

Cariogenic and Pro Health Taxa in the Oral Cavity Among Children and Adults A Scoping Review

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Abstract

Introduction: Dental caries are not due to a single organism, but to complex interactions among multiple microbes found in the oral cavity. Microbiome studies have identified multiple organisms associated with dental caries in both the saliva and dental plaque, but taxa identified vary largely by study. Our scoping review aims to create a comprehensive list of cariogenic and prohealth taxa found in saliva and dental plaque among healthy children and adults that compare caries-active and caries-free populations.

Methods: We searched published studies querying the PUBMED and EMBASE databases using the following keywords: (plaque OR saliva) AND caries AND (next generation sequencing OR checkerboard OR 16s rRNA or qPCR). Studies were limited to human studies published in English between January 1, 2010 and June 24, 2020.

Results: Our search strategy identified 298 identified articles. After applying the exclusion criteria, 22 articles were included (Figure 1, Table 1 and 2). Taxa associated with caries or health varied widely among the studies reviewed, with notable differences by age and biologic sample type. While no single taxa was associated with caries in all studies, *Streptococcus mutans* was significantly associated with caries in 12/24 studies (50%) and *Fusobacterium periodonticum* was significantly associated with prohealth in 4/24 studies (16.7%).

Conclusion: No taxa in plaque and salivary microbiomes were consistently associated with caries or prohealth across all studies. This may be due to the inconsistency of timing of sample collection during the caries process, differing sequencing methods, lack of correction for multiple testing or possibly indicate that there are multiple ways that the oral microbiome can be cariogenic or prohealth.

Introduction

Dental caries are the most prevalent oral disease in both children and adults (1), and can greatly compromise quality of life (2). Caries result from an interaction between cariogenic species in the mouth, poor oral hygiene and a high sugar diet (3), but can be prevented or limited by regular cleaning to remove cariogenic microbes within the oral cavity, increasing the acid-resistance of the teeth (via sealants), and controlling the carbohydrate composition of the diet (4). Improved understanding of which taxa are cariogenic, and which are protective will lead to additional strategies for oral disease prevention and treatment.

Dental caries are not due to a single organism, but to complex interactions among multiple microbes found in the oral cavity (5,6). Studies using methods that do not require microbial culture have identified multiple organisms associated with dental caries in both the saliva and dental plaque (7,8). However, the taxa identified vary by study. This may reflect differences in caries definition, study population, biologic sampling and collection procedures, laboratory methods and sample size. We found only one review of these studies, and it focused on children (9). Our scoping review fills this gap, by creating a comprehensive list of cariogenic and prohealth taxa found in saliva and dental plaque among children

and adults. We focused our review on results from oral microbiome studies comparing caries-active and caries-free populations that were free of underlying illnesses.

Materials And Methods

Search Strategy

We searched published studies querying the PUBMED and EMBASE databases using the following keywords: (plaque OR saliva) AND caries AND (next generation sequencing OR checkerboard OR 16 s rRNA or qPCR). Studies were limited to human studies published in English between January 1, 2010 and June 24, 2020. Initially, the PUBMED database was searched on June 24, 2020 followed by a search on the EMBASE database on August 20, 2020. D.B and B.F reviewed each full text article for inclusion (Fig. 1). Studies were included if they met the following criteria: (1) a human study; (2) comparison of a healthy (free from any diagnosed disease or illness) caries-free population to a caries-active population; (3) sample size greater than 10 for each population; (4) assessment of the entire bacterial community (sequencing, checkerboard, DGGE); and (5) had taxa resolved to the species level.

Data Synthesis

From each study, we included all taxa occurring statistically significantly more frequently among the caries-active group than caries-free group (cariogenic) or vice versa (prohealth) and noted if the comparisons were corrected for multiple testing. The frequency of each taxa among all the studies included for review was calculated. We further stratified the frequency rates according to age group (children versus adults) and sample type (saliva versus plaque).

Results

Study Selection

Our search strategy identified 298 identified articles (Additional File 1). After applying the exclusion criteria, 22 articles were included (Fig. 1, Tables 1 and 2). Overall, 6 studies were conducted in adults, 15 conducted in children, and 1 conducted in both adults and children. Fifteen of the articles used 16 s rRNA amplicon sequencing, 4 used HOMINGS, one used 16 s rDNA PCR-DGGE, and 2 used checkerboard. Eight analyzed saliva, 12 analyzed supragingival plaque and 2 analyzed both saliva and plaque. For presentation, we included each of the 2 studies analyzing plaque and saliva as separate studies of plaque and saliva, giving us a denominator of 24 studies. Only 8 studies corrected for multiple comparisons.

