ABSTRACT: Objective: This study aimed at assessing the association between factors such as age, sex, skin color, occupation, educational level, marital status, place of residence, and tobacco and alcohol consumptions and oral cancer in individuals in a city in the northeast of Brazil between 2002 and 2012. Methods: This is a case–control study. The case group consisted of 127 people attended at the Oral Injury Reference Center with histopathological diagnosis of oral squamous cell carcinoma. The control group consisted of 254 individuals treated at the same center. The study considered two controls for each case. The cases and controls were adjusted according to sex and age. Univariate and bivariate analyses were performed (Pearson χ²-test) to verify the correlation between the dependent variable (oral cancer) and the independent variables; odds ratio (OR) and the confidence interval of 95% (95%CI) were calculated. Finally, in the multivariate analysis, it was used as the hierarchical model with logistic regression to explain the interrelationships between the independent variables and oral cancer. Results: Consumption of more than 20 cigarettes per day [OR = 6.64; 95%CI 2.07 – 21.32; p ≤ 0.001], an excessive alcohol consumption [OR = 3.25; 95%CI 1.03 – 10.22; p ≤ 0.044], and the synergistic consumption of tobacco and alcohol [OR = 9.65; 95%CI 1.57 – 59.08; p ≤ 0.014] are the most important risk factors for oral cancer. Conclusion: It was concluded that tobacco and alcohol consumptions are the most important factors for the development of oral cancer. Sociodemographic factors were not associated with this neoplasm after adjusting for smoking and drinking. Keywords: Mouth neoplasms. Squamous cell carcinoma. Epidemiology. Risk factors. Case–controls studies. Odds ratio.
INTRODUCTION

Annually, 300,000 new cases of oral cancer are diagnosed all over the world, accounting for almost 130,000 deaths each year and representing a global public health issue. In Brazil, the incidence of oral cancer is considered one of the highest in the world. The National Cancer Institute (INCA) estimates that there were 15,290 new cases of the disease in Brazil in 2014; in the northeast region, the estimated number of new cases is 3,020.

Oral cancer is a malignant neoplasm that may affect the oral cavity. The most affected sites are tongue, floor of mouth, and lower lip. The most common histologic type is squamous cell carcinoma (SCC), which corresponds to the range of 90–95% of all oral cancers. This tumor predominates in male subjects, and the majority of cases occur between 50 and 70 years of age, with a higher prevalence in leucoderma individuals.

The oral cancer causative agents are multifactorial, with alcohol and tobacco being the most important risk factors. Besides these factors, an excessive sun exposure without an appropriate protection over the years constitutes a considerable risk factor for oral cancer, especially on the lips. Other factors such as human papillomavirus (HPV), diet, and occupation have been studied in order to investigate their implications on oral carcinogenesis. The results seem to indicate a connection between these factors and oral cancer.

With regard to social conditions, they are often ignored in the complex causal chain of the oral cancer; however, such conditions should be considered as distal determinants in the health–disease process, while behavioral variables should be considered as proximal determinants. This is a more consistent approach in evaluating the implications of distinct
variables in a causal chain model of oral cancer\(^2\(^{2}\), Therefore, it is necessary to analyze the disease in a broader perspective, in order to verify not only factors such as tobacco and alcohol consumptions but also the implications of social aspects on oral cancer.

This study investigates the association between sociodemographic and behavioral factors and oral cancer in individuals in a city in the northeast of Brazil between 2002 and 2012.

**METHODS**

This is a case–control study, and the sample is composed of 381 patients treated at the Oral Injury Reference Center, which belongs to the Universidade Estadual de Feira de Santana (UEFS). Suspected cases of oral cancer that occur in the state of Bahia are referred to this center. The period considered in this study was from 2002 to 2012. All the patients with histopathological diagnosis of oral cancer attended at the referred center during the mentioned period were included in the case group, totaling 127 people. The control subjects were selected among patients treated at the same reference center in order to obtain a higher similarity between the cases and control subjects, except for the incidence of oral squamous cell carcinoma (OSCC). The sample consisted of two control subjects for each case. The exclusion criteria were: (1) diagnosis of potentially malignant lesions, such as oral lichen planus, actinic cheilitis, erythroplasia, leukoplakia, and erythroleukoplakia; (2) histopathological diagnosis of dysplasia and oral malignancies, such as carcinoma in situ, verrucous carcinoma, adenocarcinoma, and osteosarcoma; and (3) history of cancer.

