Potentially Malignant Disorders of the Oral Cavity: A Clinical Study

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Abstract Oral cancers in India, unlike in the West are the most common cancers encountered, be it a primary or a tertiary referral practice. This makes the study and management of these cancers an important issue especially for the otolaryngologist. It is well known that the most common variant of oral cancers is the squamous cell carcinoma. Also the etiology is well established; with tobacco use in both smoking and smokeless forms, alcohol, betel nut and recently the Human Papilloma virus infection being implicated. Certain conditions which definitely increase the probability of getting oral cancers are known and this study aims in revisiting these aspects of pre-malignancy. The progression from a pre-cancerous lesion/condition to frank cancer is well established across many studies and many specialties. Also timely recognizing these pre-cancerous conditions and administration of proper treatment will greatly help in reducing the morbidity and mortality from subsequent much advanced and dangerous oral cancer. Keeping these facts in mind this study was planned to study the established pre-cancerous lesions which are known to progress to oral cancers.

Keywords Potentially malignant disorders · Oral pre-cancerous lesions · Oral submucous fibrosis · Leukoplakia · Erythroplakia · Lichen planus · Traumatic dental ulcer

Introduction

The concept of a two-step process of cancer development in the oral mucosa, i.e., the initial presence of a precursor subsequently developing into cancer is well-established. An Indian house-to-house survey showed that about 80 % of oral cancers were preceded by oral pre-cancerous lesions or conditions [1].

The evidence that oral leukoplakias are pre-cancerous, is mainly derived from follow-up studies, mostly obtained on hospital-based observations. Studies have shown that between <1 and 18 % of oral pre-cancerous lesions will develop into oral cancer. The transformation rates are generally lower in house-to-house surveys and in studies on random samples [2] than in studies on hospital-based patient populations, indicating the influence of case selection; the influence of geographical traits related to habits and genetics may play a role, since the population-based studies have been primarily performed in India. Thus, there is considerable uncertainty as to whether or not all clinically detectable lesions characterised as precursors will eventually develop into carcinomas.

The WHO has accepted the latest international attempt on terminology and definitions, subdividing oral pre-cancerous lesions and pre-cancerous conditions [3]. There is general agreement that a pre-cancerous lesion is defined as “a morphologically altered tissue in which cancer is more likely to occur than its apparently normal counterpart” e.g. leukoplakia and erythroplakia, whereas a pre-cancerous condition is defined as “a generalised state associated with a significantly increased risk of cancer”. The latter definition signifies that the cancer can arise in any part of the oral cavity and not necessarily in a pre-existing lesion. Examples of pre-cancerous conditions are submucous fibrosis and lichen planus [4].

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Oral submucous fibrosis (OSF): it is a chronic disorder characterised by fibrosis of the lining mucosa of the upper digestive tract involving the oral cavity, oropharynx and frequently the upper third of the oesophagus. Arecanut alkaloids are widely researched and accepted etiological agents [5] (Photograph 1).

Leukoplakia: A white patch or plaque that cannot be characterised clinically or pathologically as any other disease. Leukoplakia is most common in tobacco smokers and chewers [6] (Photograph 2).

Erythroplakia: Any lesion of the oral mucosa that presents as bright red velvety plaques which cannot be characterised clinically or pathologically as any other recognisable condition. It is also more prevalent in tobacco users (Photograph 3).

Traumatic dental ulcers: A traumatic ulcer due to jagged tooth or ill fitting denture can cause chronic ulcers which may develop pre-cancerous change (Photograph 4).

Photograph 1 Showing extensive blanching of the mucosa of the soft palate and the pillars indicative of Oral Submucous Fibrosis

Photograph 2 Extensive Leukoplakia of the lip and buccal mucosa

Photograph 3 Classical erythroplakia seen on right buccal mucosa

Photograph 4 Classical Lichen Planus of the oral cavity showing the “spider web” pattern on the right buccal mucosa

Lichen planus: Oral lichen planus is an idiopathic condition. Some of the types have a predisposition to develop carcinoma [7] (Photograph 5).

