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Clinical Studies

Associations of chairside salivary aMMP-8 findings with periodontal parameters, potentially periodontal pathogenic bacteria and selected blood parameters in systemically healthy adults☆

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ABSTRACT

The aim of this cross-sectional study was to investigate associations between salivary active matrix-metalloproteinase 8 (aMMP-8) and periodontitis severity, potentially periodontal pathogenic bacteria as well as blood parameters in generally healthy participants.
Therefore, 188 participants with a mean age of 48.9 ± 8 years were examined. The periodontitis severity was assessed based on periodontal probing depth and clinical attachment loss. Both, aMMP-8 and microbiological analysis were performed using a validated, commercially available test system. Blood values were utilized from regular differential blood count.
The aMMP-8 findings were associated with the periodontitis severity ($P < 0.01$), as well as with the prevalence of *Porphyromonas gingivalis, Tannerella forsythia, Prevotella intermedia, Parvimonas micra, Camphylobacter rectus* and *Eubacterium nodatum* ($P_i < 0.05$). No associations between aMMP-8 and the examined blood parameters were found ($P_i > 0.05$).
In conclusion, salivary aMMP-8 findings seem to reflect periodontal disease severity as a result of an immunoreaction, especially against bacteria with high periodontal pathogenic potential.

1. Introduction

Periodontitis is an inflammatory disease primarily caused by a dysbiosis of oral microbiota, which is influenced by different modifiable (e.g. smoking) and non-modifiable (e.g. genetics) factors (Kinane et al. 2017). The high burden of periodontal disease affecting more than 700 million of patients worldwide (Richards 2014) leads to growth of interest regarding their sufficient diagnosis and therapy and forwards research in this field (Slots 2017). While clinical parameters are still the main issue in periodontal diagnostics, different novel approaches have developed, especially regarding non-invasive methods (Slots 2017). In this context, the active matrix-metalloproteinase 8 (aMMP-8) became a biomarker of increasing relevance in recent years (Sorsa et al. 2016). In response to a bacterial infection, the enzyme aMMP-8 causes destruction of collagen-Typ I, II and III, leading to a damage of periodontal soft and hard tissue (Sorsa et al. 2004; Sorsa et al. 2006). Accordingly, increased activity and expression of aMMP-8 is reported to reflect current periodontal inflammation and disease progression (Sorsa et al. 2004; Sorsa et al. 2006).

The highest potential benefit might bring a non-invasive saliva based point-of-care testing of aMMP-8, as described in recent review articles (Sorsa et al. 2016; Alassiri et al. 2018). Meanwhile, it is repeatedly described that this salivary aMMP-8 testing is able to reflect periodontal disease, but there is still a necessity of research regarding its diagnostic and preventive potential in management of periodontal diseases (Alassiri et al. 2018; Zhang et al. 2018; Lorenz et al. 2017; Izadi Borujeni et al. 2015). Moreover, the immunological response to bacterial load and thus aMMP-8 expression is potentially influenced by general diseases and medication (Ziebolz et al. 2017; Schmalz et al. 2017). Furthermore, aMMP-8 could be influenced by specific bacterial load and associated to specific potentially periodontal pathogenic bacteria. Periodontal bacteria with a high pathogenic potential like *Porphyromonas gingivalis* or *Treponema denticola* could be associated with a strong immune reaction and in this way with a higher aMMP-8 expression (Ramseier et al. 2009; Yakob et al. 2012; Yakob et al. 2013; Salminen et al. 2014). However, data regarding associations between aMMP-8 and specific bacteria are

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still rare, making clear statement impossible and further clinical investigations necessary.

Periodontitis as an inflammatory disease could also influence blood parameters, especially C-reactive protein as a marker for acute immunoreaction to bacterial infection (Bolla et al. 2017). Although blood parameters are neither part of routine nor of adjunctive periodontal diagnostics, it could be relevant whether non-invasive aMMP-8 salivary test could also be associated to blood parameters and thus reflect systemic inflammatory reaction in healthy adults.