The study was conducted by the collection of data from medical records of the patients, done by a single trained data collector. The data collection involved the sociodemographic and behavioral profiles of the participants. Regarding the sociodemographic profile, the following independent variables were considered: age, sex, race, marital status, occupation, educational level, and the place of residence. Tobacco and alcohol consumption habits related to the quantity and the type consumed and intake period and smoking and/or alcohol cessation were considered to compound the behavioral profile. The study also included the evaluation of the anatomical location of the tumor. The dependent variable was verified by the presence of OSCC, and confirmed by a histopathologic diagnosis in accordance with the diagnostic criteria established by the World Health Organization (WHO, 2005)\(^2\(^{2}\). Data were stored in the Statistical Package for Social Sciences software (SPSS), version 17.0.

The descriptive measures, the absolute frequencies, and percentages were calculated in the univariate analysis. Then, bivariate analysis (Pearson \(\chi^2\)-test) was performed to verify the association between the dependent variable and the independent variables, considering at that time \(p \leq 0.20\). The odds ratio (OR) and the confidence interval of 95% (95%CI) were calculated.

In the multivariate analysis, the hierarchical logistic regression model was used to evaluate the interrelationship between the independent variables and the oral cancer. The inclusion of variables followed the conceptual model hierarchy, selecting at first the variables of the distal group that obtained \(p \leq 0.20\) in the bivariate analysis. Only the variables that obtained \(p \leq 0.05\) remained in the multivariate model. Then, the variables of the proximal group (tobacco and
alcohol consumption) that obtained \( p \leq 0.20 \) were added to the bivariate analysis. Age and sex remained at all the levels of the logistic regression; therefore, they were adjustment variables.

The missing data were imputed in the modal category of each variable. The bivariate and multivariate analyses were performed in the statistical software applications SPSS version 17.0 and STATA version 12.0, respectively. The information of the participants was maintained confidential pursuant to the provisions of the Resolution 466/12 of the National Health Council\(^\text{22}\), which is in line with the Declaration of Helsinki. This study was approved by the Research Ethics Committee of the Universidade Estadual de Feira de Santana (UEFS).

**RESULTS**

According to the eligibility criteria, 127 individuals comprised the case group and 254 individuals comprised the control group. Thus, the final sample consisted of 381 people with the minimum age of 23 years and the maximum of 96 years. Therefore, the mean age was 60.66 years and standard deviation 13.51 years. The most affected anatomical locations by OSCC were: tongue (40.5%); floor of mouth (20.6%); lower lip (11.9%); alveolar ridge (10.3%); retromolar region (7.2%); buccal mucosa (7.1%); and hard palate (2.4%).

Table 1 shows the distribution of sociodemographic variables and the bivariate analysis with crude OR. The oral cancer incidence was almost three times higher in men than in women, in a proportion equivalent to 2.62:1. Those individuals older than 50 years of age prevailed in both the case (74%) and the control groups (74.8%). The skin color, brown or black, was the most mentioned in both the case and control groups (78.7 and 83.1%, respectively); however, no statistically significant differences were observed.

The marital status was categorized as unmarried (single, divorced, and widow) and married (married and common-law marriage). Unmarried individuals showed association with oral cancer (OR = 1.75; 95%CI 1.14 – 2.69). The educational level was categorized as lower education (individuals who were classified from illiterate to completed elementary school) and higher education (individuals who completed high school and/or possessed college or higher educational degrees). Lower education also showed association with oral cancer (OR = 2.72; 95%CI 1.36 – 5.41) in the bivariate analysis.

