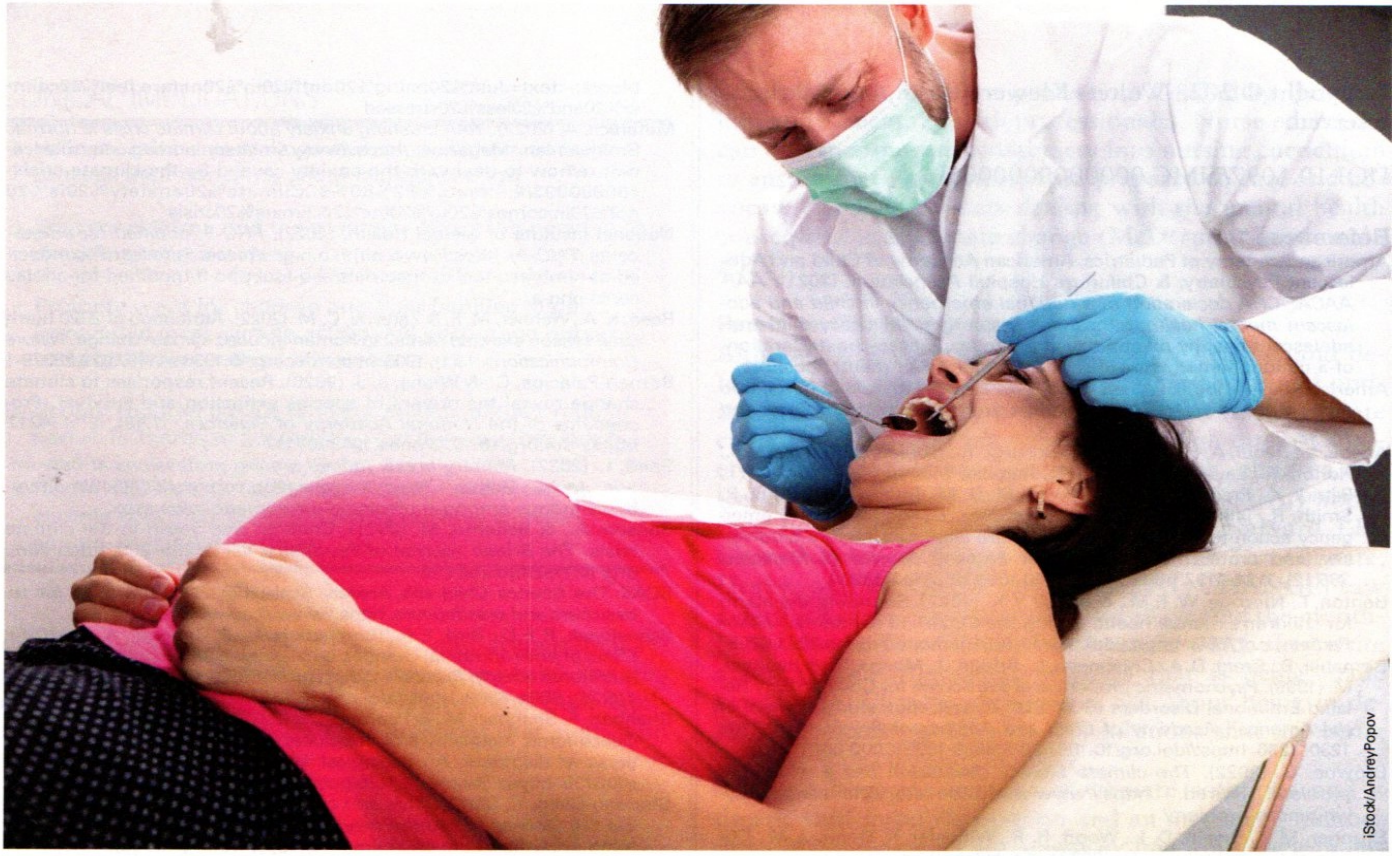

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THE ORAL MICROBIOME THROUGHOUT PREGNANCY: A SCOPING REVIEW

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Abstract

Introduction: Oral health is associated with systemic health, including adverse pregnancy outcomes. Understanding the oral microbiome during pregnancy may lead to targeted interventions for prevention of adverse outcomes. The purpose of this review is to examine the literature on the oral microbiome throughout pregnancy.

Methods: We conducted a literature search with four electronic databases for original research conducted between 2012 and 2022 that examined the oral microbiome longitudinally using 16s rRNA sequencing during pregnancy.

