Exploring the relationship among dental caries, nutritional habits and peri-implantitis

Javi Vilarrasa*, Marta Peña*, Laura Gumbau†, Alberto Monje*‡, José Nart*

*Department of Periodontology. Universitat Internacional de Catalunya, Barcelona, Spain

†Faculty of Dentistry, Universitat Internacional de Catalunya, Barcelona, Spain

‡ Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI.

Corresponding author:

Dr José Nart

Department of Periodontology. Universitat Internacional de Catalunya.

C/ Josep Trueta, sn/n Sant Cugat del Vallés (08195), Barcelona, Spain

+34 93 504 20 00

josenart@uic.es

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Short running title: Relationship between caries, nutrition and peri-implantitis

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Key findings: Assessment of caries risk profile and nutritional habits should be considered as part of the armamentarium for the prevention of peri-implant diseases

Abstract

Background: A study was made of the prevalence, co-occurrence and association among caries, nutritional habits and peri-implant disease, with an analysis of the influence of other patient and implant factors upon peri-implant disease.

Material and methods: The included subjects underwent a clinical examination and were asked to complete a questionnaire. Demographic data and potential lifestyle/behavioral variables were collected. Clinical and radiographic assessment allowed calculation of the decayed, missing and filled teeth (DMFT) index and peri-implant diagnosis. Uni- and multivariate multinomial logistic regression analyses were applied to identify predictors of peri-implant disease.

Results: A total of 169 patients with 311 implants were studied. At patient level, 92.2% of the subjects presented at least one carious lesion, while 22.5% and 56.2% were diagnosed with peri-implantitis and mucositis, respectively. Those patients with more than two caries had a higher risk of mucositis (OR = 3.33). Statistically significant associations for peri-implantitis included full mouth periodontal indexes, sugar-rich diets, keratinized mucosa width, number of missing teeth and interproximal untreated caries or fillings adjacent to implants.

Conclusion: High caries risk profiles and mucositis/peri-implantitis tended to accumulate within subjects. A sugar-enriched diet and untreated caries or fillings adjacent to implant sites may be further considered as risk indicators of peri-implantitis.

Key words: Mucositis; Peri-implantitis; Dental caries; Diet, Food and Nutrition; Risk factors.

1. INTRODUCTION

Dental caries and periodontitis are considered the most common oral infectious diseases[1] Indeed, the Entire Global Burden of Diseases 2010 Study estimated the overall prevalence of untreated cavitated caries in the permanent dentitions to be 35%. [2] Similarly, the prevalence of periodontitis remains high, affecting approximately 42% of the adult population - though the most severe forms of periodontitis affect 7.8% of the population as reported in a recent national US survey. [3]

Dental caries and periodontitis are complex chronic disorders that may share similar etiological factors with different physiopathological processes.[4] The EFP/ORCA Workshop on the boundaries of caries and periodontal disease [4] identified the potential risk factors for both disorders such as inherited (i.e. genetic variants) and acquired factors (i.e. bacterial biofilm, socio-economic status, hyposalivation, smoking, obesity or carbohydrate intake). Interestingly, the accumulation of pathogenic bacteria in the proximity of the gingival crevice or across the enamel/cementum is a prerequisite for the development of caries and periodontitis in a susceptible host.[5] Carious lesions are caused by demineralization derived from acid production by bacteria exposed to dietary sugars[6], while periodontitis is conceived as an inflammatory condition promoted by putative microbial challenge[7]. Nonetheless, the progression of both disorders may be modulated by other factors such as lifestyle habits,

acquired oral or systemic diseases and the socioeconomic profile of the individual[4]. As interest, nutritional factors, together with hyposalivation, smoking and suboptimally controlled diabetes and obesity, are the most important acquired and shared risk factors between caries and periodontitis [4]. In this regard, an optimum diet for health, low in carbohydrates, high in non-vegetable fats, high in micronutrients and containing sufficient proteins, has been suggested to prevent dental caries and improve periodontal conditions.[8]

Strikingly, there is little evidence on the co-occurrence of dental caries and periodontitis[9–11]. Nevertheless, Mattilla et al. showed, in the Finnish population, that subjects with periodontitis had a significantly higher number of caries (33%).[9] Similarly, subjects with caries had significantly higher proportions of periodontitis (31%). It was concluded that periodontal disease, especially in its severe forms, and dental caries may occur simultaneously in the same subjects - thus suggesting a possible association between the two diseases [9]. Likewise, a recent study by Nascimento et al. found an association between caries and periodontitis among Danish adolescents. [10] Interestingly, it has been reported that the severity of periodontitis is negatively associated to enamel/dentin caries, while its extent is positively associated to dentin caries. [10]