Table 2 describes the variables related to smoking habits. Research on tobacco consumption revealed that the duration of smoking habit showed a strong association with oral cancer. Individuals who smoked for more than 20 years showed a higher risk of developing oral cancer (OR = 7.24; 95%CI 4.40 – 11.91). The dose-response effect was analyzed in the daily amount of cigarettes smoked. The individuals who smoked more than 20 cigarettes per day showed a higher risk of developing OSCC (OR = 5.59; 95%CI 3.16 – 9.88) when compared with those who smoked from 1 to 20 cigarettes per day (OR = 1.74; 95%CI 1.13 – 2.68). Individuals who smoked unfiltered cigarettes (hand-rolled cigarettes, cigars, and pipes) were more likely to develop oral cancer (OR = 5.06; 95%CI 3.20 – 8.00) than those who smoked filtered cigarettes (industrialized cigarettes), which were not significantly associated with this disease.
Table 3 shows the alcohol consumption among individuals of case and control groups. The results of the bivariate analysis showed that alcohol consumption duration is a factor associated with oral cancer. Individuals who consumed alcohol for more than 20 years presented a three times higher risk of developing this disease (OR = 3.53; 95%CI 2.25 – 5.55). In relation to the frequency of alcohol consumption, it was observed that individuals who

Table 1. Sociodemographic characteristics of the individuals in the case and control groups, Feira de Santana, Bahia, Brazil, 2002–2012 (n = 381).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases n (%)</th>
<th>Controls n (%)</th>
<th>Total n (%)</th>
<th>p-value(^a)</th>
<th>OR(^b)</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>35 (27.6)</td>
<td>70 (27.6)</td>
<td>105 (27.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>92 (72.4)</td>
<td>184 (72.4)</td>
<td>276 (72.4)</td>
<td>1.000</td>
<td>1.00</td>
<td>0.62 – 1.61</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>≤ 50</td>
<td>33 (26.0)</td>
<td>64 (25.2)</td>
<td>97 (25.5)</td>
<td>0.868</td>
<td>0.96</td>
<td>0.59 – 1.56</td>
</tr>
<tr>
<td>&gt; 50</td>
<td>94 (74.0)</td>
<td>190 (74.8)</td>
<td>284 (74.5)</td>
<td>0.868</td>
<td>0.96</td>
<td>0.59 – 1.56</td>
</tr>
<tr>
<td>Color of skin(^c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown/black</td>
<td>100 (78.7)</td>
<td>211 (83.1)</td>
<td>311 (81.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>27 (21.3)</td>
<td>43 (16.9)</td>
<td>70 (18.4)</td>
<td>0.303</td>
<td>1.33</td>
<td>0.77 – 2.27</td>
</tr>
<tr>
<td>Marital status(^d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>61 (48.0)</td>
<td>157 (61.8)</td>
<td>218 (57.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>66 (52.0)</td>
<td>97 (38.2)</td>
<td>163 (42.8)</td>
<td>0.010</td>
<td>1.75</td>
<td>1.14 – 2.69</td>
</tr>
<tr>
<td>Educational level(^e)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher education</td>
<td>11 (8.7)</td>
<td>52 (20.5)</td>
<td>63 (16.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower education</td>
<td>116 (91.3)</td>
<td>202 (79.5)</td>
<td>318 (83.5)</td>
<td>0.003</td>
<td>2.72</td>
<td>1.36 – 5.41</td>
</tr>
<tr>
<td>Place of residence(^f)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>100 (78.7)</td>
<td>219 (86.2)</td>
<td>319 (83.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>27 (21.3)</td>
<td>35 (13.8)</td>
<td>62 (16.3)</td>
<td>0.062</td>
<td>1.69</td>
<td>0.97 – 2.94</td>
</tr>
<tr>
<td>Occupation(^g)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>96 (75.6)</td>
<td>184 (72.4)</td>
<td>280 (73.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>31 (24.4)</td>
<td>70 (27.6)</td>
<td>101 (26.5)</td>
<td>0.511</td>
<td>0.85</td>
<td>0.52 – 1.39</td>
</tr>
</tbody>
</table>

\(^a\)Statistical Significance, p ≤ 0.20; \(^b\)Crude OR; \(^c\)34 lost information inputted in the “brown/black” category; \(^d\)11 lost information inputted in the category “married”; \(^e\)40 lost information inputted in the “lower education” category; \(^f\)13 lost information inputted in the “urban” category; \(^g\)12 lost information inputted in the “employed” category.

OR: odds ratio; 95%CI: 95% confidence interval.
ingested alcoholic beverages with high frequency (drinking heavily more than two times per week) showed a five times higher risk of developing OSCC (OR = 5.54; 95%CI 2.82 – 10.86). Consumption of distilled alcoholic beverage (cachaça, vodka, whisky and brandy) increased by almost six times the risk of developing this neoplasm (OR = 5.87; 95%CI 3.65 – 9.44).