Accordingly, aim of this study was to detect associations between aMMP-8 and clinical periodontal parameters as well as prevalence of selected potentially periodontal pathogenic bacteria and blood parameters. To ensure that there is no influence by general health or medication, only generally healthy participants should be included in the study. It was hypothesized that aMMP-8 would be associated to periodontal disease severity and potentially periodontal pathogenic bacteria with high pathogenic potential.

2. Methods

2.1. Study design

This current study was designed and performed as a clinical cross-sectional study. It has been reviewed and approved by the ethics committee of the University Medical Center Goettingen, Germany (No: 1/6/12). All participants were informed verbally and in writing and gave their written informed consent.

2.2. Patients

All participants were blood donors at the Department of Transfusion Medicine, University Medical Center Goettingen, Germany. Only generally healthy individuals with a minimum age of 35 years were included. Accordingly, the presences of any general disease (especially immunosuppression, infections, diabetes mellitus, autoimmune diseases, renal insufficiency or neurological diseases) as well as pregnancy, alcohol- or drug abuse were exclusion criteria. Moreover, participants with the necessity of an antibiotic prophylaxis or an antibiotic therapy in the previous 3 months before examination were also excluded from the examination. The generally healthy condition of the participants was assessed based on their recent regular physical and laboratory examinations in context of blood donation procedures.

2.3. Clinical examination

The patients were examined between 01.11.2012 and 30.11.2013 under standardized conditions by two experienced and calibrated dentists in the Department of Preventive Dentistry, Periodontology and Cariology, University Medical Centre Goettingen, Germany. All patients, who visited the Department of Transfusion Medicine during the examination period and met the criteria for participation, were included in the current study. The clinical examination comprised the detection of gingival inflammation (papilla bleeding index) and periodontal disease severity (periodontal status). The papilla bleeding index (PBI) was executed, which contained the smooth straining of the gingival sulcus with a periodontal probe (PCP 15, Hu-Friedy, Chicago, IL, USA). The resulting occurrence of bleeding was recorded as PBI score between 0 (no bleeding/inflammation-free gingiva) to 4 (profuse bleeding/severe inflammation). Furthermore periodontal parameters were recorded, including the periodontal probing depth (PPD) and clinical attachment loss (CAL). These parameters were assessed based on 6 measurements (mesio-buccal, buccal, disto-buccal, mesio-oral, oral, and disto-oral) each tooth using a millimeter-scaled periodontal probe (PCP 15, Hu-Friedy, Chicago, IL, USA). Based on these values, the periodontal disease severity was determined according to AAP/CDC criteria into no/mild, moderate or severe periodontits (Page and Eke 2007).

2.4. aMMP-8 chairside test

The applied chairside test currently exists as reader equipped computerized quantitative test (Sorsa et al. 2017, Alassiri et al. 2018, Ahmed et al. 2018). A commercially available test system (Periomarker®, Hager & Werken GmbH & Co. KG) was used following the manufacturers' instructions and in accordance to previously published studies of this working group (Schmalz et al. 2018; Schmidt et al. 2017). The sample collection was performed before any clinical dental/periodontal examination was done. All participants were instructed to refrain from eating, drinking and oral hygiene on the same day prior to the test performance. For saliva collection, all participants needed to rinse their mouth with the (test) mouth rinse liquid for 30 seconds. Afterwards, participants had to spit the rinse into the test tube. Of the filtered mixture of saliva and solvent, three drops were pipetted into the fluid recess of the chairside test. This applied aMMP-8 chairside test is qualitative, showing a positive or negative result based on the measured quantity of 25 ng/ml as threshold level. The underlying analysis is a lateral flow-immunochromatographic assay, which has already been described previously (Schmalz et al. 2018). In brief, the solvent passes a dissolved salt-sugar mixture with an antibody-immobilizing surface. The resulting solvent-conjugate mixture with linked antibody interacts with another molecule that is provided on stripes. The accumulation of molecule-interacted conjugate-antibody mixture causes a color reaction. The minimum measured quantity of 25 ng/mL aMMP-8 in sample is displayed by a blue test stripe and shows a “positive” result. A second control stripe verifies that the test is working correctly.

