Universitat Internacional de Catalunya
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Association between caries experience and peri-implantitis: a cross sectional clinical study

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Final Degree Project

Association between caries experience and peri-implantitis: a cross sectional clinical study

5th year dentistry

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I. Introduction

The introduction of the present study is focused on the review of definition, diagnosis, prevalence and main etiologic factors of caries lesions, periodontitis and peri-implantitis (PI).

I. Dental caries

I.I. Definition

Dental caries is a widespread process defined as the result of a localized chemical dissolution of the tooth surface caused by acid production by dental biofilm exposed frequently to sugars (1, 2). Caries lesions can affect enamel, dentin and cementum. Their extension and severity are variable and they can be active or inactive. Mainly, caries lesions can occur at crown and/or surface level in both primary and permanent dentitions throughout all life.

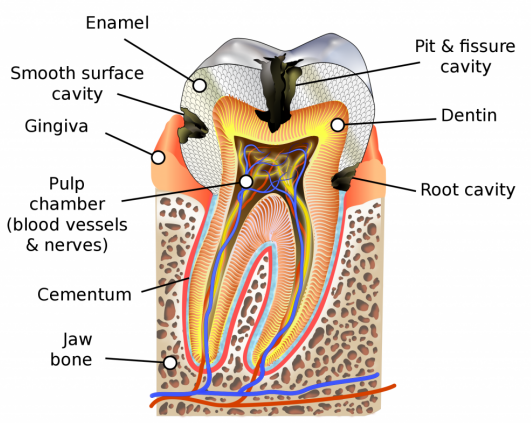

Figure 1. Tooth structure and different caries lesions

As Black stated on 1914 (2), the caries onset occurs at such points of the teeth where microorganisms attachment is favored, such as pits, grooves and fissures in oclusal surfaces, approximal surfaces cervical to the contact point and gingival margin (Figure 1). The biofilm tends to remain “undisturbed” there for long periods of time (3).

The caries mechanism is illustrated in the following flowchart (Figure 2):

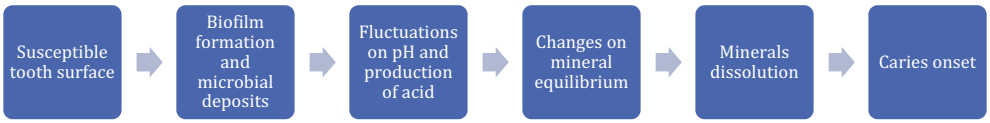

Figure 2. Caries initiation mechanism

Firstly, the formation of biofilm on any solid susceptible surface initiates the caries process. The acid-producing microorganisms (*lactobacilli, mutans streptococci, Bifidobacterium dentium or Scardovia wiggsiae*) that form the biofilm are metabolically active and are able to cause changes on pH that may produce the minerals tooth loss (4). In fact, this demineralization process leads to dissolution of the dental hard tissues (enamel, dentin and cementum) and the caries lesion appears.

If the decay spreads to the dentin, the semiclosed environment produces a rise of a very low pH and, as a consequence the process is accelerated. After a while, when it gets close to the innervated pulp, the patient may feel pain (intermittent or continuous) (3, 5).

I.II. Diagnosis

Clinical detection of dental caries implies the evaluation of depth and demineralization's degree, made by visual inspection. Also, a radiographic exploration (bite wing) should be performed particularly to asses interproximal caries lesions. Moreover, it is important to point out that the biofilm should be always removed before making a correct diagnosis.

At the initial stages, no changes are seen on the enamel surface. After two weeks of undisturbed biofilm, caries lesion is clinically seen as a subsurface lesion (called "white spot"). If the biofilm remains undisturbed, the lesion will progress to a cavitation on the tooth surface. Interestingly, it is not recommended to use dental probes as they don't provide an additional diagnostic benefit. The use of

them can be harmful provided that are sharp pointed, likely causing a cavity that may lead to biofilm stagnation.

Clinical and radiographic manifestations of dental caries are illustrated in Figure 3.

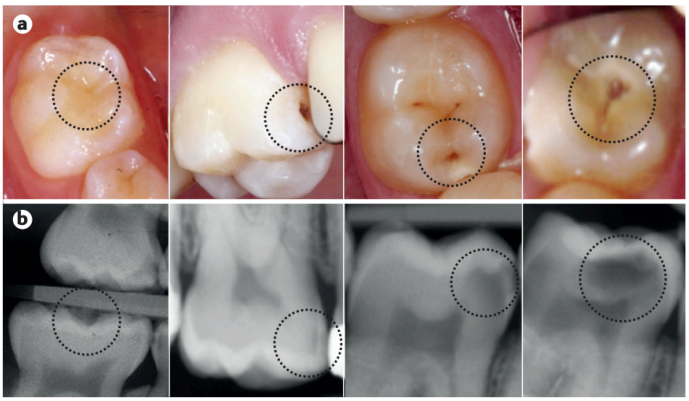

Figure 3. Clinical appearance (a) and corresponding bite-wing radiograph (b). Extracted from Nigel B. Pitts et al. (6)

I.III. Prevalence

Untreated caries in permanent teeth was the most prevalent diseases according to Marcenes et al. on 2013 (7). In this study, a total of 291 diseases and injuries were investigated. It was reported that caries disease showed a global prevalence of 35% (2,431,636) at all ages and 621 millions of children had untreated caries in primary dentition. Interestingly, a systematic review evidenced that caries is prevalent at all ages with three peaks at 6, 25 and 70 years old (8). However, prevalence and incidence may change between regions and countries.

I.IV. Etiologic factors

There are four important factors directly contributing to caries development: tooth, time, bacteria in biofilm and diet (Figure 4).

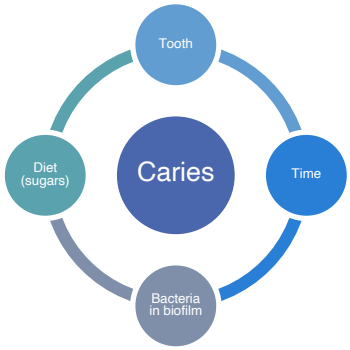

Figure 4. Major factors influencing dental caries development

Several studies in experimental animals between 1950 and 1970

demonstrated that the presence of some microorganisms were needed to form dental plaque and cause dental carious lesions. Thus, a cariogenic high-sugar diet is not able to induce dental caries by itself, in the absence of such microorganisms (9-11). Therefore, caries entails interactions among the tooth structure, the biofilm on its surface, sugars from diet and other factors such as salivary and genetic factors.

Some physical and biological risk factors may determine the likelihood of mineral loss and are involved in the development of caries lesions. Some of these factors are the salivary characteristics (flow and composition), the amount of cariogenic bacteria, lacking of fluoride exposure, gingival recession as well as genetic and immunologic factors (3). In addition, other factors related to an increase on the caries risk' are the behavior, lifestyle (poor oral hygiene and dietary habits, for example), social status, income, poverty, education and dental insurance (2).

II. Periodontal diseases

Periodontal diseases (PD) (mainly gingivitis and periodontitis) are considered inflammatory diseases with microbiological origin (12). Periodontitis is the progression of untreated gingivitis, but not all patients with gingivitis will develop periodontitis (13). In figure 5, the transition from periodontal health to periodontitis is clearly illustrated.

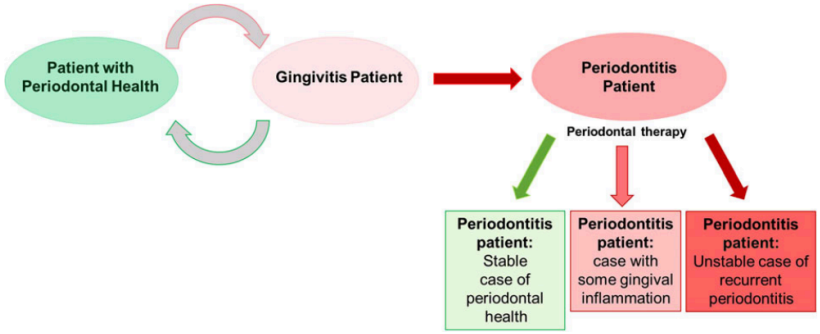

Figure 5. Transition from periodontal health to periodontitis. Image extracted from the Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (14).

II.I. Periodontal health

II.I.I. Definition

The Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (14) stated that gingival health can be classified as: 1) Clinical gingival health on an intact periodontium or 2) Clinical gingival health on a reduced periodontium in non-periodontitis patients or those with stable periodontitis.

II.I.II. Diagnosis criteria

Clinical characteristics of patients with intact periodontium include the lack of bleeding on probing, edema, erythema, patient symptoms, as well as attachment loss and bone loss. It should be considered that the physiological bone levels vary within 1 to 3 mm apical to the CEJ (cementoenamel junction) (14).

Similarly, patients with a reduced periodontium have the same clinical characteristics as the ones listed above except from the reduced clinical attachment levels and bone levels. Gingival health in stable periodontitis patients and non-periodontitis patients must be distinguished because the risk for periodontal disease progression is different between them. Stable periodontitis patients are at a higher risk of progression of periodontitis and must be well controlled; yet non-periodontitis patients, are not at a higher risk of developing periodontitis.

II.II. Gingivitis

II.II.I. Definition

The Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (14)

defined gingivitis as a non-specific inflammatory condition caused by the accumulation of the plaque biofilm at an apical position to the gingival margin, it does not extend to the periodontal attachment, it remains contained within the gingiva.

As mentioned before, gingivitis is a pre-requisite and the major risk factor for periodontitis and the inflammation can be produced at a specific site or at all dentition (it depends on local and systemic risk factors). However, it is a reversible condition, which means that if treated properly, it should not progress to periodontitis.

II.II.II. Diagnosis criteria

The diagnosis of gingivitis is made clinically and it is based on signs of inflammation such as swelling, bleeding and discomfort on probing, redness and pain. Generally, a gingivitis patient may come to the dental clinic complaining about pain (soreness), halitosis, difficulty eating, bleeding gums (altered taste), swollen red gums and a decreased oral health-related quality of life (14).

II.III. Periodontitis

II.III.I Definition

Periodontitis is a multifactorial chronic inflammatory disease which is associated with a dysbiosis of the plaque biofilm. Its main characteristics include: loss of clinical attachment and bone loss (assessed radiographically), gingival bleeding and periodontal pocketing (15).
It represents the progression of gingivitis and it is not a reversible condition, as the bone loss can’t be naturally recovered.

II.III.II. Diagnosis criteria

The Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (15) considered a periodontitis case when an interdental clinical attachment loss is appreciable at ≥ 2 non-adjacent teeth, or if a vestibular clinical attachment loss ≥ 3 mm with pocketing ≥3 mm is detectable at ≥2 teeth.

However, sometimes the clinical attachment loss is due to a non-periodontitis-associated causes, for example: 1) gingival recession of traumatic origin; 2) dental caries reaching the tooth's cervical area; 3) clinical attachment loss on the distal part of a second molar associated with malposition or extraction of the third molar, 4) endodontic lesion draining through the marginal periodontium; and 5) vertical root fracture.