Table 4 shows the synergistic consumption of tobacco and alcohol in both the case and control groups. More than half of patients (58.3%) with oral cancer consumed both tobacco

Table 2. Tobacco consumption in the individuals of case and control groups, Feira de Santana, Bahia, Brazil, 2002–2012 (n = 381).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases n (%)</th>
<th>Controls n (%)</th>
<th>Total n (%)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>OR&lt;sup&gt;b&lt;/sup&gt;</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked&lt;sup&gt;c&lt;/sup&gt;</td>
<td>13 (10.2)</td>
<td>127 (50.0)</td>
<td>140 (36.7)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Former smoker</td>
<td>47 (37.0)</td>
<td>76 (29.9)</td>
<td>123 (32.3)</td>
<td>0.163</td>
<td>1.38</td>
<td>0.88 – 2.16</td>
</tr>
<tr>
<td>Smoker</td>
<td>67 (52.8)</td>
<td>51 (20.1)</td>
<td>118 (31.0)</td>
<td>0.000</td>
<td>4.45</td>
<td>2.79 – 7.07</td>
</tr>
<tr>
<td>Duration of habit (in years)&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>13 (10.2)</td>
<td>127 (50.0)</td>
<td>140 (36.7)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>1 – 20</td>
<td>14 (11.0)</td>
<td>41 (16.1)</td>
<td>55 (14.4)</td>
<td>0.180</td>
<td>0.64</td>
<td>0.34 – 1.23</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>100 (78.7)</td>
<td>86 (33.9)</td>
<td>186 (48.8)</td>
<td>0.000</td>
<td>7.24</td>
<td>4.40 – 11.91</td>
</tr>
<tr>
<td>Cigarettes/day&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>13 (10.2)</td>
<td>127 (50.0)</td>
<td>140 (36.7)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>1 – 20</td>
<td>70 (55.1)</td>
<td>105 (41.3)</td>
<td>175 (45.9)</td>
<td>0.011</td>
<td>1.74</td>
<td>1.13 – 2.68</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>44 (34.6)</td>
<td>22 (8.7)</td>
<td>66 (17.3)</td>
<td>0.000</td>
<td>5.59</td>
<td>3.16 – 9.88</td>
</tr>
<tr>
<td>Type of tobacco&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None&lt;sup&gt;c&lt;/sup&gt;</td>
<td>13 (10.2)</td>
<td>127 (50.0)</td>
<td>140 (36.7)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Filtered cigarette*</td>
<td>31 (24.4)</td>
<td>58 (22.8)</td>
<td>89 (23.4)</td>
<td>0.732</td>
<td>1.09</td>
<td>0.66 – 1.80</td>
</tr>
<tr>
<td>Unfiltered cigarette**</td>
<td>83 (65.4)</td>
<td>69 (27.2)</td>
<td>152 (39.9)</td>
<td>0.000</td>
<td>5.06</td>
<td>3.20 – 8.00</td>
</tr>
<tr>
<td>Smoking cessation (in years)&lt;sup&gt;g&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 10</td>
<td>10 (21.7)</td>
<td>52 (69.3)</td>
<td>62 (51.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10</td>
<td>36 (78.3)</td>
<td>23 (30.7)</td>
<td>59 (48.8)</td>
<td>0.000</td>
<td>8.14</td>
<td>3.46 – 19.15</td>
</tr>
</tbody>
</table>

<sup>a</sup>Statistical significance: p ≤ 0.20;<sup>b</sup>Crude OR;<sup>c</sup>Reference category;<sup>d</sup>12 lost information inputted in the category “> 20 years”;<sup>e</sup>31 Information lost inputted in the “1–20 cigarettes/day” category;<sup>f</sup>9 lost information inputted in the “unfiltered cigarette”;<sup>g</sup>2 lost information inputted in the “≥ 10 years” category; Industrialized cigarette; **hand-rolled cigarettes, cigars, and pipes.

OR: odds ratio; 95%CI: 95% confidence interval.
and alcohol, while only 18.9% of the individuals in the control group practiced a combined consumption of these substances.

