Chapter 86

Pregnancy and periodontal disease: A review of the literature

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Fernando Mauricio Villalta Mendoza
Universidad de Cuenca, Ecuador
E-mail: fernandovillalta4@gmail.com

Scarlett Maribel Pesántez Correa
Universidad Católica de Cuenca, Ecuador
E-mail: scarlett17pc@gmail.com

Jhonny Leonel González Ortega
Universidad de Cuenca, Ecuador
E-mail: jgonzalez3.95@live.com

Andrea Belén Ochoa Ávila
Universidad de Cuenca, Ecuador
E-mail: belenochoaav@hotmail.com

Christian Daniel Piedra Arpi
Universidad de Cuenca, Ecuador
E-mail: cpiedra99@gmail.com

Jorge Antonio Reinoso Ortiz
University of Cuenca, Ecuador
E-mail: parkingjorge@gmail.com

ABSTRACT
Objective: The objective of the study is to determine the relationship and the impact that periodontal diseases have during pregnancy for both the pregnant woman and the fetus. Methodology: An exhaustive search of the literature was carried out in the "PUBMED", "Science Direct", "Scopus" and "Ebsco" databases using the keywords: "Pregnancy", "Periodontal Disease", "Gingivitis", " Periodontitis"; where a total of 20 articles that met the inclusion and exclusion criteria could be obtained. Results: Periodontal disease has serious consequences on the development of the fetus due to the imbalance between the patient's immunity and the presence of pathogenic periodontal microorganisms. Conclusion: Periodontal disease is a risk factor to be taken into account during pregnancy, its early diagnosis and effective treatment will avoid any type of complication in the short or long term.

Keywords: Pregnancy, Periodontal disease, Gingivitis, Periodontitis.

1 INTRODUCTION

In recent years, it has been estimated that approximately 6 million perinatal deaths have occurred worldwide, where the main cause is premature birth. There is a relationship between periodontal diseases during pregnancy and alterations in the term of pregnancy. This is due to a gram-negative anaerobic bacteremia generated by the presence of gingival bacterial plaque, leading to the production of proinflammatory mediators that enter the hematogenous pathway through the gingival submucosa (Carvajal et al., 2020). All this leads to the development of an inflammatory response, which allows the suppression of growth factors at the fetal level and influences the labor process. All these alterations allow the long-term development of cardiovascular and metabolic pathologies in the neonate (Barbirato et al., 2019; Puertas et al., 2018; Uwitonze et al., 2018) .

Pregnancy generates several transitory changes in the female organism and compensatory modifications in several organs such as the oral cavity. Pregnant women are more predisposed to the development of periodontitis, gingivitis and gingival hyperplasia. Hormonal changes are believed to be the

direct link between periodontal disease and pregnancy. The presence of estrogen and progesterone receptors in the human periodontium affect the gingival inflammatory response due to the influence of chemotaxis, cytokine and antioxidant production from inflammatory cells by neutrophils, gingival fibroblasts and periodontal ligament cells which contributes to increased gingival inflammation. All this is exacerbated by the presence of periodontopathogenic microorganisms such as Porphyromona gingivalis, Prevotella intermedia and Campylobacter rectus (Barbirato et al., 2019; Puertas et al., 2018). The aim of the present research is to describe the impact of periodontal disease during pregnancy and the consequences that may occur for both the pregnant woman and the fetus.

2 METHODOLOGY

Narrative literature reviews are characterized by presenting a critical and objective analysis of a particular topic in the scientific literature. According to Barker et al. the search for information in the scientific literature and its subsequent analysis will allow obtaining solid results that contribute to obtain an answer to any topic (Baker, 2016). The present research was carried out based on an exhaustive search currently available, using the databases "PUBMED", "ScienceDirect", "Scopus" and "Ebsco" using the keywords: "Pregnancy", "Periodontal Disease", "Gingivitis", "Periodontitis" by means of the Boolean operator "AND", where a total of 20 scientific articles could be obtained.

The inclusion criteria consisted of secondary scientific studies related to the main research topic present in the previously described databases, which had to be publications in the English language. The search was limited to the last 5 years (2017-2022). On the other hand, the exclusion criteria were studies based on case reports, protocols, opinions, letters and short communications as well as research where the methodology was not clear and the probability of bias was high. Initially, the articles were selected based on their titles, to later analyze their abstracts and finally the complete article. Table 1 and Figure 1 are attached below, where the scheme used for the selection of the articles used in this research can be summarized in an orderly manner.