The workgroup classified periodontitis on four stages depending on the severity (level of clinical attachment loss, the radiographic bone loss and tooth loss), the complexity, the extent and the distribution. It also was determined three grades of periodontitis reflecting biologic features of the disease (evidence/risk of rapid progression or anticipated treatment response).

II.III.III. Prevalence

A report conducted by Eke et al on 2012 in the US confirmed that approximately 50% of the adult population aged ≥ 30 years and 68% of the adult population aged ≥ 65 years presented periodontitis (16). Worldwide, the mildest form of periodontitis affects between 45% and 50% of adults, and its most severe form between 9% and 11% of adult population (17, 18). Due to its high prevalence, periodontitis is a worldwide public health problem.

II.III.IV. Risk factors

Every patient presents different susceptibility to periodontitis; thus, risk factors play an important role in the initiation, progression and severity of the

disease. The presence of these risk factors implies an increase in the probability of the occurrence of periodontitis. The elimination or modification of one risk factor may not necessary solve the disease because its causal pathway is affected by multiple factors. The main etiologic factors of periodontitis are discussed below:

II.III.IV.I. Biofilm

Microbial biofilm was early described by Costerton et al. in 1987 (19) and Hall-Stoodley et al. in 2004 (20) as an organized accumulation of different species of microorganisms which are enclosed in an extracellular matrix and adhered to biological or non-biological surfaces. Socransky, S. S. et al in 2005 (21) explained that there were some factors needed for the formation of microbial complexes as the existence of a colonizable surface at the appropriate time, the capability to survive in bad conditions, the provision of nutrients from the ecosystem, the ability to tolerate other environmental features (temperature, pH, osmotic pressure) and the capacity to adhere to the correct surface.

The biofilm associated with PD is formed basically by proteolytic and anaerobic microorganisms, and its main source of nutrients comes from the gingival crevicular fluid (4). The role of microbial biofilms in the pathogenesis of periodontitis is very important and constitutes the main risk factor.

II.III.IV.II. Smoking habit

Smoking cigarettes is one of the major risk factors of periodontitis and it appears a large body of literature that demonstrates their association (22-24). In fact, nicotine, carbon monoxide, carcinogens and oxidizing radicals are toxic substances that are contained on cigarettes and may affect the periodontium by different mechanisms. Tobacco components were found to interact with specific periodontal pathogens and caused an alteration on the neutrophils function, enhancing their degranulation and making them more sensitive to bacterial challenge. Moreover, levels of proinflammatory cytokines are increased, as well as levels of pathogenic T- cells. The gingival blood flow is reduced because of

the peripheral constriction caused associated with low doses of nicotine, which also explains the compromised microvascular response (25).

II.III.IV.III. Diabetes Mellitus

Diabetes Mellitus (DM), a metabolic disorder characterized by hyperglycemia, is able to cause defects on insulin action or/and production because of the abnormal glucose metabolism. It is a growing public health concern and it shares a bidirectional relationship with periodontitis. Indeed, patients suffering from DM (with poor glycemic control) are more likely to have severe periodontal conditions. Thus, worsened glycemic control increases the prevalence, severity, extent and progression PD. At the same time, periodontal infection may affect glycemic control on those patients (26-28).

II.III.IV.IV. Other risk factors

II.III.IV.IV.I. Obesity and metabolic syndrome

Overweight and obesity have an impact on insulin resistance and chronic systemic inflammation, being associated with some entities like DM, cardiovascular disease, cancer as well as PDs. There is evidence that obese individuals have a greater mean clinical attachment loss as well as changes in the proinflammatory and immune responses (29-31) that increase their susceptibility for periodontitis. However, the pathophysiological mechanisms are not yet clear and more studies are needed to unravel them.

In the same line, patients who suffer from a metabolic syndrome also have an increased chronic systemic inflammatory response that exacerbates the destructive immunopathologic response to the periodontal flora (32).

II.III.IV.IV.II. Osteoporosis, calcium from the diet and vitamin D

Osteoporosis is a systemic disorder characterized by low bone mass throughout the skeletal system (including jaws) with a consequent increased risk for bone fracture. The diminished alveolar bone mass may result in accelerated

immunological responses when an oral biofilm infection occurs (32, 33). On the other hand, low dietary calcium and vitamin D levels may also influence periodontitis and bone loss (34), especially in women.

II.III.IV.IV.III. Alcohol

Alcohol may also be related with a greater attachment loss in a dose-dependent manner (35), but further studies are necessary to understand the role of alcohol as a risk factor.

II.III.IV.IV.IV. Psychological stress, distress and coping skills

Some studies show a positive relation between the severity of PD and patients stress (36-38). When a subject is exposed to psychological stress, the immune response and behaviors are affected, leading to an immunosuppressive response that can enhance periodontal tissue destruction. Interestingly, patients who have the ability to cope with stress are less prone to the progression of PD.

II.III.IV.IV.V. Genetic susceptibility

It has been studied that some genes, and interactions between them, may modify PD. In fact, polymorphisms and some interleukins, MMP-9 genes and other genetic factors are associated with an increased risk of periodontitis development (39, 40), but further studies are needed.

II.III.IV.IV.VI. Gender

Generally, males have a higher prevalence of periodontitis compared to females. However, this association seems to be more closely related to lifestyle (32, 41).

III. Dental caries and PD: common features

Periodontal diseases and dental caries are the most common diseases of humans and the main cause of tooth loss. They have an important impact if

untreated due to the fact that tooth loss can lead to discomfort and inability to chew properly, edentulism, loss of oral function and poor diet in addition to a loss of self-esteem, social problems and a decreased quality of life (42).

Periodontal diseases and dental caries both are caused by a disequilibrium in the interaction between the biofilm, the host and the microenvironment (17, 43).

The consensus report of EFP/ORCA Workshop (1) on caries and PD found that both diseases share common risks factors such as a pathogenic plaque biofilm, which is the major biological determinant for their progression (4).

III.I. Plaque biofilm

Oral health means a balancing microbiota, an efficient host response and an undisturbed microenvironment. But when a dysbiosis between biofilm, host and environment occurs, caries and PD are manifested. Biofilms are present on all intra-oral surfaces and differ in terms of composition and metabolism, therefore levels of pathogenicity in health and disease also change (43).

The progression of caries and periodontitis entails numerous interactions between the biofilm's microorganisms, but these interactions are driven by distinct stressors. In caries, a sugar's rich diet and their fermentation to organic acids, results in an increase of acidogenic species that enhances the acidity of the environment that favors caries' progression. Whereas, the progression of gingivitis occurs due to an increase of inflammatory molecules associated to the accumulation of those microorganisms in the gingival margin (4).

III.II. Interactions of lifestyle, behavior and systemic diseases

In the consensus report of EFP/ORCA Workshop (1) several interactions of lifestyle, behavior and systemic diseases were also reported in both diseases. Those interactions are discussed below:

III.II.I. Diet

In this line, the intake of fermentable carbohydrates (sugars and starches) were the most common dietary risk factors for both diseases, but associated mechanisms differed. Fermentable carbohydrates cannot initiate caries by itself, but they are necessary for the caries onset and progression (44-46). Gingival bleeding and inflammation are also increased by intake of sugars (47-50). Morevoer, some micronutrient deficiencies, such as vitamin C, D or B12 may as well be related to the onset and progression of both diseases (1, 51).

III.II.II. Systemic risk factors

There are several acquired systemic risk factors, such as hyposalivation, rheumatoid arthritis, tobacco, undiagnosed or suboptimal controlled DM and obesity, that are common for both diseases, caries and PD (1).

III.II.III. Genetic factors

As mentioned before, genetic factors have also been studied to explain the susceptibility of some individuals of suffering from caries and PD (52).
Chronic periodontitis is strongly associated with VDR (vitamin D receptor), Fc gamma receptor IIA and Interleukin 10 (IL10). There are also some genes that may impact on caries susceptibility affecting enamel formation (AMELX, AMBN, ENAM,…), immune regulation (LTF), salivary function (AQP5) and dietary preferences (TAS2R38, TAS1R2).

Several potential common genetic pathways have been described but there is no strong and clear evidence of an association of genetic variants that may modulate susceptibility of both diseases. Moreover, this moderate association is altered by lifestyle and environmental factors, key determinants for the development and progression of both diseases.

III.II.IV. Socioeconomic position

There is also evidence for an association between socioeconomic position (SEP) and dental caries (53). Schwendicke et al. (54) reported that components such as low income, low social position and low parental educational or occupational background are correlated with a higher risk of having caries lesions or caries experience. It can be explained because low-income individuals have less access to dental care, both professional and at home (toothpastes, dental floss…). Similarly, low socioeconomic status is associated with a major prevalence of periodontitis (53, 55).

III.II.V. Behavior

Behavioral aspects including oral hygiene with fluoride toothpaste and smoking have a clear influence on dental caries and PD (1, 17, 56, 57). Therefore, it is necessary to be aware of patients' socioeconomic and behavioral background to recognize risk groups.

IV. Peri-implant diseases

The use of dental implants to restore lost tissues and function became a revolution in modern dentistry in the 1980s (58). Currently, osseointegrated dental implants are the treatment of choice for the replacement of a missing tooth or teeth.

The tissues around osseointegrated dental implants are known as peri-implant tissues. These tissues are composed by two compartments: the soft tissue (peri-implant mucosa) formed during the wound healing process after the implant or abutment placement protecting the underlying bone (59); and the hard tissue (bone), in direct contact with the implant surface to provide implant stability (60).

Dental implants have shown survival rates of 90-95% over periods of 5-10 years (61, 62), and up to 95.7 % from 9-14 years of follow-up (63). Nevertheless,

implants are not exempt of biological or mechanical complications that could affect the long-term outcomes of dental implants.

In the consensus report of workgroup 4 of the 2017 World Workshop (64), a classification on peri-implant diseases and conditions was reported considering peri-implant health (65), peri-implant mucositis (66) and PI (67).

IV.I. Peri-implant health

IV.I.I. Definition

A healthy peri-implant tissue (64, 65, 68) is defined by the lack of redness, bleeding on probing, swelling and suppuration. Histologically, healthy peri-implant mucosa measures approximately 3 to 4 mm in height and is covered by a masticatory mucosa (keratinized epithelium) and a lining mucosa (non-keratinized epithelium).

