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Association of trace elements with oral submucous fibrosis.

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ABSTRACT… Objectives: Clinical assessment of OSMF patients visiting Isra dental college Hyderabad Sindh and correlation of trace elements in OSMF pathogenesis. **Study Design:** Observational Study. **Setting:** Outpatient Department, Oral Surgery Isra Dental College Hyderabad Sindh. **Period:** February 2016 January 2017. **Material & Methods:** Sixty research participants were categorized into control (group-II) and experimental group (group-I). Both clinical and physiological demographics of the research participants were recorded on a pre-designed questionnaire. In next phase, estimation of serum copper and serum zinc levels were determined for both control and OSMF patients by using spectrometric analysis. Patient data analysis was done by using Chi-square test and student's t test. Where Microsoft office 2010 tools were also used for data presentation. **Results:** Based on clinical presentation 80 % patient were presenting with burning sensation in oral cavity in thirty OSMF patients. Where in control group only 3.3% patients were facing burning sensation in oral cavity. By assessing the functional staging of oral submucosa fibrosis about 50 % patients were presenting stage-II OSMF cytology. Where all the thirty participants in experimental group were presenting mucosal blanching. About 36 % patients suffering from OSMF were using Gutka and 33 % patients were using areca nut. Serum Zn mean value estimation in controls (Group II) and cases (Group I OSMF) was noted as 68.06 ± 17.10 and 94.20 ± 15.11 μg/dl respectively (t = 6.27, p=0.001). **Conclusion:** The present study concludes that increased serum trace element levels has significant correlation in the development and progression of OSMF.

Key words: LYSYL Oxidase Activity Causing, Oral Submucous Fibrosis, Sindh-Pakistan.

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INTRODUCTION

Oral submucous fibrosis (OSF) is recognized as an irreversible chronic disease impacting the mucus lining of oral, pharyngeal and esophageal cavity. The general appearance of OSF represents turgidity of affected tissues and ends up with proliferation into squamous cellular carcinomas. The major changes within oral tissues include localized systemic sclerosis. The tobacco-based products and areca nut chewing were reported as potential etiological agents of the OSF yet.[1] Many young people in the community are consuming the areca nut which precipitates the OSMF condition.[2] Areca nut alkaloids stimulate the proliferation of fibroblast within oral submucosa and increase the collagen synthesis. Areca nut contains alkaloids like tannins and arecoline which are the potent stimulators of fibroblast proliferation. Overuse of areca nut particularly night quid are reported as stimulator of malignant growths. Duration and frequency of areca nut chewing is directly related to the OSMF progression.[3] Areca nut is also reported to contain traces of elements- the zinc, magnesium, copper and iron. Severity of OSMF is related with the trace elements levels and the stage of disease has a definite relationship. Increased copper concentration in certain areca nut mix has been reported as a possible risk of OSMF in predisposed people.[4] Salivary copper is raised in areca nut users. Elevated salivary copper stimulates the activity of lysyl oxidase enzyme which is copper dependent enzyme. The lysyl oxidase is fibrogenic as it stimulates the fibroblasts in the presence of copper. This is

how the copper plays role in the pathogenesis of OSMF.[5-7] Another mechanism of stimulated fibrogenesis is through the mutagenesis of P53 aberrations. Aberrations of P53 plays potentially significant role in the induction of oncogenesis of oral squamous cell carcinoma. Thus, the serum copper levels are directly proportional to the grade and severity of OSMF in areca nut chewers.[4] The subjected study aims to assess the correlation of trace elements with oral submucous fibrosis among patients enrolled from Sindh Pakistan.

MATERIAL & METHODS

Current observational study was conducted on patients of oral submucosal fibrosis (OSMF) attending the Outpatient Department, Oral Surgery Isra Dental College Hyderabad Sindh during January-2016 to December 2017.