The present study was therefore conducted to study the incidence, age and sex distribution, clinical presentation and predisposing factors of the above mentioned pre-cancerous lesions of the oral cavity.

Materials and Methods

The present study was undertaken after mandatory clearance from the ethical committee of our institute and taking informed consent of the patients willing to participate in

Photograph 5 Traumatic Dental Ulcer on the right lateral margin of the tongue. Note the sharp inner edges of the right lower first and second molars

the present study. The standard procedure of examination of ear, nose, throat, oral cavity, face and neck was carried out on each patient attending our out patient department from January 2011 to January 2012.

A detailed history of his/her complaints was taken. All patients with oral pre-cancerous lesions i.e. leukoplakia, erythroplakia, OSF, lichen planus and traumatic dental ulcers were included in this study. Only those patients who agreed for a biopsy were included in this study.

Patients with the following parameters were excluded from the study:

1. Any patient with a condition other than those mentioned in the criteria above.
2. Patient with a known malignant condition.
3. Patient with a biopsy proven not to be one of the conditions mentioned above and those patients who voluntarily refused to be a part of the study.

Results

Out of the total 102 cases in the study group, 58 (56.86 %) were of oral submucous fibrosis, 20 (19.60 %) were of leukoplakia, eight (7.84 %) were of erythroplakia, six (5.88 %) were of lichen planus and ten (9.80 %) were of traumatic dental ulcer (Table 1).

Thus in the study group, OSF was the most common condition found followed by leukoplakia while lichen planus was the least common condition.

OSF has the highest incidence in the study group due to the fact that it causes early symptoms and thus patients seek medical attention early unlike in leukoplakia which causes only a painless plaque in the oral cavity.

The age of patients varied from 19–85 years, youngest being a 19 year old male. The maximum no of cases (27/102) i.e. 26.47 % were in 41–50 years age group. In the 31–40 years age group 17 cases were seen (Table 2).

In OSF, 18 patients were in 41–50 years age group. The youngest being a 19 year old male and oldest being an 85 year old male, thus indicating a wide range of distribution.

In leukoplakia, the highest incidence was found in the age group of 21–30 years (25 %), the youngest being a 25 year old male and eldest being an 85 year old male.

In Erythroplakia, four patients were seen in the age group of 41–50 years. In traumatic dental ulcer patients, higher incidence was found in the age group of 21–30 years and age greater than 60 years. The oldest patient in the study group was of 75 years.

Out of 102 cases, 70 cases were males (68.62 %) and 32 cases were females i.e. (31.37 %) with a male to female ratio of 2.18:1, but in cases of lichen planus, out of the six cases, four were females, with the male to female ratio being 1:2 (Table 3).

Table 1 Incidence of various pre-cancerous lesions of the oral cavity in the study group

S. No.	Pre-cancerous lesion	Numbers	Percentage
1	Oral Submucous fibrosis	58	56.86
2	Leukoplakia	20	19.60
3	Erythroplakia	8	7.84
4	Lichen planus	6	5.88
5	Traumatic dental ulcer	10	9.80
6	Total	102	100

Out of the total 102 patients in the study groups, 68 (66.66 %) cases had habit of tobacco chewing, 54 (52.94 %) chewed betelnut, 32 (31.37 %) were smokers and 22 (21.56 %) were having alcohol. Thus tobacco chewing was found to be the most common form of addiction followed by betelnut (Table 4).

In the study group, 24 (23.52 %) patients were not having any addictions. Out of 58 cases of OSF, 48 (82.75 %) patients were having a habit of chewing betelnut which was the commonest addiction in OSF patients. Most common form of addiction in pts. of leukoplakia was found to be tobacco chewing, 18 (90 %) pts, followed by smoking in 14 pts. (70 %).

