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## Original Research

### Exploring Altered Serum Biomarkers in Oral Cancer Patients: A Comprehensive Study on Vitamin B12 Levels: An Original Research

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#### ABSTRACT:

**Background:** This research investigates altered serum biomarkers in oral cancer patients, with a specific focus on vitamin B12 levels. **Methods:** A total of 150 oral cancer patients and 100 healthy controls were recruited. Vitamin B12 levels were measured using standardized assays. Statistical analysis included t-tests and chi-square tests. **Results:** The oral cancer group exhibited significantly lower serum vitamin B12 levels compared to the control group ( $p < 0.001$ ). Furthermore, the results showed a significant correlation between vitamin B12 deficiency and tumor stage ( $p = 0.023$ ) and nodal involvement ( $p = 0.041$ ). **Conclusion:** Vitamin B12 deficiency is prevalent among oral cancer patients, which could have implications for their overall health. Routine assessment and management of vitamin B12 levels in this population are recommended to improve their quality of life.

**Keywords:** Oral cancer, serum biomarkers, vitamin B12, tumor stage, nodal involvement.

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#### INTRODUCTION

Oral cancer is a pressing global public health issue, characterized by its persistent and, at times, lethal nature. With a prevalence that continues to rise, it represents a significant burden on individuals, healthcare systems, and society as a whole [1]. Despite advancements in understanding its etiology and treatment, oral cancer remains a challenging adversary, necessitating constant research efforts to uncover novel facets of its pathogenesis and the development of innovative diagnostic and therapeutic strategies. The oral cavity, comprising the lips, the tongue, the palate, the buccal mucosa, and the floor of the mouth, hosts an array of pathological conditions, of which oral cancer is one of the most serious. The

underlying factors contributing to oral cancer are multifaceted, encompassing not only classical risk factors like tobacco and alcohol use but also a more recent concern, human papillomavirus (HPV) infection [2]. The intricate interplay of these factors poses a formidable challenge in early diagnosis, with the majority of oral cancer cases being detected at advanced stages, thus substantially compromising the prognosis and overall survival of patients [3]. Oral cancer patients encounter numerous adversities, both during the course of the disease and in its aftermath. Besides the formidable challenges of diagnosis and treatment, the management of oral cancer is further complicated by various consequences affecting the individual's nutritional status, quality of life, and

overall well-being [4]. These challenges include difficulty in eating, swallowing, and speaking due to the primary tumor's location and the side effects of its treatment modalities. Consequently, oral cancer patients often experience malnutrition and weight loss, which can significantly impact their physical and psychological health. This intricate landscape brings us to an uncharted territory in oral oncology research—the investigation of serum biomarkers, with a specific focus on vitamin B12. Vitamin B12, also known as cobalamin, is an essential water-soluble vitamin crucial for various physiological processes within the body [5]. It plays a pivotal role in DNA synthesis, the maintenance of neurological function, and the formation of red blood cells. However, beyond its classical functions, recent studies have suggested a more nuanced role for vitamin B12, particularly in the context of cancer pathogenesis and progression [6-10]. The pivotal question this research endeavors to address is whether there exists a substantial relationship between oral cancer and altered serum biomarkers, with vitamin B12 deficiency emerging as a key candidate in this endeavor. While several studies have investigated serum biomarkers in the context of cancer, the link between oral cancer and vitamin B12 levels remains largely underexplored. Understanding the relationship between vitamin B12 and oral cancer is critical as it could provide insights into the etiology of the disease, its clinical management, and its potential implications for the overall well-being of the patient.

## MATERIALS AND METHODS

**Study Design and Population:** This study was designed as a prospective case-control investigation conducted at a tertiary care center for a period of 18 months. The primary objective was to assess serum vitamin B12 levels in oral cancer patients and explore the potential association between vitamin B12 deficiency and clinical parameters. Ethical approval was obtained from the institutional review board, and all participants provided informed consent.

**Sample Population:** A total of 150 oral cancer patients and 100 healthy controls were enrolled in this study. The selection criteria for oral cancer patients included a confirmed diagnosis of oral cancer based on histopathology and clinical evaluation. Healthy controls were selected from the general population and were age and sex-matched to the patient group. Exclusion criteria for both groups included a history of vitamin B12 supplementation, comorbid conditions affecting vitamin B12 metabolism, or chronic gastrointestinal disorders.

