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Systematic Review

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Evaluating Preventive Health Strategies: Salivary Biomarkers as Non-Invasive Indicators of Caries Risk in School Children

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ABSTRACT

Dental caries, a prevalent oral health condition affecting 514 million children aged <6 years, globally, was a significant public health concern. Salivary biomarkers offer a non-invasive approach to assessing caries risk. However, research on the specific role of salivary components in caries progression and prevention was limited. This systematic review aimed to evaluate the potential of salivary biomarkers as a valuable tool for predicting caries risk in school children. **Objective:** To evaluate the role of Salivary Biomarkers in risk assessment of caries in school children. **Methods:** A systematic review of literature published between January 2009 and February 2024 focused on studies investigating the association between salivary biomarkers and caries risk in school-aged children. PubMed, Google Scholar, Cochrane Library, Springer, and Science Direct were searched, and the PRISMA guidelines were followed. 500 full-text papers were screened for eligibility, and 43 studies meeting the inclusion criteria were evaluated, relevant information was extracted, and a systematic review was conducted with 43 included studies. **Results:** Salivary biomarkers, including proteomics, microbiota, sugar metabolization, IgA levels, and salivary metabolic profiles, were significantly correlated with the risk of developing caries. Salivary samples demonstrated superior sensitivity, specificity, cost-effectiveness, and patient acceptance compared to blood samples for predicting caries risk. **Conclusions:** The findings suggested that salivary biomarkers hold promise as valuable non-invasive tools for stratifying caries risk in school children. Further research was needed to validate these biomarkers and integrate them into routine dental care to improve preventive strategies.

INTRODUCTION

Dental caries in children or Early Childhood Caries (ECC) is the major chronic disease affecting more than 600 million children globally. Its prevalence is estimated to be more than the combined number of 5 leading Noncommunicable Diseases (NCDs) namely Cardiovascular Disease (CVD), mental health conditions, Diabetes Mellitus (DM), chronic respiratory disorders, and cancers. Nearly, 35% of the world's population is affected with caries, becoming a major public health burden worldwide. Globally, 2.3 billion populations are reported with untreated caries followed by periodontitis affecting nearly 1 billion populations. Sathiyakumar T *et al.*, reported that sociodemographic factors such as age, gender, and ethnicity play a pivotal role in determining the risk of caries development. They concluded that the male child population (aged <11 years) compared to the female child population was highly attributable to dental caries [1]. The estimated prevalence of dental caries in Pakistan is around 60% [2]. ECC is