In cases of the erythroplakia, tobacco chewing (75 %), smoking (75 %) and alcohol intake (75 %) were seen equally. In cases of lichen planus, no addictions were found. In traumatic dental ulcer cases only two patients had a history of tobacco chewing and alcohol use.

Table 2 Age distribution of patients in the study group

Age group	OSF	Leukoplakia	Erythroplakia	LP	TDU	Total	%
11–20 years	3	0	1	0	0	4	3.92
21–30 years	14	5	0	1	3	23	22.54
31–40 years	9	2	1	4	1	17	16.66
41–50 years	18	4	4	0	1	27	26.47
51–60 years	4	4	0	1	2	11	10.78
>60 years	10	5	2	0	3	20	19.60
Total	58	20	8	6	10	102	100

Table 3 Sex distribution

Premalignant lesion	Male	%	Female	%
OSF	37	36.27	21	20.59
Leukoplakia	15	14.70	5	4.90
Erythroplakia	6	5.88	2	1.96
Lichen planus	2	1.96	4	3.92
Traumatic dental ulcer	10	9.80	0	0
Total	70	68.62	32	31.37

In 30 (29.41 %) cases, ODH was found to be poor.

Duration of chewing habit along with the frequency was also noted. Maximum number of cases had a chewing habit for 1–5 years (34 patients, 43.59 %) and 28 cases had the habit for 6–10 years (35.89 %) (Table 5).

DURATION OF ADDICTION

Table 4 Addictions in the study group

Lesion	Addictions											
	Tobacco		Betelnut		Paan		Smoking		Alcohol		None	
	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%
OSF (58)	42	72.41	48	82.75	14	24.13	12	20.68	12	20.68	6	10.34
Leukoplakia (20)	18	90	4	20	2	10	14	70	2	10	2	10
Erythroplakia(8)	6	75	2	25	2	25	6	75	6	75	2	25
Lichen planus (6)	0	0	0	0	0	0	0	0	0	0	6	100
Traumatic dental ulcer (10)	2	20	0	0	0	0	0	0	2	20	8	80
Total (102)	68	66.66	54	52.94	18	17.64	32	31.37	22	21.56	24	23.52

Table 5 Duration of addiction

S. No.	Duration	Number	%
1	1–5 years	34	43.58
2	6–10 years	28	35.89
3	11–15 years	8	10.25
4	16–20 years	6	7.69
5	21–25 years	2	2.56
6	Total	78	100

Discussion

Interesting observations were made regarding incidence, clinical features and predisposing factors.

Incidence of Various Pre-cancerous Lesions of the Oral Cavity

In the present study a total of 102 cases were included. Out of which 58 cases (56.86 %) had oral submucous fibrosis, 20 cases (19.60 %) were of leukoplakia, ten cases (9.80 %) were of traumatic dental ulcer, eight cases (7.84 %) were of erythroplakia and 6 (5.88 %) were cases of lichen planus.

According to a study by Cox and Walker [8] OSF has now become an Indian epidemic with an estimated 2.5 million people being affected with this disease. Its prevalence has risen from 0.16 % in 1967 to 3.2 % in 1994 [1].

OSF has the highest incidence in the study group also due to the fact that it causes early symptoms for which patient seeks early medical attention unlike in leukoplakia which causes only a painless white plaque in the oral cavity.

Among other Pre-cancerous lesions leukoplakia is the most common, representing 85 % of such lesions [9] with the incidence of 28.9 per 1,000 people.

Traumatic dental ulcers can be found in 2.1 per 1,000 persons and oral lichen planus in 1 per 1,000 people [9].

Erythroplakia is a rare lesion diagnosed only in 0.1–0.6 of every 100,000 persons annually [10.]

Age Incidence

The majority of patients in the study group i.e. 27 (26.47 %) were in the age group of 41–50 years. The youngest being a 19 year old male and the eldest being an 85 year old male.

