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Systematic Review

Pediatric oral lichen planus

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Abstract – Background: Oral lichen planus (OLP) is a rare chronic inflammatory mucocutaneous disorder in children, with limited research on its prevalence and clinical features. Therefore, more comprehensive studies are needed. The aim of this review was to synthesize the available evidence on pediatric OLP, its, clinical manifestations, etiology, and treatment options. **Methods:** The search of articles was conducted on Medline between January 2001 and December 2023. The search strategy was based on relevant keywords and Medical-Subject-Headings terms related to OLP and children. After selecting articles, data were extracted and analyzed. **Results:** Twenty-eight articles were included in the review. Clinical manifestations of pediatric OLP varied with common presentations. Its etiology remains unclear, although genetic factors, immune dysregulation, viral infections, and environmental triggers have been implicated. Topical corticosteroids were used as first-line therapy. Other treatment modalities; immunomodulatory agents, phototherapy and systemic corticosteroids; were also explored in the included studies. However, the evidence base for these interventions efficacy and safety in children was limited. **Discussion and conclusion:** OLP as one of the most common oral mucosal diseases in adults, has been rarely described in children. The findings of this review can guide healthcare professionals in diagnosing and managing OLP in pediatric patients based on the current evidence.

Introduction

lichen planus (LP) is known as a common chronic autoimmune affection, in which both skin and mucosal surfaces can be affected. High percentage of patients with oral mucosa lesions have an incidentally discovered vulvar lichen planus. While its exact cause remains unknown, a respected number of authors attributed a cell-mediated immune response. Oral lichen planus (OLP) predominantly affects middle-aged and elderly individuals; however, it is extremely rare in the young population, with only few limited cases documented in the literature. Various factors can explain its rarity in this population such as the minimized autoimmune and systemic diseases incidence, lower stress levels, milder symptoms and the reduced awareness. Pediatric lichen planus incidence is still unknown, but several studies have reported a prevalence less than 2–3% among children [1,2]. Since OLP is recognized as an Oral Potentially Malignant Disorder, carrying a 1–2% risk of malignant transformation in adults [3,4], early diagnosis and timely management are critical and it is notably important in pediatric patients, where the malignant potential is insufficiently studied and its incidence is uncommon.

The aim of this work was to highlight the different characteristics of oral lichen planus in the pediatric population regarding the clinical presentation and management.

Materials and methods

To conduct this review, Preferred Reporting Items for Systematic Review and Meta-Analysis PRISMA 2020 guidelines were followed [5].

Inclusion and exclusion criteria

This narrative review utilized the PICOS framework to formulate an evidence-based question, defined as follows: P (Population): children under 18 years old with a clinical and histological diagnosis of OLP. I (intervention): interventions of all types were considered (topical treatment, systematic drugs, non-pharmacological intervention). C (comparator): none. O (outcome): The main outcome or endpoint of interest of the review in question was to assess current evidence on pathogenic factors, clinical features and management of OLP in children. S (study design): Randomized controlled trial, retrospective and prospective cohorts, case reports, case series.

