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Expression of Glucose Transporter-1 (Glut-1) in Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma

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ABSTRACT

Aim of the study: Expression of Glucose Transporter-1 (GLUT-1) in Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma.

Material & methods: A total of 50 cases formed the study, which were divided into two main groups; Group I - Oral Epithelial Dysplasia (n=30) and Group II - Oral Squamous Cell Carcinoma (n=20).

Results: The results were tabulated using Chi-square test and Fischer's exact test for comparison of GLUT-1 expression in Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma. GLUT-1 has a consistent role in oral premalignant and malignant lesions and that its expression level and activity appear to be associated with malignant transformation and aggressiveness.

Conclusion: The expression of GLUT-1 increased with disease severity; OSCC showed the highest intensity, followed by OED and NOM.

Keywords: *Oral Epithelial Dysplasia, Oral Squamous Cell Carcinoma, Glucose Transporter-1, Immunohistochemistry.*

1. INTRODUCTION

Mammalian cells are compartmentalized by intracellular biological membranes present formidable barriers to the passage of ionic and polar substances so that they can transverse membranes only through the action of certain transport proteins. Such proteins are therefore required to mediate all transmembrane activities of ions, glucose, amino acids and even water.[1,21]

One such group of transporter proteins essentially involved in transmembrane movement of glucose molecules are the glucose transporter proteins (GLUTs), which consist of a family of 13 proteins among which GLUT1 is the first to be cloned and the dominant one.[2,22]

It was reported that there is a pronounced elevation of GLUT1 protein in many tumors to supply energy that is necessary for tumor cell proliferation. It is also known to regulate proteins that have a role in increased proliferative activity, cancer invasiveness and metastasis. Oral cancer is a serious problem in many parts of the world. Oral squamous cell carcinoma is the most common form, accounting for over 90% of the cases of these malignancies. Some oral squamous cell carcinomas have also been documented in association with or preceded by a potentially malignant lesion, such as Oral Epithelial Dysplasia (OED).[3,19]

Assessing the GLUT1 in the epithelial dysplasia could bring new insights into their molecular nature and hence our study is aimed to evaluate the expression of GLUT1 in epithelial dysplasia and oral squamous cell carcinoma by immunohistochemistry.[4,20]

2. MATERIAL AND METHODS

A total of 60 cases formed the study, which were divided into three main groups; Group I- Normal Oral Mucosa(NOM): (10 cases), Group-II - Oral Epithelial Dysplasia(OED) comprised of total 30 cases including Mild Dysplasia (14 cases), Moderate Dysplasia (11 cases), Severe Dysplasia (4 cases), Mild to Moderate Dysplasia (1 case) and Group III - Oral Squamous Cell Carcinoma(OSCC) comprised of 20 cases including Poorly Differentiated (8 cases), Well Differentiated (6 cases), Moderately Differentiated (6 cases). Histological slides of all the cases were stained using Haematoxylin and Eosin stain and Immunohistochemical staining for evaluation of GLUT-1 positivity in both the study samples. Therefore, total of 120 slides were stained.[5,18]

Immunohistochemical analysis of GLUT-1 was expressed on the basis of four criteria. First, percentage of positivity (Score 0: Absence of expression, Score 1: 1-25% cells showing positivity, Score 2: 25-50% cells positive, Score 3 : >50% positive expression. Second, intensity of staining (Score 0: No expression, Score 1: Mild expression, Score 2: Intense expression. Third, Location of GLUT-1 expression (Score 0: No expression, Score 1: Membrane only, Score 2: Cytoplasmic location, Score 3: Nuclear expression, Score 4: Combination of membrane and cytoplasm, Score 5: Combination of cytoplasm and nucleus). Forth, Extent of staining (Score 0: No expression, Score 1: Expression limited to the basal and suprabasal layer. Score 2: Expression extending into spinous layer, Score 3: Expreesion extending to the granular layer, Score 4: Expression extending to the corneal layer.[7]

