

## SERUM URIC ACID LEVELS IN ORAL CANCER PATIENTS SEEN AT TERTIARY INSTITUTION IN NIGERIA

A.O. Lawal<sup>1</sup>, B. Kolude<sup>1</sup> and B.F. Adeyemi<sup>1</sup>

1. Department of Oral Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria.

### Correspondence:

**Dr. A.O. Lawal**

Department of Oral Pathology,  
College of Medicine, University of Ibadan.  
E-mail: toytoy219@yahoo.com  
Tel: +2348055133964  
Fax: +23422411768

### SUMMARY

**Introduction:** Toxicity by oxygen radicals has been considered as an important cause of cancer. It is proposed that the antioxidant properties of uric acid may act to prevent formation of oxygen radicals and thereby protect against carcinogenesis. This study aims to assess the role of uric acid in the aetiology of oral cancer.

**Materials and Methods:** Thirty one oral cancer patients and thirty normal patients had serum uric acid measured using spectrophotometer. The data obtained was analyzed using the Statistical Package for the Social Sciences, version 19.0 (SPSS19). Statistical significance was determined at  $P < 0.05$ .

**Results:** The mean serum uric acid level in oral cancer patients was 5.18 mg/dl ( $SD \pm 1.96$ ) while the mean was 7.09 mg/dl ( $SD \pm 1.84$ ) for the control group and this difference was statistically significant ( $p=0.000$ ,  $t= -3.914$ , C.I. = - 2.885 to - 0.933). The risk of oral cancer was 3.98 times more in patients who had low serum uric acid.

**Conclusion:** This study showed that serum uric acid was lower in oral cancer patients compared with healthy volunteers and low serum uric acid was associated with increased risk of oral cancer development. However, further prospective cohort studies are suggested to better understand the role of serum uric acid in aetiology of oral cancer.

### INTRODUCTION

Toxicity by oxygen radicals has been suggested as an important cause of cancer, heart disease and aging.<sup>1</sup> Oxygen radicals and other oxidants are toxic mainly because of their ability to initiate the chain reaction of lipid peroxidation. Lipid peroxidation in turn, generates reactive species such as radicals, hydro peroxides, aldehydes, and epoxides with the capability of causing cellular, DNA, and RNA injuries.<sup>1</sup>

The protective systems against these injuries include enzymes, such as superoxide dismutase, the selenium containing glutathione peroxidase and antioxidants and radical scavengers; such as  $\alpha$ -tocopherol and  $\beta$ -carotene in the lipid portion of the cell and glutathione and ascorbic acid in the aqueous phase.<sup>1</sup> These protective mechanisms are now recognized as anti-carcinogenic and even having ability to increase life-span.<sup>1</sup>

Uric acid is the final product of purine metabolism in humans, and its circulating concentrations are regulated by the balance in its production and excretion<sup>2</sup>. Uric acid is a known antioxidant,<sup>1</sup> and thus may prevent cancer by mopping up free radicals that may cause

cellular and genetic injury. It is also said to help in stabilization of ascorbate in biological fluids<sup>3</sup>, and because its serum concentration is higher than that of ascorbate, it is thought to potentially have a higher antioxidant property than ascorbate.<sup>3</sup>

Humans and other primates have higher serum urate and lower hepatic uricase levels compared to lower mammalian species.<sup>4</sup> Ames *et al.*<sup>1</sup> proposed that the uric acid may act to prevent formation of oxygen radicals and thereby protect against carcinogenesis. Only few studies have tested the association between uric acid and carcinogenesis with inconsistent results<sup>5, 6</sup>, however, to the best of our knowledge, no study has examined the role of uric acid in the aetiology of oral cancer.

The aim of this study was to analyze the serum uric acid levels in oral cancer patients and compare them with those of normal patients in order to examine the possible role of uric acid in the aetiology of oral cancer.

## MATERIALS AND METHODS

Thirty one histological confirmed oral cancer patients and thirty healthy volunteers were recruited from the Out-patient department of the Dental Centre University College Hospital Ibadan over an eighteen months period. Ethical clearance was obtained from the joint ethical committee of University of Ibadan and the University College Hospital. All patients were duly informed of the aim of the procedure and consented to participate in the study. Healthy volunteers

ratio and logistic regression, where applicable. Statistical significance was determined at  $P < 0.05$ .

