Estimation Of Serum B2-Microglobulin In Oral Precancerous Lesions And Oral Squamous Cell Carcinoma

Pratik Rupakar*, Akilahmed Kureshi, Aanal Balar***, Mahammadhusen Khatri****, Mayur Parmar*****, Piyush Pujara******, Maitri Shah*******

*Department Of Dentistry,G.M.E.R.S. Medical College, Sola, Ahmedabad, Gujarat, India.

**Department Of Oral Pathology, Government Dental College, Ahmedabad, India

Abstract: Background & objectives:The purpose of this study was to assess the serum levels of β2 microglobulin in oral squamous cell carcinoma and oral leukoplakia and to evaluate the possible role of β2 microglobulin as a biochemical parameter in the diagnosis of oral cancer.Methods: Serum β2 microglobulin levels were evaluated using ELISA in thirty patients with oral squamous cell carcinoma, thirty patients with oral leukoplakia, and thirty age-&sexmatched disease-free controls.Results: It was observed that there was a significant increase in serum β2 microglobulin levels in oral squamous cell carcinoma patients as compared to oral leukoplakia and controls. Progressively higher values were obtained as the cancer advanced clinically with respect to clinical staging, tumor size and nodal status. Although, serum β2 microglobulin levels were increased in oral leukoplakia compared to controls, it was found to be statistically insignificant.Interpretation & conclusion**:** From these results, it seems that evaluation of serum β2 microglobulin levels may be useful as one of the battery of tests in assessment of oral carcinoma and leukoplakia. [Pratik Rupakar NJIRM 2016; 7(4):51-55]

Key words: β2 microglobulin, ELISA, leukoplakia; Oral squamous cell carcinoma.

Author For Correspondence: Dr. Pratik Rupakar, Department Of Dentistry,G.M.E.R.S. Medical College, Sola, Ahmedabad, Gujarat, India. **Email Address**:Pratikrupakar@Yahoo.Com, **Phone**: 079 23600216 **Mobile:** 91 9723339724.

Introduction: "Oral squamous cell carcinoma is one of the most common malignant neoplasms worldwide. In India it is the most common cancer in males and third most common in female. As per cancer registries in India, cancer of the oral cavity is one of the five leading sites of cancer in either sex.

Tobacco consumption is the most important risk factor for oral cancer. Epidemiologic studies have established that the high incidence of oral cancer is due to tobacco chewing and smoking habits.The importance of tobacco as an etiologic factor in oral precancerous lesion has been incorporated in its current definition. Oral precancerous lesion has attracted much attention because of its tendency to develop carcinoma within it.[2]

Early detection is also called secondary prevention. The programs for cancer control are based on the premise that the earlier cancer is diagnosed, the better the outcomes in terms of increased survival and reduced mortality. Oral cancer lesions are usually preceded by the occurrences of premalignant lesions and ⁄ or conditions**.**

Recently, there have been a number of scientific approaches to the problem of precancerous lesions, with the aim to establish a fundamental biochemical basis of understanding. The goal of such methods is to find a reliable indicator of the biological potential of precancerous and cancerous lesions. In the biochemical evaluation of cancers it has been found that various substances change quantitatively in the serum during tumor development and are collectively termed as tumor markers or biochemical serum markers.

Currently, tumor markers have been introduced for early detection of malignancy. In the
carcinomas of oral cavity, various serum markers have been studied: these include oncofetal proteins (alpha-fetoprotein, CEA), other proteins like B-protein and enzymes (LDH) etc. One such marker is beta 2 microglobulin. β2 -microglobulin is a low molecular weight, 11800 kD protein found on the surface of all cells except erythrocytes as the invariable light chain of the histocompatibility antigen.[3]

So present study was performed with an objective to correlate the serum levels of beta 2 microglobulin in Oral precancerous lesion and Oral squamous cell carcinoma."

Methods: This study is carried out in the Department of Dentistry, Medical College, Sola, Ahmadabad during December 2015 to April 2015 which includes 30 patients with oral precancerous lesion, which include 20 patients with leukoplakia and 10 patients having erythroplakia, 30 patients with oral squamous cell carcinoma and 30 age- and sex- matched controls for comparison of results. Ethical approval was taken from

ethical committee of the institute and written informed consent was taken from the participants.

Subjects clinically and histopathologically diagnosed as leukoplakia/erythroplakia and OSCC, which had not received any treatment before and the conditions where the serum β2-m level may be elevated like acute and chronic leukemias, non-Hodgkin's lymphoma, myeloma, tumors of breast, lung, colon, stomach, cervix, uterus, hepatobiliary disorders, systemic lupus erythematosus were included while the subjects having such conditions and treatment were excluded from these study. Biopsy and was performed to confirm the diagnosis.

