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EVALUATION OF SERUM BETA 2-MICROGLOBULIN LEVELS IN LEUKOPLAKIA AND SQUAMOUS CELL CARCINOMA OF ORAL CAVITY

Pathology

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ABSTRACT

Introduction: Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity, accounting for approximately 90% of all oral cancers worldwide, requires timely diagnosis for successful treatment. Beta-2 microglobulin, a supplementary biomarker, is being explored for its potential to improve risk assessment and inform treatment strategies, potentially indicating the progression and early detection of pre-malignant oral lesions. **Objectives:** The study investigates the clinical significance of serum Beta-2 microglobulin levels in oral leukoplakia and squamous cell carcinoma, and its potential role in early oral cancer diagnosis. **Methods:** There were 100 patients; 15 had leukoplakia and 85 had OSCC. Demographic information, beta 2 microglobulin levels and tumor characteristics were gathered. Serum beta-2 microglobulin levels were analyzed using the Enzyme-Linked Immunosorbent Assay (ELISA) indirect method. The relationship between beta 2 microglobulin levels and histopathological characteristics were investigated statistically. **Results:** The study found that the 31–60 age group was most affected overall in leukoplakia and malignant cases , while OSCC was most prevalent in males aged 51–60. Tobacco chewing showed a strong association with both conditions. Leukoplakia commonly appeared as white patches in 66.66% present on the buccal mucosa in 46.67%, whereas OSCC typically presented as ulceroproliferative lesions in 74.03% on the lateral border of tongue in 37.65%. Elevated beta-2 microglobulin levels strongly correlated with malignant transformation in the oral cavity. **Conclusion:** Elevated beta 2-microglobulin levels were linked to poorer histological grades, indicating its potential as a marker of oral squamous cell carcinoma aggressiveness. Further research is necessary to validate these findings and improve patient management by integrating beta 2-microglobulin with current prognostic tools.

KEYWORDS

Oral squamous cell carcinoma, leukoplakia, serum beta 2 microglobulin

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity, accounting for approximately 90% of all oral cancers worldwide (1) .Globocan 2020 reported 377,713 new cases of OSCC worldwide, with a high mortality rate due to late-stage detection. India bears a substantial disease burden, contributing nearly 30% of global OSCC cases, with 77,000 new cases annually (2,3).The prevalence of OSCC is highest in South Asia, Southeast Asia, and parts of Europe.The Indian Council of Medical Research (ICMR) reports that over 77,000 new oral cancer cases are identified in India in each year, with a male-to-female ratio of 2:1.[4]. Oral squamous cell carcinoma (OSCC) is a very aggressive tumor with a very bad outlook because it is multistage process ,usually found late and has a high chance of recurrence[5]. Early detection and treatment plays an important role, especially in Indian setup where treatment modalities and costs are high for invasive procedures.

Serum β2M is a non-Invasive biomarker and plays a role in antigen presentation, immune modulation, and tumor surveillance[6]. β2M was identified as a urine protein by the late I. Berggerd in the mid-1960s, and defined in 1968 by Berggird and Bearn. The molecular weight is 11,600, it is present in the serum and urine of humans and several other animals, and it seems to function at the cell surface as a component of the HLA complex [7-9].β2M functions as a significant tumor marker in both hematological and solid cancers, with its levels closely associated with tumor burden, prognosis, and metastatic capability. [10,11]

The tumor microenvironment (TME) in OSCC is characterized by immune evasion mechanisms, including the suppression of cytotoxic T-cell responses and the promotion of M2 macrophages.[6] β2M is involved in: Regulating T-cell responses by altering MHC class I expression.[12]

Facilitating tumor progression by promoting macrophage polarization toward M2 phenotype, which aids angiogenesis and metastasis.[13]

MATERIAL AND METHOD

Sample Collection: Prospective and retrospective analytical comparative study was conducted at Baba Raghav Das (BRD) Medical College, Gorakhpur, Uttar Pradesh, India over a period of one year, after obtaining clearance from the Ethical Committee of the college. The sample comprised of 15 clinically and later on histologically confirmed oral leukoplakia and 85 OSCC patients

Inclusion Criteria: Patients who were clinically suspected and histopathologically confirmed as cases of oral premalignant lesions and oral squamous cell carcinoma (OSCC) were included in the study.

Exclusion Criteria:

- Patients who denied consent for participation.
- Cases with inadequate biopsy specimens that were unsuitable for histopathological analysis.
- Patients diagnosed with systemic diseases known to cause increased beta-2 microglobulin levels, such as active tuberculosis, chronic kidney disease, hepatitis, or HIV infection.

Specimen Collection And Preparation:

4-5ml of blood sample was collected from ante cubital vein into an appropriately labelled plain tube and allowed to clot .After centrifugation serum layer was carefully separated and stored at -20^0 C until use for β2-M level estimation.

Beta 2 microglobulin Estimation:

Serum beta-2 microglobulin levels were analyzed using the Enzyme-Linked Immunosorbent Assay (ELISA) indirect method using ELISA kit - Diagnostic Biochem Canada Inc. (Ref: CAN-B- 4300) in which mouse Anti β2-microglobulin Antibody coated microplate were present. Comparison of mean values of β2M between OSCC and leukolpakia was done using ANOVA and t test.The expected normal value of β2M was 0.8-1.5 mg/L.