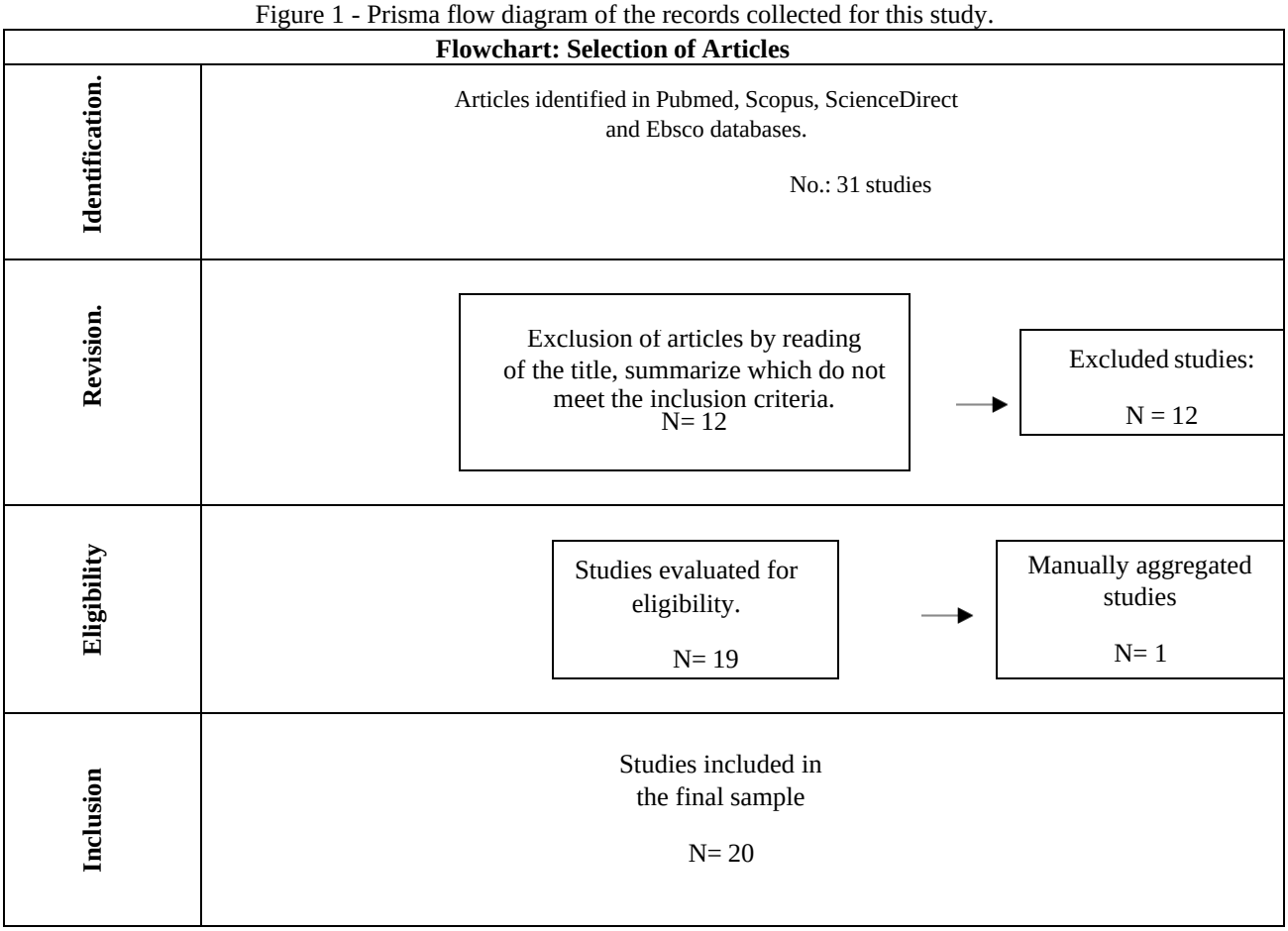
Table 1 - Articles selected for research.

