

Association of Salivary Biomarker Concentration and Activity Between Caries-free and Caries-affected Children: An Umbrella Review

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INTRODUCTION

Dental caries is a prevalent and chronic disease in humans. Dental caries is a highly prevalent multifactorial disease. It afflicts a large proportion of the world's population.

Since teeth are regularly exposed to saliva, the composition and characteristics of this fluid in the mouth are crucial factors influencing the development and advancement of tooth decay.¹

This is because caries results from an imbalance in cariogenic microorganism in the biofilm. This imbalance results in loss of minerals from dental hard tissues.² However, when considering the microorganisms involved in caries progression, one must also exam the environment in which they live. Because teeth are constantly immersed in saliva, the properties and components of this oral fluid are crucial in the onset and advancement of cavities.²

Salivary proteins help maintain tooth health and prevent cavities through various mechanisms, including the production of AEP and the prevention of demineralization on exposed tooth surfaces.²

Numerous salivary proteins play a defensive role in the oral cavity including carbonic anhydrase, lactoferrin, immunoglobulins (Igs), proline-rich proteins (PRPs), and mucins1.

Taking these established, and researched salivary proteins into consideration, examining if there is a relationship in their concentration in caries free vs caries affected patient is plausible.³

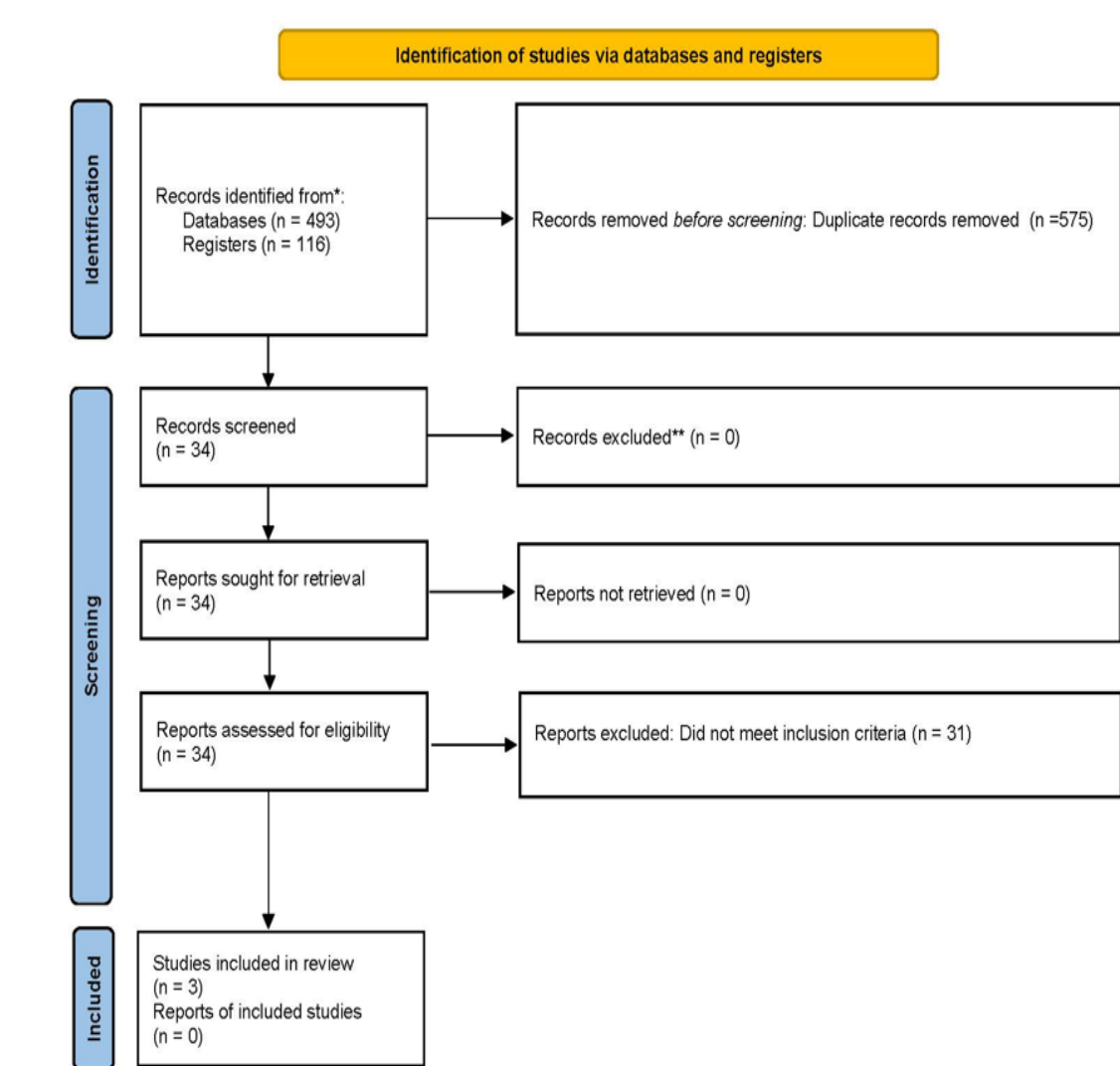
PURPOSE

•Purpose: The purpose of this umbrella review was to retrieve and assess the available systematic reviews reporting on association of salivary biomarker concentration and activity between caries-free and caries-active children.

METHOD

- A literature search was conducted on electronic bibliographic databases to locate systemic reviews reporting on salivary biomarker concentration and activity between caries-free and caries-active children (age 9 and under).
- Literature searches were performed until January 2024 in: PubMed, Embase, CINAHL, Cochrane Library, Prospero, Scopus, Web of Science, Google Scholar, Doss, Health and Psychosocial Instruments (HaPI), Medline.
- Eligible publications were reviewed independently by reviewers and reviews were selected, and their methodological qualities were assessed using Assessing the Methodological Quality of Systematic Reviews (AMSTAR 2) tools (16 items) and PRISMA flow diagram.

