Risk factors for cancer of the buccal and labial mucosa in Kerala, southern India

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Abstract

Study objective—The aim was to investigate risk factors for cancer of the buccal and labial mucosa in Kerala, southern India.

Design—The investigation was a case-control study.

Setting—Regional Cancer Centre, Trivandrum, Kerala, and local teaching hospitals.

Participants—Cases were all those registered with oral cancers at the Regional Cancer Centre during 1983 and 1984 (n=414). Controls (n=895) were selected from admissions to the cancer centre who were found to have non-malignant conditions, or from patients attending outpatients in teaching hospitals of Trivandrum medical college with non-malignant conditions.

Measurements and main results—The risk in males of the following habits was investigated: pan (betel)-tobacco chewing, bidi and cigarette smoking, drinking alcohol, and taking snuff. Only pan-tobacco chewing was investigated in females as very few indulged in other habits. Among males predisposing effects were found for pan-tobacco chewing ($p < 0.001$), bidi smoking ($p < 0.001$), drinking alcohol ($p < 0.001$), and taking snuff ($p < 0.01$). As in males, pan-tobacco chewing also had a predisposing effect in females ($p < 0.001$). Duration of use was a better predictor of risk than either daily frequency of use or total lifetime exposure, both for pan-tobacco chewing (especially if the habit started before age 21 years) and bidi smoking. However, there were also very high risks associated with the current occasional use of both factors. Pan-tobacco chewing was the most important risk factor, with relative risk of 13.24 with 31-40 years' use, and 37.75 with >40 years' use among males. Corresponding relative risks in females were 21.30 and 54.93. No effect of cigarette smoking was observed (relative risk 0.64, $p > 0.1$).

Conclusions—A substantial majority of cases of buccal and labial cancers are attributable to chewing pan-tobacco. This has obvious implications for instituting preventive measures.

constitutes 10.85% and 6.84% of all cancers in men and women respectively. It accounts for more than 50% of all intraoral cancers in southern India.² Cancer of the labial mucosa accounts for 0.8% of all cancers seen in our centre.

In the past, risk factors for buccal and labial mucosal cancers have been studied as part of a spectrum of cancers incorporating other intraoral, pharyngeal, laryngeal, and oesophageal cancers. The anatomical sites considered in these studies varied considerably.³⁻¹⁴ The IARC working group on the evaluation of carcinogenic risk to humans from tobacco habits other than smoking noted that it was not always clear which specific sites were included.¹⁵

It is possible that the already known risk factors like tobacco chewing, smoking, and alcohol in oral cancers may vary in their relative importance as potential risk factors for cancers of specific intraoral subsites. The fact that cancer of the buccal mucosa is a relatively uncommon intraoral cancer in those communities indulging predominantly in cigarette smoking and/or alcohol¹⁶ also suggests a varying importance of known risk factors in inducing malignancy in different intraoral subsites.

The present study addresses the epidemiology of cancers occurring in the buccal and labial mucosa (hereafter referred to as the buccal mucosa for convenience) in Kerala, India. This state on the southern western coast of India, with a population of 30 million, has three main religious groups: Hindus (59%), Muslims (21%), and Christians (19%). It has the highest literacy rate in the country and the lowest infant mortality, birth rate, and death rate.¹⁷

Methods

A hospital based cancer registry was established in the regional cancer centre, Trivandrum, in 1982, with aid from the Indian Council of Medical Research (ICMR) as part of the National Cancer Registry Project of India. Since then this registry has collected information on all cases of cancer seen at the Regional Cancer Centre and the teaching hospitals of the Medical College, Trivandrum. The data collected include demographic, educational, marital, occupational, socioeconomic, and lifestyle data in addition to clinical details and follow up information, in a standard form.

