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Discerning Oral Lichen Planus from Oral Lichenoid Reactions: A Comprehensive Analysis of Clinical, Histological and Molecular Signatures

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Abstract

Background:- The complex clinical, histological, and genetic features that differentiate these diseases are explored in this narrative review. The review summarizes recent research with an emphasis on the thorough investigation of these oral mucosal illnesses, **Aim:-** Investigating histological, clinical, and molecular markers in detail was the main goal, with a focus on differentiating between oral lichen planus (OLP) and oral lichenoid reaction (OLR). The objective was to present an in-depth understanding of the intricate components that go into the differential diagnosis, **Methodology:-** Inclusion criteria which covered material from 2000 to 2023 and focused on English-language studies including human patients with OLP and OLR. A thorough investigation was guaranteed by a methodical search approach using a variety of databases (such as Pubmed Central, Google scholar, Scopus, Web of Science, etc.) and manual searches. MeSH phrases and free-text keywords made it easier to explore the subtleties of histology, clinical, and molecular aspects, **Results:-** The results were categorized into molecular markers, histological features, and clinical presentations using thematic data synthesis. A clear and thorough analysis was provided by the qualitative transformation of the synthesized data, which revealed subtle distinctions between OLR and OLP.**Conclusion:-** For pathologists, doctors, and researchers negotiating the complex terrain of OLP and OLR, this article is an invaluable resource. It helps improve treatment plans and diagnostic precision for these intricate oral diseases by combining several elements.

Key words:-Autoimmune response. Molecular profiling, Oral mucosal disorders, Oral lichen planus, Oral Lichenoid reactions

Introduction

The oral cavity is significantly affected by complex chronic inflammatory mucocutaneous illnesses known as oral lichenoid reactions (OLRs) and oral lichen planus (OLP). Although these disorders share certain clinical and histological aspects, they also have unique characteristics that require a sophisticated understanding to properly diagnose and treat the problem.

Terminology and Nomenclature

OLRs and OLP get their namesake from lichen, a symbiotic organism of fungi and algae, which has lacy, white streaks. On the other hand, "lichen planus" and "lichenoid reactions" signify different things.[1,2]Lichen planus is an immunologically driven mucocutaneous condition affecting the skin, scalp, nails, oral mucosa, and

vaginal mucosa. It is characterized by recurrent and chronic exacerbations and remissions. Dr. Erasmus Wilson first used the term "lichen" in 1869 to refer to symbiotic relationships. Because of characteristics like lichen, Sir Jonathan Hutchinson officially named it in 1887. Subtypes have been found via ongoing study, which has improved our understanding of the etiology and clinical manifestations. This historical account highlights the breadth and prospective nature of investigations on oral lichen planus[3].

Primary Aim and Objective

This articlecarefully examines the histological, clinical, and genetic subtleties that differentiate oral lichen planus (OLP) from lichenoid reactions. It attempts to assist pathologists, doctors, and researchers in accurately diagnosing and providing the best possible care for these difficult oral illnesses by synthesizing the state of the art.

Methodology

Objective:

- The main objective of this narrative review was to conduct a comprehensive investigation and examination of the various features that include histological, clinical, and molecular markers, with a particular emphasis on distinguishing between lichenoid reactions and oral lichen planus (OLP). A detailed view of the complex elements that contributed to the differential diagnosis of these unique oral mucosal organisms by exploring their entire environment was explored in this review.

Timeline:

- The narrative evaluation covered a wide range of literature, including works published between 2000 and 2023. This purposeful time period was selected to guarantee a current and comprehensive analysis of the growing corpus of information concerning the clinical, histological, and molecular aspects of OLP and lichenoid reactions.

Inclusion and exclusion criteria:

- With clearly specified inclusion and exclusion criteria, the narrative review concentrated on English-language studies including human subjects diagnosed with oral lichen planus (OLP) and lichenoid reactions. The included publications provided information about the differences between these entities on a clinical, histological, and molecular level. Publications written in a language other than English, studies irrelevant to the comparison of OLP and Lichenoid Reactions, and studies unrelated to the research topic were also excluded. This approach guaranteed accuracy and application by ensuring the chosen literature made a direct contribution to the thorough investigation of the molecular, histological, and clinical aspects.