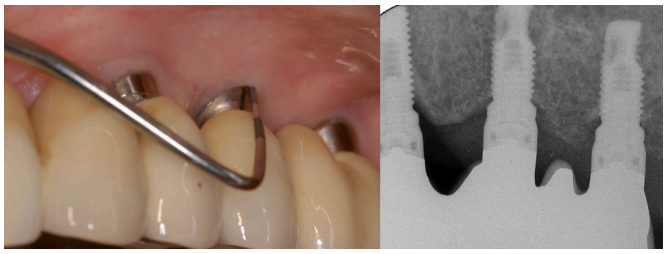

Figure 6. Peri-implant health (69)

IV.I.II. Diagnostic criteria

The diagnostic of peri-implant health is made by visual inspection (Figure 6), digital palpation as well as probing with a periodontal probe (64). The clinical characteristics of a healthy peri-implant site are the absence of erythema, bleeding on probing, suppuration and swelling. In peri-implant health there is not an increase in probing depth over time. In implants is not possible to determine a range of probing depth associated with health, so baseline examination should be done to have reference probing compatible with health. Although at implants sites the probing depths are frequently higher than at tooth sites, there are no

perceptible differences between periodontal and peri-implant tissues in health. The only variation could be the length of the papillae at the interproximal sites, which tends to be shorter at implant sites. Interestingly, a peri-implant health can be diagnosed in implants with diminished bone support.

IV.II. Peri-implant mucositis

IV.II.I. Definition

Peri-implant mucositis is defined as an inflammation of the peri-implant mucosa in absence of continuous marginal peri-implant bone loss. It represents the precursor of PI (64, 67, 70).

This condition is initiated due to the accumulation of bacterial biofilms around osseointegrated implants, that causes a disruption of the host-microbe homeostasis at the implant-mucosa interface.

IV.II.II. Diagnostic criteria

Peri-implant mucositis (64, 66, 68) should be diagnosed when clinical signs of inflammation (redness, swelling and/or suppuration) and bleeding on gentle probing (Figure 7) can be detected. Probing depth could increase compared to baseline data (supra-structure in place) but there is no further bone loss beyond physiologic bone remodeling. To asses bone level around implants should always be assessed with an intraoral radiograph at baseline (supra-structure in place).

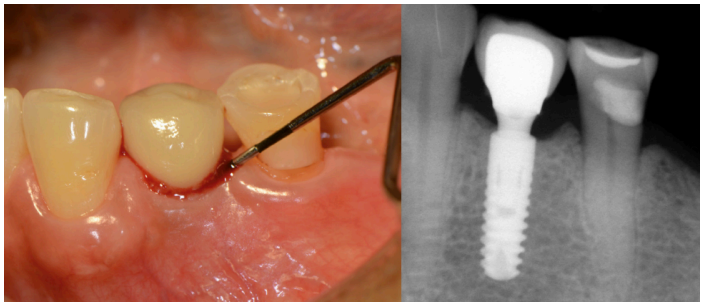

Figure 7. Peri-implant mucositis (69)

IV.II.III. Prevalence

Several systematic reviews have reported epidemiologic data of peri-implant diseases, but the results should be cautiously interpreted because of the influence of different variables such as the lack of comparable studies, the different case definitions criteria and the data heterogeneity between studies. A summary of epidemiologic data of peri-implant disease is presented in Table 1
The results of a meta-analyses conducted by Derks et al. (71) reported that the estimated prevalence of peri-implant mucositis was 43%, but the case definitions, follow-up times and selection of patients were very different among the studies assessed. Lee et al (72) published a systematic review were the prevalence of peri-implant mucositis at subject level was 46,83% and at implant level was 29,48%. A recent cross-sectional study conducted by Rodrigo D. et al (73) evaluated the prevalence of peri-implant diseases in Spain. They concluded that the prevalence at subject level of peri-implant mucositis was 27%.Similarly, another cross-sectional study performed by Vignoletti et al (74) in university setting with a total sample of 237 patients and 831 implants concluded that 38,8% of the patients and 37,7% of the implants were diagnosed with peri-implant mucositis.

IV.III. Peri-implantitis

IV.III.I. Definition

PI is defined as a pathologic condition around dental implants characterized by the presence of an inflammatory lesion with a progressive bone loss (64, 67). This condition represents the progression of peri-implant mucositis and it is not reversible.

IV.III.II. Diagnostic criteria

PI is characterized by the presence of signs of inflammation (bleeding on gentle probing, redness, swelling and/or purulent exudate) in addition to an increased probing depth compared to previous examinations (Figure 8). In some cases, a recession of the mucosal margin can be observed (64, 67, 68).

The difference between peri-implant mucositis and PI is based on the alveolar bone loss. In implants with PI, a radiographic bone loss compared to baseline radiograph should be evidenced.

However, if there are no baseline data references (baseline radiograph and probing depths) to asses clinical and radiographic changes over time, diagnosis of PI should be based on the presence of signs and symptoms of inflammation together with probing depths of ≥ 6 mm and bone levels ≥ 3 mm apical from the most coronal portion of the intraosseous part of the implant.

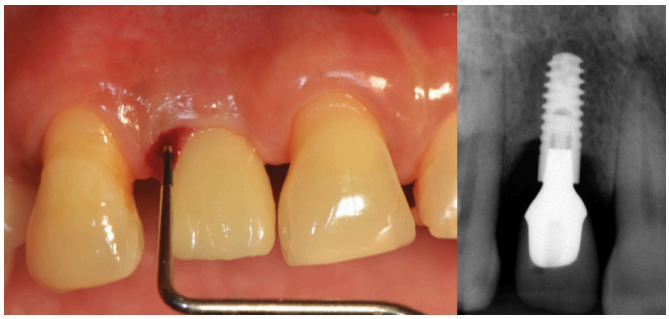

Figure 8. PI (69)

IV.III.III. Prevalence

Again, Table 1 shows the main epidemiologic data of peri-implant disease. Firstly, the meta-analyses conducted by Derks et al. concluded that the estimated prevalence of PI was 22% (71). While the systematic review published by Lee et al (72) show a prevalence of 9,25% at implant level and a prevalence of 19,83% at subject level. Moreover, the cross-sectional study conducted by Rodrigo et al. (73) described a prevalence of PI in Spain of 24% at subject level. In contrast, Vignoletti et al. (74) estimated a 35% of PI at subject level and 17.1% at implant level.

	Implant level		Suject level	
	Mucositis	**PI**	**Mucositis**	**PI**
Derks et al (71)			43%	22%
Lee et al (72)	29,48%	9,25%	46,83%	19,83%
Rodrigo et al (73)			27%	24%
Vignoletti et al (74)	37,7%	17,1%	38,8%	35%

Table 1. Prevalence of peri-implant diseases

IV.III.IV. Risk factors

Early identification of the risk factors is essential to prevent peri-implant diseases and minimize the complications associated with dental implants. Briefly, the most associated risk factors and indicators of PI are summarized below:

IV.III.IV.I. Poor plaque control and irregular attendance to supportive treatment

The most important risk factor for the development of PI is the accumulation of dental plaque biofilm around the mucosal margin (75, 76). Scientific evidence shows that patients with poor plaque control and erratic patients, who do not attend maintenance visits were at a higher risk of suffering from PI (64, 67).

IV.III.IV.II. History of periodontitis

According to the recent published literature (58, 67, 76-81), another strong risk factor of PI occurrence is history of periodontitis. Moreover, it has been reported that implants replacing teeth due to chronic periodontitis showed inferior survival and success rates than those replacing teeth due to caries, trauma or agenesia (81).

IV.III.IV.III. Indicators for peri-implantitis

There are some risk factors with not enough evidence to demonstrate a strong association with PI. Thus, these factors are being categorized as risk indicators for PI instead of risk factors. Some examples of these risk indicators are smoking, DM and lack of keratinized mucosa (KM) (79), which are summarized below.

V. Periodontitis and Peri-implantitis

PI have strong similarities with periodontitis in terms of etiology and clinical features. However, both diseases represent different entities from a histopathologic point of view (82).

V.I. Related pathogens

Alike to healthy teeth, healthy implants are mainly colonized by gram-positive rods and cocci (83). However, both diseases periodontitis and PI are infectious diseases and several studies have reported a high prevalence of common pathogens (75, 84-89). Microorgnisms of the orange complex (*Prevotella intermedia* and *Fusobacterium sp.*) and microorganisms of the red complex (*Porphyromonas gingivalis*, *Tannerella forsythia* and *Treponema denticola*), as described by Socransky et al (21), as well as *actinomycetemcomitans* (90, 91) were found in both diseases. Nevertheless, PI is also associated with opportunistic microorganisms such as *Candida Albicans* and *Staphylococcus aureus* in contrast to periodontitis (92-96). Moreover, it has been demonstrated the transmission of putative periodontal pathogens from the microbiota around teeth to implant sites (97-100).

V.II. Onset and progression

The onset of both diseases depends on bacterial biofilm. The initial host response contains a similar inflammatory cell infiltrate within the apical extension of the junctional epithelium. Nevertheless, the mechanisms of bacterial adhesion

and biofilm formation at implants are different from periodontitis because it may be affected by chemical and physical properties of implants such as titanium purity, surface roughness, type of coating and free energy (101, 102).

In addition, the inflammatory infiltrate in the peri-implant mucosa appears to be significantly greater in size after persistent biofilm accumulation, being in direct contact to the bone (103-105). Thus, as peri-implant lesion is not walled off from the alveolar bone by a supracrestal connective tissue compartment, the progression of this condition is faster (103, 105, 106).

VI. Justification

As discussed above, caries and periodontitis are different diseases that may share common etiologic factors. Similarly, periodontal and peri-implant disease may, to some extent, be mirror pathologies on teeth and implants.

Strikingly, there is scarce solid evidence evaluating the co-occurrence of dental caries and periodontitis. Nevertheless, Mattilla et al (107) showed, in the Finnish population, that subjects with periodontitis had significantly higher number of caries (33%). Similarly, subjects with caries had significantly higher proportions of periodontitis (31%). Therefore, it was concluded that periodontal disease, specially its severe forms, and dental caries may simultaneously occur in the same subjects, thus suggesting a possible association between both diseases. Likewise, in the German population (108) it was found a significantly higher attachment loss and probing depths at sites with caries experience compared to sites without caries experience, respectively. Moreover, a recent study by Nascimento et al (109) found an association between caries and periodontitis among adolescents. Noteworthy, it was also reported that the severity of periodontitis was negatively associated with enamel/dentin caries, while its extent was positively associated with dentin caries (109). To our knowledge, there is no scientific evidence approaching the association between caries experience and peri-implant disease; in other words, we wonder if a patient with a high level of caries experience is at a higher risk of developing peri-implant disease.

II. Objectives

The purposes of the present study are listed below:

1. The main objective of this study was to assess the prevalence, co-occurrence and association between caries history and peri-implantitis.
2. The second objective of this study was to analyze the influence of other patient and implant factors with peri-implantitis.

III. Hypothesis

I. Hypothesis of primary objective

H0: Caries experience and peri-implantitis occurrence are not associated and accumulated in the same subjects.
H1: Caries experience and peri-implantitis occurrence are associated and not accumulate in the same subjects.

II. Hypothesis of secondary objective

H0: The analyzed patient and implant related factors do not have an influence in the development of peri-implantitis.
H1: The analyzed patient and implant related factors may have an influence in the development of peri-implantitis.

