

Assessment of the presence of ceruloplasmin and Selenium in the serum of the subjects having oral cancer and potentially malignant disorders

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ABSTRACT

Background: *Despite various advancements for screening, detection, prevention, and treatment of Oral cancer, potentially malignant oral carcinomas remain one of the most prevalent cancers contributing to significant mortality raising concern. Modifiable factors identified in oral cancer are immunity and diet.*

Materials and Methods: *30 subjects (10 healthy and 20 with oral lesions) from both the genders and age range of 25-55 years were divided into 3 groups of 10 subjects each. Group I: normal healthy, group II: oral leukoplakia, and group III: oral carcinoma subjects followed by blood investigations. The diamine oxide method was used to evaluate ceruloplasmin and the atomic absorption spectrometer method of Sir Alan Walsh was used to analyze selenium. Collected data were subjected to statistical evaluation for results formulation.*

Results: *On intergroup comparison, it was seen that the mean value for selenium in ng/ml were 119.935, 109.15, and 99.6228 for Group I, Group II, and Group III respectively, whereas for ceruloplasmin these values were 31.748, 81.413, and 90.7122 respectively for group I, group II, and group III.*

Conclusion: *The present study concludes that the most important defense system to prevent cell damage by free radicals is the use of antioxidants. Detection of selenium and ceruloplasmin in the serum of the affected subject can serve as a reliable biomarker in subjects having precancerous lesion (leukoplakia) and oral carcinomas (squamous cell carcinoma).*

Keywords:

Antigen- antibody complex, ceruloplasmin, oral precancerous lesions, oral Neoplasm's, Selenium

INTRODUCTION

Prevalence of the premalignant and the malignant lesions is higher in the Indian subjects compared to the other parts of the globe. This can be attributed to widely prevalent habits in India including mechanical irritation, alcohol consumption, tobacco chewing, and/or smoking. Excess intake or dietary deficiencies are also found to be associated with the

occurrence of various premalignant lesions.¹ Previous literature data has reported that trace elements play a vital role as causative or inhibitory factors of these lesion occurrences. These trace elements include selenium, ceruloplasmin, iron, zinc, and copper. The most commonly seen premalignant and malignant lesion in the oral cavity is leukoplakia and squamous cell carcinoma respectively. High occurrence of Oral carcinoma and leukoplakia is attributed to the betel quid and tobacco chewing as etiologic and a risk factor for these lesions.²

Decreasing delays in diagnosis can help in the early detection of these lesions which is found to be between 3 months and 6 months in primary care centers. Significant negative impact on patient survival and outcome is seen by delay in referral to specialist and delay in diagnosis of the lesion. Hence, a widely accessible, inexpensive, non-invasive, and simple test method is needed for detection in the primary care center.³ A close association between cancer and oxidative challenge has been reported in the literature. Free radical action leads to lipid peroxidation resulting in harmful effects on cells and causing cell damage. Also, by lipid peroxidation, metabolic conversion of various carcinogens to free radicals is seen.⁴

Previous literature data has also reported that selenium acts as a cancer-protective agent. Measuring selenium in the serum has gained popularity recently owing to the nutritional and toxicological importance of selenium. A recent study assessed serum concentration of ceruloplasmin and selenium in subjects with squamous cell carcinoma and oral leukoplakia had helped in diagnosis and tumor burden assessment and served as a tumor marker to help in assessing diagnosis and prognosis of these oral lesions.⁵

MATERIALS AND METHODS

The present study was conducted to assess the presence of ceruloplasmin and selenium in subjects with premalignant and malignant oral lesions. The study was conducted at Shyam Shah Medical College And Sanjay Gandhi Memorial Hospital, Rewa, Madhya Pradesh after obtaining clearance from the concerned Ethical committee. The study included a total of 30 subjects from both genders, within the age range of 25-55 years and the mean age of 34.2 ± 2.43 years. The study population was comprised of the subjects visiting the Outpatient Department of Oral and Maxillofacial Surgery of the Institute. The exclusion criteria for the study were subjects having previous cancer therapy, nephrotic syndrome, liver disease, acute infections, hypertension, diabetes mellitus, autoimmune diseases, and known allergies.

