Open Access

OBM Genetics

LIDSEN Publishing Inc.

Case Report

Papillon-Lefèvre Syndrome and Vitamin D Deficiency: An Intriguing Clinical Observation

Hela Mhiri [†,*], Manel Chalbi [†], Nesrine Dridi [†], Faten Ouled Brahim [†], Med Ali Chemli [†]

La Rabta Hospital, Tunis, Tunisia; E-Mails: Mhirihala@gmail.com; manelchaalbi@gmail.com; nisrint61@gmail.com; fatenaouledbra@gmail.com; hemlimedali@gmail.com

† All authors contributed equally to this work.

* **Correspondence:** Hela Mhiri; E-Mail: Mhirihala@gmail.com

Academic Editor: Thomas Liehr

OBM Genetics
2025, volume 9, issue 2
doi:10.21926/obm.genet.2502297

Received: April 06, 2025
Accepted: June 10, 2025
Published: June 24, 2025

Abstract

We report the case of a 3-year-old girl from a consanguineous marriage, initially diagnosed with vitamin D deficiency–associated periodontitis following early tooth mobility. Despite supplementation, her condition worsened with the onset of palmoplantar hyperkeratosis. Further investigations revealed the diagnosis of Papillon-Lefèvre Syndrome (PLS), a rare genetic disorder causing severe periodontitis and palmoplantar keratosis. The patient was managed with vitamin D supplementation, dental extractions, and a removable partial denture. A multidisciplinary approach led to the confirmation of PLS and appropriate management, highlighting the importance of considering genetic disorders in a severe form of periodontitis. This case underscores the potential role of vitamin D deficiency in exacerbating periodontal disease in genetically predisposed individuals, warranting further research into its impact on PLS progression.

Keywords

Vitamin D; Papillon-Lefèvre Syndrome; periodontitis

© 2025 by the author. This is an open access article distributed under the conditions of the Creative Commons by Attribution License, which permits unrestricted use, distribution, and reproduction in any medium or format, provided the original work is correctly cited.

1. Introduction

Early tooth loss is clinically defined as the premature shedding of any deciduous tooth, occurring at least two years before the average age of physiological exfoliation [1]. While trauma and dental diseases, such as caries and periodontitis are the most common causes of early tooth loss in children, it may also represent a manifestation of a systemic condition [2].

In physiological exfoliation, tooth loss occurs due to root resorption. However, in particular genetic or metabolic conditions, such as Papillon–Lefèvre syndrome (PLS) or hypophosphatasia, premature tooth loss occurs with retention of the dental roots, reflecting a different pathophysiological mechanism [3, 4].

PLS, initially described by French physicians Papillon and Lefèvre [5], is a rare monogenic (Mendelian) autosomal recessive disorder characterized by palmoplantar hyperkeratosis and a severe form of periodontitis beginning in early childhood. It is caused by biallelic mutations in the *cathepsin C* (*CTSC*) gene, located on chromosome 11q14.1, which encodes a lysosomal protease expressed in epithelial tissues and immune cells. This progressive periodontal destruction leads to premature loss of both primary and permanent teeth, often before the age of five. The prevalence of PLS is estimated at 1 to 4 cases per million births [6, 7].

The diagnosis of PLS remains challenging due to its clinical overlap with other rare conditions associated with early tooth loss, such as Chediak–Higashi syndrome and hypophosphatasia, especially before the age of four.

Therefore, PLS should be considered a diagnosis of exclusion, once the more common causes have been ruled out.

In this context, we report the case of a 3-year-old girl who initially presented with early tooth mobility and was first diagnosed with periodontitis associated with vitamin D deficiency. Despite supplementation, her condition worsened, with the appearance of progressive palmoplantar lesions. Further investigations confirmed the diagnosis of Papillon-Lefèvre Syndrome, underscoring the importance of considering genetic conditions in cases of early severe periodontitis.

2. Case Report

2.1 Ethics Statement

This study was conducted by ethical guidelines and was approved by the Comité d'Éthique pour la Recherche Biomédicale (CERB). The approval identification code is CERB 14/2025. This law establishes the ethical and legal framework for biomedical research, ensuring the protection of participants' rights, dignity, and well-being. informed consent was obtained from the legal guardian.

