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Research Article

Salivary metabolomics as an early predictor of childhood ECC before lesion formation

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ABSTRACT

Early childhood caries (ECC) remains one of the most prevalent chronic oral diseases affecting children worldwide, with conventional diagnostic approaches often detecting disease only after irreversible enamel damage has occurred. Salivary metabolomics has emerged as a promising non-invasive strategy for identifying biochemical alterations associated with ECC susceptibility before visible lesion formation. By analyzing complex metabolic profiles present in saliva, this approach can detect early changes related to microbial activity, carbohydrate metabolism, host responses, inflammation, and oxidative stress. Advanced metabolomic platforms, including mass spectrometry and nuclear magnetic resonance-based techniques, enable the identification of potential biomarker patterns that may predict caries risk and progression. Integration of salivary metabolomics with microbiome analysis, proteomics, and artificial intelligence-driven predictive models may improve early risk assessment and support personalized preventive dental care. This molecular-based approach has the potential to transform ECC management from reactive treatment toward proactive prevention by enabling timely interventions, targeted behavioral modifications, and individualized therapeutic strategies. However, clinical implementation requires standardized protocols, validation of reliable biomarkers, and development of practical chairside diagnostic technologies. Salivary metabolomics represents a promising frontier in precision pediatric dentistry for early ECC prediction and prevention.

INTRODUCTION

Early childhood caries (ECC) is a highly prevalent and complex oral disease affecting young children, characterized by rapid progression of dental decay and significant impacts on oral health, nutrition, quality of life, and future dental outcomes. ECC develops through a multifactorial interaction between cariogenic microorganisms, dietary factors, host susceptibility, and environmental influences. Although advances in preventive dentistry and restorative materials have improved disease management, conventional diagnostic approaches mainly identify ECC after visible enamel changes or cavitation, limiting opportunities for early intervention (Hajishengallis et al., 2017; Singh, 2025).

Recent advances in molecular dentistry have highlighted the importance of detecting biological alterations that occur before clinical lesion formation. The oral microbiome

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Table 1: Key Biological Components Detected by Salivary Metabolomics in ECC Prediction

Biological Component	*Examples*	*Role in ECC Prediction*
Organic acids	Lactate, acetate, succinate	Reflect bacterial acid production and cariogenic activity
Amino acid metabolites	Glutamate, alanine, phenylalanine	Indicate microbial and host metabolic responses
Carbohydrate metabolites	Glucose-related compounds	Demonstrate fermentation activity and dietary influence
Inflammatory metabolites	Oxidative stress-related molecules	Suggest early host response changes
Microbial metabolic products	Biofilm-derived compounds	Reveal microbial dysbiosis associated with ECC

plays a central role in ECC initiation and progression, with microbial communities undergoing metabolic shifts that influence acid production, enamel demineralization, and disease advancement. Understanding these microbial and biochemical changes provides opportunities for developing predictive diagnostic approaches (Duque et al., 2023; Li et al., 2023).

Salivary metabolomics has emerged as a promising non-invasive technology capable of identifying metabolic signatures associated with early cariogenic activity. By evaluating small-molecule profiles in saliva, metabolomic approaches can reveal alterations in carbohydrate metabolism, organic acid production, amino acid pathways, and host response mechanisms before structural tooth damage occurs. Studies have demonstrated the potential of salivary metabolic profiles and biomarker panels for distinguishing children with different levels of caries risk (Kim et al., 2023; Schulz et al., 2020).

Furthermore, integration of metabolomics with proteomic and microbiome-based analyses may enhance ECC prediction accuracy and support personalized preventive strategies. Salivary biomarkers offer potential applications in early risk assessment, monitoring disease progression, and guiding minimally invasive interventions (Shivaprakash et al., 2025; Singh et al., 2026). Therefore, salivary metabolomics represents a transformative approach toward precision pediatric dentistry by enabling early detection and prevention of ECC before irreversible lesions develop.

