



Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Baghdad
College of Dentistry



**IMMUNOHISTOCHEMICAL ASSESSMENT OF
PERINEURAL INVASION IN SALIVARY GLAND
CARCINOMAS IN RELATION TO
HISTOLOGICAL VARIANTS AND TUMOR
GRADE**

A thesis submitted to the Council of the College of Dentistry/ University of
Baghdad in Partial Fulfillment of the Requirements for the Degree of
Doctor of Philosophy in Oral and Maxillofacial Pathology

By

Alyaa Kadhim Mohammed

B.D.S. M.Sc.

Supervised by

Assist. Prof. Dr. Ban F. Al-Drobie

B.D.S., M.Sc., Ph.D.

(Oral and Maxillofacial Pathology)

2023 A.D

1444 A.H

ABSTRACT

Introduction: Perineural invasion is a type of metastatic tumor spread in which cancer cells travel along nerves far away from the primary lesion. Perineural invasion is linked to an increased risk of metastasis and a lower chance of survival in oral salivary gland cancer. The migration of cancer cells towards nerves necessitates the activation of numerous signaling pathways involving numerous growth factors. In many types of cancer, neurotrophins and molecules like neuropeptides contribute to survival, proliferation, and migration signaling pathways. These molecules are thought to mediate invasion, depending on the tumor's origin. The aims of the study are to investigate perineural invasion among salivary gland carcinomas confirmed by immunohistochemical evaluation using Protein Gene Product 9.5 and S100 protein with their association, to detect neurite outgrowth by immunohistochemical assessment of Nerve growth factor and Nerve growth factor receptor, the role of Galanin involved in perineural invasion and finally association of perineural invasion among salivary gland carcinomas using the aforementioned markers in relation to histological variants and tumor grade.

Materials and Methods: Fifty paraffin embedded tissue blocks of salivary gland carcinomas that were retrieved from the archives of the Department of Oral & Maxillofacial Pathology/College of Dentistry/University of Baghdad, and from Ghazi Al-Harerri Hospital-Medical City, which were collected from the date 2000 to 2021, diagnosed as (mucoepidermoid carcinoma, adenoid cystic carcinoma and polymorphous adenocarcinoma). The immunohistochemical procedure was used to evaluate perineural invasion and its association with tumor grade and histological variants, and then immunohistochemical evaluation of Nerve growth factor, Nerve growth

factor receptor and Galanin for their role in perineural invasion in salivary gland carcinomas.

Results: 39 (78%) cases of salivary gland carcinomas had perineural invasion. There was a non-significant difference in the distribution of perineural invasion in (H&E, S100 and PGP9.5) across salivary gland carcinoma variants (P value = 0.1, 0.49 & 0.11) respectively. Protein gene product 9.5 and S100 recognized perineural invasion more accurately than H&E. Specificity of protein gene product 9.5 (92%) higher than that of H&E (59%), and S100 (64.1%). Perineural invasion was significantly associated with tumor grade, histological variants, (H&E, S100, protein gene product 9.5, nerve growth factor and Galanin). There was a significant association between nerve growth factor, nerve growth factor receptor and Galanin.

Conclusion: Perineural invasion is associated with tumor grade and histological variants and is a predictive factor for tumor development and metastasis. Protein gene product 9.5 immunostaining increase the detection of perineural invasion when compared to H&E and S100. Protein gene product 9.5 might be used instead of S100 or as part of an immunostaining panel for detection of perineural invasion. Nerve growth factor, nerve growth factor receptor and Galanin may induce tumor cell dispersion and migration, thereby boosting perineural invasion and metastasis of salivary gland carcinomas.