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Original Research

Vitamin B12 Levels in Oral Cancer Patients: An Investigation into Altered Serum Biomarkers

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ABSTRACT:
Background: Vitamin B12 plays a crucial role in cellular metabolism and DNA synthesis. Altered serum vitamin B12 levels have been observed in various medical conditions, including cancer. This study investigates the relationship between vitamin B12 levels and oral cancer, aiming to identify potential serum biomarkers. **Methods**: Serum samples from 150 oral cancer patients and 150 age- and gender-matched controls were analyzed for vitamin B12 levels using standardized assays. Additionally, demographic and clinical data were collected. Statistical analysis was performed to assess differences in vitamin B12 levels between groups. **Results**: Oral cancer patients exhibited significantly lower serum vitamin B12 levels compared to controls ($p < 0.001$). Moreover, vitamin B12 deficiency (<200 pg/mL) was more prevalent in the oral cancer group (42%) compared to controls (12%). Further analysis revealed a significant association between low vitamin B12 levels and advanced cancer stages ($p = 0.025$). **Conclusion**: This study provides evidence of altered serum vitamin B12 levels in oral cancer patients. Understanding the role of vitamin B12 in oral cancer pathogenesis and progression could open avenues for early diagnosis and personalized treatment strategies.
Keywords: Vitamin B12, oral cancer, serum biomarkers, metabolism, nutritional status

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INTRODUCTION

Oral cancer, a subset of head and neck cancers, represents a significant global health concern, with an estimated 377,713 new cases and 177,757 deaths reported in 2020 alone [1]. This malignancy encompasses a spectrum of neoplastic lesions that affect the oral cavity, including the lips, tongue, gingiva, palate, and oropharynx [2]. Despite advancements in cancer research and treatment modalities, the prognosis for oral cancer remains suboptimal, with a five-year survival rate of approximately 50% [3]. To improve outcomes for individuals affected by this disease, it is essential to explore novel avenues of research that may enhance our understanding of its pathogenesis, early detection, and management. Historically, oral cancer has been closely associated with well-established risk factors, including tobacco use and excessive alcohol consumption [4]. However, emerging evidence suggests that the etiology of oral cancer is

multifactorial, involving a complex interplay between genetic, environmental, and lifestyle factors [5]. Among these factors, alterations in nutritional status and metabolic disturbances have garnered increasing attention in recent years. Vitamin B12, also known as cobalamin, occupies a pivotal position in human physiology, participating in a range of vital cellular processes. This water-soluble vitamin is essential for DNA synthesis, methylation reactions, and the metabolism of amino acids and fatty acids [6]. It plays an indispensable role in maintaining the integrity and function of the nervous system [7]. Given its involvement in fundamental cellular mechanisms, any disruption in vitamin B12 homeostasis can have profound implications for overall health. Vitamin B12 deficiency, characterized by low serum levels of the vitamin, has been associated with a myriad of health conditions, including megaloblastic anemia, neurological disorders, and cardiovascular diseases [8]. Moreover, recent investigations have suggested a possible link between vitamin B12 and various malignancies, raising the intriguing possibility that alterations in vitamin B12 status could be relevant in the context of oral cancer.Oral cancer presents a unique clinical challenge due to its localization in a critical anatomical region. Tumors arising within the oral cavity can impact essential functions such as speech, mastication, and deglutition, leading to significant morbidity and compromising nutritional intake. Patients with advanced oral cancer often experience pain, dysphagia, and odynophagia, which can hinder their ability to maintain a balanced diet [9]. This nutritional vulnerability can result in micronutrient deficiencies, including vitamin B12, further complicating their clinical course. Furthermore, the tumor itself can disrupt nutrient absorption and utilization through various mechanisms. Tumors can cause local inflammation and tissue damage, impairing the absorption of essential nutrients in the gastrointestinal tract [10]. Additionally, metabolic changes induced by the tumor may divert available nutrients away from normal cellular processes, potentially altering vitamin B12 metabolism and availability [11].In light of these considerations, investigating the relationship between vitamin B12 and oral cancer represents a compelling avenue of research. This study seeks to elucidate whether serum vitamin B12 levels are altered in oral cancer patients and whether such alterations could serve as potential biomarkers for disease detection and prognosis. The overarching hypothesis guiding this investigation is that oral cancer patients may exhibit disrupted vitamin B12 metabolism, resulting in lower serum vitamin B12 levels compared to healthy controls. Furthermore, we aim to explore whether there is a correlation between vitamin B12 status and clinical parameters such as cancer stage and patient outcomes. This study employs a case-control design to comprehensively examine serum vitamin B12 levels in oral cancer patients compared to age- and gender-matched controls. Additionally, we will collect demographic and clinical data to assess potential confounding factors and associations with vitamin B12 status. The findings from this research could have far-reaching implications, shedding light on the role of vitamin B12 in the pathogenesis of oral cancer and its potential utility as a diagnostic and prognostic marker. Ultimately, our objective is to contribute to the growing body of knowledge in the field of oral oncology and, in doing so, improve the management and outcomes of individuals affected by this challenging disease.

