3.6. Preterm birth

The odds ratio of association between pre-term birth and periodontal treatment was −0.31 (OR; 95 CI (−0.70 – 0.09), $P > 0.05$) ($I^2 = 80.44\%$; $P = 0.00$). Figure 5 shows a statistically significant relationship between pre-term birth and periodontal treatment during pregnancy ($P = 0.03$) (Figure 5). Periodontal treatment can reduce the odds ratio of preterm birth by 31%.

3.7. Birth weight

The mean difference in birth weight between the periodontal treatment group and control group was 1099.37 gr (MD; 95 CI (1095.18 g, 1103.57 g), $P < 0.05$) ($I^2 = 98.34\%$; $P = 0.00$). Figure 6 shows a statistically significant relationship between birth weight and periodontal treatment during pregnancy ($P = 0.00$) (Figure 6). Based on this, birth weight increases with periodontal disease treatment.

4. Discussion

According to the available evidence, women are more prone to oral diseases during pregnancy due to microbial changes in the mouth that increase during pregnancy. In the present study, reviewing the articles attempted to report the relationship between pregnancy and oral microbial changes. Selected studies have reported that oral microbes are more common in pregnant women than in non-pregnant or postpartum women. Based on the present meta-analysis, this evidence is confirmed. The expansion of pathogenic bacteria or opportunistic pathogens

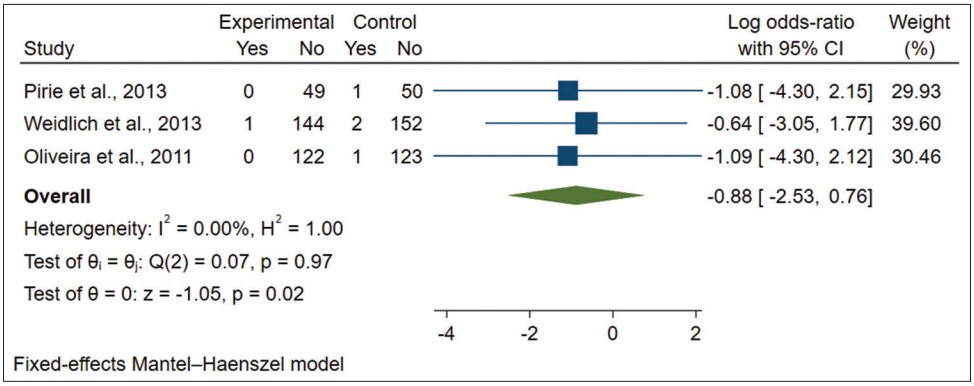

Figure 4. The forest plot showed perinatal mortality.

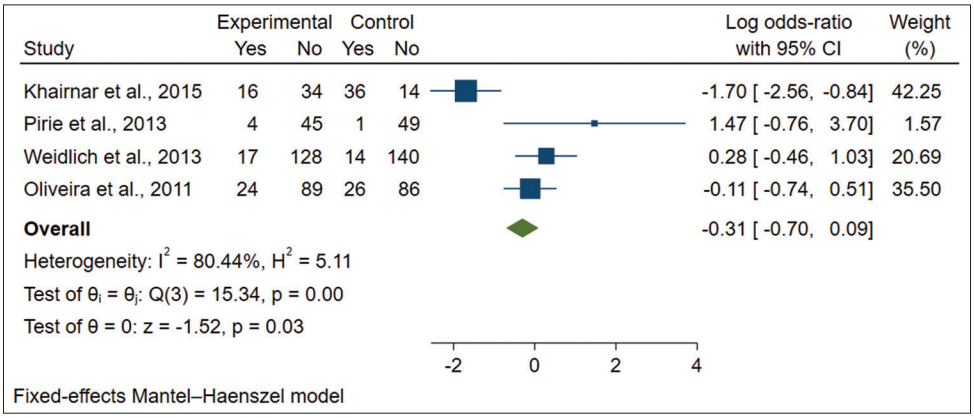

Figure 5. The forest plot showed Preterm birth.

