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ORIGINAL RESEARCH

BCL-2 AND MDM2 EXPRESSION IN ORAL LICHEN PLANUS: AN IMMUNOHISTOCHEMICAL STUDY

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Abstract

Background: Oral lichen planus (OLP) is a chronic T-cell mediated inflammatory disease that affects the basal keratinocytes of the epithelium. Bcl-2 and MDM2 are important markers used to assess cell cycle regulation and apoptosis. The present study aimed to evaluate the expression of Bcl2 and MDM2 in oral lichen planus.

Materials and methods: Thirteen histopathologically confirmed cases of OLP were included in the present study. Immunohistochemistry was performed with BCL2 and MDM2 primary antibodies and analyzed by two oral pathologists. Statistical analysis was performed using SPSS software Version 23.

Results: The study comprised of 6 males and 7 females. The buccal mucosa was the most common site affected, followed by the retromolar trigone. Mild expression of BCL2 was noted in seven cases (53.8%) and moderate in one case (7.7%) of oral lichen planus. Mild expression of MDM2 was noted in three cases (23.1%) and moderate expression in nine cases (69.2%) of lichen planus.

Conclusion: The findings of this study highlight that oral lichen planus (OLP) exhibit immunoexpression of MDM2 and BCL2, suggesting a potential role in apoptosis and risk of malignant transformation.

Keywords**:** MDM2, BCL-2, immunohistochemistry, lichen planus, buccal mucosa

INTRODUCTION

Oral lichen planus (OLP) is a chronic T-cell-mediated autoimmune disorder that commonly affects the skin and the mucous membrane of the oral cavity [1]. Clinically, six variants of OLP have been reported which include reticular, papular, plaque-like, atrophic, erosive, and bullous types [2]. Although the etiology of OLP remains unclear, several factors have been speculated, including medications (e.g., ibuprofen, NSAIDs, aspirin), infections (e.g., viral hepatitis C virus), antimalarial and retroviral therapy, genetic factors, dental materials, trauma, stress (both external and internal), diabetes, hypertension, malignant neoplasms, immunodeficiency, and bowel disorders [3]. The etiopathogenesis of OLP has been postulated by various authors. This involves immune dysregulation through mechanisms such as nonspecific mechanisms, autoimmune responses, humoral immunity, and antibody-mediated immune responses [4]. According to Roopashree et al., activated CD8+ T

cells attack the basal keratinocytes of the epithelium, and these cytotoxic T cells secrete TNF-alpha, triggering apoptosis of basal keratinocytes[5]. Keratinocytes produce collagen IV and laminin V, which are essential for the structure of the epithelial basement membrane [5].

The apoptosis of keratinocytes leads to disruption of the basement membrane [5,6,7].

Various proteins involved in cell cycle regulation and apoptosis are known to play an important role in the pathogenesis of OLP. Murine double minute 2 (MDM2) is a negative regulator of the p53 tumor suppressor protein. The primary function of MDM2 is to suppress p53 activity. Overexpression of MDM2 can inactivate p53, and promote tumor progression [8,9]. Cancer genomics datasets have reported overexpression of MDM2 in various malignancies, including lung, breast, esophageal, colorectal, gastric, liver, and oral cancers [9]. BCL2, an anti-apoptotic protein. The abnormal expression of Bcl2 results in inhibition of apoptosis and is frequently observed in various malignancies. The present study aims to evaluate the expression of BCL2 and MDM2 in oral lichen planus

MATERIALS AND METHODS

Sample collection

This retrospective cross-sectional comparative study was conducted between April and June 2024, after obtaining approval from the Institutional Ethics Committee (SRB/SDC/OPATH-2202/24/203). The study included 13 histopathologically proven cases of oral lichen planus reported at a private dental college and hospital in Tamilnadu, India. Age, gender and site of the lesion was noted down from the departmental records.

Histopathological analysis

The hematoxylin and eosin (H&E) slides were retrieved from the department archive and re-evaluated by two oral pathologists to confirm the diagnosis of oral lichen planus. Subsequently, two sections were prepared on coated slides for further analysis.