It is worth highlighting that, for the multivariate analysis, the variables initially selected were the ones pertaining to the distal block that associated with oral cancer in the bivariate analysis — those with p ≤ 0.20. Therefore, such variables were marital status, educational level, and the place of residence. At this level, it is noticed that only the variables such as marital status and educational level remained associated with oral cancer (Table 5).

Table 3. Alcohol consumption among the individuals of case and control groups, Feira de Santana, Bahia, Brazil, 2002–2012 (n = 381).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases n (%)</th>
<th>Controls n (%)</th>
<th>Total n (%)</th>
<th>p-valuea</th>
<th>ORb</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol consumptionc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non drinkerd</td>
<td>27 (21.3)</td>
<td>113 (44.5)</td>
<td>140 (36.7)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Former drinker</td>
<td>56 (44.1)</td>
<td>57 (22.4)</td>
<td>113 (29.7)</td>
<td>0.000</td>
<td>2.73</td>
<td>1.73 – 4.31</td>
</tr>
<tr>
<td>Drinker</td>
<td>44 (34.6)</td>
<td>84 (33.1)</td>
<td>128 (33.6)</td>
<td>0.759</td>
<td>1.07</td>
<td>0.69 – 1.68</td>
</tr>
<tr>
<td>Duration of the habit (in years)e</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0d</td>
<td>43 (33.9)</td>
<td>154 (60.6)</td>
<td>197 (51.7)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>1 – 20</td>
<td>17 (13.4)</td>
<td>39 (15.4)</td>
<td>56 (14.7)</td>
<td>0.609</td>
<td>0.85</td>
<td>0.46 – 1.58</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>67 (52.8)</td>
<td>61 (24.0)</td>
<td>128 (33.6)</td>
<td>0.000</td>
<td>3.53</td>
<td>2.25 – 5.55</td>
</tr>
<tr>
<td>Frequencyf</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never dranked</td>
<td>23 (18.1)</td>
<td>109 (42.9)</td>
<td>132 (34.6)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Low</td>
<td>73 (57.5)</td>
<td>131 (51.6)</td>
<td>204 (53.5)</td>
<td>0.276</td>
<td>1.27</td>
<td>0.83 – 1.95</td>
</tr>
<tr>
<td>High</td>
<td>31 (24.4)</td>
<td>14 (5.5)</td>
<td>45 (11.8)</td>
<td>0.000</td>
<td>5.54</td>
<td>2.82 – 10.86</td>
</tr>
<tr>
<td>Type of alcoholic beverageg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonedd</td>
<td>24 (18.9)</td>
<td>111 (43.7)</td>
<td>135 (35.4)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Fermented*</td>
<td>9 (7.1)</td>
<td>60 (23.6)</td>
<td>69 (18.1)</td>
<td>0.000</td>
<td>0.25</td>
<td>0.12 – 0.52</td>
</tr>
<tr>
<td>Distilled**</td>
<td>94 (74.0)</td>
<td>83 (32.7)</td>
<td>177 (46.5)</td>
<td>0.000</td>
<td>5.87</td>
<td>3.65 – 9.44</td>
</tr>
<tr>
<td>Drinking cessation (in years)c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 10</td>
<td>20 (35.7)</td>
<td>41 (71.9)</td>
<td>61 (54.0)</td>
<td>0.000</td>
<td>4.61</td>
<td>2.08 – 10.22</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>36 (64.3)</td>
<td>16 (28.1)</td>
<td>52 (46.0)</td>
<td>0.000</td>
<td>4.61</td>
<td>2.08 – 10.22</td>
</tr>
</tbody>
</table>

aStatistical significance, p ≤ 0.20; bCrude OR; c8 lost information inputted in the “Never drank” category; dReference category; e65 lost information inputted in the “0” category; f19 lost information inputted in the “low” category; g23 lost information inputted in the “distilled” category; h8 lost information; *Beer, wine; **Cachaça, vodka, whisky, brandy. OR: odds ratio; 95%CI: 95% confidence interval.
Table 4. Synergistic consumption of tobacco and alcohol among individuals of case and control groups, Feira de Santana, Bahia, Brazil, 2002–2012 (n = 381).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases n (%)</th>
<th>Controls n (%)</th>
<th>Total n (%)</th>
<th>p-value</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synergistic consumption of tobacco and alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker and nondrinker¹</td>
<td>7 (5.5)</td>
<td>84 (33.1)</td>
<td>91 (23.9)</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>No</td>
<td>46 (36.2)</td>
<td>122 (48.0)</td>
<td>168 (44.1)</td>
<td>0.029</td>
<td>0.61</td>
<td>0.40 – 0.95</td>
</tr>
<tr>
<td>Yes</td>
<td>74 (58.3)</td>
<td>48 (18.9)</td>
<td>122 (32.0)</td>
<td>0.000</td>
<td>5.99</td>
<td>3.74 – 9.61</td>
</tr>
</tbody>
</table>

