

REVIEWER'S REPORT

Manuscript No.: IJAR- 59128

Title: SQUAMOUS CELL CARCINOMA OF THE MOBILE TONGUE: AN EMERGING EPIDEMIOLOGICAL PROFILE BEYOND CLASSICAL RISK FACTORS IN A SERIES OF 30 CASES.,

Recommendation:

Accept after minor revision

Rating	Excel.	Good	Fair	Poor
Originality		✓		
Techn. Quality			✓	
Clarity			✓	
Significance	✓			

Reviewer's ID: Bilquees Hamza

Detailed Reviewer's Report

The manuscript entitled "Squamous Cell Carcinoma of the Mobile Tongue: An Emerging Epidemiological Profile Beyond Classical Risk Factors in a Series of 30 Cases" investigates the epidemiological characteristics and potential non-traditional risk factors in a cohort of 30 patients diagnosed with mobile tongue squamous cell carcinoma (MTSCC) over a four-year period. The primary focus of the study is to evaluate the clinical profile of patients presenting without conventional carcinogen exposures—specifically tobacco and alcohol—and to analyze the prevalence and spatial relationship of chronic dental-related mechanical irritation (CMI) in tumor development.

In this single-center retrospective study, the authors evaluate 18 men (60%) and 12 women (40%) with a mean overall age of 64.1 years. The primary finding of the manuscript is the identification of a distinct epidemiological subgroup: 43.3% of the overall cohort (13/30 patients) had no history of tobacco or alcohol use. This non-traditional profile was predominantly observed among female patients, where 91.7% (11/12) were non-smokers and non-drinkers. Furthermore, local chronic mechanical trauma from traumatic crowns, ill-fitting prostheses, fractured teeth, or sharp dental edges was identified in 50% of all cases (15/30) and 83.3% of female patients (10/12). Notably, anatomical concordance between the site of dental trauma and the primary tumor location on the lateral free border of the tongue was documented in 46.7% of all patients (14/30) and 75% of female patients (9/12).

The manuscript addresses a highly relevant and evolving paradigm in head and neck surgical oncology: the increasing clinical frequency of oral tongue carcinomas occurring in patients lacking traditional risk

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factors. The paper is concisely written, logically structured, and presents well-tabulated preliminary clinical data. However, to ensure the manuscript meets the rigorous standard required for indexed publication, several major methodological, analytical, and manuscript-completion items must be systematically addressed.

Major Strengths

- **Topical Clinical Relevance:** The study contributes valuable clinical data to the ongoing global discussion surrounding the changing epidemiology of oral tongue squamous cell carcinoma, particularly among female non-smokers and non-drinkers.
- **Anatomical Mapping:** The evaluation of spatial/anatomical concordance between specific local irritants (e.g., sharp teeth or ill-fitting prostheses) and the exact primary tumor site adds clinical granularity to the hypothesis of mechanical trauma as a potential co-factor.
- **Subgroup Differentiation:** The clear distinction between male patients (who predominantly exhibited traditional tobacco and alcohol risk profiles, 88.9% and 55.6% respectively) and female patients (who overwhelmingly presented with non-habit profiles and high CMI exposure) highlights distinct epidemiological phenotypes.

Suggestions for Improvement

1. Completion of Draft Placeholders and Data Tables

- **Table 1 Missing Data:** In Table 1, the columns for "Women (\$n=12\$)" and "Men (\$n=18\$)" leave the "Age, mean $\pm$ SD" and "Age, median [range]" cells blank. These subgroup demographic figures must be calculated and populated.
- **Table 1 Items without Subgroup Breakdown:** The rows for "Fractured or severely damaged tooth" (\$30.0\%\$) and "Traumatic dental edge" (\$40.0\%\$) contain overall values but lack gender-specific counts/percentages in the Women and Men columns.
- **Table 2 Unresolved Staging Category:** Table 2 includes a row labeled "*TNM to be verified (1/30, 3.3%)*". Pathological or clinical TNM staging must be finalized for all 30 patients prior to publication; leaving staging unverified compromises the rigor of the clinical dataset.
- **Declarations Section Placeholders:** Lines 127–129 contain template placeholders ("*Ethical approval: To be completed according to institutional and journal requirements*", "*Consent: To be specified...*", "*Data availability: To be specified...*"). These declarations must be updated with explicit ethics committee review numbers, patient consent parameters, and data repository access protocols.