Results: We identified six studies that examined the oral microbiome longitudinally throughout pregnancy, though comparisons of oral niches, oral microbiome measures, and findings between studies were not consistent. Three studies identified alterations in alpha diversity throughout pregnancy and two studies identified increased pathogenic bacteria during pregnancy. Three studies reported no changes in the oral microbiome throughout pregnancy, and one study identified differences in the composition of the microbiome based on socioeconomic status and antibiotic exposure. Two studies examined adverse pregnancy outcomes in association with the oral microbiome, one reporting no associations and one reported difference in community gene composition in those diagnosed with preeclampsia.

Clinical Implications: There is limited research on the composition of the oral microbiome throughout pregnancy. There may be alterations in the oral microbiome during pregnancy such as increased relative abundance of pathogenic bacteria. Socioeconomic status, antibiotic use, and education may contribute to differences in the microbiome composition over time. Clinicians should evaluate oral health and educate on the importance of oral health care during the prenatal and perinatal time period.

Key words: Microbiota; Oral health; Pregnancy; Prenatal care; Saliva.

Epidemiologic studies identify associations between oral health and adverse pregnancy outcomes (Ide & Papapanou, 2013; Manrique-Corredor et al., 2019; Sanz & Kornman, 2013). Adverse pregnancy outcomes such as preterm birth, gestational diabetes mellitus, and hypertensive disorders during pregnancy have long-term implications for women and their infants. Women with these conditions are at increased risk of adverse pregnancy outcomes in subsequent pregnancies (Malacova et al., 2018; Wainstock et al., 2021) and long-term systemic diseases such as type 2 diabetes (T2D; Vounzoulaki et al., 2020).

Adverse pregnancy outcomes associated with poor oral health may result directly or indirectly from bacteria or their metabolites reaching the fetal–placental interface or by inducing systemic inflammation (Martínez-García & Hernández-Lemus, 2021), thus significantly contributing to maternal and infant morbidity and mortality (Figuero et al., 2020; Sanz & Kornman, 2013). Previous research is limited to bacterial cultures in the presence of oral disease as opposed to the full microbiome by 16s rRNA sequencing. Oral microbiome analysis may yield biologically plausible pathways in which oral health influences adverse pregnancy outcomes.

The *microbiome* refers to the collective genome of the microbes within a niche (Amon & Sanderson, 2017). The oral cavity contains a core microbiome of over 700 different species identified by the Human Oral Microbiome Database. The most prominent phyla in the oral cavity are Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria, Spirochaetes, and Fusobacteria (Dewhirst et al., 2010). Many of the bacterial populations identified in the oral microbiome cannot be cultured in the laboratory (Dewhirst et al., 2010).

Whole genome sequencing allows all microorganisms in a sample to be identified, whereas next-generation sequencing targets bacterial microbes (Deo & Deshmukh, 2019). Next-generation sequencing and whole genome sequencing allow for calculation of the relative abundance of both commensal and pathogenic bacteria (Deo & Deshmukh, 2019). Disruption to the normal balance of bacteria in the oral cavity, also referred to as dysbiosis, may be caused by an overgrowth of pathogenic bacteria or a decrease in commensal bacteria (Petersen & Round, 2014).

In comparison to knowledge of gut and vaginal microbiomes during pregnancy, little is known about how the oral microbiome might change throughout gestation, or how changes during pregnancy might affect outcomes. Pregnancy is associated with a variety of immunologic, metabolic, and hormonal shifts that can affect the microbiome (Nuriel-Ohayon et al., 2016). Factors such as poor oral health, gingival disease, and stress have the potential to negatively impact the oral environment leading to oral microbiome dysbiosis (Sedghi et al., 2021). During pregnancy, increases in hormones can lead to increased gingival inflammation (Lin et al., 2018). Gingivitis has been associated with an increased risk of preterm birth (Erchick et al., 2020; Kruse et al., 2018; Novák et al., 2020) and the increased presence of gram-negative bacteria such as *Fusobacterium nucleatum* (Kruse et al., 2018), which is also associated with preterm birth (Vander Haar et al., 2018). Other periodontal pathogens associated with poor oral health and adverse pregnancy outcomes, such as *Porphyromonas gingivalis*, and *Aggregatibacter actinomycetemcomitans* may also increase during pregnancy (Fujiwara et al., 2017).