Taxa statistically significantly associated with caries in plaque and saliva

We tallied all taxa that were positively or negatively associated with dental caries in saliva and plaque with a p value ≤ 0.05 (Fig. 2). Four studies found no taxa that were statistically significantly associated as either cariogenic or prohealth, while 2 studies found significant taxa only for caries and 2 studies found significant taxa only for prohealth. Overall, the most common statistically significant cariogenic taxa among the 24 articles were *Streptococcus mutans* (12/24, 50%), *Veillonella dispar* (6/24, 25%), and *Veillonella parvula* (4/24, 16.7%). When limited to the 8 studies that corrected for multiple comparisons, *Streptococcus mutans* was found in 4/8 (50%) studies and *Veillonella dispar* in 3/8 (37.5%) studies as cariogenic taxa. The most common statistically significant prohealth taxa were *Fusobacterium periodonticum* (4/24, 16.7%) and *Haemophilus parainfluenzae* (3/24, 12.5%). Among the studies that corrected for multiple comparisons, *Fusobacterium periodonticum* and *Haemophilus parainfluenzae* were both found in 3/8 studies (37.5%).

We further analyzed papers to determine if there were differences in taxa by age or biologic specimen (saliva or plaque). *Streptococcus mutans* was statistically significantly associated with caries in 60% of the studies (6/10) conducted in children analyzing supragingival plaque and 50% of studies analyzing saliva (3/6). Multiple taxa were significantly associated with prohealth in children but not consistently across studies. In 2/10 (20%) plaque studies in children, *Streptococcus sanguinis* was significantly associated with prohealth, and in 2/6 (33.3%) saliva studies in children *Granulicatella elegans*, *Gemella haemolysans*, *Haemophilus parainfluenzae*, and *Fusobacterium periodonticum* were statistically associated with prohealth. Among adults, *Streptococcus mutans* was statistically significantly associated with cariogenesis in 2/4 (50%) saliva studies and only 1/3 (33%) in plaque studies. There were no overlapping taxa that were statistically significantly associated with prohealth in either saliva or plaque studies among adults for at least 2 studies. When limited to studies in children that corrected for multiple comparisons, *S. mutans* in plaque was significantly associated with caries in 2/2 (100%) and in saliva in 2/3 (66.7%) studies. *Prevotella denticola* was also significantly associated with caries found in 2/3 (66.7%) of the children salivary studies. Prohealth significant taxa among the multiple comparisons studies was only found to be overlapping within saliva studies taken in children, with *Haemophilus parainfluenzae* found in 2/3 (66.7%) of the studies.

Discussion

Overall Findings

Cariogenic and prohealth taxa identified varied widely among the studies reviewed, with notable differences by age and biologic sample type. No one taxon was significantly associated with caries or prohealth in all studies. However, *Streptococcus mutans* and *Veillonella dispar* were associated with caries in 12/24 studies (50%) and 6/24 (25%), respectively. The most common taxa significantly associated with prohealth were found less frequently: *Fusobacterium periodonticum* (4/24, 16.7%) and *Haemophilus parainfluenzae* (3/24, 12.5%). These four taxa were also identified when the review was limited to studies that corrected for multiple testing in roughly the same proportions.

S. mutans is widely accepted as cariogenic; its cariogenicity is attributed to its superior acidogenic and aciduric potential (9,10). Reasons for a lack of association with caries in all studies may be attributed to differences in study design, conduct or analysis or reflect true differences by study population or disease process. Some of the studies included enamel lesions and dentinal caries; these have distinct microbiomes (11,12), and the oral microbiome changes between childhood to adulthood (13–15). Further, bacterial composition changes with disease progression; therefore associations with some taxa may not be detected if taxa abundance varies by when during the disease process samples were collected (16). Plaque bacteria are shed in the saliva (17), but the amount may also vary by disease stage. It is also possible that saliva plays an ancillary role in cariogenesis or in preventing caries (18). There also may be multiple pathways to dental caries, and/or the processes leading to caries may depend on behavioral or physiologic factors associated with age, for example, diet, or dentition.

While several studies reviewed reported associations between *Veillonella dispar* and dental caries, we found no previous studies suggesting a mechanism for this association. Further, at least one report suggested that increased *Veillonella dispar* abundance is negatively associated with periodontitis (19). The consistent association of *F. periodonticum* with prohealth - observed in children and adults - is somewhat surprising, as this taxa is positively associated with periodontitis (20,21) and oral squamous cell carcinoma (22). However, one study reviewed that tested saliva among adults (23) identified *F. periodonticum* as cariogenic. *Haemophilus parainfluenzae* is considered a pathobiont, and has been associated with respiratory disease (24). Although 4 studies found significant associations of *Haemophilus parainfluenzae* with prohealth, one study among adults flagged it as cariogenic.