By following random model analysis at 95 % confidence interval and Solvin's formula, patient sample size was determined. The study was approved by Isra University, Dental College ethical committee (IURR-10 /AQK/BASR/-24/2016/1310) and written informed consent was obtained prior to study. In very first phase of the subjected research study, research participants were equally categorized into group- I (control group participant) and group-II (experimental group participants).

Similarly, participants from each group were presented with a questionnaire for complete data acquisition including patient demographic details and disease history. Once patient clinical assessment was made. The patient specific clinical parameters include, functional staging, mucosal blanching, tongue movement and pain sensation in general. In next phase estimation of serum copper and zinc was achieved by following standard blood collection and serum isolation method. The 6ml blood sample was collected in gel tube and then we centrifuged at 3000 rpm gravity for 10min to separate the serum from blood. The 4 to 5ml serum collected in this way was analyzed by spectrophotometric method on Hitachi 902(Roche Germany). The levels of copper and zinc were estimated from serum samples of both groups. Patient data analysis was done by Chi-square test and student's t test was employed for mean values determination.

RESULTS

In current observational research study equal number of participants were placed in control group (Group-I) and experimental group (Group-II), each group participants were tested for clinical and biochemical analysis. Based on clinical presentation, only 3.3% patients complained of burning sensation within oral cavity in control group participants. Where in participant's group 80% patient were suffering from burning sensation. The symptomatic difference between each group participant was found statistically significant ($p = 0.0001$) and chi square value ($X^2 = 30$), Table-I.

Enlightening functional staging of experimental and control group participants represents that, most of patients in OSMF group (Group-I) represent stage-II and stage-III oral submucous fibrosis. The functional staging was done to assess the severity of disease and interventions in the routine physiology. In control group participants only, limited cases were presenting oral submucous fibrosis in control group healthy participants. The healthy participants representing 96.6% functional staging-I outcomes ends up without further progression suggested normal regulation of trace elements and their content ($p=0.033$) ($X^2 = 30$) as mentioned in Table-II.

Discussing, the mucosal blanching, 0% ($n=0$) controls group participants were found. In contrast to control group participants 100% ($n=30$) cases were presenting mucosal blanching in OSMF participants group. The mucosal blanching was assessed on the behalf of patient clinical characterization. As patients were presenting mixed inflammatory edema, epithelial atrophy, fibroblasts and fibrous bands of mucous in oral cavity. The difference was statistically significant P value ($p = 0.001$) and chi square value ($X^2 = 31$), Table-III The tongue immobility was noted in 0% ($n=0$) participants in control group and 73.3% ($n=22$) in OSMF patients. While 26.6% ($n=8$) showed no tongue immobility. The difference was statistically significant P value ($p = 0.0001$) and

chi square value (X^2= 33), Table-III.

The assessment of type of areca nut consumption include, Sweet scented areca nut, Manipuri and Gutkha were noted in 10 (33.3%), 15 (50%) and 11 (36.6%) in both group participants respectively. Results showed that, most of the patients were using Manipuri and least was the sweet-scented areca with P-value (p= 0.0001) and chi square value (X^2= 29) (df = 29).

In next phase of the subjected research study, Serum Cu and serum Zn levels were calculated, serum Cu mean ± SD in controls (Group II) and cases (Group I OSMF) was noted as 114.0 ± 13.8 and 86 ± 4.20 μg/dl respectively (p=0.0001).

The estimation of Serum Zn mean ± SD in controls (Group II) and cases (Group I OSMF) was noted as 68.06 ± 17.10 and 94.20 ± 15.11 μg/dl respectively (t = 6.27, p=0.001) Table-VI.

DISCUSSION

Trace element refers to the chemical elements, which are present or required in minute quantities.[8] These TEs play an imperative role in numerous physiological and metabolic processes in humans. Metal ions are necessary for humans as >25% of the enzymes need to be activated by them.[9]

Study Groups	Yes	No	Df	X^2	P-value
Group-I. OSMF (n=30)	24 (80%)	6 (20%)	29	30.0	0.033
Group-II. (n=30) Controls	1 (3.3%)	29 (96.6%)	29		

Table-I. Burning sensation in oral cavity (n=60).