There is evidence supporting differences in the composition and diversity of the oral microbiome during pregnancy compared to nonpregnant individuals (Balan et al., 2021; Sparvoli et al., 2020). Studies have also reported variations in the oral microbiome during pregnancy in comparison to preconception (La et al., 2022) and postpartum (Crusell et al., 2020). Much of the research focused on the oral microbiome during pregnancy has a cross-sectional study design (Balan et al., 2021; Cortez et al., 2019; Paropkari et al., 2016; Sparvoli et al., 2020; Tuominen et al., 2018; Wang et al., 2020; Wang et al., 2018; Xu et al., 2020; Yang et al., 2020; Yang et al., 2019). Cross-sectional studies do not, however, allow researchers to make inferences about when changes occur during pregnancy, or clinicians to understand when to intervene. The purpose of this review is to determine if the oral microbiome changes in diversity or abundance throughout pregnancy, and to learn what factors are associated with changes in oral microbiome throughout pregnancy.

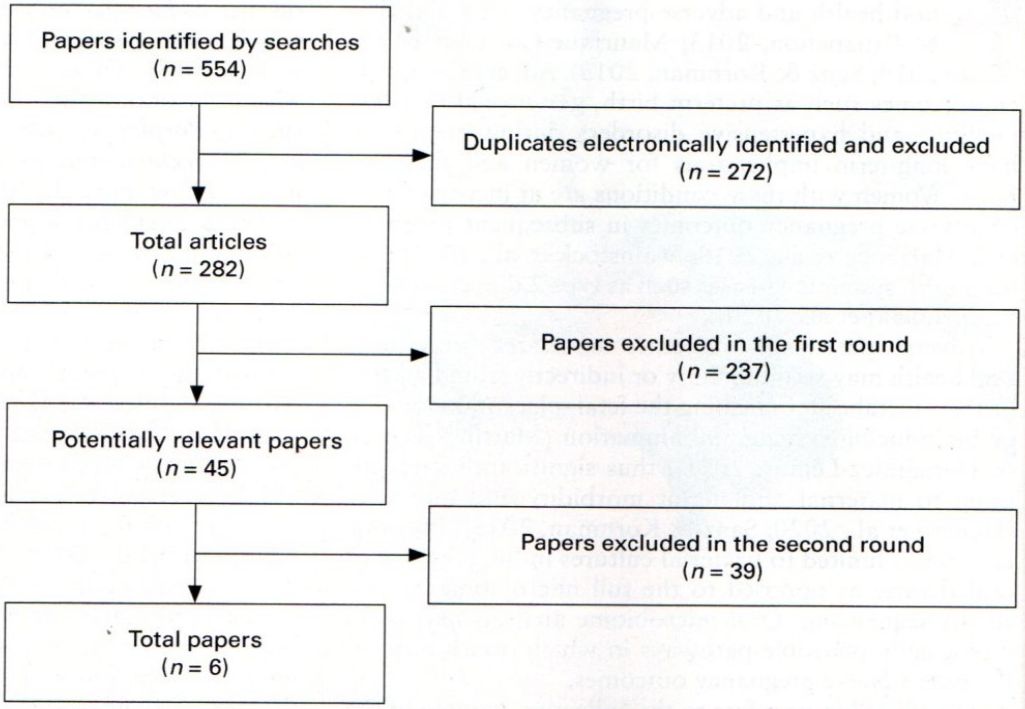
Methods

The aim of this review is to search the literature for original research that examines the oral microbiome longitudinally throughout pregnancy. This review is guided by the Arskey and O'Malley framework (Arksey & O'Malley, 2005). We searched four electronic databases, PubMed, Embase, Web of Science, and Scopus between February and March 2022. We also examined manuscript references to ensure that outliers were included in this review. We consulted a medical librarian to assist with the search strategy. We included the search terms: "*mouth* OR *saliva* OR *mouth mucosa* OR *oral* OR *salivary* OR *subgingival* OR *supragingival*" AND "*microbiome* OR *microbiota*" AND "*pregnancy* OR *pregnant* OR *perinatal* OR *antenatal* OR *peripartum*" AND "*sequencing* OR *16s rRNA*." We included appropriate MeSH terms when searching PubMed. The search term *microflora* was added when searching in EMBASE as it is a keyword identified by the database. Inclusion criteria: 1) original research in a longitudinal design that examines the oral microbiome during pregnancy using next-generation sequencing or whole genome sequencing, 2) published in English, 3) peer-reviewed, and 4) published between 2012 and 2022. Exclusion criteria: 1) publications of study protocols, 2) conference abstracts, or 3) literature reviews.