Search strategy:

- A thorough search was conducted using a methodical manner across important academic databases, such as PubMed, Scopus, Google Scholar, and Web of Science. A thorough manual search of relevant medical journals, conference proceedings, and the reference lists of important papers supplemented this method. Using a two-pronged approach, the goal was to find important and little-known research that added to the overall story.

Search keywords and terms:

- In crafting a comprehensive search strategy, an extensive selection of controlled vocabulary terms (MeSH terms) and free-text keywords was strategically employed.This approach aimed to cast a broad net across the intricate landscape of clinical, histological, and molecular signatures distinguishing Oral Lichen Planus (OLP) from Lichenoid Reactions.The carefully chosen MeSH terms, including "Oral Mucosal Diseases," "Oral Lesions," "Autoimmune Diseases," "Immunohistochemistry," "Differential Diagnosis," "Immunopathogenesis," "Oral Pathology," "Mucosal Immunology," "Autoantibodies," and "Lichenoid Tissue Reaction," were combined withfree-text keywords such as "Lichenoid Oral Lesions," "Autoimmune Response," "Molecular Profiling," "Oral Immune Microenvironment," "Inflammatory Mediators," "Cellular Immunology," "Epithelial Dysplasia," "Immunomodulation," "Salivary Biomarkers," and "Oral Preneoplastic Lesions.The strategic use of Boolean operators (AND, OR) in constructing refined search queries facilitated a discerning exploration of the literature, ensuring a thorough examination of the diverse aspects ofclinical, histological, and molecular intricacies in the context of OLP and Lichenoid Reactions.

Data extraction:

- Systematic data extraction emerged, capturing a wide range of study features, approaches, and important conclusions related to the genetic, histological, and clinical aspects that set apart OLP from lichenoid reactions. This procedure followed the use of a uniform form, guaranteeing careful and accurate extraction.

Data synthesis:

- After being systematically organized into thematic groups, the synthesized data experienced a qualitative metamorphosis. The main components of these categories were clinical presentations, histological characteristics, and molecular markers. The narrative that emerged was skilfully constructed to offer a clear and comprehensive examination, elucidating the nuanced differences between lichenoid reactions and OLP from a histological, clinical, and molecular standpoint.

Results

A thorough summary of studies contrasting oral lichen planus (OLP) and oral lichenoid reactions (OLR) is given in Table 1. McCartan et al. (2000)[5] identified a lichen planus-specific antigen, while Al-Hashimi et al. (2007)[4] concentrated on diagnostic and therapeutic features. A thorough overview of the etiopathogenesis, diagnosis, and treatment was provided by Ismail et al. (2007)[6]. Boorghani et al. (2010)[7] investigated the cause, course of treatment, and clinical features. Mast cells and eosinophils were assessed along with histological characteristics by Reddy et al. (2012)[8]. Gueiros and colleagues (2012)[9] examined Langerhans cells. Aminzadeh and colleagues (2013)[10] carried out a comparative study. Saraceno et al. (2013)[11] talked about new discoveries. Clinicopathologic connection was investigated by Mravak-Stipetić et al. (2014)[12]. Gorouhi et al. (2014)[13] examined lichen planus of the skin and mucosa. After replacing dental restorations, lesion regression was investigated by Mårell et al. (2014)[14]. In 2015, Czerninski et al. conducted a comparison of histological and clinical features. On oral lichenoid lesions, Kamath et al. (2015)[16] provided an update. Dudhia et al. (2015)[17] talked about the progression of lichenoid lesions from OLP. Clinical variables were evaluated by Grossmann et al. [18] in 2015. An updated review of the literature was provided by Agha-Hosseini et al. (2019)[19]. In a narrative review, Rotaru et al. (2020) provided diagnostic criteria. Villa and colleagues (2021)[20] emphasized the microbiological perspective. AdditionallyGhier et al. (2023)[21] carried out a retrospective study on oral lichenoid mucositis, and Andabak-Rogulj et al. (2023)[22] assessed the options for OLP therapy.

Incidence/prevalence, gender predominance, age prevalence, clinical features, histopathology, immunohistochemistry, diagnostic criteria, association with other systemic diseases or conditions, association with medications, treatment modalities, prognosis, malignant transformation, and follow-up period are just a few of the factors that Table 2 compares between OLP and OLR. The differences between OLP and OLR for each of these characteristics are highlighted in the table.

