RESEARCH ARTICLE

ESTIMATION & COMPARITIVE EVALUATION OF SERUM COPPER AND ZINC LEVELS IN PATIENTS WITH OSMF

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ARTICLE INFO	ABSTRACT
	Background and objectives: Copper and Zinc are important trace elements that play a vital role in maintaining various functions of the body at cellular level. Copper and Zinc are involved in many of the anabolic and catabolic enzymatic reactions in the body which determine the cellular growth and differentiation. Copper is responsible for up-regulation of collagen synthesis by regulation of enzyme lysyl oxidase thus enhancing fibrosis in OSMF. Zinc is involved in maintaining cell membrane integrity that is disturbed in OSMF. The purpose of the study was to evaluate the changes in the serum Cu and Zn levels and to relate these alterations with the severity and progression of the disease. **Materials and methods**: In this hospital-based study, 20 clinically diagnosed cases of OSMF and 20 healthy age and sex matched controls were taken. The subjects were screened properly and an informed consent was obtained from all the patients and controls following which blood samples were collected. After serum separation, analysis for Cu and Zn was done. **Results**: Serum Cu was found to be increased in patients with OSMF and serum Zn was found to be depleted in patients when compared to the control group. Furthermore, a progressive trend was seen in the levels of serum Cu with the increasing grades of OSMF. No significant relation was observed in the levels of Zn with the disease progression. **Conclusion**: The above findings suggest a correlation of serum Cu and Zn levels to OSMF. Increasing levels of serum Cu in the progressive grades of OSMF can be used as a marker of disease progression and severity. Serum Zn can be considered as an early marker of the disease.

INTRODUCTION

Oral submucous fibrosis is (OSMF) is a chronic insidious disease of the oral cavity, which is characterized by an epithelial and sub epithelial inflammatory reaction followed by fibro elastic changes in the submucosa (Tadakamadla, 2011). It is a premalignant and crippling condition of the oral mucosa (Shettar, 2010). It has been present most probably for centuries but was not described in the medical literature until 1952. The concept of precancer was put forward by the World Health Organization (WHO) in 1972. According to this concept, a premalignant condition is defined as "a generalized state associated with significantly increased risk of cancer". Thus by definition the oral submucous fibrosis is classified as a premalignant condition (Gupta, 2011). The pathogenesis of OSMF is believed to be multifactorial. Factors that trigger the disease include consumption of chewing areca nut, chillies, nutritional deficiencies such as iron and immunologic processes.

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Certain factors such as genetics, autoimmunity and Human Papilloma virus (HPV) and Herpes simplex virus (HSV) infections are also found to be involved in the etiopathogenesis of OSMF exerting a direct or indirect effect by mediating the immune system which is compromised in OSMF. The most important risk factor however is the chewing of betel quid and this has been supported by epidemiological, case control, experimental studies on animals and tissue culture studies (Sudarshan, 2012). Trace elements have been extensively studied in recent years to assess whether they have any modifying effects in the etiology of cancer. Copper, iron, zinc and selenium are essential for numerous enzymes and therefore it is reasonable to assume that variations in the serum levels of these biochemical markers may be associated with pathogenesis of oral cancer (Khanna, 2006). The present study is being undertaken to evaluate the levels of Copper and Zinc and the Cu /Zn ratio in the serum of patients with oral submucous fibrosis with the view to have a better prospect on the role of these trace elements in the pathogenesis of the condition such that better diagnostic and treatment modalities may be framed to cure this precancerous condition.

MATERIALS AND METHODS

The present study was a case control study and was conducted in the Department of Oral Medicine and Radiology in collaboration with Department of Oral Pathology & Microbiology of Seema Dental College &Hospital, Rishikesh (Uttarakhand) over a period of 11 months from May 2013 to June 2014. The study group consisted of 40 patients, taken from outpatient department of Seema Dental College & Hospital, Rishikesh, out of which 20 patients were diagnosed clinically as Oral submucous fibrosis and 20 patients were clinically diagnosed without any oro-mucosal lesions with age and sex matched with the case group. The serum copper and zinc levels were measured using the RANDOX copper and zinc estimation kits using the calorimetric methods in Dabral Pathology Lab (Dehradun Road, Rishikesh).

