

# Research Article

## Serum Protein Levels as Potential Biomarkers in Oral Cancer and Oral Precancer

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### ABSTRACT:

**Background:** The reactive free radicals may interact with intracellular macromolecules such as proteins leading to carcinogenesis. This study was conducted to assess the use of proteins as potential biomarkers in oral premalignant and malignant lesions.

**Materials & Methods:** This study was conducted on 15 individuals with oral potentially malignant disorders, 15 patients with oral cancer, and 15 healthy controls.

**Results:** Our results showed that serum protein levels were decreased in OPMDs, but increased in Oral cancer.

**Conclusion:** It may be concluded that serum protein can be used a potential biomarker for Oral precancer and oral cancer.

**KEY WORDS:** OPMDs, Oral cancer, leukoplakia, OSMF, biomarkers

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### INTRODUCTION:

Oral cancer is the 6<sup>th</sup> most common cancer in the world with a 5-year mortality rate of about 50%. Delayed detection is likely to be a primary reason for the high mortality rate of oral cancer patients.<sup>1</sup> Detection of cancer at the early stage is of utmost importance to decrease the morbidity and mortality of the disease. Hence, there is an imperative need of a sensitive biomarker to improve early detection of oral cancer<sup>2</sup>.

Oral cancers are generally preceded by Oral Potentially Malignant Disorders (OPMDs) like Oral Leukoplakia, OSMF, etc. During oncogenesis, various biochemical alterations occur at every stage, during which, various substances change quantitatively in the serum and are collectively termed as tumour markers or

serum biomarkers<sup>3</sup>.

Serum biomarkers are defined as substances changing quantitatively in the serum during tumour development<sup>4</sup>. The biochemical markers may provide evidence of the changes taking place in the body at a time whenever changes at tissue and cellular level are not obvious to be taken as an evidence of frank malignancies<sup>5</sup>. Many biochemical substances deviate from their normal values; these may include proteins of body fluid. Measurement of total protein concentration provides general information, reflecting disease states in many organs systems, so alternation in serum total protein concentration is used commonly in clinical practice as an indicator for underlying disease or monitoring disease activity<sup>6</sup>. Hence, we carried out the present study with an aim to estimate serum protein levels in oral precancer and oral cancer patients and in

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Table 1: Master chart.

Case Number	Age/Sex	Habits	Provisional Diagnosis	Serum protein levels (g/dl)
1	55/F	Tobacco	Leukoplakia	3.93
2	24/M	Tobacco, Gutkha	OSMF+ Leukoplakia	4.33
3	44/F	Mishri	Leukoplakia	2.7
4	60/M	Smoking	Initial leukoplakia	2.23
5	55/M	Tobacco , smoking, Gutkha chewing	OSMF	4.09
6	19/M	Smoking	Smokers palate, tobacco pouch kerstosis	4.10
7	39/F	Tobacco, Gutkha	OSMF	6.45
8	25/M	Tobacco	Leukoplakia	4.24
9	41/F	Tobacco	Leukoplakia	3.3
10	50/M	Mishri	leukoplakia	3.44
11	70/F	Tobacco	melanosis	3.52
12	60/M	Mishri	LESION	2.27
13	60/M	Tobacco	Pre leukoplakia	2.9
14	65/M	Bidi	Lichenoid reaction	3.93
15	29/M	Tobacco	Lichenod reaction	4.25
16	25/F	None	Normal	5.88
17	27/F	None	Normal	6.11
18	26/F	None	Normal	2.8
19	63/M	None	Normal	5
20	68/M	None	Normal	7.17
21	33/M	None	Normal	1.85
22	36/F	None	Normal	3.60
23	34/M	None	Normal	3.67
24	29/M	None	Normal	4.36
25	25/F	None	Normal	1.78
26	32/M	None	Normal	4.12
27	54/F	None	Normal	3.41
28	45/M	None	Normal	4.27
29	41/F	None	Normal	3.8
30	51/M	None	Normal	4.01
31	72/F	Mishri	CA	4.78
32	55/M	Tobacco, Gutkha	CA	13.9
33	63/M	Tobacco	CA	5.7
34	48/F	Tobacco, Mishri	CA	7.6
34	33/F	Gutkha	OSMF CA	7.2
36	34/M	Tobacco	CA	4.4
37	28/M	Tobacco, Mishri	CA	4.77
38	59/M	Tobacco	CA	5.19
39	69/M	Mishri	CA	3.99
40	36/M	Tobacco	CA	6
41	49/M	Bidi	CA	4.12
42	45/M	Tobacco	CA	6.5
43	54/M	Gutkha	CA	9.1
44	28/M	Tobacco, Gutkha	OSMF CA	8.03
44545	59/M	Tobacco	CA	6.56

healthy controls to evaluate their role in diagnosis and prognosis of oral cancer.