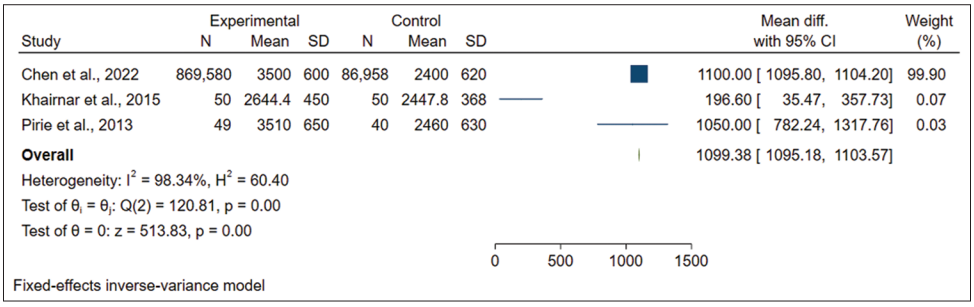

Figure 6. The forest plot showed Birth weight.

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that cause oral diseases, including tooth decay and periodontal disease, might result from an unstable oral microbial community environment [38,39]. According to the previous studies, changes in pregnancy, including changes in the hormones estrogen and progesterone, can affect the microbial balance of the mouth and increase the pH of the oral cavity as a result of vomiting during pregnancy and high simple sugar intake during gestation make these people more susceptible to oral diseases and put teeth [40]. Pregnant women have higher levels of *P. gingivalis*, prevotella intermedia, and more gingivitis [41]. This increase makes pregnant women susceptible to periodontal disease [8,42]. Based on the previous studies and the findings of the present meta-analysis, a significant relationship was observed between adverse birth outcomes and periodontal disease during pregnancy. In addition, the meta-analysis showed that pregnant women with periodontal disease had a higher risk of preterm delivery.

The findings of other studies are consistent with the present study [42]. In the previous studies, *P. gingivalis* levels were higher in women who gave birth prematurely [43]. Women with preeclampsia who had adverse birth outcomes were more likely to be diagnosed with periodontal disease with *P. gingivalis* and *Eikenella corrodens*. In the present study, because one variable was mentioned in each article and some studies could not perform a meta-analysis; few studies were included in the meta-analysis. By examining the findings of the meta-analysis, it was found that there is a direct relationship between the adverse outcomes of childbirth and microbial changes in the mouth during pregnancy. Meta-analysis showed a direct relationship between low birth weight and pre-term delivery. Other studies confirm the results of the present study [43]. Some recent studies are inconsistent with the present study's findings and have not reported an association between adverse delivery outcomes and periodontal disease [44,45]. Therefore, more studies should be done because this issue is very controversial and challenging. Study findings also show that higher levels of quantitative microorganisms are observed in women with pre-term delivery [18,43]. Based on the findings of other studies, no significant relationship has been reported between the level of bacteria under the gums and the increased risk of adverse birth outcomes [19,46]. Some studies have reported that maintaining good oral hygiene during pregnancy can reduce the risk of periodontal disease, or treating periodontal disease before 21 weeks of gestation can prevent adverse birth outcomes and the risk of pre-term birth. Reduce to 6% [47]. As a result, pregnant women should take care of their oral health and not miss a visit to the dentist, and effective treatments should be considered to reduce the adverse consequences of childbirth.

Due to the high heterogeneity between studies in some investigated parameters, the results of the present study should be interpreted with caution; this heterogeneity can be related to the cognitive methodology of the studies. More studies with a larger statistical population and using similar tools are needed.

5. Conclusion

Based on the findings of the present study, it is observed that during pregnancy, there is a direct relationship between periodontal disease with low birth weight, perinatal mortality, and preterm delivery; however, the high association of microorganisms between pregnancy and postpartum requires further study. Oral microforms are reported to be affected in pregnant women, and they should take extra care of their mouth and teeth; further studies are needed to confirm the available evidence. Extensive studies are also needed to understand the relationship between periodontal disease and adverse birth outcomes due to the differences between study results. Sufficient and strong evidence can help to improve the health outcomes of mothers and children.

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Conflicts of Interest

The authors declared that there are no conflicts of interest.

