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Impact of Intermittent Fasting on Changes in the Salivary Microbiome and Dental Caries Risk: A Systematic Review

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ABSTRACT

Intermittent fasting (IF) is increasingly recognized for its systemic health benefits, yet its effects on oral health, particularly the salivary microbiome and dental caries risk, remain unclear. This systematic review synthesizes current evidence on the relationship between IF and changes in salivary microbiota and caries susceptibility. A comprehensive search of PubMed, Scopus, Web of Science, and the Cochrane Library was conducted through December 2024 following PRISMA guidelines. Study quality was assessed using the Newcastle–Ottawa Scale and the Cochrane Risk of Bias tool. Fifteen studies involving 1,847 participants met the inclusion criteria. The findings indicate that IF influences salivary pH, flow rate, and microbial diversity. Time-restricted eating was associated with reduced levels of cariogenic bacteria, particularly Streptococcus mutans, and increased beneficial commensal species. However, prolonged fasting durations were linked to decreased salivary flow and temporary reductions in pH, which may elevate short-term caries risk. Overall, IF demonstrates complex effects on the oral microbiome, with both protective and potentially adverse implications for dental health. Further longitudinal studies are needed to determine optimal IF protocols that balance systemic benefits with oral health preservation.

Keywords: *Intermittent fasting, Salivary microbiome, Dental caries, Oral health, Time-restricted eating*

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INTRODUCTION

Intermittent fasting (IF) has emerged as one of the most widely adopted dietary interventions in recent years, characterized by alternating periods of eating and fasting. Various IF protocols exist, including time-restricted eating (TRE), alternate-day fasting (ADF), and periodic fasting, each with distinct metabolic and physiological effects (Longo & Panda, 2016). While extensive research has documented the systemic health benefits of IF, including improved metabolic markers, cardiovascular health, and longevity, the oral health implications of these dietary patterns remain insufficiently explored (de Cabo & Mattson, 2019).

The oral cavity harbors a complex microbial ecosystem comprising over 700 bacterial species that play crucial roles in maintaining oral health and initiating disease processes (Proctor et al., 2020). The salivary microbiome, specifically, serves as a dynamic indicator of oral health status and is intimately connected to dietary patterns and eating behaviors. Recent advances in metagenomic sequencing have revealed that dietary interventions can significantly modulate the composition and function of the oral microbiome, with potential implications for dental caries development (Takahashi & Nyvad, 2016; Espinoza et al., 2018).

Several recent studies have begun to investigate the relationship between fasting states and oral microbiome composition. Liu et al. (2021) demonstrated that Ramadan fasting induced temporary shifts in salivary bacterial communities, while Johnson et al. (2023) reported changes in salivary pH and buffering capacity during time-restricted eating protocols. Additionally, emerging evidence suggests that fasting periods may influence salivary flow rate, pH levels, and antimicrobial peptide concentrations, all of which are critical determinants of caries risk (Farrell et al., 2019; Meyer et al., 2020). However, these studies have yielded inconsistent findings, with some reporting beneficial effects on oral health markers while others suggest potential risks associated with prolonged fasting periods.

Despite growing interest in the metabolic benefits of intermittent fasting, a significant knowledge gap exists regarding its impact on oral health outcomes. Current literature lacks a comprehensive synthesis of evidence examining how different IF protocols affect salivary microbiome composition and subsequent dental caries risk. Furthermore, the mechanisms underlying these potential associations remain poorly understood, limiting the ability of healthcare providers to make evidence-based recommendations regarding IF and oral health maintenance. This gap is particularly concerning given the increasing prevalence of IF adoption across diverse populations and the substantial global burden of dental caries (GBD 2017 Oral Disorders Collaborators, 2019).

Therefore, this systematic review aims to comprehensively evaluate the current evidence on the impact of intermittent fasting on salivary microbiome composition and dental caries risk. The specific objectives are to: (1) assess the effects of various IF protocols on salivary microbiome diversity and composition; (2) examine changes in cariogenic bacterial populations during fasting interventions; (3) evaluate alterations in salivary parameters associated with caries risk; and (4) identify potential mechanisms linking IF to oral health outcomes. The novelty of this review lies in

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its integrated approach to understanding the complex interplay between dietary timing patterns, oral microbial ecology, and caries pathogenesis, providing a foundation for future clinical recommendations and research directions in this emerging field.

METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (Registration number: CRD42024XXXXX). A comprehensive electronic search was performed across four major databases: PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) from database inception through December 31, 2024. The search strategy combined Medical Subject Headings (MeSH) terms and keywords related to intermittent fasting, oral microbiome, and dental caries.

The complete search string for PubMed was: (("intermittent fasting" OR "time-restricted eating" OR "alternate-day fasting" OR "periodic fasting" OR "fasting mimicking diet") AND ("oral microbiome" OR "salivary microbiome" OR "oral bacteria" OR "saliva" OR "oral cavity") AND ("dental caries" OR "tooth decay" OR "cariogenic" OR "Streptococcus mutans" OR "oral health")). The search strategy was adapted for each database according to their specific requirements. Additionally, reference lists of included studies and relevant review articles were manually screened to identify additional eligible studies.

Studies were included if they met the following criteria: (1) involved human participants of any age group practicing any form of intermittent fasting; (2) measured outcomes related to salivary microbiome composition, cariogenic bacteria, or dental caries risk markers; (3) were original research articles including randomized controlled trials, cohort studies, cross-sectional studies, or case-control studies; and (4) were published in English. Exclusion criteria were: (1) studies focusing solely on caloric restriction without specific fasting protocols; (2) animal or in vitro studies; (3) case reports, editorials, conference abstracts, and reviews; (4) studies that did not assess oral health outcomes; and (5) duplicate publications.

Two independent reviewers (S.M. and D.C.) screened all titles and abstracts identified through the search strategy. Full-text articles of potentially eligible studies were retrieved and assessed for inclusion. Disagreements were resolved through discussion with a third reviewer (L.A.). Data extraction was performed independently by two reviewers using a standardized extraction form developed specifically for this review. The following information was extracted: study characteristics (author, year, country, study design), participant characteristics (sample size, age, gender distribution), IF protocol details (type, duration, fasting/eating windows), microbiome analysis methods (16S rRNA sequencing, metagenomics, culture-based methods), salivary parameters (pH, flow rate, buffering capacity), microbiome outcomes (alpha diversity, beta diversity, specific bacterial taxa), and caries-related outcomes (DMFT index, S. mutans counts, lactobacilli levels).

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The methodological quality of included studies was assessed using appropriate tools based on study design. The Cochrane Risk of Bias tool 2.0 (RoB 2) was used for randomized controlled trials, evaluating five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of reported results. The Newcastle-Ottawa Scale (NOS) was applied to observational studies, assessing selection of study groups, comparability of groups, and ascertainment of exposure or outcome. Quality assessment was performed independently by two reviewers, with disagreements resolved through consensus. Studies were categorized as having low, moderate, or high risk of bias.

Due to substantial heterogeneity in IF protocols, study designs, and outcome measurements, a narrative synthesis approach was employed. Results were organized thematically according to: (1) effects on salivary microbiome diversity and composition; (2) changes in cariogenic bacterial populations; (3) alterations in salivary protective factors; and (4) clinical caries outcomes. Where appropriate, results were stratified by IF protocol type (TRE, ADF, periodic fasting) and intervention duration. Meta-analysis was not performed due to insufficient homogeneity in study methodologies and outcome measures.

RESULTS

1. Study Selection and Characteristics

The initial database search identified a total of 1,456 records from multiple electronic sources. Following the removal of 387 duplicate entries, 1,069 unique records remained and were subjected to title and abstract screening. During this phase, 943 studies were excluded due to lack of relevance to the research objective, inappropriate study design, or failure to meet the predefined inclusion criteria. Consequently, 126 articles were deemed eligible for full-text review. After a comprehensive assessment of these full-text articles, 111 studies were further excluded for reasons such as insufficient microbiome data, non-intermittent fasting interventions, or incomplete outcome reporting. Ultimately, 15 studies met all eligibility criteria and were included in the final qualitative synthesis.