Immunohistochemical analysis

Immunohistochemistry was performed according to the standard operating protocol of the laboratory. Paraffin embedded blocks were sectioned in 3µ thickness onto a charge slide and incubated overnight at 70°C, deparaffinized in xylene followed by antigen retrieval (Traigunya -ARS CellKraft) in an electrical pressure cooker for 20 minutes and tampering it to room temperature. The slides were blocked by endogenous peroxidase blocking (EnVision Flex Dako) for 30 minutes. After each steps pH was maintained by keeping it in Tris buffer solution for 6 mins (pH - 7.4) followed by primary mouse monoclonal antibody anti-human incubation of BCL2 (Clone : IHC514-7 GeneAb™) and MDM2 (Clone : PM263 PathnSitu) for 90 minutes. Followed by buffering for 6 mins and treating it in a secondary antibody (Envision Flex/ HRP Dako) for 30 minutes. Then 3,3′-Diaminobenzidine + chromogen (3,30-diaminobenzidine tetrahydrochloride) for 5 to 10 minutes and counterstained it in hematoxylin. Following the slides were dehydrated and mounted permanently with mounting media (Dibutyl Phthalate Polystyrene Xylene). Immunohistochemical stained slides were evaluated by two oral pathologists and scoring has been given as -(negative), +(mild), ++(moderate), +++(intense).

RESULTS

Clinico-demographic details

The mean age of patients with lichen planus was noted as 44.07 years. A slight female predilection was observed, with a male-to-female ratio of 0.86:1 (46.2% - males; 53.8% - females). Oral lichen planus was most commonly reported on the buccal mucosa (61.5%). The reticular type of lichen planus was observed in 9 cases (69.2%), and erosive type was seen in 4 cases (30.8%) (Table 1).

Bcl-2 and MDM2 immunoexpression

In the epithelium, BCL2 was not expressed in five cases (38.5%), mild expression was noted in seven cases (53.8%) and moderate in one case (7.7%). MDM2 was not expressed in one case (7.7%) of lichen planus, mild expression was noted in three cases (23.1%) and moderate expression in nine cases (69.2%) in epithelium (Figure 1).

Statistical analysis

Statistical analysis was performed using chi- square test with IBM SPSS software 23. Chi square analysis performed to assess the significance (p value) of the study. P value ≤ 0.05 is considered a significant value.

BCL2 expression in epithelium showed no significant difference in relation to site and gender (p= 0.874; p = 0.237 respectively). Furthermore, MDM2 expression in epithelium also showed no significant difference in relation both site and gender (p = 0.890, p = 0.503).

Table 1. Clinicodemographic details of included patients

Sl no	*Age*	*Gender*	*Site*	*Type*
1	*37*	*Male*	*Buccal mucosa*	*Reticular type*
2	*29*	*Male*	*Buccal mucosa*	*Reticular type*
3	*29*	*Male*	*Palate*	*Reticular type*
4	*59*	*Female*	*Buccal mucosa*	*Erosive type*
5	*59*	*Female*	*Buccal mucosa*	*Erosive type*
6	*59*	*Female*	*Retromolar trigone*	*Reticular type*
7	*28*	*Male*	*Tongue*	*Reticular type*
8	*28*	*Male*	*Buccal mucosa*	*Reticular type*
9	*37*	*Female*	*Buccal mucosa*	*Reticular type*
10	*61*	*Female*	*Buccal mucosa*	*Erosive type*
11	*39*	*Male*	*Buccal mucosa*	*Reticular type*
12	*49*	*Female*	*Marginal gingiva*	*Erosive type*
13	*59*	*Female*	*Retromolar trigone*	*Reticular type*

