DOI: 10.21088/rjeas.2456.5024.10125.2

RFP Journal of ENT and Allied Sciences
Volume 10 Number 1/January - June 2025

ORIGINAL ARTICLE

Clinical Prognostic Factors of Oral Leukoplakia

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HOW TO CITE THIS ARTICLE:

Keshav Gupta, Ajay Kumar Singh. Clinical Prognostic Factors of Oral Leukoplakia. RFP J ENT Allied Sci 2025; 10(1): 13–18.

ABSTRACT

Background: Oral Leukoplakia is a common pre-cancerous condition observed worldwide which often leaves physician in dilemma regarding its benign or malignant nature. Biopsy is the method followed to rule out its malignant nature which is invasive and painful. Patient has to wait for the histopathology report which is usually available after a week, and sometimes even a repeat biopsy is needed.

Methods: Here we did a detailed prospective study on morphological characteristics of 156 patients of oral leukoplakia and compared these with the biopsy outcome. Results were analysed statistically by chi square test using IBM SSPS 28 package and p values were calculated. P values less than 0.05 were taken to be significant.

Results: Smoking and tobacco chewing habits, age of patient, duration, location, margins, tenderness, texture, tendency to peel easily and Induration of Oral Leukoplakia were found to be statistically significant.

Conclusion: Complete morphological description of Oral Leukoplakia provides significant insight to its nature during its first encounter with the physician, with confirmatory results provided by the biopsy.

KEYWORDS:

- Clinical prognosis oral leukoplakia doctor cancer.

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➢ **Received:** 14-04-2025 ➢ **Accepted:** 24-05-2025

INTRODUCTION AND REVIEW OF LITERATURE

Leukoplakia is a white patch or plaque that cannot be ascribed to any other clinical disease. World Health Organization defines Leukoplakia as "Clinical white patches that cannot be wiped off the mucosa and cannot be classified clinically or microscopically as another specific disease entity".[1] Many oral cavity diseases such as vitamin and mineral deficiencies, candidiasis, oral lichen planus, diphtheria, oral warts and oral cancers can present with whitish discolouration of oral mucosa. Physicians have to investigate thoroughly to diagnose them. Oral Leukoplakia is a relatively rare disease with an estimated prevalence of less than 1%.[2] Oral cancers are believed to be preceded by precancerous lesions, defined clinically based on appearance that is leukoplakia (whitish discolouration of mucosa), erythroplakia (a well-defined reddish patch of the oral cavity), and oral submucous fibrosis (irreversible fibrosis of the submucous tissue). However, histopathological evaluation is required to identify dysplasia.[3-6] Histopathological confirmation should be sought in all cases of leukoplakia. Even leukoplakia with dysplasia may still contain carcinomatous foci.[1] Even though diagnosis is possible by history and clinical examination, there are several knowledge gaps regarding the identification and the work-up of pre-cancerous stages.[7,8] The chances of progression of oral leukoplakia to invasive oral cancer are variable. The literature says that 0% to 36% of pre-cancer progresses to cancer if it grows unopposed.[3,9-12] These existing lacunae in the scientific knowledge of the most common oral pre-cancerous lesion highlight the need for more scientific contributions.

AIM

To study various clinical prognostic factors of oral leukoplakia.

OBJECTIVES

1. To study the gender preponderance of oral leukoplakia.
2. To study the age distribution of oral leukoplakia.
3. To study the effect of the duration of oral leukoplakia.
4. To study the effect of nicotine on oral leukoplakia and malignant conversion
5. To study the effect of the presence of other clinical symptoms on oral leukoplakia.
6. To study the effect of the various clinical morphological factors on oral leukoplakia.

METHODS

Study Design

This was a prospective study. The study was conducted after ethical approval from the Institutional Ethical Committee.

Inclusion Criteria

Patients of all ages and both sexes presenting to ENT Outpatient Department who had white patches on oral cavity examination which could be peeled off by gentle pressure of Lack's tongue depressor and which could not be attributed to any other disease during 1st January 2021- 1st January 2023 at a Tertiary Care Hospital in India were included in this study.

Exclusion Criteria

Patients with known dermatological and auto immune conditions which present with white patches of oral cavity.

Study Procedure

Informed and written consent was taken from all the patients satisfying the inclusion criteria before enrolling them in the study. Detailed history was taken. Morphological characters namely location, colour, size, margins, border, texture, tenderness, induration, tendency to bleed on touch and whether it could be peeled easily with slight pressure of oral speculum and duration of lesion were noted. Basic blood investigations including CBC, PT, INR, HBsAg, HCV and HIV were sent. After availability of reports, Xylocaine sensitivity was done, the area of lesion and surrounding the lesion was anesthetised, A layer of mucosal lesion was gently peeled off with sharp edges of a glass slide till a healthy bleeding base was visible. It was uniformly spread over another glass slide to get a thin smear composed of a single layer of cells in thickness, dried and stained with eosin-haematoxylin and sent for histopathological examination.