Results from our electronic database search were imported into a bibliographic management program, Rayyan (Ouzzani et al., 2016). Duplicates were removed, and articles that did not meet inclusion criteria based on title and abstract review were excluded. Full-text review

determined final articles included in this review. We then independently extracted data from articles that met the purposes of this scoping review into a spreadsheet. Data extraction included authors, year of publication, study population and sample size, study design and methods, results, and limitations. No conflicts arose during inclusion or exclusion of articles or data extraction and charting.

FIGURE 1. PRISMA DIAGRAM OF SEARCH RESULTS



Results

We identified 554 articles in our initial search. After removing duplicates, 282 articles remained. We reviewed the full text of 45 articles after removing articles deemed irrelevant during the abstract review. Six articles met inclusion and exclusion criteria and are included in this review. A PRISMA diagram detailing the process of article selection is presented in Figure 1.

Characteristics of Included Studies

Four included studies are longitudinal cohort studies (Balan et al., 2018; DiGiulio et al., 2015; Dunlop et al., 2019; Lin et al., 2018), one study was a secondary data analysis of one of the included studies (Goltsman et al., 2018), and one was a randomized controlled trial (Bisanz et al., 2015). Balan et al. (2018) conducted a longitudinal study but includes a cross-sectional analysis as some participants only provided samples during one trimester, whereas six participants provided samples during each trimester, for longitudinal analysis. Study characteristics and findings are presented in Table 1.

Studies were conducted in Tanzania (Bisanz et al., 2015), China (Balan et al., 2018; Lin et al., 2018), and the United States (DiGiulio et al., 2015; Dunlop et al., 2019; Goltsman et al., 2018). Collection sites included an oral swab of the tongue or hard palate and gum line (Dunlop et al., 2019), subgingival plaque (Balan et al., 2018), supragingival plaque (Lin et al., 2018), and/or saliva (Balan et al., 2018; Bisanz et al., 2015; DiGiulio et al., 2015; Goltsman et al., 2018; Lin et al., 2018). Amplification of 16s rRNA gene hypervariable regions, which contain sequences to classify microbes at various taxonomic levels, varied between studies and included the V4 region (Balan et al., 2018; Bisanz et al., 2015), the V3-V5 regions (DiGiulio et al., 2015), the V3-V4 regions (Dunlop et al., 2019), and the V4-V5 regions (Lin et al., 2018). Databases for taxonomy classification of operational taxonomic units (OTUs) or amplicon sequencing variants included the Greengenes database (Bisanz et al., 2015; Lin et al., 2018) and the Ribosomal Database Project (Balan et al., 2018; DiGiulio et al., 2015; Dunlop et al., 2019). Only Dunlop et al. (2019) used amplicon sequencing variants, which are more sensitive and specific than OTUs, resulting in more precise results (Callahan et al., 2017).

Characteristics of Participants

The sample of studies include 267 participants. Sample sizes ranged from 10 (Goltsman et al., 2018) to 110 participants (Dunlop et al., 2019); however, one study evaluated only 6 of their participants longitudinally (Balan et al., 2018). Participants age, on average, ranged from 23 years to 34 years old. Participant data were collected during the first, second, and third trimesters in five of the included studies (Balan et al., 2018; Bisanz et al., 2015; DiGiulio et al., 2015; Goltsman et al., 2018; Lin et al., 2018), with Dunlop et al. (2019) collecting samples between 8–14 weeks and 24–30 weeks. Postpartum data were included in two studies (Balan et al., 2018; Lin et al., 2018). Studies varied on different exclusion criteria with participants being excluded if they had chronic or systemic diseases (Balan et al., 2018; Dunlop et al., 2019; Lin et al., 2018), were a current smoker or drinker (Balan et al., 2018; Lin et al., 2018), recently visited the dentist (Balan et al., 2018), had less than 20 teeth or untreated oral health conditions (Lin et al., 2018), and/or recently used antibiotics (DiGiulio et al., 2015; Lin et al., 2018).