## RESULTS

The male to female ratio in the oral epithelial cancer group was 1:1.7. The age range was 18 to 83 years while the mean age was 53.7 years ( $SD \pm 17.3$ ). The male: female ratio in the control group was 1.3:1 and the mean age was 54.8 years ( $SD \pm 10.9$ ) while the age range was 40-78 years. Student t test showed there

Uric acid levels	Oral cancer N (%)	Control N (%)	Total N (%)
Low (<3mg/dl)	5(16.1)	1(3.3)	6(9.8)
Normal (3-6 mg/dl)	21(67.7)	16(53.3)	37(60.7)
High serum (>6 mg/dl)	5(16.1)	13(43.3)	18(29.5)
Total	31(100)	30(100)	61(100)

**Table 1:** Serum levels in Oral cancer patients and control group

under age 40 years and all those with known systemic diseases were excluded from the study (this is because things like alcohol, fructose containing sugars and purine containing foods may increase serum uric acid levels). Patients who previously had any form of radio therapy, chemo therapy or surgical interventions were excluded from the study.

10mls of intravenous blood was taken from all participants after an overnight fast. The blood was centrifuged at 3,000 rpm for 5 minutes and separated serum was aspirated into tubes and analyzed for uric acid with a DM520 spectrophotometer (Beckman USA).

The data obtained was analyzed using the Statistical Package for the Social Sciences, version 19.0 (SPSS19). Differences between the two groups were analyzed for statistical significance using the student t- test, odd

was no statistical significant difference between the mean ages of patients with oral cancer and the control group. ( $p = 0.788$ ,  $t = 0.270$ , C.I. = - 6.337 to +8.308). The mean serum uric acid level in oral cancer patients was 5.18 mg/dl ( $SD \pm 1.96$ ) while the mean was 7.09 mg/dl ( $SD \pm 1.84$ ) in the control group. There was a statistically significant difference between the mean serum levels of oral cancer patients compared to that of the control group. ( $p=0.000$ ,  $t= -3.914$ , C.I. = - 2.885 to -0.933).

Table 1 shows that more (16.1%) oral cancer patients had low serum uric acid (<3 mg/dl) compared with the control group in which only 3.3% had low serum uric acid levels. The risk of oral cancer was 3.98 times more in patients who had low serum uric acid, while tobacco and alcohol use were associated with 4.05 and 1.09 times increased risk of oral cancer respectively (Table 2).

Risk Factors	Oral cancer N (%)	Control N (%)	P	OR	95.0% CI for OR
Low serum uric acid	5(16.1)	1(3.3)	0.027*	3.98	0.076, 0.834
Alcohol intake	8(25.8)	7(24.1)	0.881	1.09	0.34, 3.53
Tobacco intake	6(23.1)	2(6.9)	0.131*	4.05	0.74, 22.20

\*Fishers exact test used

**Table 2:** Comparison of risk factors for oral cancer

## DISCUSSION

This study showed that serum uric acid level was significantly lower in oral cancer patients compared to the control group. Previous studies showing relationship between serum uric acid and cancer incidence have been rather inconsistent. Mazza *et al*<sup>6</sup>, in a study in Italy, found that serum uric acid could protect against cancer. This was corroborated by Bozkir *et al*<sup>7</sup> who reported a significantly lower Serum uric acid in lung cancer patients compared to healthy controls. In a study by Willet *et al*<sup>7</sup> in the Netherlands, 672 men aged 47-66 years were followed up for a 10 years period, found that lower levels of SUA were associated with lung cancer mortality but no increase in mortality of other cancer types. After controlling for age and smoking, the relationship of serum uric acid to lung cancer was significant.

Many other studies such as Strasak *et al*<sup>8</sup> in Austria, Levine *et al*<sup>4</sup> in USA, Bengston *et al*<sup>5</sup> and Petterson *et al*<sup>10</sup> all found that high serum uric acid was associated with higher risk of cancer mortality, although, they did not observe serum uric acid association with cancer incidence and other factors. However, Hiatt and Fireman<sup>2</sup> in prospective cohort study, found no association between serum uric acid with cancer incidence after adjusting for age, race, education, tobacco, alcohol intake, and body mass index.

The increased risk of cancer mortality obtained in some of these studies may be due to the markedly high serum uric acid observed in some cancer patients, which may be attributed to the malignant process itself, resulting from the increased nucleic acid turnover in the rapidly proliferating diseased tissue.<sup>9</sup>

It is also possible that the effect of serum uric acid on 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.