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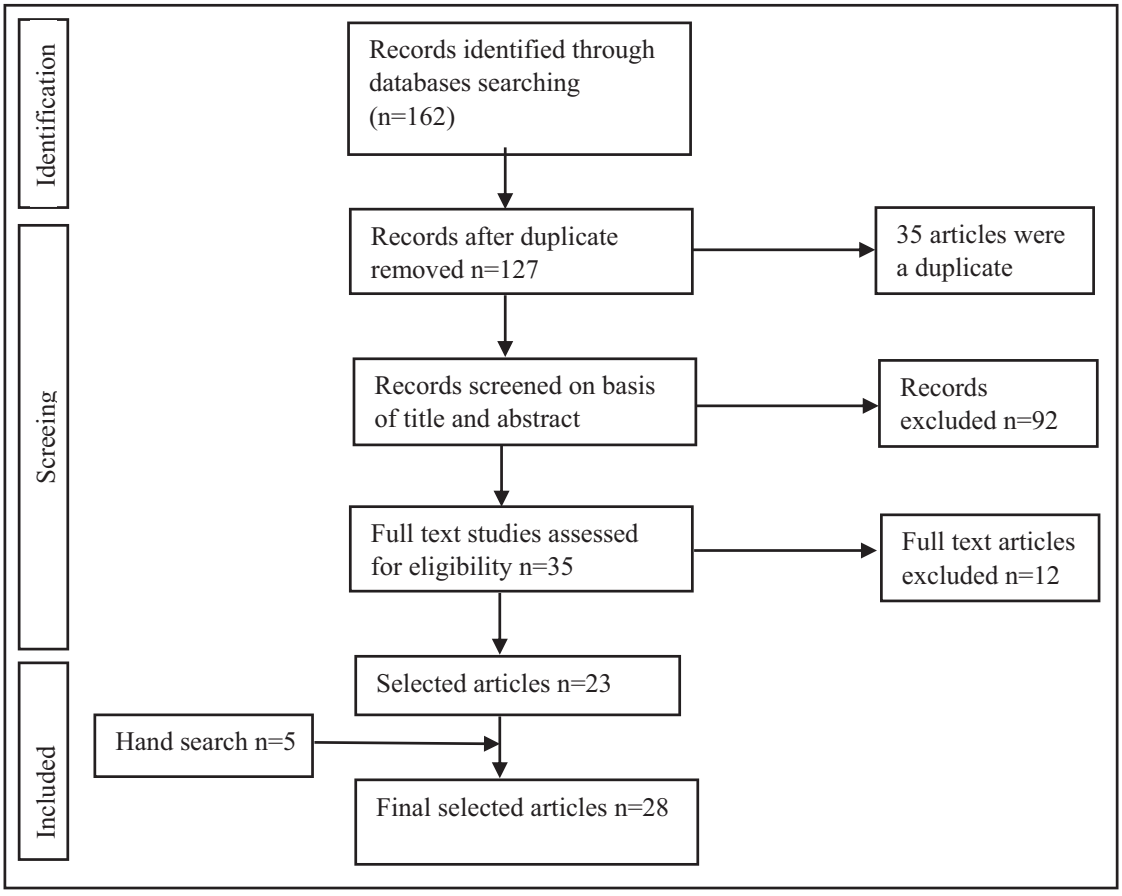

Fig. 1. PRISMA flow chart for selection of studies in this review.

The study excluded editorial letters, articles lacking complete clinical data, case reports on oral lichenoid lesions/reactions, articles not answering the research question, and those published in languages other than English.

Search strategy

A systematic literature search was conducted from the inception of the electronic databases MEDLINE (via PubMed) and the Cochrane collaboration from January 2001 to December 30st, 2023. The search was conducted using the following keywords: "Oral, lichen planus" (Mesh), "OLP" (Mesh), "Childhood" (Mesh) and "Pediatric" (Mesh). The search algorithm was: (lichen planus, oral (MeSH Terms)) OR ("OLP" (MeSH Terms) AND ("Childhood" (MeSH Terms) OR "Pediatric" (MeSH Terms)).

Study selection

Abstracts of the screened articles were reviewed by two authors from the work group for eligibility independently. Disagreements regarding inclusion were solved by discussion between each other. Full text documents of the articles were retrieved and reviewed for final inclusion in the review.

Data extraction

Two reviewers independently extracted data from each article. The extracted information included the author's name, publication year, patient gender, age, medical history, family history of OLP, confirmatory histological findings, clinical presentation, oral sites affected, oral symptoms, extraoral involvement, and treatment used. In the beginning, the extraction of the data was performed independently. Then, it was revised between the authors.

Results

Study selection

The initial search of databases using keywords and the equation mentioned above yielded 162 articles. A detailed overview of the selection process is illustrated in PRISMA flowchart diagram in Figure 1. Thirty-five articles Were a duplicate, and therefore, removed. All remaining titles and abstracts, 127 were analyzed on the first screening, The titles' screening process resulted in excluding 92 articles and 35 articles qualified for full text assessment. A full-text analysis was carried out when the abstract indicated that the inclusion criteria were fulfilled, 12 articles were excluded because they

Table I. Summary table.