Title	Author	Year	DOI
The Purpose, Process, and Methods of Writing aLiterature Review	Baker, J. D	2016	10.1016/j.aorn.2016.01.016
Association Between Periodontal Diseases and Adverse Gestational Outcomes: a Reviewof the Current Literature.	Barbirato, D., Rodrigues, M., Alves, J.,Castro, H., & Fogacci, M.	2019	10.1007/s40496-019-0209-3
Periodontal disease and adverse pregnancy outcomes.	Bobetsis, Y. A., Graziani, F., Gürsoy,M., & Madianos, P. N.	2020	10.1111/prd.12294
Periodontal disease and its impact on general health in Latin America. Section II: Introductionpart II.	Carvajal, P., Vernal, R., Reinero, D., Malheiros, Z., Stewart, B., Pannuti, C. M., & Romito, G. A.	2020	10.1590/1807-3107bor-2020.vol34.0023
Periodontal Disease and Pregnancy Outcomes:Overview of Systematic Reviews.	Daalderop, L. A., Wieland, B. V., Tomsin, K., Reyes, L., Kramer, B. W.,Vanterpool, S. F., & Been, J. V.	2018	10.1177/2380084417731097

Periodontal diseases and adverse pregnancy outcomes: Mechanisms.	Figuero, E., Han, Y. W., & Furuichi, Y		10.1111/prd.12295
Placental colonization with periodontal pathogens:the potential missing link.	Fischer, L. A., Demerath, E., Bittner-Eddy, P., & Costalonga, M.	2019	10.1016/j.ajog.2019.04.029
Periodontal disease and its impact on general health in Latin America. Section V: Treatment ofperiodontitis.	Fischer, R. G., Lira Junior, R., Retamal-Valdes, B., Figueiredo, L. C., Malheiros, Z., Stewart, B., & Feres, M.	2020	10.1590/1807-3107bor-2020.vol34.0026
Periodontal Conditions and Pathogens Associatedwith Pre-Eclampsia: A Scoping Review.	Gare, J., Kanoute, A., Meda, N., Viennot, S., Bourgeois, D., & Carrouel, F.	2021	10.3390/ijerph18137194
Periodontal diseases and adverse pregnancy outcomes.	Komine-Aizawa, S., Aizawa, S., & Hayakawa, S.	2019	10.1111/jog.13782
Can periodontal disease affect conception? A literature review.	Ludovichetti, F. S., Signoriello, A. G., Gobbato, E. A., Artuso, A., Stellini, E.,& Mazzoleni, S.	2021	10.1530/raf-20-0043
Pregnancy, parity and periodontal disease.	Morelli, E. L., Broadbent, J. M., Leichter, J. W., & Thomson, W. M.	2018	10.1111/adj.12623
Association of periodontitis with preterm birth andlow birth weight: a comprehensive review.	Puertas, A., Magan-Fernandez, A., Blanc, V., Revelles, L., O'Valle, F., Pozo, E., Mesa, F.	2018	10.1080/14767058.2017.1293023
Periodontology and pregnancy: An overview ofbiomedical and epidemiological evidence.	Raju, K., & Berens, L.	2021	10.1111/prd.12394
Periodontitis, female fertility and conception (Review).	Ricci, E., Ciccarelli, S., Agnese Mauri,P., Gerli, S., Favilli, A., Cipriani, S., Vignali, M., and Vignali, M., among others.	20221	10.3892/br.2022.1569
Oral microbiome and pregnancy: A bidirectionalrelationship.	Saadaoui, M., Singh, P., & Al Khodor,S.	2021	10.1016/j.jri.2021.103293
Calcium and Vitamin D Supplementation as Non-Surgical Treatment for Periodontal Disease with aFocus on Female Patients: Literature Review.	Sllamniku Dalipi, Z., & Dragidella, F.	2022	10.3390/dj10070120
Association between Maternal Periodontitis and Development of Systematic Diseases in Offspring.	Starzyńska, A., Wychowański, P., Nowak, M., Sobocki, B. K., Jereczek- Fossa, B. A., & Słupecka-Ziemilska, M.	2022	10.3390/ijms23052473
Pregnancy and periodontal disease: does a two-way relationship exist?	Tettamanti, L., Lauritano, D., Nardone,M., Gargari, M., Silvestre-Rangil, J., Gavoglio, P., & Tagliabue, A.	2017	10.11138/orl/2017.10.2.112
Periodontal diseases and adverse pregnancy outcomes: Is there a role for vitamin D?	Uwitonze, A. M., Uwambaye, P., Isyagi, M., Mumena, C. H., Hudder, A.,Haq, A., Razzaque, M. S.	2018	10.1016/j.jsbmb.2018.01.010
Oral microbiome shifts during pregnancy and adverse pregnancy outcomes: Hormonal and Immunologic changes at play.	Ye, C., & Kapila, Y.	2021	10.1111/prd.12386

Source: Authors (2022).