Table 3 presents a comparison between the clinical appearance and distribution of OLP and OLR, with reference to Rotaru et al[23]. OLP commonly manifests in multiple forms, such as bullous, reticular, papular, plaque-like, erosive, and atrophic. Lesions are symmetrically and bilaterally distributed. On the other hand, OLR manifests in diverse forms akin to OLP, sharing a comparable distribution; nonetheless, it is frequently linked to external agents. The appearance and distribution features of both situations are explained in depth by the table

Discussion

Prevalence and Incidence

The epidemiological landscape of OLRs and OLP is complicated by the geographical and ethnic variations in their prevalence and incidence. Although OLP is

thought to affect 1% to 2% of the world's population, the prevalence of OLRs is harder to pin down because of the wide range of possible causes [19,20]. Clinicians dealing with a variety of patient populations need to have a thorough awareness of the epidemiology of these disorders.

Examining the historical background of oral lichen planus, notable advancements have been made in the identification and description of the ailment. Standardized techniques to diagnosis have been made easier by the introduction of diagnostic criteria and classifications, such as those put forth by Dr. ErasylbekOmarbekov in 1972 and later modified by the World Health Organization (WHO). These criteria provide a thorough framework for researchers and physicians alike, considering clinical, histological, and immunological factors [2]. The way that diagnostic terms and standards have changed over time highlights how dynamically we are understanding oral lichen planus.

Because of this, the historical contributions of early medical pioneers are the source of the language and nomenclature related to oral lichen planus. These terminology' development mirrors the advancement of our knowledge of this complicated illness, influencing the classifications and diagnostic standards that direct modern therapeutic management.

Pathogenesis of OLP and OLR

Chronic inflammatory disorders affecting the oral mucosa, oral lichen planus (OLP) and lichenoid reactions (OLR) are caused by a complex interplay between genetic predisposition, immunological dysregulation, and environmental stimuli [1,2,3,31,34,41]. Polymorphisms in pro-inflammatory cytokines contribute to vulnerability, and genetic variables are important [34]. The persistent inflammatory process seen in these disorders can be caused by an abnormal immune response brought on by this genetic variant [1].

Immunological dysregulation is present in OLP and OLR, and T-cell-mediated immunity is linked to their pathogenesis [31]. CD8+ T cells in particular, which infiltrate the oral epithelium, indicate a cytotoxic immune response [49]. The deregulation of immune response and the chronic inflammatory milieu in afflicted tissues are caused by pro-inflammatory cytokines such as TNF-α and IFN-γ [34]. One set of environmental factors linked to the development of OLP and OLR include viral infections and metal exposures. It is debatable whether these disorders and viral infections are related [41], however exposure to metals such as mercury and dental amalgam is investigated as a possible trigger [25, 36]. There is still debate over the exact method by which these factors help trigger or intensify the inflammatory response.

Due to similar clinical and histological features, differentiating OLP from OLR and other oral mucosal disorders is difficult, making clinicopathologic correlation difficult when diagnosing OLP using current criteria. To clarify the complex

complexities of these illnesses and improve diagnostic criteria, more study is necessary [1,23,49]

Immunopathogenetic insights

T-cell mediated responses:- In their insightful investigation of the T-cell-mediated reactions involved in OLP pathogenesis, Sugerman et al. [31] identified T-lymphocytes, in particular CD8+ cells, as having a pivotal role. The coordinated mobilization and enlistment of these T-cells plays a major role in the persistent inflammatory infiltration that is seen in OLP lesions. Notably, immune-mediated damage to oral mucosal epithelial cells is largely driven by dysregulated cell-mediated immunity.