## MATERIALS & METHODS:

The prospective study was carried out in the

Department of Oral Pathology & Microbiology of our institute. After obtaining Institutional ethical clearance and written informed consent from the patients, 5 ml of blood was aspirated from right/left antecubital vein and was centrifuged at 2000 rpm for 10 minutes to separate

**Table 2:** Descriptive statistics.

	Serum Protein Levels			95% confidence interval to the mean		Minimum	Maximum
	Mean	Standard deviation	Standard error	Lower bound	Upper bound		
Normal (n=15)	4.20	1.73	0.522	3.03	5.31	1.78	7.17
OPMDs (n=15)	4.08	0.95	0.25	3.52	4.63	2.27	4.63
OSCC (n=15)	5.31	2.84	0.76	3.66	6.95	3.01	13.90

the serum. The serum was then analysed for total proteins. Assessment of serum total protein was done using the Biuret method with absorption at 540 nm. Serum total proteins were expressed as g/dL. Only patients with histopathological diagnosis were considered. Patients with systemic diseases and those with a follow-up of oral precancer or oral cancer and past history of surgery were excluded. The study subjects were divided into 3 groups- 15 healthy controls, 15 individuals with OPMDs, and 15 patients with oral cancer. Participants from age group 25-60 years from same socioeconomically condition were included in the study.

## RESULTS:

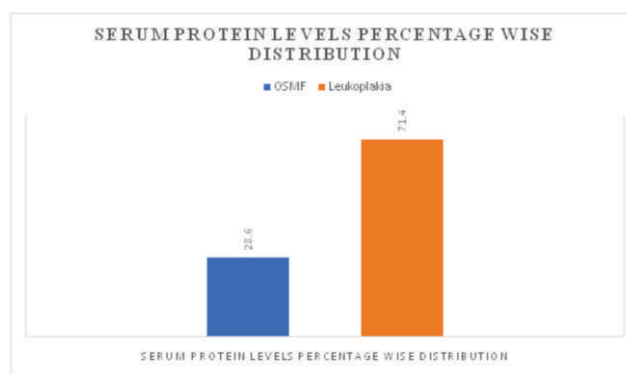
The serum protein levels were estimated in all three groups and tabulated (Table-1). The statistical difference was analyzed by using one-way ANOVA test. The mean value of total protein was minimum ( $4.08 \pm 1.73$ ) g/dl in the OPMD group and was maximum ( $5.31 \pm 2.84$ ) in the oral cancer group (Tables-2 & Table 3). Percentage-wise comparison of proteins in OSMF and leukoplakia patients showed that OSMF patients had decreased serum protein levels as compared to leukoplakia patients (Graph- 1).

**Table 3:** Mean Rank by Kruskal-Wallis test.

Groups	Serum protein values - Mean Rank
Normal (n=15)	6.0
OPMDs (n=15)	7.5
OSCC (n=15)	7.5

## DISCUSSION:

The free radicals are said to be highly reactive and short-lived and are known to be involved in the process of carcinogenesis<sup>[5]</sup>. Free radicals in high concentrations interact with intracellular macromolecules such as DNA, proteins, carbohydrates, and lipids, initiating and promoting carcinogenesis. Free radicals attack the body's healthy cells, leading to loss of structure and function. In

**Graph 1:** Percentage wise distribution of serum protein levels between OSMF and Leukoplakia patients.

carcinogenesis, increased oxidative stress and weakened antioxidant defense produce damage to the macromolecules like proteins. Thus, proteins can be potential biomarkers in oral premalignant and malignant lesions<sup>[7]</sup>. Oxidation of proteins plays an important role in the pathogenesis of cancer. Previous studies have demonstrated decreased protein levels in the cases of OPMDs and oral malignancies<sup>[8]</sup>. In oral cancer, tobacco and areca nut chewing are the main etiologic factors leading to tissue damage and resultant free radicals play a major role as carcinogens.

Our results showed that serum protein levels were decreased in OPMDs, but increased in Oral cancer. Our results were consistent with the results of More CB et al in OSMF and Oral leukoplakia patients (OPMD), Ahmad S et al, Patidar KA et al, and Rajendran R et al, in OSMF patients (OPMD) and Dawood RM et al, in oral cancer patients<sup>[2,7,8,9,10]</sup>. But our results were not consistent with the results of Chandran V et al, in the Oral cancer group in which the plasma protein levels were found to be decreased<sup>[11]</sup>. The increased serum protein levels may be associated with inflammatory reactions associated with oral malignancy. One of the reasons for the decrease in total proteins in oral precancer patients is a decrease in serum albumin level and the other reason is tobacco's effect on the liver which results in a reduction in the synthesis of protein and ultimately total protein level decreases<sup>[8]</sup>. Due to reduced mouth opening in OSMF patients, there

is a reduced overall intake of food leading lack of nutrients which may be responsible for reduced serum protein levels in OSMF patients.

### CONCLUSION:

The present study showed decreased serum protein levels in OPMDs, but increased serum protein levels in oral cancer. It may be concluded that serum protein can be used a potential biomarker for Oral precancer and oral cancer.

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Nil.

### Conflicts of Interest

There are no conflicts of interest.

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