2.2 Patient Information and Initial Presentation

We report the case of a 3-year-old girl, born at full term via vaginal delivery, from a first-degree consanguineous marriage. The family originates from Testour and Bousselem, with no history of early childhood mortality or recurrent infections. Importantly, no family history of periodontal disease or early tooth loss was reported; specifically, no cases of early-onset periodontitis or other periodontal pathologies were identified among first-degree relatives. The maternal grandfather had pancreatic cancer at the age of 63. The mother has a history of desquamation of the palms and soles.

The patient had an unremarkable perinatal history, with a birth weight of 3350 g, timely umbilical cord detachment within 10 days, exclusive breastfeeding for 24 months, and normal psychomotor development (walking at 1 year, first words at 19 months, simple phrases at 2.5 years). She received routine vaccinations per the 2020 Tunisian immunization schedule. At 2 years and 9 months, she developed desquamative palmo-plantar plaques diagnosed as atopic dermatitis (Figure 1).

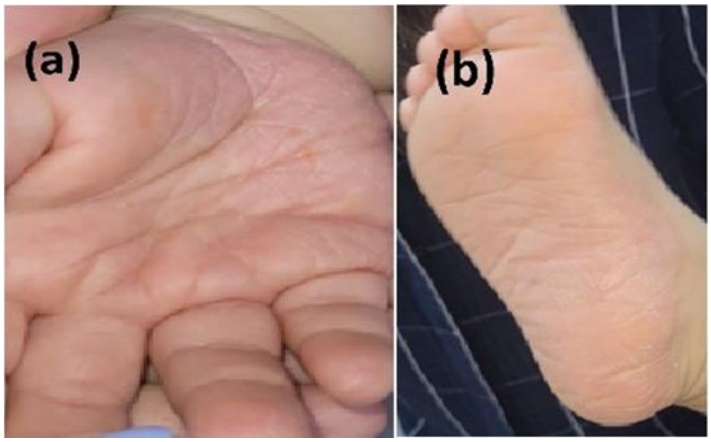

Figure 1 Desquamative palmo-plantar plaques diagnosed as atopic dermatitis.

At 3 years and 2 months, following a minor facial trauma, dental examination revealed periodontitis with dental mobility and gingival recession (Figure 2).

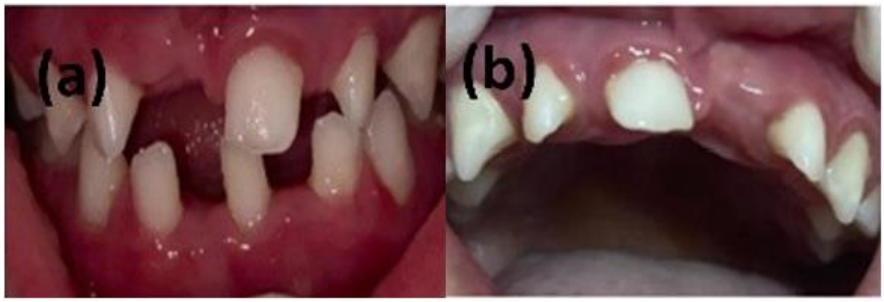

Figure 2 General gingival inflammation.

A comprehensive periodontal assessment indicated a mean probing depth (PD) ranging from 4 to 5 mm, bleeding on probing (BOP) present in approximately 70% of sites, and a plaque index (PI) of 20%, reflecting severe periodontal inflammation despite satisfactory oral hygiene.

A panoramic radiograph showed severe periodontal and alveolar destruction (Figure 3).

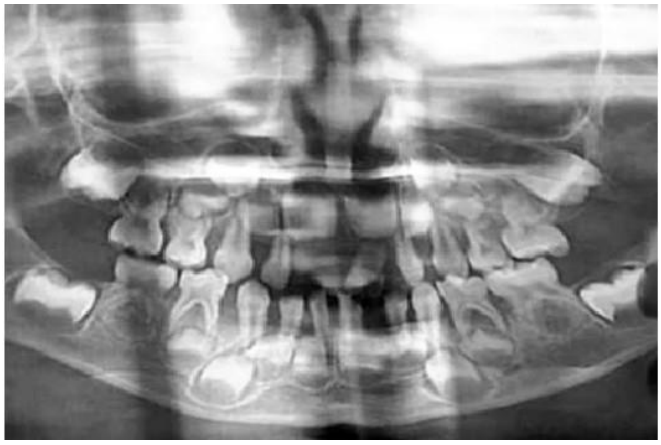

Figure 3 Panoramic radiograph with bone loss.