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characterized by the formation of tooth decay in children aged less than six years [3]. It is also known as a family disease due to its ability to transmit caries-causing bacteria from caregivers to children. Several studies showed that caries prevalence rates are higher among females than males [4]. According to the WHO, approximately 3 in every 4 caries cases are reported in Low and Middle Income Countries (LMICs) [5]. Universal Health Coverage (UHC) comprises no treatment for oral health conditions. Consequently, this leads to potential preventable barriers associated with the delivery of effective and equal oral health services. Dental caries is generally caused by the bacterial fermentation of dietary carbohydrates in the susceptible host. Smooth surface caries in primary maxillary anterior teeth, and missed, or decayed surfaces are indicative of ECC in children <6 years [6]. ECC can cause poor ability of children to eat or drink, malnutrition, speaking and sleeping issues, impaired social and behavioural patterns, and low self-esteem. According to Hemadi AS *et al.*, ECC can affect the Quality of Life (QoL) of children. It may be influenced by weak immune systems of children, prevalent cariogenic bacteria, feeding type, and oral hygiene among children. The presence of cariogenic bacteria such as *Mutans streptococcic*, *Lactobacilli*, and *Candida spp.* in saliva has been strongly associated with the risk of ECC [7]. Caries risk assessment also known as, CRA, is essential for the optimum management of ECC. There are four CRA tools, namely CAMBRA form, Cariogram model, American Dental Association (ADA), and American Academy of Pediatric Dentistry (AAPD) CRAs [8]. The goal of CRA is to accurately evaluate and prevent the development of carious lesions in children and adults [9]. Traditionally, epidemiological studies related to ECC performed by using biomarkers such as blood in school children have remained a challenging task. They are known as invasive procedures causing great stress and pain among school children aged <6 years [10]. Currently, non-invasive procedures such as saliva biomarkers are being used as blood sample alternatives for the risk assessment of dental caries among school children. They cause less stress, improve participation rates, increase samples, and reduce risk to children and healthcare providers, and more economical and less painful procedures. These properties make saliva samples more favorable than blood samples when evaluating risk assessment of caries in children [11]. Saliva is a complex biomolecule containing essential organic and inorganic compounds including bacteria. Salivary biomarkers have been used in various oral health studies, evaluation of metabolic disease risk, and identification of taste sensitivity [12]. Saliva is also an essential innate defense mechanism in humans [13]. Saliva contains protein compounds that are crucial for the maintenance of oral health hygiene and homeostasis [14]. It is also estimated that changes in salivary proteome concentrations may increase the risk of oral diseases [15]. Proteomics in saliva such as defensins, lactoferrin, and proline peptides are associated with regulating oral normal flora by the release of antibacterial compounds [16]. Our systematic review identified limited high-quality epidemiological evidence on the use of saliva as a biomarker for the risk assessment of ECC. Furthermore, the literature lacks enough data evaluating the correlation between saliva and the risk of caries, the use of saliva as a non-invasive sample collected, evaluation of saliva analyte to determine oral health hygiene among school children. Therefore, it created a need to conduct a detailed systematic review on the role of salivary biomarkers for the risk assessment of caries in school children.

METHODS

PubMed, Cochrane Library, ScienceDirect, Springer and Google Scholar were systematically searched to collect all the potential studies conducted during the last 15 years (January 2009 to February 2024) by using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and following search keywords "Caries Risk Assessment", "salivary biomarkers", "salivary biomarkers efficacy", "saliva", "dental caries". "Salivary biomarkers caries assessment", "caries predictive models", "CRA". We primarily focused on research articles containing relevant studies on the role of salivary biomarkers in caries risk assessment for school children. Reference lists of selected relevant studies were further screened for other potentially eligible studies. Titles and abstracts of full research papers were screened for their relevancy and defined as original research focusing on the topic "the role of salivary biomarkers in caries risk assessment for school children". In this systematic review, initially, a total of 18,198 studies were identified. After excluding duplicates, reviewing titles of the papers, editorials, irrelevant full-text papers, and full-text papers not in English, a total of 2,000 studies were included for screening. After thoroughly screening the abstract of the remaining papers, 1500 more studies were excluded for reasons such as insufficient data for analysis, duplicates, citations in the abstract form, non-English citations, interventions not related to salivary biomarkers, studies conducted among the adult population which was outside the target population (school going children, aged <9 years). Followed by an in-depth reading of 500 remaining full-text articles that led to the exclusion of 457 papers, for reasons such as not mentioning the salivary biomarkers for CRA in school children, and the inclusion of school children aged <6 years. Ultimately, 43 studies were included for qualitative synthesis (Figure 1).

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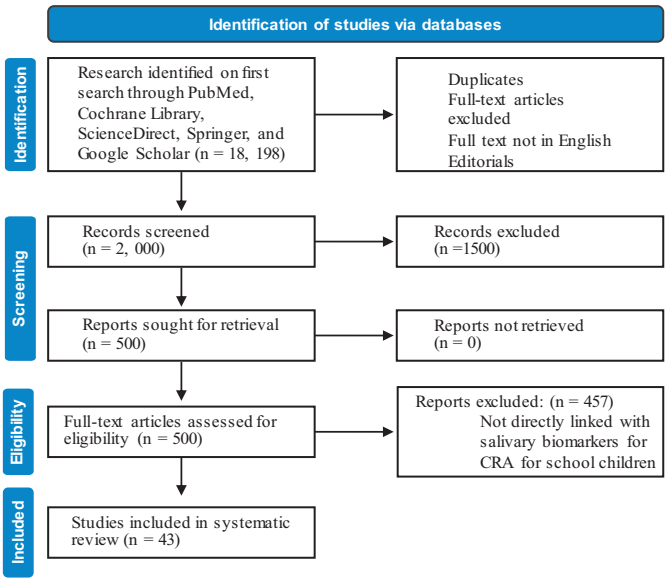

