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Research article

Relationship between Serum Albumin and Oral Epithelial Cancers in Patients Seen at a Nigerian Tertiary Hospital

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ABSTRACT: Oral cancer is the sixth most common cancer worldwide, and displays great geographic variation in its incidence worldwide. While tobacco and alcohol are the major aetiological factors, other important aetiological factors include diet, infections, and exposure to ultraviolet radiation. This study attempts to determine whether there is any association between serum albumin levels and the risk of oral epithelial cancer. Thirty-three oral cancer patients seen over an eighteen months period and thirty control patients were recruited from the Dental Clinic of the University College Hospital, Ibadan, Nigeria. Blood samples from these patients were analyzed for albumin using a spectrophotometer. The mean serum albumin level was significantly lower in the oral cancer patients than in the control group ($p < .001$). The risk of oral cancer was 32 times more in patients with low serum albumin levels ($< 3.5 \text{g/dl}$) compared to 1.09 and 4.05 for alcohol and tobacco respectively. On logistic regression analysis, low serum albumin independently predicted the occurrence of oral cancer. Further studies are required to substantiate if the low serum albumin is a cause or an effect of oral cancer.

Keyword: Oral cancer, Hypoalbuminemia, Oral pathology

INTRODUCTION

Oral cancer is defined as a malignant neoplasm involving the oral cavity, which is a region extending from the lips to the anterior pillars of the fauces (Zakrzewska 1999). Oral cancer is estimated to be the sixth most common cancer worldwide, and displays great geographic variation in its incidence worldwide, with highest prevalence rates of 35 to 50% occurring in India (Boyle *et al* 1992). Malignant oral neoplasms represent 2-4% of all cancers in the United States of America, 2% in Britain and 1% in Australia

(Krutchkoff *et al* 1990, Binnie 1976 and Sugeran *et al* 1999)

Tobacco and alcohol are regarded to be the most important aetiological factors in the development of oral cancer (Zakrzewska 1999, Krutchkoff *et al* 1990). Other important aetiological factors are the areca nut, viral and fungal infections, and exposure to ultraviolet radiation. Many studies have also implicated diet and nutrition in the aetiology of oral cancer. Franceschi *et al* (Winn 1995) suggested that inadequate nutrition enhances cancer risk and this was corroborated by a study in India which showed that subjects with oral cancer were less likely than control subjects to eat meat, eggs, milk and fish at least once per week (Notani *et al* 1976). Other studies, however, showed conflicting relationships between diet and oral cancer (Knekt *et al* 2000).

Since serum albumin may be a reflection of nutritional status and protein intake (Knekt *et al* 2000), it can be suggested that low serum albumin

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levels are associated with an increased risk of oral cancer (Ko *et al* 1986). Previous studies have shown varying results of serum albumin levels and risk of other types of cancer but very few studies have been done on oral cancer risk and serum albumin (Ko *et al* 1986, Glattre *et al* 2001 and Richter *et al* 2000). The aim of this study is to compare serum albumin levels in oral cancer patients and a control population in order to determine any association between serum albumin levels and the risk of oral cancer.

MATERIALS AND METHODS

Thirty-three patients with histologically confirmed oral epithelial cancer and thirty control patients who did not have oral cancer were recruited from outpatients attending the Dental Clinic of the University College Hospital, Ibadan in Nigeria during an eighteen months period (July 2005 to January 2007). 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 procedure and consented to participate in the study. Normal

patients under age 40 years and all those with known systemic diseases were excluded from the study.

Ten millilitres 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 albumin using the Bromocresol Green method with a DM520 spectrophotometer (Beckman, USA) (Varley 1976).

The data obtained was analyzed using the SPSS Statistical Package (SPSS, Version 11.0). Difference between the two groups was analyzed for statistical significance using the student t- test. Statistical significance was determined at $P < 0.05$.

RESULTS

The mean age of the oral cancer group was 53.7 years ($SD \pm 17.3$) while that for the control group was 54.8 years ($SD \pm 10.9$). There was no statistically 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).