2.5. Microbiological analysis

After aMMP-8 analysis, biofilm samples for microbiological diagnostic were collected. Firstly, supragingival plaque was carefully removed from the tooth surface without affection of the gingival margin to avoid any bleeding. Furthermore, the working field was drained using dental rolls. Three sterile paper tips were placed in the deepest periodontal pockets for 20 s to collect subgingival biofilm and pooled for each patient. The microbiological analysis of potentially periodontal pathogenic bacteria was executed using polymerase chain reaction analysis (PCR) in the clinical laboratory of the Department of Preventive Dentistry, Periodontology and Cariology, University Medical Center, Goettingen. For the semi-quantitative detection of the bacterial colonization of samples, a commercial test system was used (Micro-IDent plus-Test, HainLifescience, Nehren, Germany) according to manufacturers´ instructions. With this analysis, 11 potentially periodontal pathogenic bacteria were analyzed: *Aa: Aggregatibacter actinomycetemcomitans* (detection threshold $>10^2$); *Pg: Porphyromonas gingivalis; Tf: Tannerella forsythia; Td: Treponema denticola; Pi: Prevotella intermedia; Pm: Parvimonas micra; Fn: Fusobacterium nucleatum; Cr: Campylobacter rectus; En: Eubacterium nodatum; Ec: Eikenella corrodens; and Cs: Capnocytophaga species* (detection threshold $>10^3$).

2.6. Blood parameters

The blood sample collection was executed during the regular blood donation appointment of the participants. The blood for the current study has been collected into two EDTA and one lithium-heparin-gel monovettes (Sarstedt AG & Co, Nümbrecht, Germany) with 2.7 milliliters each. The samples were analyzed at the Department for Clinical Chemistry of the University Medical Centre Goettingen, Germany. Thereby, samples were centrifuged at 2500 g and a differential blood count at the Sapphire (Abbott GmbH & Co. KG, Ludwigshafen, Germany) was performed. The following blood parameters were analyzed: c-reactive protein (CRP), procalcitonine (PCT), thrombocytes, leucocytes, lymphocytes, monocytes as well as eosinophil, basophil and neutrophil granulocytes.

2.7. Statistical analysis

The statistical analysis was performed with Statistica, version 9, 2010 (StatSoft, Hamburg, Germany). Normal distribution was tested with Kolmogorov–Smirnov test. Depending on normal distribution, two samples were analyzed with *t*-test or Mann-Whitney *U* test, respectively. For comparisons with more than two variables, an ANOVA or Kruskal Wallis test was applied, respectively. Statistical significance was determined by the *P*-value of 0.05.

3. Results

3.1. Patients

A total of 188 patients with a mean age of 48.9 ± 8 years were included. The gender distribution was balanced with 94 male and female participants, respectively. The minority of participants (18%) were active smokers and the majority was aMMP-8 positive (76%; Table 1).

Table 1: Patients characteristics of all included patients.

Parameter		Patients (n = 188)
Age (mv ± SD)		48.9 ± 8
Gender n (%)	Male	94 (50%)
	Female	94 (50%)
Smoking n (%)	Non-smoker	108 (57.5%)
	Former smoker	46 (24.5%)
	Smoker	34 (18%)
aMMP-8 findings n (%)	Positive	139 (74%)
	Negative	49 (26%)

aMMP-8 = active matrix-metalloproteinase 8, mv = mean value, SD = standard deviation.

3.2. aMMP-8-findings and periodontal parameters

The examined periodontal parameters, including PBI, PPD and CAL ($p_i < 0.01$) were significantly higher in aMMP-positive participants (table 2). More than half of the participants suffering from no/mild periodontitis were aMMP-8 positive (27/50 [54%]). Nevertheless, positive aMMP-8 findings were associated to increased periodontitis severity ($P < 0.01$; table 2). Considering the amount of false-positive and false-negative aMMP-8 findings, a sensitivity of 0.81 and a specificity of 0.46 for the detection of moderate or severe periodontitis with aMMP-8 chairside test were determined.