Biological Basis of Salivary Metabolomics in ECC Prediction

Saliva as a Diagnostic Biofluid in Early Childhood Caries

Saliva represents a dynamic biological fluid containing microbial metabolites, host-derived molecules, proteins, peptides, and signaling compounds that reflect the physiological status of the oral environment. In early childhood caries (ECC), metabolic alterations occur before clinically visible enamel destruction due to changes in microbial composition, acid production, and host–microbial interactions. These early biochemical variations make saliva a valuable medium for identifying children at increased caries risk through non-invasive molecular assessment (Duque et al., 2023; Li et al., 2023). Unlike conventional visual examination, salivary metabolomics provides insight into disease initiation pathways and may support preventive interventions before irreversible tooth damage occurs.

Metabolic Alterations Associated with ECC Development

ECC progression is strongly associated with increased activity of acidogenic and aciduric microorganisms, particularly those involved in carbohydrate fermentation and biofilm maturation. These microbial processes generate metabolic changes, including elevated organic acids, altered amino acid pathways, and modifications in energy metabolism, which contribute to enamel demineralization and caries progression (Hajishengallis et al., 2017). Salivary metabolomic profiling can identify

Table 2: Major Salivary Metabolomic Technologies and Their Predictive Applications in ECC

Technology	*Main Function*	*Application in ECC Prediction*
NMR spectroscopy	Global metabolic profiling	Detects overall metabolic shifts linked to caries risk
LC-MS	High-sensitivity metabolite identification	Identifies specific ECC-associated biomarkers
GC-MS	Volatile and small metabolite analysis	Evaluates microbial metabolic products
Multi-omics integration	Combines metabolome, microbiome, and proteome data	Improves predictive accuracy and personalized risk assessment

Table 3: Clinical Applications, Benefits, and Challenges of Salivary Metabolomics in ECC Prediction

Application Area	*Clinical Benefit*	*Current Challenges*
Early ECC prediction	Detects molecular changes before cavitation	Need for validated biomarkers
Risk assessment	Enables personalized preventive care	Influence of age, diet, and saliva variability
Disease monitoring	Tracks metabolic changes over time	Limited chairside diagnostic availability
Multi-omics integration	Combines microbiome, metabolome, and proteome data	Requires standardized analytical protocols
Precision dentistry	Supports individualized treatment planning	Cost and technical complexity

these biochemical signatures and distinguish healthy children from those with early metabolic patterns associated with ECC.

Studies evaluating salivary and pellicle metabolites have demonstrated differences in metabolic profiles among children with varying caries activity, supporting the potential use of metabolite patterns as predictive indicators (Schulz et al., 2020). Furthermore, specific salivary metabolic biomarker panels have shown promise for ECC detection by identifying combinations of metabolites associated with disease status (Kim et al., 2023).

Integration of metabolomic data with microbiome and proteomic profiles may enhance predictive accuracy and facilitate personalized preventive strategies in pediatric dentistry (Li et al., 2023; Shivaprakash et al., 2025). Such molecular approaches complement preventive and minimally invasive treatments aimed at preserving tooth structure and controlling disease progression (Singh, 2025; Singh et al., 2026).

Metabolomic Technologies and Predictive Applications in ECC

Salivary metabolomics has emerged as a powerful molecular approach for identifying early biochemical changes associated with early childhood caries (ECC) before clinical lesion development. By characterizing small-molecule metabolites in saliva, metabolomic technologies provide insights into microbial metabolism, host responses, and disease-associated pathway alterations. These approaches complement traditional clinical examination by detecting subtle metabolic disturbances linked to cariogenic activity (Hajishengallis et al., 2017).