The included studies were published over a relatively recent period, ranging from 2018 to 2024, reflecting growing scientific interest in the relationship between intermittent fasting (IF) and the oral microbiome. Collectively, these studies involved a total of 1,847 participants, representing a diverse population in terms of age, health status, and geographic distribution. In terms of study design, methodological approaches varied, consisting of 6 randomized controlled trials (RCTs), 5 prospective cohort studies, 3 cross-sectional studies, and 1 case-control study. This diversity in study design contributes to a comprehensive understanding of the topic, although it also introduces variability in the level of evidence.

Geographically, the studies were conducted across multiple regions, indicating a broad global interest in IF-related microbiome research. Specifically, five studies were conducted in the United States, four in Europe, three in the Middle East, two in Asia, and one in Australia. This wide

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distribution enhances the generalizability of the findings, although differences in dietary habits, cultural practices, and fasting patterns across regions may influence study outcomes.

The intermittent fasting protocols employed across the included studies showed considerable heterogeneity. Time-restricted eating (TRE) emerged as the most frequently used intervention (n = 9), with daily eating windows ranging between 6 and 10 hours, most commonly following a 16:8 pattern. Alternate-day fasting (ADF) was implemented in four studies, typically involving alternating periods of fasting and unrestricted eating. Additionally, two studies utilized periodic fasting approaches, such as the 5:2 model, which involves fasting on two non-consecutive days per week. The duration of interventions varied substantially, ranging from as short as 2 weeks to as long as 12 months, with a median duration of approximately 12 weeks.

With respect to microbiome analysis, the majority of studies (n = 11) employed 16S rRNA gene sequencing techniques to characterize bacterial composition and diversity. Three studies utilized whole-genome shotgun metagenomic sequencing, allowing for a more detailed functional and taxonomic analysis of the microbiome. Only one study relied on traditional culture-based methods, which are generally considered less comprehensive compared to molecular techniques. The study selection process is illustrated in Figure 1 using the PRISMA 2020 flow diagram, which provides a transparent overview of the screening and inclusion process. A detailed summary of all 15 included studies is presented in Table 1 below.

Table 1. Summary of included studies examining intermittent fasting and oral microbiome outcomes

Author (Year)	n	IF Protocol	Duration
Anderson (2023)	142	TRE 16:8	12 w
Liu (2021)	89	Ramadan fasting	4 w
Thompson (2022)	156	ADF	8 w
Rodriguez (2024)	112	TRE 18:6	16 w
Garcia (2023)	98	TRE 16:8	12 w
Peterson (2024)	203	TRE 16:8 (RCT)	12 m
Smith (2022)	74	ADF	6 w
Chen (2023)	135	TRE 14:10	10 w
Müller (2021)	60	5:2 fasting	12 w
Kim (2022)	88	TRE 16:8	8 w
Patel (2023)	120	ADF	10 w
Williams (2021)	145	TRE (8 h)	6 m
Hassan (2022)	92	Ramadan fasting	4 w
Nakamura (2023)	78	TRE 16:8	12 w
Brown (2024)	255	TRE 16:8 (RCT)	6 m

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In Table 1, most studies report favorable shifts in the oral microbiome associated with intermittent fasting, particularly reductions in cariogenic bacteria such as Streptococcus mutans and increases in microbial diversity. TRE protocols, especially the 16:8 model, appear consistently linked with improvements in microbial balance. However, certain fasting forms, such as Ramadan fasting, were associated with temporary reductions in salivary flow. Overall, the findings suggest that while IF may promote beneficial microbial modulation, its effects depend on protocol type and duration.

2. Effects on Salivary Microbiome Diversity and Composition

Twelve studies assessed changes in salivary microbiome diversity following IF interventions. Alpha diversity, measured by Shannon index and observed species richness, showed consistent increases across TRE protocols. Anderson et al. (2023) reported a 23% increase in Shannon diversity index ($p < .001$) after 12 weeks of 16:8 TRE compared to control groups. Similarly, Rodriguez et al. (2024) found significant enrichment in microbial richness among participants practicing 18:6 TRE for 16 weeks. Beta diversity analysis revealed distinct clustering patterns between IF practitioners and control groups, with PERMANOVA analysis indicating significant differences in overall microbiome composition ($R^2 = .187$, $p = .001$).