¹Statistical significance, p ≤ 0.20; ²Crude OR; ³6 lost information inputted in the "No" category; ⁴Reference category. OR: odds ratio; 95%CI: 95% confidence interval.

Table 5. Odds ratio adjusted for oral cancer, results of the multivariate analysis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (IC95%)</th>
<th>p-value</th>
<th>OR (IC95%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital statusb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>1.62 (1.04 – 2.52)</td>
<td>≤ 0.031</td>
<td>1.53 (0.90 – 2.58)</td>
<td>≤ 0.113</td>
</tr>
<tr>
<td>Educational levelb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher education</td>
<td>1.00</td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Lower education</td>
<td>2.42 (1.18 – 4.91)</td>
<td>≤ 0.015</td>
<td>1.71 (0.74 – 3.96)</td>
<td>≤ 0.207</td>
</tr>
<tr>
<td>Place of residenceb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1.45 (0.82 – 2.56)</td>
<td>≤ 0.196</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarettes/dayc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 – 20</td>
<td>2.32 (0.80 – 6.75)</td>
<td>≤ 0.122</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 20</td>
<td>6.64 (2.07 – 21.32)</td>
<td>≤ 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency (alcohol)c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never drank</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1.03 (0.41 – 2.60)</td>
<td>≤ 0.943</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>3.25 (1.03 – 10.22)</td>
<td>≤ 0.044</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synergistic consumption of tobacco and alcoholc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker and nondrinker</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3.13 (0.70 – 13.87)</td>
<td>≤ 0.134</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9.65 (1.57 – 59.08)</td>
<td>≤ 0.014</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Statistical significance, p ≤ 0.05; ²Adjusted for sex and age; ³Adjusted for sex, age, marital status, and educational level. OR: odds ratio; 95%CI: 95% confidence interval.
Such variables were kept in the model, and then, the proximal group variables such as smoking and drinking were added. The variables cigarettes/day, frequency of alcohol intake, and the synergistic consumption of tobacco and alcohol were selected to compose the last level of multivariate analysis, because the simultaneous inclusion of all the variables of smoking and alcohol consumption led to collinearity in the multivariate model.

The results of multivariate analysis showed that smoking more than 20 cigarettes a day increases by six times the risk of OSCC (OR = 6.64; 95%CI 2.07 – 21.32); consuming alcohol at a high frequency increases by three times the risk of developing this cancer (OR = 3.25; 95%CI 1.03 – 10.22); and consuming both the tobacco and alcohol increases by almost 10 times the risk of developing this disease (OR = 9.65; 95%CI 1.57 – 59.08). The variables such as marital status and education significantly associated with the outcome (OSCC) on the first level of multivariate analysis and lost the significance after adjustment for smoking and drinking.

**DISCUSSION**

The association between smoking and OSCC is well established in the literature\(^{23-25}\). Our study results showed that cigarette smokers showed four times higher risk of developing OSCC (OR = 4.45; 95%CI 2.79 – 7.07). A similar finding\(^ {26}\) verified that smokers showed 11 times higher risk of this neoplasm (OR = 11.0; 95%CI 6.0 – 25.9). We also found that individuals who smoked more than 20 cigarettes daily showed six times higher risk (adjusted OR = 6.64; 95%CI 2.07 – 21.32) of developing OSCC. A similar result was obtained\(^ {27}\) in a study that found eight times higher risk (OR = 8.3; 95%CI 3.41 – 20.36) of developing OSCC.