3.3. aMMP-8 findings and microbiology

More than half of the investigated potentially periodontal pathogenic bacteria were associated to aMMP-8 findings. Thereby, the prevalence of *Pg* ($P = 0.02$), *Tf* ($P = 0.02$), *Pi* ($P = 0.04$), *Pm* (0.04), *Cr* ($P = 0.03$) and *En* ($P = 0.02$) was higher in aMMP8-positive compared to aMMP-8 negative participants (table 3).

Table 2
Association of aMMP-8 findings to periodontal parameters.

		aMMP-8 negative	aMMP-8 positive	*P*-value
Mean age (mv ± SD)		46.6 ± 6.9	49.7 ± 8.2	**0.02**
PBI (mv ± SD)		0.54 ± 0.39	0.91 ± 0.59	<**0.01**
PPD in mm (mv ± SD)		2.02 ± 0.34	2.25 ± 0.42	<**0.01**
CAL in mm (mv ± SD)		2.16 ± 0.41	2.39 ± 0.47	<**0.01**
Periodontitis severity n(%)	no/mild	23 (45)	27 (54)	
	moderate	25 (23)	86 (77)	<**0.01**
	severe	1 (4)	26 (96)	

aMMP-8 = active matrix-metalloproteinase 8, mv = mean value, SD = standard deviation, PBI = papilla bleeding index, PPD = periodontal probing depth, CAL = clinical attachment loss; significant results are highlighted in bold ($P < 0.05$).

Table 3
Association of aMMP-8 findings with potentially periodontal pathogenic bacteria.

Bacteria	Total prevalence n = 188 (n [%])	aMMP-8		*P*-value
		negative n = 49	positive n = 139	
Aa n (%)	15 (8)	4 (8)	11 (8)	0.98
Pg n (%)	57 (30)	7 (14)	50 (36)	**0.02**
Tf n (%)	143 (76)	29 (59)	114 (82)	**0.02**
Td n (%)	112 (60)	24 (49)	88 (63)	0.14
Pi n (%)	35 (19)	2 (4)	33 (24)	**0.04**
Pm n (%)	138 (73)	29 (59)	109 (78)	**0.04**
Fn n (%)	186 (99)	47 (96)	139 (100)	0.67
Cr n (%)	102 (54)	19 (39)	83 (60)	**0.03**
En n (%)	38 (20)	2 (4)	36 (26)	**0.02**
Ec n (%)	143 (76)	35 (71)	108 (78)	0.52
Cs n (%)	161 (86)	41 (84)	120 (86)	0.78

aMMP-8 = active matrix-metalloproteinase 8, Aa = *Aggregatibacter actinomycetemcomitans*, Pg = *Porphyromonas gingivalis*, Tf = *Tannerella forsythia*, Td = *Treponema denticola*, Pi = *Prevotella intermedia*, Pm = *Parvimonas micra*, Fn = *Fusobacterium nucleatum*, Cr = *Campylobacter rectus*, En = *Eubacterium nodatum*, Ec = *Eikenella corrodens* and Cs = *Capnocytophaga spp.*; detection threshold = $>10^2$, significant results are presented in bold ($P < 0.05$).

3.4. aMMP-8 findings and blood parameters

Beside of procalcitonine, all examined blood parameters were found to be within the reference values. None of the investigated parameters showed any association to the findings of salivary aMMP-8 test ($P > 0.05$, table 4).

4. Discussion

Summary of the main results: The aMMP-8 chairside test was associated with all selected periodontal parameters in the current study. From the tested potentially periodontal pathogenic bacteria, *Pg, Tf, Pi, Pm, Cr* and *En* were significantly associated to positive aMMP-8 findings. Furthermore, non out of the selected blood parameters showed associations to aMMP-8 results.