2.3 Investigations and Initial Management

All biological parameters (Table 1) are within the reference ranges, except for vitamin D, which is slightly below the recommended threshold.

Table 1 Biological Values of the Patient.

Parameter	Patients values	unit
Calcium	97	mg/L
phosphorus	1.7	mmol/L
Alkaline phosphatase	192	U/L
leukocytes	11,430	/mm^3
platelets	272,000	/mm^3
PNN (neutrophils)	5,589.27	/mm^3
Red blood cells (erythrocytes)	5.17	million/mm^3
Vitamin D	16.9	ng/mL

2.4 Therapeutic Approach

2.4.1 Management of Vitamin D Deficiency–Associated Periodontitis

Based on the clinical findings, the child was initially managed for vitamin D deficiency–associated periodontitis, with supplementation provided by the pediatrician's recommendations based on the child's specific needs and condition.

- **Vitamin D Supplementation**: The patient was given an initial dose of 200,000 IU of vitamin D for 3 months. After this period, a maintenance protocol was followed, consisting of 200,000 IU administrated twice a year, every 3 months. At a re-evaluation after 6 months, the vitamin D level increased to 70 ng/mL, showing significant improvement.
- **Dental Management**: Based on clinical findings and radiographic results, the mobile teeth 81, 82, 71, and 61 were extracted. Simultaneously, oral hygiene education was provided, with specific instructions on brushing techniques suitable for the child's age.

- **Follow-up**: Although gingival inflammation has improved, mobility and radicular exposure of teeth 72 and 84 persist (Figure 4).

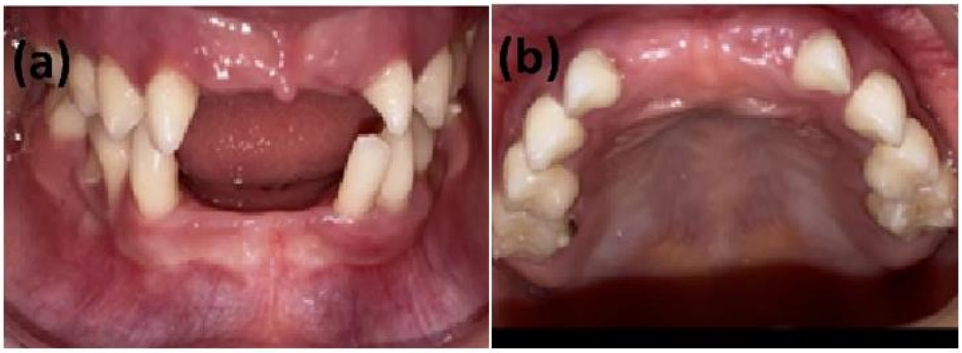

Figure 4 Oral follow-up.

2.4.2 Progression of Dermatological Manifestations

By the age of 4 years, the palmoplantar lesions worsened (Figure 5), becoming more erythematous and hyperkeratotic, with an incomplete response to topical hydrating and anti-inflammatory treatments.

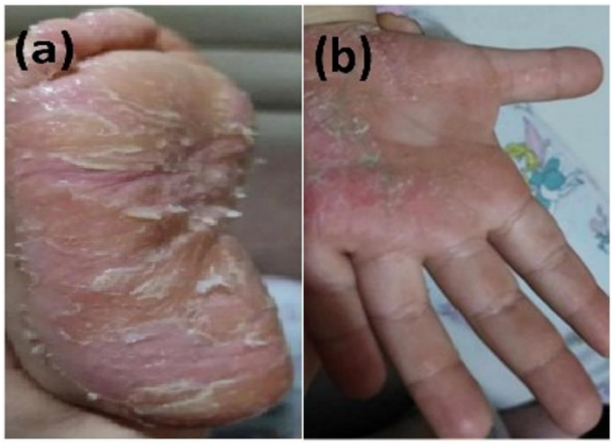

Figure 5 Palmoplantar hyperkeratosis.

