

# Risk Assessment of Alcohol Consumption for Oral Cancer: A Case-Control Study in Patients Attending the National Cancer Institute (Apeksha Hospital, Maharagama) of Sri Lanka

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## Abstract

**Background:** Oral squamous cell cancer (OSCC) is one of the commonest cancers in Sri Lanka. **Objectives:** This study aimed to determine the use of alcohol, its duration and consuming pattern in relation to the risk of developing OSCC in patients attending the National Cancer Institute of Sri Lanka. **Methods:** A case-control study was carried out on 105 patients with a histologically confirmed primary OSCC and 210 age-sex matched controls. Information on alcohol consumption was obtained via an interviewer-administered questionnaire. **Results:** Participants who had consumed alcohol at some point in their life had a 3.8-fold risk of developing OSCC ( $p=0.000$ ). Current consumers had a higher risk compared to who have consumed previously. Former consumers had a lower risk of developing OSCC compared to current consumers. Individuals who had consumed alcohol for more than 20 years had a greater risk [Odds ratio (OR)=4.69] of developing OSCC compared to those who had consumed alcohol for less than ten years (OR=3.25). Those who consumed the locally-made illicit liquor (Kasippu) had the greatest risk (OR=8.45;  $p<0.05$ ) of developing OSCC when considering the type of alcohol consumed. **Conclusions:** Alcohol consumption is a risk factor for OSCC. The OSCC risk increased with longer duration of alcohol use, the consumption of locally-made illicit liquor and current consumers of alcohol.

**Keywords:** Squamous cell carcinoma- alcohol drinking- risk factors- Sri Lanka

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## Introduction

Oral cancers comprise of tumours involving the oral cavity, pharynx, and salivary glands. Tumours in the oral cavity are an emerging type of cancer in various parts of the world. They accounted for an estimated 354,864 new cancer patients (2.1% of all new cancer patients) and 177,384 deaths (1.9% of all deaths) in 2018 while another study reports that the standard incidence of OSCC in the world was 4 per 100,000 people (Salehiniya and Raei, 2020; Bray et al., 2018).

Squamous cell carcinoma is the commonest malignant epithelial neoplasm in the oral cavity and accounts for more than 90% of oral malignant lesions (Warnakulasuriya, 2009). In the Indian subcontinent and other parts of Asia, oral squamous cell carcinoma (OSCC) is one of

the commonest forms of cancer. In South-Central Asia to which Sri Lanka belongs, it is the third most common type of cancer (Petersen, 2003). According to data from GLOBOCAN 2018, when considering both the incidence and the mortality data of lip and oral cancer, South Central Asia accounts for the highest age-standardized incidence rates and mortality rates compared to the rest of the Asian, African and European data (Bray et al., 2018). The National Cancer Control Program of Sri Lanka reported that 1941 new cases were diagnosed in the year 2011(NCCP, 2011), while 2199 new patients were detected in 2014(NCCP, 2014). These data imply that there is a rise in newly diagnosed OSCC cases.

A cross sectional study carried out in 7 of the 9 provinces in Sri Lanka between 2005 and 2006 revealed the overall prevalence of alcohol consumption to be 23.7%.

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It had a higher prevalence among the urban population, reaching up to 29.5% (Katulanda et al., 2014). Given the high prevalence of alcohol consumption, and irritation effect of alcohol on oral mucosa it may be worthwhile to study the possible relationship between alcohol consumption and the presence of OSCC. Therefore, the objective of this study was to determine the risk of alcohol use for OSCC in patients attending the National Cancer Institute of Sri Lanka (Apeksha Hospital), Maharagama.

## Materials and Methods

The sample size was calculated based on the literature relating to case-control studies in two independent groups (Daly and Bourke, 2000) and a case-control study was carried out on 105 patients over the age of 18 years with a histologically confirmed primary OSCC recruited from Apeksha Hospital, Maharagama. The patients were either being treated at the institute at the time of recruitment or were awaiting clinic visits at the same institute. Two hundred and ten age-matched ( $\pm 5$  years from the age of each case) and gender-matched individuals attending the general clinics at Colombo South Teaching Hospital and community were selected as controls using an open advertisement over twelve months. Controls were excluded of the disease, after inspecting for oral lesions for any oral malignant or pre malignant lesions. The patient to control ratio was 1: 2. Ethical approval for the study was granted by the Ethics Review Committee, University of Sri Jayewardenepura, Colombo South Teaching Hospital (29/16) and Apeksha Hospital, Maharagama. Informed and written consent was obtained from all participants. Patients who do not gave the informed consent and did not belong to ICD-O-3 site codes: 00 to 06 categories were excluded from the study population. Both cases and controls were selected randomly in order to reduce the confounding errors.