Generally speaking, untreated caries and periodontitis are often leading causes of tooth loss.[12]. In consequence, patients may be affected by reduced masticatory function, poorer nutritional status and low self-stem and quality of life.[13] Nowadays, when replacing missing teeth, implant supported restorations appear to be one of the most predictable treatment options, with long-term implant survival rates. [14] Over the years, clinical practice and scientific research have confirmed that dental implant therapy is not exempt of biological, aesthetic and technical complications.[15] Indeed, peri-implant diseases are plaque-mediated and are characterized by site-specific infections mainly predisposed by local, environmental and/or genetic factors [16,17] - thus resembling to a certain extent the pathogenesis of periodontal disease. [18]

In this context, the scientific rationale behind this study was to explore a possible relationship between dental caries and peri-implantitis as both pathologies are biofilm-induced[5,18] while frequent among population[1,19]. Although the pathophysiology of caries and peri-implantitis differs[18,20], several acquired factors such as lifestyle habits may merge concomitantly in both disorders. Therefore, in pursuance of a better understanding of peri-implant diseases and in order to efficiently implement preventive measures, it was hypothesized that patient caries risk and lifestyle habits could be viewed as potentially relevant factors.

To our knowledge, there is no scientific evidence on the association among caries, nutritional habits and peri-implant diseases. The primary objective of the present study therefore was to assess the prevalence, co-occurrence and association among caries history, nutritional habits and peri-implant diseases. A secondary objective was to analyze the influence of patient and implant-related factors upon peri-implant diseases.

2. MATERIAL AND METHODS

2.1. Study design

The present cross-sectional study was conducted after approval from the Ethics Committee from Universitat Internacional de Catalunya (Ref. PER-ECL-PER-2017-08) and in accordance with the Helsinki Declaration of 1975, as revised in 2013. The study also followed the STROBE statement recommendations. [21] Selected subjects were informed about the aims of the research, and written consent was obtained before starting the study.

2.2. Study population

Patients visiting the Postgraduate Periodontology Clinic of the Faculty of Dentistry of the Universitat Internacional de Catalunya (Barcelona, Spain) from January 2018 to December 2019 were consecutively enrolled in the study by one of the researchers (JV), if they met the following criteria:

- Males or females ≥ 18 years of age.
- One or more dental implants with an implant-supported fixed restoration.
- Subjects needed to have implants with at least one adjacent natural tooth.
- A minimum of one year elapsed from implant-supported restoration delivery.
- Partially edentulous patients with ≥ 20 teeth in the mouth.

The following criteria exclusion criteria were established:

- Inaccuracy in recording peri-implant parameters due to prosthesis design.
- Implant cemented-retained prosthesis.
- Patients previously treated for peri-implantitis.
- Patients taking medications known to modify bone metabolism or with established degenerative diseases of bone (hyperparathyroidism, osteoporosis).
- Patients who had taken antibiotics, nonsteroidal anti-inflammatory drugs or corticosteroids for more than two weeks in the three months before the study.

2.3. Data collection

Data collection comprised a patient interview and clinical and radiographic assessment. Initially, a previously trained examiner (MP) collected the following data:

- Age (years).
- Gender (female/male).
- Smoking habit: smoker, non-smoker or ex-smoker. In the case of smokers, the total amount of cigarettes per day was categorized as < 10 or ≥ 10 cigarettes per day.
- Systemic diseases: presence or absence.
- Diabetes mellitus: presence or absence. In the case of diabetic patients, glycemic control was assessed on the basis of a previous blood test.
- Body mass index (BMI): recorded as weight (kg)/ height $(m)^2$.
- Dietary habits: assessed by the Mediterranean Diet Score (MDS) questionnaire [22] and classified as low adherence (score ≤ 5), medium adherence (score 6-9) or high adherence (score ≥10).
- Regular sugar consumption: yes or no. Sugar consumers were also asked about their level of sugar intake (low, medium, high).
- Nutrient or vitamin deficiencies: presence or absence.
- Oral dryness: patient perception of dry mouth (presence or absence).
- Educational level (EL): primary and secondary or professional and university.
- Oral hygiene measures: frequency of teeth brushing and interproximal hygiene.
- Supportive periodontal treatment (SPT): regular (≥ 2 times/year) or irregular (< 2 times/year).
- Cause of tooth loss: caries, periodontitis, both, and trauma/fracture.

