ESTIMATION AND COMPARISON OF SERUM β2-MICROGLOBULIN IN ORAL SQUAMOUS CELL CARCINOMA AND ORAL LEUKOPLAKIA

Bhavana Agrawal1, R. N. Mody2, Arun Tadas3

1 Department of Oral Medicine and Radiology, Jodhpur Dental College General Hospital, Jodhpur, India
2 Department of Oral Medicine and Radiology, Mithran Dental College, Jodhpur, India
3 Department of Biochemistry, Vasant Rau Govt. Medical College, Tevateal, India

CORRESPONDING AUTHOR: drbhavana_1@yahoo.com

ABSTRACT

**Aim:** To estimate and compare serum β2-microglobulin levels in oral leukoplakia and oral squamous cell carcinoma patients with that of control group.

**Material and Methods:** The study was carried out on 70 subjects divided into three groups (20 oral leukoplakia patients, 30 oral squamous cell carcinoma patients and 20 controls). Serum β2-microglobulin was estimated by an enzyme linked immunosorbent assay (ELISA).

**Results:** A significant increase in serum levels of β2-microglobulin was observed in oral squamous cell carcinoma patients as compared to control group.

**Conclusions:** Results of this study suggest that estimation of serum β2-microglobulin can be useful in as biomarker for diagnosis of oral squamous cell carcinoma.

**KEYWORDS:** serum β2-microglobulin, oral squamous cell carcinoma, tumor markers

INTRODUCTION

Squamous cell carcinoma is the most common malignancy of oral cavity representing 90-95% of all oral malignancies in India. It is a major health problem in India, forming about 10% of the new cancers that occurs in all parts of body each year. The current research focuses on faster, specific and sensitive tests to detect cancer in early stages. In this context, many tumor markers have been studied. In the oncogenic process, specific events occur at each step and these can be studied by assessing the associated biological markers.

The tumor markers are substances that are produced by body in response to cancerous growth or by the cancer tissue itself and released in blood and other body fluids. There are only a few well-established tumor markers that are being routinely used like prostate specific antigen (PSA), α-fetoprotein for hepatocellular carcinoma, cancer antigen-125 for ovarian cancer etc. For the detection of oral malignancy various markers like oncofoetal protein, carcinoembryonic antigen (CEA), other proteins like B-Protein & β2-microglobulin, and enzymes like lactate dehydrogenase (LDH). These markers have wide range of potential applications like screening, diagnosis, prognosis, and
monitoring the response to treatment.

The search for “ideal tumour marker” has become a major goal in research oncology.

β2-microglobulin is a tumor marker, which has received considerable attention. It was described and isolated from the urine of patients with tubular proteinurias by Berggard and Bearn. It was described and isolated.

Studies have reported increased prevalence of oral malignancy in India, precancer. Considering the high prevalence of oral malignancy in India, the present study was carried out to estimate and compare serum β2-microglobulin levels in patients with oral squamous cell carcinomas and in patients with oral leukoplakia with that of healthy controls.

MATERIAL AND METHODS

For the present study, 70 patients were selected at random from Department of Oral Medicine and Radiology, Govt. Dental College, Nagpur, Maharashtra, India. The informed consent was obtained from all patients and ethical clearance was obtained from institutional ethical committee. The patients were divided into three groups:

G1: control group consisted of 20 age and sex matched individuals who gave no history of any habit nor presented with any signs of systemic disease or pathological oral lesions; G2: consisted of 20 patients in age range of 21 to 69 years, with clinically and histopathologically confirmed leukoplakia; G3: consisted of 30 patients in age range of 25 to 70 years, with clinically staged and histopathologically confirmed squamous cell carcinoma of oral cavity.

None of the patients had received any treatment before study and were free from conditions where β2-microglobulin level may be elevated (acute and chronic leukemia, non-hodgkins lymphoma, multiple myeloma, tumors of breast, lung, colon, cervix, uterus, hepatobiliary disorders & systemic lupus erythematosus). To avoid false positive results, care was taken to exclude subjects with other malignancies or with history of systemic diseases.

Under aseptic conditions, five ml of blood was collected from antecubital vein and allowed to clot at room temperature for two hours and then serum was separated by centrifuging at 3000 rpm for 10 minutes.

The serum was stored in Laxbro storage vials at −70°C until assayed β2-microglobulin was estimated by an indirect solid phase Enzyme Linked Immunosorbent Assay (ELISA), which was designed for the quantitative measurement of β2-microglobulin in human serum. Quantitative estimation of serum β2-microglobulin was done using Immunometric Enzyme Immunoassay kit manufactured by Orgentec Diagnostika GmbH, Mainz, Germany.

The data was analyzed by using statistical package for social sciences (SPSS) software. Cases and controls were tested for statistical significance by Students’ unpaired t-test. Values of p<0.05 were considered significant. Analysis of variance (ANOVA) was used to compare β2-microglobulin in various age groups of control group.