Analytical Platforms for Salivary Metabolomics

Advanced technologies such as nuclear magnetic resonance (NMR) spectroscopy, liquid chromatography–mass spectrometry (LC-MS), and gas chromatography–mass spectrometry (GC-MS) enable comprehensive profiling of salivary metabolites. NMR provides reproducible global metabolic analysis, whereas LC-MS and GC-MS offer high sensitivity for identifying specific biomarkers. Targeted metabolomic studies have demonstrated differences in salivary and pellicle metabolic profiles between children with different levels of caries activity, supporting their diagnostic potential (Schulz et al., 2020).

Identification of Predictive Biomarker Signatures

Salivary metabolic profiling has enabled the discovery of biomarker panels associated with ECC risk. Alterations in organic acids, amino acids, carbohydrates, and lipid-related metabolites reflect increased bacterial fermentation, acid production, and host–microbial interactions. Kim et al. (2023) identified a salivary metabolic biomarker panel capable of distinguishing children with ECC, highlighting the potential for early molecular diagnosis. Furthermore, combined salivary microbiome and metabolome analyses have demonstrated improved understanding of metabolic pathways involved in severe ECC progression (Li et al., 2023).

Integration with Multi-Omics and Predictive Models

Combining metabolomics with microbiome sequencing, proteomics, and artificial intelligence-based predictive algorithms may enhance ECC risk prediction. Oral microbial signatures provide important context for interpreting metabolic changes associated with disease initiation and progression (Duque et al., 2023). Salivary biomarker approaches may support personalized preventive strategies and minimally invasive interventions, complementing modern restorative and preventive concepts in pediatric dentistry (Singh, 2025; Singh et al., 2026).

Clinical Applications, Advantages, Challenges, and Future Perspectives

Clinical Applications

Salivary metabolomics offers significant potential for transforming ECC management through early molecular detection before visible lesion development. Metabolic profiling can identify children at high risk by detecting alterations in salivary metabolites associated with cariogenic bacterial activity, host responses, and disease progression (Kim et al., 2023; Schulz et al., 2020). These biomarkers may support individualized preventive

strategies, including targeted dietary counseling, fluoride interventions, and monitoring of caries-risk changes. Integration with oral microbiome analysis can further improve prediction accuracy by linking microbial dysbiosis with metabolic alterations involved in ECC initiation and progression (Duque et al., 2023; Li et al., 2023). Salivary metabolomics may also complement minimally invasive treatment approaches by enabling early intervention before extensive restorative procedures are required (Singh et al., 2026; Singh, 2025).

Advantages

Salivary metabolomics provides a non-invasive, child-friendly diagnostic approach with high potential for repeated monitoring. It offers deeper biological insights than conventional examination by identifying early metabolic disturbances associated with ECC development (Schulz et al., 2020). Combined metabolomic and proteomic approaches may enhance diagnostic reliability and improve preventive decision-making (Shivaprakash et al., 2025).

Challenges and Future Perspectives

Major limitations include biological variability, lack of standardized biomarker panels, and the need for large-scale clinical validation. Future developments will focus on artificial intelligence-assisted metabolic interpretation, portable chairside devices, and integrated microbiome–metabolome platforms for real-time ECC risk prediction. These advances may facilitate precision pediatric dentistry by enabling earlier, personalized, and preventive management of childhood caries (Kim et al., 2023; Li et al., 2023).

Conclusion

Salivary metabolomics represents a promising advancement in the early prediction and prevention of early childhood caries (ECC) by enabling detection of molecular changes before the appearance of clinically visible lesions. Through comprehensive analysis of salivary metabolic profiles, this approach provides valuable insights into microbial activity, host responses, and biochemical pathways associated with caries initiation and progression. The integration of metabolomics with oral microbiome analysis, proteomic profiling, and artificial intelligence-based predictive models may enhance risk assessment accuracy and support personalized preventive strategies. Although challenges related to biomarker validation, standardization, cost, and clinical translation remain, continued technological development is expected to improve the feasibility of chairside applications. Ultimately, salivary metabolomics has the potential to shift pediatric dentistry from conventional disease management toward precision-based prevention, allowing early intervention, improved oral health outcomes, and reduced burden of ECC in children.

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