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## Original Research

### Analysis of salivary copper and zinc levels in patients with potentially malignant and malignant disorders: A case-control study

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#### ABSTRACT:

**Background:** Trace elements are chemical elements required in minute amounts, usually as part of a vital element. The present study was undertaken to assess and compare salivary copper and zinc levels in patients with potentially malignant and malignant disorders. **Materials & methods:** A total of 40 subjects were enrolled in the present study. Among these 40 subjects, 10 subjects were of oral leukoplakia (OL), 10 subjects were of oral submucous fibrosis (OSMF), 10 subjects were of oral lichen planus (OLP), 10 subjects were of oral squamous cell carcinoma (OSCC) and remaining 10 subjects were healthy controls. Unstimulated salivary samples were obtained from all the patients in sterilized vials. All the samples were sent to laboratory where an auto-analyser was used for assessing the salivary copper and zinc levels. **Results:** Mean salivary copper levels of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 74.5, 80.1, 79.2, 92.6 and 10.2 ppb respectively. Mean salivary Zinc levels of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 289.2, 295.1, 294.8, 415.2 and 178.9 ppb respectively. Mean salivary copper and zinc levels of the potentially malignant group and the malignant group was significantly higher in comparison to the healthy controls. Also, mean salivary copper and zinc levels of the subjects of the malignant group was significantly higher than that of potentially malignant group. **Conclusion:** Salivary copper and zinc levels show significant alteration in premalignant and malignant disorders; thus highlighting their role in the pathogenesis of the disease.

**Key words:** Copper, Malignant, Zinc.

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#### INTRODUCTION

The human body contains various elements which can be classified as abundant elements and trace elements. The normal function of the human body is reliant on a number of complex physiologic processes, and this function of the living body is through the maintenance of osmotic pressure and membrane potential.<sup>1-3</sup> Growth and development of human body is influenced by his/her daily nutritional intake. The nutrients important for the healthy growth, development, and maintenance are micronutrients and macronutrients or trace elements. Trace elements are chemical elements required in minute amounts, usually as part of a vital element.<sup>4,5</sup> The present study was undertaken to assess and compare salivary copper and zinc levels in patients with potentially malignant and malignant disorders.

#### MATERIALS & METHODS

The present study aimed to competitively evaluate salivary copper and zinc levels in patients with potentially malignant and malignant disorders. A total of 40 subjects were enrolled in the present study. Among these 40 subjects, 10 subjects were of oral leukoplakia (OL), 10 subjects were of oral submucous fibrosis (OSMF), 10 subjects were of oral lichen planus (OLP), 10 subjects were of oral squamous cell carcinoma (OSCC) and remaining 10 subjects were healthy controls. Only those subjects were enrolled in which confirmed histopathologic diagnosis was confirmed according to their respective groups. Complete demographic and clinical details of all the subjects were obtained. Special instructions were given to all the patients that do not drink or eat anything one hour prior to sample collection. Unstimulated salivary samples were obtained from all the patients in sterilized vials. All the samples were sent to

laboratory where an auto-analyser was used for assessing the salivary copper and zinc levels. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software. Mann Whitney U test and chi- square test was used for assessment of level of significance.

**RESULTS**

A total of 40 subjects were enrolled in the present study. Among these 40 subjects, 10 subjects were of OL, 10 subjects were of OSMF, 10 subjects were of OLP, 10 subjects were of OSCC and remaining 10 subjects were healthy controls. Mean age of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 42.6, 44.8, 45, 49.8 and 44.1 years respectively.

In the present study, mean salivary copper levels of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 74.5, 80.1, 79.2, 92.6 and 10.2 ppb respectively. Mean salivary Zinc levels of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 289.2, 295.1, 294.8, 415.2 and 178.9 ppb respectively. Mean salivary copper and zinc levels of the potentially malignant group and the malignant group was significantly higher in comparison to the healthy controls. Also, mean salivary copper and zinc levels of the subjects of the malignant group was significantly higher than that of potentially malignant group.