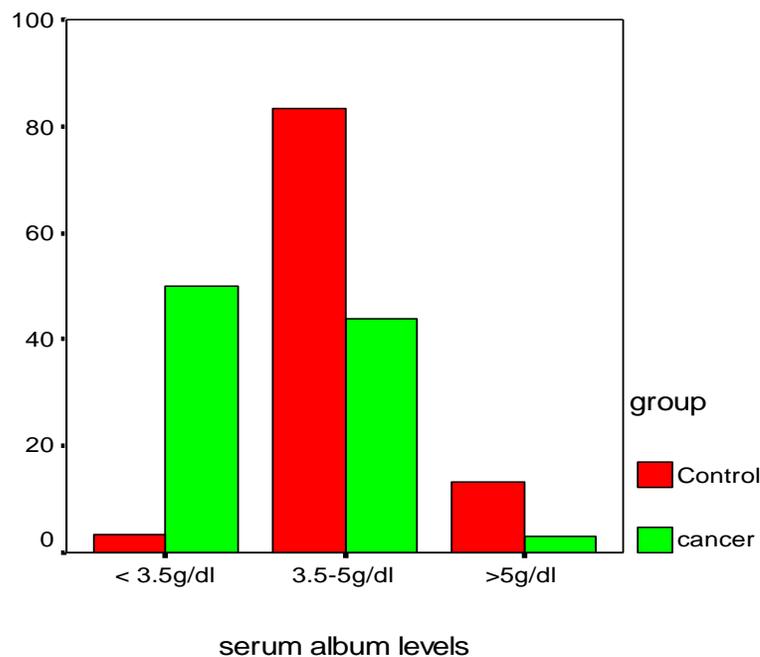


Fig 1
Comparison of serum albumin levels in oral cancer and normal patients

Table 1

Assessment of risk of oral cancer with low serum albumin, alcohol intake and tobacco intake

| | Oral cancers | | | | P | OR | 95.0% CI for OR |
|-------------------|--------------|------|-----------|------|--------|-------|-----------------|
| | Yes (n=32) | | No (n=30) | | | | |
| | N | % | n | % | | | |
| Low serum albumin | 17 | 53.1 | 1 | 3.3 | 0.000* | 32.87 | 3.98, 271.34 |
| 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 |

* *fishchers exact test used***Table 2:**

Logistic regression analysis of risk of oral cancer with low serum albumin, alcohol intake and tobacco intake

| | B | P | OR | 95.0% CI for OR |
|------------------------------|--------|-------|-------|-----------------|
| Low serum albumin | -3.957 | 0.000 | -3.96 | -6.21, -1.76 |
| Alcohol intake (>5g/day) | 0.418 | 0.668 | 0.42 | -1.49, 3.33 |
| Tobacco intake (>2pack/week) | -2.023 | 0.089 | -2.02 | -4.34, 0.31 |
| Constant | 1.250 | 0.005 | 1.25 | |

The mean serum albumin level was lower in the oral cancer patients with a value of 3.5g/dl (SD±0.7) while the control group had a higher mean serum albumin level of 4.5g/dl (SD ± 0.49). Student t test showed a statistically significant difference in the mean serum levels between the oral cancer group and control group (p=.000, f=1.13) (CI 0.19-0.76). Majority (83.3%) of control group had serum albumin levels within the normal range (3.5-5.0g/dl) while only 45.2% of the oral cancer patients had normal serum albumin levels. More oral cancer cases (51.6%) had serum levels of albumin below the lower limit of normal (<3.5g/dl), compared with only 3.3% of control patients who had below the lower limit of normal (fig 1).

The risk of oral cancer was 32 times more in patients with low serum albumin levels (<3.5g/dl) compared to 1.09 and 4.05 for alcohol and tobacco respectively (Table 1). More so, on logistic regression analysis, low serum albumin independently predicted the occurrence of oral cancer (Table 2).

DISCUSSION

The mean serum level of albumin for oral epithelial cancer in this study was statistically significantly lower than in controls. There is a

paucity of studies on the relationship between serum albumin and oral cancer. Daae *et al*, in a study from Norway observed that serum albumin levels in patients with cancer of the oral cavity and throat were lower than normal, which is in agreement with our findings (Daae *et al* 1997). However, studies attempting to correlate low serum albumin with cancer of other anatomical sites have yielded conflicting results (Glattre *et al* 2001 and Richter *et al* 2000).

Low serum albumin in patients with oral cancer may partly be due to the effect of cytokines such as interleukin-6 (IL6) and tumour necrosis factor (TNF). These inflammatory mediators are produced by tumour and host cells in malignancies. TNF and IL6 may act both by increasing the local transcapillary escape of albumin in the tumour bed and by decreasing the hepatic synthesis of albumin (Richter *et al* 2000).

It should be noted that albumin acts as an extracellular antioxidant, but unlike antioxidant vitamins that scavenge reactive oxygen radicals, albumin scavenges mainly carbon-centred free radicals (Soriani *et al* 1994). Low serum albumin may thus reduce the role of albumin in mopping up free radicals and thus increase the potential for toxic cellular injuries that could trigger the process of carcinogenesis.

In addition, low serum albumin may be an indication of malnutrition, which is known to be

associated with general immunosuppression and impaired salivary gland function and thus reduced oral mucosal immunity (Chojnowska 1996).

Malnutrition is also associated with a significant reduction in the number of helper CD4+ cells and depressed natural killer cell activity (Enwonwu 1995). This suggests a diminished capacity of the malnourished to mount effective tumour surveillance (Enwonwu 1995) and thus increased risk of developing cancers.

Although this study showed a statistically significant lower serum albumin in oral cancer patients and a markedly increased risk of oral cancer in patients with low serum albumin, there is still the dilemma of which event preceded the other. That is, does chronic hypoalbuminaemia precede oral cancer? On the other hand, does oral cancer predispose to hypoalbuminaemia? Further prospective cohort studies are desirable to help resolve this dilemma.

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