IV. Material and methods

I. Study design

The present cross-sectional study was conducted after the approval of the Ethics Committee (PER-ECL-PER-2017-08). All selected subjects were informed about the aims of the research. If agreed to participate, a written consent (Annexe VI) was signed before initiating the study.

II. Subjects population

Patients attending the Postgraduate Periodontology Clinic of the School of Dentistry of Universitat Internacional de Catalunya (UIC), were consecutively enrolled in the study, by one of the researchers (JV), if they meet the following criteria:

- Male or female ≥18 years old.
- One or more dental implant with an implant-supported restoration.
- Minimum of one year after implant supported restoration delivery.
- Partially edentulous patients with ≥ 20 teeth in mouth.

However, patients were excluded on the basis of the following criteria:

- Inaccuracy in recording peri-implant parameters due to prosthesis design.
- Implant cemented-retained prosthesis.
- Patients who underwent surgical treatment of peri-implantitis.

III. Data collection

Data collection process was performed in two steps: patient's interview and clinical and radiographic assessment.

III.I. Patients interview

Initially, one trained examiner (LG) interviewed the patient and collected patient related information (Annexe VII). Demographic data was obtained, as well as other factors such as tobacco consumption, systemic diseases, reason of tooth loss, dietary habits, xerostomia perception, socioeconomic status, oral hygiene habits, supportive periodontal treatment compliance, among others. Any doubts that came out during the questionnaire were solved by the examiner.

III.II. Clinical and radiographic assessment

Afterwards, a previous calibrated examiner (LG) conducted the intraoral examination. The exploration was conducted to assess caries and implant site parameters:

- Periodontal indexes: full mouth plaque score (FMPS) (110) and full mouth bleeding score (FMBS)(111).
- Number of decayed, missing and filled teeth (DMFT) assessed by visual inspection and radiographic assessment following ICDAS (112). All tooth surfaces were examined but the observations were recorded by tooth.
- Probing pocket depth (PPD), bleeding on probing (BoP), suppuration (SUP), keratinized mucosa (KM) were measured at 6 sites per implant with a PCP UNC 15 probe (Hu-Friedy ®).
- Radiographic bone loss assessed at mesial and distal implant site using the parallel cone technique.

If patients presented with either caries, periodontal or peri-implant disease, it was referred and treated in the appropriate clinical department.

IV. Outcome measures

The main outcome of the study were dental caries and peri-implant disease prevalence. Firstly, caries prevalence was assessed as the number of patients

with at least one caries recorded in the dentition. Similarly, peri-implant disease diagnosis was obtained on the basis of the following case definition from 8th European Workshop on Periodontology (64):

- **Peri-implant Health (H)**: an absence of erythema, bleeding on probing, suppuration and swelling without additional bone loss after initial marginal bone remodeling.
- **Peri-implant mucositis (M)**: presence of bleeding and/or suppuration on gentle probing with or without increased probing depth compared to anterior examinations without additional bone loss after initial marginal bone remodeling.
- **Peri-implantitis (PI)**: bleeding on probing with or without concomitant deepening of peri-implant sites with a progressive bone loss after 6 months of prosthetic loading. If previous radiographs were not available, PPD>6 mm and vertical threshold distance of 3 mm from the expected marginal bone remodelling was used.

All the exposure variables obtained from questionnaire and clinical examination were expressed as follows:

- FMBS and FMPS
- Number of decayed, missing, filled teeth (DMFT).
- Cause of tooth loss: caries, mobility, caries and mobility and trauma/fracture.
- History of periodontitis: assessed radiographically by the presence or absence of bone loss.
- Tobacco habit: smoker, non-smoker or former smoker patient. In case of smokers, total amount of cigarettes per day was registered and categorized as < 10 or ≥ 10 cigarettes per day.
- Systemic diseases: presence or absence.
- Diabetes Mellitus: presence or absence. In case of diabetic, subjects were asked if glycemia was controlled on the basis of previous blood test.
- Body Mass Index (BMI): obtained as weight (kg)/ height (m^2).

- Nutrient or vitamin deficiencies: presence or absence.
- Dietary habits: assessed by the Mediterranean Diet Score (MDS) questionnaire. Patients were classified as low adherence (score ≤ 7) or high-adherence (score 8-9, or 10) to the Mediterranean diet.
- Regular sugar consumption: yes or no. Sugar consumers were asked as well for the level of sugar consumption (low, medium, high).
- Oral dryness: patient subjective perception of dry mouth (presence or absence).
- Oral hygiene measures: frequency of brushing teeth and interproximal hygiene performance.
- Educational level (EL): assessed in two different categories (primary and secondary, professional and university).
- Supportive periodontal treatment (SPT): regular (≥2 times/year) or irregular (<2 times/year).

V. Sample size calculation

A logit model for the association between the outcome diagnosis at the patient level (health or peri-implantitis) and every independent variable were conducted to reach a power of 82,7% to detect an OR = 2.5 as statistically significant. Assuming a level of 95% a total of 169 subjects were recruited. At the implant level, the power was 96.2% under the same previous conditions. Due to the multi-level design of the data (multiple implants per patient), potency had to be corrected. Assuming a moderate intra-subject correlation ($\rho = 0.5$), a power of 87.7% was estimated.

VI. Statistical analysis

Assuming a multi-level design study, data was calculated at patient-and-implant level. Descriptive analysis provided the most relevant statistics for all the variables collected: absolute and relative frequencies (for the categorical

variables) and means, standard deviation, range and median (for the continuous ones).

Inferential analysis was carried out as follows. At the patient-level, simple binary logistic regression models were estimated to study the association between the patient's diagnosis and each of the independent variables of the study. On one hand, the “healthy” diagnosis was compared to “peri-implantitis”. The model estimated unadjusted odds ratios (OR) along with the 95% confidence interval. Once the relevant independent variables were identified ($p<0.10$), they were incorporated into a multiple model to obtain adjusted OR. At the implant-level, simple binary logistic regression models were estimated using generalized estimating equations (GEE) to explain the probability of the status of the implant. The models estimated OR from the Wald Chi^2 statistic. The GEE approach addressed the intra-subject correlation or dependency between observations due to the multiplicity of implants per patient. The relevant independent variables were incorporated into a multiple model to obtain adjusted OR.

The SPPS software, version 21.0 (SPSS Inc, Chicago, IL, USA) will be used for statistical analysis. The level of significance used in the analyses was 5% ($\alpha=0.05$).

V. Results

I. Sample description

All the sample description is summarized in Table 1 Annexe VIII. The study was composed by 169 patients. Of these, 87 were men (51.5%) and 82 were women (48.5%), with a mean age of 54.5 ± 11.7 years (age range 20-82).

Briefly, most of the patients were systemically healthy (67.5%), non-diabetic (92.9%) and almost half of the subjects were non-smokers (43.8%) and of normal weight (44.4%). A high adherence to Mediterranean diet was reported in 60.4% of the sample, while 29.6% consumed routinely sugar. Fewer subjects presented with nutrient (3%) or vitamin deficiency (8.3%) and almost half of them reported oral dryness (45.8%). Most of the included patients carried out professional or university studies (67.5%), brushed their teeth with ≥ 2 times per day (84.6%) and used interproximal hygiene (71.6%). Most of the patients presented with history of periodontitis (74.6%), but few of them attended regularly to SPT (30.9%). As a matter of interest, the vast majority of teeth were lost due to caries (63.9%).

Furthermore, a mean of 1.84 implants were included per patient with the following distribution: 37.9%, 40.2% and 3 21.9% of the subjects carried one, two and three implants, respectively. Almost all the implants were located in posterior maxilla/mandible (96.1%) and surrounded by ≥ 2 mm of KM (76.9%). The mean PPD was 3.4 ± 1.2 and suppuration appeared in 3.2% of the implants. Interestingly, almost 60% of the implants displayed an untreated caries or filling adjacently.

II. Prevalence of caries and peri-implant disease

The prevalence of caries among population was 92.2%. In detail, 8.8% of the patients did not present with any caries, while 32.6% and 58.6% presented at least one/two and more than two caries, respectively. The mean number of caries per patient was 3.1±1.9 (range 0-12) (Table 1). Additionally, males presented

significantly higher mean of caries when compared to females (3.40 ± 2.15 vs 2.76 ± 1.58; p=0.028) (data not reported).

At patient level, the prevalence of H, M and PI were 21.3%, 56.2% and 22.5%, respectively. On the other hand, 27.7%, 55.6% and 17.7% of the implants were diagnosed as H, M and P, respectively.

III. Association and co-occurrence between caries and peri-implantitis

Table 2 Annexe VIII reports the descriptive data and ORs between caries, filled, missing teeth and DMFT index with PI.

The mean distribution of caries was 2.8 ± 1.9 and 3.2 ± 1.9 in H and PI group, respectively (p=0.36) (Table 1). In other words, subjects with PI exhibited a similar prevalence of caries than those without peri-implant disease (51.3% vs 48.7%; p=0.788). Nonetheless, PI patients had a higher prevalence of more than two caries in mouth (>2: 71.1% vs 1: 15.79% and vs 0:13.16%). Similarly, subjects with more than two caries showed a greater prevalence of PI versus H (61.3% vs 38.4%) and an increased risk of PI (OR=1.27; p=0.746) when compared to non-caries patients.

Furthermore, it was estimated that one additional caries lesion in mouth increased the risk of PI by 12%. Interestingly, Figure 9 illustrates the probability of PI on the basis of the number of caries; note that the probability increases as the number of caries rises up.

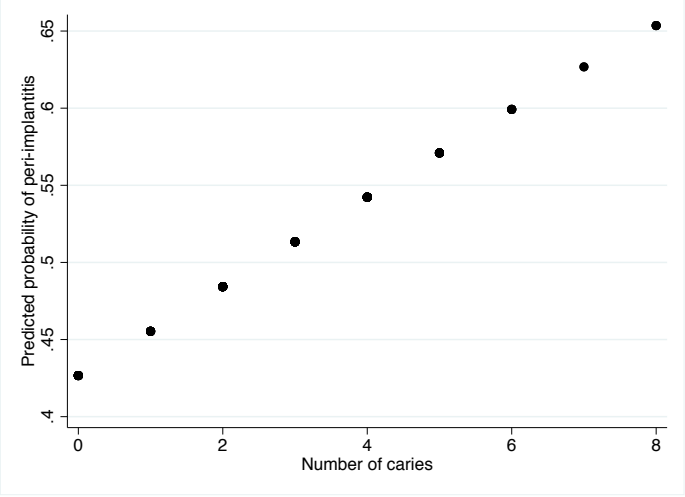

Figure 9. Peri-implantitis predicted probability depending on the number of teeth remaining in the mouth.