Figure 1: PRISMA Flowchart Diagram of the Screened Studies Included in the Systematic Review

RESULTS

Table 1 listed the different standard references used in included studies to evaluate the salivary biomarkers and their roles in caries risk assessment.

Table 1: Table of Reference used for Analytical Methods of Saliva Sample used in Studies Included

Characteristics	Standard Reference Used in Studies
Caries Classification	ICDAS (reference values = 0-6, Ranging from noEvidence of Caries to Distinct Cavity with Visible Dentine)
Salivary Proteomic Profile	Human Metabolome Specialised Dataset
Salivary Microbiome Profile	CRT* guideline chart (<105 CFU/ml saliva or ≤ 105 CFU/ ml saliva)
Salivary pH	Silver-silver Chloride Electrode (≤ 6.6 and >6.6)
The Buffering Capacity of Saliva	Titration (≤9 and >9)
Statistical Analysis	SPSS, the area under the ROC Curve
Immunology of Saliva (inflammatory Markers,Beta -defensin 3, TLRs)	ELISA test kit

*ICDAS; International caries detection and assessment system, TLRs; toll-like receptors, ELISA; enzyme-linked immunosorbent assay, CRT; caries risk test. *Caries risk test was a reliable, simple, and effective caries diagnostic test to detect cariogenic bacteria. CRT kit uses selective culture media for the CRA.*

The most common type of salivary parameters used for CRA were salivary microbiota, metabolic, and molecular salivary profile. Eleven studies evaluated the association of salivary microflora and caries development. Seventeen studies explored the role of salivary proteomics and sugar profile for the CRA. Four studies examined the salivary pH and buffering capacity in caries progression. Six studies evaluated the role of salivary IgA, and inflammatory markers in the development of caries. The remaining five studies examined the risk prediction accuracy of CRA models using salivary biomarkers (Table 2).

Table 2: Summary of Study Findings Evaluated

S.No.	Study Design	Country	Total Participants/ Total Studies Included	Salivary Parameters	Increased/ decreased conc.In Caries	Methods	References
1	Prospective Study	Australia	208 Children	*Mutans streptococci*	Increased	CFU	Fernando *et al.*,2021 [19]
2	Longitudinal Study	Australia	239 Children	*Mutans streptococci*	Increased	Mann-Whitney U Test	Lallo *et al.*, 2019 [20]
3	Clinical Study	China	90 Children	*Lactobacillus, Arthrospira spp*	Increased	PCR	Lin *et al.*, 2023 [21]
4	Cohort Study	Finland	11,400 Children	*Paludibacter, labrenzia*	Increased	PCR and Illumina HiSeq	Manzoor *et al.*, 2021 [22]
5	Prospective Case-Control Study	Iraq	89 Children	*Streptococcus mutants*	Increased	Chairside Diagnostic Kit	Hamalaw, Kareem and Gul 2021 [24]
6	Case-Control	India	160 Children	*Streptococcus mutants, Lactobacillus*	Increased	ELISA, CFU	Menon and Bhat 2019 [25]
7	Longitudinal	Japan	85 Children	*Salivary ALT, P. gingivalis*	Increased	Mann-Whitney U Test	Nomura *et al.*, 2012 [26]
8	Cohort	Mexico	110 Children	Salivary microbiota, flow rate	Useful Predictors for CRA	Synder tests, Fissure Morphology, Caries Experience	Sánchez-Pérez *et al.*,2009 [27]