Figure 1 - Prisma flow diagram of the records collected for this study.



Source: Authors (2022).

3 RESULTS AND DISCUSSION

3.1 PERIODONTAL DISEASES: EPIDEMIOLOGY

Periodontal disease represents a very serious problem for pregnant women, as there is a predisposition for the development of gingivitis or periodontitis for them. In some ethnic groups, prevalences of 66.7% have been reported. Certain factors such as age, degree of education among others can negatively influence the importance of proper personal hygiene and dental checkups in pregnant patients (Starzyńska et al., 2022).

In 2010 periodontitis affected 743 million people around the world aged 15 - 99 years (Starzyńska et al., 2022). According to Raju K et al, the prevalence of periodontal diseases in pregnant women varies from 20-50%(Raju & Berens, 2021). Saadaoui et al. report that gingivitis affects 60-70% of pregnant women. However, gestation is not the causative agent in the development of any form of periodontal disease, but it does aggravate and exacerbate pre-existing conditions due to hormonal changes, lack of education, social inequity and other factors, which contribute negatively to the onset of periodontal disease in pregnancy (Saadaoui et al., 2021).

According to the CDC (Centers for Disease Control and Prevention) in the United States, the incidence of periodontal disease is 47.2% in populations over 30 years of age. Periodontal disease is much more common in patients of advanced age, low socio-economic strata, low education and smoking patients.

Similarly, the presence of concomitant systemic diseases such as diabetes mellitus provides the necessary risk for its progression (Starzyńska et al., 2022).

Unequal access to a public health system in populations with a vulnerable socioeconomic level can lead to the establishment of periodontal pathologies, being a risk factor for the development of any alteration periodontal, which is why intra- and extra-oral motivation and training by health professionals towards pregnant women is of utmost importance for the prevention of any oral morbidity (Morelli et al., 2018).

3.2 ETIOLOGY

Periodontal diseases have historically been described as gingivitis and periodontitis and are characterized by having a multifactorial component both in their onset and progression to more severe forms (Fischer et al., 2020). Initially, inflammation of bacterial origin occurs at the level of the gingival tissue, with time it progresses and negatively affects the supporting tissues: periodontium, alveolar bone, and tooth structure.

The first symptoms of gingivitis are: inflammation, bleeding gums, gingival pockets, redness at gingival level. When the etiological factors are not adequately treated, it can lead to progression of the disease and adding risk factors such as inadequate hygiene or systemic alterations it progresses to the appearance of periodontal pockets (<4mm depth at probing), destruction of periodontal connective tissue, alveolar bone, tooth movement, enlargement of the clinical crown of the tooth and even tooth loss(Starzyńska et al., 2022).

The main etiological cause of periodontal diseases is bacterial plaque, which predominantly presents Gram-negative bacteria such as: Aggregatibacter actinomycetemcomitans, Porphyromona gingivalis, Tannerella forsythia and Treponema denticola (Komine-Aizawa et al., 2019; Morelli et al., 2018; Puertas et al., 2018; Starzyńska et al., 2022). Gingivitis is a nonspecific inflammatory reaction where an increase in the number of bacteria (gram-positive and gram-negative) in or on the gingival sulcus are determinant for its establishment. In contrast, periodontitis is associated with the multiplication of gram- negative species inside the periodontal pockets which in turn favors a greater accumulation of bacteria and alterations in the type of microbiota (Starzyńska et al., 2022).

The inflammatory process is enhanced by the presence of inflammatory cells such as plasma cells, macrophages, T and B lymphocytes, which produce inflammatory mediators and immune complexes such as C-reactive protein (CRP), nitric oxide (NO), interleukin 1 (IL-1), interleukin 6 (IL-6) and tumor necrosis factor (TNF) which together with enzymes such as matrix metalloproteinases can destroy periodontal connective tissue and alveolar bone (Puertas et al., 2018). The development of periodontitis is not due to a history of gingivitis but is characterized as a multifactorial disease where an alteration of the balance between the host immune system and the periodontal pathogenic bacteria is generated, resulting in an alteration of immunity, which added to predisposing factors such as advanced age, genetic factors, smoking,

diabetes, stress, osteoporosis and other comorbidities allow its development (Saadaoui et al., 2021; Starzyńska et al., 2022).

