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Risk of Oral Tongue Cancer Among Immunocompromised Transplant Recipients and Human Immunodeficiency Virus-Infected Individuals in the United States.
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Summary:

A retrospective cohort study evaluating the Risk of Oral Tongue Cancer Among Immunocompromised Transplant Recipients and Human Immunodeficiency Virus-Infected Individuals in the United States was conducted by Joseph E. Tota, Eric A Engles, Margaret M Madeleine, et al. This study was published in the *American Cancer Society Journals* in April 2018 ([https://pubmed.ncbi.nlm.nih.gov/29645080/](https://pubmed.ncbi.nlm.nih.gov/29645080/)). DOI:10.1002/cncr.31359

This cohort study uses the information from the US Transplant Center Match and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) to assess the risk of oral tongue squamous cell carcinoma (SCC) along with four other head and neck cancers (oropharyngeal SCCs, oral cavity/pharynx cancer, other oral cavity SCCs) among two immunosuppressed groups i.e. HIV infected individuals and transplantation recipients. The results derived from the statistical analysis suggest the moderate, elevated risk of all SCCs among transplantation recipients. The risk of oral tongue SCC was observed to be higher among HIV-infected individuals. A high prevalence of oral tongue SCC was found among the HIV-infected men who have sex with other men (MSM). The authors concluded that the viral etiology has no association with the moderate risk of oral tongue SCCs observed among immunosuppressed individuals.

Article information:

A retrospective cohort study conducted by Joseph E. Tota, Eric A Engles, Margaret M Madeleine, et al. investigates the “Risk of Oral Tongue Cancer Among Immunocompromised Transplant Recipients and Human Immunodeficiency Virus-Infected Individuals in the United States”. This study was published in the *American Cancer Society Journals* in April 2018 ([https://pubmed.ncbi.nlm.nih.gov/29645080/](https://pubmed.ncbi.nlm.nih.gov/29645080/)). DOI:10.1002/cncr.31359 The research reported in this article was partly supported by the Intramural Research Program of the National Cancer Institute. In addition, support was provided by the HIV/AIDS and cancer registries of the following states, California, Colorado, Connecticut, Illinois, Iowa, Maryland, Massachusetts, New Jersey, New York, Texas, Utah, Washington. Furthermore, this research was supported by the individuals Scientific Registry of Transplant Recipients (SRTR) and the Health Resources and Services Administration.

Study analysis:
Type of study:

A retrospective, cohort study was conducted in 2018 using the data from the two prospective studies i.e. Transplant Cancer Match (TCM) study (1987-2012) and HIV/AIDS Cancer Match (HACM) Study (1996-2012).

Study Purpose:

To examine the role of an infectious agent (virus) in increasing the risk of oral tongue squamous cell carcinoma (SCC) among immunosuppressed individuals. The potential cause of increment in the occurrence of oral tongue cancer among young white individuals in the United States is unascertained. However, certain epidemiological studies have been conducted that investigated the impact of viruses leading to the development of cancers in patients infected by the Human immunodeficiency virus (HIV/AIDS) and immunocompromised transplant recipients. Moreover, the inducement of human papillomavirus (HPV) infection to cause oropharyngeal cancer and the association of Merkel cell carcinoma with acquired immunodeficiency syndrome (AIDS) stimulated the further investigation of the impact of viruses in immunosuppressed patients.

Experimental design:

