Journal of Population Therapeutics & Clinical Pharmacology

Sialic Acid in Diagnosis of Oral Malignancy & Premalignancy

Dr Jinal K. Chavada[1*], Dr Viral Bhatt[2], Dr Mamatha M.T. [3], Dr Rohan Thaker[4],

Dr Priyanshi Parikh[5], Dr Honey Patel[6]

Department of Oral Pathology and Microbiology, College of Dental Science and Research Centre, Bopal, Ahmedabad

Corresponding Author: Dr Jinal K. Chavada, Senior Lecturer, Dept of Oral Pathology and Microbiology, College of Dental Science and Research Centre, Bopal, Ahmedabad. Email: jinalchavada1994@gmail.com

Abstract

Background: Oral sqamous cell carcinoma (OSCC) an epithelial origin tumor has highest prevalence rate in India and is a former disease following precancerous conditions and lesions. **Aim:** To compare the sialic acid levels in blood and saliva of OSCC patients with Leukoplakia and Oral Sub Mucous Fibrosis (OSMF) with normal health individual. **Material and Methodology:** The saliva and serum sample collected from patients and normal individual were analyzed biochemically using Yao et al method. **Result:** The sialic acid level hiked in OSCC and Premalignant group compared with controls. **Conclusion:** As the levels increased, the sialic acid can be used as diagnostic marker as well as prognostic marker post treatment. A larger study is required to be conducted for to check specificity of sialic acid as marker.

Keywords: Sialic Acid, Oral Malignancy, Premalignancy

Introduction: Cancer is a life threatening condition and among which oral cancer is the 6th most common type in India.(1) Around two third of the cases of head and neck cancer are diagnosed in there advanced stages causing significant deaths due to cancer.(2) According to the data of 2004 to 2009 over 3 lakh cases were reported globally among which 7000 of them died.(3) Potentially

malignant disorder transforming into malignancy also contributes to this numbers. Hence looking at the data it is necessary to research on a technique which can provide fast diagnosis.

Talking about diagnosis of Cancer and precancer the hallmark is biopsy, but the process is very time consuming and is invasive so here we are taking salivary sialic acid and serum sialic acid as a less invasive diagnostic approach.

The term 'Sialic Acid', was first introduced by Swedish biochemist, Gunnar Blix in 1952.[4] Cell surface undergo changes during carcinogenesis which is necessary foruncontrolled potential growth and malignant nature of the neoplastic cells.[5] They are attached to the non-reducing residue of thecarbohydratechains of glycoproteins and glycolipids. Among the glycoconjugates, it is seen in 30% of various glycoproteins.[6] It has major role in cell-cell recognition, invasiveness, adhesiveness, and immunogenicity.[7] The structural component of cell membrane and glycoproteins are altered due toneoplastic transformation of the cell. One of these is increased levels ofsialic acid on the cell surface. Hence, Neoplasms often show increase in concentration of sialic acid on the tumor cell surface and are shed or secreted by someof these cells which increase the concentration in blood. [6,8]

The present study was conducted to determine the serum and salivary levelsof sialic acid in patients with oral premalignancy and oral squamous cell carcinomawhich can be used to differentiate premalignancy from cancer. This study also intendsto assess the importance of sialic acid levels as an adjunctive diagnostic marker in headand neck cancer by evaluating serum and salivary total sialic acid levels in oral premalignancy and oral cancer.

Material and Method: This study was conducted to estimate serum and salivary sialic acid level in patientsclinically diagnosed and histopathologically confirmed with oral premalignancy that isOSMF, leukoplakia and oral malignancy (SCC). Further the levels of sialic acid werecompared with that of healthy individuals which are comprised of same age group and geoghraphical region. The patients were selected from the Department of Oral Medicine and Radiology.

Patients were grouped in three groups oral premalignancy, oral malignancy and controls each having 20 individuals (Figure1 to 6). Thecollected saliva and serumsample were then subjected to biochemical analysis of sialic acid through Yao et al. method. This biochemical analysis was based on the reaction between sialic acid andninhydrin in the presence of acidic medium (according to Yao et al.).[9] This leads to the formation of a colored product which can be measured by using spectrophotometer at 470 nm.