3.3 PERIODONTAL DISEASE AND PREGNANCY:

According to the European Federation of Periodontology they describe two mechanisms that allow understanding the relationship between periodontal disease and alterations during gestation, these are:

-Direct mechanism: where oral microorganisms with their components invade the placenta through hematogenous dissemination (Figuero et al., 2020).

-Indirect mechanism: given by local inflammatory mediators produced by periodontal tissues that directly affect the placenta-foetus unit (Figuero et al., 2020).

Gingival inflammation can lead to pathological changes in the oral cavity, adding the immune response and the production of inflammatory mediators will favor the appearance of periodontitis, which in turn generates a greater inflammation cascade thanks to the presence of several types of microorganisms (Figuero et al., 2020).

Similarly, sex steroid hormones represent a key factor to consider due to the presence of specific receptors for these hormones at the level of gingival fibroblasts and epithelial cells, which are involved in gingival changes during pregnancy. These hormones act at the level of blood vessels increasing vascular permeability and contributing to gingival changes. Progesterone is the main hormone related to these changes, but estrogen is also considered to be responsible for several vascular changes at the level of the gingiva as well as at the uterine level (Morelli et al., 2018).

Hormonal changes at the end of the pregnancy period allow the release of proinflammatory cytokines in maternal serum, which initiates the production of prostaglandins in the myometrium and leads to uterine contraction. The presence of these mediators such as IL6, IL 8 and IL1 are secreted by inflammatory cells from the periodontium into the blood vessels and can spread to various organs and tissues. It has been hypothesized that this inflammatory cascade may indirectly influence the onset of labor in the last weeks of gestation (Bobetsis et al., 2020; Ye & Kapila, 2021).

The relationship between periodontal diseases and pregnancy is closely linked to the biological activity of periodontopathogenic bacteria, which together with inflammatory mediators generated locally in the periodontium can travel through the bloodstream and reach the fetus in the placenta. Certain bacterial species such as Fusobacterium nucleatum, Campylobacter rectus, Porphyromona gingivalis and others are most commonly associated with abnormalities during pregnancy. Microorganisms such as Bergeyella are considered an important factor in oro-uterine infectious transmission. Similarly, Fusobacterium nucleatum is negatively associated with the course of pregnancy as it could be identified in several areas of the placenta, fetal tissues, amniotic fluid, umbilical cord (Fischer et al., 2019; Starzyńska et al., 2022).

3.4 CONSEQUENCES OF PERIODONTAL DISEASE DURING PREGNANCY

In recent years, a bidirectional link has been established between periodontal disease and alterations in female fertility and gestation period. The development of polycystic ovary syndrome, endometriosis and bacterial vaginosis has been described. Similarly, periodontal diseases negatively affect the early stages of pregnancy even at the level of conception (Ludovichetti et al., 2021; Ricci et al., 2022). There is a large body of evidence relating the short-term consequences of periodontal disease at the fetal level, as well as long-term alterations. In the short term there are alterations in the size of the fetus as well as premature births. On the other hand, in the long-term consequences, low birth weight, cardiovascular alterations and metabolic diseases in adulthood such as hypertension, coronary heart disease, obesity, type II diabetes and an increased risk of reproductive and neurological alterations are described. Insulin resistance, alterations in the development of the central nervous system and an increased risk of a pulmonary allergic inflammatory pulmonary response have also been reported (Daalderop et al., 2018; Ricci et al., 2022; Starzyńska et al., 2022). Among other alterations we find the relationship between periodonto-pathogenic microorganisms and the development of preeclampsia, this is characterized as an angiogenic and inflammatory dysregulation that generates the development of arterial hypertension, organ dysfunction and proteinuria after 20 weeks of gestation. This can lead to serious maternal and fetal consequences such as intrauterine growth restriction, premature delivery, detachment of the fetus, and the development of a preeclampsia. placenta and fetal death in utero (Gare et al., 2021).

