EVALUATION OF SERUM URIC ACIDS WITH ORAL CANCER, POTENTIALLY MALIGNANT DISORDERS AND IN PATIENTS WITH TOBACCO HABIT: A CASE CONTROL STUDY

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ABSTRACT:
Introduction: Uric Acid (UA) is a known antioxidant which inhibits carcinogenesis and have protects cells against oxidative damage by mopping up free radicals. Oral cancer is considered as one of the commonest cancer affecting human population worldwide with high mortality and morbidity rate. Most of these cancers are associated with consumption of tobacco. Usage of tobacco leads to changes in the oral mucosa in the form of potentially malignant disorders which further causes oral cancer. Hence this study was aimed to evaluate serum UA in patients with oral cancer (OC), potentially malignant disorders (PMD) and in patients with tobacco habit.

Materials and Method: This case control study consisted of 80 subjects which were divided into mainly two groups; study and control groups. The study group consisted of a total of 60 patients, 20 patients in each subgroups ie, OC, PMD, tobacco habits but without any lesions at the time of study. Control group consisted of 20 healthy individuals without lesions or tobacco habits. Fasting venous blood of all subjects was collected the serum which was separated using centrifuge and subjected for biochemical evaluation. The biochemical evaluation is done using BS-380 chemist auto analyzer using and URICASE – POD method with DHBS. The values obtained were statistically analyzed using SPSS 19.0 version software.

Results: A significant decrease in UA was observed in the patients with OC and PMD as compared to the control group and no significant decrease was found in patients with tobacco habit.

Conclusion: Low UA is associated with increased risk of PMDs and OC development and UA has got no direct and overall significant influence associated in tobacco users.

Keywords: Oral cancer (OC), potentially malignant disorders (PMD), Tobacco habit, Uric acid (UA),

INTRODUCTION:
Oral cancer is one of the most common malignancies in Southeast Asia and is one of the 10 most common causes of death. More than 11 million people are diagnosed with cancer every year. It is estimated that there will be 16 million new cases every year by 2020.[¹] Most of oral cancers occur as squamous cell carcinomas. Most affected patients are middle-aged or elderly individuals. In male, OC represents 4% of total body cancer; in females, 2% of all cancers are OC.[²] Many Oral squamous cell carcinoma (OSCC) develops from PMD of the oral cavity. The use of tobacco has been well established as a significant risk

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for the development of OSCC and Potentially malignant disorders (PMDS) like leukoplakia, erythroplakia and oral submucous fibrosis.

OC is found to be associated with tobacco habit, in one or the other form. The risk of developing malignancy is 5-9 times greater for smokers than non-smokers which is dose dependent.\[3\] It is believed that tobacco carcinogens induce generation of free radicals and reactive oxygen species, which are responsible for high rate of oxidation and peroxidation of polyunsaturated fatty acids. This peroxidation further releases peroxide radicals. This affects essential constituents of cell membrane and might be involved in carcinogenesis.

Uric acid (UA) is the final product of purine metabolism in body. Its circulating concentrations are regulated by the balance in its production and excretion.\[4\] It is a known antioxidant which prevents cancer by mopping up free radicals that causes injury to the cells. Antioxidants are inhibitors of initiation, promotion and transformational stage of carcinogenesis and protect cells against oxidative damage produced by free radicals. Only few studies have tested the association between UA as biomarker and carcinogenesis with inconsistent results.\[5\]

The present study was aimed to i) evaluate the serum UA in OC, PMDS, and patients with tobacco habit ii) to compare the obtained values with normal individuals who do not have disease or habit of tobacco in any form and, iii) finally attempt was made to examine the possible role of UA in the etiopathogenesis of oral cancer.