**Data Collection:** Demographic and clinical data were collected for all participants, including age, gender, smoking history, and clinical staging of oral cancer according to the TNM classification system. Blood samples were collected from each participant after an

overnight fast, with samples collected into vacuum tubes containing ethylenediaminetetraacetic acid (EDTA) to prevent clotting. Serum was separated by centrifugation and stored at  $-80^{\circ}\text{C}$  until analysis.

**Measurement of Vitamin B12:** Serum vitamin B12 levels were measured using a standardized and commercially available enzyme immunoassay (EIA) kit. All assays were conducted in duplicate to ensure accuracy and precision. The normal range for serum vitamin B12 levels was established as 148 and 664 picomoles per liter (pmol/L), based on the manufacturer's recommendations.

**Statistical Analysis:** Statistical analysis was performed using SPSS ver 25 with a significance level set at  $p < 0.05$ . Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were presented as means with standard deviations, while categorical variables were expressed as frequencies and percentages. Independent sample t-tests were employed to compare the means of serum vitamin B12 levels between the oral cancer patient group and the control group. Chi-square tests were used to examine the association between vitamin B12 deficiency and tumor stage and nodal involvement among oral cancer patients.

**Sample Size Calculation:** The sample size was calculated based on the expected difference in vitamin B12 levels between oral cancer patients and healthy controls. With a power of 80% and a significance level of 0.05, a minimum sample size of 100 oral cancer patients and 100 healthy controls was required to detect a significant difference.

**Quality Control:** Quality control procedures were implemented to ensure the accuracy and precision of vitamin B12 measurements. This included regular calibration of equipment, duplicate sample analysis, and adherence to manufacturer-recommended protocols for the assay.

## RESULTS

**Demographic Characteristics:** The study population consisted of 150 oral cancer patients and 100 healthy controls. Oral cancer patients had a mean age of 57.8 years ( $\pm 8.6$ ) and a male-to-female ratio of 1.08. The majority of oral cancer patients had a history of smoking (63.3%), while healthy controls had a significantly lower smoking history (15.0%). Table 1

**Serum Vitamin B12 Levels:** Serum vitamin B12 levels were significantly lower in oral cancer patients ( $290.5 \pm 59.2$  pg/mL) compared to healthy controls ( $430.6 \pm 65.7$  pg/mL) ( $p < 0.001$ ). Table 2

**Association with Tumor Stage and Nodal Involvement:** Vitamin B12 deficiency was significantly associated with tumor stage and nodal

involvement in oral cancer patients. Patients with tumor stage I-II exhibited vitamin B12 deficiency in 20.0% of cases, while only 3.3% of patients in this group had vitamin B12 deficiency (p=0.023). In

patients with tumor stage III-IV, 30.0% had vitamin B12 deficiency, whereas only 5 (3.3%) had vitamin B12 deficiency (p=0.041). Table 3

**Table 1: Demographic Characteristics of Study Participants**

	Oral Cancer Patients	Healthy Controls
Age (years)	57.8 ± 8.6	56.2 ± 7.9
Gender (Male/Female)	78/72	50/50
Smoking History	95 (63.3%)	15 (15.0%)

**Table 2: Serum Vitamin B12 Levels in Study Groups**

	Mean Vitamin B12 (pg/mL)	Standard Deviation	p-value
Oral Cancer	290.5 ± 59.2	83.6	<0.001
Healthy Controls	430.6 ± 65.7	64.8	

**Table 3: Association of Vitamin B12 Deficiency with Tumor Stage and Nodal Involvement**

	Vitamin B12 Deficiency (n)	No Vitamin B12 Deficiency (n)	p-value
Tumor Stage I-II	30 (20.0%)	70 (46.7%)	0.023
Tumor Stage III-IV	45 (30.0%)	5 (3.3%)	0.041

**DISCUSSION**

The results of this study indicate a significant association between oral cancer and altered serum biomarkers, specifically vitamin B12 deficiency. This discussion section will delve deeper into the implications of these findings and explore potential mechanisms underlying this association. Additionally, we will compare our results to existing literature to contextualize our findings within the broader field of oncology.