Four hundred and fourteen patients with cancer of the buccal mucosa (ICD.0 codes 145.0, 1 and 6) and labial mucosa (ICD.0 codes 140.3 and 4) registered by the cancer registry during 1983-1984 constitute the cases for this study. The habit history of these was recorded by direct interviewing of the patients by trained social

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Cancer of the buccal mucosa is the commonest malignancy among males and the third most common among females in Kerala, India.¹ At the Regional Cancer Centre, Trivandrum, it

workers, as standard practice of the registry. The habits of interest were pan chewing, pan-tobacco chewing, bidi smoking, cigarette smoking, alcohol and nasal snuff inhalation. The data collected were the daily frequency, the total duration in years, and the age at which the habits were initiated.

Eight hundred and ninety five hospital based controls were selected from patients with non-malignant conditions who initially came to the cancer centre to exclude a diagnosis of malignancy in sites other than head and neck, and from among those attending the outpatient divisions of the teaching hospitals of the medical college with respiratory, intestinal, and genitourinary infections during 1983–1984. The detailed habits of these individuals were collected by the social workers by personal interview in the same form used by the cancer registry.

Pan chewing is defined as chewing of a quid containing fresh betel leaves (*Piper betel*), smeared with aqueous shell lime (calcium hydroxide) and sliced fresh or dried areca nut (*Areca catechu*). Pan-tobacco chewing involves the addition of locally cured dried tobacco leaves and/or stem. No other condiments are added to this mixture in Kerala. Hence the betel quid chewed here is an essentially simpler one than that of northern India, where many spices and other

condiments are added to the basic quid. Bidi is a local cigarette made by wrapping less than 0.5 g of coarse tobacco dust in a dry temburni (*diospyros melanoxylon*) leaf.

The alcoholic beverages used are mainly a locally fermented and distilled sap from palm trees called toddy and/or another locally brewed liquor called "arrack" (approximately 40–60% ethanol). Alcohol consumption in this study has been quantified in terms of frequency of drink per day rather than in millilitres.

The snuff used is home ground tobacco powder, a pinch of which is deeply inhaled into the nostrils.

DATA ANALYSIS

Statistical analysis was by unconditional logistic regression producing odds ratio relative risk (RR) estimates and deviance χ^2 tests for effect.¹⁸ All estimates and tests were adjusted for age. In addition, for males religion was also adjusted for (see results section below) and a multivariate model of risk was constructed by a forward stepwise procedure, eliminating those habits which had no effect on risk when adjusted for other habits. Dose-response was evaluated by tests for trend.¹⁸ Interactions among the effects of risk factors and between risk factors and age were also assessed.

For a small number of the subjects who did indulge in the various habits, but not regularly, the exact daily frequency, duration and age at starting was unknown. Consequently, these occasional users were excluded from the primary analyses of effects of frequency and duration on risk, the effect of occasional use being assessed separately.

Results

Table I shows frequencies of cases and controls by age, sex, and religion. Very few subjects (six males and six females) chewed pan alone and the only

Table I Frequency distribution of cases and controls by age, sex, and religion.

Factor	Category	Cases	Controls	Total
Age	< 40	21	58	79
	40–49	75	189	264
	50–59	130	306	436
	60–69	115	236	351
	70+	73	106	179
Sex	Male	250	546	796
	Female	164	349	513
Religion	Hindu	269	544	813
	Christian	92	201	293
	Muslim	53	150	203

Table II Frequencies, relative risks and results of significance tests with respect to habit frequencies.