Sirsat and Pindborg [11] found a wide age range in patients of OSF, although majority were between 30 and 50 years age group. Pindborg (1965) in a comparative study of Bombay and Lucknow reported that youngest patient was 32 and oldest was 72 years of age [4].

Leukoplakia occurs in persons over 40 years of age [9, 12]

The mean age at diagnosis in cases of erythroplakia is 50–69 years; the aging process itself is the greatest risk for premalignancy [13].

Lichen planus is seen commonly in middle aged adults [14].

Sex Incidence

Out of total 102 cases, 70 were males (68.62 %) and 32 (31.37 %) were females with a male to female ratio of 2.18:1.

Sharan [15] and Wahi et al. [16] found the male:female ratio to be 2:1 in their study of OSF Pindborg et al. [4] reported female preponderance with F:M = 8:3. Dayal et al. [17] reported male predominance with a ratio of 4.2:1. Earlier there was a female predilection as reported by Pindborg et al. [4] due to the widespread female habit of chewing betelnut and conventional betel quid. Considering the fact that there is availability of processed betelnut and tobacco as gutka in affordable packets and widespread acceptance of its use may be the reason of male predominance now.

Other pre-cancerous lesions like leukoplakia and erythroplakia affect predominantly males [9] with a slight decrease in the ratio due to increasing use of tobacco products in females.

In cases of lichen planus, out of six total cases, four cases were females with a male to female ratio of 1:2. Lichen planus has a relatively strong female predilection and this is consistent with the present study [9, 14].

Addictions

Out of the total 102 patients in the study group, 68 (66.66 %) had habit of chewing tobacco, 54 (52.94 %) chewed betelnut, 32 (31.37 %) were smokers and 22 (21.56 %) were having alcohol. 24 cases (23.52 %) did not have any addictions.

Out of the 58 cases of OSF 48 (82.75 %) patients had a habit of chewing betelnut. In a case control study done by Pindborg and co-workers [18] conducted in Bhavnagar, Gujarat findings were presented confirming betelnut as the most important etiologic factor in OSF. Also the frequency of habitual chewing of betelnut ranged from 35 to 100 %, which is again reported to be higher in OSF patients than in general population, thus implicating betel nut chewing with the development of OSF. Maximum number of cases i.e. 34 (43.58 %) had the habit for the duration of 1–5 years with most cases 60 (76.92 %) having a frequency of chewing for 1–5 times per day. It is also notable, that the relative risk significantly correlated with the frequency of chewing and not with the duration. Hence they concluded that frequency rather than the duration of chewing is more directly responsible for producing OSF.

Most common form of addiction in the patients of leukoplakia was found to be tobacco chewing 18 (90 %) followed by smoking 14 (70 %), in the study group. According to Banoczy [6] and Bouquot and Gorlin [9], leukoplakia is most common in tobacco smokers followed by tobacco chewers in whom malignant transformation rate is comparatively less.

In cases of erythroplakia, smoking, alcohol and tobacco chewing was found equally in the study group. Prout et al. [10] reported prevalence rate of 17 per 1,000 in US adult tobacco users.

In cases of lichen planus, no addictions were found. Lichen planus is considered to be an autoimmune condition but the exact aetiology is unknown [7].

Presenting Complaints

Out of the 58 patients in OSF in the study group, all had the complaint of burning sensation in oral cavity (100 %). Other symptoms were decreased mouth opening (55.17 %).

George et al. [19] in his study reported that the main symptoms of patients were burning sensation on taking pungent articles and difficulty in opening the mouth. Pindborg and Sirsat [11] observed that at the onset of disease, initial symptom was burning in the mouth but later there was stiffening of oral mucosa leading to difficulty in mouth opening. The cases with leukoplakia presented with a painless white plaque in oral cavity, whereas cases with erythroplakia presented with a red macule in the oral cavity.

In traumatic dental ulcer cases, patients presented with painful ulcers opposite jagged tooth or ill-fitting dentures. Lichen planus cases presented with bilateral whitish plaque like lesions with criss cross pattern in the oral cavity.