This review is limited by variations in samples used, study population, and how taxa were detected. The number of studies conducted that met our criteria, conducted using otherwise healthy populations, and comparing individuals with caries to those caries free with 10 or more participants per group, was relatively small. Further, virtually all were conducted at a single point in time. Nonetheless, this review revealed some general insights. All 4 taxa significantly associated with cariogenesis or prohealth across all studies reviewed or when limited to studies correcting for multiple testing were detected in plaque and saliva. This suggests that studies using saliva can provide insights into cariogenesis. Further, although the most proximal cause of caries might be found in dental plaque (25), saliva might contribute to or thwart cariogenesis.

Abbreviations

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Provided in the supplementary material

Competing interests

The authors declare no conflicts

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Author Contributions

All authors contributed extensively to the work presented in this manuscript. DB and BF contributed to the conception and design of the study. DB, BF, and DM screened articles for eligibility and synthesized the information into tables. DB performed data analysis and interpretation. DB and BF were contributors in writing the manuscript. All the co-authors critically reviewed the manuscript, read and approved its final version to be published.

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Table

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Figures

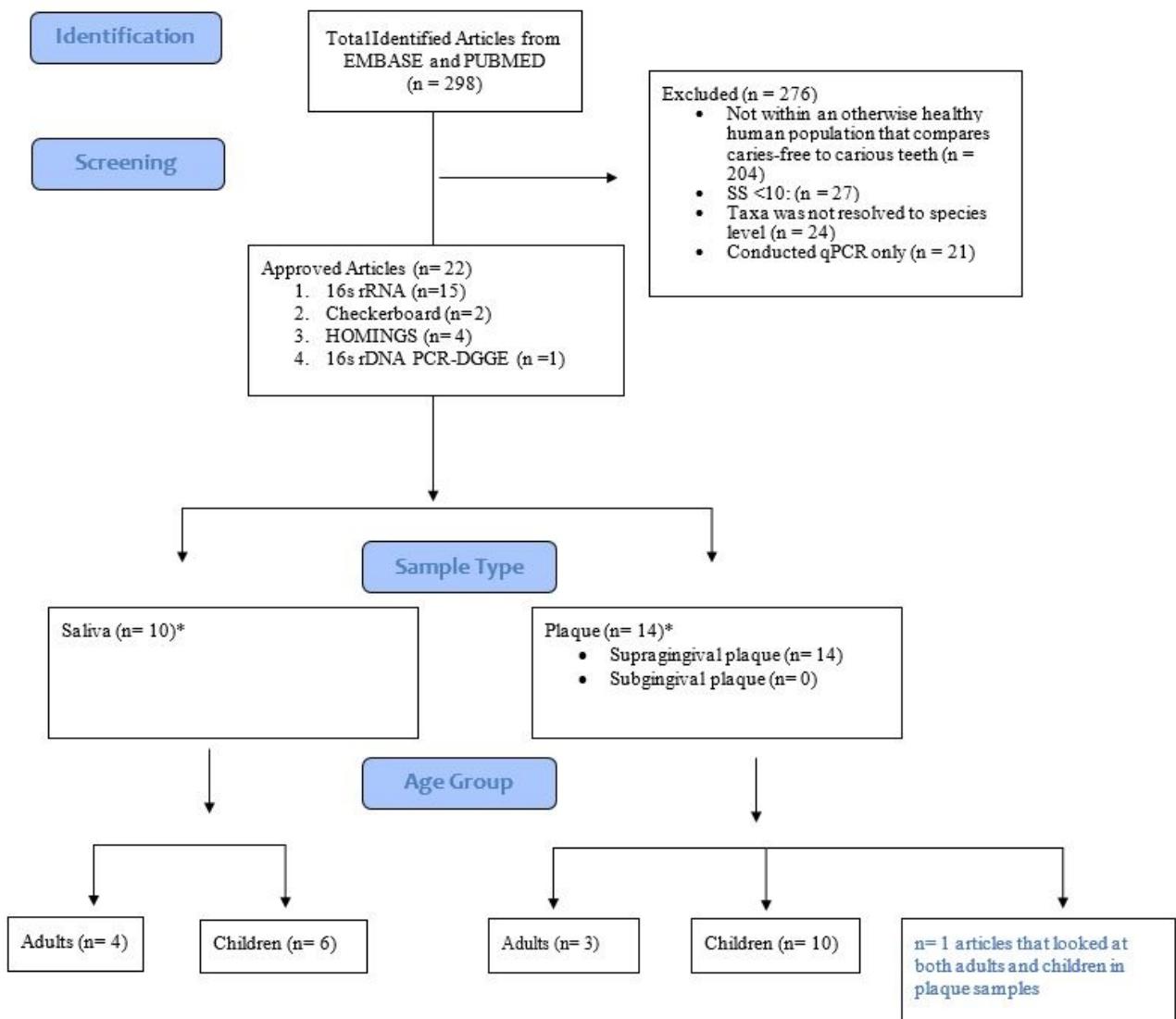


Figure 1

Schematic diagram depicting literature search process for oral microbiome studies conducted in the past 10 years from EMBASE and PUBMED.

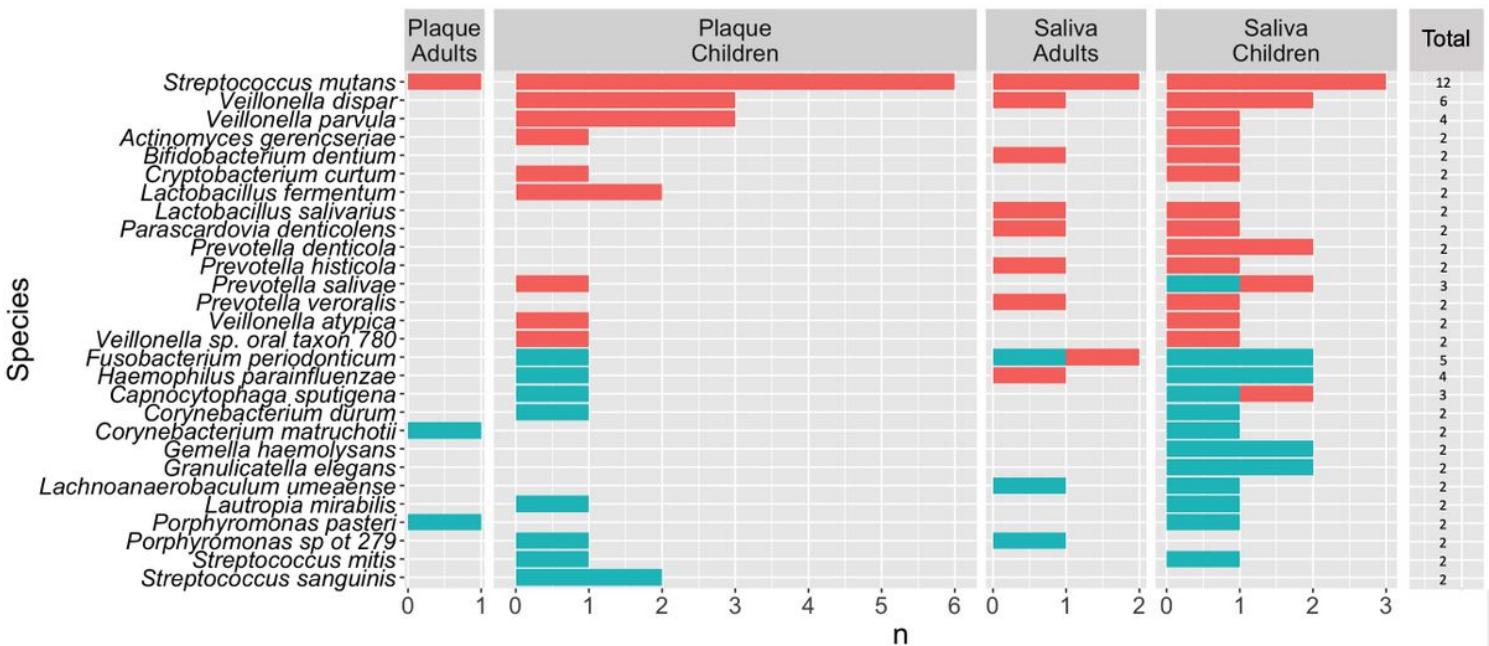


Figure 2

Number of studies that found statistically significant taxa identified as cariogenic (red) or pro health (green) from the total 24 studies found eligible in this scoping review, stratified by sample type and age group. Studies that looked at plaque in adults (n = 3), plaque in children (n = 10), saliva in adults (n = 4), saliva in children (n = 6), and saliva in both children and adults (n = 1). Only one study looked at plaque in both children and adults, and had no overlapping taxa found. Note: Only taxa that were found to be statistically significant in at least 2/24 studies are presented.

Supplementary Files

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