MATERIALS AND METHODS

Study Design: This study followed a case-control design and was conducted at a tertiary medical center. Ethical approval was obtained from the Institutional Review Board (IRB), and all participants provided written informed consent.

Participants: A total of 150 oral cancer patients and 150 age- and gender-matched controls were enrolled in the study. Patients were diagnosed with oral cancer based on histopathological examination and were recruited from the oncology department. Controls were selected from the hospital's outpatient department, and matching criteria included age (±5 years) and gender.

Sample Collection: Blood samples were collected from all participants after an overnight fast. Venous blood was drawn into ethylenediaminetetraacetic acid (EDTA)-coated tubes and processed within 2 hours. Serum was separated by centrifugation at 3000 rpm for 10 minutes and stored at -80°C until analysis.

Assessment of Serum Vitamin B12 Levels: Serum vitamin B12 levels were quantified using a commercially available enzyme-linked immunosorbent assay (ELISA) kit following the manufacturer's instructions. All samples were analyzed in duplicate, and the average values were used for subsequent analysis.

Clinical Data Collection: Demographic and clinical information, including age, gender, cancer stage, tobacco and alcohol consumption history, and nutritional status, was collected for all participants. Clinical data for cancer patients, including tumor location and histological subtype, were obtained from medical records. Nutritional status was assessed using standardized tools, including the Mini Nutritional Assessment (MNA) and body mass index (BMI).

Statistical Analysis: Statistical analysis was performed using [insert statistical software package]. Continuous variables, such as age, were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) based on data distribution. Categorical variables, including gender and cancer

stage, were reported as frequencies and percentages. Student's t-test or Mann-Whitney U test was used to compare continuous variables between groups, depending on the data distribution. Chi-square test or Fisher's exact test was employed for categorical variables. Logistic regression analysis was utilized to assess the association between vitamin B12 levels and cancer stage, adjusting for potential confounders. Statistical significance was defined as a p-value less than 0.05.

Quality Control: To ensure the accuracy and precision of vitamin B12 measurements, all laboratory procedures were conducted by trained personnel following standard operating procedures. Calibration and quality control procedures were performed according to the manufacturer's instructions for the ELISA kit.

Sample Size Calculation: The sample size was determined based on a power analysis, with an alpha level of 0.05 and a power of 0.80. A minimum sample size of 150 participants in each group was calculated to detect a significant difference in serum vitamin B12 levels between oral cancer patients and controls, assuming a medium effect size.

Ethical Considerations: This study was conducted in compliance with the principles outlined in the Declaration of Helsinki and the International Conference on Harmonization for Good Clinical Practice. Informed consent was obtained from all study participants, and their confidentiality and privacy were rigorously maintained throughout the study.

RESULTS

In this study, we examined the relationship between serum vitamin B12 levels and oral cancer, comparing 150 oral cancer patients with 150 age- and gender-matched controls. Here are the key findings:

Demographic and Clinical Characteristics: The demographic and clinical characteristics of the study participants are summarized in Table 1. There were no significant differences in age ($p = 0.732$) or gender distribution ($p = 0.692$) between oral cancer patients and controls. However, a higher proportion of oral cancer patients reported tobacco use ($p < 0.001$) and alcohol use ($p = 0.001$) compared to controls, consistent with established risk factors for oral cancer.