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9	Comparative Study	Spain	35 Children	Statherin	Increased	ELISA	Angarita-Díaz *et al.*,2021 [28]
10	Case-Control	USA	41 Children	Statherin, cystatin S	Increased	MS	Rudney, Staikov and Johnson 2009 [29]
11	Prospective	Serbia	213 Children	Salivary pH	Decreased	Digital pH Meter	Stojković *et al.*, 2020 [30]
12	Systematic Review	Saudi Arabia	18 Studies	Salivary Biomarkers	Potent CRA Biomarker	ELISA, DMF, Spectro photometry	Alamoudi *et al.*,2022 [31]
13	Case-Control	Iran	163 Children	Oxidative Stress	Decreased	Spectro photometry	Salman *et al.*, 2021 [32]
14	Clinical Study	India	100 Children	Buffering Capacity	Decreased	Digital pH Meter, Titration	Jayaraj and Ganesan 2015 [33]
15	Prospective Case-Control	Serbia	40 Children	Leptin	Decreased	ELISA	Petrović *et al.*, 2022 [34]
16	Case-Control Study	India	120 Children	Salivary Ferritin	Increased	Chemiluminescence Micro particle Immunoassay	Rajkumaar and Mathew 2020 [35]
17	Case-Control Study	Saudia Arabia	64 Children	Salivary Cortisol	Increased	ECL Immunoassay	Pani *et al.*, 2013 [36]
18	Case-Control Study	Greece	36 Children	(alpha-Amylase 2B, beta-Defensin 4A)	Downregulated	LC-MS	Pappa *et al.*, 2021 [37]
19	Case-Control Study	UK	61 Children	Fluoride	Decreased	Validated Questionnaires	Idowu *et al.*, 2020 [38]
20	Case-Control Study	China	28 Children	Salivary Protein (SMR-3B)	Differentially Expressed	LC-ESI-MS	Zhou *et al.*, 2021 [41]
21	Randomized Controlled	India	400 Children	Salivary pH, Buffering Capacity	Decreased	pH Test Strips, Buffer pH Pad	Choudhary *et al.*, 2022 [42]
22	Case-Control Study	Russia	20 Children	Salivary Mineral Organic, Carbon-Phosphate	Improved CRA	FTIR	Seredin *et al.*, 2018 [45]
23	Systematic Review and Meta-Analysis	Brazil	5419 Papers	No_2-	Decreased	Newcastle-Ottawa Scale Assessment	Díaz-Fabregat *et al.*, 2024 [46]
24	Case-Control	india	100	Nitric Oxide	Increased	Griess Reaction Method	Syed, Sachdev and Chopra 2016 [47]
25	Case-Control	Pakistan	80 Children	Salivary Beta Defensin-3	Decreased	ELISA	Faheem *et al.*, 2021 [48]
26	Exploratory, Cross-Sectional Study	Norway	176 Children	Salivary Inflammatory Markers (macrophage CSF1)	Increased	LASSO	Børsting *et al.*, 2022 [49]
27	Meta-Analysis	China	30 Case-Control Studies	Salivary IgA	Decreased	Sensitivity Analysis, Funnel Diagram	Wu *et al.*, 2020 [50]
28	Prospective non-Randomized Clinical Study	USA	40 Children	Soluble TLR-2	Increased	ELISA	Zhao *et al.*, 2014 [51]

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29	Systematic Review and Meta-Analysis	Pakistan	28 Papers	Salivary IgA	Decreased	Newcastle Ottawa Quality Assessment Scale	Hamid *et al.*, 2020 [52]
30	Systematic Review	Italy	16 Papers	Interleukins (IL-2 RA, 4-13), mucins, glycoproteins (sCD14)	Increased	ICDAS	Antonelli *et al.*, 2024 [53]
31	Case-Control	Spain	68 Children	Salivary lactate, acetone, proline, mannose	Increased	NMR spectroscopy	Musalem-Dominguez *et al.*,2023 [54]