The results obtained were used to construct the database in an excelsheet and the data was afterwards transfered to the software programme SPSS-17.0. For satistical analysis, the chi- square test and the Fischer's exact test were done for the final comparison of GLUT-1 expressions between OED, OSCC and ONM.[6,17]

3. RESULTS

There was male predominance in dysplasia cases and there was equal sex ratio in case of Squamous Cell Carcinoma. The habit of tobacco usage was predominant in dysplasia cases and usage of bidi was higher in case of Oral Squamous Cell Carcinoma. The results varied with the scoring criteria as:

4. PERCENTAGE

Percentage of positivity increased with the disease severity i.e. Oral Squamous Cell Carcinoma showed the higher number of positive cells for GLUT-1 as compared to Oral Epithelial Dysplasia and normal oral mucosa. In NOM, the expression seems to be absent (Score-0), in OED cases 1-25% cells showed positivity (Score-1), in OSCC cases >50% cells showed positivity. A statistically significant increase in the percentage was noted in OSCC with progression from OED to OSCC (**p – value < 0.001).**[8,16]

5. INTENSITY

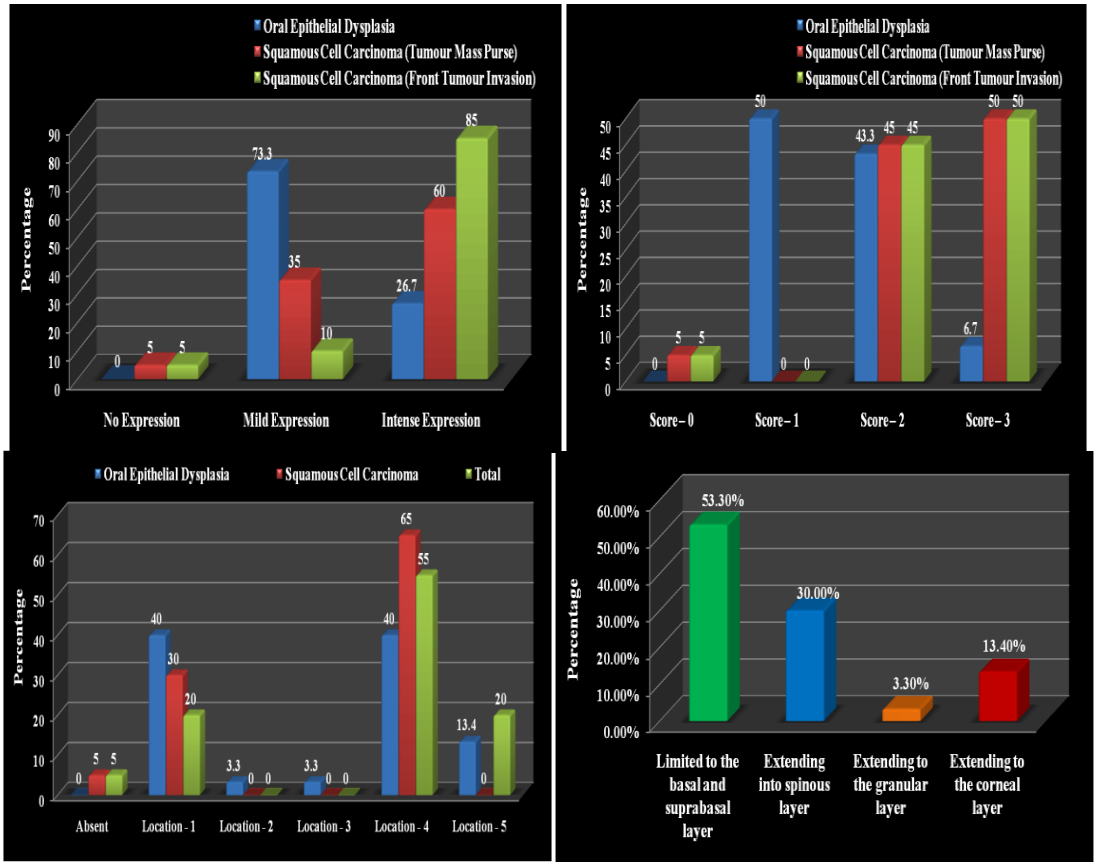
Mild staining was observed in OED cases (Score-1) and intense staining was observed in OSCC cases with exception of one case which doesn't show any expression. Results were statistically significant (**p – value < 0.001).**[9,15]