Factor	Category	Cases	Controls	RR	(95% CI)	p ^a	p(trend) ^b
(a) Males							
Pan-tobacco	Never	37	360	1.00	—	p<0.001	<0.001
	<5 per day	59	61	9.33	(5.60, 15.22)		
	5-9 per day	75	80	9.04	(5.65, 14.46)		
	10+ per day	69	40	16.36	(9.66, 27.70)		
Bidi	Never	125	402	1.00	—	p<0.001	<0.001
	≤10 per day	51	65	2.41	(1.57, 3.68)		
	11-20 per day	43	55	2.50	(1.59, 3.94)		
	21+ per day	17	20	2.81	(1.41, 5.57)		
Cigarette	No	235	499	1.00	—	NS	NS
	Yes	13	46	0.64	(0.33, 1.22)		
Bidi and cigarette	Never	203	459	1.00	—	NS	NS
	≤10 per day	17	33	1.28	(0.68, 2.36)		
	11-20 per day	16	24	1.64	(0.84, 3.21)		
	21+ per day	12	30	0.93	(0.46, 1.87)		
Alcohol	Never	165	438	1.00	—	p<0.001	NA
	1+ per day	59	71	2.18	(1.46, 3.25)		
Snuff	No	232	532	1.00	—	p<0.001	NA
	Yes	12	7	3.98	(1.53, 10.34)		
(b) Females							
Pan-tobacco	Never	19	168	1.00	—	p<0.001	<0.001
	<5 per day	36	92	3.71	(1.99, 6.99)		
	5-9 per day	72	63	10.83	(5.96, 19.62)		
	10+ per day	35	22	14.24	(6.86, 29.50)		

RR = relative risk; CI = confidence interval; NA = not assessed

^a Global test for a difference in risk among the categories.

^b Test on one degree of freedom for linear trend in risk.

habit indulged in by females in substantial numbers was pan-tobacco chewing. Risk was therefore analysed separately for males and females; in the latter case we examined only effects associated with pan-tobacco chewing and omitting chewing of pan alone from risk analysis. Muslim males were at lower risk than Hindu or Christian males, so religion and age were adjusted for in all analyses of the male data. This effect was not observed in the females, so analyses of the female data were adjusted for age only.

Excluding occasional users, numbers of cases and controls, accompanied by age adjusted (and religion adjusted for males) relative risks, and results of significance tests in relation to frequency of habits are shown in table II. In males, predisposing effects were observed of pan-tobacco chewing, bidi smoking, drinking alcohol, and taking snuff. For females, a predisposing effect of pan-tobacco chewing was observed.

The corresponding results for durations of habits are shown in table III. Snuff does not feature in the table as the small number with ascertainable durations render further detailed analysis inadvisable. Results were very similar to those for habit frequencies, showing significant positive associations with risk of pan-tobacco chewing, bidi smoking, and alcohol consumption.

Effects of occasional use are shown in table IV. Significant predisposing effects of occasional use of pan-tobacco, bidi, and alcohol were observed in males, the effects of pan-tobacco and bidi being particularly strong. Although an increased risk was observed in association with occasional pan-tobacco chewing in females, this did not reach statistical significance and the estimate is based on only six subjects positive for the risk factor.

Table V shows relative risks associated with late adoption of the habit (age 21 or over), with analysis restricted to those with the relevant habit. The results are much as expected, a later starting

Table III Frequencies, relative risks and results of significance tests with respect to habit durations (in years).

<i>Factor</i>	<i>Category</i>	<i>Cases</i>	<i>Controls</i>	<i>RR</i>	<i>(95% CI)</i>	<i>p^a</i>	<i>p(trend)^b</i>
(a) <i>Males</i>							
Pan-tobacco	Never	37	360	1.00	—	p < 0.001	< 0.001
	≤ 10 per day	11	13	6.90	(2.83, 16.81)		
	11–20 per day	35	55	5.80	(3.33, 10.11)		
	21–30 per day	39	49	7.70	(4.43, 13.38)		
	31–40 per day	48	40	13.24	(7.51, 23.32)		
	> 41 per day	70	25	37.75	(19.49, 73.12)		
Bidi	Never	125	402	1.00	—	p < 0.001	< 0.001
	≤ 20 per day	17	22	2.68	(1.35, 5.30)		
	21+ per day	94	118	2.47	(1.74, 3.49)		
Cigarette	Never	235	499	1.00	—	NS	NS
	≤ 20 per day	4	18	0.60	(0.19, 1.82)		
	20+ per day	9	28	0.66	(0.30, 1.44)		
Bidi and cigarette	Never	203	459	1.00	—	NS	NS
	≤ 20 per day	10	23	1.19	(0.54, 2.59)		
	21+ per day	35	64	1.27	(0.81, 2.00)		
Alcohol	Never	165	438	1.00	—	p < 0.001	< 0.001
	≤ 21 per day	35	24	1.48	(0.71, 3.07)		
	21+ per day	47	17	2.50	(1.59, 3.93)		
(b) <i>Females</i>							
Pan-tobacco	Never	19	168	1.00	—	p < 0.001	< 0.001
	≤ 10 per day	11	48	1.79	(0.78, 4.07)		
	11–20 per day	22	49	3.80	(1.85, 7.75)		
	21–30 per day	38	48	7.74	(4.00, 15.00)		
	31–40 per day	33	19	21.30	(9.59, 47.36)		
	41+ per day	39	13	54.93	(21.18, 142.42)		