Any doubts coming from the interview were solved by the examiner. A previously calibrated examiner (LG) conducted the intraoral examination (with a Cohen inter-agreement kappa index > 85%). The exploration was conducted to assess the following parameters:

- Periodontal indexes: full mouth plaque score (FMPS)[23]and bleeding score (FMBS)[24]
- History of periodontitis: assessed radiographically by the presence or absence of bone loss.
- Number of decayed, missing and filled teeth (DMFT) assessed by visual inspection and radiographic assessment following the International Caries Detection and Assessment System (ICDAS) [25]. All tooth surfaces were examined, but the observations were recorded per tooth.

- Probing pocket depth (PPD) (in mm), bleeding on probing (BoP) (yes/no), suppuration (SUP) (yes/no), keratinized mucosa (KM) (in mm), attached mucosa (AM) were all recorded at 6 sites per implant using a PCP UNC 15 probe.
- Radiographic bone level (in mm) at mesial and distal to the implant site using the parallel cone technique.
- Implant position (anterior maxilla, anterior mandible, posterior maxilla, posterior mandible).
- Interproximal untreated caries or fillings adjacent to implants: yes/no. If these conditions were present, their location was recorded (mesial, distal or both).

Patients presenting with caries or periodontal or peri-implant disease were referred to the corresponding clinical department within the Universitat Internacional de Catalunya for further evaluation and management.

2.4. *Outcome measures*

The main outcome measure of the study was the prevalence of dental caries and peri-implant disease. Firstly, caries prevalence was assessed as the proportion of patients with at least one clinically (ICDAS 1 to 6) and/or radiographically detectable caries in their dentition. In turn, peri-implant disease was diagnosed following the case definition from the World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions:[26]

- **Peri-implant health (H)**: absence of erythema, BoP, SUP and swelling, without additional bone loss after initial marginal bone remodeling.
- **Peri-implant mucositis (M)**: presence of BoP/SUP with or without increased PPD compared to previous examinations, without additional bone loss after initial marginal bone remodeling.
- **Peri-implantitis (P-I)**: BoP with or without concomitant PPD deepening, with progressive bone loss after 6 months of prosthetic loading. If previous radiographs were not available, PPD > 6 mm and a vertical threshold distance of 3 mm from expected marginal bone remodeling were used.

All other variables obtained from patient information and clinical examination were regarded as secondary outcome measures.

2.5. Sample size calculation

A logit regression model used to associate the outcome diagnosis at the patient level and each exposure variable reached a statistical power of 82.5% in detecting odds ratio (OR) = 2.5 as being significant in the recruited sample (n= 169), assuming a confidence level of 95%. At the implant level, the power was 96.2% under the same previous conditions. Due to the multi-level design, the power had to be corrected. In this regard, assuming a moderate intra-subject correlation (ρ = 0.5), a power of 87.7% was estimated.

2.6. *Statistical analysis*

A descriptive analysis was carried out, with the calculation of absolute and relative frequencies (categorical variables) and the mean and standard deviation (SD) (continuous variables).

§ PCP UNC 15, Hu-Friedy, Rockwell St, Chicago, IL

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the exposure variables (see Table S1 in online Journal of Periodontology). Specifically, the peri-implant diagnosis in subjects with multiple implants was assigned by the worst status between all the carried implants. At implant level, simple multinomial logistic regression models were estimated using generalized estimating equations (GEEs) (see Table S2 in online Journal of Periodontology). The models estimated OR from the Wald chi-squared statistic. The GEE approach addressed intra-subject dependency between observations due to the multiplicity of implants per patient. Relevant exposure variables ($p<0.10$) were incorporated into a multiple logistic regression model at patient and implant level to obtain adjusted ORs. The SPPS v21.0 statistical package was used throughout. The level of significance was 5% ($\alpha = 0.05$).

3. RESULTS

3.1. Sample description

The study sample characteristics are summarized in Table 1. Of the total 169 patients, 87 were males (51.5%) and 82 females (48.5%), with a mean age of 54.5 ± 11.7 years.