Review cases (n = 53)		Number	Percent
AGE	Overall age range	3 to 17	
	Mean age	10.42	
GENDER	Males	28	52,84%
	Females	25	47,16%
Familial OLP		4	7,54%
Confirmatory histology		53	100%
OLP clinical pattern	Reticular	45	84,90%
	Papular	8	15,09%
	Plaque-like	12	21,30%
	Ulcerative	1	1.88%
	Erosive/ Atrophic	21	39,62%
	Bullous	2	3,77%
	Mixed	33	62,26%
OLP site involvement	Buccal mucosae	43	81.13%
	Tongue	25	47.16%
	Gingiva	8	15,09%
	Retromolar fossae	3	5,66%
	Lips	10	18,86%
Extraoral involvement		9	16,98%

OLP: Oral lichen planus.

were not meeting our objectives. Finally, 28 articles were included in this review by adding 5 articles, found through manual search [6–33].

Epidemiological clinical data

The following results have been extracted from the included studies according to the PICO elements. Our findings were summered in Table I.

This study included a total of 53 pediatric OLP cases, with the earliest case reported in 2001. Patient ages ranged from 3 to 17 years, with a mean age of 10.42 years. Fifty-two-point eighty-four percent (**n =** 28) of the patients were males and 47.16% (**n =** 25) were females. The ratio of men to women was 1,12/1. Sixty-seven percent (**n**=30) of the patients were Asian and 33% (**n**=14) were Caucasian. The Ethnicity was not mentioned in 9 cases. Of all 53 cases, only 4 patients (7,54%) have a positive family history of OLP. In the case of wang al 2020, both parents were diagnosed with OLP only after the positive diagnosis of their 3-year-olds child.

Confirmatory histology

In all 53 cases, an incisional biopsy was performed, and the histopathological results confirmed a diagnosis of OLP. Key histopathological features included a superficial band-like infiltration of T lymphocytes, basal cell liquefaction degeneration, and a normal epithelial maturation pattern. Additional characteristics observed were jagged, spindly rete ridges, Civatte bodies, and separation of the epithelium from the lamina propria. Direct immunofluorescence (DIF) was conducted in 5 cases, revealing the deposition of fibrin as irregular strands along the basement membrane zone (BMZ) extending into the superficial lamina propria.

Site of involvement

OLP may be present anywhere in the oral cavity, in our narrative review of 28 articles reports and 53 patients in total the most common sites were the buccal mucosae (81.13%) and the tongue (47.16%). Other sites of involvement included labial mucosa (18.86%), gingiva (15.09%) and retromolar fossae (5.66%). Nine cases showed extraoral involvement, with the skin being the most frequently affected area (16.98%).

Clinical presentation

According to the present study we found the following results: the reticular pattern appeared to be the most common in childhood (86,53%) followed by Erosive/ Atrophic (39,62%), Plaque-like (21.30%), popular (15.09%). Bullous type (3.77%) was seen only in two cases (Pendyala *et al*. 2012; Cascone *et al*. 2017). Ulcerative type was seen only in one case (Laeijendecker *et al*.) It was not uncommon for the same patient to present with multiple forms of OLP, we found mixed forms in (62.26%) of the cases.

Therapeutic modalities

The majority of patients received topical steroids as their primary treatment. Some were also treated with topical calcineurin inhibitors (De Moraes *et al.*, 2011; Laeijendecker *et al.*, 2005) and systemic steroids (Laeijendecker *et al.*, 2005; Woo *et al.*, 2007; Anuradha *et al.*, 2011; Sanjaya *et al.*, 2013; Zychowska *et al.*, 2015; Morankar *et al.*, 2016). Other treatment options recommended included topical retinoids (Mohan Das *et al.*, 2009; Khandelwal *et al.*, 2013; Sharma *et al.*, 2017), low-level laser therapy (Pedro *et al.*, 2018), and topical bovine recombinant fibroblast growth factor (Wang *et al.*, 2020). Topical antifungal medications were prescribed in some of the cases in order to avoid overlapping fungal overgrowth due to the compromised oral tissues in OLP. No treatment was required in 10 patients who were asymptomatic.

Malignant transformation

All of the patients responded well to therapy and showed improvement in symptoms and lesion regression. No Malignant transformation was mentioned in all of the 53 cases.

