

## Original Article

### Malignant Transformation of Oral Leukoplakia: Study of 50 Patients

Rathi Rela

Senior Resident, Patna Medical College & Hospital, Patna, Bihar, India

#### ABSTRACT:

**Background:** Oral leukoplakia (OL) is the best-known potentially malignant disorder. The objective of this study is to estimate the rate of malignant transformation in a patients with leukoplakia for more than 5 years and identify significant risk factors of OL malignant transformation. **Methods:** A total of 50 patients with clinical and histopathological diagnosis of OL were retrospectively reviewed. The mean follow-up period was 5.3 years. **Results:** Among 50 cases, 10 (20 %) OL patients developed oral cancer, with a mean duration of 5.2 years. Statistical analysis revealed that dysplasia was an independent risk factor for OL malignant transformation, but age, gender, lesion site, diet habit, smoking and ethanol intake were not risk factors. Consistent with this result, high-risk dysplastic OL had significantly higher malignant incidence than low-risk dysplasia, particularly during the first 2-3 years. **Conclusions** The utilization of high-risk dysplasia as a significant indicator for evaluating malignant transformation risk in patients with OL was suggested, which may be helpful to guide treatment selection in clinical practice.

**Key words:** Leukoplakia, Oral squamous cell carcinoma, precancer.

Received: 14 October 2018

Revised: 27 October 2018

Accepted: 28 October 2018

**Corresponding author:** Dr. Rathi Rela, Senior Resident, Patna Medical College & Hospital, Patna, Bihar, India

**This article may be cited as:** Rela R. Malignant Transformation of Oral Leukoplakia: Study of 50 Patients. J Adv Med Dent Scie Res 2018;6(11):107-109.

#### INTRODUCTION:

Oral squamous cell carcinoma (OSCC) is widely recognized as the most common type of head and neck cancer, with a 50% survival rate over 5 years despite various treatments in the past three decades.<sup>1,2</sup> Oral leukoplakia (OL) is defined as “A white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer”, which is the best-known potentially malignant disorder of the oral mucosa.<sup>3</sup> Reports indicate that 15.8-48.0% of OSCC patients were associated with OL when diagnosed.<sup>4</sup> Histopathologically, oral epithelial dysplasia currently is the most important prognostic indicator for determining the malignant transformation risk of OL.<sup>5</sup> Traditionally, OL lesions are classified as non-dysplasia (hyperplasia) and dysplasia (mild, moderate or severe).<sup>6</sup>

The risk factors of clinical features and lifestyle habits associated with transformation of OL into carcinoma have been evaluated in previous studies. Studies suggest the clinical predictors of malignant transformation in oral leukoplakia, such as age, gender and lesion site, but the results from different study populations vary.<sup>7</sup> The role of smoking and ethanol intake as important risk factors related to malignant transformation remains controversial and unclear.<sup>8</sup> Thus, assessment of these factors for OL malignant transformation is still needed. The objective of the present study is to estimate the malignant transformation rate of 50 patients with OL (mean follow-up of 5.3 years), and identify significant risk factors of OL malignant transformation.



Figure 1 Oral leukoplakia

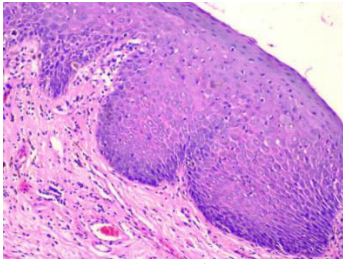


Figure 2 Low power photomicrograph shows changes from basal or parabasal layer.

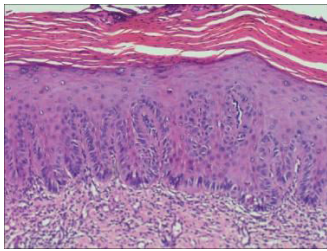


Figure 3 Lesion shows hyperkeratosis of the surface epithelium (H & E, X 40) The fibrous connective tissue Stroma exhibit mild chronic inflammation.

**METHODS**

**Study population**

Information regarding gender, age, site of lesions at the time of the initial diagnosis of OL and diet habit, history of smoking and ethanol intake was all documented in detail.

**Exclusion Criteria:**1.) Patient without the initial histopathologic examination of OL and development of OSC.2.) Clinical history and histopathologic changes of oral white or predominantly white oral benign diseases, for example, linea alba, leukoedema, leukokeratosis; and oral precancerous conditions 3.) Patient with diagnosis of OSCC at first visit. 4.) patient with a follow-up period of less than 12 months. According to the binary grading system newly proposed by WHO<sup>12</sup>, re-examination of the sample confirmed the diagnosis of epithelial dysplasia. The architecture (a total of 7 scoring) and cytology (a total of 9 scoring) criteria for epithelial dysplasia were as follows: Architecture: 1) Irregular epithelial stratification; 2) Loss of polarity of basal cells; 3) Drop-shaped rete ridges; 4) Increased number of mitotic figures;

5) Abnormally superficial mitoses; 6) Premature keratinization in single cells; 7) Keratin pearls within rete ridges.