Briefly, most of the patients were systemically healthy (67.5%), and almost half of the subjects were non-smokers (43.8%). Medium to high adherence to the Mediterranean diet was reported in 21.3% of the sample, while 29.6% routinely consumed sugar. Most of the patients presented with a history of periodontitis (74.6%), but few of them regularly received SPT (30.9%). Most teeth were lost due to caries (63.9%).

An average of 1.84 implants were included per patient, with the following distribution: 37.9%, 40.2% and 21.9% of the subjects carried one, two and three implants, respectively. Almost all the implants were located in the posterior maxilla/mandible (96.1%), surrounded by ≥ 2 mm of KM (76.9%) and < 1 mm of AM (73.3%). Interestingly, almost 60% of the implants presented adjacent untreated caries or fillings.

3.2. Prevalence of caries and peri-implant disease

The prevalence of caries was 92.2%. More in detail, 8.8% of the patients did not present 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).

At patient level, the prevalence of H, M and P-I was 21.3%, 56.2% and 22.5%, respectively. At implant level, 27.7%, 55.6% and 17.7% were diagnosed as H, M and P-I, respectively.

[II] SPSS Inc., Chicago, IL, USA

3.3. Association and co-occurrence between caries and peri-implant diseases

As reported in Table 1, the mean distribution of caries was 2.8 ± 1.9, 3.1 ± 2.0 and 3.2 ± 1.9 in the H, M and P-I groups, respectively (H versus M: p=0.37; H versus P-I: p=0.36) (Table 1). Nonetheless, the prevalence of P-I was seen to be greater in subjects displaying ≥ 2 caries (>2 = 71.0% versus 1: 15.8% and versus 0=13.2%). Similarly, subjects with ≥ 2 caries showed a greater prevalence of P-I versus H (61.3% versus 38.4%) and an increased risk of M (OR=3.33; p=0.148) when compared to non-caries patients. Figure 1 illustrates the probability of M and P-I on the basis of the number of caries; it should be noted that the probability of M and P-I increased as the number of caries increased.

3.4. Association between patient-related factors and peri-implant diseases

The results of the multiple multinomial logistic regression analysis for M and P-I are reported in Table 2. It should be noted that FMBS and FMPS were the parameters most significantly associated to M and P-I on applying the simple logistic regression analysis. Data showed that males were significantly associated to a decreased risk of M (OR=0.31; p=0.019), whereas the number of missing teeth and presenting >2 caries showed a tendency to develop M (OR 1.36; p=0.064, OR: 3.33; p=0.148, respectively). Conversely, the results indicated that an enriched sugar diet and the number of missing teeth were significantly associated to P-I (OR=5.38; p= 0.015, OR: 1.44; p=0.046).

3.5. Association between implant-related factors and peri-implant disease

The results of the multiple multinomial logistic regression analysis at implant site (Table 3) showed mean PPD to be significantly associated to M (p <0.001) and P-I (p=0.001), increasing the risk of M and P-I from 4- to 8-fold respectively. Moreover, the risk of M and P-I significantly increased in those patients with < 2 mm of KM (M: OR= 2.77, p=0.030; P-I: OR=4.85; p=0.007) when compared to patients with ≥ 2 mm of KM. As a matter of interest, the presence of an interproximal untreated caries or filling mesially adjacent to the implant showed a tendency to develop M (OR= 2.15, p=0.083) and was significantly associated to P-I (p=0.012). In fact, the presence of this condition increased the risk of P-I 4.26-fold.

4. DISCUSSION

To the best of our knowledge, this is the first study to evaluate the co-occurrence and association among caries, nutritional habits and peri-implant diseases. The mean distribution of caries was found to be similar in patients with M and P-I when compared to H patients. As a matter of fact, subjects with M and P-I presented a higher prevalence of two or more caries when compared to H patients, whereas the presence of two or more caries represented a risk of M (OR= 3.33) when compared to no caries. Interestingly, a survey in the Finnish population [9] found subjects with periodontal disease to have significantly more dental caries - this association being more evident in cases of severe periodontal disease. Similarly, it was found that subjects with dental caries more often presented with severe periodontal disease. [9] Thus, on the basis of our study, it could be suggested that both caries and P-I may accumulate within the same subjects, provided the number of caries is greater than two.