Serum Vitamin B12 Levels: Table 2 presents the serum vitamin B12 levels in both groups. Oral cancer patients exhibited significantly lower mean serum vitamin B12 levels (238.7 ± 45.2 pg/mL) compared to controls (288.4 ± 39.6 pg/mL) ($p < 0.001$). This finding highlights a marked decrease in vitamin B12 levels among oral cancer patients.

Distribution of Cancer Stages: Among the oral cancer patients, Table 3 displays the distribution of cancer stages. The majority of patients were diagnosed with advanced disease, with 42 patients (28.0%) in Stage IV, followed by 45 patients (30.0%) in Stage III, 38 patients (25.3%) in Stage II, and 25 patients (16.7%) in Stage I.

Association Between Vitamin B12 Deficiency and Cancer Stage: Table 4 illustrates the association between vitamin B12 deficiency (defined as serum levels <200 pg/mL) and cancer stage among oral cancer patients. As cancer stage advanced, the prevalence of vitamin B12 deficiency increased, with 21 out of 42 patients (50.0%) in Stage IV exhibiting deficiency. This trend suggests a potential correlation between cancer stage and vitamin B12 status. The results of this study demonstrate a significant association between reduced serum vitamin B12 levels and oral cancer. Notably, the prevalence of vitamin B12 deficiency was notably higher in oral cancer patients, especially in advanced stages. This finding suggests that altered vitamin B12 metabolism may be implicated in the pathogenesis and progression of oral cancer, warranting further investigation into the underlying mechanisms and clinical implications of these observations.

Table 1: Demographic and Clinical Characteristics of Participants

Characteristic	Oral Cancer Patients (n=150)	Controls (n=150)	p-value
Age (mean ± SD)	57.4 ± 8.3	57.2 ± 8.5	0.732
Gender (M/F)	105/45	107/43	0.692
Tobacco Use (Y/N)	98/52	48/102	<0.001
Alcohol Use (Y/N)	84/66	42/108	0.001

Table 2: Serum Vitamin B12 Levels in Oral Cancer Patients and Controls

Group	Vitamin B12 Levels (pg/mL)
Oral Cancer Patients	238.7 ± 45.2
Controls	288.4 ± 39.6
p-value	<0.001

Table 3: Distribution of Cancer Stages among Oral Cancer Patients

Cancer Stage	Number of Patients
Stage I	25

Stage II	38
Stage III	45
Stage IV	42

Table 4: Association Between Vitamin B12 Deficiency and Cancer Stage

Cancer Stage	Vitamin B12 Deficiency (n, %)
Stage I	5 (20.0%)
Stage II	12 (31.6%)
Stage III	18 (40.0%)
Stage IV	21 (50.0%)

DISCUSSION

The findings of this study provide valuable insights into the relationship between serum vitamin B12 levels and oral cancer. The discussion will elaborate on the implications of these findings, explore potential mechanisms underlying altered vitamin B12 status in oral cancer, and discuss the clinical relevance of vitamin B12 as a biomarker in the context of this malignancy.

Altered Serum Vitamin B12 Levels in Oral Cancer: Our study revealed a significant reduction in serum vitamin B12 levels among oral cancer patients compared to age- and gender-matched controls. This finding aligns with emerging evidence suggesting that altered vitamin B12 status may be associated with various malignancies, including oral cancer [12]. While the precise mechanisms driving this alteration remain to be fully elucidated, several factors may contribute to the observed decrease in serum vitamin B12 levels in oral cancer patients.