All subjects were screened clinically, biochemically, and biophysically to exclude any infections, renal, hepatobiliary disorders, systemic lupus erythematosus, lymphoproliferative disorders as well as other malignancies, previous history of allergy or autoimmune disease. None of the included patients had received any treatment before the study.

Under aseptic precautions, 5 ml venous blood was drawn and serum was separated out. The samples were frozen at 20°C until assay. The serum β2-m level was analyzed by enzyme linked immunosorbent assay using commercially available kit (β2-mEIA kit, Orgentec, Germany).

Statistical Methods: Analysis was done with SPSS version 15. Analysis of variance has been used to find the significance of 2M mg/lbetween thethree groups and post-hoc Tukey test has been used to find the pairwise significancebetween the groups. Confidence interval and level of significance was set as 95% and 5% respectively.

Results: In our present comparative study, the serum β2 microglobulin levels were estimated in3 groups consisting of 30 subjects each with oral squamous cell carcinoma (OSCC)designated as Group A, 30 subjects with oral precancerous lesion designated as Group B &30 controls designated as Group C.

In Group A of 30 cases with OSCC, 3 cases were in age group of 31-40 years (10%), 6cases were in age group of 41-50 yrs (20%), 14 cases were in age group of 51-60 yrs(46.7%), 6 cases were in age group of 61-70 yrs (20%) and one case was >70 yrs old(3.3%) (Table 1).

The oral squamous cell carcinoma cases selected included more females (66.7%) thanmales (33.3%) (Table 2).

The mean pattern of β2 microglobulin was noted to be increasing progressivelyaccording to the stage of OSCC (Table 3) but no significant correlation was obtained in relation to serum β2 microglobulinandhistopathological grading of OSCC.

Serum β2 microglobulin was significantly elevated in cases with mild, moderate andsevere dysplasia compared to cases without dysplasia ($p<0.001$). Significance was notnoted when the serum β2 microglobulin levels were compared between cases of mildand cases of moderate to severe dysplasia ($p=0.040$) (Table 4).

Upon comparison of serum β2 microglobulin in oral squamous cell carcinoma versus control for p value less than 0.001, the statistical difference was found to be highly significant (Table 5).

Upon comparison of serum β2 microglobulin in oral squamous cell carcinoma with oral precancerous lesion for p value less than 0.001, the statistical difference was found to be highly significant(Table 5).

Upon comparison of serum β2 microglobulin in oral precancerous lesion versus control for p value less than 0.067, the statistical difference was found to be insignificant (Table 5).

Table 1:-Table 1Age distribution

Age in years	Group A	Group B	Group C
≤ 30	-	4(13.3%)	2(6.7%)
31-40	3 (10.0%)	9(30.0%)	8(26.7%)
41-50	6 (20.0%)	6(20.0%)	7(23.3%)
51-60	14(46.7%)	8(26.7%)	9(30.0%)
61-70	6(20.0%)	2(6.7%)	4(13.3%)
>70	1(3.3%)	1(3.3%)	-
Total	30	30	30

Table 2:-Sex distribution

SEX	GROUP A	GROUP B	GROUP C
MALE	10 (33.3%)	16(53.3%)	12(40.0%)
FEMALE	20(66.7%)	14(46.7%)	18(60.0%)
TOTAL	30	30	30

Table 3:-Mean pattern of serum ß 2 microglobulin levels in mg/l according to stage of OSCC.

Stage of OSCC	Mean ±SD
Stage I	2.52±0.59
Stage II	2.59±0.48
Stage III	2.93±0.36
Stage IV	3.17±0.31
P value	P=0.014*

Table 4:- Comparison of serum ß 2 microglobulin levels in mg/l with Epithelial Dysplasia.

EpithelialDysplasia	ß2 microglobulin levels in mg/l		
	Range	Mean±SD	95% CI
Without Dysplasia(n=6)	1.10-.45	1.22□0.14	1.07-1.37
Mild ED (n=18)	1.25-.83	1.71□0.17	1.62-1.79
Mod-Sev. D(n=6)	1.80-.94	1.89□0.05	1.84-1.94
Interface	F=33.345, P<0.001		
P value	Comparition between Without Dysplasia &Mild ED : P<0.001 Comparition between Without Dyslasia& Mod-Sev ED: P<0.001 Comparition between Mild ED & Mod-Sev ED: P=0.040		

Table 5:- Comparison of serum ß2microglobulin levels in mg/l between the groups.

