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## Assessment of copper status in oral submucosa fibrosis patients

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### ABSTRACT

To determine the level of trace elements especially copper in oral submucous fibrosis. The objective of the study is to evaluate the levels of circulating trace elements especially copper in oral submucous fibrosis. 30 OSMF patients and 30 healthy individuals from the OPD of Saveetha Dental College. Serum samples were analyzed for serum Copper level DiBrom-PAESA method using ERBA CHEM 5 plus analyzer. There is a highly significant increase in copper levels ( $p < 0.001$ ) in OSMF patients compared to controls, by the influence of OSMF on metabolisms. Our findings suggest that increased Copper values can be used as a diagnostic marker for the manifestation of OSMF.



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### INTRODUCTION

Oral submucous fibrosis (OSMF) is high risk precancerous condition mostly seen in south and south-east Asian countries like India, Bangladesh, Sri Lanka, Pakistan, Taiwan, China, and other Asiatics (Samiha Bari *et al.*, 2017, Yesha Vijaykumar Jani *et al.*, 2017, Tupkari TV *et al.*, 2007). Oral cancer is the sixth most commonly seen cancer worldwide (Sunita N Dyavanagoudar, 2009). Oral squamous cell carcinomas (OSCCs) is the most commonly seen in the case of oral cancer (Shah JP *et al.*, 2003). OSMF is caused due to chewing of Areca nut. The introduction of areca quid product like Gutkha (AQ tobacco), Pan Masala (areca quid) in the Indian market as commercial preparation in the 1980s made an increase in the use of Pan Masala and Gutkha in younger age groups (Sunita N Dyavanagoudar, 2009).

According to the World Health Organisation (WHO), OSMF is "a generalized pathological state of the oral mucosa associated with a significantly increased risk of cancer. OSMF shows several symptoms like Burning sensation in the mouth during consumption of spicy food, Appearance of blisters especially on the palate, Ulceration, Excessive salivation, Defective gustatory sensation and dryness of the mouth (Shah JP *et al.*, 2003). The pathogenesis of the disease is not well established, but the cause of OSMF is believed to be multifactorial (Rajendran R, 2009). The present study was made to trace the amount of copper in the blood serum of normal individual vs OSMF patients.

### MATERIALS AND METHODS

Patients were selected from those attending the outpatient department of Saveetha Dental College, and hospitals and divided into two groups as follows

Group I – Normal healthy individuals – 30 individuals

Group II - Patients with OSMF – 30 individuals

### Inclusion Criteria

Individuals with the age group of thirty-five to Sixty-five years  
OSMF Patients

## Exclusion Criteria

Individuals with other systemic illness like cardiovascular disease, Renal failure, Stroke, endocrine illness.

Immunocompromised individuals

## Sample collection and Procedure

Informed consent was obtained from the patient before sample collection. 3ml of venous blood was collected and distributed in plain collection tubes and centrifuged in 3000rpm for 10 minutes. Then the serum was separated and then it is analyzed for serum Copper level DiBrom-PAESA method using ERBA CHEM 5 plus analyzer.

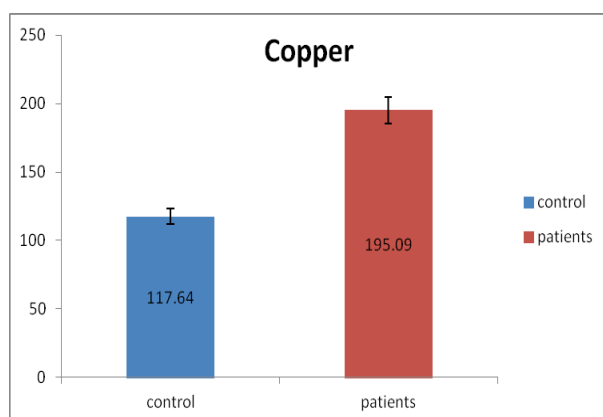
## Principle

The reducing agent Guanidine hydrochloride releases copper bound to ceruloplasmin in an acidic medium. Dibromo-PEASA (4-(3,5-dibromo-2-Pyridylazo)-N-ethyl-N-Sulfopropylaniline) reacts with the free copper to form a stable coloured complex. The intensity of this colour is proportional to the copper concentration in the sample and is measured photometrically at 580nm.