Cytology: 1) Abnormal variation in nuclear size; 2) Abnormal variation in nuclear shape; 3) Abnormal variation in cell size; 4) Abnormal variation in cell shape; 5) Increased nuclear-cytoplasmic ratio; 6) Increased nuclear size; 7) Atypical mitotic figures; 8) Increased number and size of nucleoli; 9) Hyperchromasia.

We reclassified all lesions as low-risk dysplasia and high-risk dysplasia in the present study. A low-risk lesion was based on observing less than four architectural changes or less than five cytological changes. A high-risk lesion was based on observing at least four architectural changes and five cytological changes.

**Statistical analysis**

A descriptive analysis was performed on clinical and pathologic factors and P values < 0.05 were considered statistically significant.

**RESULTS**

**Patient Characteristics**

A total of 50 patients were enrolled in this retrospective study, with a mean follow-up period of 5.3 years. Of these, 10 (20%) patients developed invasive oral cancer, with the mean time of malignant transformation of 5.2 years. For all the subjects, the gender ratio was equal (40 males: 10 females). The average age at diagnosis was 42.7 years old (range 21-84). The peak incidence was fourth decade of life (33.0%). Tongue was affected in 51.4% patients with OL, followed by buccal mucosa (32.6%). Few lesions were located on the floor of mouth and lip. There were 12.8% patients with spicy dietary habit. The history of smoking and ethanol intake were observed in 29.8% and 6.9% cases, respectively. We found 41 (82.6%) OL cases were low-risk dysplastic lesions and 9 (17.4%) OL cases were high-risk dysplastic lesions. Among 50 OL lesions, 6 of 41 low-risk dysplasia and 5 of 9 high-risk dysplasia developed into cancer, respectively. We observed that a high-risk dysplastic OL was associated with an increased oral cancer risk.

L Size of OL	L1 Lesion less than or equal to 2
	L2 Lesion of 2-4 cm
	L3 Lesion greater than 4cm
	L <sub>x</sub> Site of lesion not specified
P Histopathological picture	P0 No dysplasia
	P1 Dysplasia
	PX Presence of dysplasia not specified
C Clinical presentation	C1 Homogenous leukoplakia
	C2 Non- homogenous leukoplakia
Stage of leukoplakia	Evaluation of leukoplakia based on histopathological examination
	Evaluation of leukoplakia based on clinical manifestation

Table 1 Staging of OL

## DISCUSSION

In the present study, we evaluated the malignant transformation rate of patients with OL, and identified the risk factors of malignant transformation during a relatively long follow-up period. Of the 50 cases, 39 (17.9%) patients developed invasive cancer, with a mean malignant transformation period of 5.2 years. Dysplasia was an independent risk factor for OL malignant transformation, but age, gender, site, diet habit, smoking and ethanol intake were not risk factors. In our series, according to the WHO criteria, we considered the time elapsed from the initial diagnosis of OL to the development of cancer. In this context, we excluded patients with diagnosis of OL concomitant OSCC at the first visit or patients with a followed-up period of less than 12 months after the initial diagnosis of OL. Although it is a well-known fact that the histological classification of OL lesions is imperfect, which may involve subjectivity, we cannot do without it to date.<sup>12</sup> Notwithstanding it had been elucidated that oral lesions with epithelial dysplasia more often develop into cancer than those with hyperplasia in previous findings<sup>13</sup> few studies have examined the risk of malignant development in different grades of dysplastic OL. In an American population, moderate or severe dysplastic OL was associated with 2.30-fold increased risk of malignant transformation, compared with mild dysplasia or hyperplasia<sup>14</sup>. In a Dutch study<sup>19</sup>, OL diagnosed with moderate or severe epithelial dysplasia had a significantly higher risk of malignant development than leukoplakia with lower dysplasia grades (P < 0.01). These findings were similar to ours. Consistent with this result, patients with high-risk dysplastic OL had significantly higher oral cancer incidence than low-risk dysplasia, particularly during the first 2-3 years of follow-up. It is suggested that rigorous follow-up in the first 2-3 years for patients with diagnosis of dysplastic OL may be important to detect early malignant events. We observed the average age at diagnosis of OL is 52.7 years, while other study populations had an average age closer to 60 years<sup>15</sup>. The peak incidence of OL was in the fifth decade of life in our study, earlier than the sixth decade in other reports<sup>16</sup>. The predominant sites of lesions are the tongue and buccal mucosa, and few lesions were located on the floor of mouth, whereas the tongue and floor of mouth were reported as the most common sites in Western countries<sup>17</sup>. Moreover, it may be generally accepted that smoking and ethanol intake play significant roles in the development of OL, but the roles of those in the malignant transformation of OL is conflicting and yet unclear. Studies<sup>18</sup> have demonstrated an increased risk of malignant transformation in the non-smoking cohort, while the study by Ho et al<sup>14</sup> and our present study found smoking was not a significant factor in transformation risk. Further studies are needed to investigate the roles of lifestyle habits in the malignant process of OL.

