SUPREME COURT VOLUME-5

ANNEXURES

SLP (C) No. 16308/2007-Ankur Gutkha Vs Indian Asthama Care Society & Ors-regarding.

Annexe 112

Addiction Biology (2002) 7, 139–146

ARECA NUT SYMPOSIUM

Socio-economic aspects of areca nut use

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Abstract

The socio-economic aspects of areca nut consumption have been overlooked. A narrative review was conducted to establish some of these features of areca nut consumption. Medline, Pubmed and the World Wide Web were searched using the terms: areca nut, betel nut, areca catechu and pan masala. Further analysis was conducted of datasets describing aspects of United Kingdom areca nut sales and consumption. South Asian economies at different stages of development have varying areca nut cultivation practices, employment opportunities and marketing strategies. Attempts at regulation of areca nut import and sales are described. Retail practice among the South Asian communities of the United Kingdom was found to reflect the diverse consumer practices current in their countries of origin. A study of areca nut consumption patterns and motivations among Bangladeshi women resident in East London identified differences between those chewing areca nut in paan with and without tobacco. Further research into the socio-economic aspects of areca nut consumption is needed which should be multidisciplinary in focus, of sound scientific quality and incorporating the opinions of consumers.

Introduction

To discuss socio-economic aspects of areca nut use provides belated recognition of a neglected aspect of a multidimensional behaviour. The main thrust of research into areca nut use has been epidemiological, seeking to identify trends in behaviour and the resulting disease outcomes. Less attention has been given to the social aspects of areca nut consumption. This focus would widen the debate from a disease to a social model of health, recognizing that the determinants of health are broader than individual behaviours. The preventive focus has been upon developing messages for individual consumers, disregarding opportunities to introduce other policies and initiatives that focus upon other determinants of this behaviour. Changing social and economic policies may lead to changing cultivation and marketing practice which will, in turn, affect individual consumption. The search for a preventive message has given inadequate attention to variations in areca nut use. In the United Kingdom the emphasis has been upon understanding a South Asian model of consumption, which is linked to positive sociocultural messages perceived as promoting increased consumption.[1] In other populations consumption could be different, because areca is associated with abundant availability and tradition.[2,3] Current estimates that 10% of the world's population are regular consumers, comprising perhaps 600 million people, suggest the desirability of widening per-

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ISSN 1355-6215 print/ISSN 1369-1600 online/02/010139-08

Carfax Publishing, Taylor & Francis Ltd
DOI: 10.1080/13556210120091518

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spectives. A review was therefore conducted to establish and describe some of the relevant socio-economic features of areca nut consumption.

Methods

This review has two strands. First, a search of existing literature sources was undertaken. Medline and Pubmed were searched using the search terms: areca nut, betel nut, areca catechu and pan masala. In addition the World Wide Web was accessed for a supplementary search focusing upon the production, processing and marketing of areca nut. Secondly, further analysis of data sets which describe aspects of areca nut sales and consumption within the United Kingdom was conducted.[3–5] Reflecting the limited nature of the resources available to describe the socio-economic aspects of areca nut use, the data are presented as a series of case studies.

Results

Changing areca nut cultivation

Areca catechu, of which areca nut is a fruit, is one of the palm species. Palms are one of the oldest flowering plants. Initially native to Malaysia, *A. catechu* is now cultivated widely throughout India, Sri Lanka, Thailand and the Phillipines.[6] Palms offer a multiplicity of uses in a rural agrarian economy. They provide fodder for cattle, edible fruits, building materials, fuel and fibres. Gandhi argued that one species of palm had such a multiplicity of use that its cultivation and harvest would banish poverty from the land, while 1000 separate uses have been identified for the coconut palm.[7] The date palm is considered the staff of life by Moslems, recognizing the importance of the date in the breaking of the fast during Ramadan. The cultivation of *A. catechu* is traditionally described as an intercrop in India, alongside the piper betle, as a forest garden in Sumatra or as part of a private allotment.[8,9] The Nepalese government has introduced initiatives to encourage the private planting of species such as *A. catechu*.[10] This individual method of cultivation was mirrored by the complementary consumption of fresh perishable products, based around individual preferences and tastes.

The liberalization of economic policy, trends to urbanization and increased prosperity have introduced tensions into this traditional scenario. *A. catechu* may now be grown and prepared to meet the needs of a mass market. The development of pan masala, a pre-packaged mix of areca nut, lime and spices, in India has been one response to this need. More pan masala is sold in urban than rural areas.[11] While still individually cultivated, the *A. catechu* tree is found increasingly in privately owned plantations to which a community will have limited access. Communities may well feel exploited and aggrieved, following the loss of a traditional right.[9] The development of areca nut as a market crop has resulted in it replacing other crops such as rice, cultivated previously for subsistence, and the introduction of fertilizer and pesticide applications to improve yields. As a cash crop rather than a rural garden tree, it has to be used to achieve maximum profit. Additional uses have been identified for the nut such as toothpaste, while the husk can be used to make paper or as a source of fuel for electrical power generation.[12,13]

The national and regional companies producing pan masala do so as part of a diverse range of products. The Kothari Group produce Pan Parag, a premium pan masala of fresh areca nuts, cardamom and lime, as part of a product range which includes tobacco products, coconut oil, washing powder, greeting cards, mineral water and writing pens.[14] Suppliers of the raw product for export can be located on the Web, most usually from Indonesia, where it is possible to purchase different qualities of nut in 50- or 85-kg sacks.[15]

The price for harvested areca nut in India appears volatile. In 1997 the government of India was asked to stop imports of areca and prevent smuggling, while by 1999 there were reports of a single premium quality areca nut costing more than a coconut (at 4–5 rupees). In general, the wholesale price appears to have fallen by about 30%, reflecting concerns about the impact of government bans on sales of the processed packaged product either as pan masala or, with tobacco added, as gutkha.[16–18]

Changing employment opportunities

The processing of areca nut in India has traditionally required the employment of a labour force, especially in preparing the nut for consumption. The nut has then been supplied to individual pan wallahs, from whom individual purchases could be made. Changing cultivation practices have resulted in the recruitment of a

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permanent labour force to tend the trees who, in return, receive regular cash wages.[8] The aggressive marketing of pan masala has jeopardized the pan wallahs' livelihoods. There are reports of pan wallahs striking in one Indian town because of reduced profit margins due to the price they pay for areca nut doubling in 12 months.[19] The production of pan masala requires the integration of supplies of individual ingredients in addition to areca nut alone, all of which may be produced in different parts of India. Other industries associated with pan masala production are the spice and silver foil industries. This use of indigenous suppliers enables the Indian pan masala trade association to make the claim that their product is 'swadeshi', signifying a product using domestically supplied ingredients.[20]