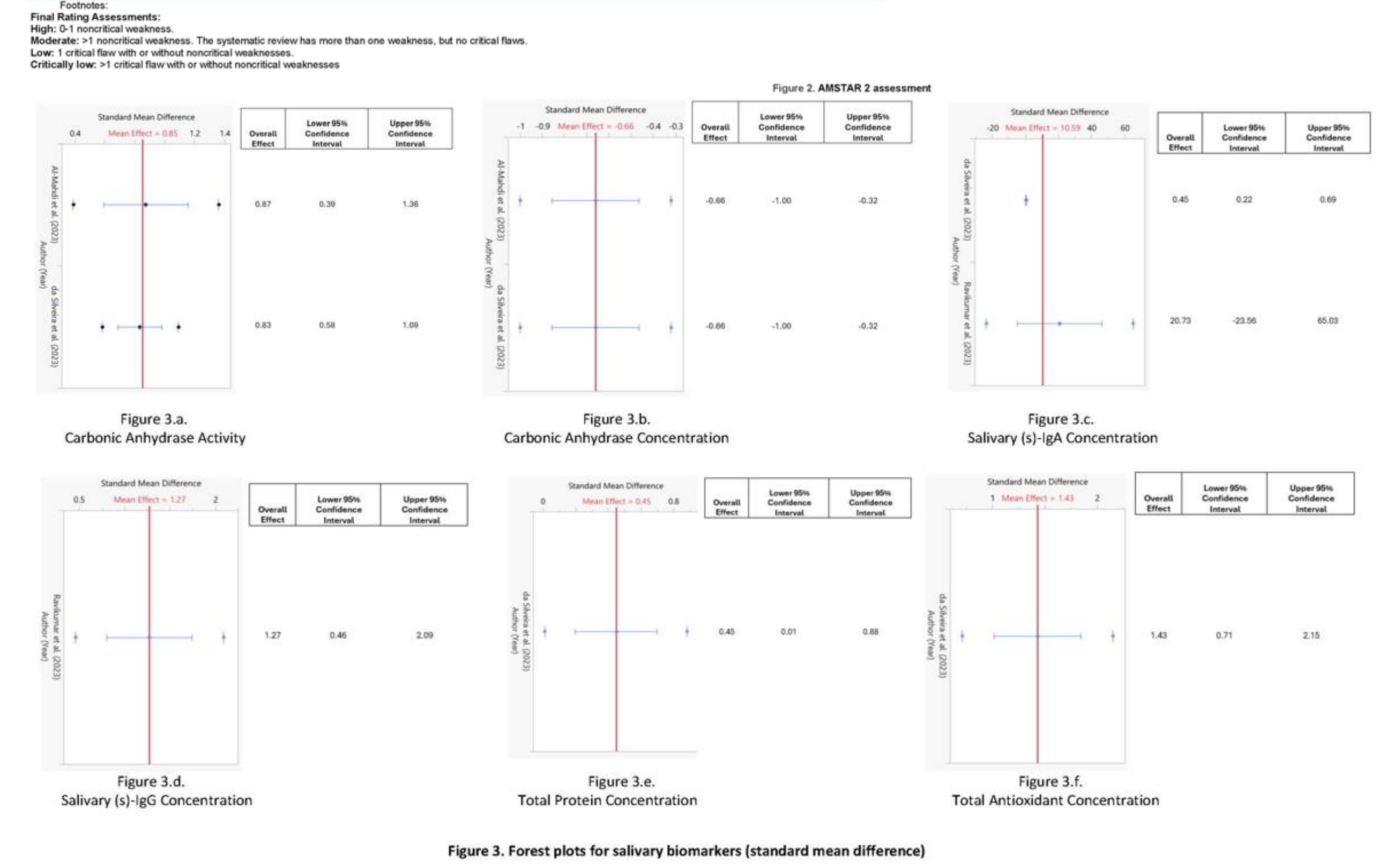
FIGURES



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Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

AMSTAR 2 domain items	Al-Mahdi et al. (2023)	da Silveira et al. (2023)	Ravikumar et al. (2023)
1. Did the research questions and inclusion criteria for the review include the components of PICO?			
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?			
3. Did the review authors explain their selection of the study designs for inclusion in the review?			
4. Did the review authors use a comprehensive literature search strategy?			
5. Did the review authors perform study selection in duplicate?			
6. Did the review authors perform data extraction in duplicate?			
7. Did the review authors provide a list of excluded studies and justify the exclusions?			
8. Did the review authors describe the included studies in adequate detail?			
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual non-randomized studies of interventions (NRSI) studies that were included in the review?			
10. Did the review authors report on the sources of funding for the studies included in the review?			
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of non-randomized studies of interventions (NRSI) results?			
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?			
13. Did the review authors account for RoB in primary studies when integrating/biasing the results of the review?			
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?			
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?			
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?			
Number of negatively answered critical domains (Item #s 2,4,7 & 11,13,15)	1	0	1
Final Rating	High	Low	High
Color Code:			
Restrictions:			
Final Rating Assessments:			
High: 0 critical weaknesses.			