RESULTS

Mean serum β2-microglobulin level in control group was 1.88 µg/ml with standard deviation of 0.82, it was 2.23 ± 0.84 µg/ml in oral leukoplakia group and 3.23± 0.96 µg/ml in oral squamous cell carcinoma group (Table 1). The increase in serum β2-microglobulin level in oral carcinoma group compared with control group was statistically highly significant (p<0.001). Statistically significant increase was also found when oral squamous cell carcinoma group was compared with oral leukoplakia group (p<0.05). Though, increased β2-microglobulin levels were observed in oral leukoplakia, it was not found to be significant when it was compared with control group (P>0.05) (Table 2). Serum β2-Microglobulin levels were also found to be increasing with advancing age in...
control group. This increase was statistically highly significant (Table 3).

In control group the mean serum $\beta_2$-microglobulin level in females was $1.7 \pm 0.50 \mu g/ml$ and in males it was $2.07 \pm 1.04 \mu g/ml$ which was higher than in females, but found to be statistically non-significant (Table 4).

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Groups</th>
<th>$\beta_2$-microglobulin (µg/ml) Mean ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Group I [Controls (n= 20)]</td>
<td>1.88 µg/ml ±0.82</td>
</tr>
<tr>
<td>2</td>
<td>Group II [Oral Leukoplakia (n=20)]</td>
<td>2.23 µg/ml ±0.84</td>
</tr>
<tr>
<td>3</td>
<td>Group III [Oral squamous cell carcinoma (n=30)]</td>
<td>3.23 µg/ml ±0.96</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In present study, increased mean serum $\beta_2$-microglobulin level in oral squamous cell carcinoma patients as compared to control group was found. This is in accordance with studies by: Scully\(^{13}\), Lin\(^{17}\), Vinzez et al\(^2\), Manzar et al\(^{14}\), Anil et al\(^{18}\), Delphine Silva et al\(^{19}\) and Singh\(^{20}\). However, Wennerberg et al\(^{15}\) reported that only 12% of patients with oral squamous cell carcinoma had elevated serum $\beta_2$-microglobulin. Teasdale et al\(^{21}\) reported that serum $\beta_2$-microglobulin more than 3 mg/l are frequently associated with advanced and persistent malignant disease even after allowing for the effects of age and non-specific illness. No correlation between various stages of oral squamous cell carcinoma and serum $\beta_2$-microglobulin level could be established. This is in accordance with Vinzez et al\(^2\) and Manzar et al\(^{14}\). However, Delphine Silva\(^{19}\) reported that progressively higher values were obtained as the oral squamous cell carcinoma advanced clinically. There was increase in mean serum $\beta_2$-microglobulin levels in oral leukoplakia group as compared with control group. This is in accordance with Scully\(^{13}\) and Anil et al\(^{18}\). When serum $\beta_2$-microglobulin level was compared between various age groups of control, it was observed that values increased with the advancing age and this difference was statistically highly significant, however no co-relation between age and serum $\beta_2$-microglobulin could be established in oral squamous cell carcinoma group. These finding were consistent with study of Teasdale et al\(^{21}\) and Parildar\(^{22}\).

When serum $\beta_2$-microglobulin level in males and females in control group was compared, it was found that mean serum $\beta_2$-microglobulin level in male patients was higher compared to female patients of same group however statistically it was not significant. This finding is in contrast with Teasdale et al\(^{21}\).
al.21, who found mean serum β2-
microglobulin levels consistently
higher in females than males. The
increased β2-microglobulin levels
reflect a heightened level of immune
activation as reported by Wanchu et al.23
in a study of HIV/TB co-infection.
Also increased serum β2-microglobulin
levels are reported in old age which
again reflects decreased host
immunity. These findings prompt us
to think that malignancies either develop
in immunocompromised host or there
is immune deficiency secondary to
malignant process.

In the present study, following
findings were also noted which were
not the objectives of study. These are
(oral carcinoma group had 30 patients)
20 males and 10 females and in oral
leukoplakia group, out of 20 patients,
only 1 was female. From this, it can be
concluded that oral pre-cancer and
cancer are more common in males
which can be attributed to relatively
higher indulgence of males in tobacco
and alcohol habits in India. Out of 30
oral carcinoma patients, only two
patients had stage I, 4 patients had
stage II and 24 patients had stage III
and stage IV oral squamous cell
carcinoma. The most common habit
was tobacco plus lime chewing in both
oral squamous cell carcinoma and oral
leukoplakia group. In both oral
leukoplakia and oral squamous cell
carcinoma group elderly patients were
affected most. The mean age in oral
leukoplakia group was 46.45 ± 14.77
years and in oral carcinoma group
mean age was 46.47 ± 9.96 years.

CONCLUSIONS

Decreased mortality and
morbidity can be achieved in oral
cancer and pre-cancer by identification
of tumor bio-markers which assist in
early diagnosis and monitoring of
progression of disease. This study
confirms the results of other
investigators, that β2-microglobulin
levels are increased with progression
from precancer to oral cancer. From
the results presented it can be
concluded that β2-microglobulin can be
used as an adjunct to clinic-pathological
diagnosis or in combination assay
along with other relevant tumor
markers in diagnosis of oral squamous
cell carcinoma. Further studies are
necessary to find out whether serum
β2-microglobulin would be of help as
an individual tumor marker in clinical
diagnosis.

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