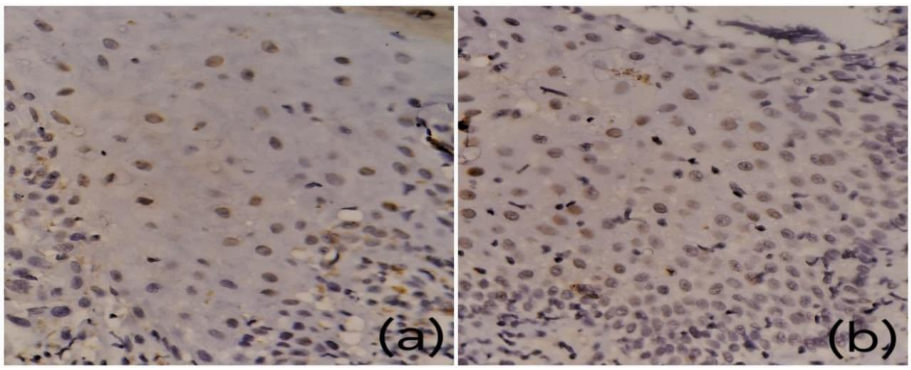

Figure 1. MDM2 expression in lichen planus

DISCUSSION

Oral lichen planus is a chronic T-cell mediated autoimmune disorder commonly affecting skin and mucous membranes having a malignant potential of 0.4% to 12.5% [10,11]. OLP usually affects middle-aged and older adults, with a higher prevalence in females. In the present study, the mean age of affected individuals was 44.07 years, with a slight female predilection. This finding is consistent with previous studies, such as those by Leyva-Huerta et al. who reported a mean age of 53 ± 12.3 years and a female predominance of 76.2% and Hazdi-Mihailovic et al. showed similar mean age of 56.3 years [12,13]. The higher prevalence in females may be attributed to hormonal fluctuations, particularly in perimenopausal women, which can lead to variations in stress hormone levels [14]. Cases of lichen planus turning into oral squamous cell carcinoma have also been reported [15,16]. OLP is characterized by molecular alterations, including the overexpression of Murine

Double Minute 2 (MDM2) and B-cell lymphoma 2 (BCL2), both of which contribute to tumor progression [17]. MDM2 is a proto-oncogene (locus: 12q14.3) encoding an E3 ubiquitin ligase that acts as a negative regulator in the MDM2–p53 autoregulatory pathway. It binds directly to p53, represses its transcriptional activity, and promotes proteasomal degradation [18]. Overexpression of MDM2 negatively regulates the tumor suppressor gene p53, leading to p53 inactivation. Consequently, in response to DNA damage, cells are less able to undergo apoptosis or halt the cell cycle because p53 activity is limited. BCL2 is an anti-apoptotic protein expressed in apoptotic keratinocytes of OLP, and its overexpression has been associated with malignant transformation [16,19]. In our study, the reticular type of OLP was the most commonly reported, followed by the erosive type. Both showed overexpression of BCL2 and MDM2, consistent with the findings of Giuliani et al. and Guan G et al. [16,18].

Previous studies have reported that MDM2 overexpression is linked to malignant transformation [20]. MDM2 overexpression has been associated with a poor prognosis in various carcinomas, including breast carcinoma, esophageal carcinoma, hepatocellular carcinoma, and renal cell carcinoma [21.22.23.24.25]. In early oral squamous cell carcinoma (OSCC), MDM2 overexpression may serve as a marker for tumor development and aggressiveness [26]. The lichen planus is known to cause invasive oral squamous cell carcinoma [27,28]. Overall, the overexpression of MDM2 in OLP is related to the regulatory mechanisms of apoptosis and indicates a favorable environment for malignant transformation.

CONCLUSION

The findings of this study highlight that oral lichen planus (OLP), particularly erosive types, exhibit overexpression of MDM2 and BCL2, suggesting a potential role in apoptosis and increased risk of malignant transformation.

