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# Salivary Metabolomics for Early Detection of Oral Squamous Cell Carcinoma: A Systematic Review and Meta-Analysis

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## Abstract

Recent years have seen increasing research on potential of salivary biomarkers for detection of various diseases, including oral cancers. However, the plethora of unverified data available adds to the conundrum in using them on a more regular basis for this purpose. In order to appraise the present scientific evidence and analyze whether and which metabolomics can be used for early detection of oral squamous cell carcinoma, this review was conducted. The review followed PRISMA 2020 guidelines and was registered in PROSPERO. A comprehensive literature search was conducted across multiple databases to identify studies published over the last 10 years. Two reviewers independently performed study selection. Later, data extraction and quality assessment were done using QUADAS-2 and the Newcastle-Ottawa Scale. A meta-analysis was conducted for diagnostic studies that reported similar outcomes. Of the 19 included studies, 12 were diagnostic and 7 observational. Meta-analysis of diagnostic studies showed a pooled sensitivity of 84%, specificity of 82%, and AUC of 0.88. Lactate, choline, and phenylalanine were the most consistent biomarkers. LC-MS was the most accurate platform (AUC: 0.91). Moderate heterogeneity ( $I^2=58-62\%$ ) reflected methodological and population differences. Salivary metabolomics demonstrates strong potential for non-invasive OSCC detection. Standardization, larger sample sizes, and validation in diverse populations are needed for clinical translation.

**Keywords:** biomarker, head and neck squamous cell carcinoma, metabolomics, saliva