Furthermore, some patient-related factors appeared to be positively associated to M and P-I. Firstly, FMBS and FMPS were the most discriminating clinical parameters associated to both diseases, increasing the risk significantly (p<0.001). It is widely known that poor plaque control may be the most important risk factor for caries, periodontal disease and per-implant disease, since all of them are biofilm-initiated conditions. [5,26] Indeed, several studies have demonstrated a strong correlation between the plaque score and the occurrence and severity of per-implant diseases. [27–29] Additionally, the inflammatory status of the patient may play an important role in the diagnosis of peri-implant disease[30]. The findings of the study conducted by Vignoletti et al. evidenced that subjects with FMBS > 25% were at a greater risk of P-I (OR=8.15). [30]

Although there are no studies investigating the role of sugary diets and peri-implantitis, our study showed patients with an enriched sugar diet to be at greater risk of M (OR=3.24; p=0.060) and P-I (OR=5.38; p=0.015). In fact, it has been reported that high carbohydrates intake may increase the risk for dental caries and gingival bleeding. [8] More in detail, sugar consumption drives oxidative stress and advanced glycation end-products, which may trigger a hyperinflammatory state evidenced in periodontal disease. [4] Interestingly, we found in the bivariate analysis that patients with high adherence to the Mediterranean diet showed

a protective effect against peri-implant diseases, thus suggesting that unhealthy dietary habits may be related to poorer peri-implant conditions. In this respect, the Mediterranean diet has not only been considered to be a protective factor against cardiovascular disease, overall cancer incidence, neurodegenerative disease and diabetes, but has also been linked with greater longevity and quality of life. [31,32] In the periodontal field, recent promising research has suggested that increased adherence to the Mediterranean diet might reduce the amount of periodontopathogenic bacteria in the saliva of systemically compromised patients. [33] Similarly, the implementation of a particular anti-inflammatory diet significantly reduced the gingival bleeding index. [34] Thus, clinicians should advise and promote healthy dietary habits among patients for preventing the aforementioned oral diseases.

Patients with a history of periodontitis and a lack of SPT compliance were associated to P-I (OR=3.74; p=0.174). Consistently, a history of periodontitis has been suggested as the primary risk factor for P-I. Similarly, several studies have confirmed that a lack of SPT is associated to the development of P-I. [28,35,36] Our study also found that those implants surrounded by < 2 mm of KM had a significantly higher risk of M (OR=2.77; p=0.030) and P-I (OR=4.85; p= 0.007). Although the association between KM width and peri-implant disease remains controversial [37],most studies report more plaque accumulation, mucosal recession, brushing discomfort and peri-implant tissue inflammation when there is a lack of KM width. [38–42] Indeed, a recent study has concluded that the absence of 2 mm of KM width around implants seems to be associated to peri-implant disease in erratic compliers [40]. Therefore, it may be suggested that 2 mm of KM are recommended for maintaining peri-implant health.

This study has also found that patients reporting oral dryness showed a tendency to develop M (OR=1.99; p=0.171) and P-I (OR=2.16; p=0.188). Similarly, in a recent cross-sectional study conducted in Brazil it was shown that dry mouth increased, but not significantly, the risk of per-implant disease by 2.16-fold [43]. Although evidence is scarce in associating both diseases, oral dryness is considered to be an important acquired risk factor for caries and periodontal disease [4]. Indeed, oral dryness is a clinical condition manifesting as a lack of salivary flow and as changes in the quantity and quality of saliva - this leading to lessened dental plaque removal and enhanced gingival inflammation. [44,45] Nevertheless, our results should be interpreted with caution, since oral dryness was assessed by questioning the patient instead of using objective methods to detect diminished salivary flow, such as stimulated and unstimulated saliva tests. [46]

Lastly, the presence of interproximal untreated caries or fillings adjacent to implants was associated to P-I, especially when located mesially to the implant (OR=4.26; p=0.009). One possible explanation for this could be the interproximal open contacts frequently observed between an implant-supported restoration and a contiguous natural tooth over the long term. [47–49] Accordingly, the presence of an open contact may lead to food trapping which, in the absence of proper interproximal oral hygiene, may lead to caries formation and peri-implant inflammation. [48,49] Thus, it could be tentatively suggested that the presence of interproximal untreated caries or fillings adjacent to implants may be considered as a local risk indicator of P-I.