2.4.3 Diagnostic Confirmation and Systemic Management

In the absence of facial dysmorphism, skeletal malformations, growth delay, or neurological abnormalities, the combination of early-onset periodontitis and palmoplantar hyperkeratosis in the context of consanguinity raised suspicion of a genetic disorder.

The patient was referred to a specialized dermatology center, where further evaluation confirmed the diagnosis of Papillon-Lefèvre Syndrome.

Antibiotic Treatment. An antibiotic regimen of amoxicillin (50 mg/kg) combined with metronidazole (30 mg/kg) was prescribed for 10 days, following established recommendations for the management of severe periodontitis in Papillon-Lefèvre Syndrome. This combination targets key anaerobic pathogens, particularly *Aggregatibacter actinomycetemcomitans*, implicated in the

pathogenesis of the disease. Although no microbial culture was performed, this treatment protocol is widely endorsed in recent literature

- **Post-treatment Care**: After completing the antibiotic therapy, regular follow-ups were scheduled to continue monitoring the patient's oral health and prevent future complications.
- **Final Oral Rehabilitation**: Following the resolution of the infection and improvement in the oral health, a removable partial denture was placed to replace the missing teeth and improve both function and aesthetics (Figure 6).

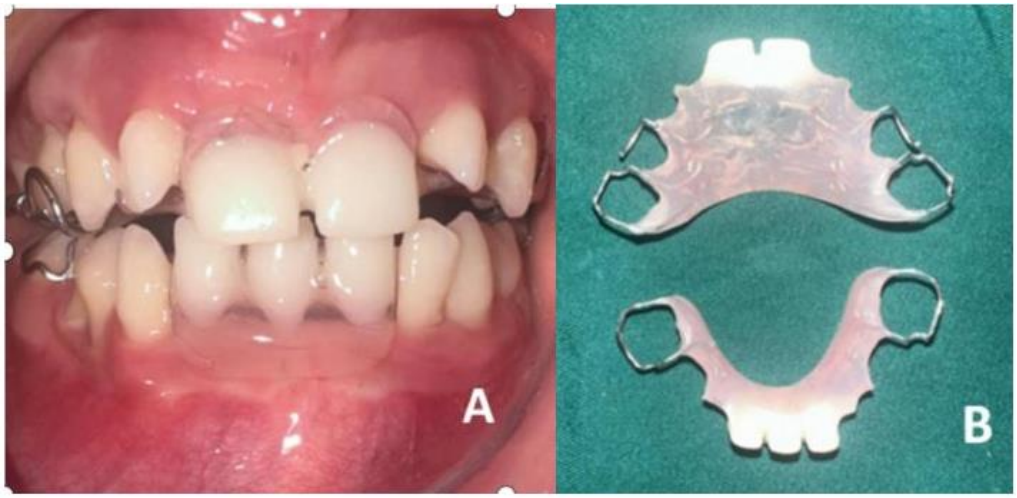

Figure 6 Final dental rehabilitation.

3. Discussion

The etiology and underlying risks of periodontitis have remained a subject of controversy. In this case, after excluding infectious and traumatic causes, we considered multiple systemic diseases as potential diagnoses. A multidisciplinary approach was undertaken in collaboration with pediatricians and dermatologists. Comprehensive investigations were performed, and the only plausible diagnosis identified was a low vitamin D level. Indeed, vitamin D deficiency has been associated with increased periodontal destruction, more severe stages of periodontitis, and greater tooth loss [1].

To better understand the systemic conditions contributing to early tooth loss, we referred to the literature review by Karolina Spodzieja, focusing on non-carious and non-traumatic causes. Several systemic diseases and syndromes have been associated with premature tooth loss, often presenting with distinct clinical signs and requiring specific hematological and biochemical investigations for accurate diagnosis. The following table (Table 2) summarizes the key systemic conditions associated with early tooth loss, including their clinical manifestations and relevant laboratory findings [2].

Table 2 Clinical, Hematological, and Biological Findings in Pathologies Associated with Early Tooth Loss [8].