After final inclusion, 30 subjects were divided into three groups having 10 subjects each where Group I had 10 healthy subjects, Group II had 10 subjects with a confirmatory diagnosis of leukoplakia on histologic and clinical examination, and Group III subjects had confirmed diagnosis of squamous cell carcinoma of stage III and IV in the oral region. The venous blood of 2ml was collected from the antecubital vein under aseptic and strict sterile conditions of all the study subjects as a medium for investigation. The collected blood was subjected to centrifugation to separate serum for estimating ceruloplasmin and selenium.

Diamine oxidase method was used for ceruloplasmin estimation and the atomic absorption spectrometer method of Sir Alan Walsh of 1950 was used to analyze selenium. The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p < 0.05$.

RESULTS

The present study was conducted to assess the presence of ceruloplasmin and selenium in subjects with premalignant and malignant oral lesions. The study included a total of 30 subjects from both genders, within the age range of 25-55 years and the mean age of 34.2 ± 2.43 years. The normal range of ceruloplasmin in the serum is 20-60 ng/dl. The mean

ceruloplasmin value in group I was 31.748 ± 2.656 ng/dl with a maximum value of 35.85 and a minimum value of 27.04. The mean ceruloplasmin value was 81.413 ± 10.117 ng/dl in group II with a maximum and minimum value of 93.41 and 59.84 respectively. These values for Group III subjects having squamous cell carcinoma were 90.7122 ± 3.648 ng/dl with a minimum value of 86.42 and a maximum value of 93.41. These differences were statistically significant between the three groups with $p=0.0005$ (Table 1).

Table 1: Estimation of serum Ceruloplasmin and intergroup comparison in the study subjects

Ceruloplasmin levels	Mean \pm S.D	Maximum	Minimum
Group I	31.748 \pm 2.656	35.85	27.04
Group II	81.413 \pm 10.117	93.41	59.84
Group III	90.7122 \pm 3.648	97.07	86.42
Conclusion	P=0.0005		
p-value			
Group I vs Group II	0.0005		
Group I vs Group III	0.0005		
Group II vs Group III	0.0005		

On intergroup analysis, it was seen that on comparing Group I (healthy subjects) with Group II (subjects having leukoplakia), it was seen that there existed a statistically significant difference with $p < 0.00005$. A similar statistically significant difference was seen comparing Group II (subjects having leukoplakia) with Group III (squamous cell carcinoma), and subjects of Group I (healthy subjects) to Group II (subjects having leukoplakia) with $p < 0.0005$ (Table 1).

The normal range of selenium in the serum is 115-35 ng/dl. The results of the present study also showed that the mean selenium value in group I was 119.935 ± 2.109 ng/dl with a maximum value of 122.52 and a minimum value of 116.07. The mean ceruloplasmin value was 109.15 ± 3.823 ng/dl in group II with a maximum and minimum value of 115.02 and 102.64 respectively. These values for Group III subjects having squamous cell carcinoma were 99.6228 ± 4.053 ng/dl with a minimum value of 104.59 and a maximum value of 92.06. These differences were statistically significant between the three groups with $p=0.0005$ (Table 2).

Table 2: Estimation of serum Selenium and intergroup comparison in the study subjects

Selenium levels	Mean \pm S.D	Maximum	Minimum
Group I	119.935 \pm 2.109	122.52	116.07
Group II	109.15 \pm 3.823	115.02	102.64
Group III	99.6228 \pm 4.053	104.59	92.06
Conclusion	P=0.0005		
p-value			
Group I vs Group II	0.0005		
Group I vs Group III	0.0005		
Group II vs Group III	0.0005		

On intergroup analysis, it was seen that on comparing Group I (healthy subjects) with Group II (subjects having leukoplakia), it was seen that there existed a statistically significant difference with $p < 0.00005$. A similar statistically significant difference was seen comparing Group II (subjects having leukoplakia) with Group III (squamous cell carcinoma), and

subjects of Group I (healthy subjects) to Group II (subjects having leukoplakia) with $p < 0.0005$ (Table 2).