One focus of this marketing activity has been on the urban Indian consumer. However, it is estimated that 70% of Indians live in rural areas. Growing rural affluence has led to the creation of a developing market for packaged goods which manufacturers have not been able to meet. This has been ascribed to factors such as inefficiencies in distribution through a fragmented transportation infrastructure. It has been noted that innovative methods of packaging have been introduced to bring down overall costs and create markets. As with products such as hair shampoo and toothpaste, the packaging of pan masala has been changed from containers to 10-g sachets. This change is considered responsible for an increase in sales in India from five million dollars in 1985 to 66 million dollars in 1991.[21]

The regulation of areca nut marketing

The regulation of areca nut and products such as pan masala is extremely difficult. First, the traditional method of consumption has involved the assembly of a quid with ingredients reflecting individual preferences. Secondly, there is a large informal sector, highly decentralized and unlicensed, which operates outside of official control. While the Indian government seeks to impose excise duty upon the sale of pan masala, it is also recognized that there is wholesale evasion of payment of the duty. Recently, pan masala with no tobacco and no more than 10% of areca nut by weight has had the rate of excise duty reduced from 40% to 16%.[22]

Within North America the US Food and Drugs Administration maintains an import 'alert' for areca. Imports are automatically detained if detected on the grounds of it being 'adulterated, containing a poisonous or deleterious substance or unsafe food additives'. There are also reports of attempts to import areca nut by misbranding the product as 'fragrant wood slice'. This 'alert' is supported by the US Department of Agriculture. Commentators note the need for clarification of the status of this alert since US Customs advise that dried betel nuts should pay an import duty of 11 cents per kilo.[23]

Areca nut for personal consumption, 'pure nut, chopped and ready to chew', is readily available to purchase on the World Wide Web from American suppliers, at $10 for 60 g and $25 for 240 g, along with advice on consumption.[24] Possession of areca nut in the Californian public school system is grounds for suspension. The Food and Drugs Administration has also formally expressed a view to the US House of Representatives that individual possession for personal consumption should not be allowed.[25]

Within the United Kingdom, analysis of prepackaged pan masala products has identified a group of problems.[26] First, labelling on the packaging was sometimes non-existent. Instructions as to use were also omitted. Secondly, the labelling might be unsatisfactory in omitting items which, on analysis, were found to be present. Thirdly, products contained non-permitted food additives, sometimes in excessive amounts. Samples of the raw ingredients such as pan leaves were also examined and found to be contaminated with salmonella. The labelling inadequacies would be expected to lead to prosecution of the importer of the product.

The marketing of areca nut in the United Kingdom

Two contrasting studies of retail practice in the United Kingdom have been carried out in London and Leicester.[3,4] The first investigation was carried out in 1996 to map the availability of paan ingredients in the London Boroughs of Tower Hamlets and Newham. First, the addresses of retail outlets selling paan ingredients were mapped. Secondly, a structured interview schedule was administered to the owners of each shop. The overall response rate for the interview was 76%. The schedule contained questions about the type of shop and its opening hours, which paan ingredients were sold, in what quantity and for what price. One hundred and twenty-eight shops

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were identified as selling paan ingredients, 95 in Tower Hamlets and 33 in Newham. Reflecting both this geographic distribution and the dispersal of South Asian communities in London, more shops were owned by members of the Bangladeshi community in Tower Hamlets, while in Newham paan shops were owned predominantly by members of the Indian and Pakistani communities. Shopkeepers supplied products which reflected the expectations of their communities. The shops serving the Bangladeshi community provided a predominantly traditional product, i.e. supplies of loose areca nut, the betle leaf, lime and tobacco which were purchased for individual assembly and consumption. The shops supplying the diverse South Asian populations of Newham had a greater availability of pre-packaged areca nut.

The trade in all paan products (betle leaf, lime, areca nut and tobacco) in Tower Hamlets and Newham was estimated as approximately £1 million per year. Areca sales averaged 64 lbs weight a week for each retailer, with a range of 500–600 pounds weight. The retail price was approximately £1 per pound weight and the estimated weekly sales were £8538. These sales of areca nut were estimated to comprise approximately half of the total weekly sales of all paan products.

The hypothesis that retailers supply the products that they perceive their customers as needing has been supported by a second study carried out in Leicester. Adopting a methodology which mirrored the East London study, 60 retail outlets which served the predominantly Gujerati community and which had the potential to sell paan products were identified. Just over half of these retailers sold paan ingredients. However, in contrast to the East London retailers, the sale of pre-packaged pan masala products was much more common than the sale of individual ingredients. Most shops sold only pre-packaged products, although it was also reported that the Bangladeshi community primarily bought the fresh products. The authors' report suggests that the practice of consuming pre-packaged pan masala would start following visits to the Indian subcontinent. This argument would have less validity in Bangladesh. As the population is largely rural and poor and the transport infrastructure is undeveloped, visitors returning there would find that plain paan products would continue to be preferred.[27]

The prevalence of areca nut consumption

Within the United Kingdom there has been a series of studies of paan chewing, usually with or without the addition of tobacco.[28–33] Estimates of the prevalence of chewing paan vary from 45 to 95%. There are several possible reasons for this variation. First, the samples may not have been drawn from the same South Asian community. Secondly, there may have been variation in the wording of the questions. Studies may ask about experience of use ('have you ever had'), while others have inquired about current use. Questions have not always adequately defined the terms used, failing to distinguish between paan with and without tobacco. Thirdly, there has been variation in sampling practice. These studies are reviewed by Warnakulasuriya in this issue.

Commonly used factors to explain any variation might be age, gender and social class. As suggested above, the data to identify variation around these factors is not always available. Within these constraints:

- Several UK studies suggest that the age of starting to chew areca, usually in paan, is about 10 years.[34–36]
- At age of onset there appears to be no variation in gender, although older people eat more areca.[11]
- Consumption decreases with educational attainment.[11]
- Rural rather than urban communities consume more paan. In this context the rural–urban continuum may be interpreted as a proxy measure of social class, with urban communities being of higher social status.[11]
- The Bangladeshi community is the most socially disadvantaged of the three South Asian communities. Estimates of paan chewing in this community are high, reflecting its adoption by women as a method of consuming tobacco.[34]

The validated prevalence of paan chewing with tobacco by UK resident Bangladeshi women has been investigated.[5] The study design and data collection have been described elsewhere but, in brief, the investigation involved the selection at random of a group of 242 women resident on two local authority housing estates in the London Borough of Tower Hamlets. The study was conducted during 1998. The participants were interviewed using a previously piloted structured