DECLARATIONS

Ethics approval and consent to participate

Not applicable

Conflicts Of Interests

None

Author Contribution

Funding

None

REFERENCES

1. Srivastava KC, Saini RS, Lin GSS, Heboyan A, Shrivastava D. A Decadal Bibliometric Analysis on the Therapeutic Strategies in Oral Lichen Planus. Health Sci Rep. 2025;8(2):e70403. doi: 10.1002/hsr2.70403.
2. Chiang CP, Yu-Fong Chang J, Wang YP, Wu YH, Lu SY, Sun A. Oral lichen planus - Differential diagnoses, serum autoantibodies, hematinic deficiencies, and management. J Formos Med Assoc. 2018 Sep;117(9):756-765.
3. Cassol-Spanemberg J, Rodríguez-de Rivera-Campillo ME, Otero-Rey EM, Estrugo-Devesa A, Jané-Salas E, López-López J. Oral lichen planus and its relationship with systemic diseases. A review of evidence. J Clin Exp Dent. 201810(9):e938-e944.doi: 10.4317/jced.55145.
4. Srinivas K, Aravinda K, Ratnakar P, Nigam N, Gupta S. Oral lichen planus - Review on etiopathogenesis. Natl J Maxillofac Surg. 2011;2(1):15-6.doi:10.4103/0975-5950.85847.
5. Roopashree MR, Gondhalekar RV, Shashikanth MC, George J, Thippeswamy SH, Shukla A. Pathogenesis of oral lichen planus--a review. J Oral Pathol Med. 2010 Nov;39(10):729-34. doi: 10.1111/j.1600-0714.2010.00946.x.
6. Maheswari TN, Choudhary M. Management of oral lichen planus based on the existing clinical practice guidelines. J Indian Acad Oral Med Radiol. 2020;32(3):284. doi:10.4103/jiaomr.jiaomr_55_20.
7. Karatsaidis A, Hayashi K, Schreurs O, Helgeland K, Schenck K. Survival signalling in keratinocytes of erythematous oral lichen planus. J Oral Pathol Med. 2007 Apr;36(4):215-22. doi: 10.1111/j.1600-0714.2007.00519.x.
8. Vijayan A, Muthukrishnan A. p53 polymorphism in oral lichen planus: A comprehensive review. Int J Health Sci. 2022;6(S5):7733-7744. doi:10.53730/ijhs.v6nS5.10441.
9. Zheng J, Miao F, Wang Z, Ma Y, Lin Z, Chen Y, Kong X, Wang Y, Zhuang A, Wu T, Li W. Identification of MDM2 as a prognostic and immunotherapeutic biomarker in a comprehensive pan-cancer analysis: A promising target for breast cancer, bladder