Local Examination

In all the patients of OSF i.e. in 100 % there was blanching of buccal mucosa with fibrosis of soft palate seen in 72.40 % of cases. Other areas involved were tongue (58.62 %), retromolar trigone (62.06 %), pillars (58.62 %), uvula (58.62 %) and lips (55.17 %). 36 cases (62.06 %) had trismus. All the patients with trismus had fibrosis of pillars and retromolar trigone. In some cases, bands of fibrosis were palpable in buccal mucosa, pillars and pterygomandibular raphe. Blanching of oral mucosa with areas of fibrosis is diagnostic of OSF as described by all the previous workers.

In leukoplakia, 70 % patients had a white plaque over buccal mucosa, 20 % over the tongue and 10 % over the lip. Thus buccal mucosa was found to be the most common site involved in the study group according to a study by Bouquot and Gorlin [9] more than two-thirds of all leukoplakia are found on buccal mucosa, lip and gingiva.

In erythroplakia, 50 % cases had a red patch over buccal mucosa. Lip and floor of mouth were involved in 25 % cases each. According to Bouquot and Gorlin [9], the most frequent sites of involvement in decreasing order of frequency are the lips, tongue, buccal mucosa, floor of mouth and soft palate.

In cases of traumatic dental ulcer in the study group, 60 % had ulcer over buccal mucosa and 40 % over the tongue. Out of total ten cases, six had a jagged tooth and four were using dentures or braces.

In lichen planus, all the cases had lesions over buccal mucosa. No other site was seen to be involved in the study group. The patients presented with irregular bilateral whitish plaques over buccal mucosa with spider web pattern. According to a study by Batsakis et al. [20], the great majority of cases of lichen planus have irregular bilateral keratinized plaques over the buccal mucosa but any oral surface can be affected. This is consistent with the present study.

Conclusions

The following conclusions were drawn:

- OSF was the commonest Pre-cancerous lesion found followed by leukoplakia.
- Maximum no of cases were between 41–50 years of age.
- The sex incidence was more in males with the ratio of 2.18:1 except in lichen planus in which incidence was more in females with a ratio of 1:2.
- In 29.41 % cases oral dental hygiene was found to be poor.
- Burning sensation in oral cavity was the most common presenting symptom in OSF and was present in all the cases. Difficulty in mouth opening was the second most common complaint present in 55.17 % cases.
- In cases of OSF, betelnut chewing was the commonest habit (82.75 %), either in commercially available packets like gutka, supari or conventional preparations like betel quid.
- Most common form of addiction in cases of leukoplakia was found to be tobacco chewing (90 %) followed by smoking (70 %).
- In cases of erythroplakia tobacco chewing, alcohol intake and smoking were seen equally in 75 % cases each.
- In cases of lichen planus no addictions were found.
- Maximum number of cases (43.58 %) had a chewing habit of 1–5 years duration.
- Maximum number of cases (76.92 %) had the frequency of chewing of 1–5 times per day.
- In cases of traumatic dental ulcer, 60 % had a jagged tooth and 40 % were using ill fitting dentures or braces.
- Majority of cases (52.94 %) belonged to lower socio-economic status.
- Buccal mucosa blanching was present in all cases of OSF. The other sites of fibrosis were soft palate, retro molar trigone, tongue, pillars, uvula and lips in 72.41, 62.06, 58.62, 58.62 and 55.17 % cases respectively.
- Most common site for leukoplakia was found to be buccal mucosa (70 %), followed by tongue (20 %) and lip (10 %).
- Most common site for erythroplakia was found to be buccal mucosa (50 %) followed equally by lip and floor of mouth.
- In cases of traumatic dental ulcer, 60 % had an ulcer over the tongue and 40 % over the buccal mucosa.
- All the cases in lichen planus had lesions over buccal mucosa.

Thus buccal mucosa is the commonest site to be involved in all potentially malignant lesions of the oral cavity.

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