IV. Association between filled, missing teeth and DMFT with peri-implantitis.

The mean number of filled teeth in the H and PI group was 6.9 ± 5.1 and 7 ± 3.6 respectively, without statistically significant differences between groups (p=0.96) (Table 2)

Interestingly, the mean number of missing teeth in the H and PI group was 2.6 ± 1.7 and 4.1 ± 2.1 respectively, showing statistically significant differences between groups (p = 0.004). In fact, it was estimated that an additional missing tooth lead to a 48% increase in the probability of presenting PI. The main reasons of tooth loss are reported in Table 2; note that caries, as mentioned before, was the most frequent reason of tooth loss.

Similarly, the mean DMFT index in the H group was significantly lower than in the PI group (12.3 ± 5.7 vs 14.2± 4.3) (p=0.10). Indeed, one additional tooth with this condition (decayed, missing or filled teeth) increased by 8 % the probability of PI. The following figures (10 and 11) depicts that PI probability was dependent on the number of missing teeth and DMFT index; note that the increase in the number of missing teeth and DMFT index incremented the probability of PI.

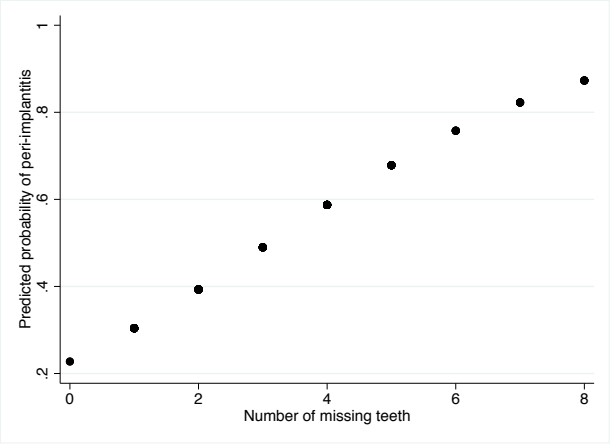

Figure 10. Predicted probability of peri-implantitis depending on the number of missing teeth.

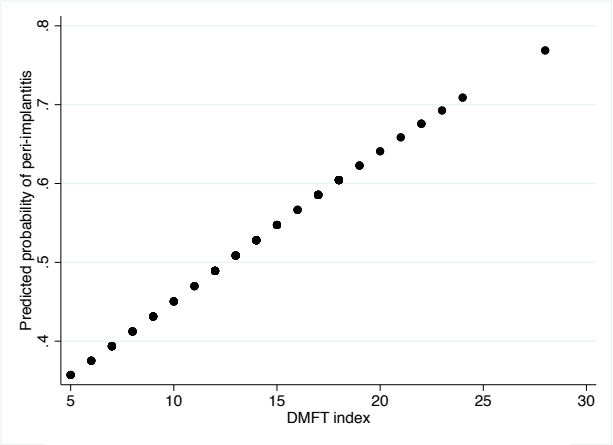

Figure 11. Predicted probability of peri-implantitis depending on the DMFT index.

V. Association between patient related factors and peri-implantitis (H vs PI)

The association between exposure variables and PI at patient-level in the bivariate simple logistic regression is described in Table 3 Annexe VIII.

The results from Table 3 indicated that several exposure variables were significantly associated with PI in the univariate analysis. As such, history of periodontitis and SPT compliance were strongly associated with PI (p=0.04; p=0.04); note that patients with history of periodontitis and without regular SPT compliance presented almost three to four times higher risk of PI (OR= 3.01, p=0.05; OR 4.33, p=0.049). Lastly, FMPS and FMBS were the more discriminating parameters between H and PI patients (p>0.001). Indeed, FMPS and FMBS were almost 20 percentage points greater among PI patients. It could be estimated that the risk of PI increased by 10% and 15% respectively for each additional percentage point in *full mouth* index.

However, a couple of exposure variables suggested a certain tendency of association with PI. As such, an enriched sugar diet and patients referring dry mouth were at a higher risk of PI and close to statistically significance (OR=2.55, p=0.071; OR=2.42, 0.07, respectively). In addition, subjects with a high adherence to Mediterranean diet reduced half the risk of presenting PI (OR=0.50, p=0.149)

The multiple binary logistic regression results are reported in Table 4 Annexe VIII. Note that FMBS and FMPS, the two parameters most associated with PI in the simple binary logistic analysis, were excluded from the model as they played an excessive role. The results indicated that an enriched sugar diet was significantly associated with PI (OR=4.71; p= 0.038); yet, the number of missing teeth also increased the risk of PI, without reaching statistical significance (OR=1.41; p= 0.052).

VI. Association between implant related factors and peri-implantitis

The results from Table 5 Annexe VIII indicated that several local implant-site factors were significantly associated with PI in the univariate analysis. Not surprisingly, the mean PPD was significantly higher in PI implants when compared to H implants (2.5 ± 0.7 vs 4.4 ± 1.3; $p < 0.001$); in other words, it was estimated that one additional millimeter in PPD measurement increased almost 7 times the risk of PI. Moreover, the risk of PI significantly increased in those patients with < 2 mm of KM (OR=4.7; $p< 0.001$) when compared to patients with ≥ 2 mm of KM. As a matter of interest, the presence of an interproximal untreated caries or filling adjacent to the implant was significantly associated with PI ($p=0.021$); in fact, the presence of this condition increased almost two and a half times the risk of PI.

The results of the multiple logistic regression analysis at implant site (seen in Table 6 Annexe VIII revealed that mean PPD and the presence of an interproximal untreated caries or filling adjacent to the implant were still significantly associated with PI ($p<0.001$ and $p=007$, respectively), thus increasing from 5 to 7 times de risk of PI.

VI. Discussion

The present cross-sectional study aimed to evaluate the prevalence and co-occurrence of caries and peri-implantitis. Moreover, the possible association between certain patient-and implant related factors with peri-implantitis was further analysed.

Initially, the prevalence of dental caries in the present study (92.2%) was similar to the data reported in a recent nationwide Spanish survey carried out in 2015 (113). Accordingly, this national survey outlines a prevalence of 95 to 100% in permanent dentitions of subjects over 35 years of age. Moreover, the mean DMFT index in our sample was 13.3, while in the Spanish survey the DMFT ranged from 8.43 (35-44 years) to 16.27 (63-74 years).

On the other hand, the prevalence of patients with peri-implantitis and peri-implant mucositis was 22.5% and 56.2%, respectively. In fact, the reported prevalence for peri-implantitis at patient-level is similar to the one recently published in Spain (24%) (73) and slightly higher when compared to previous national cross-sectional studies (15.1%-16.3%) (114, 115) and to other population studies (14.5%-16.4%) (78, 116). The variability in prevalence estimation between studies may be derived by the use of convenience samples, different case definitions criteria of peri-implant disease and subjective interpretation of bleeding on probing and bone levels as outcomes (73).

To our knowledge, this is the first study evaluating the co-occurrence and association between caries and peri-implantitis. Hence, it could be elucidated that the distribution of caries was quite similar in patients with peri-implantitis when compared to healthy patients. As a matter of fact, subjects with peri-implantitis presented a higher prevalence of two or more caries in mouth when compared to healthy patients, whereas the presence of two or more caries represented a risk of peri-implantitis (OR=1.27) when compared to none caries. Interestingly, a survey study in the Finnish population (107) observed that subjects with periodontal disease had significantly more dental caries, being this fact more evident in cases of severe periodontal disease. Similarly, it was found as well that subjects with dental caries presented more often with severe periodontal disease

(107). Thus, on the basis of the present cross-sectional study it could be suggested that both caries and peri-implantitis may accumulate in the same subjects as long as the number of caries is higher than two.

Furthermore, some patient-related factors appeared to be positively associated with peri-implantitis. Firstly, FMBS and FMPS were the most discriminating clinical parameters associated with peri-implantitis, increasing significantly the risk. It is widely known that poor plaque control may be the most important risk factor for caries, periodontal disease and per-implant disease, as all of them are biofilm-initiated conditions (4, 64). Indeed, several studies have demonstrated a strong correlation between plaque score and occurrence and severity of per-implant diseases (73, 76, 117). Additionally, the inflammatory status of the patient may play an important role in the diagnosis of peri-implant disease. In this line, the findings in the study conducted by Vignoletti et al. (74) evidenced that subjects with FMBS >25% were at a greater risk of peri-implantitis (OR=8.15).

High carbohydrates diets are known to increase the risk for dental caries and gingival bleeding (51). In detail, sugar intake drives oxidative stress and advanced glycation end-products, which may trigger a hyperinflammatory state evidenced in periodontal disease (1). Although there are no studies investigating the role of a dietary sugar and peri-implantitis, our study revealed that patients with an enriched sugar diet were at a higher risk of peri-implantitis (OR=4.71). Noteworthy, patients reporting a high adherence to Mediterranean diet presented a protective effect against peri-implantitis (OR=0.50), thus suggesting that unhealthy dietary habits may be associated with worse peri-implant conditions. Interestingly, a recent study (118) that aimed to investigate the influence of an anti-inflammatory diet (based on low processed carbohydrates and animal proteins, rich in omega-3 fatty acids, vitamin c and d, antioxidants, plant nitrates and fibres for 4 weeks) on different parameters in patients with gingivitis, observed a significant reduction in gingival bleeding index in the modified anti-inflammatory diet. Thus, in the light of these promising results, clinicians may advise and promote health dietary habits among patients.

Patients with history of periodontitis and lack of SPT compliance were associated with PI in the multiple logistic regression analysis (OR=2.39; p=0.289). Consistently, patients with history of periodontitis, especially those with severe forms, are clear risk factors of peri-implantitis as reported in many cross sectional (76, 119) and longitudinal studies (116, 120). Similarly, several studies have confirmed that the lack of SPT predisposed the development of peri-implantitis (74, 121, 122).

This study has also found that patients reporting oral dryness showed a tendency to develop peri-implantitis (OR=2.42; p=0.07). Although there is no evidence associating both diseases, oral dryness is considered an important acquired risk factor of caries and periodontal disease (1). Indeed, oral dryness is a clinical condition that exhibits as lack of salivary flow and as changes in quantity and quality of saliva, this leading to a reduced cleansing of tooth surface. This saliva alteration, in turn, may be associated with reduced dental plaque removal and enhanced gingival inflammation (14, 123). Nevertheless, our results should be interpreted with caution as oral dryness was assessed by asking to the patient instead of using objective methods to detect a reduction in salivary flow, such as stimulated and unstimulated saliva tests (124).

Another risk factor studied in our sample was smoking habit. Smoking has been associated with a major risk of periodontitis in many studies (14, 125), but there is no conclusive evidence when referring to PI even though the impact of smoking on peri-implant tissues has been reported in several studies (63, 79, 126). Our study has failed to demonstrate a significant association between smoking and PI, which is in agreement with findings of other studies (78, 127, 128). However, it has found that smoker patients are more than 2 times more likely to suffer PI. Nevertheless, it should be considered that smoking habit was only assessed by asking to the patient, which may underestimate the role of smoking.

