

# A study of the natural history of oral preleukoplakia

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Daftary, D.K., Pitkar, V.K., Gupta, P.C., Pindborg, J.J. & Mehta, F.S. A study of the natural history of oral preleukoplakia. *Acta Odontol. Scand.* 36, 327-331

A preleukoplakia, conceived as a precursor stage of leukoplakia, is grey or greyish-white area with indistinct borders. The paper describes 659 preleukoplakias detected among 20,358 individuals in two districts in India. In Bhavnagar district 99.5 % of the preleukoplakias were among men. 23.5 % of the hookli (clay pipe) smokers had preleukoplakias. In Ernakulam district 79.6 % of the preleukoplakias were found among men and the mixed habit group of bidi smoking and tobacco chewing had the highest prevalence (6.1 %). The preleukoplakias showed a marked tendency to regress; among the bidi smokers in Bhavnagar, 75 % regressed. In two patients preleukoplakia turned into carcinoma.

*Key-words:* Epidemiology; leukoplakia; neoplasms; precancer

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In an initial pilot study to our main project (4, 5) carried out in some villages of the Poona district of Maharashtra, a lesion of the oral mucosa was observed which was similar to leukoplakia but did not fulfill the criteria of leukoplakia. This lesion was so frequently encountered (3 to 4 %) that it was necessary to register it separately as an entity. The term preleukoplakia was suggested because it was used by one of the authors (J.J.P.) in a survey of oral mucosal changes among Papuans (6). As preleukoplakia was thought to be a precursor stage of leukoplakia, it was decided to study the behavior of this lesion. Preleukoplakia is defined as a low grade of very mild reaction of the mucosa,

appearing as a grey or greyish-white, but never completely white area, with a slight lobular pattern and indistinct borders blending into adjacent normal mucosa.

## MATERIAL AND METHODS

The present material is derived from a study conducted by Metha et al. 1969, among Indian villagers. Two districts, Bhavnagar and Ernakulam, were chosen for different chewing and smoking habits practised in these areas. A total of 20,358 villagers were examined in the two districts in 1967. The examination took place in the natural light

using two mouth mirrors. The team of dentists were trained by and calibrated to one of the authors (J.J.P.). Before examination all the individuals were questioned about their age, chewing and smoking habits. All lesions were recorded and photographed. Biopsies were taken whenever the patients consented.

The first survey was carried out in 1966–67. The follow-up study started in 1969 and the present results are based on 10-year follow-up observations.

At the end of 10-year follow-up study, lesions which reversed back to normal mucosa were termed "regressed". Lesions which changed to leukoplakias were termed "progressed to leukoplakia". Lesions which persisted as preleukoplakia were termed "persistent". The lesions which regressed but reappeared subsequently were termed as "variable".

## RESULTS

### *Epidemiologic findings*

Table 1 shows age and sex distribution of preleukoplakias in the two districts at the first examination survey. In Bhavnagar, out of 409 cases of preleukoplakias, 407 were

males, whereas in Ernakulam, out of 250 cases of preleukoplakias, 199 were males and 51 females. The highest number of cases were found in the age group of 35–44 years. In Bhavnagar district 24.9% and in Ernakulam district 28.0% of all preleukoplakias were from the 35–44 years age group.

Table 2 shows correlation of preleukoplakia lesions with the tobacco habits. In Bhavnagar district, the highest number of preleukoplakias were found among bidi (an Indian form of a cheap cigarette) smokers. An interesting observation was a very high prevalence (23.5%) of preleukoplakias among hookli (clay pipe) smokers (3) on the labial mucosa. The group of individuals smoking both bidi and hookli also showed a fairly high prevalence (12.7%) of preleukoplakias. In Ernakulam district, though the highest number of preleukoplakias (91) were diagnosed among bidi smokers, the prevalence was highest (6.1%) in the mixed habit group. In the chewing habit group, though the number of preleukoplakias was the same as that in the mixed habit group, the prevalence was much lower compared to the bidi and the mixed habit groups. The lowest prevalence was in the no habit group. In Bhavnagar district, 0.03% and in Ernakulam district, 0.2% of the preleukoplakias were