Oral Microbiome throughout Pregnancy and Postpartum

Researchers in three of the studies reported significant differences in alpha diversity measures during pregnancy (Balan et al., 2018; DiGiulio et al., 2015; Lin et al., 2018). Measures of alpha diversity include the Chao 1

TABLE 1. CHARACTERISTICS OF LONGITUDINAL STUDIES EXAMINING THE ORAL MICROBIOME DURING PREGNANCY

First Author and Year of Publication	Primary Outcome(s)	Study Design, Sample Size, Population, and Oral Niche(s) Sampled	Findings	Limitations
Balan (2018)	Examine changes to the OM from pregnancy to PP.	Mixed cross-sectional and longitudinal analyses ($n = 24$) Pregnant women in Singapore in their 1st, 2nd, 3rd trimesters, and PP. • SAL • SUB	Alpha diversity (Observed species, Chao 1 and Simpson index) was significantly different in SUB between the second and third trimester ($p < .05$). Observed number of species and Chao 1 index were significantly higher in the third trimester in SUB samples ($p < .05$). Weighted UniFrac indicated there were no distinct grouping of bacterial communities during pregnancy or PP in SAL or SUB samples ($p = .209$). In SUB and SAL, there was a significant drop in the abundance of pathogenic species from pregnancy to PP ($p < .05$).	Small sample size, and pilot study with no indication of statistical power. No identification of adverse pregnancy outcomes. No inclusion of other covariates such as SES or recent antibiotic use in analysis.
Blisanz (2015)	Examine the effect of probiotic yogurt on oral, gut, vaginal, and breastmilk microbiomes.	Randomized controlled trial ($n = 56$) Pregnant women from Tanzania during their second and third trimesters and 1 month postpartum. • SAL	Nutritional status was not correlated with a difference in microbiome between groups based on alpha/beta diversity or taxa. No significant difference in beta diversity throughout pregnancy in either group.	Small sample size, based on participant availability. 12 participants with HIV but did not discuss differences in microbiota.
DiGiulio (2015)	Examine the temporal dynamics of the maternal microbiome throughout pregnancy.	Longitudinal, case-control study ($n = 49$) Pregnant women from California during their 1st, 2nd, and 3rd trimesters. • SAL • Molar tooth surface swab	No significant difference in alpha diversity throughout pregnancy in SAL (Shannon index [$p = .264$], Chao 1 [$p = .297$], Simpson index [$p = .246$]) or tooth/gum (Shannon index [$p = .068$], Simpson index [$p = .109$]). Chao 1 index was significantly different for tooth/gum ($p = .0008$). No difference in beta diversity throughout pregnancy in SAL (Bray-Curtis dissimilarity [$p = .370$], Jensen-Shannon dissimilarity [$p = .745$], weighted UniFrac [$p = .58$]) or tooth/gum (Bray-Curtis dissimilarity [$p = .525$], Jensen-Shannon dissimilarity [$p = .743$], weighted UniFrac [$p = .613$]). Taxonomic composition in saliva and tooth/gum did not significantly differ from early and late pregnancy. No change from predelivery to postdelivery in SAL (Bray-Curtis dissimilarity [$p = .135$], Jensen-Shannon dissimilarity [$p = .71261$], weighted UniFrac [$p = .2861$]) or tooth/gum (Bray-Curtis dissimilarity [$p = .1913$], Jensen-Shannon dissimilarity [$p = .2762$], weighted UniFrac [$p = .2161$]).	Collected information about stress, SES, and other comorbidities but did not report on their associations with the microbiome. Periodontal status or associations with adverse pregnancy outcomes were not examined. Small number of cases ($n = 11$) compared to controls. Sample size lacking in diversity with 59% ($n = 29$) of participants being White and only 4% ($n = 2$) Black.

(*continued on next page*)

TABLE 1. CHARACTERISTICS OF LONGITUDINAL STUDIES EXAMINING THE ORAL MICROBIOME DURING PREGNANCY (*CONTINUED*)