Some studies have reported a lack of association between Diabetes Mellitus and PI (63, 78, 126, 128). In the same way, our study also failed to find a significant association between Diabetes Mellitus and PI, although it was suggested that patients with those patients were at a higher risk of PI. One

possible explanation might be the small number of diabetic patients in our study (7.1%). Another reason may be the fact that assessment was based on patient-reported information and probably a percentage of prediabetic patients were classified as non-diabetic. Nevertheless, as reported by Monje et al. (129), data is currently inconclusive.

There is strong evidence that low socio-economic status is associated with a higher risk of dental caries and periodontitis (17, 53, 54). In a study conducted by Sabbah et al. (130), level of education was used as an indicator for socio-economic position. They found that lower educational level was associated with greater PPD as well as higher extent of gingival bleeding and loss of attachment. Our study also analyzed educational level as an indicator for socio-economic status and showed that patients with university and professional studies had a higher risk of peri-implant disease, although it was not statistically significant. Strikingly, patients with primary or secondary studies were less likely to suffer PI. This may be explained by the fact that patients with lower socioeconomic status are associated with less replacement of lost teeth (131) probably due to lower financial recourses, less knowledge about the different rehabilitation treatments and more social acceptance of the absence of prosthetic replacement of missing teeth.

In our study, only patients with ≥ 20 teeth were included to symmetrize the DMFT distribution. The mean number of missing teeth and implants per patient was 3.4 and 1.81, respectively. As previously stated, the main reason of tooth loss in the present study was dental caries (63.9%). In addition, the most prevalent tooth replaced by an implant was the mandibular first molar (29.2%), followed by maxillary first molars (21.9%). This is not surprisingly because first permanent molars, as erupting early (6-7 years old), are more exposed to caries risk factors. Interestingly, it was found that the mean number of missing teeth was substantially associated with peri-implantitis; it was estimated that an additional missing tooth lead to a 48% increase in the probability of presenting PI. Our findings are partially in agreement with Derks et al. (116), as it was stated that ≥ 4 implants increased 15 times the risk of PI. Thus, it could be suggested, in

partially edentulous patients, that the more teeth lost, if replaced by implants, the more risk to develop peri-implantitis.

Furthermore, there were a couple of implant site-related factors strongly associated with peri-implantitis. In accordance with previous investigations (116, 132), our study has found that an increase on PPD is significantly associated with PI. Each additional millimeter of PPD increased almost 7 times the risk of PI. This might be explained by the fact that, as in natural teeth, microflora components of peri-implant tissues differ between shallow and deep pockets. As reported by Mombelli et al. (96), a PPD > 5 mm might be a protective habitat for putative pathogens that may challenge host response and trigger tissue destruction. Indeed, two studies demonstrated that each 1 millimeter increase in PPD, the risk of BOP was 1,6 (133) and 1,8 (134) times higher, which indicates that deeper pockets present higher levels of inflammation, and an increased risk of PI.

Moreover, our study encountered that those implants surrounded by < 2 mm of KM presented significantly higher risk of PI (OR=4.7; p< 0.001). Although the association between KM width and peri-implant disease has remained controversial over the years (135), most of the studies indicated more plaque accumulation, mucosal recession, brushing discomfort and peri-implant tissue inflammation when there was a lack of KM width (136, 137). Indeed, a recent study (138) has concluded that the absence of 2 mm of KM width around implants seems to be associated with peri-implant disease in erratic compliers patients. Therefore, in the light as well of our results, it may be suggested that 2 mm of KM are recommended for maintaining peri-implant health.

Lastly, the presence of inteproximal untreated caries or fillings adjacent to implants was associated with peri-implantitis (OR=2.41; p=0.021), especially when those were located mesially to the implant. Although this phenomenon has been rarely studied, one possible explanation could be the interproximal open contacts frequently observed, especially in the mesial aspects, between an implant-supported restauration and a contiguous natural tooth in the long term (139-141). Therefore, bearing the above mentioned in mind, it could be cautiously suggested that the presence of interproximal untreated caries or fillings adjacent to implants may be considered as a local risk indicator of peri-implantitis.

Certainly, this present study presents some limitations that should be addressed for a proper understanding of the results. Initially, the inherent cross-sectional design of the study makes virtually impossible to identify causality relationship between the exposure variables and peri-implantitis. Another possible limitation could be the patient's sincerity in answering the questionnaire. Moreover, some data was collected by asking to the patient instead of using more objective methods of assessment (such as oral dryness). With regard to implant measurements, it could be acknowledged that the lack of standardized baseline radiographs (at prosthesis delivery) may have interfered in the accuracy of bone level measurements. Finally, other possible exposure factors, such as the mean function time of the implant, the type of prosthesis (single or fixed partial bridge) or the presence of open contacts at implant site could had also been registered.

VII. Conclusions

This study has concluded that:

1. The prevalence of dental caries was similar among healthy and PI. However, high caries risk profiles and peri-implantitis tended to accumulate in the same subjects.
2. FMBS, FMPS and an increase in PPD were the most significantly associated factors increasing the risk of PI. Nevertheless, a sugar enriched diet and untreated caries or fillings adjacent to implant sites may be further considered as risk indicators of peri-implantitis.

VIII. Future research

This study will probably serve as a pilot study for future research in the association between caries experience and the development of peri-implant disease. Studies with greater sample sizes would be useful to unravel the mechanisms underlying the association between both diseases.

Moreover, studies investigating and understanding their association would be of special importance for the implementation of common preventive and therapeutic approaches that reduce the incidence of dental caries and peri-implant diseases. These approaches could be based on the daily use of oral hygiene measures, changes in diet, tobacco cessation or xerostomia treatment, which could be effective for the prevention of both pathologies.

Additionally, studies exploring the mechanisms through which high sugar consumption could increase the risk of PI, would clarify to what extent the changes towards a healthier diet could reduce the risk of PI and highlight the need to encourage dietary changes at risk patients.

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X. Annexes

Annexe I:

FACULTAD DE ODONTOLOGÍA
Trabajo Final de Grado

FORMULARIO PROPUESTA TRABAJO (RESUMEN, máximo 450 palabras).

DATOS ESTUDIANTE:

Nombre completo: Laura Gumbau Larriba

Correo electrónico: od095342@uic.es

DEPARTAMENTO EN EL QUE SE QUIERE REALIZAR EL TRABAJO

MORE	
Patología médico-quirúrgica y maxilofacial	
Odontopediatría	
Ortodoncia y ortopedia dentofacial	
PeriodÓncia	X
Preventiva y pacientes especiales	
Clínica integrada	
Endodoncia	

Título del TFG

Association between caries history and peri-implantitis: a cross sectional clinical study

☐ Estudio *In Vitro* ☐ Estudio Retrospectivo ☒ Estudio *In Vivo* ☐ Revisión Bibliográfica

☐ Encuesta ☐ Caso Clínico/Revisión Bibliográfica ☐ Revisión Bibliográfica/Diseño protocolo

Nº DE CEIC (para estudios clínicos iniciados): PER-ECL-2017-08

IP del estudio: Dr. Jose Nart Molina

***Los alumnos de TFG no pueden iniciar estudios que requieran la aprobación de un CEIC, deben adherirse a estudios ya iniciados**

Firma alumno

Firma tutor

Annexe II:

FACULTAT DE ODONTOLOGÍA
Trabajo Final de Grado

Nº ID TFG: TFG-87/2019-A61

Sr/a. GUMBAU LARRIBA, Laura

Desde la Coordinación de Trabajos de Final de Grado se le comunica que se ha aceptado que realice el trabajo que lleva por título "Association between caries history and peri-implantitis: a cross sectional clinical study", una vez superados sus estudios lo pueda defender ante un tribunal previa aprobación de su tutor y de la coordinación de TFG.

La persona encargada de tutorizarle durante este período de tiempo será el Dr/Dra. MARTA PEÑA

Adicionalmente, se le informa que la normativa de la UIC establece que hace falta obtener una evaluación favorable del Comité de Ética en la Recerca (CER) o del Comité de Ética de Estudios Clínicos (CEIC), antes de iniciar la investigación. Deberá aportar este informe cuando lo obtenga.

Le saluda cordialmente

Dr. Oscar Salomó
Coordinador Trabajo Final de Grado Odontología

Sant Cugat del Vallés a 29 de Noviembre 2019

Annexe III:

Comitè Ètic d'Investigació Clínica

Clínica Universitària d'Odontologia | Universitat Internacional de Catalunya

APROVACIÓ ESTUDI PEL CEIC / APROBACIÓN ESTUDIO POR EL CEIC / RESEARCH ETHICAL COMMITTEE APPROVAL STUDY

Codi de l'estudi / Código del estudio / Study Code: PER-ECL-2017-08
Versió del protocol/ Versión del protocolo / Study version: 1.2
Data de la versió/ Fecha de la versión/ Version date: 01/02/18
Títol/ Título / Title: Association between caries history and peri-implantitis: a cross sectional clinical study
Investigador Principal / Main researcher: Dr. Jose Nart
Investigador Secundari/ Second reseracher: Javi Vilarrasa Sánchez

Sant Cugat del Vallès, 15 de febrer de 2018

Benvolgut Doctor,

Els membres del CEIC de la Clínica Universitària d'Odontologia, els hi agraeixen l'aportació científica en el camp de la investigació i la presentació del Protocol en aquest Comitè per a la seva avaluació.

Valorades les noves aportacions realitzades a l'estudi, sol·licitades pel nostre CEIC, el dia 1 de febrer de 2018, li comuniquem que el dictamen final ha sigut FAVORABLE.

Li informem que s'haurà de presentar al Comitè d'Ètica d'investigacions clíniques de la CUO, i a través de la Comissió Científica, un informe preliminar mensual del seguiment de l'estudi i un informe final un cop finalitzat aquest.

El Comitè, tant en la seva composició, com en els PNT, compleix amb les normes de BPC (CPMP/ICH/135/95) i amb el Real Decreto 1090/2015, i la seva composició actual és la següent:

- Dr. J.Manuel Ribera Uribe (Presidente, Medico-estomatólogo)
- Dr. Pau Ferrer Salvans (Vicepresidente, Farmacólogo clínico)
- Sra. Noelia Nogales (Secretaria técnica, Bióloga)
- Dr. Joan Janáriz Roldán (Miembro, Médico especialista en medicina interna i oncología)
- Dr. Andreu Hernando Chaure (Miembro, Jurista)
- Sra. Patricia Dominguez Tordera (Miembro, Farmacéutica Hospitalaria)
- Sra. Klaudia Oboloñczyk (Miembro, Farmacéutica de Atención Primaria)
- Dr. Christian Villavicencio-Chávez (Miembro, Médico gerontólogo)
- Sra. Laia Wennberg Capellades (Miembro, Enfermera)
- Sr. Antonio Alcáraz Gibert (Miembro lego, Persona ajena a la profesión sanitaria)

Que en aquesta reunió del Comitè Ètic d'Investigació Clínica es va cumplir amb el quorum preceptiu legalment.

