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Chewing and Smoking Habits in Relation to Precancer and Oral Cancer*

Fali S. Mehta, P.C. Gupta, and J.J. Pindborg

Basic Dental Research Unit, Tata Institute of Fundamental Research, Homi Bhabha Road, Bombay 400005, India

Summary. In a prospective epidemiologic house-to-house survey of a random sample in the district of Ernakulam in Kerala State, the annual incidence rate of leukoplakia per 1,000 adults was found to be 2.1 for males and 1.5 for females. The rate was highest in the mixed tobacco habits group and lowest (0) in the no habits group. During the same period, oral cancer developed only among the individuals, who had a history of a previously diagnosed oral lesion. Malignant transformation was significantly higher among the speckled leukoplakia cases. The rate of malignant transformation was also highest among leukoplakias associated with tobacco chewing habits. These results suggest that leukoplakias associated with different tobacco habits may have a different natural history.

Key words: Prospective epidemiology of oral cancer – Tobacco habits – Leukoplakia

The natural history of oral leukoplakia is not very clear. It is believed to be a precancerous lesion. However, the reported rates of malignant transformation vary from less than 1% (Mehta et al. 1972) to 33% (Weisberger 1957). To date incidence rates for oral leukoplakia have not been reported in the literature.

An extensive, prospective epidemiologic house-to-house survey has been conducted in India for 10 years to investigate the natural history of oral leukoplakia, other possible oral precancerous lesions, and oral cancer. It also seeks to determine if there is any association between these lesions and the various kinds of tobacco habits prevalent in different parts of the country (Mehta et al. 1971).

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Offprint requests to: Fali S. Mehta (address see above)

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Table 1. Age-specific incidence rate per 1,000 person-years for leukoplakia from a 10-year follow-up study

Age-group	Male			Female		
	Person-years of observation	New leukoplakias detected	Incidence per 1,000 per year	Person-years of observation	New leukoplakias detected	Incidence per 1,000 per year
15–24	5,748	—	—	5,444	—	—
25–34	9,504	10	1.0	10,256	7	0.7
35–44	7,039	21	3.0	9,627	13	1.4
45–54	5,095	17	3.3	7,156	21	2.9
55–64	3,620	13	3.6	4,646	14	3.0
65 and above	3,033	12	4.0	3,516	5	1.4
Total	34,039	73	2.1	40,645	60	1.5

Material and Methods

In a cross-sectional survey a random population sample of 50,915 adults was examined by dental teams, who were fully trained and calibrated for diagnosing oral precancerous lesions. Thus, baseline registries were established in five rural districts of India, these are (1) Ernakulam in Kerala, (2) Bhavnagar in Gujarat, (3) Srikakulam in Andhra Pradesh, (4) Singhbhum in Bihar, and (5) Darbhanga in Bihar. Each registry contained detailed information of the results of oral diagnostic examination and tobacco habits for over 10,000 individuals examined in each district. Lesions were documented by Polaroid color photographs and biopsies were obtained for all leukoplakias and other lesions, whenever possible.

For the purposes of this study, leukoplakia was defined as a raised white patch, measuring 5 mm or more, which could neither be scraped off nor attributed to any other diagnosable disease.

In evaluating the clinical features of leukoplakia, the following three types were taken into consideration: (1) homogeneous leukoplakia – the most frequent form, characterized by fairly uniform, raised, white plaque formation; (2) speckled leukoplakia – characterized by white nodular patches intermingled with erythematous areas; and (3) ulcerated leukoplakia – a white plaque with ulceration. This terminology was used in a purely clinical sense, without any histological connotation intended. A detailed account of the diagnostic criteria, methods of examination, and standardization of techniques has been previously reported by Mehta et al. (1971).

Annual follow-ups of all screened individuals have been conducted in three of the five rural districts. In the present report, we shall discuss the 10-year follow-up results on the natural history of leukoplakia from the Ernakulum district, Kerala State, in the southern part of India.

The most common tobacco habits in this region are "pan" chewing and "bidi" smoking. "Pan" is a chewing quid composed of a basic combination of betel leaf, lime, areca nut, and tobacco. "Bidi" is a cheap cigarette measuring 4–7 cm, made by rolling about 0.2 g of coarse tobacco in a dry temburni (diospyros melanoxylon) leaf.

Incidence rates and the rates of malignant transformation have been calculated using the person-year method (MacMahon and Pugh 1970).

Results

Table 1 shows the annual age-specific incidence rates per 1,000 for oral leukoplakia in Ernakulam. For males the incidence rate increase steadily from 1.0 in the age group of 25–34 years. The peak (4.0) is attained in the age group of 65 years and over.