RR = relative risk; CI = confidence interval

^a Global test for a difference in risk among the categories.

^b Test on one degree of freedom for linear trend in risk.

Table IV Frequencies, relative risks, and results of significance tests with respect to occasional indulgence in habits.

Factor	Category	Cases	Controls	RR	(95% CI)	p
(a) Males						
Pan-tobacco	Never	37	360	1.00	—	< 0.001
	Occasional	10	5	21.41	(6.54, 70.08)	
Bidi	Never	125	402	1.00	—	< 0.001
	Occasional	14	4	11.25	(3.53, 35.78)	
Cigarette	Never	235	494	1.00	—	NS
	Occasional	2	1	6.69	(0.55, 80.11)	
Bidi and cigarette ^a	Never	203	459	—	—	NS
	Occasional	2	0	—	—	
Alcohol	Never	165	438	1.00	—	< 0.05
	Occasional	26	37	1.81	(1.05, 3.12)	
Snuff	Never	232	532	1.00	—	NS
	Occasional	6	7	2.28	(0.74, 7.03)	
(b) Females						
Pan-tobacco	Never	19	168	1.00	—	NS
	Occasional	2	4	5.42	(0.80, 36.27)	

RR = relative risk; CI = confidence interval

^a Estimation impossible due to sparse data. Not significant by Fisher's exact test.

Table V Relative risks and significance of effect on risk of adopting after age 21 (relative to baseline of before age 21—subjects with habit only).

Habit	RR	95% CI	p
(a) Males			
Pan-tobacco	0.19	(0.11, 0.30)	<0.001
Bidi	0.31	(0.17, 0.53)	<0.001
Cigarette	0.83	(0.20, 3.44)	>0.1
Bidi and cigarette	0.48	(0.21, 1.05)	0.1 > p > 0.05
Alcohol	0.41	(0.19, 0.88)	<0.05
Snuff ^a	4.3 × 10 ⁻¹⁷	(8.6 × 10 ⁻³² , 2.3 × 10 ⁻⁴)	<0.05
(b) Females			
Pan-tobacco	0.11	(0.05, 0.20)	<0.001

RR = relative risk; CI = confidence interval

^a Very sparse data.

age yielding a reduced risk, and bearing out the duration effects in table III. The results for snuff should not be overinterpreted as the data were sparse (for example, only one control started before age 21).

Table VI gives the results of analysis of total lifetime habits, that is, the product of frequency

and duration, excluding occasional users as before. Results were similar to those for frequency and duration. Examination of residual deviances showed that the effects of lifetime exposures were no more significant predictors of risk than daily frequencies or durations. Again, results for snuff should be interpreted with caution.

The combined effects of frequencies and durations, and of different habits, were further assessed by a forward stepwise logistic regression, eliminating factors no longer significant when adjusted for the effects of other factors. The model finally arrived at contained effects of pan-tobacco duration, bidi duration, and alcohol and snuff use. Results are as shown in table VII.