Several clinical implications may be derived from findings of our study. Firstly, the number of caries may be viewed as a potential factor influencing the severity of peri-implant diseases. Accordingly, caries risk profile, which may be subjected to patients' oral hygiene

and lifestyle factors, should be assessed and monitored throughout implant therapy. Special attention should be paid to interproximal caries or fillings adjacent to implants as its presence could denote deficient self-performed interproximal oral hygiene, thus predisposing peri-implant disease occurrence.[50] Finally, nutritional habits such as sugar intake or adherence to Mediterranean diet may play a protective role against peri-implant disease, without overlooking as well the impact of oral dryness. Healthy dietary habits consisting in a reduced sugar consumption, anti-inflammatory aliments and water ingestion may be able to alter bacterial metabolism and reduce inflammatory status. Thus, clinicians should be encouraged to promote healthy lifestyle habits among patients to prevent the occurrence of the abovementioned oral diseases.

Our study has some limitations that should be addressed for proper understanding of the results. The study design inherently makes it virtually impossible to identify causal relationships between outcomes. Likewise, the lack of standardized baseline radiographs may have interfered in the accuracy of the bone level measurements. Finally, other possible exposure factors, such as the mean time of function of the implant, the socio-economic status, the type of prosthesis (single or fixed partial bridge) or the presence of open contacts at the implant site, could also have been registered.

Longitudinal prospective studies involving larger sample sizes would be useful to clarify the mechanisms underlying the association between nutritional and dietary habits and peri-implant disease. This would be of special importance for the implementation of preventive strategies aiming to reduce the incidence of dental caries and periodontal and peri-implant diseases.

5. CONCLUSIONS

The present study found the prevalence of dental caries to be similar among healthy patients and individuals with peri-implantitis. However, high caries risk profiles and mucositis/peri-implantitis tended to accumulate in the same subjects. A sugar enriched diet and untreated caries or fillings adjacent to implant sites may be further considered as risk indicators of peri-implantitis.

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Table 1. Description of the included patients (n=169) and implants (n=311) in the study.

Variable	Health	Mucositis	Peri-implantitis	Total
Patient-related variables				
N implants, mean ± SD	1.39 ± 0.60	1.92 ± 0.77	2.08 ± 0.72	1.84 ± 0.76
Implants/patient, % (1-2-3)	37.5-50.0-12.5	14.7-57.4-27.9	5.4-64.9-29.7	37.9-40.2-21.9
Peri-implant diagnosis, n (%)	36 (21.3)	95 (56.2)	38 (22.5)	-
Gender, % (male-female)	63.9-36-1	42.1-57.9	63.2-36.8	51.5-48.5
Age (years), mean ± SD	53.0 ± 10.3	55.1 ± 11.4	54.5 ± 13.7	54.5 ± 11.7
Smoking habit, % (non-smoker- <10 cig/d- ≥ 10 cig/d- former smoker)	47.2-13.9-8.3-30.6	47.4-10.5-8.4-33.7	31.6-21.0-15.8-31.6	43.8-13.6-10.1-32.5
Systemic disease, % (yes, no)	27.8-72.2	32.6-67.4	36.8-63.2	32.5-67.5
Diabetes mellitus (no-yes controlled- yes uncontrolled)	97.2-2.8-0	93.7-6.3-0	86.9-10.5-2.6	92.9-6.5-0.6
BMI, % (underweight-normal-overweight-obesity)	0-44.5-33.3-22.2	0-45.3-39.0-15.7	0-42.1-39.5-18.4	0-44.4-37.8-17.8
Diet, % (low adherence-medium-high adherence)	5.6-69.4-25.0	10.5-69.5-20.0	15.8-63.2-22.2	10.7-68.1-21.3
Sugar-rich diet, % (no-yes)	77.8-22.2	72.6-27.3	57.9-42.1	70.4-29.6
Level of sugar intake, % (low-medium-high)	22.2-44.4-33.3	7.7-73.1-19.2	13.3-53.3-33.4	12-62-26
Nutrient deficiency, % (no-yes)	97.2-2.8	96.8-3.2	97.4-2.6	97.0-3.0
Vitamin deficiency, % (no-yes)	94.4-5.6	89.5-10.5	94.7-5.3	91.7-8.3
Dry mouth, % (no-yes)	68.6-31.4	51.6-48.4	47.4-52.6	54.2-45.8
Educational level, % (primary and secondary-professional and university)	33.3-66.7	33.7-66.3	29.9-71.1	32.5-67-5
Number of brushings/day, % (0 or 1- ≥ 2)	16.7-83.3	15.8-84.2	13.2-86.4	15.4-84.6
Interproximal hygiene, % (no-yes)	22.2-23.1	27.4-72.6	36.8-63.2	28.4-71.6
History of periodontitis, % (no-yes)	36.1-63.9	25.3-74.7	15.8-84.2	25.4-74.6
SPT compliance, % (erratic-≥ 2)	81.3-18.7	74.2-25.8	50.0-50.0	69.1-30.9
Cause of tooth loss, % (caries-periodontitis- both-fracture/trauma)	72.2-5.6-16.6-5.6	64.2-6.3-25.3-4.2	55.3-2.6-26.3-15.8	63.9-5.3-23.7-7.1
FMBS, mean ± SD	20.4 ± 11.6	32.7 ± 12.0	39.2 ± 12.6	31.7 ± 13.5
FMPS, mean ± SD	36.3 ± 13.5	46.2 ± 16.0	57.3 ± 17.2	46.5 ± 17.1
Caries number, mean ± SD	2.8 ± 1.9	3.1 ± 2.0	3.2 ± 1.9	3.1 ± 1.9
Number of caries, % (0-1-≥ 2)	11.1-41.7-47.2	6.3-35.8-57.9	13.2-15.8-71.0	8.9- 32.5-58.6
Filled teeth, mean ± SD	6.9 ± 5.1	6.7 ±3.2	7 ± 3.6	6.8 ±3.8
Missing teeth, mean ± SD	2.6 ± 1.7	3.5 ± 1.9	4.1 ± 2.2	3.4 ± 2.0
DMFT index, mean ± SD	12.3 ± 5.7	13.4 ± 3.9	14.2 ± 4.3	13.3 ± 4.5
Implant-related variables				
Implant position (max-anterior-mand anterior-max posterior-mand posterior)	0-2.4-52.4-42.2	3.4-0.6-52.6-43.4	5.5-0-60.0-34.5	2.9-1.0-54.6-41.5