Study groups	Stage 1	Stage 2	Stage 3	df	X^2	p-value
Group I. OSMF (n=30)	7 (23.3%)	15 (50%)	8 (26.6%)	29	30	0.033
Group II. Controls (n=30)	29 (96.6%)	1 (1.3%)	0 (0%)	29		

Table-II. Functional staging (n=60).

Study group	Yes	No	df	X^2	p-value
Group II. Controls (n=30)	0 (0%)	30 (100%)	29	31	0.001
Group I. OSMF (n=30)	30 (100%)	0 (0%)	29		

Table-III. Mucosal blanching (n=60).

Study Groups	Yes	No	df	X^2	p-value
Group I. OSMF (n=30)	22 (73.3%)	8 (26.6%)	**29**	33	0.0001
Group II. Controls (n=30)	0 (0%)	30 (100%)	29		

Table-IV. Tongue immobility (n=60).

Group B. OSMF (n=30)	Sweet Sented areca nut	Manipuri	Gutkha	df	X^2	p-value
	10 (33.3%)	15 (50%)	11 (36.6%)	29	29	0.001

Table-V. Types of areca nut consumption (n=60).

Study Groups	Mean	SD	df	t-value	p-value
Group I. OSMF (n=30)					
Copper Level	86	4.2	29	10.6	0.0001
Zinc Level	94.2	15.11	29	6.27	0.001
Group II. Controls (n=30)					
Copper Level	114	13.88	29	10.6	0.0001
Zinc Level	68.06	17.1	29	6.27	0.001

Table-VI. Serum copper and Zinc (μg/dl) of study population (n=60).

Schwartz reported the importance of TEs as resourceful anti-cancer agents, which thereby led to the discovery of new diagnostic and therapeutic events in the fields of medicine and specifically in oncology.[10-11] Shockingly, the oral potentially malignant disorder (PMDs) and cancer are spreading like an epidemic. Oral PMDs occurs much higher than oral cancer and these lesions have been predicted to be a useful clinical marker for the detection of oral cancer.[12] Findings of types of areca nut consumption, total duration, quantity, duration of chewing, and areca nut chewing during sleep are consistent to previous studies.[13-14]

Zn is physiologically and biologically essential for the normal development, growth and function in mammals.[15] Zn is basically involved as a cofactor in carbonic anhydrase, carboxy peptidase, leucine peptidase and SOD. Zn is also an essential component for regulating cell cycle and cell division and is also an essential ion needed for the activation of DNA polymerase enzyme.[16] In the present study, serum copper and Zinc levels were low in control group A compared to OSMF group B which showed raised serum Zn levels. In the present study, serum Zn, mean ± SD in controls (Group II) and cases (Group I OSMF) was noted as 68.06 ± 17.10 and 94.20 ± 15.11 μg/dl respectively ($t = 6.27$, $p=0.001$).

The findings of serum Zn levels of present study are in keeping with previous studies.[17-18] They reported raised salivary Zn may provide protective role against free radicals because Zn is antioxidant as it is needed for enzymes biological activity, hence its levels are increased once oxidative stress is increased as occurs by areca nut chewing.

CONCLUSION

Current study confirms that, patient who had habit of areca nut chewing showed increased amounts of trace elements (serum copper and zinc). Research reports revealed that, Copper and Zinc could contribute to the pathogenesis of OSMF complications. Role of copper and zinc has been documented and confirmed by the present study. The present study concludes that increased serum trace element levels has significant role in the development and pathogenesis OSMF patients.

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3	Surwaich Ali Channa	Manuscript review.	
4	Khalid Yousuf	Data analysis.	
5	Shahzaman Memon	Manuscript writing.	
6	Shafquat Hussain Khuwaja	Review of literature.	