RESULTS

The age wise distribution of the study group including the cases and the controls is illustrated in Table 1.
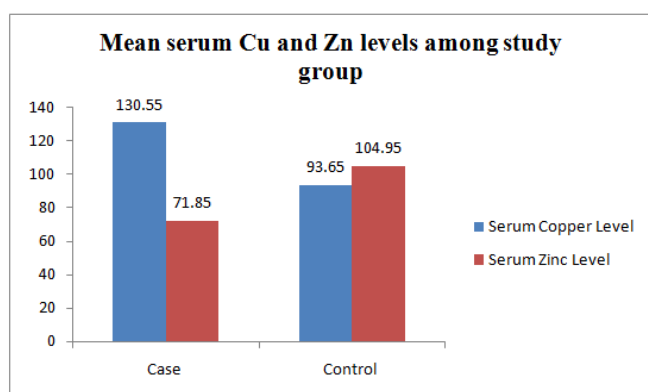
Table 1. Age wise distribution

Age Group	Case (n=20)	Control (n=20)
20 – 30	6	6
31 – 40	7	8
41 – 50	3	4
51 – 60	3	2
> 60	1	0

The study group was divided according to sex of the patients as shown in Table 2.

Table 2. Sex wise distribution

Sex	Case (n=20)	Control (n=20)
Male	17	16
Female	3	4

The comparison of mean serum copper and zinc levels among the study group is depicted in the graph below.

The distribution of cases according to staging system (Chandramani More et al, 2011) is illustrated in the graph below. The comparison of serum copper and zinc levels among the patients with different grades of OSMF is depicted in Table 3 below. The graph below shows the distribution of the patients included in the study on the basis of their habits of betel quid or gutkha chewing.
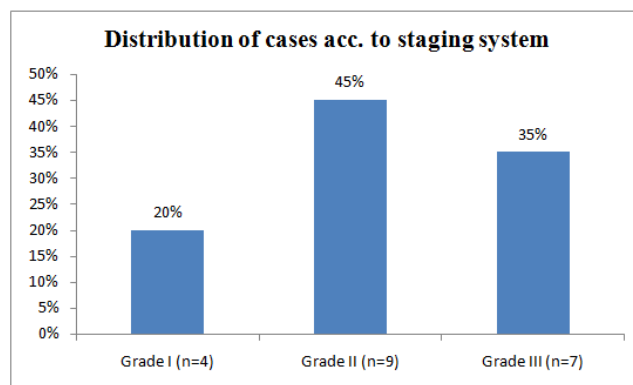

Table 3. Comparison of serum copper and zinc levels among patients with different grades of OSMF

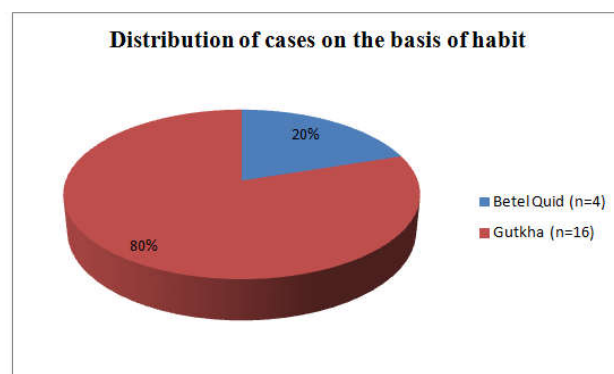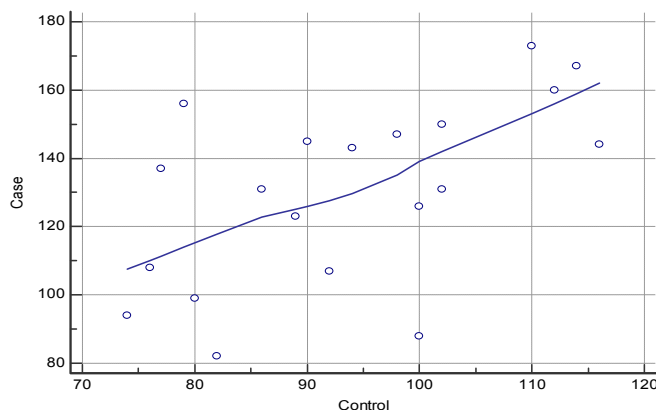|	Serum Copper Level	Serum Zinc Level	t	P value
Grade I (n=4)	90.75±7.36	85±8.16	1.04	0.335
Grade II (n=9)	131.88±16.61	66.77±14.41	8.88	0.001
Grade III (n=7)	151.57±16.85	70.85±15.96	9.20	0.001

Table 4 shows the comparison of mean serum copper and zinc levels among the patients with different habits.