cancer and ovarian cancer immunotherapy. Life Sci. 2023 Aug 15;327:121832.doi: 10.1016/j.lfs.2023.121832.
10. M D, Tn U, Ramalingam K, S S. Use of the Hospital Anxiety and Depression Scale in Patients with Oral Lichen Planus: An Institutional Experience. Cureus. 2024;16(9):e70521.doi: 10.7759/cureus.70521.
11. Rotaru DI, Sofineti D, Bolboacă SD, Bulboacă AE. Diagnostic Criteria of Oral Lichen Planus: A Narrative Review. Acta Clin Croat. 2020 Sep;59(3):513-522. doi: 10.20471/acc.2020.59.03.16.
12. Leyva-Huerta ER, Ledesma-Montes C, Rojo-Botello RE, Vega-Memije E. P53 and bcl-2 immunoexpression in patients with oral lichen planus and oral squamous cell carcinoma. Med Oral Patol Oral Cir Bucal. 2012 Sep 1;17(5):e745-50. doi: 10.4317/medoral.18013
13. Hadzi-Mihailovic M, Petrovic R, Raybaud H, Stanimirovic D, Ozar Koray M. Expression and role of p53 in oral lichen planus patients. J BUON. 2017 Sep-Oct;22(5):1278-1286.
14. Mohan RPS, Gupta A, Kamarthi N, Malik S, Goel S, Gupta S. Incidence of Oral Lichen Planus in Perimenopausal Women: A Cross-sectional Study in Western Uttar Pradesh Population. J Midlife Health. 2017;8(2):70-74.doi: 10.4103/jmh.JMH_34_17.
15. Kaplan BR. Oral lichen planus and squamous carcinoma: case report and update of the literature. R I Dent J. 1991 Winter;24(4):5-9, 11-4. PMID: 1819863.
16. Giuliani M, Troiano G, Cordaro M, Corsalini M, Gioco G, Lo Muzio L, Pignatelli P, Lajolo C. Rate of malignant transformation of oral lichen planus: A systematic review. Oral Dis. 2019 Apr;25(3):693-709. doi: 10.1111/odi.12885.
17. Tampa M, Caruntu C, Mitran M, Mitran C, Sarbu I, Rusu LC, Matei C, Constantin C, Neagu M, Georgescu SR. Markers of Oral Lichen Planus Malignant Transformation. Dis Markers. 2018 Feb 26;2018:1959506. doi: 10.1155/2018/1959506.
18. Guan G, Mei L, Polonowita A, Hussaini H, Seo B, Rich AM. Malignant transformation in oral lichen planus and lichenoid lesions: a 14-year longitudinal retrospective cohort study of 829 patients in New Zealand. Oral Surg Oral Med Oral Pathol Oral Radiol. 2020 Oct;130(4):411-418. doi: 10.1016/j.oooo.2020.07.002.
19. Arreaza AJ, Rivera H, Correnti M. Expression of COX-2 and bcl-2 in oral lichen planus lesions and lichenoid reactions.Ecancermedicalscience. 2014;8:411. doi: 10.3332/ecancer.2014.411.
20. Barak Y, Juven T, Haffner R, Oren M. mdm2 expression is induced by wild type p53 activity. EMBO J. 1993;12(2):461-8. doi: 10.1002/j.1460-2075.1993.tb05678.x.
21. Cuny M, Kramar A, Courjal F, Johannsdottir V, Iacopetta B, Fontaine H, Grenier J, Culine S, Theillet C. Relating genotype and phenotype in breast cancer: an analysis of the prognostic significance of amplification at eight different genes or loci and of p53 mutations. Cancer Res. 2000 Feb 15;60(4):1077-83.
22. Jiang M, Shao ZM, Wu J, Lu JS, Yu LM, Yuan JD, Han QX, Shen ZZ, Fontana JA. p21/waf1/cip1 and mdm-2 expression in breast carcinoma patients as related to prognosis. Int J Cancer. 1997 Oct 21;74(5):529-34. doi: 10.1002/(sici)1097-0215(19971021)74:5<529::aid-ijc9>3.0.co;2-5.
23. Shimada Y, Imamura M, Shibagaki I, Tanaka H, Miyahara T, Kato M, Ishizaki K. Genetic alterations in patients with esophageal cancer with short- and long-term survival rates after curative esophagectomy. Ann Surg. 1997 Aug;226(2):162-8. doi: 10.1097/00000658-199708000-00007.
24. Endo K, Ueda T, Ohta T, Terada T. Protein expression of MDM2 and its clinicopathological relationships in human hepatocellular carcinoma. Liver. 2000 Jun;20(3):209-15. doi: 10.1034/j.1600-0676.2000.020003209.x.
25. Uchida T, Gao JP, Wang C, Jiang SX, Muramoto M, Satoh T, Minei S, Shimura S, Irie A, Kameya T, Baba S. Clinical significance of p53, mdm2, and bcl-2 proteins in renal cell carcinoma. Urology. 2002 Apr;59(4):615-20. doi: 10.1016/s0090-4295(01)01601-6.

Katayama A, Ogino T, Bandoh N, Takahara M, Kishibe K, Nonaka S, Harabuchi Y. Overexpression of small ubiquitin-related modifier-1 and sumoylated Mdm2 in oral squamous cell carcinoma: possible involvement in tumor proliferation and prognosis. Int J Oncol. 2007 ;31(3):517-24.

26. Sowmya, S; Sangavi, R. Evaluating the Antioxidant and Anti-Inflammatory Effects of Nano Encapsulated Vitamin A with Chitosan Gel- In vitro Study. Journal of Indian Academy of Oral Medicine & Radiology 37(2):p 210-214, Apr–Jun 2025. | DOI: 10.4103/jiaomr.jiaomr_291_24
27. Muthusamy M, Ramani P, Arumugam P, Rudrapathy P, Kangusamy B, Veeraraghavan VP, Jayaraman S, Kannan B, Pandi A. Assessment of various etiological factors for oral squamous cell carcinoma in non-habit patients- a cross sectional case control study. BMC Oral Health. 2025 Jan 13;25(1):62. doi: 10.1186/s12903-024-05406-z.