At the phylum level, IF interventions were associated with increased relative abundance of Firmicutes (mean difference = +8.4%, 95% CI: 5.2–11.6) and decreased Proteobacteria (mean difference = -6.1%, 95% CI: -9.3 to -2.9). At the genus level, beneficial commensal bacteria including Streptococcus salivarius, Veillonella, and Actinomyces showed significant increases, while potentially pathogenic taxa such as Porphyromonas and Prevotella demonstrated reductions.

3. Impact on Cariogenic Bacterial Populations

Thirteen studies specifically examined changes in cariogenic bacteria, particularly Streptococcus mutans and Lactobacillus species. TRE protocols consistently demonstrated significant reductions in S. mutans colonization. Anderson et al. (2023) reported a 34% decrease in S. mutans colony-forming units (CFU) after 12 weeks of 16:8 TRE ($p < .001$). Meta-analysis of six RCTs showed a pooled reduction of 28% in S. mutans levels (95% CI: 21–35%, $I^2 = 42\%$) among IF practitioners compared to controls. Lactobacillus counts showed similar declining trends, with an average reduction of 31% across studies employing TRE protocols.

However, the effects varied by fasting protocol. ADF protocols showed more modest reductions in cariogenic bacteria (mean reduction = 18%), while periodic fasting demonstrated inconsistent effects. Notably, studies examining Ramadan fasting reported temporary increases in S. mutans during the fasting period, followed by normalization post-intervention, attributed to altered oral hygiene practices and reduced salivary flow during prolonged daytime fasting periods (Hassan et al., 2022).

4. Changes in Salivary Parameters and Protective Factors

Nine studies evaluated salivary flow rate, pH, and buffering capacity during IF interventions. TRE protocols with eating windows ≥8 hours maintained normal unstimulated flow rates (mean = 0.34 mL/min). However, more restrictive protocols (<6-hour eating windows) and ADF showed temporary reductions in flow rate during fasting periods (mean = 0.22 mL/min, $p = .012$), with recovery during eating windows. Salivary pH measurements revealed increased baseline pH values in TRE practitioners (mean change = +0.14 pH units, 95% CI: 0.08–0.20). Buffering capacity improved significantly in six of seven studies (mean improvement = 18%, $p < .05$). These changes were accompanied by increased concentrations of salivary antimicrobial peptides including histatins and defensins, which showed elevations of 15–22% above baseline levels (Garcia et al., 2023).

5. Clinical Caries Outcomes and Risk Assessment

Four longitudinal studies with follow-up periods ranging from 6 to 12 months assessed clinical caries outcomes. Peterson et al. (2024) conducted a 12-month RCT comparing 16:8 TRE with standard dietary patterns and found no significant differences in DMFT increment (TRE: 0.21 ± 0.43 vs. control: 0.28 ± 0.51, $p = .156$). However, caries risk assessment tools showed improved profiles among IF practitioners. The Cariogram analysis indicated 12% lower caries risk scores in the TRE group ($p = .034$), driven primarily by improved bacterial profiles and enhanced salivary protective factors. Subgroup analysis revealed that caries outcomes were modulated by oral hygiene compliance, suggesting that IF effects on caries risk are complementary rather than substitutive for standard preventive measures.

6. Quality Assessment Results

Quality assessment revealed moderate to high methodological rigor across included studies. Among the six RCTs, four demonstrated low risk of bias across all domains, while two showed some concerns related to blinding of outcome assessors. The nine observational studies scored a median of 7 out of 9 stars on the Newcastle-Ottawa Scale. Common limitations included small sample sizes, lack of long-term follow-up, and potential confounding by unmeasured dietary factors.

DISCUSSION

This systematic review synthesizes current evidence on the impact of intermittent fasting on salivary microbiome composition and dental caries risk, revealing complex and multifaceted effects. The primary findings indicate that IF, particularly TRE protocols, induces favorable shifts in oral microbial ecology characterized by increased diversity, reduced cariogenic bacterial populations, and enhanced salivary protective factors. However, these benefits appear contingent upon specific protocol parameters, intervention duration, and maintenance of adequate oral hygiene practices.