References

[1] Remaschi G, Ricci S, Cortimiglia M, De Vitis E, Iannuzzi L, Boni L, *et al.* TREC and KREC in Very Preterm Infants: Reference Values and Effects of Maternal and Neonatal Factors. J Matern Fetal Neonatal Med 2021;34:3946-51.

[2] Ekwebene OC, Nnamani CP, Edeh CG, Obidile CV, Tyotswame YS. Prevalence of Falciparum Malaria in Conjunction with Age, Gravidity, Abo Blood Group/ Rhesus Factor, and Genotype among Gravid Women in South-Eastern Nigeria. Int J Sci Res Dent Med Sci 2021;3:12-7.

[3] Neuman H, Koren O. The Pregnancy Microbiome. In: Intestinal Microbiome: Functional Aspects in Health and Disease. Vol. 88. Playa del Carmen: Nestlé Nutrition Institute Workshop; 2017. p. 1-10.

[4] Yao Y, Cai X, Chen C, Fang H, Zhao Y, Fei W, *et al.* The Role of Microbiomes in Pregnant Women and Offspring: Research Progress of Recent Years. Front Pharmacol 2020;11:643.

[5] Sugino KY, Paneth N, Comstock SS. Michigan Cohorts to Determine Associations of Maternal Pre-pregnancy Body Mass Index with Pregnancy and Infant Gastrointestinal Microbial Communities: Late Pregnancy and Early Infancy. PLoS One 2019;14:e0213733.

[6] Javed M, Chaudhry SI, Butt S, Ijaz S, Awais F, Khan A. Transmission of *Streptococcus mutans* from Mother to Child. Pak Oral Dent J 2012;32:493-6.

[7] Kloetzel MK, Huebner CE, Milgrom P. Referrals for Dental Care during Pregnancy. J Midwifery Womens Health 2011;56:110-7.

[8] Borgo PV, Rodrigues VA, Feitosa AC, Xavier KC, Avila-Campos MJ. Association between Periodontal

Condition and Subgingival Microbiota in Women during Pregnancy: A Longitudinal Study. J Appl Oral Sci 2014;22:528-33.

[9] Emmatty R, Mathew JJ, Kuruvilla J. Comparative Evaluation of Subgingival Plaque Microflora in Pregnant and Non-pregnant Women: A Clinical and Microbiologic Study. J Indian Soc Periodontol 2013;17:47-51.

[10] Jang H, Patoine A, Wu TT, Castillo DA, Xiao J. Oral Microflora and Pregnancy: A Systematic Review and Meta-analysis. Sci Rep 2021;11:16870.

[11] Corbella S, Taschieri S, Del Fabbro M, Francetti L, Weinstein R, Ferrazzi E. Adverse Pregnancy Outcomes and Periodontitis: A Systematic Review and Meta-analysis Exploring Potential Association. Quintessence Int 2016;47:193-204.

[12] Dörtbudak O, Eberhardt R, Ulm M, Persson GR. Periodontitis, a Marker of Risk in Pregnancy for Preterm Birth. J Clin Periodontol 2005;32:45-52.

[13] Uriza CL, Velosa-Porras J, Roa NS, Lara SM, Silva J, Ruiz AJ, *et al.* Periodontal Disease, Inflammatory Cytokines, and PGE_2 in Pregnant Patients at Risk of Preterm Delivery: A Pilot Study. Infect Dis Obstet Gynecol 2018;2018:7027683.

[14] Turcu-Duminică A, Dumitriu AS, Paunica S, Gică C, Botezatu R, Gică N, *et al.* Periodontitis as a Potential Risk Factor for Premature Delivery. J Mind Med Sci 2021;8:27-33.

[15] Santana DD, Kac G, Dos Santos PP, da Silva TC, Benaim C, Cocate PG, *et al.* Association between Pre-pregnancy BMI and Inflammatory Profile Trajectories during Pregnancy and Postpartum in Brazilian Women with Periodontitis: The IMPROVE Trial. Int J Environ Res Public Health 2022;19:2705.