Abbreviations: CFU; colony-forming unit, PCR; polymerase chain reaction, CRA; caries risk assessment, ELISA; enzyme-linked immunosorbent assay, MS; mass-spectroscopy, ECL; Electrochemiluminescence, LC-MS; Liquid-chromatography-mass spectrometry, LC-ESI-MS; Liquid chromatography-electrospray ionization tandem mass spectrometry, SELDI-TOF-MS; Surface-enhanced laser desorption/ionization time-of-flight mass spectrometry, FTIR; Fourier transform infrared spectroscopy, PLS; Partial least square, LASSO; Least absolute shrinkage and selection operator, ICDAS; International caries detection and assessment system, NMR; Nuclear magnetic resonance, TLR-2; toll-like receptors-2, CSF1; colony-stimulating factor 1, PR3; proteinase 3, ALT; Alanine aminotransferase, DMF; decayed, missing, filled teeth

DISCUSSION

Salivary biomarkers can be a potential source for the Caries Risk Assessment (CRA) in school children [17]. The included studies used the processes which generally include 3 steps. The first step involves saliva sample collection of case and control groups proceeded by the application of analytical methods such as mass spectrometry, PCR amplification and sequencing and ELISA test [18-20]. Through these procedures, potential salivary biomarkers such as salivary peptidome, metabolome profile, pH, buffering capacity, and IgA levels were identified. A prospective study comprising of 208 children (aged <17 years) was conducted by Siddiqui AA *et al.*, in Australia [2]. The study found children with a high load of Mutants Streptococci (MS) ($p = 0.03$) and Lactobacilli (LB) ($p = 0.004$) in the saliva. It was determined by Colony Forming Units (CFU) using a CRT guideline chart as reference and low salivary flow rates ($p < 0.01$) measured by using GC Saliva Check test kits, reported with advanced carious cases [3]. These findings were similar to a longitudinal study consisting of 239 Aboriginal children (aged <17 years) conducted by Lallo R *et al.*, in Australia [21-24]. A clinical study involving 90 participants (High Caries Activity (CA) = 30, medium CA = 30, low CA = 30) was conducted by Lin X *et al.*,in China [21]. The study highlighted a positive correlation between CA and salivary microbial structure and PCR amplification of the bacterial 16S rRNA gene amplicon sequencing compared with PICRUSt2 revealed increased number of Scardiovia and Selenomonas in the high CA group, genus Abiotrophia and Lautropia in the low CA group, and Lactobacillus and Arthrospira spp. in the medium CA group ($p < 0.05$) [25]. A cohort study consisting of 617 children was conducted by Manzoor M *et al.*, in Finland [22]. The study indicated that sugar-metabolizing bacteria such as Paludibacter and Labrenzia promote sugar acidification in the development of dental caries ($p < 0.001$) as indicated by bacterial 16S rRNA gene (V3-V4 region) using PCR and Illumina HiSeq [26]. Similar findings were also reported in two prospective case-control studies conducted by Divaris K *et al.*, in Iraq and a case-control study conducted by Menon and Bhat in India [23, 27-30]. A cohort study undertaken by Hamalaw SJ *et al.*, and a literature review conducted by Menon I *et al.*, in the USA also shared similar results [29, 30]. Similar findings were also reported in a longitudinal study conducted by Nomura Y et al [26, 31, 32]. Angarita-Díaz MP *et al.*, compared High-Aggregation Adherence (HAA) and Low-Aggregation Adherence (LAA) in Spain among 35 children (Caries-Free (CF) children = 12, children with caries = 23). The study found that the CF group compared to the caries group demonstrated a higher concentration of statherin (CF median = 94, 734.6, caries group median = 90, 875.0) ($p = 0.03$) and low levels of format as indicated by Cloud Cone Corp and BioVision colorimetric tests, respectively (format levels = 0.02, 0.10, respectively) [28, 33]. These findings were similar to a case-control study conducted by Rudney JD *et al.*, in the USA [29, 34]. A prospective 1-year study involving 213 children (aged <13 years) was conducted by Stojkovic B *et al.*, in Serbia. The study found that salivary pH and oral hygiene index (OR; 0.270, $P = 0.043$, OR; 1.886, $p = 0.042$, respectively) were the major independent caries risk predictors among early adolescents as determined by using Hosmer-Lemeshow test [35]. These findings were similar to a systematic review of 18 papers published between 2010 to 2022 (multiple countries), including a combined total number of 1454 participants conducted by Alamoudi A *et al.*, in Saudi Arabia [31, 36]. A case-control