6. LOCATION

Most of the OED and OSCC cases from our study reveal predominantly membranous and cytoplasmic expression although one case from OSCC cases didn't show expreesion for GLUT-1 staining. The results were not statistically significant **(p – value = 0.200).**[13,23]

7. EXTENT

Maximum of the OED cases showed strong expression in the basal layer it showed expression in all layers as disease progress from mild dysplasia to severe dysplasia.



8. DISCUSSION

The present study evaluated the pattern as described in the literature regards to the epidermology of OED and OSCC. GLUTs (Glucose Transporters) are the means through which glucose is transported into the all types of cells. GLUT-1, 3 were the 1st one to be identified from the total 12 members who then appeared to be regulated by the proto- oncogenes, which are present in both normal cells as well as in the growth factors.[10,24]

In the cells of the normal tissue GLUT-1 is not detected in large proportions, with the deviation of erythrocytes, germinative cells of the testes, renal tubuless, and the perineurium of the peripheral nerves and endothelial cells of the blood brain barrier. The alterations in GLUT-1 expression have been described as an early event during the development of various types of carcinomas.[11]

In the previous literature various methods have been used to study GLUT-1 protein like the Positron emission tomography, Polymerase chain reaction, [^{18}F]-2-flluoro-2 deoxy-D-glucose and Immunohistochemistry (IHC). In the present study, we have used IHC to analyze GLUT-1 expression which is a method for localizing specific antigens in tissue/cell based on antigen antibody recognition; it seeks to exploit the specificity provided by an antibody with its antigen at a light microscope level and is inexpensive and can be performed with ease.[12]

Chewing tobacco and smoking are distinct risk factors particularly among males in certain countries; however, other countries have noted that females or non-smokers may be also at risk of malignant transformation. The marking pattern strongly present in the cell membrane found in the present research was similar to that found in the studies of Haber et al (1998), Kato et al (2007), and Ayala et al (2010).[14]

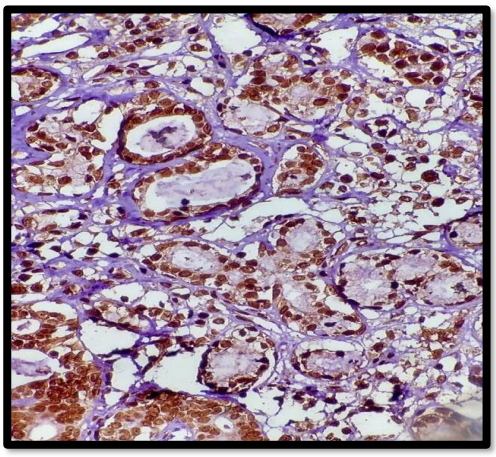


Fig.1 Intense GLUT-1 expression in blood vessels and RBC's used as internal positive control

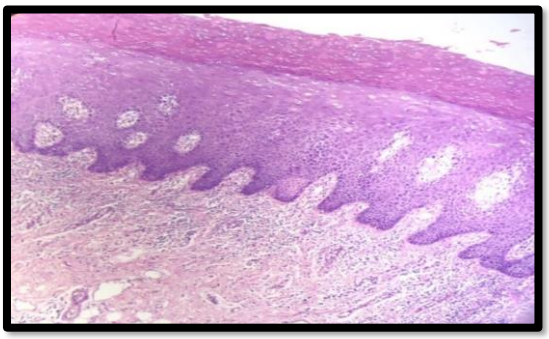


Fig.2 Photomicrograph showing Mild Epithelial Dysplasia (H&E)(10x)