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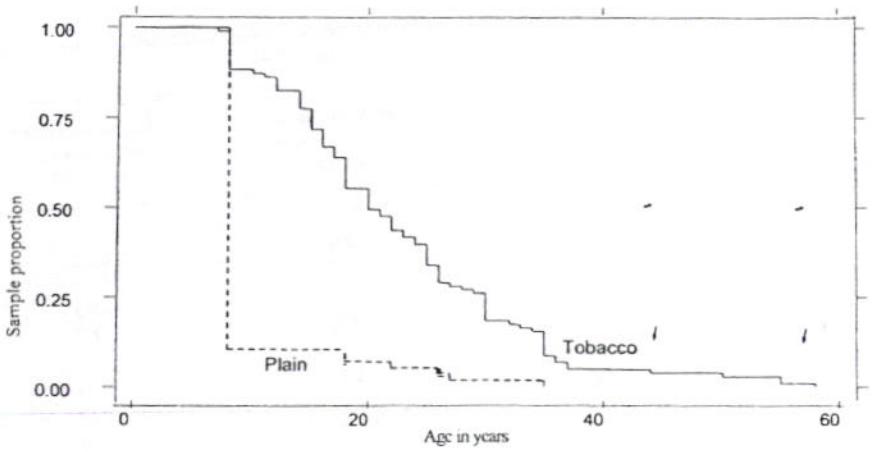

Figure 1. *Retrospective age of starting current paan use (with and without tobacco) in a sample of Bangladeshi women (n = 166)*

interview schedule containing questions about age, aspects of tobacco use and the degree of self-reported dependence upon tobacco. Validation of responses was achieved with carbon monoxide and cotinine concentration analysis. This validation exercise enabled the identification of a group of paan chewers without tobacco.

The outcomes of this study showed that 75% ($n = 169$) of the whole sample were currently chewing either paan without or paan with tobacco. While 49% ($n = 111$) of the whole sample were classified as current paan with tobacco chewers, 25% ($n = 58$) were currently chewing a plain paan with basic ingredients of betle leaf, areca nut and lime without tobacco. Current plain paan chewers had a significantly younger mean age (32.4 years vs. 39.0 years, $t = 4.0194$, $p = 0.000$). The consumption patterns of plain paan chewers and paan with tobacco chewers differed in terms of the mean number of paan chewed daily (2.23 vs. 9.00, $t = 6.905$, $p = 0.000$), the age of starting their current practice (9.7 vs. 21.2 years, $t = 8.342$, $p = 0.000$) and the length of their chewing career (22.7 years vs. 17.9 years, $t = 2.179$, $p = 0.031$).

Figure 1 further clarifies the age at which the current paan chewing practice had commenced. The majority of plain paan chewers had started their current practice at or around the age of 8 years, while the impetus for starting to add tobacco to paan occurred at different times in the respondents' life spans. Fifty per cent of the paan with tobacco chewers had still to start their current tobacco consumption at the age of 20 years. These differences were tested using the log-rank test for equality of survivor functions and were found to be statistically significant.

The plain paan and paan with tobacco chewers also differed in their motivations and practice (Table 1). Plain paan chewers were more likely to cite 'refreshing' as their main reason for chewing whereas those chewing paan with tobacco most commonly cited 'habit' as their reason for chewing. While the paan with tobacco chewers were more likely to have their first paan of the day within 1 hour of waking, for those chewing plain paan this was more likely to happen at least 2 hours after waking. Finally, plain paan chewers reported only a moderate intention to stop this practice, compared to the paan chewers with tobacco who were more likely to report a strong intention to stop adding tobacco to their paan. These differences were tested using the chi-square test for trend and were found to be statistically significant.

Discussion

This paper has reviewed some of the socio-economic aspects of areca nut consumption. Data to support a comprehensive systematic review, reflecting the wide use of areca nut, is lacking. The sources used have their limitations, being dependent upon the geographic location and focus of academic research interest in areca nut and the geographic development of the World Wide Web. An emerging outcome has been the identification of a heterogeneous method of use,

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Table 1. *Paan quid consumption, with and without tobacco. Beliefs and behaviours in a sample of Bangladeshi women (n = 169)*

Questionnaire item	Chew pan quid without tobacco ($n = 58$)	Chew pan quid with tobacco ($n = 111$)	Significance
Reason for chewing (%)			
habit	22.8	61.2	
refreshing	63.2	12.6	
helps teeth and gums	7.0	22.3	0.000
other	7.0	3.8	
First paan quid of the day (%)			
within 1 hour	1.8	39.8	
within 1–2 hours	7.0	26.2	
2+ hours	91.2	34.0	0.000
Intention to quit (%)			
none	28.1	21.4	
moderate	54.4	3.0	
strong	17.5	45.6	0.002

with variation within and between populations. The areca nut may be placed in a quid along with the piper betle leaf and lime, drunk in a beverage or shredded into pre-packaged pan masala. The areca nut itself may be consumed as a 'wet' or 'dry' solid. The quid may be chewed vigorously by some populations, while in others it is placed in the cheek for a more gentle mastication. All these factors inhibit the development of a robust evidence base, indicating the need to proceed on a case-study basis.

A second outcome has been the recognition that socio-economic trends in South Asia may serve to either reinforce existing patterns of consumption or lead to the development of marketing innovation. There is currently inadequate evidence to argue that the Bangladeshi socio-economic profile will lead to the diffusion of pan masala there, a mass-produced product reflecting the pattern of socio-economic change in India.

Thirdly, a focus on the health and behaviours of the United Kingdom South Asian communities, who make up about half of the United Kingdom ethnic minority population, has developed. This community is not a homogeneous group, differing along variables such as geographic distribution in the United Kingdom, educational attainment and economic prosperity. It cannot be assumed that their patterns of areca nut consumption will be similar. Further data collection should establish factors such as return travel to their families' country of origin where areca nut consumption started, and any change in this behaviour over time.

Fourthly, accessible and robust data clearly distinguishing between individuals chewing areca nut in a made-up paan, pan masala or with tobacco is limited. Data from East London suggests that, in community samples, a group of adults reported their current areca nut chewing to be in paan without tobacco. This group was clearly distinguishable from a larger group chewing areca nut in paan with tobacco, with a differing consumption frequency, pattern and motivation. Reflecting these consumption patterns, epidemiological outcomes among those who chew paan without tobacco need further clarification against the international concensus reached in 1985.[37]

It may be concluded that the socio-economic aspects of areca nut production and consumption have been largely overlooked, inhibiting the identification of clear conclusions. This research should be multidisciplinary in focus and of high scientific quality. The consumer voice is currently ignored in the development of this research activity.

Acknowledgements

Sharif Islam is an MRC Health Services Research Training Fellow. Dr K. Chaudhry, from the Indian Council of Medical Research, made constructive comment on an earlier draft.

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J Oral Pathol [illegible]; [illegible]: [illegible]

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Oral submucous fibrosis: study of 1000 cases from central India

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BACKGROUND: Very few reports have been published on the gender specificity of oral submucous fibrosis (OSF) in relation to habit patterns and the severity of disease in the world literature. The purpose of the study was to ascertain the gender specificity for different habits and severity of OSF.

METHODS: A hospital-based cross-sectional study on various habit patterns associated with OSF was performed in Nagpur over a 5-year period. A total of 1000 OSF cases from 266 418 out patients comprised the study sample.