## RESULTS

**Table 1: Mean, SD and Significance value of Level of Copper in control vs OSMF patients**

Parameters	Controls	OSMF patients	p-Value
Copper	117.64 ± 28.07	195.09 ± 34.82	<0.001



**Figure 1: Significance value of Level of Copper in control vs OSMF patients**

## DISCUSSION

The Copper levels of OSMF patients  $195.09 \pm 34.82$  were significantly high when compared with healthy individuals  $117.64 \pm 28.07$  the significant value is  $p < 0.001$

OSMF is a well recognized potentially malignant condition of the oral cavity. Controlling the consequence of OSMF requires intervention in at risk of persons before the disease becomes untreatable. Detection of the precancerous condition and preventing it from becoming cancer seems to be the best method to treat oral cancer (Akanksha Yadav *et al.*, 2015).

Hence the study has been carried out and the content of copper seems to be increased on OSMF patients as compared to normal patients. On chewing areca nut or its commercial products, the level of soluble copper is released into saliva, which is absorbed into the oral mucosa (Trivedy C *et al.*, 1997).

Increased serum copper in OSMF is due to copper present in areca nut increases the collagen production in oral fibroblasts by upregulating lysyl oxidase leading to crosslinking of collagen and elastin (Philips Mathew *et al.*, 2014, Shetty SR *et al.*, 2013). However, studies tracing the source of the increased copper content are rare in the literature. Interestingly, on review of literature, it was found that the areca nut plantations in South India commonly use Bordeaux mixture (BM), a copper-based fungicides on areca nut palms which would increase the level of copper in areca nut (Sastry MN *et al.*, 1988, Nayaka S *et al.*, 2005). One of the most important ingredients for Bordeaux mixture is copper sulphate (Kurian A *et al.*, 2007). The copper-induced mutagenesis through the p53 aberrations in OSMF, which can be critical in the progression of the potentially malignant lesions to squamous cell carcinoma (Philip Mathew *et al.*, 2015). Several studies have reported the increased tissue and serum copper levels in OSMF patients (Trivedy CR *et al.*, 2000, Trivedy C *et al.*, 2001, Trivedy C *et al.*, 1999). OSMF can also be stated as a "collagen metabolic disorder" where there is an increased production of collagen and there is a decrease in collagen degradation which lead to fibrosis (Richa Goel *et al.*, 2014, Trivedy C *et al.*, 2014, Noguchi Y *et al.*, 2006, Archana Venugopal *et al.*, 2016, George A *et al.*, 2011). Thus there is lots of evidence to prove that there is an increase in the level of trace element copper in OSMF patients.

## CONCLUSION

Oral carcinoma develops from oral potentially malignant disorders. Our research findings conclude that an increase in the level of copper is a remarkable criterion in diagnosis and manifestation of OSMF.

## REFERENCES

Akanksha Yadav. *et al.* Estimation of serum zinc, copper, and iron in the patients of oral sub