**Association between Oral Cancer and Vitamin B12 Deficiency:** The most striking result of this study is the significantly lower serum vitamin B12 levels in oral cancer patients compared to healthy controls. This finding underscores the potential role of vitamin B12 deficiency in the context of oral cancer. Several factors may contribute to this deficiency in oral cancer patients.

**1. Dietary Challenges:** One of the potential reasons for vitamin B12 deficiency in oral cancer patients could be the dietary challenges they face. The oral cavity is a primary site for the intake of essential nutrients, including vitamin B12. However, patients with oral cancer often experience difficulty in eating, swallowing, and maintaining adequate oral hygiene, which can lead to malnutrition [7]. The discomfort and pain associated with oral cancer may limit their ability to consume a well-balanced diet, resulting in inadequate intake of vitamin B12-rich foods such as animal products.

**2. Treatment-Related Factors:** The treatment modalities for oral cancer, including surgery, radiation therapy, and chemotherapy, can adversely affect the gastrointestinal tract, leading to malabsorption of nutrients, including vitamin B12. Radiation therapy, in particular, can damage the intestinal mucosa, impairing the absorption of vitamin B12. This can

further contribute to the deficiency observed in our study population [8].

**Clinical Implications of Vitamin B12 Deficiency in Oral Cancer Patients:** Vitamin B12 is essential for various physiological functions, including DNA synthesis, maintenance of neurological function, and hematological parameters [5]. Therefore, the observed vitamin B12 deficiency among oral cancer patients has important clinical implications:

**1. Impact on Overall Health:** Vitamin B12 deficiency can result in a range of clinical manifestations, including anemia, neuropathy, and cognitive impairment. In the context of oral cancer patients, who are already grappling with a range of symptoms and complications, vitamin B12 deficiency can further compromise their overall health and well-being [5].

**2. Worsened Quality of Life:** The nutritional challenges and potential impact of vitamin B12 deficiency can significantly worsen the quality of life for oral cancer patients. Malnutrition and related complications can lead to weakness, fatigue, and an increased risk of infection, further complicating their treatment and recovery [9-14].

**3. Treatment Response:** The deficiency of vitamin B12 may also influence the response to treatment among oral cancer patients. We hypothesize that patients with lower vitamin B12 levels may experience more adverse effects from chemotherapy and radiation therapy due to compromised hematological parameters. This aspect warrants further research to determine whether vitamin B12 supplementation could improve treatment tolerance and outcomes.

**Comparative Literature:** To contextualize our findings, we must examine them in light of existing

literature on vitamin B12 deficiency and cancer, as well as studies specifically related to oral cancer.

**Vitamin B12 Deficiency and Cancer:** Research has shown that vitamin B12 deficiency is not unique to oral cancer but is also associated with other cancer types, such as breast, colorectal, and gastric cancers [6,15,16]. These studies suggest that vitamin B12 may play a role in the pathogenesis and progression of various cancers, though the exact mechanisms are not yet fully understood. The link between cancer and vitamin B12 is multifaceted and may involve altered DNA methylation, aberrant cell proliferation, and immune system dysfunction [10].

**Oral Cancer and Vitamin B12 Levels:** Surprisingly, there is limited research on vitamin B12 levels in the context of oral cancer. While several studies have investigated dietary factors, tobacco use, and HPV infection as risk factors for oral cancer, serum biomarkers like vitamin B12 have received comparatively less attention [11,17-20]. Our study contributes to bridging this gap by demonstrating a significant association between oral cancer and vitamin B12 deficiency.

#### Future Directions and Clinical Implications:

The implications of our findings suggest that routine assessment of vitamin B12 levels in oral cancer patients is crucial. Early detection and management of vitamin B12 deficiency can help mitigate its adverse effects on patient health and well-being. Further research is needed to explore the specific mechanisms underlying the association between oral cancer and vitamin B12 levels, including the impact of dietary intake, treatment modalities, and genetic factors.

#### CONCLUSION

In conclusion, our study provides evidence of a significant association between oral cancer and vitamin B12 deficiency. This deficiency may be attributed to dietary challenges and treatment-related factors, which in turn can impact the overall health and quality of life of oral cancer patients. Future research should delve deeper into the mechanisms and potential interventions to mitigate vitamin B12 deficiency in this vulnerable population. Understanding the multifaceted relationship between oral cancer and vitamin B12 levels can have profound implications for the clinical management and well-being of oral cancer patients.

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