2. Methodological Rigor and Bias Mitigation

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- **Definition and Retrospective Assessment of CMI:** Assessing chronic mechanical irritation retrospectively carries significant risk of recall and observer bias. The authors must detail the objective criteria used to define CMI. Was CMI verified via pre-treatment dental records, standardized oral/dental photography, or clinical examination by an oral surgeon/dentist at the time of initial diagnosis? Clarifying who performed the dental assessment and how "sharpness" or "traumatic potential" was standardized is essential.
- **Lack of a Control Cohort:** As acknowledged in the discussion, the lack of a control group (e.g., age- and sex-matched patients without oral malignancy or patients with non-tongue oral lesions) prevents the calculation of odds ratios or relative risk for CMI. The authors should explicitly reframe their conclusions to emphasize that CMI is an associated finding rather than an established risk factor, expanding on how future prospective case-control studies should be designed to test this hypothesis.

3. Statistical Analysis and Comparative Testing

- **Inferential Statistics:** Currently, the manuscript only presents descriptive percentages and means. Given that the paper emphasizes a stark difference between male and female cohorts regarding habits vs. CMI, the authors should perform basic comparative statistical testing (e.g., Fisher's exact test or Chi-square test for categorical variables such as smoking status, alcohol use, and presence of CMI across sexes; Mann-Whitney U test or Student's t-test for age). Reporting exact p-values will strengthen the assertion that these subgroup profiles differ significantly.

4. Expansion of the Etiological and Molecular Framework

- **HPV / p16 Status:** Although human papillomavirus (HPV) is predominantly associated with oropharyngeal carcinoma rather than mobile tongue SCC, p16 immunohistochemistry or HPV-DNA testing is routinely evaluated in non-smoker/non-drinker head and neck cancer cohorts. The manuscript should state whether p16/HPV testing was performed. If testing was not conducted, this should be explicitly listed as a study limitation, accompanying a brief discussion on the low expected prevalence of HPV in oral tongue sites compared to the base of tongue.
- **Additional Non-Traditional Risk Factors:** The discussion should briefly incorporate other potential non-habit risk factors reported in non-smoking oral cancer cohorts, such as human leukocyte antigen (HLA) genomic susceptibility, oral microbiome dysbiosis, chronic periodontal disease, and nutritional deficiencies (e.g., iron, vitamin A/C).

5. Inclusion of Treatment Modalities and Follow-up Data

- **Surgical and Oncologic Management:** The manuscript focuses on epidemiology and staging but omits treatment details. Adding a brief section or summary table outlining primary treatment (e.g.,

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partial glossectomy margins, rate of neck dissection, administration of adjuvant radiotherapy or chemoradiotherapy) would enhance the clinical completeness of the series.

- **Clinical Outcomes:** If follow-up data are available over the four-year study period, including brief figures on local recurrence rates, regional failure, or overall survival would significantly elevate the manuscript's impact.

6. Writing, Style, and Literature Refinement

- **Language and Terminology:** Minor typographical and structural adjustments are needed (e.g., reconciling duplicate words in line 33: "*mechanical trauma; ma; mechanical irritation.*").
- **Literature Context:** Ensure references [1] and [2] are properly integrated into the discussion, contrasting the mean age of this cohort (64.1 years) with studies reporting rising tongue cancer incidence in younger non-smoking cohorts (<45 years).

Final Recommendation**Decision: Accept with Minor Revisions**

This manuscript presents a compelling clinical series that highlights an important epidemiological pattern in mobile tongue squamous cell carcinoma, particularly among non-smoking, non-drinking female patients with dental-related mechanical trauma. The data are concise, clinically relevant, and well-organized. Provided the authors address the minor revisions outlined above—specifically filling in missing subgroup data in Table 1, finalizing the TNM staging category in Table 2, completing the ethical declarations, adding basic inferential statistical comparisons (p-values), and expanding the discussion regarding CMI assessment criteria and p16/HPV status—the article will be suitable for publication.

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