For this study, the population-based registry linkage information was obtained from the US Scientific Registry of Transplant recipients (SRTR) or state HIV registries. The authors have utilized the data from two Cancer Match Studies for research purposes i.e. Human Immunodeficiency virus/acquired immunodeficiency syndrome HACM study, and the US Transplant Cancer Match TCM study. The data restricted to investigating the characteristics of 242,022 solid-organ transplantation recipients from the TCM study and 465,429 HIV-infected individuals from the HACM study was analyzed to find out whether the exposure to the risk factor (the infectious agent) has a significant impact on the development of oral tongue cancer. These two immunosuppressed populations were then compared with the general population to assess the risk of oral tongue cancer, HPV-related oropharyngeal cancer, EBV-related oral cavity/pharynx cancer, and tobacco/alcohol-related squamous cell carcinoma (SCC). Both populations (HIV-infected individuals and transplantation recipients) were separately analyzed in correspondence to the general population to recognize the risk of four potential cancer sites mentioned above. For the TCM study conducted by the authors, data from only 1 out of 16 US state/metropolitan area cancer registries was utilized. According to the authors, the follow-up for
this study began after transplantation, or the start of “cancer registry coverage,” and ended at the
time of death, or the last date of “cancer registry coverage for the patients. For the available data,
the patient's characteristics and need for organ transplantation were analyzed. Furthermore, for
the HACM study, the authors obtained the data of the patients who underwent antiretroviral
therapy in the year 1996-2012. The following data was restricted to the HIV-infected patients in
8 US states and Puerto Rico. For this study, follow-up began at the time of diagnosis of
HIV/AIDS, or the start of “cancer registry coverage,” and ended at the time of death, or the end
of “cancer registry coverage.” For the HACM study, the available data were analyzed with
respect to CD4 counts 12 months preceding cancer. For both studies, ethical approval was
obtained from the National Cancer Institute and from the Institutional Review Boards (IRB) for
all of the registries that were a part of this research. For comparative research purposes, the data
was analyzed to assess the proportion that leads to the development of oral tongue SCC,
oropharyngeal SCC, oral cavity/pharynx non-Hodgkin lymphoma (NHL), and oral cavity SCC
(related to tobacco/alcohol). The data obtained from each cancer registry participating in this
research were arranged according to age, sex, race/ethnicity, and year (when data was collected).
The available data were statistically analyzed by calculating the cancer rate in all the registries to
the particular time or the particular individual (HIV infected group or transplantation recipients)
at risk. The quantitative investigation of both the studies i.e. HACM and TCM were conducted
and incidence rate ratios (IRRs) were accessed. For this study, the probability level (P Values)
of <0.05 was set to be acceptable. Moreover, the quantitative assessment of the risk of all four
cancer sites i.e. oral tongue SCC, oropharyngeal SCC, oral cavity/pharynx (NHL), and oral
 cavity SCC (related to tobacco/alcohol) among the immunosuppressed populations (HIV-
infected group and transplantation recipients) with respect to the general population was
accomplished and standardized incidence ratios (SIR) were calculated. For this study, the
confidence intervals (CIs) were set at 95% by the researchers.

Results:

According to available data, the solid-organ transplantation recipients (242,022) were
mostly white men (61%). 53% of those men were less than 50 years of age at the time of
transplantation. 82% of the transplant surgeries were performed after 1996 and 58% of them
were kidney transplants. Furthermore, for the HACM study, HIV-infected individuals (465,429)
were mostly men (72%) out of which 52% were black men, aged less than 50 years. The follow-
up for this study entry started between 2001-2005. Most importantly, in the HACM study, 33% of the HIV prevalence was found among men who have sex with men (MSM). Among TCM study participants, researchers discovered the occurrence of 36 oral tongue SCCs, 203 oropharyngeal SCCs, 86 oral cavity SCCs, and 48 oral cavity/pharynx NHLs. Notably, the risk of all 4 cancer sites was found to be higher among participants who qualified for liver transplant surgery due to alcoholic cirrhosis. According to the authors, factors like sex and race have no influence over the risk of oral tongue SCCs among organ transplant recipients. The only factor that leads to the higher risk of oral tongue SCCs among this group was age and the post-transplant time. However, for the other three head and neck cancers i.e, the higher risk of oral cavity SCCs, oral cavity/pharynx SCCs, and oropharyngeal SCCs is due to the influence of gender and race. A higher incidence of these three head and neck cancers was reported among white men. When the data of TCM were compared with the general population of the US, researchers found a significantly higher rate of cancers in transplantation recipients. The standardized incidence ratio (SIR) was comparatively higher for oral cavity/pharynx NHL cancers i.e. 8.2; 95% CI, 6.0-10.8.

The data available under observation for the HACM study revealed the occurrence of 70 oral tongue SCCs, 117 oral cavity SCCs, 144 oral cavity/pharynx NHLs, and 311 oropharyngeal SCCs. Similar to the higher incidence of oral cavity/pharynx in the TCM study, results for the HACM study also exhibited a higher prevalence of oral cavity/pharynx NHLs among HIV-infected individuals. However, a higher proportion of oral tongue SCCs risk was significant as compared to oropharyngeal SCCs in the HIV-infected individuals. Although, one-half of the oral tongue SCCs were detected in the “MSM HIV risk group” but resulted in lesser SIR, while other heads and neck cancers were detected in a lesser proportion but lead to higher SIR. Moreover, researchers reported the CD4 (cells per cubic millimeter) count for all head and neck cancers as 350 cells/mm^3 except for the oral cavity/pharynx NHLs which was 150 cells/mm^3. The risk of oral tongue cancer SCC, oropharyngeal SCC, oral cavity/pharynx NHL was reported to be higher among white men. Except for oral cavity/pharynx NHL, the risk of the remaining three head and neck cancers was reported to climb as age increases. Lastly, the onset of AIDS and progression of the disease are important factors leading to an increased risk of oral tongue SCCs, oral cavity SCCs, and oropharyngeal SCCs. Since the P-value of this data analysis is <0.05, the significance level set by researchers, it can be concluded that the results are statistically significant.
Conclusion:

The authors of this study assessed the modest elevation of oral tongue SCCs, other oral cavity SCCs, and oropharyngeal SCCs in comparison to the US general population. However, the risk of oral cavity/pharynx SCCs was observed to be significantly higher among both HIV-infected individuals and transplantation recipients. Notably, the risk of oral tongue SCCs was found to be higher among HIV-infected individuals. Surprisingly, the increased risk of oral tongue SCCs, other oral cavity SCCs, and oropharyngeal SCCs in immunosuppressed individuals corresponded with the risk among the general US population which lead to a conclusion that the use of tobacco and alcohol is synergistically linked with an increased risk of all head and neck cancers. Although the risk of oropharyngeal SCCs caused by human papillomavirus (HPV) is perceived to be higher among immunosuppressed individuals, the etiological role of HPV in oral tongue cancers remains unidentified. Furthermore, the authors observed the increased occurrence rate of oral tongue SCCs (½ of oral tongue SCCs) among men who have sex with other men (MSM risk group) as compared to other HIV-infected individuals. The incidence proportion of oropharyngeal SCCs among the MSM group was as follows: oropharyngeal SCCs (23%), oral cavity SCCs (32%), and oral cavity/pharynx NHLs (30%). The authors concluded that the onset of AIDS and the post-transplant period are the critical factors leading to an increased risk of oral tongue SCCs, oropharyngeal SCCs, and other oral cavity SCCs among the immunosuppressed population. Opposinglly, the incidence of oral cavity/pharynx NHLs was observed to be highest among organ transplant recipients immediately after the transplant surgery. An important observation marked by the authors is that before cancer diagnosis, the intensity of immunosuppression tends to fluctuate as it is severe among oral cavity/pharynx NHLs and moderate among oral tongue, oropharyngeal, and other oral cavity SCCs. Lastly, the results of the available data indicated that “onset of AIDS” is the leading factor in increasing the risk of cancers, hence, proving the significance of the etiological effect of “long-term immunosuppression”. Due to oral cavity/pharynx cancers being uncommon and difficulty in sub-groups analysis, the generalizability of this study was quite affected. Since authors had limited information about the impact of HPV-associated tumors, its correlation with oral cancers was not assessed for this study. This study’s standardized incidence ratio (SIR) depicted that immunosuppression is not affected by viral etiology. However, similar to oropharyngeal cancer, the increased risk of oral tongue cancer among “HIV-infected MSM” and
“time since AIDS onset” can be linked to the viral etiology (sexually transmitted virus). Furthermore, the authors have acknowledged that the global rise in the incidence of oral tongue cancer among white men and women needs further research and evaluation.

**Your impression:**

This study reinforces the importance of oral cancer screening and patient education concerning the potential threat of oral cancer. As a future dental hygienist, this study has helped me learn the importance of precisely evaluating any changes in the normal tissue and reporting any abnormal findings in the mouth. According to the National Institute of Dental and Craniofacial Research, the five most common factors to oral cancers are the use of tobacco and alcohol, age of an individual, infections caused by “sexually transmitted human papillomavirus” (HPV), sun exposure, and the omission of fruits and vegetables in the body ("The details of oral cancer screening", 2021). The viral infection can lead to potential oral health issues in an individual therefore a detailed oral health examination can save a patient’s life. Moving on, this article highlights the association of human immunodeficiency virus (HIV)/AIDS with head and neck cancers i.e. oral tongue cancer, oropharyngeal cancer, oral cavity/pharynx cancers, and other oral cavity cancers. As a dental hygienist, if I encounter any HIV-infected patient, I will inquire about their CD4 levels to understand the current level of their health. Furthermore, the authors of this study observed an increased risk of oral tongue cancer among HIV individuals, hence, proper oral health education should be provided to the patient to decrease the viral load in the mouth. Similar to HIV-infected individuals, another risk group studied in this research was organ transplant individuals. The authors have concluded that there is a moderate increase in the risk of head and neck cancers among “transplantation recipients. Therefore, a comprehensive oral examination can help a health care professional identify any oral malignancies in the patient’s mouth. Considering the alarming revelations that are made in this article, it will be accurate to state that the role of a dental hygienist in the prevention of oral cancers and the progression of infectious diseases is exceptionally vital.