[16] Tettamanti L, Lauritano D, Nardone M, Gargari M, Silvestre-Rangil J, Gavoglio P, *et al.* Pregnancy and Periodontal Disease: Does Exist a Two-way Relationship? Oral Implantol (Rome) 2017;10:112-8.

[17] Lee YL, Hu HY, Chou SY, Lin CL, Cheng FS, Yu CY, *et al.* Periodontal Disease and Preterm Delivery: A Nationwide Population-based Cohort Study of Taiwan. Sci Rep 2022;12:3297.

[18] Andonova I, Iliev V, Živković N, Sušič E, Bego I, Kotevska V. Can Oral Anaerobic Bacteria Cause Adverse Pregnancy Outcomes. Pril (Makedon Akad Nauk Umet Odd Med Nauki) 2015;36:137-43.

[19] Costa EM, de Araujo Figueiredo CS, Martins RF, Ribeiro CC, Alves CM, Sesso ML, *et al.* Periodontopathogenic Microbiota, Infectious Mechanisms and Preterm Birth: Analysis with Structural Equations (Cohort-brisa). Arch Gynecol Obstet 2019;300:1521-30.

[20] Mardany A, Pornamazeh T, Ahmadvand A, Vatandoust MT, Mirmalek SP, Soltanian M. The Comparison of the Bonding Performance between the New Flash-free Orthodontic Bracket Bonding System and the Traditional Bracket Bonding System: A Systematic Review and Meta-analysis. Int J Sci Res Dent Med Sci 2022;4:196-200.

[21] Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, *et al.* The Cochrane Collaboration's Tool for Assessing Risk of Bias in Randomised Trials. BMJ 2011;343:d5928.

[22] Elfeky A, Gillies K, Gardner H, Fraser C, Ishaku T, Treweek S. Non-randomised Evaluations of Strategies to Increase Participant Retention in Randomised Controlled Trials: A Systematic Review. Syst Rev 2020;9:224.

[23] Chen JJ, Wu DR, Lin WS, Chen IC, Liu JF, Chen HL, *et al.* Impact of Scaling and Periodontal Treatment during Pregnancy on the Risk of Adverse Birth Outcomes. J Pers Med 2022;12:137.

[24] Aikulola OO, Okoje VN, Adesina OA. Comparative Study of Oral Health and Microbial Flora in Pregnant and Non-pregnant Women in Ibadan, Nigeria. Afr J Biomed Res 2020;23:31-5.

[25] Huang Z, DerGarabedian BP, He L, Sha Y, Chen Z, Kang J, *et al.* Impact of Periodonto-pathogenic Microbiota and Sociodemographic Variables on Periodontal Status during Pregnancy and Postpartum Period. Oral Health Prev Dent 2020;18:855-64.

[26] Sparvoli LG, Cortez RV, Daher S, Padilha M, Sun SY, Nakamura MU, *et al.* Women's Multisite Microbial Modulation during Pregnancy. Microb Pathog 2020;147:104230.

[27] Wagle M, Basnet P, Vartun Å, Trovik TA, Acharya G. Oxidative Stress Levels and Oral Bacterial Milieu in the Saliva from Pregnant vs. Non-pregnant Women. BMC Oral Health 2020;20:245.

[28] Escalante-Medina RP, Asmat-Abanto AS, Ruiz-Barrueto MA. Effect of a Commercial Toothpaste Containing Xylitol on the Count of *Streptococcus Mutans* in Saliva of Pregnant Women: Randomized Controlled Clinical Trial. Int J Odontostomatol 2019;13:316-20.

[29] Xiao J, Fogarty C, Wu TT, Alkhers N, Zeng Y, Thomas M, *et al.* Oral Health and *Candida* Carriage in Socioeconomically Disadvantaged US Pregnant Women. BMC Pregnancy Childbirth 2019;19:480.

[30] Asad R, Khan KA, Javed T, Arshad MB, Chaudhary A, Khan AA. Effect of Atraumatic Restorative Treatment on *Streptococcus mutans* Count in Saliva of Pregnant Women: A Randomized Controlled Trial. Ann King Edward Med Univ 2018;24:957-60.