PPD (mm), mean ± SD	2.5 ± 0.71	3.5 ± 1.0	4.4 ± 1.3	3.41 ± 1.21
SUP, % (no-yes)	100-0.0	96.5-3.5	92-7-7.3	96.8-3.2
Keratinized mucosa width, % (≥ 2-< 2mm)	89.2-10.8	75.1-24.9	63.6-36.4	76.9-23.1
Attached mucosa, % (<1 mm, ≥ 1 mm)	61.5-38.5	77.5-22.5	78.2-21.8	73.3-26.7
Interproximal untreated caries or filling adjacent to implant, %(no-yes)	45.8-54.2	42.4-57.6	25.4-74.6	40.3-59.7
Localization of untreated caries or filling adjacent to implant, % (mesial-distal-both)	35-6-48.9-15.5	43.4-39.4-17.2	45-32.5-22.5	41.9-40.2-17.9

Notes: SD: standard deviation; N: number; cig: cigarettes; BMI: Body Mass Index; SPT: Supportive Periodontal Therapy; FMBS: Full Mouth Bleeding Score; FMPS: Full Mouth Plaque Score; DMFT: Decayed Missing Filled Teeth; max: maxilla; mand: mandible; PPD: probing pocket depth; SUP; suppuration

Table 2. Association between exposure variables and M and P-I at patient level. Results of multiple multinomial logistic regression model, adjusted OR and 95% CI.

	H vs M		**H vs P-I**	
Variable	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Gender				
Female	1		1	
Male	0.31 (0.12-0.83)	0.019*	0.61 (0.19-1.99)	0.411
Sugar-rich diet				
No	1		1	
Yes	3.24 (0.95-11.12)	0.060	5.38 (1.39-20.87)	0.015*
Oral dryness				
No	1		1	
Yes	1.99 (0.74-5.33)	0.171	2.16 (0.69-6.82)	0.188
History of periodontitis and SPT compliance				
No	1			
Yes, ≥ 2 times/year	0.96 (0.31-2.92)	0.936	1.13 (0.26-4.94)	0.869
Yes, <2 times/year	1.12 (0.22- 5.72)	0.883	3.74 (0.56- 25.11)	0.174
Number of caries				
None	1		1	
1-2	3.01 (0.54-3.67)	0.208	0.42 (0.06-3.02)	0.393
>2	3.33 (0.65-17.03)	0.148	0.93 (0.16-5.36)	0.938
Missing teeth	1.36 (0.98-1.88)	0.064	1.44 (1.01-2.06)	0.046*

Table 3. Association between exposure variables M and P-I at implant level. Results of multiple multinomial binary logistic regression models with GEE and adjusted odds ratio (OR) and 95% CI.

