

## Original Research

### Salivary Copper Levels in Oral Leukoplakia Patients

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#### ABSTRACT:

**Background:** This study had been conducted to assess salivary copper levels among oral leukoplakia patients. **Material and mods:** A total of 100 participants were enlisted for this study. The participants were categorized into two groups: group 1, which served as the control group, and group 2, designated as the leukoplakia group. The concentration of copper was measured in the saliva of 50 patients diagnosed with oral leukoplakia through the use of inductively coupled plasma mass spectrometry (ICP-MS). These measurements were then compared to those of 50 control subjects matched for age and sex. **Results:** The age range of the subjects of group 1 was 38-52 years whereas the age range of the subjects of group 2 was 23-62 years. There were 50 subjects in control group and 50 subjects in the second group. There were 25 males and 25 females in control group. There were 40 males and 10 females in group 2. The salivary copper levels in the control group and leukoplakia group were  $10.23 \pm 2.6$  mg/dl and  $69.54 \pm 1.7$  mg/dl, respectively. A notable disparity was observed in the average salivary copper concentrations of individuals with leukoplakia in comparison to the normal control group. An increase in salivary copper levels was identified among the subjects diagnosed with leukoplakia. **Conclusions:** Saliva has the potential to serve as a diagnostic tool, effectively utilized to assess copper concentrations in pre-malignant lesions within the oral cavity.

**Keywords:** Copper, leukoplakia, saliva.

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#### INTRODUCTION

Cancer of the oral cavity represents the most prevalent neoplasm in developing nations. A notably high rate of oral cancer has been documented in Kerala, South India, in comparison to other regions globally. Likewise, the occurrence of precancerous lesions in the oral cavity, such as oral leukoplakia, is also significantly elevated.<sup>1</sup>

The reasons behind this high incidence remain largely unclear. This elevated rate has been linked to various factors, including chewing, smoking, and viral infections. Regardless of the underlying causes, there is a scarcity of information regarding the biochemical and immunological disturbances involved. The influence of certain trace metals, particularly copper, on the pathology of various diseases has been extensively reviewed.<sup>2,3</sup>

Copper is the trace element that has been most thoroughly investigated in patients with premalignant and malignant conditions, and the levels of these elements in serum have proven to be a reliable

diagnostic and prognostic indicator in cases of craniofacial tumors.<sup>4</sup> Recent advancements in technology have enabled the use of saliva as a diagnostic tool for a variety of conditions, including hormone imbalances, liver function, immunodeficiency, and even cancer.<sup>5</sup> So, the present study was undertaken to evaluate the levels of copper in saliva of premalignant and lesions of oral cavity.

#### MATERIAL AND METHODS

The study population was made up of 100 patients in total, who were divided into two groups. 50 healthy volunteers made up Group 1, while 50 people with oral leukoplakia made up Group 2. This study only included cases that had been histopathologically confirmed and those who had been clinically assessed as having no systemic disorders. The subjects selected for the control group had no oral illnesses. Through the use of questionnaires, the nutritional status of each subject was assessed.

One hour prior to the sample collection, the subjects were asked to refrain from eating, drinking, or rinsing, and to immediately rinse with deionized water before saliva was collected. Each person was instructed to collect saliva in their mouths for two minutes before spitting into sterile plastic vials. The entire unstimulated saliva was collected using this method for six minutes. The samples were centrifuged for five minutes at 3,000 rpm and 4 °C. This method yields a saliva sample devoid of significant debris and with reduced viscosity, enabling a considerably more

precise and repeatable examination. In 10 ml/L nitric acid, each specimen was multiplied by five, and the trace elements were determined using inductively coupled mass spectrometry (ICP- MS).

The results were given as parts per billion (ppb) or g/L. The student's independent t-test and one-way analysis of variance (ANOVA) were used in the statistical analysis to compare the means in the two study groups and the two independent groups, respectively.

## RESULTS

The age and sex distribution of all the subjects in the present study is presented below:

**Table 1: age distribution of subjects in leukoplakia group and control group.**

Groups	Range	Mean age	P value
Group 1 (control)	38-52	48.53	p>0.05
Group 2	23-62	45.97	Not significant

The age range of the subjects of group 1 was 38-52 years whereas the age range of the subjects of group 2 was 23-62 years.

**Table 2: sex distribution of subjects in leukoplakia group and control group.**

Groups	Number of subjects	No. of males	No. of females
Group 1(control)	50	25(50%)	25(50%)
Group 2	50	40(80%)	10(20%)

There were 50 subjects in control group and 50 subjects in the second group. There were 25 males and 25 females in control group. There were 40 males and 10 females in group 2.

**Table 3: salivary copper levels in leukoplakia group and control group.**

Groups	Range	Mean	P value
Group 1(control)	5.83-12.79	10.23±2.6	P<0.01 (significant)
Group 2	40.38-213.50	69.54±1.7	P<0.01 (significant)

The salivary copper levels in the control group and leukoplakia group were 10.23±2.6 mg/dl and 69.54±1.7 mg/dl, respectively.

A notable disparity was observed in the average salivary copper concentrations of individuals with leukoplakia in comparison to the normal control group. An increase in salivary copper levels was identified among the subjects diagnosed with leukoplakia.

## DISCUSSION

Trace elements are crucial, either directly or indirectly, in numerous physiological metabolic processes within humans. Over 25% of the body's enzymes require activation by metal ions to perform their metabolic roles. Bioelements such as copper and zinc participate in essential biochemical functions, including various redox reactions and the formation of free radicals, as well as the maintenance of cellular proton homeostasis. Copper is a component of several enzymes that facilitate oxidation, including tyrosinase, ceruloplasmin, amine oxidase, and cytochrome oxidase. Zinc plays a role in carbonic acid metabolism (via carbonic anhydrase) and in proteolytic processes (such as those involving carboxypeptidase and leucine aminopeptidase).<sup>6</sup>

Hence, the present study was undertaken to evaluate the copper levels in the unstimulated whole saliva of normal and premalignant lesions of the oral cavity.

In this study, the age range of the subjects of group 1 was 38-52 years whereas the age range of the subjects

of group 2 was 23-62 years. There were 50 subjects in control group and 50 subjects in the second group. There were 25 males and 25 females in control group. There were 40 males and 10 females in group 2. The salivary copper levels in the control group and leukoplakia group were 10.23±2.6 mg/dl and 69.54±1.7 mg/dl, respectively. A notable disparity was observed in the average salivary copper concentrations of individuals with leukoplakia in comparison to the normal control group. An increase in salivary copper levels was identified among the subjects diagnosed with leukoplakia.

Nasulewicz et al.<sup>7</sup> proposed that copper metabolism is profoundly altered in neoplastic disease and serum copper correlates with tumor incidence and burden, malignant progression, and recurrence in variety of human cancers. Copper plays an important role in tumor angiogenesis, especially in early stages. Copper is necessary for endothelial cell activation as it stimulates their proliferation and activation. Copper activates several angiogenic factors (VEGF, TNF- $\alpha$ ,

IL -1, b-FGF) which bind to endothelial cells switch from G0 into G1 phase and force proliferation. The level of ceruloplasmin, the principal copper transporting protein, increases four to eight folds during malignant progression, often tumors become palpable.

### CONCLUSION

A notable increase in salivary copper concentrations was observed in individuals with oral leukoplakia when compared to those in the control group. Therefore, it was determined that salivary copper levels in cases of oral leukoplakia could serve as a promising diagnostic indicator.

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