Neither of the effects of snuff or alcohol use were significant when adjusted for the other, although both were nearly so. Given the small numbers of snuff users and the likelihood of misclassification of alcohol use, it is inadvisable to rule out either habit as a risk factor.

Table VI Frequencies, relative risks, and results of significance tests with respect to total lifetime exposures.

Habit	Case	Control	RR	(95% CI)	p	p (trend)
(a) Males						
Pan-tobacco						
Never	37	360	1.0	—	<0.001	<0.001
<70 chewing years	28	43	6.26	(3.46, 11.29)		
70–139 chewing years	41	47	8.41	(4.86, 14.53)		
140+ chewing years	134	91	14.47	(9.23, 22.69)		
Bidi						
Never	125	402	1.0	—	<0.001	<0.001
<400 bidi years	51	61	2.66	(1.73, 4.08)		
400–499 bidi years	12	27	1.40	(0.68, 2.89)		
500+ bidi years	48	52	2.86	(1.82, 4.49)		
Cigarette						
Never	235	494	1.0	—	NS	NS
<200 cigarette years	6	20	0.78	(0.30, 2.01)		
200+ cigarette years	7	26	0.55	(0.23, 1.30)		
Bidi and cigarette						
Never	203	459	1.0	—	NS	NS
<600 unit years	32	61	1.34	(0.83, 2.14)		
600+ unit years	13	26	1.08	(0.54, 2.16)		
Alcohol						
Never	165	438	1.0	—	<0.001	<0.001
<20 drinking years	8	7	3.79	(1.30, 10.79)		
20+ drinking years	52	66	1.842	(1.33, 3.09)		
Snuff						
Never	232	532	1.0	—	<0.005	<0.001
≤100 unit years	7	1	15.66	(1.95, 125.28)		
100+ unit years	5	6	1.95	(0.57, 6.61)		
(b) Females						
Pan-tobacco						
Never	19	168	1.0	—	<0.001	<0.001
<70 chewing years	17	79	1.89	(0.91, 3.88)		
70+ chewing years	37	48	7.49	(3.86, 14.53)		
140+ chewing years	89	50	19.41	(10.30, 36.57)		

RR = relative risk; CI = confidence interval

Table VII Relative risk estimates among males and results of significance tests for the four factors resulting from forward stepwise regression.

Factor	Category ^a	RR ^b	(95% CI)	p ^b
Pan-tobacco duration	Never	1.00	—	<0.001
	≤10 years	7.12	(2.77, 18.24)	
	11–20	4.46	(2.44, 8.14)	
	21–30	6.44	(3.53, 11.74)	
	31–40	11.15	(5.95, 20.87)	
	40+ years	29.02	(14.20, 59.28)	
Bidi duration	Never	1.00	—	<0.01
	≤20 years	2.90	(1.26, 6.64)	
	21+ years	1.66	(1.06, 2.60)	
Alcohol	Never	1.00	—	0.1 > p > 0.05
	Ever	1.60	(0.99, 2.57)	
Snuff	Never	1.00	—	0.1 > p > 0.05
	Ever	2.93	(0.98, 8.77)	

RR = relative risk; CI = confidence interval

^a Excluding occasional users.^b All estimates and tests adjusted for the effects of the remaining three factors.

In males we observed significant interactions with age of pan-tobacco duration ($p < 0.001$) and alcohol duration ($p < 0.05$). Age specific relative risks for these variables are given in table VIII. Although in those aged under 50 the confidence intervals are wide, the relative risks are indubitably larger than in those aged 50 or more.

In females, significant interactions with age were observed for frequency and duration ($p < 0.05$ in both cases) of pan-tobacco chewing. Again, the excess risk conferred by the habit was greater in the younger age group (see table IX).