An association of low serum uric acid level with lung cancer was thought to be plausible under the Ames hypothesis, since the high oxygen environment of lung tissue could be more susceptible to the carcinogenic activity of oxygen radicals.<sup>4</sup>

Increased risk of prostate cancer associated with elevated serum uric acid may be an indirect reflection of androgen (testosterone and dihydrotestosterone) metabolism which has been associated with increased prostate cancer risk. These hormones are associated with increased muscle mass and increased muscle mass may lead to greater tissue turnover and DNA

catabolism and thus high serum uric acid levels.<sup>10</sup> These possibilities may be in part, responsible for the inconsistent results gotten from studies in the relationship between serum uric acid and cancer incidence and mortality.

The low Serum uric acid in oral cancer patients in this study may be due to nutritional compromise of the patients due to Tumour necrosis Factor (TNF) and Interleukin 6 (IL-6) produced in cancer patients, which cause loss of appetite.<sup>10</sup> Serum uric acid level is determined by both endogenous production and exogenously by ingestion from dietary sources. It is believed that up to 50% of serum uric acid is from dietary sources including liver, mussels, sardines and sausages.<sup>3</sup> Serum uric acid level is also affected by alcohol consumption, fructose containing sugars, and defects in purine metabolism, impaired renal function, hyperinsulinemia, drugs such as diuretics and genetic factors.<sup>11,12</sup>

Although, this study does not entirely resolve the controversy of the role of serum uric acid in cancer aetiology, it is probably one of the first to examine possible role of serum uric acid in oral cancer aetio-pathogenesis and showed that low serum uric acid is associated with increased risk of oral cancer development but further prospective cohort studies are suggested to better understand the role of serum uric acid in aetiology of oral cancer.

## ACKNOWLEDGMENTS

The authors wish to acknowledge Mr. Olabiyi of the Department of Chemical Pathology, University College Hospital, Ibadan who did the laboratory analysis.

## REFERENCES

1. **Ames BN**, Cathcart R, Schwiers E, Hochstein P. Uric acid provides an antioxidant defense in humans against oxidant-and radical-caused aging and cancer: A hypothesis. *Proc. Natl. Acad. Sci. USA.* 1981; 78:6858-6862.
2. **Voruganti VS**, Nath SD, Cole SA *et al.* Genetics of variation in serum uric acid and cardiovascular risk factors in Mexican Americans. *J Clin Endocrinol Metab.* 2009; 94:632-638.
3. **Kolonel LN**, Yoshizawa C, Nomura A M, *et al.* Relationship of serum uric acid to cancer occurrence in a prospective male cohort. *Cancer Epidemiol Biomarkers Prev.*1994; 3:225-228.
4. **Levine W**, Dyer AK, Shekelle RB, Schoenhenger JA, Stamler J. Serum uric acid and 11.5 year mortality of middle aged women: Findings of

- the Chicago Heart Association Detection Project in Industry. *J. Clin. Epidemiol.* 1989; 42:257-267.
5. **Bengston C**, Lapidus L, Stendahl C, Waldenstrom J. Hyperuricemia and risk of cardiovascular disease and overall health. *Acta Med. Scand.* 188; 224:549-555.
  6. **Mazza A**, Pessina AC, Pavei A *et al.* Predictors of stroke mortality in elderly people from the general population. The cardiovascular study in elderly. *Eur J Epidemiol* 2001; 17: 1097–1104.
  7. **Bozkir A**, Simsek B, Grungor A, Torun M. Ascorbic acid and uric acid levels in lung cancer patients. *J Clin Pharm Ther.* 1999; 24:43-47.
  8. **Strasak AM**, Rapp K, Hilbe W, Oberaigner W. The role of serum uric acid as an antioxidant protecting against cancer: prospective study in more than 28,000 older Austrian women. *Annals of Oncology.* 2007; 18:1893-1897.
  9. **Sevanian A**, Davis KJ, Hochstein P. Serum urate as an antioxidant for ascorbic acid. *Am. J. Clin. Nutr.* 1991; 54:1129S-1134S.
  10. **Richter E**, Connelly RR, Moul JW. The role of pre-treatment serum albumin to predict pathologic stage and recurrence among radical prostatectomy cases. *Prostate Cancer Prostatic Dis.* 2000; 3:186-190.
  11. **Schachter M**. Uric acid and hypertension. *Curr Pharm Des.* 2005; 11:4139-4143.
  12. **Cameron JS**, Simmonds HA. Hereditary hyperuricemia. *Semin Nephrol* 2005; 25: 9–18.