DISCUSSION

The present study was conducted to assess the presence of ceruloplasmin and selenium in subjects with premalignant and malignant oral lesions. The study included a total of 30 subjects from both genders, within the age range of 25-55 years and the mean age of 34.2 ± 2.43 years. The normal range of ceruloplasmin in the serum is 20-60 ng/dl. The mean ceruloplasmin value in group I was 31.748 ± 2.656 ng/dl with a maximum value of 35.85 and a minimum value of 27.04. The mean ceruloplasmin value was 81.413 ± 10.117 ng/dl in group II with a maximum and minimum value of 93.41 and 59.84 respectively. These values for Group II subjects having squamous cell carcinoma were 90.7122 ± 3.648 ng/dl with a minimum value of 86.42 and a maximum value of 93.41. These differences were statistically significant between the three groups with $p = 0.0005$. These results were consistent with the findings of Mohammad AA et al⁶ in 2018 and Bhattacharya PT et al⁷ in 2016 where authors reported comparable values of ceruloplasmin in subjects with oral lesions in their respective studies.

The normal range of selenium in the serum is 115-35 ng/dl. The results of the present study also showed that the mean selenium value in group I was 119.935 ± 2.109 ng/dl with a maximum value of 122.52 and a minimum value of 116.07. The mean ceruloplasmin value was 109.15 ± 3.823 ng/dl in group II with a maximum and minimum value of 115.02 and 102.64 respectively. These values for Group III subjects having squamous cell carcinoma were 99.6228 ± 4.053 ng/dl with a minimum value of 104.59 and a maximum value of 92.06. These differences were statistically significant between the three groups with $p = 0.0005$. These findings were in agreement with the results of Garg P et al⁸ in 2012 and Rahal A et al⁹ in 2014 where authors showed comparable values of selenium in subjects with oral lesions.

On intergroup analysis for ceruloplasmin, it was seen that on comparing Group I (healthy subjects) with Group II (subjects having leukoplakia), it was seen that there existed a statistically significant difference in ceruloplasmin levels with $p < 0.00005$. A similar statistically significant difference was seen comparing Group II (subjects having leukoplakia) with Group III (squamous cell carcinoma), and subjects of Group I (healthy subjects) to Group II (subjects having leukoplakia) with $p < 0.0005$. On intergroup analysis of selenium levels, it was seen that on comparing Group I (healthy subjects) with Group II (subjects having leukoplakia), it was seen that there existed a statistically significant difference with $p < 0.00005$. A similar statistically significant difference was seen comparing Group II (subjects having leukoplakia) with Group III (squamous cell carcinoma), and subjects of Group I (healthy subjects) to Group II (subjects having leukoplakia) with $p < 0.0005$. These results were comparable to the results by the studies of Kadkol S et al¹⁰ in 2020 and Tsao AS et al¹¹ in 2004 where authors reported similar significance in ceruloplasmin and selenium levels in subjects with oral lesions.

CONCLUSION

Within its limitations, the present study concludes that antioxidants play a vital role in defense for cellular injury caused by the free radicals. These antioxidants apart from playing role in free radical injury also play a role in cases with malignancy. To neutralize the peroxidant state, excessive antioxidants are produced by humans including α -tocopherol, glutathione, and ceruloplasmin. Also, levels of selenium and zinc are reduced in malignancy. Levels of selenium and ceruloplasmin can be used as reliable biomarkers and can be monitored and used as disease markers in subjects with premalignant and malignant oral lesions.

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