Fig:1 UV- SPECTROPHOTOMETER

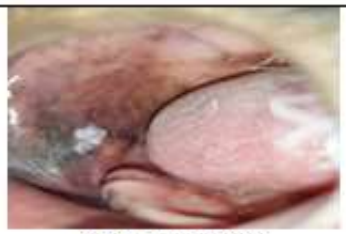

Fig:2 LEKOPLAKIA

Fig:3 ORAL SUB MUCOUS FIBROSIS

Fig:4 WELL DIFFERNTIATED SQUAMOUS CELL CARCINOMA

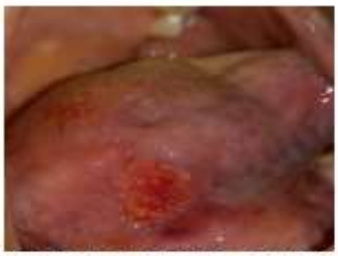

Fig:5 MODERATELLY DIFFERNTIATED SQUAMOUS CELL CARCINOMA

Fig:6 POORLY DIFFERNTIATED SQUAMOUS CELL CARCINOMA

Result: The mean salivary sialic acid level (mg/dl) with standard deviation inControl, Oral Premalignancy, and Malignancy were 16.36+1.4, 35.17+2.34 and 49.2+10.22 respectively. The mean serum sialic acid level (mg/dl) with standard deviation in Control, Oral Premalignancy, and Malignancy were 25.71+1.58, 45.7+2.2 and 80.55+4.8 respectively; which showed that there is increase in salivary and serumsialic acid level in Oral Premalignancy compared to controls.

Comparison using one way ANOVA of salivary sialic acid level (mg/dl) between the three groups shows that malignancy group has the highest value of 57.461 and Controls has the least value of 16.3625. This difference is statistically significantwith a test value of 1628.833 and p value of & lt; 0.001. Also, serum sialic acid level (mg/dl) between the three groups shows that Malignancy group has the highest value of80.5518 and Controls has the least value of 25.713. This difference is statistically Significant with a test value of 1449.61* and p value of 0.001. (Table 1)

Posthoc Tukey tests comparing salivary sialic acid level (mg/dl) in Oral Premalignancy and Malignancy groups shows a mean difference of -22.292 and is statistically significant with a p value of <0.001. Comparing Oral Premalignancy and Controls groups shows a mean difference of 18.8065 and is statistically significant with a p value of <0.001. Comparing Malignancy and Controls groups shows a mean difference of 41.0985 and is statistically significant with a p value of <0.001. Whereas in serum sialic acid level (mg/dl) in Oral Premalignancy and Malignancy groups shows a mean difference of -34.8503 and is statistically significant with a p value of <0.001. Comparing Oral Premalignancy and Controls groups shows a mean difference of 19.9885 and is statistically significant with a p value of <0.001. Comparing Malignancy and Controls groups shows a mean difference of 54.8388 and is statistically significant with a p value of <0.001. (Table 2)

Table: 1: One Way ANOVA TEST

	Oral Premalignancy (n=20)	**Malignancy (n=20)**	**Controls (n=20)**	**ONE WAY ANOVA**	
				F value (*=welch test)	**P VALUE**
SALIVARY SIALIC ACID LEVEL (mg/dl)	35.17±2.34	57.46±2.85	16.36±1.4	1628.833	<0.001
SERUM SIALIC ACID LEVEL (mg/dl)	45.7±2.2	80.55±4.8	25.71±1.58	1449.61*	<0.001

Table: 2: POSTHOC TUKEY TEST

	Oral Premalignancy vs. Malignancy difference (p value)	**Oral Premalignancy vs. Controls difference (p value)**	**Malignancy vs. Controls difference (p value)**
SALIVARY SIALIC ACID LEVEL (mg/dl)	-22.29 (<0.001)	18.81 (<0.001)	41.1 (<0.001)
SERUM SIALIC ACID LEVEL (mg/dl)	-34.85 (<0.001)	19.99 (<0.001)	54.84 (<0.001)

Discussion: Tumor markers play a significant role from diagnosis to therapy toprognosis of cancers and potentially malignant disorders which have potential of malignancy. These markers can also help in early diagnosis in recurrence cases of cancer during follow up of cases. Hence, makers are an alarming factor for deadly caseslike cancer as it is easily detected in body fluids.