RESULTS: The male-to-female ratio of OSF was 4.9:1. Occurrence of OSF was at a significant younger age group (<30 years) among men when compared with women (OR = 4.62, 3.22–6.63, $P = 0.0001$). Reduced mouth opening, altered salivation and altered taste sensation were found to be significantly more prevalent in women when compared with men. Exclusive areca nut chewing habit was significantly more prevalent in women (OR = 44.5, 25.4–79.8, $P = 0.0001$). Whereas significant increase for *Gutkha* (Areca quid with tobacco) (OR = 2.33, 1.56–3.54, $P = 0.0001$) and *kharra/Mawa* (crude combination of areca nut and tobacco) (OR = 6.8, 4.36–11.06, $P = 0.0001$) chewing was found in men when compared with women.

CONCLUSIONS: There is a marked difference in literacy, socioeconomic status, areca nut chewing habits, symptoms and disease severity in women when compared with men in the central Indian population.

J Oral Pathol Med (2007) 36: 12–7

Keywords: oral submucous fibrosis; descriptive study; gender; pan masala; oral cancer

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Accepted for publication July 5, 2006

Introduction

Oral submucous fibrosis (OSF) is a high risk precancerous condition characterized by changes in the connective tissue fibers of the lamina propria and deeper parts leading to stiffness of the mucosa and restricted mouth opening. OSF has been reported almost exclusively among Indians living in India and among other Asiatics, with a reported prevalence ranging up to 0.4% in Indian rural population (1). Epidemiological and *in vitro* experimental studies have shown that chewing areca nut (*Areca catechu*) is the major aetiological factor for OSF (2).

Although there are regional variations in the type of areca nut products used in India, the betel quid (BQ) was the most popular and prevalent habit in ancient Indian culture. But in 1980, both areca quid products such as *Pan masala* (Areca quid) and *Gutkha* (AQ + tobacco) were introduced in Indian market as commercial preparations. Since then there has been an increase in the use *Pan Masala* (Areca quid) and *Gutkha* (AQ + T) in the younger age groups, which had lead to increased incidence of OSF (3).

Pan Masala (Areca quid) includes areca nut, catechu, lime, flavours and spices. One previous hospital-based case–control study has proved strong association of *Pan Masala* (AQ) with highest relative risk (48.9) of development of OSF (4). *Gutkha* (AQ + T) contains all ingredients of *Pan Masala* (AQ) plus tobacco and other contents, that are closely guarded secretes and is a commercial substitute to local preparation popularly known as *Khurra/Mawa* (5).

Recently, it has been documented that the habit of chewing *Gutkha* (AQ + T) had gained considerable popularity among the younger men in this region. The rapidly increasing prevalence of this habit can be judged from the reports that the Indian market for *Pan masala* (AQ) and *Gutkha* (AQ + T) is worth 25 billion (US$ 500 million) (6).

Many epidemiological studies on OSF have been published in world literature (1, 2, 8, 17, 19, 20, 23, 25). However, very few reports have been published on the

gender specificity of OSF in relation to habit patterns and the severity of disease (7). Given this paucity of information, a hospital-based cross-sectional study was performed to ascertain the gender specificity for different habits associated with OSF and the prevalence of oral cancer among these patients controlling for tobacco chewing habits.

Materials and methods

A total of 266 418 patients visited the outpatient department of Government Dental College and Hospital, Nagpur, central India, in a 5-year period (from January 2000 to December 2004). Out of these, 1000 patients were diagnosed for OSF and they comprised the study sample. Criteria for diagnosis of OSF were the presence of palpable fibrous bands in the labial and/or buccal mucosa, loss of elasticity of the buccal/labial mucosa and inability to open the mouth wide (1, 6). The clinical diagnosis was confirmed by biopsy in a subgroup of cases, using established criteria: submucosal dense and avascular collagenous connective tissue, variable number of chronic inflammatory cells and epithelial atrophy (8).

Complete clinical history, including demographic details, various oral habits, the frequency (number of times per day), duration (years of consumption) and type [Areca nut, *Khaini, Mawa, Pan Masala* (AQ), *Gutkha* (AQ + T), BQ] along with tobacco use were recorded in case record forms.

Data management and analysis

For the purpose of data entry, storage and retrieval, clinician-friendly graphical software programme 'SOFPro 1.0' was specially designed and developed with the help of a qualified software programmer. Graphical user interface (GUI) screens were developed using Visual Basics 6.0 and database in MS Access. Designing of a suitable 'form' for data entry and 'format' for storage of information (computer screens) was done as per the structure of case record form for OSF.

All statistical analyses were performed using locally cooled STATA Version 8.0 (STATA corporation, Lakeway, TX, USA) software. Descriptive measures like mean values and standard deviations for continuous variables and percentage for categorical variables were calculated. The OSF cases were classified by gender for comparison purposes. Estimation of odds ratio (OR) along with 95% confidence intervals was made for comparing risk of OSF by gender. Tests of significance like unpaired *t*-test for comparing means and chi-squared test of association were performed for comparing percentages of two independent samples (men vs. women). A value of $P < 0.05$ was considered statistically significant.

Results

Year-wise prevalence of OSF in the study population is shown in Table I. The overall prevalence rate (per 1000) was found to range from 2.42 in 2000 to 6.42 per 1000 population in 2004. Fig. 1 highlights the increasing trend in prevalence of OSF since 2000.

Table I Year-wise prevalence of oral submucous fibrosis

Year	Cases	Sample size	Prevalence (per 1000 cases)
2000	152	62 587	2.42
2001	167	59 973	2.78
2002	168	48 848	3.43
2003	203	46 753	4.34
2004	310	48 257	6.42

Demographics

Table 2 shows the demographics of 1000 OSF cases. The mean age for men ($n = 830$) was 27.60 ± 9.58 (range 12–75) years and for women ($n = 170$) it was 34.78 ± 12.21 (range 9–75) years. Thus, occurrence of OSF was at a significantly younger age (< 30 years) among men when compared with women (OR = 4.62, 3.22–6.63, $P = 0.0001$). Prevalence of OSF in men (83%) was significantly ($P < 0.0001$) more than in

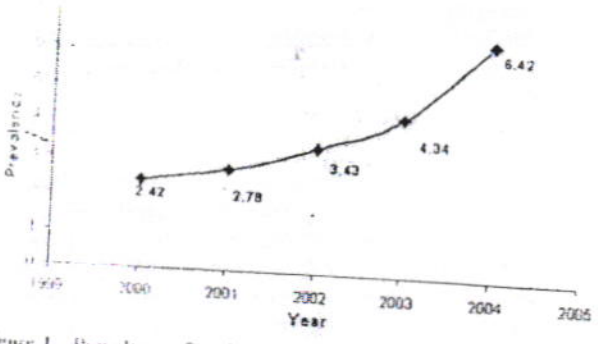

Figure 1 Prevalence of oral submucous fibrosis (per 1000 population) [illegible] years