An interviewer-administered questionnaire was given to the participants. The questionnaire comprised two main sections i.e., demographic details and risk factor assessment. The main demographic details gathered were age, sex, gender, education status, occupation and monthly income of the study population. The second section of the questionnaire was used to collect data on alcohol consumption including duration, quantity, pattern,

frequency and type of alcohol consumed. Consumption of alcohol along with other two risk factors i.e., smoking and betel chewing was also assessed as these two habits are also considered to be main risk factors for OSCC. All interviews were conducted by the primary investigator and trained five pre-intern medical officers who completed pre-survey calibration to minimize inter-observer variability.

Statistical software SPSS version 21.0 was used for general statistical analysis. The odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess the risk factor. Statistical significance for associations was calculated using the chi-square test, with statistical significance set at  $p < 0.05$ .

## Results

Out of the 105 oral cancer patients, 80 were males and 25 were females. The patients' age ranged from 35-85 years and they had a mean age of  $59.67 \pm 15.50$  years. The mean age of the male patients was  $61.22 \pm 15.75$  years, while that of the female patients was  $54.72 \pm 13.80$  years. The control group ( $n=210$ ) had 160 males and 50 females within an age range of 40-82 years (mean  $61 \pm 12$ ) with the males having a mean age of  $61 \pm 13$  years and females  $60 \pm 12$  years. Among the patients, 49.5% (52/105) were educated up to General Certificate of Education - Ordinary Level while 40.4% (82/210) of the control group were educated up to the same level.

In the sample, 82 (82/105, 78.1%) patients and 102 (102/210, 48.5%) controls had consumed alcohol at some point during their life. The overall OR for alcohol consumption was 3.77, with a 95% CI of 2.20-6.45. The risk was statistically significant ( $p=0.000$ ). Twenty-four patients claimed that they do not drink alcohol anymore but were former alcohol consumers. Fifty-eight patients were current alcohol consumers. The former alcohol consumers had a lower risk of developing OSCC compared to the current consumers. Both former and current alcohol consumption showed a significant association with oral cancer (Table 1).

There was a linear association between the duration of alcohol intake and OSCC. Of the total population, 23 patients claimed to have consumed alcohol for more than 20 years. Patients who had consumed alcohol for more

Table 1. Association between Alcohol Consumption and duration with OSCC

	Patients		Controls		Odds Ratio (95% CI)
	N	%	N	%	p value
Alcohol usage					
Former	24	22.8	48	22.8	2.34 (1.20-4.56) $p=0.01$
Current	58	55.2	54	25.7	5.04 (2.81-9.03) $p<0.05$
Never	23	21.9	108	51.4	1
Duration of alcohol consumption					
< 10 years of alcohol	27	25.7	39	18.5	3.25 (1.67-6.32) $p<0.05$
10-20 years of alcohol	32	30.4	40	19.0	3.75 (1.96-7.17) $p<0.05$
>20 years of alcohol	23	21.9	23	10.9	4.69 (2.25-9.76) $p<0.05$
No consumption	23	21.9	108	51.4	1

Table 2 Association between the Types of Alcohol and OSCC

Alcohol type	Patients		Controls		Odds Ratio (95% CI) p value
	N	%	N	%	
Beer	25	23.8	34	16.1	3.45 (1.74-6.84) p<0.05
Wine	6	5.7	16	7.6	1.76 (0.62-4.98) p=0.282
Liquor	33	31.4	42	20	3.68 (1.94-7.00) p<0.05
Kasippu	18	17.1	10	4.7	8.45 (3.45-20.67) p<0.05
None	23	21.9	108	51.4	1

Table 3. Association between Combined Use of Alcohol, Smoking, and the Betel Chewing with OSCC

Type	Patients		Controls		Odds Ratio (95% CI) p value
	N	%	N	%	
Combined use of smoking, alcohol and chewing betel	50	47.6	59	28	27.54 (6.41-118.19) p=0.000
Not smoking or using alcohol or chewing betel	2	0.01	65	30.9	1
Combined use of smoking and alcohol	66	62.8	77	36.6	5.67 (2.90-11.07) p=0.000
Not smoking or using alcohol	13	12.3	86	40.9	1
Combined use of alcohol and chewing betel	64	60.9	79	37.6	13.12 (5.01-34.32) p=0.000
Not using alcohol and chewing betel	5	0.02	81	38.5	1

than 20 years had a greater risk (OR=4.69) of developing OSCC compared to the people who had consumed alcohol for less than ten years (OR=3.25) (Table 1).