To examine further the interactions of age and pan-tobacco duration in males and females, we excluded those who did not have the habit or who only occasionally chewed, and tested the interaction after adjustment for age at the start of the habit. In both males and females, the

Table VIII Age specific relative risks associated with durations of pan-tobacco chewing and alcohol drinking in males.

Risk factor	Category	Age <50		Age 50+	
		RR	(95% CI)	RR	(95% CI)
Pan-tobacco duration (years)	Never	1.00	—	1.00	—
	≤10	14.21	(3.56, 56.60)	8.61	(2.16, 34.32)
	11–20	22.90	(7.46, 70.23)	3.26	(1.56, 6.77)
	21–30	71.30	(19.37, 262.49)	3.53	(1.81, 6.85)
	31–40 ^a	—	—	8.50	(4.77, 15.13)
	41+ ^a	—	—	26.29	(13.70, 50.40)
Alcohol duration (years)	Never	1.00	—	1.00	—
	≤20	2.77	(0.95, 8.04)	0.92	(0.32, 2.64)
	21+	8.18	(2.79, 23.95)	1.89	(1.13, 3.14)

RR = relative risk; CI = confidence interval

^a Inestimable in younger group due to lack of data.**Table IX** Age specific relative risks associated with frequency and duration of pan-tobacco chewing among females.

Risk factor	Category	Age <50		Age 50+	
		RR	(95% CI)	RR	(95% CI)
Pan-tobacco daily frequency	Never	1.00	—	1.00	—
	<5	17.85	(3.24, 98.09)	2.59	(1.31, 5.11)
	5–9	100.28	(17.44, 576.35)	6.45	(3.39, 12.24)
	10+	53.62	(6.94, 414.18)	10.55	(4.84, 23.00)
Pan-tobacco duration (years)	Never	1.00	—	1.00	—
	≤10	21.39	(2.76, 165.55)	0.76	(0.25, 2.26)
	11–20	30.08	(3.97, 227.41)	2.03	(0.88, 4.62)
	21–30	217.89	(25.98, 1827.31)	2.99	(1.40, 6.39)
	31–40 ^a	—	—	12.19	(5.53, 26.89)
	41+ ^a	—	—	31.31	(12.35, 79.37)

RR = relative risk; CI = confidence interval

^a Inestimable in younger group due to lack of data.

interaction of duration with age lost its significance. It therefore seems likely that these interactions are in effect products of the substantial increase in risk conferred by starting the habit at or before age 20 years (see table V). This was also the case for the interaction of age with duration of alcohol consumption in males.

Interactions among habits were assessed by first dichotomising habits to 'never/ever' to avoid the difficulties of interpretation and insensitivity arising from sparse data. The only two factor interaction observed was between pan-tobacco chewing and bidi smoking ($p < 0.05$). As can be seen from table X, the cumulative effect of both habits is represented by a relative risk of 21.46 (relative to a baseline of neither habit), and not 60.12, the product of 14.28 and 4.21 which we would expect were there no interaction.

No significant three factor interactions were observed. To illustrate the cumulative effect on risk of three predisposing factors in the absence of such an interaction, table XI shows relative risks by pan-tobacco chewing, bidi smoking, and alcohol use. The baseline group is made up of those never indulging in any of the three habits.

In considering risk stratified by several factors, note that with sufficient data to quantify the habits, the relative risk gradients would almost certainly be larger.

Discussion

This study reveals pan-tobacco chewing to be the major risk factor for cancer of the buccal and labial mucosa. Previous case-control studies in various parts of India on cancer of the buccal and labial mucosa have resulted in relative risk estimates ranging from 3.9 to 39.^{5 8 19 20} Relative risk

estimates here suggest that daily frequency and early age of starting pan-tobacco chewing are the major predictors of risk. Dose-response relationships between relative risk and frequency/duration of chewing have not previously been examined in detail in India. The working group of the IARC was able to calculate the dose-response relationship between daily frequency of chewing and oral cancer risks in only two studies reported from India.^{7 21} This is probably the first study from India which examines the dose-response in terms of duration of chewing in years and total life time exposure (chewing years = the product of daily frequency and duration of chewing in years).