Table 2 [illegible] graphics of oral submucous fibrosis

[illegible]	Male (N = 830)		Female (N = 170)		Total (N = 1000)	
	No.	%	No.	%	No.	%
Age group						
0–9	–	–	1	0.6	1	0.6
10–19	180	21.7	23	13.5	203	35.2
20–29	439	52.9	42	24.7	481	77.6
30–39	131	15.8	59	34.7	190	50.5
40–49	55	6.6	30	17.6	85	24.3
50+	25	3.0	15	8.8	40	11.8
Educational status						
Illiterate	161	19.4	12	7.1	173	17.3
Primary/middle	567	68.4	103	60.6	670	67
Literate	51	6.1	44	25.8	95	9.5
[illegible]	51	6.1	11	6.5	62	6.2
[illegible] status						
[illegible]	281	33.8	72	42.3	353	35.3
[illegible]	520	62.6	93	54.7	613	61.3
[illegible]	13	1.5	2	1.1	15	1.5
[illegible]	16	1.9	3	1.7	19	1.9

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Table 3 Symptoms and risk/distribution of OSF by gender

Symptom*	Male (N = 830) No.	%	Female (N = 170) No.	%	OR (95% C.I.)	P-value
Reduced mouth opening	747	90.0	161	94.7	1.98 (0.97–4.5)	0.053
Burning sensation	734	88.4	157	92.3	1.57 (0.85–3.15)	0.135
Ulceration	545	65.7	117	68.8	1.15 (0.80–1.67)	0.427
Altered salivation	307	36.9	86	50.6	1.41 (0.99–1.99)	0.043
Taste change	268	32.2	74	43.5	1.61 (1.13–2.29)	0.004
Dysphagia	205	24.7	53	31.2	1.38 (0.94–2.00)	0.078

*Some patients had more than one symptoms of OSF.

women (17%) with male-to-female ratio being 4.9:1. Significantly higher proportions of women belonged to low socioeconomic status when compared with men (OR = 1.43, 1.00–2.04, $P = 0.035$). Proportion of illiterate women was significantly higher when compared with illiterate men (OR = 5.46, 3.38–8.74, $P = 0.0001$).

Table 3 shows the gender-wise distribution of symptoms in OSF cases at first presentation. Reduced mouth opening (OR = 1.98, 0.97–4.5, $P = 0.053$), altered salivation (OR = 1.41, 0.99–1.99, $P = 0.043$) and altered taste sensation (OR = 1.61, 1.13–2.29, $P = 0.004$) were found to be significantly more prevalent in women when compared with men.

Chewing habits

Out of 1000 patients, 77.8% ($n = 778$) patients were having multiple (more than one) habits, whereas 20.5% ($n = 205$) patients were having exclusive habits (only one habit), 1.7% ($n = 17$) patients did not give history of any habit. Average length of chewing for all cases was 21.5 ± 22.6 min with a mean frequency of chewing 1.28 ± 4.03 per day and mean duration of chewing 1.4 ± 3.59 years.

Exclusive habits

Table 4 gives the distribution and risk of OSF cases having exclusive habits ($n = 192$). Females have shown statistically significant increase in exclusive areca nut chewing habit (OR = 44.5, 25.4–79.8, $P = 0.0001$) when compared with men, but significant increase for *Gutkha* (OR = 3.69, 0.93–32, $P = 0.05$) and *khara/Mawa* chewing was found in men when compared with women.

Table 4 Gender-wise risk/distribution of oral submucous fibrosis with exclusive habits

Variables	Male (N = 830), n (%)	Female (N = 170), n (%)	OR (95% CI)	P-value
Areca nut				
Yes	20 (2.40)	89 (52.35)	44.5 (25.4–79.8)	0.0001
No	810 (97.59)	81 (47.64)		
Kharra				
Yes	38 (4.57)	0 (00)	–*	
No	792 (95.42)	170 (100)		
Gutkha				
Yes	35 (4.21)	02 (1.17)	3.69 (0.93–32)	0.0557
No	795 (95.78)	168 (98.82)		
Tobacco				
Yes	05 (0.60)	03 (1.76)	2.96 (0.45–15.5)	0.1212
No	825 (99.39)	167 (98.23)		

*OR values cannot be calculated because of zero cell frequency.

Multiple habits

Table 5 gives the distribution and risk of OSF patien with multiple habits ($n = 791$). There was a statistical significant increase in areca nut chewing (OR = 24 12.10–54.17, $P = 0.0001$), *Kharra/Mawa* chewir (OR = 6.8, 4.36–11.06, $P = 0.0001$), *Gutkha* (NO + chewing (OR = 2.33, 1.56–3.54, $P = 0.0001$) and smo king habits (OR = 12.8, 5.3–40.6, $P = 0.0001$) in mc when compared with women. Although BQ chewing an the use of snuff for teeth cleaning were proportionate higher in men, they were not found to be statistical significant.

Associated lesions

In the present sample, major pre-malignant lesion associated with OSF were leukoplakia (4.8%) and liche planus (0.7%) followed by erythroplakia (0.2%) an Betel chewer's mucosa (0.7%).

Table 5 Gender-wise risk/distribution of OSF with multiple habit

Variables	Male (N = 830), n* (%)	Female (N = 170) n* (%)	OR (95% C.I.)	P-value
Areca nut				
Yes	476 (57.34)	09 (5.29)	24 (12.10–54.17)	0.000
No	354 (42.65)	161 (94.70)		
Kharra				
Yes	459 (55.30)	26 (15.29)	6.8 (4.36–11.06)	0.000
No	371 (44.69)	144 (84.70)		
Ghutka				
Yes	345 (41.56)	37 (21.76)	2.33 (1.56–3.54)	0.000
No	531 (63.97)	133 (78.23)		
Tobacco				
Yes	275 (33.13)	41 (24.11)	1.55 (1.05–2.34)	0.02
No	555 (66.86)	129 (75.88)		
Snuff				
Yes	230 (27.71)	37 (21.76)	1.37 (0.91–2.10)	0.13
No	600 (72.28)	133 (78.23)		
Smoking				
Yes	233 (28.07)	05 (2.94)	12.8 (5.3–40.6)	0.00
No	597 (71.92)	165 (97.05)		
Betal quid				
Yes	108 (13.01)	16 (9.41)	1.43 (0.81–2.68)	0.19
No	722 (86.98)	154 (90.58)		

*All of these patients had more than one habit.

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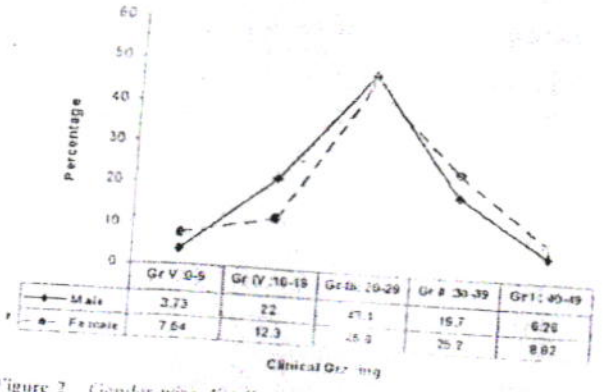

Figure 2 Gender-wise distribution of clinical grading by interincisal opening

Clinical grading

Fig. 2 depicts the gender-wise distribution of clinical grading of OSF (mouth opening in millimetres), where men and women were equally (48.3%) affected with grade III (20–29 mm) severity.