RESULTS AND OBSERVATION

Study conducted in department of Pathology at B.R.D. Medical College, Gorakhpur on a total of 100 samples comprising of 15 premalignant (leukoplakia) and 85 malignant (OSCC) lesions. A total of 100 serum samples, along with formalin-fixed, paraffin-embedded biopsy samples from patients presenting with oral lesions, were analyzed.

In the leukoplakia group, the most common age group was 31–40 years (33.33%) while, in the OSCC group, the majority of patients belonged to the 51–60 years (30.59%) , suggesting that middle-aged individuals are most commonly affected.In both, the leukoplakia and OSCC, males were the dominant gender, comprising 66.67% and 69.41% respectively; however, this difference was not statistically significant ($p = 0.832$). Both groups also exhibited a higher occurrence on the right side, with 73.33% of leukoplakia and 71.76% of OSCC cases. A significantly greater proportion of individuals in the leukoplakia group

reported tobacco use alone compared to the OSCC group (46.67% vs. 15.29%). The variation in habit patterns between the two groups was statistically significant ($p < 0.001$), highlighting a strong link between combined risk habits and the development of OSCC. The buccal mucosa was the most frequently affected site in leukoplakia cases (46.67%), while the lateral tongue was most commonly involved in OSCC (37.65%). Clinically, leukoplakia was mainly observed as white patches (66.66%), whereas OSCC commonly appeared as ulceroproliferative lesions (74.03%).The study also found a significant correlation between β2-M levels and the appearance of OSCC, with the highest levels observed in lesions exhibiting both exophytic and endophytic features.Patients with worse pattern of invasion (WPOI 4–5) had significantly higher β2-M levels than those with WPOI 1–3 ($p = 0.019$), showing a link between β2-M levels and aggressive tumor behavior. However, no significant association was found between β2-M levels and lymphovascular invasion (LVI), perineural invasion (PNI), or ulceration.

Our study shows a strong link between high levels of serum beta-2 microglobulin (β2-M) and the development of oral leukoplakia into invasive oral squamous cell carcinoma (OSCC). The normal range of β2-M levels were 0.8- 1.5 mg/L. The mean β2-M levels in patients with OSCC were 3.67 ± 1.87 mg/L, while they were only 1.62 ± 0.26 mg/L in patients with leukoplakia. This difference was statistically significant ($p < 0.001$). This result suggests that β2-M may serve as a potential biomarker for malignant transformation in the oral cavity.

Table 1 Levels Of Serum Beta-2 Microglobulin Levels Between Oral Leukoplakia And Squamous Cell Carcinoma (OSCC).

Normal range 0.8- 1.5 mg /L	Leukoplakia (n=15)		OSCC (n=85)		t	P value
s. beta 2 microglobulin levels (mg/L)	Mean	±SD	Mean	±SD	-7.32	<0.001
	1.62	0.26	3.67	1.87		

Table 2 Comparison Of Mean Serum Beta-2 Microglobulin Levels Across Different Histopathological Grades Of Oral Leukoplakia And Squamous Cell Carcinoma (OSCC)

CATEGORIES		N	Mean	±SD	F	P value
LEUKOPLAKIA N=15	Without Dysplasia	7	1.64	0.08	15.79	<0.001
	Mild Dysplasia	4	1.77	0.13		
	Moderate Dysplasia	3	2.01	0.01		
	Severe Dysplasia	1	2.07	0.08		
OSCC N =85	Microinvasive SCC	2	2.72	0.03	14.93	<0.001
	WDSCC	29	2.89	0.48		
	Verrucous Ca	2	3.64	0.03		
	MDSCC	45	3.82	0.74		
	PDSCC	7	4.44	0.12		
TOTAL		100				

DISCUSSION

The comparison of dysplasia severity scores in leukoplakia across our present study,Saddiwal et al., 2017[14] and Rupakar et al., 2016 [15] reveals trends in the progression of dysplasia severity. Thus, suggesting that it might play a part in tracking the progression of dysplasia. Also, in OSCC, β2-M levels were very different depending on the type of cancer. The highest levels were found in poorly differentiated squamous cell carcinoma (PDSCC) (4.44 ± 0.12 mg/L), while the lowest levels were found in microinvasive SCC (2.72 ± 0.03 mg/L) ($p < 0.001$) followed by WDSCC .Agarwal et al. (2024)[16] and Saddiwal et al. (2017) [14] also reveals significant correlation among different histopathological disease grade. This finding highlights the correlation between higher β2-M levels and poor tumor differentiation, suggesting its prognostic value.

CONCLUSION

Unlike histopathological grading, which requires biopsy, serum β2M levels can be measured non-invasively, offering potential for early detection and disease monitoring [17]. Since OSCC is a heterogeneous disease, combining β2M with other biomarkers such as p53, Ki-67, IL-6, and cyclin D1 may improve diagnostic accuracy.[18] Overall results in our study suggest that serum β2-M levels is a useful complementary biomarker for detecting malignant transformation, tumor differentiation, and aggressiveness in oral cavity lesions. This needs to be confirmed in larger, multi-center studies.

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