Table 4. Comparison of mean copper and zinc levels among patients with different habits

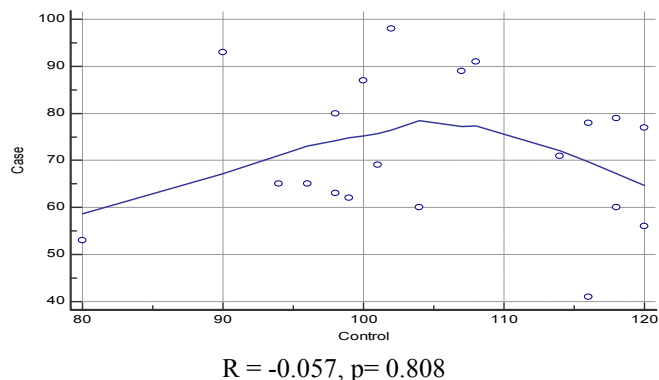|	Serum Copper Level	Serum Zinc Level	t	P value
Paan (n=4)	127.25±32.41	74.5±14.97	2.95	0.025
Gutkha (n=16)	131.37±26.22	71.18±15.51	7.90	0.001

The graphs below represent the correlation between the serum copper and the serum zinc levels in the study group.

Correlation between serum copper levels (µg/dl) in the study group

R= 0.573, p= 0.008

Correlation between serum zinc levels (µg/dl) in the study group

R = -0.057, p= 0.808

DISCUSSION

Copper is an essential trace element. Average intake of copper by adults from diet is between 0.6 – 1.6 mg/day, of which 35 – 70% is absorbed from the gastrointestinal tract (Trivedy, 2000). Copper is needed for synthesis of hemoglobin, proper iron metabolism, and maintenance of blood vessels. Areca nut has a high copper content (302 nmol/g), a substantial amount of which is released into saliva while chewing. The role of copper in the pathogenesis of oral submucous fibrosis is not clearly understood although it is known that the copper dependent enzyme, lysyl oxidase, secreted by the fibroblasts facilitates the cross linking of collagen, thereby initiating its degradation (Pillai, 2005). The nature and characteristics of copper compounds in the areca is yet unknown, though there is an evidence to suggest that the metal – matrix binding of copper in plants is associated with lectins and glycoproteins. The solubility of these complexes in physiological fluids as saliva has been related to chewing areca products in some studies (Arakeri, 2013). Zinc is an essential element for the structure and function of several enzymes. At least 20 different zinc containing proteins have been identified, which include carbonic anhydrase, alcohol dehydrogenase, leucocyte elastase and insulin (Kode, 2013). The exact role of zinc is unknown. Zinc binding may be related to carcinogenesis in the sense that the metals may affect the catabolic and the anabolic enzymes. It has been proposed that zinc being an integral part of bio-membranes may control the membrane integrity and may be involved in the stability of the membranes and in lipid peroxidation related injury. Zinc has been observed to function as a mitogen inducing blastogen transformation of lymphocytes (Schwartz, 1975). Our study has found a statistically significant correlation of the increased serum copper level and reduced serum zinc level in patients with OSMF. Also, there has been a progressive trend seen in the level of serum copper in OMSF patients with the increase in the severity of the disease.

The severity of the disease is statistically not related to the level of serum zinc in these patients, suggesting the smaller sample size as one of the possible explanation for the same.

Conclusion

On the basis of our study, it can be suggested that serum levels of these trace elements may be used as diagnostic and prognostic markers in OSMF patients. Furthermore, this biochemical assessment can be of value for proactive intervention of high risk groups. These tests can be used as auxiliary tests to contribute to the clinico-pathological diagnosis and thus determining the prognosis in a better way in OSMF patients.

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