Discussion

LP is a chronic autoimmune inflammatory disorder that affects both mucosal and cutaneous tissues. In children, the oral mucosa is generally less commonly involved compared to adults [34]. OLP is classified into six types based on its clinical presentation: reticular, papular, plaque-like, atrophic/erosive, ulcerative, and bullous. Typical OLP presents as bilateral, symmetrical, flat-topped polygonal papules and plaques. While *De Moraes et al.* described atypical presentations, *Chatterjee et al.* observed the classic pattern.

A review concluded that most cases of OLP in children are of the reticular type, with erosive OLP being rare in this age group [17]. This finding is consistent with our study, where the reticular pattern was the most common in children (84.90%). In earlier studies, the buccal mucosa was found to be the most commonly affected site in childhood OLP, with the tongue being the next most frequent site, which aligns with our observations. Other areas that may be affected include the labial mucosa, gingiva, and retromolar fossae. Lesions of OLP are typically found alone, with simultaneous involvement of multiple sites being less frequent [8,35,36]. However, a study by *Shivakumar et al.* observed simultaneous cutaneous and oral mucosal lesions in 47.06% of patients [37].

Many factors have been implicated in the development of OLP. Both antigen-specific and nonspecific processes, triggered by endogenous and/or external factors in genetically predisposed individuals, are involved [8,38]. Specifically, antigen presentation and keratinocyte death unique to an antigen are key processes [38]. Nonspecific mechanisms include chemokine RANTES-mediated mast cell degranulation, matrix metalloproteinase activation, and mast cell degranulation [38]. OLP may have a T cell-mediated autoimmune etiology. TGF-1, a protein produced by T cells that helps prevent autoimmunity, is weakly expressed in OLP, making it more susceptible to autoimmune lymphocytic inflammation and apoptosis [34,39]. The association between OLP and Hepatitis C is etiologically suggested but remains debatable with limited scientific support. Reports have documented HCV replication in epithelial cells using Reverse transcription polymerase chain reaction (RT-PCR) and the detection of HCV-specific CD4 and CD8 T lymphocytes in the subepithelial region [40,41]. Additionally, OLP may be linked to autoimmune conditions such as lupus erythematosus, ulcerative colitis, or myasthenia gravis [9]. Viral antigens in the HBV vaccine can trigger cell-mediated autoimmune destruction of keratinocytes, and a very small percentage of children who receive the HBV vaccine may exhibit LP-like reactions [42]. That's why It is important to be aware of these potential adverse reactions. Psychological Factors like stress, anxiety, and depression could also play a role in the development of OLP [43]. Additionally, inadequate oral hygiene might contribute to the initiation or worsening of gingival OLP lesions [44,45].

In pediatric cases, OLP is relatively rare. Research suggests that, among children with LP, oral mucosal involvement occurs less frequently, with a prevalence of around 0.03%, compared to 1–2% in the general population [18]. The diagnosis of OLP in children may be missed or misdiagnosed because of its asymptomatic nature and the ignorance of its clinical presentation. The superimposition of OLP lesions on a background of poor oral hygiene and irregular dental visits also contribute to fewer opportunities for diagnosis [6,8]. It has also been proposed that childhood LP is rare, possibly due to under-reporting and the infrequent presence of triggering factors such as autoimmune conditions and drug exposure in children. Graft-versus-host disease, active hepatitis, and hepatitis B vaccination are commonly cited as predisposing conditions in these reports. Our study, which spanned 23 years, also found that OLP is rare, with only 53 patients identified. Although LP is typically sporadic, a familial form has been observed in 1 to 4.3% of pediatric patients [46]. A family history of LP is considered a relevant predisposing factor in pediatric cases. In the present study, we found that 7.54% of the patients had a positive family history of OLP. The OLP diagnosis is primarily based on histological and clinical characteristics. Histologically, LP is characterized by a dense sub-epithelial lymph-histiocytic infiltrate and an increased number of intra-epithelial lymphocytes. Colloid or Civatte bodies, representing degenerated basal keratinocytes, may be observed in the epithelium. Additional features include parakeratosis, acanthosis, and "saw-tooth" rete peg formation [29]. Unlike other conditions, OLP does not consistently show immunoglobulin and complement deposits, and B-cells and plasma cells are uncommon. A mixed and occasionally more diffuse infiltrate should alert the pathologist to the possibility of a drug-induced or lichenoid condition rather than true idiopathic LP [47].