## CONCLUSIONS

In summary, we evaluated the usefulness of the new system of grading dysplasia proposed by WHO in prediction of OL malignant transformation risk. High risk dysplasia was a significant indicator for OL malignant transformation. It is thus important to detect early malignant events of OL with the diagnosis of high-risk dysplasia.

## REFERENCES

1. Parkin DM, Bray F, Ferlay J, Pisani P: Global cancer statistics, 2002. *CACancer J Clin* 2005, 55:74-108.
2. Warnakulasuriya S: Global epidemiology of oral and oropharyngeal cancer. *Oral oncol* 2009, 45:309-316.
3. Warnakulasuriya S, Johnson NW, van der Waal I: Nomenclature and classification of potentially malignant disorders of the oral mucosa. *J Oral Pathol Med* 2007, 36:575-580.
4. van der Waal I: Potentially malignant disorders of the oral and oropharyngeal mucosa; present concepts of management. *Oral Oncol* 2010, 46:423-425.
5. Scheifele C, Reichart PA: Oral leukoplakia in manifest squamous epithelial carcinoma. A clinical prospective study of 101 patients. *Mund KieferGesichtschir* 1998, 2:326-330.
6. Haya-Fernandez MC, Bagan JV, Murillo-Cortes J, Poveda-Roda R, Calabuig C: The prevalence of oral leukoplakia in 138 patients with oral squamous cell carcinoma. *Oral Dis* 2004, 10:346-348.
7. Hogewind WF, van der Waal I, van der Kwast WA, Snow GB: The association of white lesions with oral squamous cell carcinoma. A retrospective study of 212 patients. *Int J Oral Maxillofac Surg* 1989, 18:163-164.
8. Liu et al. *BMC Cancer* 2010, 10:685 <http://www.biomedcentral.com/1471-2407/10/685> Page 5 of 6
9. Petti S: Pooled estimate of world leukoplakia prevalence: a systematic review. *Oral Oncol* 2003, 39:770-780.
10. Napier SS, Speight PM: Natural history of potentially malignant oral lesions and conditions: an overview of the literature. *J Oral Pathol Med* 2008, 37:1-10.
11. Reibel J: Prognosis of oral pre-malignant lesions: significance of clinical, histopathological, and molecular biological characteristics. *Crit Rev Oral Biol Med* 2003, 14:47-62.
12. Warnakulasuriya S, Reibel J, Bouquot J, Dabelsteen E: Oral epithelial dysplasia classification systems: predictive value, utility, weaknesses and scope for improvement. *J Oral Pathol Med* 2008, 37:127-133.
13. Kujan O, Oliver RJ, Khattab A, Roberts SA, Thakker N, Sloan P: Evaluation of a new binary system of grading oral epithelial dysplasia for prediction of malignant transformation. *Oral Oncol* 2006, 42:987-993.
14. Ho PS, Chen PL, Warnakulasuriya S, Shieh TY, Chen YK, Huang IY: Malignant transformation of oral potentially malignant disorders in males: a retrospective cohort study. *BMC Cancer* 2009, 9:260.
15. Shiu MN, Chen TH, Chang SH, Hahn LJ: Risk factors for leukoplakia and malignant transformation to oral carcinoma: a leukoplakia cohort in Taiwan. *Br J Cancer* 2000, 82:1871-1874.
16. Silverman S Jr, Gorsky M, Lozada F: Oral leukoplakia and malignant transformation. A follow-up study of 257 patients. *Cancer* 1984, 53:563-568.
17. World Health Organization: World Health Organization international histological classification of tumours. In *Histological typing of cancer and precancer of the oral mucosa*. Edited by: Pindborg JJ, Reichart PA, Smith CJ, Van der Waal I. Berlin: Springer; 1997:21-23.
18. Lodi GSA, Bez C, Demarosi F, Carrassi A: Interventions for treating oral leukoplakia. *Cochrane Databases Syst Rev* 2006, CD001829.

**Source of support:** Nil

**Conflict of interest:** None declared

This work is licensed under CC BY: *Creative Commons Attribution 3.0 License*.