First Author and Year of Publication	Primary Outcome(s)	Study Design, Sample Size, Population, and Oral Niche(s) Sampled	Findings	Limitations
Dunlop (2019)	Examine the stability of the microbiome from early to late pregnancy in African American women, examine if SES is associated with microbiome composition, and if antibiotics mediate the association between SES and stability of the microbiome.	Longitudinal cohort study (n = 110) Pregnant African American women in Georgia during early pregnancy (8–14 weeks) and late pregnancy (24–30 weeks). • Tongue/hard palate/gum line swab	Exposure to antibiotics between visits was higher in women who had only completed high school or less (p = .02) and higher in women with Medicaid (p = .02) No difference in Shannon index or Chao 1 index for oral samples between visits according to SES status or antibiotic exposure. Low level of education (p = .015) and antibiotic exposure between visits (p = .008) was associated with a greater Bray-Curtis dissimilarity in the oral microbiome. Prenatal insurance was associated with the direction of oral compositional change between visits (p = .009).	Did not examine periodontal disease or smoking habits. Sample size was not large enough to detect small effect sizes. 75% of participants had Medicaid, which limits the effect of health insurance type.
Goltsman (2018)	Examine the gene content and functional potential of microbial communities in the oral, vaginal, and gut microbiome throughout pregnancy.	Secondary data analysis of a previous longitudinal, case-control study. (n = 10) Pregnant women from California during their 1st, 2nd, and 3rd trimesters. • SAL	The OM demonstrated stability over time. There were high levels of interindividual variability, as different participants demonstrated different taxa. Redundancy analysis indicated gestational age and health complications contribute to variations in community composition (p = .001).	Small sample size, with limited adverse pregnancy outcomes, which was likely not adequately powered. No demographic data provided about subsample of participants, so unable to generalize findings.
Lin (2018)	Examine the OM throughout pregnancy and compare to nonpregnant women.	Longitudinal case-control study (n = 18) Pregnant women from China during the first (less than or equal to 14 weeks), second (20–25 weeks), and third (33–37 weeks) trimesters and postpartum (6 weeks) and nonpregnant women at the same time intervals. • SUP • SAL	For alpha diversity, Shannon index was higher in the third trimester compared to all other times (p < .01). For beta diversity, there were distinct clusters based on gestational age. The dominant phylum in pregnant women was Proteobacteria (27.8%) compared to nonpregnant women, which was Firmicutes (29.76%). 64 OTUs were correlated to sex hormones (p = .003).	Small sample size and no information if it was adequately powered.

OM = oral microbiome; PP = postpartum; SAL = saliva; SES = socioeconomic status; SUB = subgingival plaque; SUP = supragingival plaque

index, which is an estimate of total number of species within a sample (Chao, 1984), the Shannon index, which is a measure of richness and evenness, giving weight to rare species (Shannon, 1948), and the Simpson index, which also estimates richness and evenness, but gives weight to common species (Simpson, 1949). Both Balan et al. (2018) and Lin et al. (2018) reported increases in alpha diversity only in the third trimester. Balan et al. reported differences in observed species, Chao 1 and Simpson indices ($p < .05$), whereas Lin et al. only reported differences with the Shannon index ($0.001 < p < .01$). Balan et al. reported significant differences only in subgingival samples, but not saliva samples, and Lin et al. reported significant differences in supragingival samples. DiGiulio et al. (2015) reported a significant decrease in Chao 1 throughout pregnancy for supragingival samples ($p = .0008$) but reported no significant differences for any other alpha diversity measures (Chao 1, Shannon, and Simpson index) for the supragingival or saliva samples.

Only one research group reported significant differences in beta diversity measures during pregnancy (Dunlop et al., 2019). Lin et al. (2018) reported clustering based on whether individuals were pregnant or not, based on principal coordinates analysis, but this finding was not significant. Dunlop et al. (2019) reported significant differences in the oral microbiome composition between early pregnancy and late pregnancy using the Bray-Curtis dissimilarity index. In this study, multivariate analyses demonstrated differences in the oral microbiome associated with antibiotic use ($p = .008$) and education level ($p = .015$). Dunlop et al. identified a significant compositional change in the oral microbiome between early and late pregnancy based on prenatal insurance type ($p = .009$) using the Manhattan index, which represents the compositional changes between the two time points. This indicates that individuals with private insurance and higher education were more likely to have a stable microbiome in comparison to individuals with Medicaid or only having completed high school or less. However, it is unclear if the composition changes resulted in alterations in the relative abundance of specific pathogenic or commensal bacteria.

Researchers of three studies reported on the relative abundance of pathogenic bacteria during pregnancy (Balan et al., 2018; Bisanz et al., 2015; Lin et al., 2018). Balan et al. (2018) reported that after pregnancy, there was a significant decrease in the relative abundance of pathogenic species in postpartum compared to pregnancy ($p < .05$). Results vary on the taxonomy of pathogenic bacteria identified during pregnancy, with Balan et al. reporting increases in bacteria belonging to the following genera: *Prevotella, Streptococcus,* and *Veillonella* and Lin et al. (2018) reported increases in bacteria belonging to the following genera: *Neisseria, Porphyromonas,* and *Treponema.* Bisanz et al. (2015) reported pregnant individuals had bacteria belonging to the following genera detected: *Streptococcus, Prevotella, Fusobacterium,* and *Porphyromonas.*