- Autoimmune associations:- The investigation of autoimmune connections in OLP by Carrozzo et al. [34] provides insight into the role of pro-inflammatory cytokines, including interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α). Variations in these cytokines turn out to be important factors that influence an individual's vulnerability to OLP, explaining the autoimmune basis of the illness. This highlights the intricate web of interactions between immunological dysregulation and genetic variables in the pathophysiology of OLP.
- Inflammatory responses in Lichenoid reactions:- Lodi et al. clearly distinguish lichenoid reactions from OLP by deciphering the complex inflammatory responses that characterize them in a consensus conference [41]. Immune cells infiltrate the oral mucosa as part of a chain of inflammatory events that ultimately results in tissue destruction. This sophisticated knowledge of inflammatory responses is crucial for distinguishing lichenoid reactions from OLP, highlighting the importance of a thorough immunological evaluation.
- Triggering factors and immune dysregulation:- The study by van der Meij et al. highlights how immunological dysregulation and trigger variables interact in OLP [49]. The fact that there is no clinicopathologic association according to current diagnostic criteria emphasizes how complex OLP diagnosis is. OLP is a complex disorder because of the dynamic interaction of genetic predisposition, environmental factors, and altered immunological responses that lead to the immune dysregulation seen in the condition.
- Shared pathways with OLP- The thorough analysis of OLP pathogenesis by Roopashree et al. [50] reveals pathways in common with autoimmune diseases, which expands our knowledge of the larger immunopathological landscape. The immune systems linked to OLP share similarities with other autoimmune disorders, providing important information on the complex network of immune responses. The identification of common pathways advances our understanding of the immunopathogenesis of OLP.

OLP's immunopathogenesis is closely linked to autoimmune connections, T-cell-mediated responses, inflammatory reactions in lichenoid circumstances,

immunological dysregulation, and common pathways with other autoimmune illnesses. By utilizing the knowledge found in these foundational papers, this thorough investigation broadens our knowledge and creates new opportunities for focused treatment approaches and improved clinical management techniques.

Histopathology of OLP and OLR

Histopathological evaluation is essential for distinguishing OLP from OLR and provides important information on the intricate changes that occur in the oral mucosal tissue. Aravind et al. emphasized the importance of mast cell distribution and basement membrane thickness as critical histopathological characteristics for this classification in their comprehensive investigation [2]. But a more comprehensive analysis of the histological terrain, as described by different investigators, demonstrates complex features.

- Basement membrane alterations:- The histopathological studies, especially the ones by Müller, provide insight into changes in the basement membrane in OLP. Müller's research highlights morphological alterations such as basal cell liquefaction, saw-toothing, and the existence of Civatte bodies in addition to thickness. These changes help to differentiate OLP from other oral mucosal disorders by providing a more detailed understanding of the histological subtleties linked to the condition [51].
- Inflammatory infiltrate- A thorough examination of the inflammatory infiltrate composition in OLP was carried out by Ismail et al. [6], who highlighted the significance of T lymphocytes in particular, CD8+ cells and antigen-presenting cells in the pathophysiology of OLP. The unique inflammatory response observed in OLP as opposed to OLR gives the histopathological characterisation more detail and sheds light on the disease's immunological components.
- Eosinophils and mast cells:- Reddy et al. investigated eosinophils' role in OLP histology and noted that they are found in the subepithelial stroma [8]. This discovery, along with the focus on mast cell dispersion by Aravind et al., paints a complete picture of the cellular elements that contribute to the histopathological landscape of OLP [2,8]. The immune response and tissue alterations seen in OLP are probably influenced by the interactions between these cell types.
- Vascular changes: Vascular modifications were highlighted by Grossmann et al., who also noted enhanced vascularity and endothelial cell enlargement in OLP. By combining these discoveries with changes to the basement membrane, OLP histopathology is better understood, and vascular dynamics influencing overall tissue pathology are clarified. [18].
- Immunohistochemical markers:- According to Agha-Hosseini et al., immunohistochemistry investigations, which include p53, are essential for

differential diagnosis and provide important information about the molecular characteristics of OLP and its possible malignancy [19].

Combining data from different research reveals the complex histopathological characteristics of OLR and OLP, including modifications to the basement membrane, the makeup of the inflammatory infiltrate, the involvement of mast cells and eosinophils, changes to the vasculature, and the functions of immunohistochemical markers. Together, these outline unique histopathological patterns that facilitate accurate diagnosis and distinction.

Immunology and Immunogenetic features

Genetics, cytokines, and immune cells all play a complex role in OLR and OLP immunology, which is characterized by a high frequency of lymphocytic infiltration, especially of CD8+ T cells. This points to a cytotoxic immune response directed against oral epithelial cells. The chronic inflammatory environment and dysregulated immune responses are facilitated by pro-inflammatory cytokines such as TNF-α and IFN-γ. Genetic variations in cytokine genes highlight the contribution of immunogenetic elements to OLP vulnerability, elucidating the diverse clinical presentations and reported treatment outcomes [31, 34].

