REVIEW

IMMUNOHISTOCHEMICAL MARKERS OF EPITHELIAL – MESENCHYMAL TRANSITION IN ORAL SQUAMOUS CELL CARCINOMA: A SYSTEMATIC REVIEW.

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Running title – Epithelial-mesenchymal transition markers in Oral Squamous Cell Carcinoma

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Abstract

Objective: The aim of this systematic review was to explore the prognostic significance of immunohistochemical markers of epithelial-mesenchymal transition (EMT) in oral squamous cell carcinoma (OSCC).

Methods: PubMed, EMBASE, and Scopus databases were thoroughly searched using various combinations of keywords, and Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines were followed for analysis.

Results: Database search yielded a total of 45 articles, out of which 13 articles were selected based on the inclusion and exclusion criteria. A total of 946 oral squamous cell carcinoma samples were

evaluated for various immunohistochemical markers. The most commonly studied immunohistochemical marker of EMT was E-Cadherin followed by Beta-catenin, CD44, N-Cadherin, EMA, vimentin, SMA, ALDH1, cyclin D1, APC, Collagen IV and MMP 9. A panel of transcription factors such as TWIST1, SNAI1/2, ZEB1, and ZEB2 and other genes intimately related to EMT (CDH1 and LAMC2) at the invasive tumor front of OSCC tissues were also studied.

Conclusion: The use of biomarkers like E-cadherin, EMA, and SMA might be a valuable tool for predicting patient outcomes and therapy. OSCC tissues had high levels of EMT phenotype as compared with the normal oral mucosa. This phenotype was characterized by reduced E-cadherin and β-catenin expression and overexpression of N-cadherin. CD44 immunoexpression was a significant predictor of lymph node metastasis, while ALDH1 high immunostaining was associated with angiolymphatic invasion. Co-expression of TWIST1 and ZEB2 was significantly prevalent in OSCC patients with poorer overall survival, especially in patients with no lymph node metastasis. The Snail family of zinc-finger transcription factors especially SNAI1/2 was significantly overexpressed in OSCC. The prognostic value of these biomarkers is proven and can be employed for evolving new therapeutic modalities.

Keywords: immunohistochemistry, oral squamous cell carcinoma, epithelial-mesenchymal transition

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