MATERIALS AND METHODS:

This study consisted of 80 subjects which were divided into mainly two groups; study and control groups. The study group consisted of a total of 60 patients, of which 20 patients were with OC, 20 patients were with PMDs, and 20 patients with habit of tobacco but without any lesions at the time of study. Control group consisted of 20 healthy individuals without lesions or tobacco related habits. Patients who had any systemic diseases like renal disease, diabetes, etc were excluded in the study.

Both groups consisted of both sexes and were in the age group of 15 years to 60 years. After informed consent a detailed history of habits was taken for all the patients who were first clinically diagnosed to have OC and PMDs. Fasting venous blood of 10ml from all subjects was collected in a test tube and the serum was separated from other constituents of blood using centrifuge. Serum from this collected blood sample is used for the evaluation. The biochemical evaluation is done using BS-380 chemist autoanalyzer and the results are analyzed and expressed. Biochemical method followed for estimation of uric acid - URICASE – POD method with DHBS.
**RESULTS:**

This case control study consisted of study and control groups. Study group involves mainly 3 subgroups with 20 patients in each subgroup. Patients with OC comprised of 14 males and 6 females, PMDs which includes oral leukoplakia and oral submucous fibrosis comprised of 13 male and 7 female and patients with tobacco habit but without any lesions at the time of study comprised of 11 male and 9 female. Control group consists of 20 healthy patients without any such lesions or tobacco related habits and comprised of 10 male and 10 female.

The values obtained were subjected to statistical analysis which is performed by using SPSS (statistical package for social sciences) 19.0 version software. The mean serum levels of UA were compared with the control, patients with OC, PMDs and patients with tobacco habits but without any lesions at the time of study.

The mean value of the UA for control group was 5.04±0.62. The mean value in OC was 3.76±0.83. The mean value in PMDs was 4.43±0.49 and in tobacco habit patients mean value was 4.52±0.68. (Table -I) (Graph- I). Comparison of the level of UA among the four groups was done by one way ANOVA and it was found that mean value between groups was statistically significant (P<0.001) (Table -II). Comparison between the 4 groups is done by Tukeys multiple post hoc test. Serum UA is reduced in oral cancer patients which is statistically highly significant (P<0.001). PMDs also showed lowered levels of uric acid when compared to patients with habit and control (P<0.05). There is no significant change of UA in patients in habit patients (P>0.05). These values suggest that there is significant decrease of UA in OC patients and PMD patients and there is decrease uric acid in habit patient also but not statistically significant. (Table-III).

**DISCUSSION:**

This case control study evaluated SUA levels in PMDs and OC. In this study, tobacco in the form of smoke and smokeless was the most significant addictive factors. On analysis, study showed that SUA level was significantly lowered in OC and PMDs when compared to the control group (P<0.001). There was no significant change of uric acid levels in tobacco habituates.

Ames et al. for the first time proposed that the uric acid has a role in primary defence, act as scavenger and prevent formation of oxygen radicals and there by protect against carcinogenesis.\[6\] Only few studies have tested the association between UA and carcinogenesis with inconsistent results. The present study showed that the decreased UA level in serum is associated with increased risk of occurrence of PMDS and OC.

In a study by Battino et al. conducted in saliva of oral lichen planus, there was significant decrease of salivary uric acid as well as in the total antioxidant...
capacity of saliva in oral lichen planus patients. The finding of this study is consistent with findings of present study which is done in serum of OC, leukoplakia and oral submucous fibrosis.

In a study by Bozkir et al. found that serum uric acid is significantly decreased in lung cancer patients compared to healthy controls, which is similar to findings of this study.

It is possible that the effect of SUA in aetiology of cancer may vary from one type of cancer to another; low serum uric acid may be associated with increased risk of lung and oral cancer for instance, while high serum uric acid may be associated with increased risk of other types of cancer. Serum uric acid levels were further positively related to deaths from malignant neoplasms of breast and female genital organs and nervous system and unspecified sites.

Mazza et al. in a study in Italy, found that SUA could protect against cancer. The role of UA in conditions associated with oxidative stress is not entirely clear.