Out of the total patients who consumed alcohol, 33 claimed that they consumed hard liquor while 25 claimed to consume beer. When considering the type of ethanol, wine consumption showed the lowest risk (OR=1.76), although the data were not statistically significant (p=0.282). Among patients those who consumed the locally-made illicit liquor (Kasippu)(18/105) had the greatest risk (OR=8.45; p<0.05) of developing OSCC (Table 2). People who consumed beer (OR=3.45) and liquor (OR=3.68) shared almost an equal risk of developing OSCC (p<0.05).

When considering the 3 main risk factors together, 47.6% (50/105) of patients were engaged in smoking, consuming alcohol and using smokeless tobacco, while among the controls, the consumers of all three risk factors were 28% (59/210). The patients who smoked and consumed alcohol were 62.8% (66/105), while was 60.9% (64/105) combined the use of alcohol and betel chewing. The OR was statistically significant and was 27.54 for the combination of all three risk factors together. The combination of alcohol and smoking showed a lower risk (OR = 5.67) compared to the combined use of alcohol and betel chewing (OR = 13.12) (Table 3).

## Discussion

Sri Lanka accounts for the world's 5<sup>th</sup> place and the 4<sup>th</sup> place among Asian countries in the incidence of lip and oral cavity cancers (Bray et al., 2018). Oral cancer is more frequent in men than in women (Vithana et al., 2021).

According to the National Cancer Control Programme of Sri Lanka, oral cancer is the commonest type of cancer found among Sri Lankan males, and the eighth most common type among females (NCCP, 2014). According to data published by the National Institutes of Health in 2018, male patients have a two to six times greater risk than female patients which could be due to their higher intake of tobacco and alcohol (NIH, 2018).

Alcohol has gained attention as a significant risk factor for oral cancer (Ribeiro et al., 2015). Furthermore, it has shown a synergistic cancer-promoting effect with tobacco and betel quid. Ethanol and its metabolites such as acetaldehyde are known carcinogenic agents present in alcoholic beverages (Cancer, 2010; Schwartz et al., 2001). It has been suggested that alcohol alters cellular metabolism and enhances the entry of carcinogenic substances into exposed cells (McCoy, 1978). However, the impact of use of alcohol alone on carcinogenesis is debatable. This may be due to the combined intake of tobacco and alcohol by most of the study subjects (Ram et al., 2011).

The present study showed that current alcohol consumers have a higher risk of having OSCC (OR=5.04; 95% CI=2.81-9.03; p<0.05) compared to former drinkers (OR=2.34; 95% CI=1.20-4.56; p=0.01). However, a study conducted in Italy and Switzerland found that the risk of having an OSCC is higher among former drinkers compared to current drinkers (OR=1.9; 95% CI=1.3-2.7) (Franceschi et al., 2000). These contrasting findings may be due to the fact that the people in the former drinking category had consumed excessive amounts of alcohol for longer periods prior to cessation. This demonstrates the importance of considering the duration and quantity of

alcohol consumed by the individual in addition to their drinking status at the time of the study. Further type of alcohol may also have contributed to these findings.

Studies have shown that the risk increases in individuals when the amount of alcohol drinking increases (Bagnardi et al., 2001; Wynder and Stellman, 1977; Silverman Jr and Griffith, 1972). A study carried out in Brazil has highlighted that the risk of oral cancer increases with the increasing frequency of alcohol consumption (OR=3.25; 95% CI=1.03-10.22) (Andrade et al., 2015). A similar finding was published in a study conducted in Spain. The study observed an increased risk for OSCC in heavy drinkers (OR=5.04; 95% CI=1.84-13.85) (Moreno-Lopez et al., 2000). This is in keeping with the findings of the present study where the relative risk of having an OSCC was higher in those who had consumed alcohol for a longer duration.