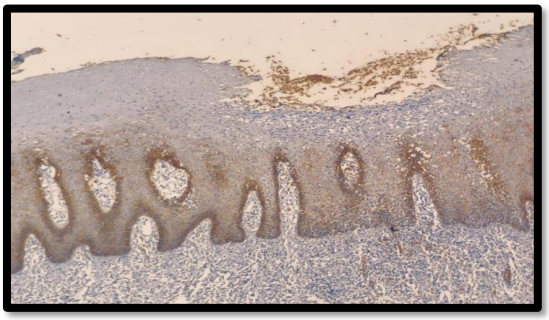


Fig.3 Photomicrograph showing Mild Epithelial Dysplasia (IHC)(10x)

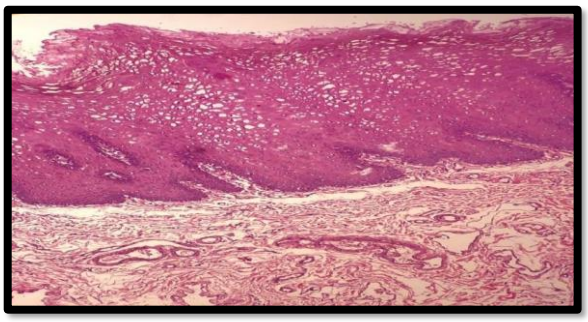


Fig.4 Photomicrograph showing Moderate Epithelial Dysplasia(H&E)(10x)

Fig.5 Photomicrograph showing Moderate Epithelial Dysplasia (IHC)(10x)

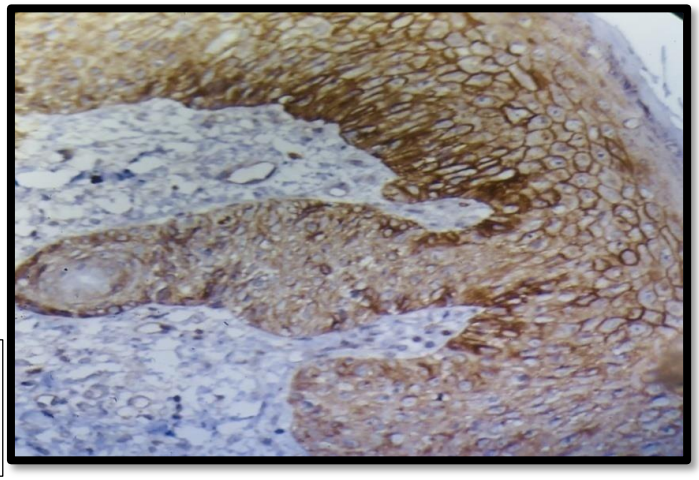


Fig.6 Photomicrograph showing Severe Epithelial Dysplasia(H&E) (10x)

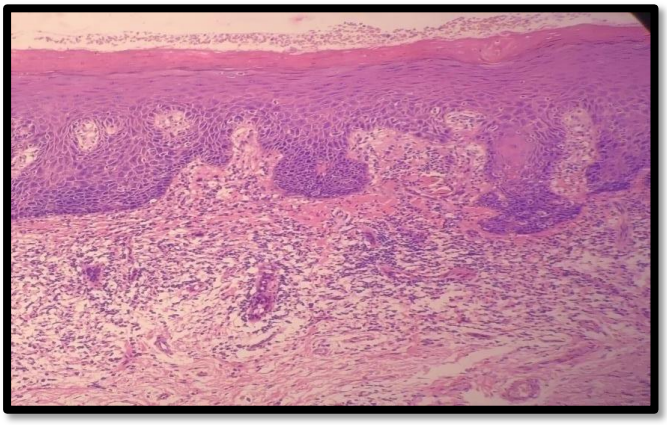


Fig.7 Photomicrograph showing Moderate Epithelial Dysplasia (IHC)(10x)