Table 1. *Age and Sex distribution of preleukoplakia*

Age groups	Bhavnagar (Gujarat)				Ernakulam (Kerala)			
	Male		Female		Male		Female	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
15–24	28	6.9	—	—	21	8.4	—	—
25–34	85	20.8	—	—	30	12.0	4	1.6
35–44	102	24.9	—	—	58	23.2	12	4.8
45–54	80	19.6	2	0.5	45	18.0	18	7.2
55–64	72	17.6	—	—	27	10.8	7	2.8
65–74	32	7.8	—	—	14	5.6	8	3.2
75 and over	8	1.9	—	—	4	1.6	2	0.8
Total	407	99.5	2	0.5	199	79.6	51	20.4
Total	409				250			

diagnosed in the no habit group. Preleukoplasias associated with chewing habits were located to the buccal mucosa and those associated with the bidi smoking habit were located to the commissures and the buccal mucosa. The majority of the preleukoplasias associated with the hookli smoking were located to the labial mucosa.

Table 3 shows the clinical behaviour of the preleukoplasias in a 10-year follow-up study. In Bhavnagar district, out of 409 preleukoplasias registered in the first survey, 274 (67%) were followed-up, while in Ernakulam district, 154 out of 250 (61.6%) preleukoplasias were followed-up. Two preleukoplasias progressed to carcinoma in Ernakulam district. One of them was a 40-year-old female who had a buccal mucosa preleukoplakia, which developed into carcinoma at the end of three years. In another case, a 70-year-old man who had preleukoplakia on the right and left buccal mucosa, developed an atrophic area, on the right buccal mucosa at the end of four years, later confirmed histologically as carcinoma. In Bhavnagar district, 6.8% and in Ernakulam district, 8% of the preleukoplasias were found to have progressed into leukoplakia. Some 50.6% of all preleukoplasias

Table 2. Correlation of preleukoplakia with tobacco habits in Ernakulam and Bhavnagar. The prevalences, in percent of each habit group, are given in brackets

Habits	Bhavnagar Gujarat	Ernakulam Kerala
Chewing habit	6 (0.5)	68 (2.1)
Smoking habit		
Bidi	199 (9.3)	91 (5.2)
Hookli	131 (23.5)	—
Others	44 (12.7)	15 (2.9)
Reverse smoking	—	—
Mixed habits	27 (8.4)	68 (6.1)
No habits	2 (0.03)	8 (0.2)
Total	409 (4.1)	250 (2.4)

in Bhavnagar and 37.6% in Ernakulam regressed to normal.

Table 4 shows the status of the preleukoplasias at the end of 10-year follow-up with their correlation to habits. The outstanding feature is a high percentage of regression in the chewer's group. In Bhavnagar, among bidi smokers also a high percentage of preleukoplasias regressed (75%).

Preleukoplakia was associated with leukoplakia in 12% of the cases in Bhavnagar and in 15% in Ernakulam.

Table 3. Follow-up results of preleukoplakia in a 10-year study

	Bhavnagar (Gujarat)		Ernakulam (Kerala)	
	Number	Percentage	Number	Percentage
Number of preleukoplasias in 1st examination (1967)	409	—	250	—
Transformed to cancer	—	—	2	0.8
Progressed to leukoplakia	28	6.8	20	8.0
Persistent	24	5.9	31	12.4
Regressed to normal	207	50.6	94	37.6
Variable	37	9.0	14	5.6
Number of individuals followed-up at the end of 10-years	274	67.0	154	61.6

*Histologic findings*

The histologic analysis was based upon 14 biopsies from buccal mucosa (11 Ernakulam and 3 Bhavnagar) and one biopsy from the labial mucosa (Bhavnagar). Eleven biopsies showed hyperorthokeratosis, 2 revealed non-keratinization and one demonstrated a combination of orthokeratosis and parakeratosis. The labial mucosa biopsy in Bhavnagar showed vacuolated hyperparakeratosis. Epithelial dysplasia was diagnosed in one case in Ernakulam. The epithelium was atrophic in 10 cases and normal in 4 cases. Inflammatory response was absent in 5, present in a slight degree in 8 cases and severe in one case.