Atentament,

Apreciados Doctores,

Los miembros del CEIC de la Clínica Universitària d'Odontologia, les agradecen su aportación científica en el campo de la investigación y la presentación del Protocolo a este Comité para su evaluación.

Valoradas las nuevas aportaciones realizadas al estudio, solicitadas por nuestro CEIC, el 1 de febrero de 2017, le comunicamos que el dictamen final ha sido FAVORABLE.

Le recordamos que deberá presentar al Comitè d'Ètica d'Investigacions Clíniques de la CUO, y a través de la Comisión Científica, un informe preliminar mensual del seguimiento del estudio y un informe final una vez finalizado el mismo.

Atentamente,

CEIC Comitè Ètic d'Investigació Clínica

CUO Clínica Universitària d'Odontologia | Universitat Internacional de Catalunya

Dear Doctors,

The members of the CEIC of the Clínica Universitària d'Odontologia, appreciate your contribution in the field of research and the presentation to this Committee of the referred study for its evaluation.

After having rated the new contributions to the study, requested by our Ethic Committee, on 1st February 2018, the decision was to APPROVE it.

We remind, that you should present a monthly preliminary report during the study and a final report when the study finishes, through the Academic Commission, to the Clinical Research Ethics Committee of the CUO.

Best regards,

Dr. J.Manuel Ribera
President CEIC

Annexe IV:

Universitat Internacional de Catalunya

Comitè d'Ètica d'Investigació amb medicaments

uic barcelona

ENMIENDA Nº 1
Fecha enmienda: 12/11/19
Protocolo: PER-ECL-2017-08
Versión del protocolo: 1.2
Fecha de la versión: 01/02/18
Título: "Association between caries history and peri-implantitis: a cross sectional clinical study"
Aprobado por el Comité en 15/02/18

Apreciados miembros del Comitè Ètic d'Investigació Clínica amb medicaments.

Mi nombre es Laura Gumbau Larriba de la Universitat Internacional de Catalunya. El motivo de esta enmienda es el de solicitar mi incoporación como investigador secundario encargado de realizar los registros clínicos del estudio "Association between caries history and peri-implantitis: a cross sectional clinical study". El motivo de tal solicitud no es otro que ayudar en la recogida de muestra del estudio mencionado anteriormente, que debería presentar durante el curso 2019-2020 al tribunal evaluador de TFG.

Agradecemos contar con su aprobación y supervisión.

Atentamente,

Investigador principal

Investigador secundario entrante

Annexe V:

Universitat Internacional de Catalunya

Comitè d'Ètica d'Investigació amb medicaments

uic barcelona

APROVACIÓ ESMENA PEL CEIm / APROBACIÓN ENMIENDA POR EL CEIm

Esmena nº / Enmienda nº: 1
Data esmena / Fecha enmienda: 12/11/2019
Codi de l'estudi / Código del estudio / Study Code: PER-ECL-2017-08
Versió del protocol/ Versión del protocolo / Study version: 1.2
Data de la versió/ Fecha de la versión/ Version date: 01/02/18
Títol/ Título / Title: Association between caries history and peri-implantitis: a cross sectional clinical study
Investigadores principales/ Main researchers: Dr. Jose Nart, Dr. Javi Vilarrassa
Tutor/a / Monitor/a:
Investigadoras Secundarias / Second researchers: Laura Gumbau Larriba

Sant Cugat del Vallès, 10 de gener de 2020

Benvolgut Doctor,

Els membres del CEIm de la Clínica Universitària d'Odontologia, li hi agraeixen l'aportació científica en el camp de la investigació i la presentació de l'esmena en aquest Comitè per a la seva avaluació.

Valorades les noves aportacions realitzades a l'esmena nº 1, sol·licitades pel nostre CEIm, el 12 de desembre de 2019, li comuniquem que el dictamen final ha sigut FAVORABLE.

Li informem que s'haurà de presentar al nostre CEIm, i a través de la Comissió Científica, un informe de seguiment anual del seguiment de l'estudi i un informe final un cop finalitzat aquest.

Atentament,

Apreciado Doctor,

Los miembros del CEIm de la Clínica Universitària d'Odontologia, le agradecen su aportación científica en el campo de la investigación y la presentación del Protocolo a este Comité para su evaluación.

Valoradas las nuevas aportaciones realizadas en la enmienda nº 1, solicitadas por nuestro CEIm, el 12 de diciembre de 2019, le comunicamos que el dictamen final ha sido FAVORABLE.

Le recordamos que deberá presentar a nuestro CEIm, y a través de la Comisión Científica, un informe de seguimiento del estudio y un informe final una vez finalizado el mismo.

Atentamente,

Dr. J.Manuel Ribera
President CEIm

Annexe VI:

CEIC Comitè Ètic d'Investigació Clínica

7a. CONSENTIMIENTO INFORMADO

Número del estudio: PER-ECL-2017-08
Versión del protocolo: 1.2
Fecha de la versión: 01/02/2018
Fecha de presentación: 14/12/2017

Investigador/a Principal: Dr. José Nart Molina
Investigador/a Secundario/a: Javi Vilarrasa Sánchez
Departamento: Periodoncia
Línea de investigación: Prevención de peri-implantitis
Título de la investigación: "Asociación entre historia de caries y peri-implantitis: estudio clínico transversal"

Yo, Sr./Sra.: .....

- He recibido información verbal acerca del estudio y he leído la información escrita que se adjunta, de la que he recibido una copia.
- He comprendido lo que se me ha explicado.
- He podido comentar el estudio y realizar preguntas al profesional responsable.
- Doy mi consentimiento para tomar parte en el estudio y asumo que mi participación es totalmente voluntaria.
- Entiendo que podré retirarme en cualquier momento sin que ello afecte a mi futura asistencia médica.

Mediante la firma de este formulario de consentimiento informado, doy mi consentimiento para que mis datos personales se puedan utilizar como se ha descrito en este formulario de consentimiento, que se ajusta a lo dispuesto en la Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal.

Entiendo que recibiré una copia de este formulario de consentimiento informado.

_____ _____

Firma del paciente o la paciente
N.º de DNI

Fecha de la firma

CEIC Comitè Ètic d'Investigació Clínica

DECLARACIÓN DEL INVESTIGADOR O LA INVESTIGADORA

El paciente o la paciente que firma esta hoja de consentimiento ha recibo, por parte del profesional, información detallada de forma oral y escrita del proceso y naturaleza de este estudio de investigación, y ha tenido la oportunidad de preguntar cualquier duda en cuanto a la naturaleza, los riesgos y las ventajas de su participación en este estudio.

_____ _____

Firma del investigador o investigadora Fecha de la firma

Nombre:

Annexe VII:

Datos a nivel de paciente

Fecha de recogida datos:

Datos personales:

Número de historia clínica:

Fecha Nacimiento:

Sexo: V / M

Talla: cm

Peso: kg

IMC=

Tabaco:

No fumador/ Exfumador/ Fumador

Si es afirmativo, cantidad: cig/d

Enfermedades sistémicas:

Enfermedad: No/Si

Diabetes: No / Si En caso afirmativo, está controlada: No/Si

Última analítica: Existe algún déficit de algún nutriente/vitamina?

Xerostomía

Se nota la boca seca? No/Si

Higiene oral

Régimen de cepillado;

N° veces día:

Limpieza interproximal: No/Si

En caso afirmativo: Hilo dental/ Cepillo interproximal

Colutorio; No/Si (especificar principio activo)

Dieta

Considera que tiene una dieta rica en azucares? No/Si (Alta/Medio/Baja en azúcares)

Para evaluar la adherencia a la dieta Mediterránea;

	Preguntas		Resultado
1.	¿Utiliza aceite de oliva para cocinar?	Sí/No	
2.	¿Cuánto aceite de oliva consume por día (freír, ensalada, etc.)?	_ veces/ día	
3.	¿Cuántos vegetales consume por día? 1 toma= 200g)	_ veces/ día	
4.	¿Cuánta fruta consume por día (incluyendo zumos naturales)?	_ veces/ día	
5.	¿Cuánto consume de carne roja, hamburguesa o carne (jamón, butifarra) por día? (1 toma= 100-150 g)	_ veces/ día	
6.	¿Cuánto consume de mantequilla, margarina o crema por día? (1 toma: 12g)	_ veces/ día	
7.	¿Cuántos azúcares o bebidas carbonatas consume por día?	_ veces/ día	
8.	¿Cuánto vino consume por semana?	_ vasos/ sem	
9.	¿Cuántas tomas de legumbres por semana? (1 toma= 150 g)	_ veces/ sem	
10.	¿Cuántas tomas de pescado o marisco por semana? (1 toma 100-150 de pescado o 4-5 unidades o 200 g de marisco)	_ veces/ sem	
11.	¿Cuántas veces por semana consume dulces comerciales o pasteles?	_ veces/ sem	
12.	¿Cuántas tomas de frutos secos por semana? (1 toma 30 g)	_ veces/ sem	
13.	¿Preferiblemente consume pollo, pavo o conejo en vez de cerdo, cordero, hamburguesa o butifarra?	Si/No	
14.	¿Cuántas veces por semana consume verduras, pasta, arroz u otros platos con sofrito?	_ veces/ sem	
			Total=

Nivel estudios

Enseñanza universitaria
Formación profesional
Enseñanza secundaria obligatoria
Enseñanza primaria
Analfabeto, sin estudios

Datos clínicos intraorales a nivel de paciente

Número de dientes (excluir 8s):

Causa de la pérdida dental: Caries/ Movilidad/ Ambas/NC

Historia de Periodontitis: Si/No

En caso afirmativo: Mantenimientos regulares (≥2v/año)

Mantenimientos irregulares (< 2v/año)

Decayed Missing Filled Teeth (DMFT): (excluir 8s)

Decay:

Missing:

Fill:

FMBS:

FMPS:

Datos clínicos intraorales a nivel de implante

Número de implantes (máximo 3 IOI):

Existe Alguna caries/restauración en el diente adyacente al implante? Si/No

(Especificar la superficie del diente donde se encuentra caries/restauración)

Posición Implante			
PS			
Sangrado			
Supuración			
EQ (mm)			
Pérdida ósea Rx (progresiva) (Si/No)			
Diagnóstico			

Annexe VIII:

Table 1:

Variable (categories)	Mean ± SD or % distribution
Patient-related variables (n=169)	
N implants, mean ± SD	1.84 ± 0.76
Implants/patient, % (1-2-3)	37.9-40.2-21.9
Gender, % (male-female)	51.5-48.5
Age (years), mean ± SD	54.5 ± 11.7
Smoking, % (non-smoker- <10 cig/d- ≥ 10 cig/d- former smoker)	43.8-13.6-10.1-32.5
Systemic disease, % (yes, no)	32.5-67.5
Diabetes Mellitus (no-yes controlled- yes uncontrolled)	92.9-6.5-0.6
BMI, % (underweight-normal-overweight-obesity)	0-44.4-37.8-17.8
Diet, % (low adherence-high adherence)	39.6-60.4
Sugar-rich diet, % (no-yes)	70.4-29.6
Level of sugar intake, % (low-medium-high)	12-62-26
Nutrient deficiency, % (no-yes)	97.0-3.0
Vitamin deficiency, % (no-yes)	91.7-8.3
Dry mouth, % (no-yes)	54.2-45.8
Educational level, % (primary and secondary-professional and university)	32.5-67-5
Number of brush/days, % (0 or 1- ≥ 2)	15.4-84.6
Interproximal hygiene, % (no-yes)	28.4-71.6
History of periodontitis, % (no-yes)	25.4-74.6
SPT compliance, % (erratic-≥ 2)	69.1-30.9
Cause of tooth loss, % (caries-mobility- caries & mobility- fracture/trauma)	63.9-5.3-23.7-7.1
FMBS, mean ± SD	31.7 ± 13.5
FMBS, mean ± SD	46.5 ± 17.1
Caries number, mean ± SD	3.1 ± 1.9
Number of caries, % (0-1-≥ 2)	8.9- 32.5-58.6
Filled teeth, mean ± SD	6.8 ±3.8
Missing teeth, mean ± SD	3.4 ± 2.0
DMFT index, mean ± SD	13.3 ± 4.5
Implant related variables (n=311)	
Implant position (max-anterior-man anterior-max posterior-mand posterior)	2.9-1.0-54.6-41.5
PPD (mm), mean ± SD	3.41 ± 1.21
SUP, % (no-yes)	96.8-3.2
KM width, % (≥ 2-< 2mm)	76.9-23.1
Interproximal untreated caries or filling adjacent to implant, %(no-yes)	40.3-59.7
Localization of untreated caries or filling adjacent to implant, % (mesial-distal-both)	41.9-40.2-17.9

Table 1: Description of the included patients and implants in the study.

Table 2:

	Diagnosis		OR	CI 95%	P-value
	Healthy	Peri-implantitis			
N (patients)	36	38			
Caries (mean)	2.8 ± 1.9	3.2 ± 1.9	1.12	1.13-1.93	0.36
Number of caries					0.045*
None	4 (11.1)	5(13.2)	1		
1-2	15 (41.7)	6 (15.8)	0.32	0.06-1.62	0.168
>2	17 (47.2)	27 (71.0)	1.27	0.30-5.41	0.746
Filled	6.9 ± 5.1	7 ± 3.6	1.00	0.90-1.11	0.96
Missing teeth (mean)	2.6 ± 1.7	4.1 ± 2.7	1.48	1.13-1.93	0.004*
DMFT index	12.3 ± 5.7	14.2 ± 4.3	1.08	0.98-1.19	0.107

n (%), mean ± SD

*p<0.05: statistically significant.

Table 2: Association between caries related variables and peri-implantitis at patient level. Results of simple binary logistic regression models, unadjusted odds ratio (OR) and 95% confidence interval.

Table 3:

	Diagnosis		OR	CI 95%	P-value
	Healthy	Peri-implantitis			
N (patients)	36	38			
Gender					
Male	13 (36.1)	14 (52.1)	1		
Female	23 (63.9)	24 (47.9)	0.96	0.37-2.50	0.948
Age	53.0 ± 10.3	54.5 ± 13.7	1.01	0.97-1.05	0.581
Smoking habit					0.467
No	17 (47.2)	12 (31.6)	1		
Yes, < 10 cig/day	5 (13.9)	8 (21.0)	2.26	0.59-8.65	0.231
Yes, ≥ 10 cig/day	3 (8.3)	6 (15.8)	2.83	0.58-13.6	0.194
Former smoker	11 (30.6)	12 (31.6)	1.55	0.51-4.65	0.439
Systemic disease					
Yes	26 (72.2)	24 (63.2)	1		
No	10 (27.8)	14 (36.8)	1.52	0.57-4.05	0.406
Diabetes Mellitus					0.246
Non-diabetic	35 (97.2)	33 (86.9)	1		
Controlled diabetic	1 (2.8)	4 (10.5)	4.24	0.45-39.94	0.207
Uncontrolled diabetic	0 (0)	1 (2.6)	-	-	-
BMI					0.505
Normal weight	16 (44.4)	16 (42.1)	1		
Overweight	11 (33.3)	15 (39.5)	1.25	0.44-3.49	0.670
Obesity	8 (2)	7 (18.4)	0.875	0.26-2.99	0.831
Diet					
Low adherence	12 (33.3)	19 (50.0)	1		
High adherence	24 (66.7)	19 (50.0)	0.5	0.20-1.28	0.149
Sugar rich diet					

No	28 (77.8)	22 (57.9)	1		
Yes	8 (22.2)	16 (42.1)	2.55	0.92-7.03	0.071
Level of sugar consumption					0.708
Low	2 (22.2)	2(13.3)	1		
Medium	4 (44.4)	8 (53.3)	2	0.20-19.9	0.554
High	3 (33.3)	5 (33.3)	1.66	0.14-18.9	0.680
Nutrient deficiency					
No	35 (97.2)	37 (97.4)	1		
Yes	1 (2.8)	1 (2.6)	1.35	0.06-15.71	0.969
Vitamin deficiency					
No	34 (94.4)	36 (94.7)	1		
Yes	2 (5.6)	2 (5.4)	0.94	0.13-7.09	0.956
Oral dryness					
No	24 (68.6)	18 (47.4)	1		
Yes	11 (31.4)	20 (52.6)	2.42	0.99-6.31	0.07
Educational level					
Primary/Secondary	12 (33.3)	11 (29.0)	1		
Professional/university	24 (66.7)	27 (71.0)	1.23	0.46-3.29	0.684
Brushing/day (n)					
1	6 (16.7)	5 (13.2)	1		
≥2	30 (83.3)	33 (86.8)	1.32	0.36-4.77	0.672
Interproximal hygiene					
No	8 (22.2)	14 (36.8)	1		
Yes	28 (77.8)	24 (63.2)	0.49	0.18-1.37	0.173
History of periodontitis					**0.04***
No	13 (36.1)	6 (15.8)	1		
Yes	23 (63.9)	33 (84.2)	3.01	1-9.11	0.050
SPT compliance					**0.04***
≥2 times/year	13 (81.3)	14 (50)	1		
<2 times/year	3 (18.8)	14 (50)	4.33	1.01-18.62	0.049
Cause of tooth loss					
Caries	26 (72.2)	21 (55.3)	1		
Mobility	2 (5.5)	1 (2.6)	0.61	0.05-7.31	0.703
Caries + mobility	6 (16.7)	10 (26.3)	2.06	0.64-6.61	0.223
Trauma/fracture	2 (5.6)	6 (15.8)	3.71	0.68-20.34	0.130
FMBS (%)	20.4 ± 11.6	39.2 ± 12.6	1.15	1.07-1.23	**<0.001***
FMPS (%)	36.3 ± 13.5	57.3 ± 17.2	1.10	1.05-1.15	**<0.001***

n (%), mean ± SD

*p<0.05: statistically significant.

Table 3: Association between exposure variables and peri-implantitis at patient level. Results of simple binary logistic regression models, unadjusted odds ratio (OR) and 95% confidence interval.

Table 4:

	Diagnosis		OR	CI 95%	P-value
	Healthy	Peri-implantitis			
N (patients)	36	38			
Sugar rich diet					
No	28 (77.8)	22 (57.9)	1		
Yes	8 (22.2)	16 (42.1)	4.71	1.09-20.37	0.038*
Oral dryness					
No	24 (68.6)	18 (47.4)	1		
Yes	11 (31.4)	20 (52.6)	1.75	0.48-6.38	0.393
History of periodontitis and SPT compliance					
No	13 (44.8)	6 (17.6)	1		
Yes, ≥2 times/year	13 (44.8)	14 (41.2)	0.79	0.18-3.54	0.760
Yes, <2 times/year	3 (10.3)	14 (82.4)	2.35	0.34-16.42	0.389
Number of caries					
None	4 (11.1)	5(13.2)	1		
1-2	15 (41.7)	6 (15.8)	0.82	0.11-6.50	0.857
>2	17 (47.2)	27 (71.0)	1.15	0.20-6.62	0.869
Missing teeth (mean)	2.6 ± 1.7	4.1 ± 2.7	1.41	1.0-2.0	0.052

n (%), mean ± SD

*p<0.05: statistically significant.

Table 4: Association between exposure variables and PI at patient level. Results of multiple binary logistic regression model, adjusted odds ratio (OR) and 95% confidence interval .

Table 5:

	Diagnosis		OR	CI 95%	P-value
	Healthy	Peri-implantitis			
N (implants)	83	52			
Implant position					0.110
Anterior Maxilla	0 (0)	3 (5.5)	1		
Anterior Mandible	2 (2.4)	0 (0)	1		
Posterior Maxilla	46 (55.4)	33 (60.0)	1.32	0.65-2.70	0.445
Posterior mandible	35 (42.1)	19 (34.5)	-	-	-
PPD	2.5 ± 0.7	4.4 ± 1.3	6.75	3.63-12.55	**<0.001***
KM width					
≥2 mm	74 (89.2)	35(63.6)	1		
<2 mm	9 (10.8)	20 (36.4)	4.7	1.94-11.37	**0.001***
Interproximal caries or filling					
No	37 (45.1)	14 (25.5)	1		
Yes	45 (54.9)	41 (74.5)	2.41	1.14-5.08	**0.021***
Interproximal caries or filling site					0.354
Mesial	16 (35.6)	18 (45.0)	1		
Distal	22 (48.9)	13 (32.5)	0.53	0.20-1.37	0.178
Both	7 (15.6)	9 (22.5)	1.00	0.35-3.78	0.827

n (%), mean ± SD

*p<0.05: statistically significant.

Table 5: Association between implant-site parameters and peri-implantitis at the implant level. Results of simple binary logistic regression models with GEE, unadjusted odds ratio (OR) and 95% confidence interval.

Table 6:

	Diagnosis		OR	CI 95%	P-value
	Healthy	Peri-implantitis			
N (implants)	83	52			
PPD	2.5 ± 0.7	4.4 ± 1.3	6.89	3.58-13.27	**<0.001***
KM width					
≥2 mm	74 (89.2)	35(63.6)	1		
<2 mm	9 (10.8)	20 (36.4)	3.05	0.80-11.73	0.104
Interproximal caries or filling					
No	37 (45.1)	14 (25.5)	1		
Yes	45 (54.9)	41 (74.5)	5.43	1.58-18-56	**0.007***

n (%), mean ± SD

*p<0.05: statistically significant.

Table 6: Association between implant-site variables and PI at implant level. Results of multiple binary logistic regression model with GEE, adjusted odds ratio (OR) and 95% confidence .