OLP and OLR are influenced by intricate genetic, immunological, and environmental variables. Understanding immunogenetic traits and performing a histopathological assessment are necessary for an accurate diagnosis. [1].

Diagnostic criteria and challenges

Since the characteristics of oral lichen planus (OLP) and oral lichenoid lesions (OLR) overlap, a comprehensive approach is necessary for diagnosis.

- ***Clinical features and challenges*** [52,53]

OLP clinical spectrum-

- ✓ Multiform Presentation: OLP can present in a variety of clinical forms, including as bullous, reticular, papular, plaque-like, erosive, atrophic, and reticular lesions. These lesions are usually symmetrically distributed in both directions.
- ✓ Challenges: Differentiating between these variances is difficult, highlighting the necessity of accurate clinical assessment.

OLR diagnostic complexity-

- ✓ Clinical Resemblance: OLR and OLP frequently have clinical similarities, necessitating a careful differential diagnosis to differentiate the two conditions.

❒ ***Histopathological evaluation*** [2,12,52]

Basement membrane thickness-

- ✓ Differentiating Factor: Changes in basement membrane thickness are emphasized by Gururaj et al. [52] as a crucial histopathological factor for differentiation.
- ✓ Significance: Determining this characteristic's worth helps classify lesions precisely.

Mast cell distribution-

- ✓ Examining Variations: Differences in the location of mast cells give diagnostic significance to the examination by influencing histological subtleties.

❒ ***Distinguishing benign from malignant lesions*** [39,40,52]

Malignant transformation risk-

- ✓ OLP Association: OLP presents a risk of malignant transformation, emphasizing the necessity of close observation.
- ✓ Potentially cancerous Character: Some lichenoid lesions, particularly those associated with amalgam restorations, have the potential to be cancerous, thus they should be carefully evaluated.

❒ ***Role of Patch testing*** [30,35,52]

Identifying Allergens-

To develop specialized management plans, patch testing is essential in pinpointing the allergens in question that cause lichenoid reactions.

❒ ***Association with dental restorations*** [25,33,38,52]

Amalgam-Related Lesions:

- ✓ Healing Potential: Research indicates that lichenoid lesions may heal clinically and histologically when dental restorations, particularly amalgam, are removed or replaced. This provides a treatment avenue.

❒ ***Immunohistochemical markers*** [9,27,28,52]

Expression of COX-2 and bcl-2:

- ✓ Possible Discriminators:- The ability of immunohistochemical markers like COX-2 and bcl-2 to differentiate OLP from other lichenoid lesions has been investigated, offering insights into the molecular characteristics of these disorders.

❒ ***Genetic, molecular and microbiological aspects*** [20,34,50,52]

- ✓ Tumor Necrosis Factor and Interferon-Gamma: According to Gururaj et al.'s study [], polymorphisms associated with these two proteins may be a factor in an individual's genetic predisposition to OLP.

- ✓ Broader Understanding: Villa et al.'s [20] suggestion to view OLP from a microbiological standpoint may help to clarify its etiology and pathology.

Treatment protocol, recurrence rate and follow-up period of OLP and OLR

Due to their chronic nature and high likelihood of recurrence, OLP and OLR require complex, tailored management that may include phototherapy and corticosteroids [7, 22, 33].Gururaj et al. [52] emphasize the significance of a step-wise approach to treatment, beginning with topical corticosteroids and moving on to systemic drugs in situations of severity. Treating triggers is essential, such as dental restorations [33, 38]. Monitoring treatment effectiveness and identifying malignant alterations require routine follow-up that includes both clinical and histological examinations [52, 53]. Since OLP recurrence rates are about 20% [52], it is imperative to do thorough long-term follow-up that takes patient compliance and trigger factors found during patch testing into account.

Conclusion

Because of their chronic nature and propensity for recurrence, oral lichen planus (OLP) and lichenoid lesions (OLR) require a customized management approach. Based on severity and clinical presentation, customized therapy regimens, involving topical and systemic drugs, must be developed. For the purpose of monitoring therapy effectiveness and identifying malignant changes, routine clinical and histological evaluations are essential. Considering their chronic nature, long-term surveillance is important. Variable recurrence rates highlight difficulties in attaining full resolution even with careful management, requiring close monitoring. Precision medicine and genetic insights may help shape future trends by improving diagnostic precision. More targeted treatments could result from a better understanding of the causal variables, underscoring the need of teamwork in the improvement of oral lichenoid lesion management.