## DISCUSSION

The prevalence rate of preleukoplakia reported here (2.4–4.1 %) is much lower than 10.6–13.4 % reported among Papuans by Pindborg et al. (6) and somewhat lower than the 6.4 % among Swedes as reported by Axéll (1). The probable reason given for the high prevalence among Papuans was the use of a more irritating tobacco (6). The highest number of preleukoplakias in this study occurred on the buccal mucosa in both the

district of Bhavnagar and Ernakulam. A similar preference of location was reported among Papuans (6). The comparatively high number of preleukoplakias recorded on the lower labial mucosa in Bhavnagar could be explained by the hooklismoking habit (3). This habit causes a high percentage of leukoplakias as well on the lower labial mucosa. Of all habit groups, the highest number of preleukoplakias were found in the hookli smoking group in Bhavnagar. In contrast to this, in Ernakulam the highest number of lesions were recorded in the mixed habit group. These results are in agreement with the results on leukoplakia (6).

Spontaneous regression of the preleukoplakias occurred in 51 % in Bhavnagar and 38 % in Ernakulam cases which is comparable to the regression rates (26 % and 43 %) reported for leukoplakias in these two districts, respectively (2). It is interesting to note that 6.8 % of the lesions in Bhavnagar and 8 % in Ernakulam progressed to leukoplakia. Of the two patients in Ernakulam who developed cancer in the preleukoplakia site, one died due to malignancy in the second year follow-up. Together with this finding and the finding of epithelial dysplasia in one preleukoplakia, the need for follow-up of this lesion is obvious.

Table 4. Percentage of preleukoplakia in each habit group according to follow-up behavior

	Bhavnagar (Gujarat)						Ernakulam (Kerala)				
	No habits	Bidi	Pipe	Other smoking habit	Chewing habit	Mixed habits	No habits	Bidi	Other smoking habit	Chewing habit	Mixed habit
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Progressive	—	9	12	7	—	—	—	8	20	19	16
Persistent	—	2	19	2	—	—	—	26	20	3	20
Regressive	100	75	54	86	100	94	100	55	60	69	57
Variable	—	14	15	5	—	6	—	11	—	9	7
Number of preleukoplakias	1	113	100	40	2	18	2	74	5	30	41

*Acknowledgement.* This study was supported by the National Institutes of Health, Bethesda, Md., U.S.A. through PL 480 Research Agreement No. 01-022-1.

## REFERENCES

1. Axéll, T. A prevalence study of oral mucosal lesions in a adult Swedish population. Thesis. *Odontol. Revy* 1976, 27, Suppl. 36
2. Mehta, F.S. & Pindborg, J.J. Spontaneous regression of oral leukoplakia among Indian villagers in a 5-year follow-up study. *Community Dent. Oral Epidemiol.* 1974, 2, 80-84
3. Mehta, F.S., Pindborg, J.J., Daftary, D.K. & Gupta, P.C. Oral leukoplakia among Indian villagers. The association with smoking habits. *Br. Dent. J.* 1968, 127, 73-77
4. Mehta, F.S., Pindborg, J.J., Gupta, P.C. & Daftary, D.K. Epidemiologic and histologic study of oral cancer and leukoplakia among 50,915 villagers in India. *Cancer* 1969, 24, 832-849
5. Mehta, F.S., Pindborg, J.J. & Hamner, J.E. Oral cancer and precancerous conditions in India. Munksgaard, Copenhagen 1971, 143 p.
6. Pindborg, J.J., Bames, D. & Roed-Petersen, B. Epidemiology and histology of oral leukoplakia and leukoedema among Papuans and New Guineans. *Cancer* 1968, 22, 379-382