The decrease SUA in oral cancer patients in this study is may attributed to nutritional compromise of the patients due to tumour necrosis factor and interleukin-6 produced in cancer and precancer patients, which cause loss of appetite. SUA level can also affected by alcohol consumption, defects in purine metabolism, hyperinsulinemia, and genetic factors.

The results of this study showed the evidence of an inverse relationship of UA in OC and PMDs. From the findings of this study, it appears that SUA as a biochemical indicator has got no direct and overall significant influence associated with tobacco habit. Variability of the values of this serum biochemical in precancerous condition and cancer patients may be due to multiple reasons, such as age, nutritional status, body mass index, alcohol consumption, exercise habits. The variability in levels of this parameter might also arise from methodological difference. Although, this study does not entirely resolve the controversy of the role of SUA in cancer etiopathogenesis, but the status of SUA can be considered as one of the biochemical markers in oral PMDs and OC.

Clinician should avoid excessively wide buccal corridors with ideal smile arcs to achieve esthetic smiles. These goals can be achieved by carefully planning treatment and by attending to arch form, the inclination of the occlusal plane, and anterior vertical tooth position, especially during finishing.

**CONCLUSION:**

This study showed that the low SUA is associated with increased risk of PMDs and OC development. SUA has got no direct and overall significant influence associated in tobacco users. But further studies are suggested in larger sample group to better understand the role of
REFERENCES:

2. Greenberg MS, Glick M. Burket’s Oral Medicine, Diagnosis and Treatment. 11th edition. India: B C Decker Inc; 2008: 153.
TABLES:

Table- I: Distribution of mean serum UA in control OC, PMD and tobacco habit groups and their statistical P-value comparisons

<table>
<thead>
<tr>
<th>group</th>
<th>Mean</th>
<th>Median</th>
<th>Std.dev.</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5.04±0.62</td>
<td>4.6</td>
<td>0.62</td>
<td>0.13</td>
</tr>
<tr>
<td>OC</td>
<td>3.76±0.83</td>
<td>3.65</td>
<td>0.83</td>
<td>0.19</td>
</tr>
<tr>
<td>PMDs</td>
<td>4.43±0.49</td>
<td>4.15</td>
<td>0.49</td>
<td>0.11</td>
</tr>
<tr>
<td>Tobacco Habits</td>
<td>4.52±0.68</td>
<td>4.45</td>
<td>0.68</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Table- II: Comparison of four groups with respect to uric acids by one way ANOVA

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Degrees of freedom</th>
<th>Sum of squares</th>
<th>Mean sum of squares</th>
<th>F-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between groups</td>
<td>3</td>
<td>16.69</td>
<td>5.56</td>
<td>12.35</td>
<td>0.001***</td>
</tr>
<tr>
<td>Within groups</td>
<td>76</td>
<td>34.23</td>
<td>0.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
<td>50.93</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

***p<0.001

Table –III: Pair wise comparison of four groups with respect Uric acids by multiple post hoc procedures.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Control</th>
<th>Oral cancer</th>
<th>Oral Precancer</th>
<th>Habit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>0.001***</td>
<td>0.026**</td>
<td>0.072</td>
</tr>
<tr>
<td>Oral cancer</td>
<td>0.001***</td>
<td>-</td>
<td>0.011**</td>
<td>0.003**</td>
</tr>
<tr>
<td>Oral precancer</td>
<td>0.026**</td>
<td>0.011**</td>
<td>-</td>
<td>0.978</td>
</tr>
<tr>
<td>Habit</td>
<td>0.072</td>
<td>0.003**</td>
<td>0.978</td>
<td>-</td>
</tr>
</tbody>
</table>

***p ≤ 0.001 represents statistically highly significant, **p ≤ 0.05 represents statistically significant, p>0.05 represents statistically not significant.

GRAPH:

Graph –I: Bar graph showing comparison of four groups with respect to uric acids.