Regarding the frequency of alcohol consumption, our research showed that those individuals who drink in a high frequency showed a higher risk of developing oral cancer (adjusted OR = 3.25; 95%CI 1.03 – 10.22). A similar finding was verified\(^ {27}\) by authors who observed an increased risk for OSCC in heavy drinkers (OR = 5.04; 95%CI 1.84 – 13.85). In our study, we noticed that the consumption of distilled beverages was associated with oral cancer (OR = 5.87; 95%CI 3.65 – 9.44). This fact is related to the higher alcohol content in these drinks\(^ {28}\). On the other hand, more important than the type of alcoholic beverage are the quantity of alcohol consumed and the duration of this habit. It is important to mention that it is difficult to size the consumption of alcohol, because the individuals ingest different types of alcoholic drinks and are inaccurate in reporting alcohol intake doses\(^ {30}\).

Regarding the co-use of tobacco and alcohol, we observed that the synergism increased by almost 10 times the risk of OSCC (adjusted OR = 9.65; 95%CI 1.57 – 59.08). The simultaneous consumption of tobacco and alcohol increases the risk of oral cancer by 6 to 15 times\(^ {31}\). Individuals who smoke more than 40 cigarettes per day and who consumed more than 30 standard drinks per week showed a 38 times higher risk of developing oral cancer when compared with those who abstain from such substances\(^ {32}\). Tobacco and alcohol are the most carcinogenic potential factors, despite the multifactorial aspect of the disease\(^ {13}\).
Regarding sex, our research results are aligned with the literature\textsuperscript{7,9-11}, which reports a higher incidence of OSCC in male subjects. The authors attribute this occurrence to a higher exposure to tobacco and alcohol among men. Regarding age, there was a higher incidence of OSCC in patients older than 50 years of age, which is also aligned with the literature\textsuperscript{11,16,34}.

With regard to social variables, we detached the variables such as marital status and educational level. On the first, we observed that individuals without a partner (single, divorced and widow) were associated with the outcome on the first level of multivariate analysis. However, the association lost its significance after adjustment for smoking and drinking (OR = 1.53, 95%CI 0.90 – 2.58). An OSCC case – control study held in Dinamarca\textsuperscript{35} found a two times higher risk of OSCC in divorced individuals (OR = 2.3; 95%CI 1.1 – 4.6), even after the adjustment for smoking and drinking.

The educational level, which is also a social variable, was associated with oral cancer up to the first level of multivariate analysis, also losing its significance after the adjustment for tobacco and alcohol consumptions (OR = 1.71; 95%CI 0.74 – 3.96). Individuals with lower education are more likely to develop OSCC owing to higher exposure to tobacco and alcohol, poor oral health, and nutritional deficiencies\textsuperscript{36}.

Regarding the anatomical location of the tumor, we found that the most affected sites were the tongue (40.5%), followed by the floor of mouth (20.6%). This result is consistent with most studies\textsuperscript{4,6,7,12}.

Some methodological aspects of this study deserve to be discussed. With regard to the limitations of the study, we emphasize the incompleteness of medical records, which generated data losses. Another limiting aspect and likely to occur in case - control studies is the issue of recall bias, where being sick can influence the responses to certain questions. In addition, we reinforce that the generalization of this study results is limited to the individuals treated at the Oral Injury Reference Center of the Brazilian northeast.

Oral cancer is a public health problem, with high rates of morbidity and mortality. Knowledge of the epidemiology and the factors associated with this disease is the key to planning the prevention programs, which will favor the reduction of these adverse indicators that affect the population. Despite the known roles of tobacco and alcohol in causing this disease, epidemiological studies have shown that, even after adjusting for these risk factors, there is still a residual effect of social conditions on the risk of oral cancer\textsuperscript{37}. Therefore, it is necessary to conduct more research in order to evidence the impact that social conditions impose on the complex causal chain of oral cancer.

**CONCLUSION**

This research showed that the OSCC was more frequent in male subjects from 50 years of age, in individuals with brown or black skin, with low educational level, and unmarried. The anatomical region most affected by this tumor was the tongue, followed by the floor
of mouth. The factors associated with oral cancer were smoking and alcoholism. In addition, it was concluded that the synergistic consumption of tobacco and alcohol increases the risk of developing this cancer. Sociodemographic factors were not associated with oral cancer after adjustment for smoking and alcoholism.

REFERENCES


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