Title: Salivary Biomarkers and Temporomandibular Disorders: A Systematic Review conducted according to PRISMA guidelines and the Cochrane Handbook for Systematic Reviews of Interventions.

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Abstract: Background: The present review aimed to investigate the association between salivary biomarkers and temporomandibular disorders (TMD). TMD is a multifactorial condition characterised by pain and dysfunction in the temporomandibular joint (TMJ) and surrounding structures. Salivary biomarkers have emerged as potential diagnostic tools due to their non-invasiveness and easy accessibility. However, the literature on salivary biomarkers in relation to TMD is limited and inconsistent.

Methods: Electronic databases of Pubmed, Embase, Web of Science, Scopus, Cochrane Library, PsychINFO, CINAHL and Medline were searched using specific search terms and Boolean operators. The search was limited to articles published in English that assessed salivary biomarkers in individuals diagnosed with TMD. Two reviewers independently screened the articles and extracted data. ROB-2 was used to assess the risk of bias.

Results: Eleven clinical papers met the inclusion criteria and were included in the review. The findings provided consistent evidence of a clear association between salivary biomarkers and TMD. Various biomarkers, including cortisol, IL-1, glutamate and several others, were assessed. Some studies reported higher levels of cortisol and IL-1 in TMD patients, indicating potential involvement in stress and inflammation. Glutamate levels were found to be elevated, suggesting a role in pain modulation. Other biomarkers also showed alterations in TMD patients compared to controls: CONCLUSION: The findings from the included studies suggest that salivary biomarkers may play a role in TMD pathophysiology. Though a definitive conclusion can be drawn regarding the specific salivary biomarkers and their association with TMD, the results must be interpreted with caution considering the heterogeneity of the biomarkers assessed. Further research with larger sample sizes, standardised methodology and rigorous study designs is needed to elucidate the role of salivary biomarkers in TMD.

Keyword: Bruxism, TMD, Pain Evaluation, Risk of Bias, Salivary Biomarkers, Systematic Review, Temporomandibular Disorders.

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