Histopathological results regarding malignancy were compared separately with each morphological characteristic applying chi square test using IBM SSPS 28. The lesions showing any sign of dysplasia were considered

malignant while non dysplastic lesions were considered benign. Variables with p value less than 0.05 were considered to be statistically significant. The results were compared with previous literature and conclusion drawn.

OBSERVATIONS

1. Sex Distribution

Table 1: Sex Distribution in patients of Oral Leukoplakia Male: Female Ratio= 1.3:1

Sex Distribution	Benign	Malignant	Total
Female	55	13	68
Male	61	27	88
Total	116	40	156

2. Age Distribution

Table 2: Age Distribution of patients of oral Leukoplakia

Age distribution (Years)	Benign	Malignant	Total
0-9	0	0	0
10-19	0	0	0
20-29	7	0	7
30-39	9	2	11
40-49	62	5	67
50-59	27	5	32
60-69	10	16	26
>=70	1	12	13
Total	116	40	156

3. Duration

Table 3: Duration of Oral Leukoplakia

Duration (Years)	Benign	Malignant	Total
<5	79	7	86
5-<10	26	10	36
>=10	11	23	34
Total	116	40	156

4. History of smoking/tobacco chewing

Table 4: Relationship between Oral Leukoplakia and smoking and tobacco chewing. Odds ratio for presence of malignancy in smokers and tobacco chewers is 10

History of smoking/ tobacco chewing	Benign	Malignant	Total
Absent	52	3	55
Present	64	37	101
Total	116	40	156

5. Presence of other clinical symptoms (Pain/ burning sensation/ irritation) in oral leukoplakia

Table 5: Presence of other clinical symptoms in oral leukoplakia

Other Clinical symptoms	Benign	Malignant	Total
Absent	88	24	112
Present	28	16	44
Total	116	40	156

6. Location

Table 6: Location of Oral Leukoplakia

Location	Benign	Malignant	Total
Lips	2	0	2
Gingiva	4	2	6
Buccal mucosa	68	11	79
Hard palate	31	14	45
Anterior two thirds of tongue	2	7	9
Floor of mouth	8	2	10
Retromolar Trigone	1	4	5
Total	116	40	156

7. Size

Table 7: Size of Oral Leukoplakia

Size in centimetres	Benign	Malignant	Total
<2	6	0	6
2-4	54	12	66
>4	56	28	84
Total	116	40	156

8 Margins

Table 8: Margins of Oral Leukoplakia

Nature	Benign	Malignant	Total
Regular	112	0	112
Irregular	4	40	44
Total	116	40	156

9. Texture

Table 9: Texture of Oral Leukoplakia

Nature	Benign	Malignant	Total
Smooth	87	26	113
Rough	29	14	43
Total	116	40	156

10. Tenderness

Table 10: Tenderness in Oral Leukoplakia

Nature	Benign	Malignant	Total
Non tender	92	12	104
Tender	24	28	52
Total	116	40	156

11. Induration

Table 11: Induration in Oral Leukoplakia

Nature	Benign	Malignant	Total
Non indurated	104	14	118
Indurated	12	26	38
Total	116	40	156

CALCULATIONS

Male-Female ratio = 88/68 =1.29 ~1.3/1

Odds ratio for malignancy as per gender distribution = 55*27/61*13 =793/1485 =1.87

Confounding Factor = Smoking

Age distribution ratios = 0/156:0/156:7/156:11/156:67/156:32/156:26/156:13/156 =0:0:.05:.07:.43:.21:.17:.08

Benign-malignant ratios in different age-groups: i:i:i:9/2:62/5:27/5:10/16:1/12 = i:i:i:4.5:12.4:5.4:.625:.083

Benign-malignant ratio in study population = 116/40 =2.9

Benign-malignant ratios in lesions of different duration = 79/7:26/10:11/23 = 11.3:2.6:.478

Odds ratio for malignancy with tobacco = 52*37/64*3 = 10

Odds ratio for malignancy with pain/burning sensation/irritation = 88*16/28*24 = 2.1

Benign-malignant ratios in lesions of different locations = i:2:6.2:2.2:.3:4:.25

Benign-malignant ratios in lesions of different sizes = i:4.5:2

Odds ratio for malignancy with regular or irregular lesions = i

Odds ratio for malignancy with smooth or rugged lesions = 87*14/29*26 =1.6

Odds ratio for malignancy with tenderness = 92*28/24*12 =8.94

Odds ratio for malignancy with induration = 104*26/12*14 =16.09

RESULT

Incidence of Leukoplakia is more in males with male:female ratio of 1.3:1

Only 3% of oral leukoplakia are found to be malignant in the study population.