Discerning oral lichen planus from oral lichenoid reactions: a comprehensive analysis of clinical, histological, and molecular signatures

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Table 1: Comparative review of OLP and OLR based on various features as published in previous literature

Author/ year	Type of article	Cause/ pathogenesis	Clinical findings	Histopathological findings	Immunological aspects	Treatment protocol (if applicable)	Conclusion of the article
McCartan BE, et al. (2000)[5]	Lichen Planus--Specific Antigen in OLP and Drug-Induced Lichenoid Reactions	Identification of a specific antigen, immunological aspects.	-	- Identifies a lichen planus-specific antigen and discusses immunological aspects.	-	Identifies a lichen planus-specific antigen and discusses immunological aspects.	
Al-Hashimi, et al. (2007)[4]	Diagnostic and Therapeutic Considerations for OLP and OLR	Diagnostic and therapeutic considerations, clinical and histological aspects.	-	-	-	Emphasizes diagnostic and therapeutic considerations for OLP and OLR, addressing clinical and histological aspects.	
Ismail SB, et al.	Comprehensive Review on OLP	Etiological factors in OLP and OLR.	Pathological features,	-	-	-	Comprehensive review

(2007)[6]	and OLR		etiological factors.				covering etiopathogenesis, diagnosis, management, and malignant transformation of OLP and OLR.
Schlosser BJ (2010)[24]	Lichen Planus and Lichenoid Reactions of the Oral Mucosa	-	Clinical and histological characteristics, diagnostic challenges.	-	-	-	Overview of clinical and histological aspects of OLP and OLR, emphasizing diagnostic challenges.
Boorghani M, et al. (2010)[7]	Clinical Features, Etiology, Treatment, and Management: A Review of Literature	-	Clinical features, etiological factors, treatment approaches.	-	-	-	Comprehensive review on clinical features, etiology, and management of OLP.
Reddy DS, et al. (2012)[8]	Evaluation of Mast Cells, Eosinophils,	-	Histological features, role of mast cells	-	-	-	Evaluates histological features and

	Blood Capillaries in OLP and OLR		and eosinophils.				the role of mast cells and eosinophils in OLP and OLR.
Gueiros LA, et al. (2012)[9]	Increased Number of Langerhans Cells in OLP and OLR	Role of Langerhans cells, comparison between OLP and OLR.	-	Investigates the role of Langerhans cells and compares OLP and OLR.	-	-	Investigates the role of Langerhans cells and compares OLP and OLR.
McParland H, et al. (2012)[25]	Oral Lichenoid Contact Lesions to Mercury and Dental Amalgam	Association with dental materials, role of mercury.	- Histological features, role of mast cells and eosinophils.	-	-	Discusses the role of mercury in oral lichenoid contact lesions and its association with dental materials.	
Aminzadeh A, et al. (2013)[10]	Retrospective Comparative Study on Clinico-Pathologic	-	Clinical and histopathological features, comparative analysis.	-	-	-	Comparative analysis of clinical and histopathological features of

	Features of OLP and OLR						OLP and OLR, aiding in differentiation.
Saraceno R, et al. (2013)[11]	Novel Acquisitions in the Pathogenesis and Treatment of OLP	Pathogenesis, novel treatment approaches.	-	-	Discusses novel insights into the pathogenesis and treatment of OLP.	Novel insights into the pathogenesis and treatment of OLP.	
Mravak-Stipetić, et al. (2014)[12]	Clinicopathologic Correlation of OLP and OLR	Histopathological findings, clinical correlation	-	Histopathological findings correlating OLP and OLR	-	-	Preliminary study providing clinicopathologic correlation
Gorouhi F, et al. (2014)[13]	Cutaneous and Mucosal Lichen Planus: A Comprehensive Review	-	Clinical subtypes, risk factors, diagnosis, and prognosis.	-	-	-	Comprehensive review of cutaneous and mucosal lichen planus, covering clinical subtypes and risk factors.