Detection of dysplastic changes in oral premalignancy is also very essential which can significantly decrease the mortality rate.

Neoplastic transformation is associated with altered cell surface components and the identification of such changes may provide the basis for using carbohydrate antigens as tumor markers. Measurements of these entities may be valuable in establishing the diagnosis, staging of disease, detecting metastasis, identifying patients at high risk for recurrence and evaluating therapeutic response.[10]

In this study, the mean serum sialic acid level in oral malignancy was increased compared to oral premalignancy and controls. On comparing these valuesusing one way ANOVA test and Posthoc Tukey test the values were having significant difference with p value of0.001. The result of comparison in our study were in accordance to study conducted by Dadhich M, et al.,[11] Chittemsetti S, et al.,[12] Rajaram S., et al,[13] Chinnannavar S. N., et al.,[14] and many more who reported that thereis significant increase in serum sialic acid levels in oral premalignancy and malignancy compared to healthy individuals .

The mean salivary sialic acid level also increased in oral malignancy andoral premalignancy compared to healthy individual its statistical comparison alsoshowed that the values were statistically significant with p value 0.001. There were limited studies conducted using saliva as sample to evaluate sialic acid as tumor marker. However the studies conducted by Jacob et al.,[15] Achalli, et al.,[16] Sanjay PR, et al.,[17]and Shivshankara AR, et al.[18] in their study also showed that there is also increase in sialic acid levels in saliva.

Thus, we estimated the salivary and serum sialic acid levels in patientswith oral premalignant and malignant lesions and compared it with controls where itwas found that sialic acid level increases in oral premalignancy patients compared tocontrols and the level also increases in malignancy patients compared to premalignancy and control. This result was also same in saliva and serum. Hence saliva can also beused as non invasive and adjuvant tool in diagnosis, therapy, and prognosis of oralcancers.

Conclusion: Oral squamous cell carcinoma (OSCC) contributes remarkably i.e. 84-97% to oral cancer. OSCC commonly results from potentially malignant lesions. Epidemiologically, In India, Kerala has the lowest incidence of oral cancer while West Bengalreports the highest.[19] Coming

to Gujarat the number of cancer patients have beenincreasing especially in areas of Saurashtra which may be due to profound tobacco chewing habit in the area.

We observed that there is increase in salivary and serum sialic acid level oral premalignancy compared tocontrols and in malignancy compared to oral premalignancy & malignancy group.

The study concluded that the level of salivary sialic acid increase along withthe serum levels in malignancy and premalignancy group and hence through result wecan conclude that saliva can also be considered as a non invasive diagnostic tool forscreening of oral malignancy. Saliva can be proved as an inexpensive and also low risktool for diagnosis of cancer in some cases like HIV or hepatitis infections. As there arelimited study conducted using saliva with sialic as tumor marker we need to conducted longitudinal study with larger sample size to evaluate the authenticity of sialic acid asspecific and reliable marker.

Conflict of interest: NIL

Source of funding: SELF

References

1. Narasannavar DA, Wantamutte DA. Prevalence of oral precancerous lesions and conditions among tobacco consumers in rural population around Belgaum. A community based cross sectional study. IOSR J Dent Med Sci 2014;13:31-4.
2. Prashant Mathur, DNB, PhD1; Krishnan Sathishkumar, MSc1; Meesha Chaturvedi, MBBS1; Priyanka Das, B-Level1;Kondalli Lakshminarayana Sudarshan, MSc1; Stephen Santhappan, MSc, MPhil1; Vinodh Nallasamy, MSc, MPhil1; Anish John, BE1;Sandeep Narasimhan, MSc1; and Francis Selvaraj Roselind, MSc1; on behalf of ICMR-NCDIR-NCRP Investigator Group. Cancer Statistics, 2020: Report From National Cancer Registry Programme, India. JCO Global Oncol 6:1063-1075.
3. Sharma P, Saxena S, Aggarwal P. Trends in the epidemiology of oral squamous cell carcinoma in Western UP: an institutional study. Ind J Dent Res 2010; 21: 316-9.
4. Available from: http://en.wikipedia.org/wiki/Neuraminic_acid [Last accessed on 2014 Nov 10].