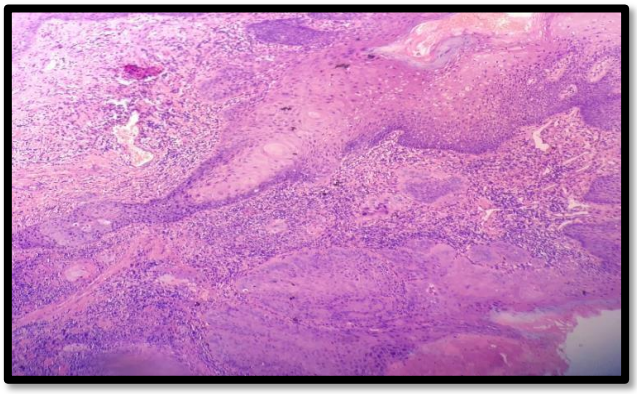


Fig 8 Photomicrograph showing Tumor mass area in OSCC (H&E) (10x)

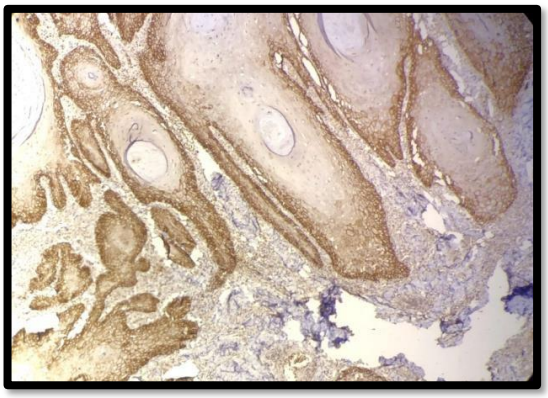


Fig 9. Photomicrograph showing Tumor mass area in OSCC (H&E) (10x)

9. CONCLUSION

The expression of GLUT-1 increased with disease severity; OSCC showed the highest intensity, followed by OED and NOM. The characteristic of Glut-1 in proliferating cells may be related to the aggressiveness of tumors and their response to various treatment modalities, thus being informative when planning individual treatment approaches.

REFERENCES

[1] Voet D, Voet J, Pratt W in Fundamentals of biochemistry life at the molecular level 2nd edition, Asia, John Wiley & Sons, 2006 (184-185)

[2] Pereira KMA, Feitosa SG, Lima ATT, Luna ECM, Cavalcante RB, Lima KCD et al. Immunohistochemical evaluation of glucose transporter type 1 in epithelial dysplasias and oral squamous cell carcinoma. 2016;17(1):147-151

[3] Younes M, Lechago V, Somoano R, Mosharaf M and Lechago J .Wide expression of the human erythrocytes glucose transport GLUT1 in human cancers.1996;56:1164-1167

[4] Reisser C, Eichhorn K, Mende HC, Born AI and Bannasch P. Expression of facilitative glucose transport proteins during development of squamous cell carcinoma of the head and neck .1998;80:194-198

[5] Kunkel M, Reichert TE, Benz P, Lehr HA, Jeong JH, Weiand S et al . Overexpression of GLUT-1 and increased glucose metabolism in tumors are associated with poor prognosis in patients with oral squamous cell carcinoma. 2003;97(4):1015-1024

[6] Varshitha A. Prevalence of oral cancer in India. Pharm. Sci & Res, 2015;7(10):845-848.