Table 2 shows the incidence rates among males and females in different habit groups. The rates are age-adjusted to eliminate the effect of differing age-distribution in various habit groups. The highest incidence was in the mixed habit group (6.0). Among females in Ernakulam, tobacco chewing habits are very common and

Table 2. Age-adjusted incidence rate per 1,000 person-years for leukoplakia in a 10-year follow-up study

Habit	Male			Female		
	Person-years of observation	New leuko-plakias detected	Incidence per 1,000 per year	Person-years of observation	New leuko-plakias detected	Incidence per 1,000 per year
No habit	5,792	—	—	24,731	—	—
Smoking habit	17,352	13	0.7	248	—	—
Chewing habit	5,016	15	2.5	15,491	60	3.0
Mixed habit	5,879	45	6.0	175	—	—
Total	34,039	73	2.1	40,645	60	1.3

Table 3. Malignant transformation of oral lesions in 1–10-years follow-up study

Previous diagnosis	Ernakulam (Kerala)	
	Number	New oral cancers detected
Leukoplakia		
Homogeneous	352	8
Speckled	14	3
Ulcerated	44	—
Preleukoplakia	389	2
Submucous fibrosis	44	1
Lichen planus	332	1
Leukokeratosis nicotina palati and Palatal lesions	65	—
Normals	6,160	—

the incidence rate in this habit group for females (3.0) was slightly higher than that for males (2.5). "Bidi" smokers exhibited the lowest incidence rate (0.7) among various habit groups. The incidence in the no habit group was zero for males as well as for females.

Table 3 shows the number of new oral cancer cases detected during the 10-year follow-up of the study population, according to previous diagnosis. Not a single new oral cancer was detected among the normal controls. Eleven more cancers were detected among individuals with leukoplakia (eight cancer cases among 352 homogeneous leukoplakias; and three cancer cases among 14 speckled leukoplakias). Four oral cancers among individuals with other oral lesions were detected. Of these, two cases were preleukoplakia, one was submucous fibrosis, and one was lichen planus. Histological typing was available for 10 cases, six were squamous cell carcinomas, and four were verrucous carcinomas.

Tables 4 and 5 show the rate of malignant transformation of leukoplakia according to age, sex, and habits, respectively. Malignant transformation of leukoplakia was not observed in the age group of less than 35 years. The rate of malig-

Table 4. Rate of malignant transformation of oral leukoplakia according to age and sex in 1–10-year follow-up study

Age group	Leukoplakia person-years	New oral cancers detected	Rate of malignant transformation per 1,000 per year
15–34	151	—	—
35–54	1,082	3	2.8
55 and above	788	8	10.2
Male	1,525	7	4.6
Female	496	4	8.1
Total	2,021	11	5.4

Table 5. Rate of malignant transformation for oral leukoplakia according to habits in 1–10-year follow-up study

Tobacco habits	Leukoplakia person-years	New oral cancers detected	Rate of malignant transformation per 1,000 per year
No habit	6	—	—
Smoking habit	500	—	—
Chewing habit	722	7	9.7
Mixed habit	793	4	5.0
Total	2,021	11	5.4

nant transformation was three-and-a-half times higher for the age group of 55 years and over (10.2) than for the age group of 35–54 years (2.8). The rate of malignant transformation was about two times higher for females (8.1) than for males (4.6) and for the tobacco-chewing habit group (9.7) than for the mixed-tobacco habit group (5.0). Malignant transformation of leukoplakia was not observed in those persons who practiced only smoking habits.

Discussion

This is the first time that the incidence rates for oral leukoplakia have been reported. Several salient points emerge from the analysis of incidence rates according to tobacco habits.

1. Oral leukoplakia shows a definite, complete association with tobacco habits. In spite of there being a sufficient number of person-years of observation for males as well as females, the incidence rate in the no-tobacco habit group was zero.
2. The association of oral leukoplakia with different tobacco habits is of different magnitude, being much higher with tobacco-chewing habits than with smoking habits.
3. When the two tobacco habits of smoking and chewing are combined, the effect appears to be synergistic.
4. There does not appear to be any real sex difference in regard to malignant transformation of leukoplakia. The apparent difference in the overall incidence rates may be ascribed to the particular pattern of the tobacco habits in two sexes.

The malignant transformation of the different types of leukoplakia confirms a previous observation (Pindborg et al. 1968) that speckled leukoplakia is more prone toward malignancy than homogeneous leukoplakia. In our case material eight of 352 homogeneous leukoplakias (2.27%) and three of 14 speckled leukoplakias (21.4%) developed into oral cancer, a difference which was statistically significant ($P < 0.05$). It is remarkable that oral cancer developed only among the individuals who had a prior diagnosis of an oral lesion.

The finding that only in the age group of 35 years or more, certain leukoplakia progressed to malignant transformation is in agreement with other reports. The risk of malignant transformation apparently being twice as frequent in females than in males is a rather unexpected finding, but that is most likely due to the fact that tobacco-chewing habits were much more common among females than among males. Table 5 verifies that only those leukoplakias which were associated with tobacco-chewing habits underwent malignant transformation.

Thus, in the study of the natural history of laukoplakia we have an inexplicable observation at hand: whereas "bidi" smoking is definitely associated with the incidence of leukoplakia, it is not associated with malignant transformation. Likewise, whereas the effect of combining "bidi" smoking with "pan" chewing appears to be synergistic for the incidence of leukoplakia, the combination does not produce a synergistic effect for the malignant transformation of leukoplakia. These results clearly indicate that leukoplakias associated with different tobacco habits are different with respect to their natural history.

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