Mårell L, et al. (2014)[14]	Regression of Oral Lichenoid Lesions after Replacement of Dental Restorations	Effect of dental restoration replacement on lichenoid lesions.	-	-	-	Study on the regression of lesions after dental restoration replacement, suggesting a potential treatment approach.	
Arreaza AJ, et al. (2014)[26]	Expression of COX-2 and bcl-2 in OLP and Lichenoid Reactions	-	Molecular markers, expression of COX-2 and bcl-2 in OLP and lichenoid reactions.	-	Investigates the expression of COX-2 and bcl-2 in OLP and lichenoid reactions.	-	Examines the molecular markers in OLP and lichenoid reactions, focusing on COX-2 and bcl-2 expression.
Gupta S, et al. (2015)[27]	An Update on Etiology, Pathogenesis, Clinical Presentation, Diagnosis, and	-	Clinical features, etiological factors, management strategies.	-	-	-	Provides an updated overview of OLP, covering etiology, pathogenesis,

	Management						clinical presentation, diagnosis, and management.
Arreaza A, et al. (2015)[28]	p53 Expression in OLP and Lichenoid Lesions	-	Molecular markers, expression of p53 in OLP and lichenoid lesions.	-	Investigates the expression of p53 in OLP and lichenoid lesions.	-	Explores the molecular aspect of OLP and lichenoid lesions, focusing on p53 expression.
Czerninski R, et al. (2015)[15]	Clinical Characteristics of Lichen and Dysplasia vs Lichen Planus Cases	-	Clinical and histopathological characteristics, dysplasia in OLP.	-	-	-	Compares clinical and histological features of OLP and dysplasia, aiding in the differentiation of lesions.
Kamath VV, et al. (2015)[16]	Review and Update on Oral Lichenoid Lesions	-	Clinical features, diagnostic updates.	-	-	-	Offers a comprehensive update on oral lichenoid lesions,

							highlighting clinical features and diagnostic advancements .
Dudhia BB, et al. (2015)[17]	Evolution or Revolution from OLP to Lichenoid Lesions	-	Clinical and histopathological evolution, diagnostic criteria.	-	-	-	Discusses the progression from OLP to lichenoid lesions, emphasizing clinical and histopathological aspects.
Grossmann SMC, et al. (2015)[18]	Review of Clinical Features, Etiologies, and Treatments	-	Clinical features, etiological factors.	-	-	-	Comprehensive review on clinical aspects of OLP, covering features, etiologies, and treatments.
Agha-Hosseini F, et al.	Literature Review on OLP and OLR	-	Differentiating features, literature	-	-	-	Provides an updated literature

(2019)[19]			overview.				review on OLP and OLR, focusing on differentiating features.
Rotaru DI, et al. (2020)[23]	Diagnostic Criteria of OLP	-	Criteria for diagnosing OLP, distinguishing features.	-	-	-	Offers a narrative review on diagnostic criteria for OLP, aiding in the accurate diagnosis of the condition.
Villa, T.G., et al. (2021)[20]	Microbiologist Point of View on Oral Lichen Planus	Role of microbiota in OLP and lichenoid lesions	Emphasizes the microbiological perspective on OLP				Emphasizes the microbiological perspective on
Andrea Elenbaas, et al. (2022)[29]	Review of Clinical Features, Etiologies, and Treatments	-		-	-	-	Comprehensive review on clinical aspects of OLP, covering features, etiologies, and

							treatments.
Alsoghier A, et al. (2023)[21]	Retrospective Study on Oral Lichenoid Mucositis	-	Histological features, clinicopathological characteristics	-	-	-	Retrospective study on oral lichenoid mucositis, highlighting clinicohistological characteristics.
Andabak-Rogulj A, et al. (2023)[22]	Different Treatment Modalities of OLP	-	Treatment modalities, outcomes.	-	-	Narrative review on treatment options for OLP, discussing various modalities and their outcomes.	