Pathologies	**Clinical Signs**	**Hematological Findings**	**Biological Findings**
Chediak-Higashi Syndrome	Recurrent infections, silver-gray hair, partial albinism (hypopigmentation), severe periodontitis	Pancytopenia	✗
Down Syndrome	Slanted palpebral fissures - Epicanthus Severe periodontitis	Decreased white blood cell count	✗
Acatalasia	- Necrosis and ulceration of soft tissues - Absence of the *foaming* phenomenon	✗	Low catalase level
Leukocyte Adhesion Deficiency (LAD)	- Recurrent skin and mucosal infections - Gingivitis and periodontitis	Leukocytosis (increased WBC count)	
Neutropenia	Recurrent infections - Periodontitis and gingivitis - Halitosis	Decreased neutrophil count	✗
Leukemia	Fever - Recurrent infections - Gingival bleeding	Leukopenia or leukocytosis	✗
Hypophosphatasia	Growth delay - Muscle weakness - Muscle fatigue	Low alkaline phosphatase	✗
Coffin-Lowry Syndrome	- Intellectual disability, short stature - Thick hands with tapered fingers - Tapered fingers	✗	✗
Papillon-Lefèvre syndrome	Palmo-plantar hyperkeratosis Aggressive periodontitis	Pancytopenia	✗
Vitamin D deficiency	Periodontitis, osteoporosis, bone pain, muscle weakness	✗	Vit D <20 ng/mL
Histiocytosis X	Diabetes insipidus Severe gingivitis Floating tooth appearance on radiograph	✗	✗
Mucocutaneous dyskeratosis	Erythematous skin patches	✗	✗

	Gingivitis and early exfoliation (Koebner phenomenon during tooth eruption)		
Erythromelalgia	Severe burning pain, redness, and inflammation of the distal extremities	✗	✗
Hajdu-Cheney syndrome (HCS)	Short stature, severe osteoporosis, acro-osteolysis, dysmorphic facial features Premature tooth loss	✗	✗
Cherubism	Chubby appearance Bilateral cystic lesions on radiograph	✗	✗
Hypophosphatemic rickets	Growth delay Genu valgum Increased pulp volume	✗	Phosphate: <2.5 mg/dL Calcium: (around 8.5-10.5 mg/dL) Vitamin D: Normal or insufficient, but often <20 ng/mL

Papillon-Lefèvre Syndrome (PLS) is an autosomal recessive disorder caused by mutations in the cathepsin C gene, leading to a rare immunodeficiency associated with severe periodontopathy, edentulism, and palmoplantar keratosis (PPK). Papillon-Lefèvre Syndrome (PLS) is characterized by early-onset, rapidly progressing periodontitis with aggressive destruction of periodontal tissues. According to the 2017 World Workshop classification on periodontal diseases, such cases fall under the category of “periodontitis as a manifestation of systemic diseases,” which recognizes the influence of genetic and immunological factors on periodontal destruction [9]. This classification provides a comprehensive approach to diagnosis and management, emphasizing the importance of systemic evaluation and multidisciplinary care in patients with syndromic periodontitis such as PLS.

The dysfunction of polymorphonuclear neutrophils (PMNs) results in gingival dysbiosis, microbial overgrowth, and intense periodontal inflammation [2].

PLS diagnosis poses many challenges. Although it is primarily established based on oral pathognomonic lesions and excessive keratosis of the palms and soles, these signs typically appear between the ages of 1 and 4 years. However, one sign may take longer to manifest than another [3].

Although the association between vitamin D deficiency and Papillon-Lefèvre Syndrome (PLS) has not been documented in the literature, it appears to be present in our clinical case. Indeed, vitamin D deficiency may have contributed to the exacerbation of the periodontitis observed in this patient. Numerous studies have highlighted the impact of vitamin D on the progression of periodontal diseases, primarily due to its role in regulating the immune system and preventing bone inflammation [1, 4].

It has been demonstrated that vitamin D supplementation can be beneficial in the treatment of periodontitis. For example, Perayil et al studied the effect of vitamin D and calcium supplementation in 82 patients with moderate chronic periodontitis after non-surgical periodontal therapy (NSPT).

The results showed that, although there were no significant differences in periodontal parameters between the supplemented group and the placebo group, a notable improvement was observed in the vitamin D supplemented group, particularly a reduction in gingival inflammation and an improvement in bone density, measured by panoramic radiography. These results suggest that vitamin D supplementation could play a key role in managing periodontitis by helping control inflammation and supporting bone repair [5].