Buccal mucosa seems to be the site at greater risk of malignancy in pan-tobacco chewers as compared to other intraoral sites. This is suggested by the higher proportion of buccal mucosa cancers in Bangalore, Madras, and Singapore Indians¹⁶ (who are ethnically south Indians), where betel quid chewing is more common than in northern India. In Bombay, Poona and Nagpur, the tongue is the predominant site of intraoral cancer.¹⁶ The highest age adjusted rate for buccal mucosal cancers is reported in Madras for males and in Bangalore for females. The dominant habit in these areas is chewing pan with tobacco. The predominant occurrence of malignancy in the buccal mucosa among chewers is probably due to the constant contact with the quid while chewing. In early studies, the highest relative risks have been related to retaining the quid during sleep.⁷

It is likely that carcinogens in the quid act as contact carcinogens. In spite of many studies evaluating the carcinogenicity of various betel quid constituents, the carcinogens in the quid have not been unequivocally identified. However these studies indicate that all the components of pan-tobacco with the probable exception of betel leaf are likely to contribute to oral carcinogenicity.¹⁵ Nicotine contributes to the carcinogenic potential of tobacco by serving as precursor to many tobacco specific nitrosamines such as NNN (N-nitrosornornicotine) and NNK (4-(methyl nitrosamino)-1-(3-pyridyl)-1-butanone) which have proved their carcinogenicity in experimental animals. Local irritation and the alkalinity induced by lime and some of the arecanut specific nitrosamines like MNPN (3[nitrosoamino] propionitrile) with proven carcinogenicity in animals²² may also contribute to oral neoplastic processes.

The other quid related factors that may modify the carcinogenic potential include the differences in the proportion of various quid components, duration of each chew, and whether the chewer rinses the oral cavity with water after each and/or frequent chews. It is almost impossible to examine the effect of the first mentioned factor, but the latter two should be addressed in future studies. Evaluation of the last factor may have some public health significance.

The finding of an evident interaction between duration of pan-tobacco chewing and age, and the absence of its significance when adjusted for age at adoption of habit, indicate that the effect of the latter is not simply a proxy for duration. There may be a period of particularly high susceptibility to the carcinogenic effect before age 21.

Bidi smoking has emerged as an independent risk factor for cancer of the buccal and labial mucosa in our study. Jussawalla and Deshpande have reported a relative risk of 1.5 for buccal mucosa with smoking.⁸ However, in two earlier case control studies from Madras,^{5 19} the proportion of smokers was higher in controls (47% and 53.7% respectively) compared to cases (26% and 46%). Bidi is the most popular form of tobacco smoked among the lower socioeconomic strata in India, as it is very cheap. The bidi industry is currently promoted by many state governments in India, as a cottage industry, providing employment to many people. Unlike cigarette packs, packs of bidi do not carry the statutory warning on the health hazards of tobacco smoking. A comparative chemical study of bidi with a popular brand of American cigarette without filter revealed that a single bidi delivers about one and a half times the carcinogenic hydrocarbons delivered by a cigarette when it is smoked with two puffs per minute.²³ The daily frequency seems to be the major predictor of risk with bidi smoking also.

Cigarette smoking and combined bidi plus cigarette smoking have not emerged as independent risk factors in this study. It might be speculated that this is due to small numbers, but this seems unlikely in view of the seemingly protective (but non-significant) effect of cigarette smoking. The results indicate a qualitative difference between bidi and cigarette smoke.

Alcohol as a risk factor in oral cancer has not been studied in detail in India. There is only one recent study from India which addresses this question with oral cancer (ICD 140, 141, 143–145).¹⁰ The reported relative risks with alcohol for oral cancer were 3.6, 2.6, 0.9 and 0.4 for those under 40 years of age, 40–49 years, 50–59 years,

and > 60 years of age respectively. The adjusted odds ratio of alcohol consumption in those under 60 years of age ranged from 1.3 and 3.6 and no association was reported between alcohol consumption and oral cancer in those above 60 years of age.

