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COMPARISON OF SERUM TRACE ELEMENT LEVELS IN PATIENTS WITH ORAL CANCER -A CROSS SECTIONAL STUDY

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ABSTRACT

Background: Iron, copper and zinc play a major role in enzymatic action in our body. Variation in their levels play a very important role in pathogenesis of oral cancer.

Aim of the study: The present study was mainly aimed to estimate and compare the serum levels of copper, iron and zinc in comparison with normal controls.

Methods: For the purpose, collected serum of cases and controls were analyzed by using standard spectrophotometric methods in spectrophotometer analyzer and the data obtained was represented as Mean ± SD, mean difference was analyzed by Student's T-test & Chi-square test for significance by using SPSSv23 software.

Results: The levels of serum trace elements in case group (N=30) were 53.8667±23.68 (iron; µg/dl), 137.10±19.52 (copper; µg/dl), 168.04±14.23 (zinc; µg/dl) and that in control group (N=30) were 85.10±27.36 (iron; µg/dl), 115.37±21.25 (copper; µg/dl), 82.46±10.26 (zinc; µg/dl). Mean serum level of iron was significantly lower and the levels of zinc and copper in patients with oral cancerous lesions were significantly higher than that of healthy individuals. ($p < 0.05$)

Conclusions: Significant changes in these parameters is evident from the study findings. This suggests the involvement of oxidative stress and trace elements in the pathogenesis of oral cancer.

KEYWORDS : Copper, Iron, Zinc, Oral cancer.

INTRODUCTION

Iron, zinc and copper have major roles in normal functioning of our body by their contributions in the enzymatic action (1-3). Oral cancer is one of the ten most common causes of cancers among men in developed countries and sixth most common cancer around the world (4) There are an estimated 6,57,000 new cases of cancers of the oral cavity and pharynx each year, and more than 3,30,000 deaths (5). Even though oral and pharyngeal cancers being one of the most mortal cancers, its quick diagnosis and referral, play crucial factors in enhancing the survival rate of the patients (6). Squamous cell carcinoma is the most prevalent cancer of oral malignancies (7). The deficiency or increased levels of these elements have to be treated in order to prevent various pathological manifestations and for early detection of oral cancer.

The development of cancer is a multi-step process which usually arises from a pre-existing potentially malignant lesion. Leucoplakia is the most common pre-cancerous lesion representing 85% of lesions that are potentially pre-malignant (8). Alcohol, tobacco chewing, viruses, genetic mutations, candida infections, and chronic irritations have modifying effects in the aetiology of oral cancer. Trace elements have an important role in carcinogenesis (9). Trace elements have been regarded as versatile anti-cancerous agents that regulate various biological mechanisms. Many researchers have observed a potential link between the trace elements with oral pre-malignant lesions and oral cancer. An alteration of serum trace elements like iron, copper and zinc are seen in metabolic disorders, oral pre-cancerous lesions and cancers. Levels of serum trace elements, also help to counteract the oxidative stress induced by free radicals which can cause serious damage to cells in oral pre-cancerous conditions and oral cancer. It can help not only in the early diagnosis and treatment but also in prognosis as the disease progresses (10). Although not established, it is plausible that disordered trace element status (if present) would contribute to morbidity and mortality among oral cancer patients. However, the incidence of abnormal trace element status in oral cancer patients has not been comprehensively studied. Therefore, a study was conducted to evaluate the possible alterations in serum levels of copper (Cu), zinc (Zn) and iron (Fe) levels in oral cancer patients which aimed to estimate and compare the serum levels of copper, iron, and zinc levels in clinically diagnosed oral cancer patients when compared to normal healthy controls.

MATERIAL AND METHODS:

Source Of Data

It was an observational analytical cross-sectional study where blood sample was collected from oncology unit and analysis was done in Father Muller Medical College Hospital, Clinical Biochemistry Laboratory over a period of 3 months. The study was conducted after getting approval from the institutional ethics committee and informed consent was obtained from all the participants. Total number of 60 subjects were included in the study (sample size was achieved by using the sample size calculator for the power of >80% and alpha value <0.05) (8).

Sample And Sampling Technique

The formula used for calculation of sampling size

$$n \geq (Z_{1-\alpha/2} + Z_{1-\beta})^2 (\sigma_1^2 + \sigma_2^2/r)/(\mu_1 - \mu_2)^2$$

n- sample size
σ-standard deviation
µ-difference between means
α-error,β-error

Inclusion Criteria:

Group I: Thirty, clinically diagnosed oral cancer patients (age: 35-80years) admitted in oncology unit of Medical College and Hospital.
Group II: Thirty, normal, healthy, age and sex-matched volunteers (age: 35-80years)

Exclusion Criteria:

People suffering from liver disease, diabetes, Chronic Kidney Diseases, infections were excluded from study. Pregnant women were also excluded from study.

Collection Of Samples:

Blood samples were collected with aseptic precautions as per requirement and processed accordingly. The samples were collected from Clinical Biochemistry Laboratory & stored in Deep Freezer for the purpose of study. Blood drawn for some other purpose was used both in cases and controls.

Assays To Be Done:

Following Biochemical parameters were analyzed using standard spectrophotometric methods in spectrophotometer analyzer.

- Iron: spectrophotometric method using ferrozine reagent (11).
Zinc: spectrophotometric method using 2-(5-nitro-2-pyridylazo)-5-(N-propyl-N-sulfopropyl amino) phenol disodium salt reagent (12).
- Copper: spectrophotometric method using Sodium diethyldithiocarbamate method (13).