[31] Fujiwara N, Tsuruda K, Iwamoto Y, Kato F, Odaki T, Yamane N, *et al.* Significant Increase of Oral Bacteria in the Early Pregnancy Period in Japanese Women. J Investig Clin Dent 2017;8:e12189.

[32] Rio R, Simões-Silva L, Garro S, Silva MJ, Azevedo Á, Sampaio-Maia B. Oral Yeast Colonization Throughout Pregnancy. Med Oral Patol Oral Cir Bucal 2017;22:e144-8.

DOI: http://dx.doi.org/10.18053/jctres.09.202303.001

[33] Khairnar MS, Pawar BR, Marawar PP, Khairnar DM. Estimation of Changes in C-reactive Protein Level and Pregnancy Outcome after Nonsurgical Supportive Periodontal Therapy in Women Affected with Periodontitis in a Rural Set Up of India. Contemp Clin Dent 2015;6(Suppl 1):S5-11.

[34] Pirie M, Linden G, Irwin C. Intrapregnancy Non-surgical Periodontal Treatment and Pregnancy Outcome: A Randomized Controlled Trial. J Periodontol 2013;84:1391-400.

[35] Weidlich P, Moreira CH, Fiorini T, Musskopf ML, da Rocha JM, Oppermann ML, *et al.* Effect of Nonsurgical Periodontal Therapy and Strict Plaque Control on Preterm/Low Birth Weight: A Randomized Controlled Clinical Trial. Clin Oral Investig 2013;17:37-44.

[36] Oliveira AM, de Oliveira PA, Cota LO, Magalhães CS, Moreira AN, Costa FO. Periodontal Therapy and Risk for Adverse Pregnancy Outcomes. Clin Oral Investig 2011;15:609-15.

[37] Volpato FC, Jeremias F, Spolidório DM, da Silva SR, Junior AV, Rosell FL. Effects of Oral Environment Stabilization Procedures on *Streptococcus mutans* Counts in Pregnant Women. Braz Dent J 2011;22:280-4.

[38] Wade WG. The Oral Microbiome in Health and Disease. Pharmacol Res 2013;69:137-43.

[39] Gao L, Xu T, Huang G, Jiang S, Gu Y, Chen F. Oral Microbiomes: More and More Importance in Oral Cavity and Whole Body. Protein Cell 2018;9:488-500.

[40] Casas R, Barquero SC, Estruch R. Impact of Sugary Food Consumption on Pregnancy: A Review. Nutrients 2020;12:3574.

[41] Kandan PM, Menaga V, Kumar RR. Oral Health in Pregnancy (Guidelines to Gynaecologists, General Physicians and Oral Health Care Providers). J Pak Med Assoc 2011;61:1009-14.

[42] Lin W, Jiang W, Hu X, Gao L, Ai D, Pan H, *et al.* Ecological Shifts of Supragingival Microbiota in Association with Pregnancy. Front Cell Infect Microbiol 2018;8:24.

[43] Ye C, Katagiri S, Miyasaka N, Bharti P, Kobayashi H, Takeuchi Y, *et al.* The Anti-phospholipid Antibody-dependent and Independent Effects of Periodontopathic Bacteria on Threatened Preterm Labor and Preterm Birth. Arch Gynecol Obstet 2013;288:65-72.

[44] Daly CG, Mitchell DH, Highfield JE, Grossberg DE, Stewart D. Bacteremia Due to Periodontal Probing: A Clinical and Microbiological Investigation. J Periodontol 2001;72:210-4.

[45] 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(Suppl 3):22-36; discussion 37-8.

[46] Lin D, Moss K, Beck JD, Hefti A, Offenbacher S. Persistently High Levels of Periodontal Pathogens Associated with Preterm Pregnancy Outcome. J Periodontol 2007;78:833-41.

[47] Merchant AT, Sutherland MW, Liu J, Pitiphat W, Dasanayake A. Periodontal Treatment among Mothers with Mild to Moderate Periodontal Disease and Preterm Birth: Reanalysis of OPT Trial Data Accounting for Selective Survival. Int J Epidemiol 2018;47:1670-8.

DOI: http://dx.doi.org/10.18053/jctres.09.202303.001