

## Original Research

### Salivary copper levels in oral submucous fibrosis patients

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#### ABSTRACT:

**Background:** The purpose of this study was to assess the concentrations of copper in saliva among individuals diagnosed with oral submucous fibrosis (OSMF). **Material and methods:** A total of 100 participants were enlisted for this study. The participants were separated into two groups: Group A, which served as the control group, and Group B, which consisted of individuals with oral submucous fibrosis (OSMF). Inductively coupled mass spectrometry (ICP-MS) was employed to assess the levels of copper in the saliva of 50 patients diagnosed with oral submucous fibrosis (OSMF). The data were compared with a control group consisting of 50 individuals who were matched in terms of age and sex. **Results:** A notable disparity was seen in the average salivary copper levels between individuals with oral submucous fibrosis (OSMF) and the control group. Subjects with oral submucous fibrosis (OSMF) exhibited elevated copper levels. **Conclusions:** Saliva has emerged as a promising diagnostic technique that holds potential for quickly assessing copper levels in precancerous lesions of the oral cavity.

**Keywords:** Copper, OSMF, saliva.

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#### INTRODUCTION

Oral Submucous Fibrosis (OSMF) is a potentially malignant disorder which was described by Schwartz in 1952 as "Atropica idiopathica mucosae oris" and later by Jens J. Pindborg in 1966 as "an insidious, chronic disease that affects any part of the oral cavity and sometimes the pharynx."<sup>1</sup> Although occasionally preceded by, or associated with, the formation of vesicles, it is always associated with a juxtaepithelial inflammatory reaction followed by fibroelastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat.<sup>1</sup> OSMF is also characterized by reduced movement and depapillation of the tongue, blanching and leathery texture of the oral mucosa, progressive reduction of mouth opening, and shrunken uvula.<sup>2-4</sup> Other terms used to describe OSMF include idiopathic scleroderma of the mouth, juxtaepithelial fibrosis, idiopathic palatal fibrosis, diffuse oral submucous fibrosis, and sclerosing stomatitis.<sup>5-8</sup> Copper has been the most extensively studied of the trace elements in patients with premalignant and

malignant disease and these elements in serum has been found to be reliable parameter as a diagnostic and prognostic index in case of craniofacial tumors.<sup>9</sup> Recent technological advances have made saliva as a tool for the diagnosis of many things; among them are hormone imbalances, liver function, immunodeficiency and even cancer.<sup>10</sup> So, the present study was undertaken to evaluate the levels of copper in saliva of subjects having OSMF.

#### MATERIAL AND METHODS

The study sample consisted of a total of one hundred patients, who were allocated into two distinct groups. Group A consisted of fifty individuals who were deemed healthy, whereas Group B had fifty individuals diagnosed with Oral Submucous Fibrosis (OSMF). This study exclusively incorporated cases that had undergone histological confirmation and individuals who had been clinically evaluated and determined to be free of systemic diseases. The individuals chosen for the control group exhibited no

oral diseases. The nutritional status of each participant was evaluated by means of questionnaires.

The participants were instructed to abstain from consuming food, beverages, or rinsing their mouths for a period of one hour before to the collection of saliva samples. Additionally, they were required to rinse their mouths with deionized water shortly before the saliva collection process. Participants were given instructions to retain saliva in their oral cavities for a duration of two minutes, after which they were directed to expel the saliva into sterile plastic vials. The complete unstimulated saliva was gathered utilizing this methodology for a duration of six minutes. The samples underwent centrifugation at a speed of 3,000 revolutions per minute (rpm) at a temperature of 4 °C for a duration of five minutes.

The utilization of this technique results in the acquisition of a saliva specimen that is free from substantial contaminants and possesses decreased viscosity, hence facilitating a significantly enhanced level of accuracy and reproducibility during analysis. The specimens were subjected to a multiplication factor of five in a solution containing nitric acid at a concentration of 10 ml/L. The determination of trace elements was carried out using inductively coupled mass spectrometry (ICP-MS).

The findings were reported in units of parts per billion (ppb) or grams per liter (g/L). The statistical analysis employed the independent t-test to compare the means in the two study groups, and the one-way analysis of variance (ANOVA) to compare the means in the two independent groups.

## RESULTS

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

**Table 1: Age distribution of subjects in OSMF group and control group.**

Groups	Range (years)	Mean age	P value
Group A (control)	38-52	41.25	p>0.05
Group B	17-55	29.36	Not significant

**Table 2: Sex distribution of subjects in OSMF group and control group.**

Groups	Number of subjects	No. of males	No. of females
Group A(control)	50	30(60%)	20(40%)
Group B	50	41(82%)	09(18%)

**Table 3: Salivary copper levels in OSMF group and control group.**

Groups	Mean concentrations	P value
Group A(control)	105.37 ± 26.75	P<0.01 (significant)
Group B	149.62 ± 46.96	P<0.01 (significant)

A notable disparity in the average salivary copper levels was observed between participants with oral submucous fibrosis (OSMF) and those in the control group. An increase in salivary copper concentrations was seen in individuals diagnosed with oral submucous fibrosis (OSMF).

## DISCUSSION

OSMF is a well-recognized, potentially malignant condition of the oral cavity. Controlling the devastating, widespread consequences of OSMF requires interventions in at-risk persons ideally before the disease becomes invasive. Detection of the premalignancies and preventing them from malignant transformation seem to be the best available tool in the fight against oral cancer. Very few studies have been conducted to find out the role of different trace elements in oral precancer and cancer.<sup>11</sup> Hence, a comprehensive study was carried out to estimate levels of serum copper in patients with OSMF.

In this study, there was significant difference of the mean salivary copper levels of OSMF subjects when compared to the normal controls. Elevation in salivary copper levels was discovered in the subjects having OSMF.

In this study, 50 subjects with OSMF were in the age range of 17–55 years with a mean age of 28.64 years. Among the fifty OSMF subjects, 41 were male and 9 were female patients, thus showing an extreme male

predominance over female with the ratio of 5.25:1. A similar male predominance was reported by Sinor *et al.*<sup>12</sup> Pindborg *et al.*<sup>13</sup>, Ahmad *et al.*<sup>14</sup>, and Hazarey *et al.*<sup>15</sup>

In this study, the serum copper level was significantly ( $P < 0.0001$ ) higher among the casethan controls. It was similar to the study by Balpande *et al.*<sup>16</sup> and Shetty *et al.*<sup>17</sup>

Increased serum copper in OSMF can be correlated to copper present in areca nut increases the collagen production in oral fibroblasts by upregulating lysyl oxidase leading to crosslinking of collagen and elastin. Trivedy *et al.* has also reported on the copper-induced mutagenesis through the p53 aberrations in OSMF, which may be critical in the progression of the potentially malignant lesions to squamous cell carcinoma.<sup>18</sup>

## CONCLUSION

Subjects with oral submucous fibrosis (OSMF) exhibited a notable increase in salivary copper levels as compared to the control group. Therefore, it may be

inferred that the measurement of copper levels in saliva could serve as a viable diagnostic tool for Oral Submucous Fibrosis (OSMF).

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