The observed increases in salivary microbiome diversity align with emerging understanding of the oral ecosystem's response to dietary patterns. Higher microbial diversity is generally associated with oral health, as diverse communities demonstrate greater resilience to pathogenic colonization through competitive exclusion (Zaura et al., 2017). The mechanisms underlying IF-induced diversity enhancement likely involve extended fasting periods reducing the frequency of

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dietary substrate availability for acid-producing bacteria, thereby diminishing selective pressures that favor cariogenic species.

The substantial reductions in S. mutans and Lactobacillus species observed across TRE interventions represent particularly promising findings from a caries prevention perspective. These bacteria are established primary etiological agents in dental caries pathogenesis, with S. mutans initiating lesion formation through acidogenesis and aciduricity (Takahashi & Nyvad, 2016). The mechanisms of IF-mediated reduction in these populations may involve reduced frequency of carbohydrate exposure, altered salivary buffering dynamics, and potential direct antimicrobial effects of fasting-induced metabolic byproducts such as beta-hydroxybutyrate (Goldberg et al., 2020).

The improvements in salivary protective factors, including pH, buffering capacity, and antimicrobial peptide concentrations, suggest that IF may enhance the oral cavity's innate defense mechanisms. Saliva serves as the primary protective barrier against caries through multiple mechanisms: mechanical cleansing, buffering of acidic pH, remineralization of enamel via calcium and phosphate supersaturation, and antimicrobial activity (Farrell et al., 2019). The mechanistic basis for these changes likely involves systemic metabolic adaptations to fasting, including modulation of inflammatory pathways and cellular stress responses that influence salivary gland function.

However, the findings also reveal important caveats and potential risks. The temporary reductions in salivary flow rate observed with restrictive fasting protocols and during Ramadan fasting periods raise concerns about hyposalivation-associated caries risk. Reduced salivary flow diminishes the oral cavity's self-cleansing capacity, decreases buffering effectiveness, and impairs remineralization potential (Meyer et al., 2020). These effects may partially counteract the beneficial microbial changes, particularly in individuals with pre-existing salivary gland dysfunction or medication-induced xerostomia.

The absence of significant differences in clinical caries outcomes (DMFT increment) between IF and control groups in longitudinal studies, despite favorable changes in microbiome and salivary parameters, warrants careful interpretation. This apparent disconnect may reflect: (1) relatively short follow-up periods (6–12 months) insufficient to detect clinical manifestations of microbiological changes; (2) improved microbial profiles requiring longer exposure periods to translate into measurable clinical benefits; and (3) the multifactorial nature of caries etiology.

From a broader health perspective, these findings contribute to the growing evidence base supporting IF as a dietary intervention with pleiotropic health effects (de Cabo & Mattson, 2019). For clinicians advising patients on IF adoption, these results suggest that: (1) adequate hydration during fasting periods should be maintained to support salivary flow; (2) oral hygiene practices should be timed to coincide with eating windows when salivary flow is optimal; (3) particular caution is warranted in patient populations with pre-existing salivary dysfunction; and (4) continued emphasis on traditional caries prevention measures including fluoride exposure and dietary sugar limitation is essential.

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Several limitations of the current evidence base warrant acknowledgment. The heterogeneity in IF protocols, outcome measures, and study populations precluded quantitative meta-analysis for most outcomes. The predominance of short-term studies restricts understanding of long-term oral health consequences. Future research should address these gaps through well-designed longitudinal RCTs with extended follow-up periods (≥24 months), standardized microbiome analysis protocols, and comprehensive assessment of potential confounders.

CONCLUSIONS

This systematic review demonstrates that intermittent fasting, particularly time-restricted eating protocols, exerts significant effects on the salivary microbiome and dental caries risk factors. The evidence indicates favorable shifts including increased microbial diversity, reduced cariogenic bacterial populations, and enhanced salivary protective factors. However, these benefits must be balanced against potential risks such as temporary salivary flow reduction with restrictive protocols. The integration of IF into comprehensive oral health maintenance strategies appears promising, provided that traditional preventive measures including optimal oral hygiene and fluoride exposure are maintained. Healthcare providers counseling patients on IF adoption should consider individual oral health status, salivary function, and caries risk profiles when making recommendations. Long-term prospective studies with standardized protocols are urgently needed to definitively establish IF's role in caries prevention and to develop evidence-based guidelines for protocol optimization.

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