Pattern of oral cancer in OSF

Out of a total of 33 malignant cases, 28 cases (2.8%) were squamous cell carcinomas and five cases (0.5%) were verrucous carcinomas. This accounts for 3.3% malignancy potential in the present study. Table 6 gives the comparison of all the habits between malignant and non-malignant OSF cases. We have found that malignancy in OSF cases was significantly associated ($P < 0.05$) with increased frequencies of BQ chewing and smoking as well as increased durations of tobacco chewing, BQ chewing and smoking habits.

Discussion

Oral submucous fibrosis is a pre-malignant condition, which has been described in detail in Asians and Asians settled in other countries. Describing the condition in five Indian women, Schwartz (9) called it 'atrophia idiopathica mucosae oris'. Subsequently, Joshi called it submucous fibrosis (10). Various aetiological factors have been suggested for OSF, which include local irritant such as capsaicin (11), pungent and spicy food (12) and areca nut use (1). In addition to the local factors, systemic factors have also been suggested to play a role in the development of OSF. These include anaemia, chronic iron and vitamin B deficiency (13) and genetic pre-disposition (14).

Chewing areca nut in its various forms is widely prevalent in the Indian subcontinent, giving rise to increased prevalence of OSF, from an estimated 250 000 cases in 1980 (15) to an estimated 5 million people in 2002 (16).

In present study, an increasing trend in prevalence for OSF was observed since 2000 (2.42 in 2000 to 6.42/1000/year in 2004). The period prevalence rate for 2004 was comparable with other Indian and Malaysian studies (17, 18), and less when compared with studies from China and Taiwan (19, 20). This striking difference between the prevalence rates may be attributable to long history of chewing habits, and an important role of areca/BQ in Taiwanese cultural activities (20).

The mean age of all cases affected with OSF was 28.8 ± 10.4 years, which is relatively a younger age when compared with south Indian (32.4 ± 10.4 years) and north Indian (30.42 ± 10.86) OSF cases (21, 22). There are very few reported cases of children affected with OSF (23, 24). In the present study, we have found OSF in the youngest, 9-year-old girl and 12-year-old boy.

Our study showed a high preponderance of OSF in men (4.9:1), which is similar to a male preponderance, reported by various authors (5, 21, 22). However, few studies have reported female preponderance (25–28). Inability to open the mouth wide was the chief complaint (90.8%), which clearly suggests that one of the diagnostic signs of the disease, is restricted mouth opening (29–31). In the present study, there were 17 cases with no history of areca nut chewing, tobacco chewing or smoking habits. Seedat and Van Wyk (32) from South Africa made similar observations in OSF patients.

In the present study, posterior one-third of oral cavity (both buccal mucosae, retromolar area and soft palate) was predominantly affected, which is similar to the observations from Pune group from Maharashtra state and in contradiction with findings from Ernakulam group from Kerala state, where labial mucosa was

Table 6 Comparison of mean frequencies (per day) and durations (years) of different habits in malignant and non-malignant oral submucous fibrosis cases

Habits	Frequency (per day)			Duration (years)		
	Malignant ($n = 33$)	Non-malignant ($n = 967$)	P-value	Malignant ($n = 33$)	Non-malignant ($n = 967$)	P-value
Areca nut	2 ± 3	1.8 ± 4.1	0.901	3.6 ± 7.3	2.85 ± 6.0	0.507
Tobacco	2.3 ± 4.1	1.9 ± 3.7	0.544	4.2 ± 7.1	2.23 ± 5.2	0.033
Khaira	3 ± 3.1	2.8 ± 6.8	0.995	4.2 ± 5.9	2.50 ± 3.4	0.015
Betel quid	1.2 ± 2.7	0.3 ± 1.3	0.001	2.4 ± 6.2	0.74 ± 3.2	0.006
Gutkha	4 ± 8.4	3.6 ± 6.3	0.732	2.6 ± 3.6	2.35 ± 3.6	0.731
Snuff	0.4 ± 0.9	0.2 ± 0.9	0.161	3.0 ± 4.4	1.21 ± 4.1	0.384
Smoking	3.4 ± 6.9	1.0 ± 3.6	0.001	5.0 ± 7.0	1.07 ± 3.5	0.005

Values are given as mean ± SD

significantly affected, which represents a regional variation with respect to various chewing habits practised in different parts of India (33).

Women have shown statistically significant increase for exclusive areca nut chewing habit when compared with men, which is mainly attributable to the local cultural practices and easy availability of areca nut. Similar finding had been reported by several studies in Asian and South African population (25, 34). Inversely, men have shown statistically significant increase in *Gutkha* (AQ + T) and *Kharra/Mawa* chewing habits. This finding justified that the commercial product *Gutkha* (AQ + T) have equated with the local preparation *Kharra/Mawa*. Negligible number of female smokers ($n = 5$) was found in our study as it was in Yang's study (27).

In the present study, majority of OSF (48.3%) cases were in grade III (20–29 mm) severity with an average mouth opening of 24.62 mm, which is in contrast with Cox's study (35), who found an average mouth opening of 34 mm in the Nepalese OSF cases. Our study also revealed a strong association between the incidence of leukoplakia (4.8%) and OSF, which might be attributed to BQ chewing and smoking habits (36).

Although this study was not designed as a case-control study, we tried to evaluate by calculating OR with group comparisons, the association between OSF and other baseline characteristics, which highlighted the significant association of OSF with younger age, illiteracy, low socioeconomic status and various chewing products.

In this study, a malignant potential of 3.3% was noted. These malignant OSF cases have shown statistically significantly increased frequencies and duration of BQ, tobacco chewing as well as smoking habits when compared with non-malignant cases. This finding confirms that tobacco plays a modifying effect on malignant transformation in OSF. A similar malignant potential (3.6%) was noted by Caniff in Durban, South Africa (37).

The present study also confirms the fact that the increased *Gutkha* (AQ + T) chewing habit, which has substituted the BQ and *Kharra/Mawa* use in this region has not only given rise to increased prevalence of OSF but also can give rise to increased incidence of oral cancer among these patients mainly because of its tobacco and other carcinogenic additives.

We hypothesize from the present epidemiological study that there is a marked difference in habits, their frequency and duration, signs and symptoms and disease severity in women when compared with men seeking dental care for OSF at tertiary level in the central Indian population. The present cross-sectional study, to the best of our knowledge, is the single largest report on OSF so far published from India.