[7] Angadi VC, Angadi PV. GLUT-1 immunoexpression in oral epithelial dysplasia, oral squamous cell carcinoma and verrucous carcinoma 2015; 57(2):115-122

[8] Li CX, Sun JL, Gong ZC, Lin ZQ and Liu H. Prognostic value of GLUT-1 expression in oral squamous cell

carcinoma.2016;95(45):1-7

[9] Rao SR, Sundaram S, Lavu V. Immunolocalization of glucose transporter 4 in human gingival. 2012;23(5):565-567

[10] Stanirowski et al. Impact of pre-gestational and gestational diabetes mellitus on the expression of glucose transporters GLUT-1, GLUT-4 and GLUT-9 in human term placenta. 2017; 55:799–808

[11] Ruddlowski et al .GLUT1 Messenger RNA and Protein Induction Relates to the Malignant Transformation of Cervical Cancer. Am J Clin Pathol2003;120:691- 698.

[12] Carvalho et al. GLUT1 expression in malignant tumors and its use as an immunodiagnostic marker. CLINICS. 2011;66(6):965-97

[13] Choi YS et al. Glucose Transporter-1 Expression in Squamous Cell Carcinoma of the Tongue. Cancer Res Treat. 2007;39(3):109-115

[14] Harshani MJ, Yeluri S, Guttikonda VR. Glut-1 as a prognostic biomarker in oral squamous cell carcinoma. Jomfp. 2014;18(3):272-278

[15] Wang XX et al. Hypoxia-inducible factor-1α and glucose transporter 1 in the malignant transformation of oral lichen planus. Int J Clin Exp Pathol. 2017;10(8):8369-8376

[16] Kato Y et al. Immunohistochemical detection of GLUT-1 can discriminate between reactive mesothelium and malignant mesothelioma. Mod pathol. 2007; 20:215–220

[17] Kurokawa T et al. Expression of glut-1 glucose transfer, cellular proliferation activity and grade of tumor correlate with [f-18]-fluorodeoxyglucose uptake by positron emission tomography in epithelial tumors of the ovary. Int. J. Cancer. 2004; 109:926–932

[18] Leino RL, Gerhart DZ, Bueren AM, Mccall AL, Drewes LR. Ultrastructural Localization of GLUT 1 and GLUT 3 Glucose Transporters in Rat Brain. Journal of Neuroscience Research. 1997; 49:617–626

[19] Wang et al. Correlation of GLUT1 and GLUT-3 expression with F-18 FDG uptake in pulmonary inflammatory lesion. JMed. 2016:95- 48

[20] Lee AF, Gown AM, Churg A. IMP3 and GLUT-1 Immunohistochemistry for Distinguishing Benign From Malignant Mesothelial Proliferations. Am J Surg Pathol 2013;37:421–426

[21] Ayala FRR. Glut1 and Glut3 as Potential Prognostic Markers for Oral Squamous Cell Carcinoma. JMpdi. 2010; 15:2374-2387

[22] Paula E, Waner P, Mizeracki A, Martin C. GLUT I: A Newly Discovered Immunohistochemical Marker for Juvenile Hemangiomas. Jomfp. 2001;31(1):11-22

[23] Fujino M et al. Expression of glucose transporter-1 is correlated with hypoxia- inducible factor 1α and malignant potential in pancreatic neuroendocrine tumors. Joncol. 2016;12: 3337-3343

[24] Muratori L et al. HERG1 positivity and Glut-1 negativity identifies high-risk TnM stage I and II colorectal cancer patients, regardless of adjuvant chemotherapy. OncoTargets and Therapy 2016;9 :6325–6332

[25] Kalir et al. Immunohistochemical Staining of GLUT1 in Benign, Borderline, and Malignant Ovarian Epithelia. J American Cancer. 2002;94(4):1078-1082.

[26] Eckert AW, Lautner MHW, Taubert H, Schubert J, Bilkenroth U. Expression of Glut-1 is a prognostic marker for oral squamous cell carcinoma patients. 2008; 20:1381-1385.

[27] Starska K et al. Gene and protein expression of glucose transporter 1 and glucose transporter 3 in human laryngeal cancer—the relationship with regulatory hypoxia-inducible factor-1α expression, tumor invasiveness, and patient prognosis. Tumor Biol. 2015; 36:2309–2321.