Only one research group reported associations between oral health and the oral microbiome throughout pregnancy (Balan et al., 2018). Two other groups examined oral health, but did not report associations with the oral microbiome (Bisanz et al., 2015; Lin et al., 2018). Lin et al. (2018) reported an increase in gingival inflammation in comparison to nonpregnant individuals and Balan et al. (2018) reported an increase in gingival bleeding during the first and second trimesters. Balan et al. reported correlations between gingivitis and 58 species of bacteria, some of which were pathogenic. Species correlated with gingivitis include *Porphyromonas gingivalis, Treponema denticola, Prevotella intermedia,* and *Porphyromonas endodontalis.*

Only two research groups reported on and evaluated associations between adverse pregnancy outcomes and the oral microbiome (DiGiulio et al., 2015; Goltsman et al., 2018). DiGiulio et al. (2015) examined associations between the microbiome and preterm birth and reported no significant differences in those who gave birth preterm compared to those who gave birth at term. Goltsman et al. (2018) used a subsample of participants from the study conducted by DiGiulio et al. and performed whole gene sequencing. Goltsman et al. reported differences in the community gene composition in those who were diagnosed with preeclampsia, T2D, or oligohydramnios in comparison to those who were healthy ($P = .001$).

Interventions

Bisanz et al. (2015) evaluated associations among maternal nutrition, use of a probiotic yogurt, and maternal microbiomes. Participants either received yogurt every day or no yogurt at all throughout pregnancy. They reported that maternal nutritional status, whether classified as nourished or undernourished at baseline, was not correlated with oral microbiota either by diversity (Shannon index) or individual taxa (Bisanz et al., 2015). There were no significant changes to oral microbiome diversity because of the yogurt consumption during pregnancy (Bisanz et al., 2015).

Discussion

We reviewed and examined the literature to guide future research studies and clinical practice. We aimed to explore the extant literature on longitudinal studies evaluating the oral microbiome and factors that are associated with changes to the oral microbiome across gestation. By examining longitudinal changes to the oral microbiome, we can better understand microbial shifts that may influence health and disease during pregnancy.

There may be alterations in the maternal oral microbiome across gestation, but there is paucity in research which longitudinally examines the oral microbiome during pregnancy. Most notably, there may be changes to the composition of the microbiome, as evidenced by the increases in pathogenic bacteria that are decreased in nonpregnant individuals and the significant changes in the relative abundance of species within samples across time. However, it is unclear how alpha diversity changes throughout the course of pregnancy, as findings were mixed. Lin et al. (2018) hypothesized alterations in diversity may be associated with

the 10-fold increase in progesterone and estrogen found by the third trimester of pregnancy.

Two groups reported on the increases in pathogenic bacteria in pregnant women compared to nonpregnant or postpartum women, some of which were low in abundance, but may play a role in altering the composition of the oral microbiome (Balan et al., 2018). As pregnancy progresses, Balan et al. (2018) reported an increase in Chao 1 alpha diversity, a measure of the total number of bacterial species present, whereas DiGiulio et al. (2015) reported a decrease using this measure. This may be due to the different populations sampled, and more research is needed to clarify and identify the implications of the variations in Chao 1 findings. Lin et al. (2018), however, reported an increase in alpha diversity as measured by Shannon diversity, a measure that is sensitive to rare species, and may be congruent with the keystone pathogen hypothesis developed by Hajishengallis et al. (2012). The keystone pathogen hypothesis states that though certain bacteria may be low in abundance, they have the opportunity to create a dysbiotic environment and influence the inflammatory cascade (Hajishengallis et al., 2012). Keystone pathogens not only increase in abundance but also reduce the abundance of commensal bacteria (Hajishengallis et al., 2012). Keystone bacteria may be critical targets for screening and intervening to reduce oral microbiome dysbiosis and subsequent systemic disease (Hajishengallis et al., 2012). Pregnancy may provide a unique period for keystone pathogens to increase in abundance due to hormonal and immunologic changes and thus alter composition and diversity of the oral microbiome, but additional research is needed.

We are unable to deduce how alpha diversity, which represents the richness and evenness of the microbiome, changes as pregnancy progresses because the research groups reported inconsistent results. One barrier to interpretation and analysis is not only that each group reported using measures that emphasize different features of the populations described, but also because each group sampled at different locations within the mouth. Although different oral sites are similar in their composition, each of these niches have varying microbial diversity (Willis & Gabaldón, 2020; Xu et al., 2015). The environmental characteristics such as surface for microbial adhesion, source of nutrition, pH, oxygen concentration, and metabolic properties of each niche provide different growth opportunities for different microbes, resulting in variations in the abundance and diversity of microbes found at each niche (Marsh & Devine, 2011). Some studies sampled from subgingival and supragingival plaque, whereas others sampled from saliva. As such, there are different adhesive properties within these niches that can result in bacterial aggregation. Studies used different primer pairs, sequenced based on different regions of the 16s rRNA gene, and the sample populations were disparate. All these variations lead to compositional differences among studies complicating comparisons.