Conclusion

The impression of emerging prevalence of OSF since 2000 (0.42–0.64%), in relatively younger population in India seems to be justified by the data observed in the present study. Urgent regulatory actions are therefore warranted to control the manufacture, marketing and the consumption of products that contain areca nut and/or tobacco, especially *pan masala* and *Gutkha*. Special efforts are needed to educate the adolescent population using available modalities such as oral health exhibitions and camps.

Endorsement

I, the undersigned, Dr (Mrs) S.M. Ganvir, hereby endorse that, the data used for the research titled 'Oral submucous fibrosis: study of 1000 cases from central India' are hospital based and were obtained from patients who visited the Department of Oral Pathology and Microbiology, Government Dental College and Hospital, Nagpur, Maharashtra, India, during the period January 2000 to December 2004.

I have verified the claimed conclusions and found them correct as per the results obtained from this study.

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Acknowledgements

The authors thank Dr (Mrs) S. M. Ganvir, Professor, Department of Oral Pathology and Microbiology, Nagpur, India, and Dr P. C. Gupta, Director Health, Sekhsaria Institute for Public Health, Navi Mumbai, for their valuable suggestions.

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Annexure 114

Cancer Causes Control. 2002 Feb;13(1):55-64.

Body mass index, tobacco chewing, alcohol drinking and the risk of oral submucous fibrosis in Kerala, India.

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Abstract

OBJECTIVE: While chewing areca nut is considered a risk factor for oral submucous fibrosis, the effects of cigarette smoking, alcohol drinking, and body mass index (BMI) have not been examined; nor are they well established. In this study we investigated the association between BMI, smoking, drinking, and the risk of oral submucous fibrosis.

METHODS: We conducted a case-control study within the framework of an ongoing randomized oral cancer screening trial in Kerala, India. Trained health workers conducted interviews with structured questionnaires and oral visual inspections to diagnose oral premalignant lesions. A total of 170 oral submucous fibrosis cases (139 women and 31 men) and 47,773 controls were identified. The odds ratios (OR) and 95% confidence intervals (CI) were calculated by logistic regression in SAS.

RESULTS: The adjusted OR for ever-tobacco chewing was 44.1 (95% CI = 22.0-88.2). An inverse dose-response relationship was seen between BMI and the risk of oral submucous fibrosis when both genders were combined (p for trend = 0.0010), with an OR of 0.5 (95% CI = 0.3-0.9) for the highest BMI quartile compared to the lowest. Alcohol drinking may possibly be associated with the risk of oral submucous fibrosis; the adjusted OR for ever drinking was 2.1 (95% CI = 1.0-4.4). Cigarette smoking did not appear to be a risk factor for women or for men. Both smoking and drinking were rare habits among women.

CONCLUSION: This study suggested, for the first time, that BMI was inversely associated with the risk of oral submucous fibrosis for both genders when potential confounding factors were adjusted. Our results indicated that alcohol drinking might be a moderate risk factor and confirmed the previous observation that chewing tobacco was a strong risk factor for oral submucous fibrosis.

Annexure 115

Cancer Epidemiology, Biomarkers & Prevention

Chewing Tobacco, Alcohol, and the Risk of Erythroplakia

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Cancer Epidemiol Biomarkers Prev 2000;9:639-645. Published online July 1, 2000.

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Chewing Tobacco, Alcohol, and the Risk of Erythroplakia[1]

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Abstract

Although chewing tobacco, smoking, and alcohol drinking have been suggested as risk factors for oral cancer, no study has examined the relationship between those factors and the risk of erythroplakia, an uncommon but severe oral premalignant lesion. In this study, we have analyzed the effects of chewing tobacco, smoking, alcohol drinking, body mass index, and vegetable, fruit, and vitamin/iron intake on the risk of erythroplakia and explored potential interactions between those factors in an Indian population. A case-control study including 100 erythroplakia cases and 47,773 controls was conducted, as part of an on-going randomized oral cancer screening trial in Kerala, India. The analysis was based on the data from the baseline screening for the intervention group, where the diagnostic information was available. The information on epidemiological risk factors was collected with interviews conducted by trained health workers. The erythroplakia cases were identified by health workers with oral visual inspections, and then confirmed by dentists and oncologists who made the final diagnosis. The odds ratios (OR) and their 95% confidence intervals (CIs) were calculated by the logistic regression model using SAS software. The adjusted OR for erythroplakia was 19.8 (95% CI, 9.8–40.0) for individuals who had ever chewed tobacco, after controlling for age, sex, education, body mass index, smoking, and drinking. The adjusted OR for ever-alcohol-drinkers was 3.0 (95% CI, 1.6–5.7) after controlling for age, sex, education, body mass index, chewing tobacco, and smoking. For ever-smokers, the adjusted OR was 1.6 (95% CI, 0.9–2.9). A more than additive interaction on the risk of erythroplakia was suggested between tobacco chewing and low vegetable intake, whereas a more than multiplicative interaction was indicated between alcohol drinking and low vegetable intake, and between drinking and low fruit intake. We concluded that tobacco chewing and alcohol drinking are strong risk factors for erythroplakia in the Indian population. Because the CIs of interaction terms were wide and overlapping with those of the main effects, only potential interactions are suggested.

Introduction

Oral cancer is the most common site of cancer for men and the third most common site of cancer for women in Trivandrum, which is located in the state of Kerala, India. The high incidence of oral cancer in Kerala has been attributed to tobacco chewing, tobacco smoking, and alcohol drinking (1–3). Tobacco is chewed predominantly as an ingredient of betel quid or pan, which is a combination of betel leaf, areca nut, and lime. It is smoked mostly in the form of bidi (a native cigarette of coarse tobacco hand-rolled in a dry tembhurni leaf) and cigarettes.

The study of oral premalignant lesions is of importance for the prevention of oral cancer because premalignant lesions may be treated to prevent their progression to oral cancer or used as surrogate (intermediate) markers for oral cancer intervention. Cessation of chewing tobacco and smoking has been associated with the regression of oral leukoplakia, a common oral premalignant lesion (4). Dietary supplements of vitamin A and β-carotene have also been implicated in the regression as well as in the prevention of oral leukoplakia (5–7). Although several studies have been conducted on risk factors for oral leukoplakia, very few have focused on erythroplakia, the most advanced type among oral premalignant lesions.

Erythroplakia is an uncommon but severe disease, defined by WHO as "any lesion of the oral mucosa that presents as bright red velvety plaques which cannot be characterized clinically or pathologically as any other recognizable condition" (8). An updated definition for erythroplakia was proposed by Bouquot (9) as "a chronic red mucosal macule which cannot be given another specific diagnostic name and cannot be attributed to traumatic, vascular, or inflammatory causes". Erythroplakia patches may be located near, or associated with, oral leukoplakias. Bouquot and Whitaker (10) suggested that erythroplakia may occur with leukoplakia in the stage called erythroleukoplakia. Erythroplakia has been considered the most severe form among all of the oral premalignant lesions because of its high malignant potential (11). When erythroplakia biopsies were studied, 91% were dysplasia, carcinoma *in situ*, or cancer (12).