Table 2: Comparison of OLP and OLR based on various aspects

Sl no.	Various aspects/ features	Oral Lichen Planus (OLP)	Oral Lichenoid Reactions (OLR)
1.	Incidence/Prevalence	Varied [6,23,27]	Associated with dental materials [24,25,30]
2.	Gender predominance	More common in females [23,24,25,27]	No clear gender predilection [24,25]
3.	Age prevalence	Wide age range, including older adults	All age groups
4.	Clinical features	Wickham striae, reticular/erosive forms; [2,27]; White striations, atrophic changes; [1,6,27]; Variable presentation, may include gingival involvement; [30]	Resembles OLP but related to external agents; Variable presentation, may include gingival involvement; [24,30]
5.	Histopathology	T-lymphocytic infiltrate, basal cell degeneration; Hyperkeratosis, hypergranulosis[2,6,23,12,31]	Similar to OLP but may lack characteristic features; Focal inflammation associated with dental materials; [30,32,33]
6.	Immunohistochemistry	Increased mast cells, CD8+ T cells [2,9]	Variable, may show features of hypersensitivity reactions [28,33]

7.	Diagnostic criteria	Clinical, histopathological and immunological. Consideration of atypical presentation [34]	Association with external factors; inclusion of patch test for identification [35,36]
8.	Association with other systemic disease or conditions	Possible association with autoimmune disorders [6,23,27]	Often associated with contact hypersensitivity [25,37]
9.	Association with medications	Linked to certain medications [31]	Frequently associated with drugs like ACE inhibitors [25,37]
10.	Treatment modalities	Topical/systemic steroids, immunosuppressants; [22,27]	Removal of triggering factors, symptomatic relief [33,38]
11.	Prognosis	Chronic, relapsing; potential for malignant transformation [27,39]	Improvement after removal of triggering factors [38,40]
12.	Malignant transformation	Variable, but potential risk; [39,40]	Limited data; potential risk from chronic irritation [40]
13.	Follow-up period	Regular follow-up due to potential malignancy; [41]	Case-dependent, monitor for resolution or exacerbation [11,26]

Table 3:- Comparison between OLP and OLR with respect to their clinical appearance and distribution

Characteristics	**OLP**	**OLR**
Appearance	• A patient may co-occur with two or more OLP types [31,42,43,44,45] • Reticular: Most prevalent; consisting of delicate white striations (Wickham striae) encircled by distinct erythematous borders. Roughness and decreased	occur in various forms that are comparable to OLP. • Reticular; erythematous; Chronic graft against host illness; oral lichenoid medication response. • Plaque-like: Long-term host disease

	mucosal flexibility might result from lesions. • Papular: Tiny, potentially converging white pinpoint papules. • Plaque-like: Generous, uniform white areas. • Erosive: White striae that faintly radiate, erythematous or atrophic ulcerations, erosions of the mucosa. • Atrophic: White striae extending from atrophic lesions encircled by erythema. In gingiva, it manifests as "desquamative gingivitis." • Bullous: Lesions packed with fluid. • Compared to erosive OLP (eOLP), non-erosive OLP lesions (reticular, papular, and plaque-like) are typically asymptomatic [43,46,44,45,47]	versus transplant. • Atrophic: Drug-induced oral lichenoid response. • Erosive: Oral lichenoid medication response, chronic graft versus host disease. [16, 47]
Distribution	Oral lesions distributed bilaterally and symmetrically • Reticular: Usually on both sides, posterior buccal mucosa may extend nearly to the commissures. Additionally, the gingiva, the vermilion border, and the lateral and dorsal surfaces of the tongue may be affected.	The disease known as Chronic Graft vs. Host (CGVHD) can impact any area of the oral mucosa. • Oral Lichenoid Contact Hypersensitivity Reaction (OLCHR): This occurs when the tongue's lateral border, buccal mucosa, or both encounter a dental restoration. • Oral Lichenoid Drug Reaction (OLDR):

	· Buccal mucosa: Papal. • Plaque-like: bilateral posterior buccal mucosa or the tongue's dorsal surface (often). • Atrophic/Erosive: frequently symmetrical and bilateral. "Desquamative gingivitis" is the term used to describe eOLP that affects the gingival mucosa. [31,43,44,45]	Usually manifests as a single oral lesion, setting it apart from OLP lesions that might show bilaterally, symmetrically, or multifocally. • Lichen Planus Pemphigoides: Mostly affects the gingiva and buccal mucosa. • Chronic Ulcerative Stomatitis (CUS): This condition affects the tongue, buccal mucosa, and gingiva and frequently mimics desquamative gingivitis. • Lupus Erythematosus: Usually affects the gingiva, buccal mucosa, and/or hard palate [46, 48]