In the present study, we also noted that those who consume locally-made illicit liquor (Kasippu) have a higher risk of having OSCC (OR=8.45; 95% CI=3.45-20.67;  $p < 0.05$ ). Kasippu is a locally made hard liquor that is made by adding different locally found ingredients without adhering to a standard protocol; thus, the alcohol content may vary. A Brazilian study showed that the consumption of distilled beverages was associated with oral cancer (OR=5.87; 95% CI=3.65-9.44) (Andrade et al., 2015). A pooled analysis of three case-control studies done in the United States of America, Italy, and China emphasized that the risk of OSCC is high in locally made distilled alcohol products because of the higher alcohol content in these drinks (Macfarlane et al., 1995). However, some studies have that the quantity and the duration of consumption of alcohol are more important than the type of alcohol consumed (Reidy et al., 2011; McDowell, 2006).

The present study also revealed that smoking, alcohol and betel chewing in combination has a very high risk of developing oral cancer (OR=27.54; 95% CI=6.41-118.19,  $p < 0.01$ ) compared to the consumption of alcohol alone (OR=3.77; 95% CI=2.20-6.450,  $p = 0.000$ ). A Brazilian study has also shown a risk increase by almost ten times in the development of OSCC (OR=9.65; 95% CI=1.57-59.08) when smoking, alcohol and betel are used in combination (Andrade et al., 2015; Edirisinghe et al., 2022). The association between the risk habits of betel quid chewing, tobacco and alcohol use was demonstrated in a recent study conducted in Sri Lanka which also showed a combined synergistic effect of the three habits (Sumithrarachchi et al., 2021). In the present study, it was found that the simultaneous consumption of tobacco and alcohol significantly increases the risk of oral cancer. Similarly, a study conducted in New York City has highlighted that the simultaneous consumption of tobacco and alcohol increases the risk of oral cancer by six to fifteen times (Cruz et al., 2007).

It is important to mention that it is difficult to measure the amount of consumption of alcohol by individuals because of the differences in the frequency of intake, the variation of the alcohol level of the drinks consumed by individuals and recall bias. Although the present study has

several limitations inherent to case-control studies such as recall bias, the advantages include the sample size, heterogeneity of distribution of exposures and a detailed assessment of lifestyle habits. A future study could also focus on the histological staging of OSCC and the site of the cancer associated with alcohol consumption. The association between gender and carcinogenic risk of alcohol consumption was not assessed in the present study and is a potential question to be answered in future studies.

In conclusion, there is a dose-dependent effect of alcohol consumption on OSCC with the locally-made illicit liquor (Kasippu) having the greatest risk for the development of OSCC. A study conducted in Sri Lanka to assess awareness about oral cancers among people revealed that only 43% were aware of oral cancers. In addition, the participants had less awareness about the association between betel chewing and OSCC as compared to that between oral cancer and tobacco smoking as well as alcohol consumption (Sumithrarachchi et al., 2021). Therefore, oral cancer prevention programs in Sri Lanka need to be strengthened to address risk factors including alcohol consumption as the public education and control of alcohol consumption appears to reduce the risk of developing OSCC.

## Author Contribution Statement

Edirisinghe ST1 (MBBS/PhD), Conceived and designed the analysis; Collected the data; Contributed data or analysis tools; Performed the analysis; Wrote the paper. Devmini KA (MBBS), Collected the data and data entry, Wrote the paper; Pathmaperuma SD (MBBS), Collected the data and data entry Wrote the paper; Weerasekera M (MBBS/PhD), Conceived and designed the analysis; Collected the data; Contributed data or analysis tools; Performed the analysis; Proofread the paper; De Silva DK (MBBS), Conceived and designed the analysis; Performed the analysis; Wrote the paper; Liyanage I (MBBS), Collected the data and data entry; Niluka M (MBBS), Collected the data and data entry; Madushika K (MBBS), Collected the data and data entry; Deegodagamage S1 (MBBS), Collected the data and data entry; Wijesundara C (MBBS), Collected the data and data entry; Rich AM (BDS/PhD), Proofread the paper; De Silva H (BDS/PhD), Proofread the paper; Hussaini HM (BDS/PhD), Proofread the paper; De Silva K (MBBS/MD), Proofread the paper; Yasawardene SG (MBBS/PhD) Conceived and designed the analysis; Collected the data; Contributed data or analysis tools; Performed the analysis; Proofread the paper.

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### Ethical approval

Ethical approval for the study was granted by the Ethics Review Committee, University of Sri Jayewardenepura (29/16), Colombo South Teaching Hospital and Apeksha Hospital, Maharagama.

### Conflicts of interest

None

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