**Table 1:** Demographic data

Parameter		OL	OSMF	OLP	OSCC	Healthy controls
Age group (years)	Less than 30	2	1	2	1	2
	30 to 45	5	6	4	3	5
	More than 45	3	3	4	6	3
Gender	Males	6	5	4	7	5
	Females	4	5	6	3	5

**Table 2:** Salivary copper and zinc levels

Salivary levels	OL	OSMF	OLP	OSCC	Healthy controls
Copper (ppb)	74.5	80.1	79.2	92.6	10.2
Zinc (ppb)	289.2	295.1	294.8	415.2	178.9

**Table 3:** Comparison of salivary copper and zinc levels

Salivary levels	Group Vs Group		p- value
Copper	OL	OSMF	0.85
		OLP	0.11
		OSCC	0.00 (Significant)
		Healthy controls	0.01 (Significant)
	OSMF	OLP	0.81
		OSCC	0.03 (Significant)
		Healthy controls	0.00 (Significant)
OSCC	Healthy controls	0.00 (Significant)	
Zinc	OL	OSMF	0.26
		OLP	0.52
		OSCC	0.00 (Significant)
		Healthy controls	0.02 (Significant)
	OSMF	OLP	0.82
		OSCC	0.00 (Significant)
		Healthy controls	0.01 (Significant)
	OSCC	Healthy controls	0.00 (Significant)

**DISCUSSION**

India has one of the highest incidences of oral cancer in the world. The development of cancer is a multistep process arising from pre-existing potentially malignant lesions. Oral leukoplakia (OL) is the most common precancer representing 85% of such lesions. Alcohol, viruses, genetic mechanisms, candida and chronic irritation have modifying effects in the etiology of oral cancer.<sup>6,7</sup> Trace elements are regarded as versatile anti-cancer agents that regulate various biological mechanisms. Many researchers have observed association between trace elements and cancer mortality. Decrease in contents of Copper (Cu) and Zinc (Zn) in the blood of patients with head and neck cancer.

Most of the molecules that are found in the body fluids like blood and urine are also found in the saliva, although in lesser concentration thus making saliva an important diagnostic tool.<sup>8,9</sup>

A total of 40 subjects were enrolled in the present study. Among these 40 subjects, 10 subjects were of OL, 10 subjects were of OSMF, 10 subjects were of OLP, 10 subjects were of OSCC and remaining 10 subjects were healthy controls. Mean age of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 42.6, 44.8, 45, 49.8 and 44.1 years respectively. Altered trace element status has been reported in both the potentially malignant and malignant stages. Microminerals are well established to be essential in metabolism as components of enzymes and hormones in the body. This research will focus on three trace minerals—Zn, Cu, and Fe—that are altered in OSF. Zinc is crucial for the normal functioning of the immune cells, antioxidant defense, wound healing, and stability of biological membranes. Chewing of areca nut generates reactive oxygen species, which can cause damage to the proteins and nucleic acids in the body. Zn induces activation of antioxidant enzyme superoxide dismutase (SOD) which inhibits production of reactive oxygen species.<sup>10, 11</sup>

In the present study, mean salivary copper levels of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 74.5, 80.1, 79.2, 92.6 and 10.2 ppb respectively. Mean salivary Zinc levels of the subjects of OL, OSMF, OLP, OSCC and healthy controls was 289.2, 295.1, 294.8, 415.2 and 178.9 ppb respectively. Mean salivary copper and zinc levels of the potentially malignant group and the malignant group was significantly higher in comparison to the healthy controls. Also, mean salivary copper and zinc levels of the subjects of the malignant group was significantly higher than that of potentially malignant group Ayinampudi BK et al evaluated the levels of copper and zinc and copper/zinc ratio in saliva of premalignant and malignant lesions of oral cavity, because of the anatomical proximity of the saliva to both premalignant and malignant oral neoplasms. The levels of copper and zinc were estimated in the saliva of 5 patients with oral submucous fibrosis, 5 patients with oral leukoplakia, 5 patients with oral lichen planus and 10 patients with oral squamous cell carcinoma of oral cavity using inductively coupled mass spectrometry (ICP- MS). The values were compared with 6 normal age and sex matched control subjects. There was significant difference of the mean salivary copper and zinc levels of premalignant and malignant lesions when compared to the normal controls. In oral cancer patients there was significant difference in the copper levels according the histodifferentiation in squamous cell carcinoma. Within the premalignant group the copper levels were more in the oral sub mucous fibrosis when compared to the leukoplakia and lichen planus. Copper zinc ratio decreased in premalignant and malignant group when compared to the normal group. Saliva may be used as a potential diagnostic tool, which can be efficiently employed to evaluate the copper and zinc levels in pre malignant and malignant lesions of oral cavity.<sup>11</sup>

## CONCLUSION

Under the light of above obtained data, the authors conclude that salivary copper and zinc levels show significant alteration in premalignant and malignant disorders; thus highlighting their role in the pathogenesis of the disease.

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