The most common differential diagnoses of OLP include oral lichenoid drug reaction, oral lichenoid contact hypersensitivity reaction, chronic graft-versus-host disease, LP pemphigoides, lupus erythematosus, oral candidiasis, and aphthous stomatitis.

There is no definitive cure for OLP; treatment focuses on symptom management and varies according to the severity of involvement. The approach to treating juvenile OLP is similar to that for adults aiming to alleviate painful symptoms, enhance the healing of erosive lesions, lower the risk of malignant transformation, and prolong periods without symptoms [48]. For patients with non-erosive OLP; asymptomatic OLP; no treatment is necessary, though close follow-up is required. The outcomes in children seem to be more positive than in adults, where symptoms often endure for many years despite aggressive treatment and extensive investigation into associated factors [18]. Topical corticosteroids are the mainstay of treatment, including triamcinolone acetonide, fluocinonide acetonide, disodium betamethasone phosphate, and more recently, super potent halogenated corticosteroids such as clobetasol [49]. However, a major drawback of topical corticosteroids is their inability to adhere to the mucosa for a sufficient period. Although studies have investigated its use associated to adhesive base (*e.g.*, carboxymethyl cellulose), they have not demonstrated superiority over topical steroids alone [50]. However, its prolonged use can lead to secondary candidiasis, necessitating antifungal treatment [50]. The corticosteroids authorized for use in children consist of clobetasol propionate 0.05%, fluocinonide 0.1%, fluocinolone acetonide 0.01%, mometasone 0.1%, fluticasone 0.05%, and betamethasone [51]. For extensive OLP, high- and super-potent corticosteroids can be administered as intralesional injections or mouthwash. When topical treatments fail to control erosive or erythematous LP, systemic corticosteroids, such as prednisolone, are used. Systemic prednisolone is preferred and should be administered at the lowest effective dosage for the shortest timeframe (40–80 mg for 5-7 days) [51]. Extreme caution is necessary due to potential significant long-term effects in young patients. Non-pharmacologic approaches include photochemotherapy using 8-methoxypsoralen and long wave ultraviolet radiation (PUVA), although it has drawbacks such as nausea, dizziness, and 24-hour photosensitivity [52]. Photodynamic therapy (PDT) targets cells using potent oxidizers that cause cellular damage, membrane lysis and protein inactivation. Hyperproliferating inflammatory cells in psoriasis and lichen planus exhibit immunomodulatory effects and may undergo apoptosis when treated with PDT [53]. Cryosurgery and various laser treatments have also been explored for patients with painful erosive OLP resistant to topical super-potent corticosteroids [52]. These laser treatments cause protein denaturation in order to eradicate the superficial epithelium containing the affected keratinocytes. Although initial studies show potential, their efficacy has not yet been conclusively established.

OLP prognosis can be influenced by multiple factors, including the severity of the disease, the effectiveness of treatment, and individual characteristics of the child. With adequate care and monitoring, most children with OLP can effectively manage their symptoms and maintain good oral health. In literature, unlike adult OLP, childhood lichen planus has not been associated with malignant transformation. Although pediatric OLP has not been linked to any malignancies, most prior studies recommend regular follow-up for as long as the condition persists, with at least one or two exams per year. This is advised despite the generally better prognosis in children compared to adults [54].

The main limitation of this study was the lack of randomized controlled trials. The included studies were case series and case reports which are rated as having a lower level of evidence than systematic reviews, meta-analyses and retrospective studies. More research is necessary to clarify the epidemiological and clinical aspects in this group of patients. The review of existing literature may be influenced by biases due to the reporting of exceptional cases, so the results of this comparison with earlier studies should be critically evaluated.

Conclusions

Oral lichen planus, although one of the most prevalent oral mucosal conditions in adults, is rarely reported in children. This review highlights the prevalence, clinical manifestations, and treatment options for juvenile OLP. The findings of this review can guide healthcare professionals in diagnosing and managing OLP in pediatric patients based on the current evidence.

Funding

No funding was received for this study.

Conflicts of interest

There are no conflicts of interest to disclose.

Data availability statement

No new data were generated or analyzed in this study. Data sharing is not applicable.

Ethics approval

As this work is a systematic review of previously published studies, it does not involve direct human or animal research and thus did not require ethical approval.

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