Groups	ß2 microglobulin levels in mg/l		
	Range	Mean±SD	95% CI
Group A	2.04±3.65	3.02±0.41	2.86±3.17
Group B	1.10-1.94	1.65□0.27	1.54-1.75
Group C	1.26-1.70	1.47□0.14	1.42-1.52
Interface	F=243.80, P<0.001		
P value	Between Group A & Group B: P<0.001 Between Group A & Group C: P<0.001 Between Group B & Group C: P=0.067		

Discussion: Oral cancer is the most life-threatening disease of oral tissues and is currently themost frequent cause of cancer-related deaths, which is usually preceded by oralprecancerous lesions like leukoplakia [4, 5]. Over 95% of oral cancer lesions aresquamous cell carcinomas. Oral cancer due to its location in anaccessible part of the body can be detected at an early stage but due to lack ofsymptoms, especially pain, in the early stages, medical attention is not sought till thedisease is advanced. This leads to poor prognosis. It is therefore important to all oralhealth. professionals to equip themselves with the knowledge to detect this disease atthe earliest possible stage6.

Leukoplakia and erythroplakiaofthe oral cavity are frequently encountered and have a well-documented potential to develop into OSCC, with a poor 5-year survival rate. The presence of epithelial dysplasia is generally accepted as one of the most important predictors of malignant development in premalignant lesions.

Histologically, 5 to 15% of oral leukoplakiahas dysplastic features[7].A tumor marker is a substance present in or produced by a tumor or by the host response to the tumor's presence that can be used to differentiate a tumor from normal tissue or to determine the presence of a tumor based on measurement in the blood or secretions. Such a substance can be found in cells, tissues, or body fluids. It can be measured qualitatively or quantitatively to determine presence of cancer[8, 9,10].

In oral carcinoma, however, the studies of tumor markers have been limited. Several tumor markers with clinical promise need further evaluation. One such tumor marker is serum β2 –microglobulin (β2 –m). β2 –microglobulin is a low molecular weight, 11800 Dalton protein found on the surface of all cells except erythrocytes.Elevated levels of β□ 2 –microglobulin have been observed in patients withmalignancy.

Our present study which involved patients visiting GMERS medical college sola and Government Dental college, Ahmedabad, consisted of 30 patients with oralsquamous cell carcinoma distributed in the range of 31-73 years with maximumincidence in the age group of 51-60 years. Our findings are in accordance to theestablished fact that the oral carcinomas are primarily the disease of the advancingage.

It is also clear from our study that female patients have outnumbered the malesamong all age groups which is similar to the sex wise incidence rates observed inSouthern India[13,14].

In The Present Study Comparison of serum β2 microglobulin in oralsquamous cell carcinoma vs. controls (p<0.001) shows that the elevation ofserum β2 microglobulin in OSCC was highly significant compared to controls. Thisnoteworthy finding was reported previously by *Manzar W et al, 1992* who studiedserum

β2 microglobulin in 50 cases of OSCC and 20 normal subjects. Similar resultshave also been obtained by *Anil S et al, 1995* who studied serum β2 microglobulininoral squamous cell carcinoma, oral submucus fibrosis & oral leukoplakia. Various other studies too have reported similar findings [15].

Serum β2 –microglobulin was previously studied in 26 patients with squamous cellcarcinoma of head and neck and a tendency towards an association between tumorsize and serum β 2 –microglobulin has been postulated 27. In our study to a similarrelationship was observed with the serum β 2 –microglobulin levels increasingprogressively with increasing tumor size. This indicates the possibility of using serumβ 2 –m as a complement to physical examination of the patient in monitoring tumorresponse to therapy and detecting recurrent disease through repeated measuring ofserum β 2 –m during and after treatment. Elevation of serum β 2 –m withadvancement of T- stage was also found by Yoneda K et al, 1990.

In our present study, the range of serum β 2 –microglobulin in oral precancerous lesion was1.10-1.94mg/L. Mean was 1.65mg/L with a standard deviation of 0.27 and apredictive value of 1.54-1.75.The serum β 2 –microglobulin in oral precancerous lesion wassignificantly less ($p<0.001$), in comparison to OSCC. Although the serum β 2 –microglobulin in oral precancerous lesion was raised compared to controls, it was found to bestatistically insignificant. Similar results were inferred by *Anil S et al, 1995*.

The increased levels of β2-m in the patients with OSCC in our study may be due toincreased production or impaired excretion. However, as the patients in the study didnot have any disorder of renal function or other systemic ailments and the patientswere matched with age, the increase in serum β2-m appears to be a true phenomenondue to the malignant process.

Conclusion: Present study shows that evaluation of serum β2 microglobulinlevelsmay be useful aid in assessment of oral squamous cell carcinoma and oral precancerous lesions.

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