Statistical Analysis:

Collected data were represented as Mean±SD, mean difference was analysed by Student's T-test & Chi- square test for significance using

SPSS v23 software.

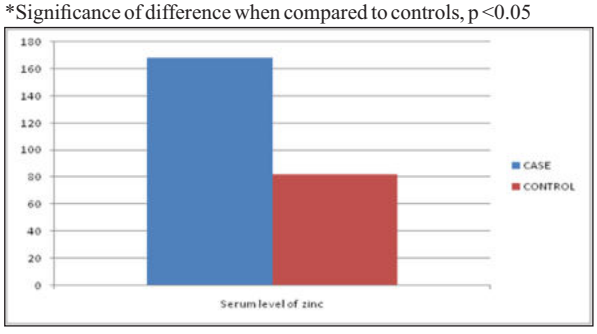
RESULTS

Results of this study are presented in (Table 1) and (Graphs 1, 2 and 3). The subjects of the study were patients with oral cancer. (Group I; n = 30) and normal healthy controls (Group II; n=30). The serum levels of zinc and copper in group I were significantly higher when compared to controls. There was a significant lower serum level of iron in Group-I when compared to controls.

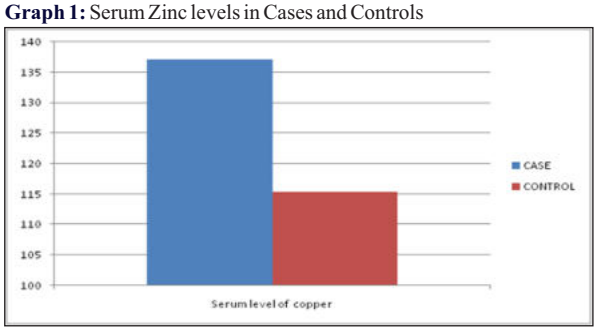
Table 1: Serum Levels Of Iron, Copper And Zinc In Both Groups

Trace Elements	Group	Sample Numbers	Mean±SD	p value
Iron (µg/dL)	Controls	30	85.10±27.36	0.026
	Cases	30	53.86±23.67*	
Copper (µg/dL)	Controls	30	115.36±21.25	0.047
	Cases	30	137.09±19.51*	
Zinc (µg/dL)	Controls	30	82.46±10.26	0.022
	Cases	30	168.03±14.22*	

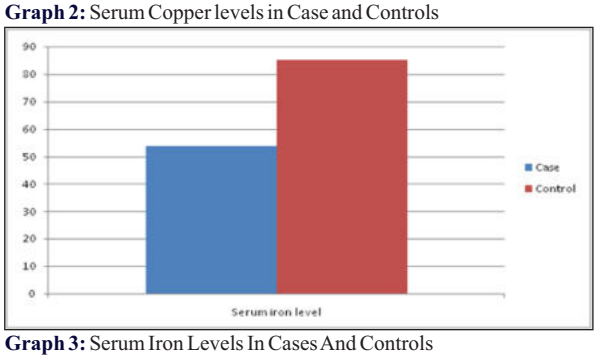
*Significance of difference when compared to controls, p <0.05



Graph 1: Serum Zinc levels in Cases and Controls



Graph 2: Serum Copper levels in Case and Controls



Graph 3: Serum Iron Levels In Cases And Controls

DISCUSSION

The rate at which oral cancerous lesion spreading like an epidemic is alarming. The oral cancer lesion provides useful clinical markers for its diagnosis. Areca nut chewing is one of the most common causes for oral cancers (14). The etiology of OSCC includes various carcinogens in tobacco and related products such as polynuclear aromatic hydrocarbons and nitrosamines (15).

The present study made an attempt to assess serum levels of iron, zinc and copper in patients with oral cancer (group I; n = 30) in comparison to normal healthy controls (Group II; n = 30).

The serum zinc and copper levels in group I patients were significantly higher compared to controls. There was a significantly lower serum iron level in group-I when compared to controls.

The serum level of copper was significantly increased and that of iron was significantly decreased with the controls in comparison to studies done by Sharada P et al., (4), Jaydeep A et al., (8) and Tadakamadla J et al.,(9). However, Sharda P et al., (4) and Jaydeep A et al., (8) observed that serum zinc levels decreased in contrast to the present study.

Even though the reason behind an increase in serum level of copper is not known, it might be due to increased production of ceruloplasmin by liver as an inflammatory response or due to decrease in catabolism of the serum ceruloplasmin (16).

Anuradha et al.,(17) attributed that decreased serum levels of iron was due to its utilisation for collagen synthesis. Hannen et al.,(18) attributed that increase in zinc levels may be due to their important role in the rapid cell proliferation as encountered in growing tumors.

Many patients neglect early symptoms till late stage of the cancer where the prognosis becomes poor. There is a delay in treatment due to self-remedies, seeking traditional healers, socioeconomic factors and lack of awareness. Better awareness on the matter and early detection is a necessity for better prognosis.

CONCLUSION

The present study has made an attempt to assess serum iron, copper and zinc in oral cancer patients. This suggests the involvement of oxidative stress and trace elements in the pathogenesis of oral cancer. The hypothesis that trace element status influenced adverse risk on clinical outcomes appears worthy of investigation. Further studies are required to evaluate the clinical significance and long-term effects of imbalances of these trace elements in oral cancer patients. Future studies with larger sample size in assessing the biomarkers for prognosis and treatment follow up of cancer is required.

Declaration

We declare no competing interests.
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