3.5 VITAMIN D: RELATIONSHIP BETWEEN PERIODONTAL DISEASE AND PREGNANCY

Vitamin D is a key factor in the regulation of calcium and phosphate homeostasis in bone metabolism. This vitamin allows calcium absorption at the intestinal level and decreases parathyroid hormone secretion thus reducing bone resorption. Similarly, vitamin D allows the stimulation of osteoclasts and alkaline phosphatase activity improving bone remodeling by a decrease in matrix protein production (Sllamniku Dalipi & Dragidella, 2022).

Vitamin D deficiency in the pregnant population presents a high prevalence with a percentage between 20-40%. Several publications report that low vitamin D levels are related to complications during pregnancy, where alterations such as preeclampsia, gestational diabetes mellitus, premature births, low birth weight and changes in the homeostasis generated by vitamin D at the calcium, phosphate and magnesium levels have been reported, which a deficit in this affects bone development leading to the genesis of hypocalcemia and lesions similar to rickets. Alterations such as pregnancy loss, premature delivery and postpartum depression have also been reported (Sllamniku Dalipi & Dragidella, 2022).

The relationship between vitamin D and periodontal diseases, lies in its anti-inflammatory effect, so providing vitamin D supplements during pregnancy positively helps periodontal maintenance and health,

so that the use of this type of supplements is of vital importance to allow proper fetal development (Sllamniku Dalipi & Dragidella, 2022; Uwitonze et al., 2018).

3.6 TREATMENT:

The treatment for periodontal pathologies consists of the mechanical elimination of bacterial plaque as well as supra and subgingival calculus by means of scaling and root planing mainly in periodontal pockets. Once the periodontal treatment has been instituted, patients require controls over long periods of time to maintain an adequate state of gingival and periodontal health. This type of non-invasive treatment allows a success rate and control of the disease in 80% of cases (Puertas et al., 2018).

The concomitant use of vitamin D and calcium with non-surgical periodontal treatment has a positive effect on the management of the disease, and can considerably reduce bone resorption and thus tooth loss (Sllamniku Dalipi & Dragidella, 2022).

According to Figuero et al., the implementation of non-surgical periodontal treatment in pregnant patients significantly reduces the concentration of IL1, IL 6 and TNF in the crevicular fluid of the gingival sulcus but not in the umbilical cord, so further quantitative and qualitative studies are needed on the level of proinflammatory mediators at the gingival level and in the placenta-fetus complex in pregnant patients with periodontal pathology (Figuero et al., 2020).

According to Raju et al. it was established that treatment for periodontal disease during pregnancy significantly decreased the risk of perinatal mortality in 8 randomized clinical trials (Raju & Berens, 2021). However, Tettamanti et al. describe that periodontal treatment does not help to prevent any complication during pregnancy, since based on their results they did not find enough evidence to corroborate this hypothesis, they also comment that periodontal treatment can generate local bacteremia, which can lead to an imbalance between the host immune response allowing the release of proinflammatory mediators. However, these authors agree that the key to maintaining periodontal health is based on education and the need to instruct pregnant women on plaque prevention and control measures by means of mechanical removal through toothbrushing (Tettamanti et al., 2017).

4 CONCLUSION

Based on what has been previously described, the importance of a correct maintenance of periodontal health in pregnant women can be evidenced. The presence of infectious foci such as those caused by periodontal-pathogenic bacteria can lead to the development of an alteration in the balance of immunity and inflammatory response of pregnant women and all this, together with the different hormonal changes that pregnant women undergo, translates into the possible establishment or exacerbation of any type of periodontal disease. And through different ways of dissemination, proinflammatory mediators can be generated that eventually reach the placenta-fetus complex and generate short or long term alterations,

which translates into negative consequences during the gestational stage as well as in the health of the future baby.

It has been possible to describe the importance of maintaining prophylactic measures through proper oral hygiene and non-surgical periodontal treatment to treat this type of morbidity. The role of vitamin D during the gestation period can reduce the risk of maternal infections and adverse pregnancy outcomes, so multidisciplinary work between dentists and gynecologists is of vital importance to obtain an effective diagnosis and allow a pregnancy free of complications where any stage of periodontal disease during gestation can be treated in a timely manner (Uwitonze et al., 2018).

Future research is recommended to establish a direct link and the impact that periodontal disease and pregnancy can have. It is also recommended to establish clinical practice guidelines to prevent the course of periodontal disease and the alterations it can cause in women's health.

DEDICATION

To all the people who were part of this 2022, I am only looking for redemption, Fernando V.

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