There are very few studies on the prevalence of erythroplakia. When 65,354 cases from two oral pathology departments were reviewed, 58 erythroplakia cases were identified

Received 6/21/99; revised 3/15/00; accepted 4/12/00.

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[1] The Trivandrum oral cancer screening project is supported by a generous grant from the Association for International Cancer Research (AICR), St. Andrews, Scotland. Additional data collection in this study is supported by the Imperial Cancer Research Fund (ICRF), United Kingdom. The analysis was carried out by M. H. under an IARC special training award during the summer of 1998, in the Unit of Descriptive Epidemiology, IARC, Lyon, France. This project is also supported in part by Grants CA77954, CA09142, and CA16042 from the National Cancer Institute, NIH, Department of Health and Human Services; by a seed grant from University of California-Los Angeles Jonsson Cancer Center Foundation; and by the Weissman Fund.

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(0.09%; Ref. 12). In a house-to-house survey in Burma among 6000 villagers over the age of 15 years, five cases were diagnosed, with a prevalence of 0.83% (13). In an oral lesion survey in Malaysia among 11,707 adults over the age of 35 years, one case of erythroplakia was identified (14).

In the study of 58 cases of erythroplakia, the disease was found to be more common among people in their 50s and 60s (12). The risk factors for oral cancer such as chewing tobacco, smoking, and alcohol drinking are assumed to be associated with erythroplakia. In a recent case-series study, erythroplakia was associated with a high prevalence of *TP53* mutations (15). *TP53* mutations may be associated with tobacco exposure for oral cancer(16–17), which would possibly indicate that tobacco exposure may play an important role in the development of erythroplakia.

To our knowledge, there have not been any case-control studies focusing on chewing tobacco, smoking, drinking, and the risk of erythroplakia in the literature, although the risk factors for erythroplakia have been assumed to be similar to those of oral cancer. The purpose of this study is to examine the independent effects of major potential risk factors, such as chewing tobacco, cigarette smoking, and alcohol drinking, and to explore possible interactions between them.

Subjects and Methods

Study Population and Data Collection. A randomized oral cancer screening trial is currently being conducted in Kerala, India, with the objective of evaluating the efficacy of oral visual inspection by trained health workers in preventing death from this cancer (18). The state of Kerala is located on the west coast of southern India with an area of approximately 38,900 km^2. Kerala is an ideal place for the screening trial because of the high prevalence of chewing tobacco and smoking habits, with 59.1% of the population practicing at least one of the tobacco habits, and because of the high risk of oral cancer. Keeping the chewing tobacco in the lower groove of the mouth is a habit especially common in Kerala.

This case-control study was conducted within the framework of the intervention trial, using data from the intervention arm. A total of 59,894 subjects, ages ≥35, resident in seven panchayaths or rural administrative structures (total resident population 172,567) were randomized to the intervention group to receive three rounds of screening at 3-year intervals. In the first round of intervention, 49,174 eligible subjects participated and were interviewed and screened in their homes by trained health workers. The 100 cases of erythroplakia and 47,773 controls in this study were identified from this group.

The health workers were required to be college graduates who were residents of the area. They were trained specifically in epidemiology, diagnosis, investigation, and management of oral precancers and cancers as described previously (18). The health workers conducted face-to-face interviews with a structured questionnaire. The subjects were asked about demographic information and their tobacco chewing, smoking, and alcohol drinking habits in terms of duration, frequency, and type of tobacco or alcohol used. For chewing tobacco, the subjects were also asked whether they kept the chewing tobacco in their mouth overnight and whether they swallowed the chewing tobacco fluid. Health workers asked whether fruits were taken frequently, vegetables were taken daily, and vitamins/iron supplements were taken currently or in the past. Their blood pressure, body weight, and height were measured. After this, the health workers conducted systematic visual inspections of the buccal and labial mucosa, gingivae, bucco alveolar sulci, tongue, and palate and floor of the mouth, under adequate light to identify lesions suggestive of oral leukoplakia, erythroplakia, submucous fibrosis, and/or oral cancer, and then referred subjects with positive findings. Subjects with tobacco and alcohol habits were advised to stop these practices. Two dentists and three oncologists who used uniform criteria were involved in the final diagnosis of these oral premalignant lesions. Of the 3585 subjects referred, a little more than one-half were examined by dentists, and various lesions were confirmed. Erythroplakia cases were defined as subjects diagnosed with erythroplakia by the dentists ($n = 100$). Controls were defined as subjects who were inspected by the health workers and diagnosed to be free of any oral condition or disease ($n = 47,773$).

Statistical Analysis. The effects of chewing tobacco, smoking, and alcohol drinking on the risk of erythroplakia were estimated with ORs[3] and their 95% CIs, derived from logistic regression analysis. Continuous variables such as years of chewing, smoking, or drinking, and frequency of use were first analyzed as continuous variables and then were categorized into groups according to categories often used in previous studies. BMI was calculated by dividing the weight in kilograms by the height in meters squared. Dummy variables were created to estimate OR for each category of exposure in logistic regression analysis. Trend tests for ordered variables were performed by assigning the score j to the jth exposure level of a categorical variable (where $j = 1, 2, \ldots$) and treating it as a continuous predictor in unconditional logistic regression.

The distributions for age, sex, religion, occupation, and education were examined for cases and controls. The distributions differed greatly between cases and controls for age, sex, and education. BMI has been indicated as a potential risk factor for oral cancer (19). On the basis of these distributions and of prior knowledge of potential risk factors for oral premalignant lesions and oral cancer, we adjusted for age, sex, education, and BMI in our data analysis.

Three models were used to assess exposure effects: (*a*) no covariates (crude analysis); (*b*) statistical adjustment for age (continuous), sex (F/M), education (categorical, as shown in Table 1), and BMI (continuous, kg/m^2); and (*c*) statistical adjustment for additional covariates, including chewing tobacco (continuous, duration in years), smoking (continuous, pack-years), and drinking (continuous, duration in years) in the logistic regression model where appropriate.

Stratified analysis was used to assess departures from additive and multiplicative effects among major potential risk factors, including tobacco chewing, cigarette smoking, alcohol drinking, low vegetable intake, and low fruit intake. The null hypotheses of additivity and multiplicativity were tested. A more than additive interaction is indicated when: $OR_{11} > OR_{10} + OR_{01} - 1$, where $OR_{11} = OR$ when both factors are present, $OR_{10} = OR$ when only factor 1 is present, $OR_{01} = OR$ when only factor 2 is present. A more than multiplicative interaction is suggested when: $OR_{11} > OR_{10} \times OR_{01}$ (20). Departures from multiplicative effects were assessed and tested by including main effects and a product term of the main effects in the logistic regression model.

Results

The general characteristics of the erythroplakia cases and controls are shown in Table 1. The erythroplakia cases were con-

[3] The abbreviations used are: OR, odds ratio; CI, confidence interval; BMI, body mass index.