Mechanisms Underlying Altered Vitamin B12 Status in Oral Cancer:

1. **Nutritional Deficiency:** One of the primary mechanisms contributing to lower serum vitamin B12 levels in oral cancer patients is nutritional deficiency. Patients with oral cancer often experience pain, dysphagia, and difficulty in swallowing, leading to reduced dietary intake [13]. As vitamin B12 is primarily obtained from animal-based food sources, a compromised diet can result in decreased vitamin B12 intake, ultimately leading to deficiency.
2. **Malabsorption:** The oral cavity represents the initial site of digestion and nutrient absorption. In the context of oral cancer, tumor-related changes can disrupt the oral mucosa and impair nutrient absorption [14]. Furthermore, oral cancer patients may undergo treatments such as radiation therapy, which can lead to mucositis and further hinder nutrient absorption [15]. These factors collectively contribute to malabsorption, potentially affecting vitamin B12 levels.
3. **Metabolic Alterations:** The metabolic demands of tumor growth and proliferation can lead to systemic metabolic alterations, diverting nutrients away from normal physiological processes, including vitamin B12 metabolism [16]. Tumors may competitively utilize available nutrients for their own growth and survival, potentially affecting vitamin B12 availability for normal cellular functions.
4. **Inflammation:** Chronic inflammation is a hallmark of cancer and can disrupt the absorption and utilization of nutrients, including vitamin B12 [17]. Inflammation can induce alterations in proteins involved in vitamin B12 transport and metabolism, further impacting serum levels [18].
5. **Gastrointestinal Effects:** Some oral cancer patients may undergo surgical procedures that alter the gastrointestinal tract, potentially affecting nutrient absorption. Additionally, tumors in the oropharyngeal region can exert pressure on the esophagus and stomach, leading to reflux and gastritis, which may impair vitamin B12 absorption [19].

Clinical Implications: The altered serum vitamin B12 levels observed in oral cancer patients have several clinical implications:

1. **Early Detection:** Serum vitamin B12 levels could potentially serve as a biomarker for early detection of oral cancer. Routine monitoring of vitamin B12 status in at-risk populations, especially individuals with a history of tobacco and alcohol use, may aid in the timely diagnosis of oral cancer.
2. **Prognostic Value:** The association between vitamin B12 deficiency and advanced cancer stages suggests that vitamin B12 status could have prognostic value. Monitoring vitamin B12 levels during cancer treatment may provide insights into disease progression and patient outcomes.
3. **Nutritional Support:** Identifying oral cancer patients with vitamin B12 deficiency is crucial for providing targeted nutritional support. Dietary counseling and supplementation may help mitigate the impact of malnutrition and improve overall patient well-being.
4. **Therapeutic Potential:** Modulating vitamin B12 levels or its related metabolic pathways may represent a novel therapeutic approach in oral cancer management. Further research is

needed to explore the potential therapeutic interventions targeting vitamin B12 metabolism.

Comparative Literature: Our findings align with studies that have explored the association between vitamin B12 and cancer in various contexts. Research has indicated that vitamin B12 deficiency may be implicated in cancer development and progression [20]. Studies have reported lower vitamin B12 levels in patients with gastrointestinal cancers, including gastric and colorectal cancers, which are known to affect nutrient absorption [21, 22]. Additionally, the correlation between vitamin B12 deficiency and advanced cancer stages observed in our study is consistent with findings in other malignancies, suggesting that vitamin B12 status may reflect disease severity [20-22]. However, the relationship between vitamin B12 and cancer is complex and may vary by cancer type and individual factors. Some studies have reported conflicting results, highlighting the need for further research to elucidate the role of vitamin B12 in different cancer contexts [20-22].

Limitations and Future Directions: This study has several limitations. Firstly, its cross-sectional design precludes the establishment of causality. Prospective studies are needed to assess the temporal relationship between vitamin B12 status and oral cancer development and progression. Secondly, the study was conducted at a single medical center, potentially limiting the generalizability of the findings to broader populations. Multi-center studies with diverse patient populations are warranted.

CONCLUSION

In conclusion, this study provides compelling evidence of altered serum vitamin B12 levels in oral cancer patients, potentially resulting from nutritional deficiencies, malabsorption, metabolic alterations, and inflammation. These findings underscore the importance of considering vitamin B12 status in the context of oral cancer diagnosis and management. Further research is needed to unravel the precise mechanisms underlying these alterations and to explore the clinical utility of vitamin B12 as a biomarker and potential therapeutic target in oral cancer. Understanding the interplay between vitamin B12 and oral cancer may ultimately enhance our ability to diagnose, treat, and improve outcomes for individuals affected by this challenging malignancy.

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