	H vs M		H vs P-I	
Variable	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
PPD	4.28 (2.76-6.65)	<0.001†	8.61 (5.10-14.54)	<0.001†
KM width				
≥ 2 mm	1		1	
< 2 mm	2.77 (1.10-6.99)	0.030*	4.85 (1.54-15.20)	0.007*
AM width				
<= 1 mm	1		1	
>1 mm	1.20 (0.59-2.47)	0.602	2.44 (0.87-6.88)	0.091
Interproximal caries or filling				
No	1		1	
Yes, mesial	2.15 (0.90-5.11)	0.083	4.26 (1.36-13.27)	0.012*
Yes, distal	1.49 (0.69-2.23)	0.310	2.82 (0.93-8.53)	0.067
Yes, both sites	1.42 (0.48-4.18)	0.522	3.98 (1.01-15.65)	0.052

Notes. OR: odds ratio; CI: confidence interval; H: healthy; M: mucositis; P-I: peri-implantitis; PPD: probing pocket depth; KM: keratinized mucosa; AM: attached mucosa.

**P* <0.05

†*P* < 0.001

Notes. OR: odds ratio; CI: confidence interval; H: healthy; M: mucositis; P-I: peri-implantitis; SPT: Supportive Periodontal Therapy

**P* <0.05

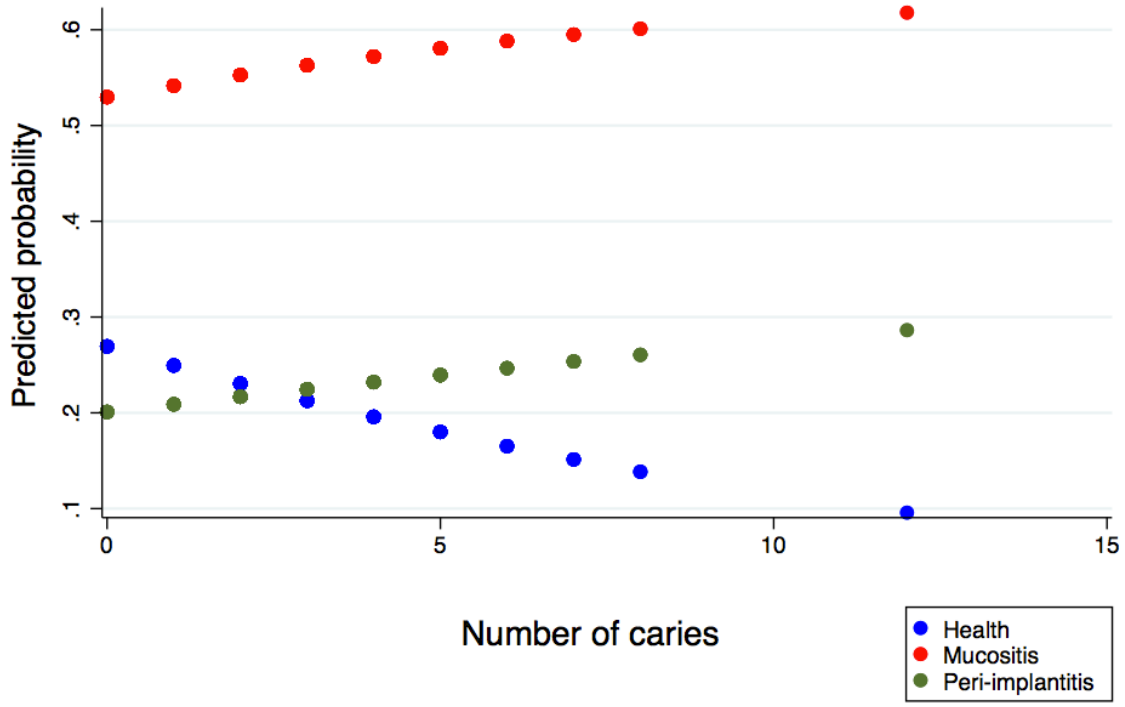

Figure 1. Predicted probability of H, M and P-I occurrence depending on the number of caries.