- mucous fibrosis. *Natl J Maxillofac Surg.* 2015 Jul-Dec;6(2):190-193.
- Archana Venugopal. *et al.* Expression of matrix metalloproteinase-9 in oral potentially malignant disorders: A systematic review. *J Oral Maxillofac Pathol.* 2016 Sep-Dec; 20(3): 474–479.
- George A, Sreenivasan BS, Sunil S, Varghese SS, Thomas J, Devi G, *et al.* Potentially malignant disorders of the oral cavity. *J Oral Maxillofac Pathol.* 2011;2:95–100.
- Kurian A, Peter KV. *Commercial Crops Technology.* Vol. 8. Horticulture Science Series. New Delhi, India: New India Publishing Agency; 2007.
- Nayaka S, Singh PK, Upreti DK. Fungicidal elements accumulated in *Cryptothecia punctulata* (Ascomycetes lichen) of an arecanut orchard in South India. *J Environ Biol* 2005;26:299-300.
- Noguchi Y, Zhang Qw, *et al.* Network analysis of plasma and tissue amino acids and the generation of an amino index for potential diagnostic use. *Am J Clin Nutr.* 2006;83(2):5135–95.
- Philip Mathew. *et al.* Effect of copper-based fungicide (Bordeaux mixture) spray on the total copper content of areca nut: Implications for increasing prevalence of oral submucous fibrosis. *J Int Soc Prevent Community Dent.* 2015;5:283-289.
- Philips Mathew. *et al.* Estimation and Comparison of Copper Content in Raw Areca Nuts and Commercial Areca Nut Products: Implication in Increasing Prevalence of Oral Submucous Fibrosis(OSMF). *J Clin Diagn Res.* 2014 Jan; 8(1): 247-249.
- Rajendran R. *Shafer's Textbook of Oral Pathology.* 6th ed. New Delhi: Elsevier; 2009. Benign and malignant tumours of the oral cavity; pp. 101–5.
- Richa Goel, *et al.* Amino Acid Profile in Oral Submucous Fibrosis: A High-Performance Liquid Chromatography (HPLC) Study. *J Clin Diagn Res.* 2014 Dec; 8(12): ZC44–ZC48.
- Samiha Bari, *et al.* An update on etiological factors disease progression, and malignant transformation in oral submucous fibrosis. *JCRT.* 2017; (13);(3):399-405.
- Sastry MN, Hegde RK. Control of fruit rot or koleroga disease of arecanut (*Areca catechu* L). *Tropical Agriculture.* 1988;65:150-2.
- Shah JP, Johnson NW, Batsakis JG. New York: Thieme Medical Publishers; 2003. Pathology and biology of oral cancer. *Oral Cancer;* pp. 33–75. 213-48.
- Shetty SR, Babu S, Kumari S, Shetty P, Hegde S, Karikal A. Role of serum trace elements in oral precancer and oral cancer – A biochemical study. *J Cancer Res Treat.* 2013;1:1–3.
- Sunita N Dyavanagoudar. *Oral Submucous Fibrosis: Review on Etiopathogenesis.* *JCST.* 2009; (1);(2):072-077.
- Trivedy C, Baldwin D, Warnakulasuriya S, Johnson N, Peters T. Copper content in Areca catechu (betel nut) products and oral submucous fibrosis. *Lancet* 1997;349:1447
- Trivedy C, Meghji S, Warnakulasuriya KAAS, Johnson NW, Harris M. Copper stimulates human oral fibroblasts in vitro: A role in the pathogenesis of oral submucous fibrosis. *J Oral Pathol Med.* 2001;30(8):465–70.
- Trivedy C, Warnakulasuriya KAAS, Hazarey VK, Tavassoli M, Sommer P, Johnson NW. The upregulation of lysyl oxidase in oral submucous fibrosis and squamous cell carcinoma. *J Oral Pathol Med.* 1999;28(6):246–51.
- Trivedy CR, Warnakulasuriya KAAS, Peters TJ, Senkus R, Hazarey VK, Johnson NW. Raised tissue copper levels in oral submucous fibrosis. *J Oral Pathol Med.* 2000;29(6):241–48.
- Tupkari TV, Bhavthankar JD, Mandale MS. Oral submucous fibrosis (OSMF): A study of 101 cases. *J Indian Acad Oral Med Radiol.* 2007;19:311–8.
- Yesha Vijaykumar Jani, *et al.* Evaluation of the role of trace elements in oral submucous fibrosis patients: A study on Gujarati population. *J Oral Maxillofac Pathol.* 2017 Sep-Dec; 21(3): 455.