Dunlop et al. (2019) reported changes in the composition to the oral microbiome when including covariates related to sociodemographic and clinically relevant factors such as antibiotic exposure. This was the only study which controlled for covariates in their analyses, and we find the effect of socioeconomic status (SES) on the oral microbiome during pregnancy potentially enlightening. Exploring how covariates affect the oral microbiome may assist in understanding mechanisms of action related to diversity, composition, and adverse outcomes and how inequity of resources may be associated with changes in the microbiota that influence health outcomes in disadvantaged populations.

Future research is needed to examine changes to the oral microbiome throughout pregnancy in large studies with adverse pregnancy outcomes, including psychosocial and relevant demographic covariates.

Only two research groups examined associations between adverse pregnancy outcomes and the oral microbiome across time and only three adverse pregnancy outcomes were evaluated, preterm birth, preeclampsia, and oligohydramnios (DiGiulio et al., 2015; Goltsman et al., 2018). Within these studies, the sample sizes of those who experienced an adverse pregnancy outcome were small in comparison to healthy controls. Although many researchers have reported associations between the oral microbiome and gestational diabetes mellitus in cross-sectional studies (Li et al., 2021; Xu et al., 2020; Zhang et al., 2021), we did not find research that longitudinally examined the oral microbiome and this adverse outcome throughout pregnancy. This is a critical gap in the extant literature and a need for future research, as understanding of potential alterations in the oral microbiome in those with adverse pregnancy outcomes would help guide future interventions.

Implications for Research

It is evident there is a paucity of research examining the oral microbiome throughout pregnancy and its contribution to adverse pregnancy outcomes. Many of the sample sizes included in this review were small and underpowered; the methods, from design, to sample collection, processing, and analysis varied; the sample populations diverse, and the regions disparate. Despite these barriers to our interpretation and analysis, we find some hints that the oral microbiota may play an important role in the health of pregnant women. It will be important for future oral microbiome studies to be conducted prospectively and longitudinally, controlled for confounders, sample standard niches, use standard collection, storage, processing, and analysis techniques to elucidate the changes in the microbiome throughout pregnancy and the microbiome's contribution to common adverse outcomes of pregnancy.

CLINICAL IMPLICATIONS

- Oral health care during pregnancy should be considered an important part of perinatal health promotion and education.
- Nurses are in a unique position to assess their patient's oral health and provide awareness about the importance of oral health maintenance during pregnancy.
- Women who are diagnosed with preeclampsia or oligohydramnios may have an altered oral microbiome and identifying those who are at risk early in pregnancy along with oral health maintenance interventions may be beneficial to reducing this adverse perinatal outcome.
- Pregnant individuals may experience an increase in gingival bleeding or inflammation, which may be associated with increases in bacteria associated with poor oral health.
- Sociodemographic factors such as education level may be associated with alterations to the oral microbiome and examining oral health literacy and providing oral health education during the perinatal period may be critical to reducing adverse perinatal outcomes.

Limitations

There are several limitations to this scoping review. Only articles that are published in the English language are included. There are few studies that reported adverse outcomes, and they are underpowered. Studies included in this review sampled multiple oral sites, using different methods of sample processing and bioinformatic analysis complicating analysis and interpretation. Different populations with different sociodemographic characteristics that are not always identified or controlled limit the generalizability of these findings.

Clinical Implications

For clinicians, findings from this review indicate that the oral microbiome may change throughout pregnancy by the increasing number of pathogenic species. There is a large gap in knowledge related to the composition and diversity of the oral microbiome as pregnancy progresses. Although only one study discussed associations between the oral microbiome and oral health measures, clinicians should continue to evaluate oral health prior to and during pregnancy and stress the importance of dental hygiene. Oral health care recommendations should be presented to all individuals during the prenatal and perinatal time periods due to its associations with systemic disease. Nurses have a unique opportunity to examine oral health and intervene by providing education on oral health and its association with health outcomes and answer patient questions about oral health care during the perinatal period. By examining the oral microbiome throughout pregnancy, we can further understand and identify biologically plausible pathways between oral health and adverse pregnancy outcomes and develop nurse-driven interventions to improve maternal and infant outcomes. ✣

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