Medium: 1 critical weaknesses. The systematic review has more than one weakness, but no critical flaws.			
Low: 1 critical flaw with or without noncritical weaknesses.			
Critically low: 2 critical flaws with or without noncritical weaknesses.			



RESULTS

- A systematic electronic search identified 3 out of 493 articles that met the inclusion criteria and were included in this review (Figure 1).
- AMSTAR 2 assessed two studies as high quality and one as low quality (Figure 2).
- The forest plot (Figure 3) reveals significant variations in salivary biomarkers between caries-affected (CA) and caries-free (CF) children.
- CA children showed:
 - **Higher activity and lower concentration of carbonic anhydrase VI:**
 - Activity: Significant increase (P < 0.0001, Mean Effect: 0.85, CI: [0.39, 1.36]) (Figure 3.a).
 - Concentration: Significant decrease (Mean Effect: -0.66, CI: [-1.00, -0.32]) (Figure 3.b).
 - **Higher salivary (s)-IgA and (s)-IgG concentrations:**
 - (s)-IgA: Significant increase (P = 0.79, Mean Effect: 10.59, CI: [0.22, 0.69]) (Figure 3.c).
 - (s)-IgG: Significant increase (P = 0.02, Mean Effect: 1.27, CI: [0.46, 2.09]) (Figure 3.d).
 - **Higher total protein concentration:** Significant increase (P = 0.0007, Mean Effect: 0.45, CI: [0.01, 0.88]) (Figure 3.e).
 - **Higher total antioxidant concentrations:** Significant increase (P = 0.00001, Mean Effect: 1.43, CI: [0.71, 2.15]) (Figure 3.f).

CONCLUSIONS

Based upon the results of this study, the following conclusions about caries-affected children can be made:

- Higher CA VI activity
- Lower CA VI concentration
- Higher s-IgA concentrations
- Higher s-IgG concentration
- Higher TAC

Salivary biomarker diagnostics is a promising opportunity for dentists to identify children at high risk for caries once commercial clinical laboratories make this service available.

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