5. Rao VR, Krishnamoorthy L, Kumaraswamy SV, Ramaswamy G. Circulating levels in serum total sialic acid, lipid associated sialic acid and fucose in precancerous lesions and cancer of the oral cavity. Cancer Detect Prev 1998;22:237-40.
6. Joshi M, Patil R. Estimation and comparative study of serum total sialic acid levels as tumor markers in oral cancer and precancer. J Cancer Res Ther2010;6:263-6
7. Baxi BR, Patel PS, Adhvaryu SG, Dayal PK. Usefulness of serum glycoconjugates in precancerous and cancerous diseases of the oral cavity. Cancer 1991;67:135-40.
8. Taqi SA. Clinical evaluation of total and lipid bound sialic acid levels in oral precancer and oral cancer. Indian J Med Paediatr Oncol2012;33:36-41.
9. Yao K, Ubuka T, Masuoka N, Kinuta M, Ikeda T. Direct determination of bound sialic acids in sialoglycoproteins by acidic ninhydrin reaction. Anal Biochem1989;179:332‑5.
10. Bose K S, Gokhale PV, Dwivedi S, Singh M. Quantitative evaluation and correlation of serum glycoconjugates: Protein bound hexoses, sialic acid and fucose in leukoplakia, oral sub mucous fibrosis and oral cancer.J Nat Sc Biol Med 2013;4:122-125
11. Dadhich M, Prabhu V, Pai VR, D'Souza J, Harish S, Jose M, *et al.* Serum and salivary sialic acid as a biomarker in oral potentially malignant disorders and oral cancer. Indian J Cancer 2014;51:214-8.
12. Chittemsetti S, Manchikatla PK, Guttikonda V. Estimation of serum sialic acid in oral submucous fibrosis and oral squamous cell carcinoma. J Oral MaxillofacPathol2019;23:156.
13. Rajaram S, Danasekaran BP, Venkatachalapathy R, Prashad KV, Rajaram S. N-acetylneuraminic acid: A scrutinizing tool in oral squamous cell carcinoma diagnosis. Dent Res J 2017;14:267-71.
14. Chinnannavar SN, Ashok L, Vidya KC, Setty SM, Narasimha GE, Garg R, *et al.* Evaluation of serum sialic acid, fucose levels and their ratio in oral squamous cell carcinoma. J Int Soc Prev Community Dent 2015;5:446-50.
15. Jacob TV, Ramesh M, Murali S, Ramesh K, Sanjay PR, Abraham P. A non-invasive study to estimate and compare salivary sialic acid level as tumor marker in patients with pre-cancer and oral cancer. J Can Res Ther 2016;12:634-9.
16. Achalli S, Madi M, Babu SG, Shetty SR, Kumari S, Bhat S. Sialic acid as a biomarker of oral potentially malignant disorders and oral cancer. Indian J Dent Res 2017;28:395-9.

17. Sanjay PR, Kaveri Hallikeri, Shivashankara AR Evaluation of salivary sialic acid, total protein, and totalsugar in oral cancer: A preliminary report Indian J Dent Res; 2008; 19(4):288-91.

18. Shivashankara AR, Prabhu MK. Salivary total protein, sialic acid, lipid peroxidation and glutathione in oral squamous cell carcinoma. Biomed Res 2011;22:355-9.

19. Ajay P., Ashwinirani S., Nayak A., Suragimath G., Kamala K., Sande A., Naik R. Oral cancer prevalence in Western population of Maharashtra, India, for a period of 5 years. *J. Oral Res. Rev.* 2018;10:11. doi: 10.4103/jorr.jorr_23_17.