In the context of PLS, this deficiency may potentially worsen periodontal destruction by weakening the immune response and impairing bone regeneration. Therefore, further investigations are necessary to understand this association better and assess its impact on the progression of periodontitis in the context of Papillon-Lefèvre Syndrome.

In the context of Papillon-Lefèvre Syndrome, vitamin D supplementation, when combined with appropriate antibiotic therapy, could potentially play a crucial role in delaying the premature loss of teeth. However, caution is advised, and further studies are needed to confirm this hypothesis.

4. Hypothesis

In the context of Papillon-Lefèvre Syndrome (PLS), vitamin D deficiency may exacerbate periodontal destruction by weakening the immune response and impairing bone regeneration. Various periodontal pathogens have been implicated in the pathogenesis of PLS, including *Fusobacterium*, *Aggregatibacter actinomycetemcomitans*, and *Eikenella corrodens* [6]. Therefore, it is hypothesized that vitamin D deficiency may contribute to the progression of periodontitis in PLS by enhancing the inflammatory response and increasing susceptibility to periodontal pathogens. Vitamin D supplementation, when combined with appropriate antibiotic therapy, could potentially play a crucial role in delaying premature tooth loss in PLS patients. However, further investigations are needed to validate this hypothesis and better understand the association between vitamin D deficiency and periodontal disease in PLS.

5. Conclusion

Papillon-Lefèvre Syndrome (PLS) is a rare genetic disorder characterized by palmoplantar hyperkeratosis and early-onset aggressive periodontitis, leading to premature tooth loss. Diagnosing PLS in young children can be challenging due to its initial clinical overlap with other conditions, such as hypophosphatasia and Chediak-Higashi syndrome. The case presented here highlights the importance of considering genetic disorders in the differential diagnosis of early periodontitis, especially when accompanied by palmoplantar lesions. While vitamin D deficiency is known to exacerbate periodontal disease, further studies are needed to explore its potential role in the progression of periodontitis in the context of PLS. The combination of genetic counseling, proper vitamin D supplementation, and multidisciplinary management can help improve the quality of life for individuals affected by this condition.

Author Contributions

Hela Mhiri: Conception and design, drafting the article. Manel Chalbi: Critical revision of the article. Nesrine Dridi: Analysis and interpretation of data. Faten Ouled Brahim: Acquisition of data. Med Ali Chemli: Critical revision of the article. All the others approved the article to be published.

Competing Interests

The authors have declared that no competing interests exist.

References

1. Zhan Y, Samietz S, Holtfreter B, Hannemann A, Meisel P, Nauck M, et al. Prospective study of serum 25-hydroxy vitamin D and tooth loss. J Dent Res. 2014; 93: 639-644.
2. Martinho S, Levade T, Fergelot P, Stephan JL. Le syndrome de Papillon-Lefèvre, à propos d'une nouvelle observation. Arch Pediatr. 2017; 24: 360-362.
3. Adamski Z, Burchardt D, Pawlaczyk-Kamieńska T, Borysewicz-Lewicka M, Wyganowska-Świątkowska M. Diagnosis of Papillon-Lefèvre Syndrome: Review of the literature and a case report. Postepy Dermatol Alergol. 2020; 37: 671-676.
4. Lu EM. The role of vitamin D in periodontal health and disease. J Periodontal Res. 2023; 58: 213-224.
5. Perayil J, Menon KS, Kurup S, Thomas AE, Fenol A, Vyloppillil R, et al. Influence of vitamin D & calcium supplementation in the management of periodontitis. J Clin Diagn Res. 2015; 9: ZC35-ZC38.
6. Rajeswari KR, Almansour R, Alrajhi F, Binmeqren AF, Albaqami MS, Abdullah Albarrak R. Papillon-Lefèvre Syndrome in dental pediatric patient: A comprehensive review. Saudi Dent J. 2024; 36: 682-687.
7. Toomes C, James J, Wood AJ, Wu CL, McCormick D, Lench N, et al. Loss-of-function mutations in the cathepsin C gene result in periodontal disease and palmoplantar keratosis. Nat Genet. 1999; 23: 421-424.
8. Spodzieja K, Olczak-Kowalczyk D. Premature loss of deciduous teeth as a symptom of systemic disease: A narrative literature review. Int J Environ Res Public Health. 2022; 19: 3386.
9. Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions. J Periodontol. 2018; 89: S173-S182.