Prevalence of malignancy is more in males as odds ratio for finding malignancy in males is 1.87 times that of females. However, smoking is a confounding factor as males are more likely to smoke than females in general population in India.

Incidence of oral leukoplakia is highest in middle age group. It rises to maximum in the age group of 40-49 and then declines a little. Likelihood of malignancy in oral leukoplakia keeps on rising as the age progresses. Also, likelihood of malignancy increases as the duration of leukoplakia increases.

Odds ratio for malignancy in tobacco addicts is high. They are 10 times more likely to have malignancy than the general population.

Odds ratio for malignancy becomes twice with pain/burning sensation / irritation in lesion.

Maximum cases of oral leukoplakia were reported from buccal mucosa followed by the hard palate. Maximum of leukoplakia of retro-molar trigone were malignant followed by anterior two-thirds of tongue. None of the leukoplakia of lip was found malignant.

Most of leukoplakia reported were large leukoplakia of size more than 4 centimetres. Maximum of malignant leukoplakia were also those of size more than 4 centimetres.

There is maximum likelihood of malignancy in irregular lesions. All of the regular lesions were benign and maximum of irregular lesions were malignant.

Odds ratio for malignancy in lesions with rough texture is 1.6

Odds ratio for malignancy is high in tender lesions (8.94)

Odds ratio for malignancy is significantly high withy induration (16.09)

DISCUSSION

Most of the studies show equal incidence of leukoplakia in both sexes. It rarely occurs in the first two decades of life. Only a minority of leukoplakias are premalignant, but identifying these cases is complex.[1] The clinical diagnosis relies on thorough history taking and oral examination.[2] Dysplasia indicates a propensity for malignant transformation.[13,14] While some studies suggested that up to 60 percent of leukoplakias regress or disappear

if tobacco use is stopped. Leukoplakias induced by smokeless tobacco may resolve if the addict abstains from this habit.[13,15,16] Most studies state that spontaneous regression of leukoplakia is exceedingly rare. Surgical and non-surgical treatments are ineffective in preventing possible future malignant transformation[2,17.] Each leukoplakia should be biopsied irrespective of its characterstics.[2,3] Compared to the general population, there is a higher incidence of oral cancer in those having Oral Leukoplakia (40.8-fold increased risk). In a study of 4886 leukoplakias, 42.5% of subjects had a history of smoking. Out of these, 65.5% were diagnosed by ENT Clinicians. They found a 68.8 % risk of malignant transformation in leukoplakia of the tongue.[3] We compared the final histopathological outcome with various epidemiological and morphological characteristics of Oral Leukoplakia and drew various generalisations. However, biopsy must be performed in every case of leukoplakia.

CONCLUSION

The 12 Point Criteria

1. The leukoplakia is tightly adherent to submucosal tissue by fibrosis. It will stay even after applying blunt pressure.
2. Oral Leukoplakia are benign (75%). However, a significant percentage is malignant (25%).
3. Most of the Oral Leukoplakia, whether benign or malignant, bears no symptom other than a whitish patch. However, the presence of other clinical symptoms favours presence of malignancy.
4. The is no sex predilection. However, the incidence of Oral Leukoplakia is slightly higher in males. Chances of malignancy are also higher in males.
5. The incidence of Oral Leukoplakia is highest in the age group of 41-50. There are negligible cases in the first two decades of life. Malignant lesions start outnumbering the benign lesions as age increases.
6. The chances of malignant conversion of Oral Leukoplakia are higher with longer duration. It was merely 8% in the first 5 years of leukoplakia. But it was as high as 67.6% in leukoplakia longer than a decade.
7. Smoking and tobacco chewing strongly favour malignancy in Oral Leukoplakia with a strong association. The association is statistically significant with a causal relationship. (Odds ratio 10)
8. Buccal mucosa is the most commonly involved site in Oral Leukoplakia. Leukoplakia of the Retromolar trigone and anterior two-thirds of the tongue carry a high malignant potential.
9. Benign Oral Leukoplakia usually has regular margins. Malignant Oral Leukoplakia is never regular.
10. Induration and tenderness in Oral Leukoplakia are more specific to malignant lesions. This association is statistically significant.
11. Presence of rough texture slightly favours malignancy in Oral Leukoplakia, but there is a weak statistical association (odds ratio 1.6).
12. Histopathological evaluation should be done in all cases of Oral Leukoplakia.

Ethical issues: None

Funding: No funding received

Conflicts of interest: As authors, we declare that no conflicts of interest are involved in the present study.

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