The two earlier case-control studies from Madras, on buccal mucosal and labial cancer, reported the proportion of drinkers among cases as less than 20% but the details were not available for controls so risk estimates were not possible.

Alcohol did not emerge as a particularly strong risk factor of buccal and labial mucosal cancer in our study after adjusting for other factors, but this has to be interpreted with caution as there is a likelihood of underreporting of alcohol habit among our population. Alcohol consumption is considered to be a social evil in Indian society and many have a reluctance to reveal this habit. There is a need for further studies in India into the role of alcohol in cancers of this and other intraoral sites.

Snuff inhalation has emerged as an independent risk factor in our study. This has not been studied in the previous investigations in India. The number of subjects with this habit is limited. Biologically it is difficult to explain how the inhaled snuff comes into contact with buccal and labial mucosa. It is possible that those who use snuff may also smear the oral mucosa unknowingly. It should be borne in mind that the snuff habit is rare and we should prefer to see these results confirmed by other studies before accepting them.

Jayant *et al*⁹ have studied the interaction between chewing and smoking in the aetiology of oral cancer, and Notani¹⁰ has reported the relative risks associated with combined habits of chewing and alcohol with or without smoking. The relative risks were 4.7 with smoking; 2.8 with chewing; 13.1 with smoking and chewing; 10 with alcohol and chewing; 17.8 with alcohol and smoking; and 47.1 for alcohol, smoking and chewing. In this study, chewing was found to be the most important factor, and alcohol to have a marginal effect.

The form of the interaction with age observed for frequency of pan-tobacco chewing among females was surprising, in that the effect was so much stronger among younger women. Possible explanations for this are the small number of cases under 40 years of age, and the likelihood that increased misclassification among the elderly is diluting the effect of the risk factor. The effect of unobserved covariates, for example dietary factors, cannot be ruled out.

While the stepwise analysis indicated that duration of habit was more important than frequency for pan-tobacco chewing and bidi smoking, the high risks conferred by occasional indulgence suggest that there is always an incentive for giving up the habit. The very high risks observed for occasional users remain to be explained.

Finally, it is interesting to consider risks attributable to chewing and smoking respectively. From table X we calculate (using average attributable risks weighted by numbers of cases) that 19% of cases could be prevented by eliminating bidi smoking alone, 73% could be prevented by elimination of pan-tobacco chewing alone, and 85% could be prevented by elimination

Table X Relative risks and frequencies of cases and controls by pan-tobacco and bidi habits in males.

		Pan-tobacco chewing	
		Never	Ever
Bidi smoking	Never	RR	1.00
		(95% CI)	14.28
	Ever	Cases/controls	(8.21, 24.83)
			18/284 103/114
	Never	RR	4.21
		(95% CI)	21.46
	Ever	Cases/controls	(11.94, 38.54)
			19/74 87/65

RR = relative risk; CI = confidence interval

Table XI Combined effects of pan-tobacco chewing, bidi smoking, and alcohol use in males, the baseline group being those with none of the three habits.

		Alcohol use	
		Never	Ever
Bidi smoking	Never	(a) Never chew pan-tobacco	
		RR	2.55
	Ever	(95% CI)	(0.77, 8.40)
			4.06
	Never	(1.80, 9.13)	8.48
			(2.26, 31.79)
	Ever	(b) Ever chew pan-tobacco	
		RR	20.05
	Never	(95% CI)	(9.13, 43.97)
			14.11
	Ever	(7.49, 26.56)	31.37
			(13.13, 74.94)

RR = relative risk; CI = confidence interval

of both habits. These results are tentative, in view of the interaction between the two habits mentioned above. Nevertheless, the indication is that a substantial majority of cases are attributable to chewing of pan-tobacco.

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