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study comprising 163 children (Aged <18 years) was conducted by Salman BN *et al.*, in Iran. Two groups were designed: 78 children with Caries Index (CI) and 85 Caries-Fee (CF) children [32]. The study highlighted salivary markers of oxidative stress as an important predictor of caries and revealed that the CI group compared to the CF group reported decreased oxidative stress levels in saliva as measured in the spectrophotometry and spectrofluorometry (Synergy 4 BioTek multi-mode reader), ($p = 0.008$) [37]. A clinical study comprising 100 children (ECC group = 50 children, CF group = 50 children) conducted by Jayaraj and Ganesan in India found that the buffering capacity of saliva may act as a potent biomarker for ECC risk prediction ($p < 0.01$) [38]. The study reported that salivary leptin levels were indicative of the development of ECC and saliva samples assessed by using commercial human ELISA kits (Abcam, Cambridge, United Kingdom) found that the ECC group compared to the CF group showed decreased levels of leptin in saliva (4.66 pg/mL and 6.64 pg/mL, $p < 0.01$, respectively) [40]. A case-control study comprising 120 children (Case = 60 children with severe ECC, control group = 60 children) was conducted by Rajkumaar and Mathew in India. The data analysis using a Statistical Package for the Social Science (SPSS) indicated that children with severe ECC compared to CF children reported statistically significant differences in salivary ferritin levels ($p < 0.001$) [41]. Another case-control study including 64 children was conducted by Pani SC *et al.*, in Saudi Arabia [36]. The study found that children with ECC compared to CF children had significantly higher concentrations of salivary cortisol as analyzed by using Electrochemiluminescence (ECL) immunoassay ($p < 0.0001$) [42]. A case-control study consisting of 36 participants (children with type 1 diabetes = 12, children with normal glycemic control = 12, control group (C) = 12 healthy participants) was undertaken by Pappa E *et al.*, in Greece [37]. The study found that salivary proteomics related to caries such as alpha-amylase 2B, beta-defensin 4A, BPI fold containing family B member 2, mucin 5B, and salivary proline-rich protein 2 were significantly downregulated in the cariogenic process among type-1 diabetic patients compared to C group as determined by Liquid Chromatography-Mass Spectrometry (LC-MS) [43]. Similar findings were also reported in a literature review conducted by Laputkova G et al., in Slovakia, a case-control study conducted by Idowu OS *et al.*, in the UK, and a systematic review undertaken by Guo and Shi in the USA [38, 44-46]. Another case-control study comprising 28 children (aged <4 years) was carried out by Zhou X et al., in China [41]. Three groups were designed; CF group = 7, caries group = 6, and healthy control group (CG) = 15. The matrix-assisted laser desorption-ionization time-of-flight (MALDI-TOF-MS) and liquid chromatography-electrospray ionization-tandem (LC-ESI-MS/MS) found two salivary proteins, namely SMR-3B and mucin-7, as the potential salivary biomarkers for CRA and found that these two peptides were differentially expressed among ECC children compared to CG ($p < 0.05$) [47]. Similar findings were also reported in a randomized controlled study by Choudhary A *et al.*, a cross-sectional study by George *et al.*, in India, [42, 48, 49]. A cohort study conducted by Sánchez-Pérez L *et al.*, among 110 schoolchildren in Mexico compared baseline data with the caries increment after 4 years and revealed that risk predictive models (Synder test; $p = 0.002$, fissure morphology; $p = 0.024$) capacity using salivary biomarkers showed a strong association with caries development in children [44, 50]. Similar findings were reported in a case-control study (combining a total of 20 participants) conducted by Seredin P *et al.*, Russia and a cohort study of 204 children conducted by Hart *et al.*, in the USA [45]. A systematic review and meta-analysis of 5419 papers was conducted by Diaz-Fabregat B *et al.*, in Brazil [46]. The study indicated that children with caries compared to CF children showed decreased levels of NO2- in the saliva as assessed by using the Newcastle-Ottawa scale recommendation and AXIS tool for case-control and cross-sectional studies, respectively ($p < 0.01$) [47]. Similar findings were reported in a case-control study conducted by Syed M *et al.*, in India [47]. A case-control study was conducted by Faheem S *et al.*, among 80 children (ECC children = 40, children without ECC = 40) in Pakistan [48]. The study found that salivary beta defensin-3 levels were lowest in the ECC group compared to children without ECC as determined by the ELISA kit (Human Beta Defensin 3 ELISA Kit Cat. No E3240Hu) ($p = 0.002$) [49]. An exploratory, cross-sectional study consisting of 176 children was carried out by Borsting T *et al.*, in Norway. The study found that salivary inflammatory markers, namely macrophage Colony-Stimulating Factor 1 (CSF1) as determined in multiplex immunoassay, were strongly associated with caries progression measured by least regression analysis, Bonferroni corrections, and least absolute shrinkage and selection operator (LASSO) (OR; 2.11, 95% CI) [50]. A meta-analysis of 30 case-control studies (combined with a total of 1545 participants; 918 caries patients, healthy control group = 627) was conducted by Wu Z *et al.*, in China. The study found that salivary IgA levels significantly decreased in the caries group compared to controls as indicated in

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ELISA (p = 0.04) which may be a major risk predictor of caries [50]. A prospective non-randomized clinical study was conducted by Zhao A *et al.*, among 40 children (aged <12 years) in the USA [51]. The study found that soluble toll-like receptors-2 (TLR-2) were significantly higher in caries saliva compared to CF saliva as measured by using a sandwich ELISA kit and standard curve of purified recombinant human CD14Fc and TLR-2Fc of known concentration (p <0.05). Similar findings were also reported in a systematic review and meta-analysis of 28 papers conducted by Hamid A *et al.*, in Pakistan and a systematic review of 16 papers conducted by Antonelli R *et al.*, in Italy [52, 53]. A case-control study consisting of 68 children (aged <12 years) (cases = 31, controls = 37) was conducted by Musalem-Dominguez O *et al.*, in Spain [54]. They concluded that salivary metabolic profiles especially saccharides and amino acids were strongly associated with the risk of caries as measured by Nuclear Magnetic Resonance (NMR) using The Human Metabolome specialized dataset and the database of spectral dataset contained fitting and quantification program included in Chenomx NMR Suite 8.1as reference (p = 0.05). While the evidence was promising, further research was needed to establish the optimal combination of salivary biomarkers for accurate and reliable caries risk prediction. Additionally, larger-scale studies were required to validate the findings in diverse populations and clinical settings.

CONCLUSIONS

This comprehensive systematic review underscores the potential of salivary biomarkers as a valuable tool for non-invasive risk assessment of caries in school children. The findings consistently demonstrate a strong association between various salivary biomarkers, including proteomics, microbiota, sugar metabolization, IgA levels, metabolic profiles, and the development of caries. By incorporating salivary biomarker analysis into routine dental care, healthcare providers can identify children at high risk for caries and implement targeted preventive interventions, ultimately improving oral health outcomes and reducing the burden of dental disease.

Authors Contribution

Conceptualization: AS
Methodology: SAM, BA, ME
Formal analysis: BA, AM
Writing, review and editing: AS, AM, SAM, ATA, BA, KA, SA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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