Comparison with literature and interpretation: the high potential benefit of salivary chairside aMMP-8 testing has been repeatedly discussed; especially the non-invasive and painless way of gaining salivary samples makes this saliva based diagnostic interesting (Sorsa et al. 2016; Alassiri et al. 2018). Thereby, the applied saliva based chairside aMMP-8 test is very suitable and functional for periodontitis screening and treatment needs assessments (Leppilahti et al. 2018; Räisänen et al. 2018). Considering the fact that majority of available literature reports reliable associations between aMMP-8 chairside testing and periodontal disease parameters (Izadi Borujeni et al. 2015; Heikkinen et al. 2016; Salminen et al. 2014; Sorsa et al. 2016; Zhang et al. 2018; Mauramo et al. 2018), the findings of the current study regarding clinical periodontal diagnostics are in line with these studies. However, previous studies of this working group were not able to show associations between salivary aMMP-8 and periodontal disease in adolescents (Schmidt et al. 2017) or for common periodontitis risk assessment parameters in patients under supportive therapy (Schmalz et al. 2018). Especially during well performed maintenance, i.e. supportive periodontal treatment, aMMP-8 concentration stays low, reflecting stable periodontal conditions (Schmalz et al. 2018). This confirms the heterogeneity of available studies mentioned in a meta-analysis by Zhang et al. (Zhang et al. 2018). Additionally, the current study shows, that the specificity of aMMP-8 in reflecting periodontal disease severity was approximately low. This could be caused by different reasons. The applied chairside test only distinguished between positive and negative based on a 25 ng/ml as threshold level. Although the agreement between qualitative and quantitative analysis were reported to be high

Table 4
Associations of aMMP-8 findings with blood parameters.

Blood parameter	Reference value	aMMP-8		P-value
		aMMP-8 negative	aMMP-8 positive	
CRP (mg/l)	≤ 5.0	1.52 ± 2.21	1.61 ± 1.90	0.36
PCT (μg/l)	≤ 0.06	0.09 ± 0.02	0.10 ± 0.07	0.90
Leucocytes (10^3/μl)	4.0–11.0	6.67 ± 1.57	6.81 ± 1.91	0.94
Lymphocytes (%)	20–45	32.9 ± 6.44	32.2 ± 8.13	0.64
Monocytes (%)	3–13	8.48 ± 1.73	8.16 ± 2.07	0.35
Eosinophil granulocytes (%)	≤ 8	2.94 ± 1.55	2.6 ± 1.64	0.14
Basophil granulocytes (%)	≤ 2	0.78 ± 0.33	0.72 ± 0.37	0.33
Neutrophil granulocytes (%)	40–76	54.84 ± 6.91	56.33 ± 8.72	0.29
Thrombocytes (10^3/μl)	150–350	250.31 ± 50.33	250.89 ± 64.80	0.70

aMMP-8 = active matrix-metalloproteinase 8, values are given as mean value ± standard deviation, CRP = c-reactive protein, PCT = procalcitonine, significance level $P < 0.05$.

(Lorenz et al. 2017), this could influence the accuracy of the test. The major reason of low specificity might be the investigation of periodontal disease severity, which does not mandatory reflect current disease progression. Meanwhile, it is known that aMMP-8 predicts labile disease progressive conditions with increased inflammatory activity, resulting in connective tissue destruction (Kiili et al. 2002; Lee et al. 1995; Sorsa et al. 2006; Sorsa et al. 2010). Additionally a recent investigation showed aMMP-8 to be an indicator especially for early periodontitis (Heikkinen et al. 2018). Thus the aMMP-8 test could indicate that several participants within the current study show no/mild periodontitis indeed, but might have an early but progressive inflammation of periodontal soft tissue. This assumption might be confirmed by the association of gingival inflammation reflected by PBI with aMMP-8 test in the current study and would be in line with the association of aMMP-8 with gingival inflammation in a previous study by this working group (Schmalz et al. 2018). Accordingly, a negative test result indicates inactive phase/stage of the periodontal disease (Alassiri et al. 2018, Ahmed et al. 2018). A major benefit of the applied test system is that it never causes bacteremia, differing clearly in this regard from clinical diagnostic with assessment of bleeding on probing (BOP) that always causes bacteremia (Alassiri et al. 2018). Consequently, the non-invasive chairside aMMP-8 test seems recommendable for detection of periodontal disease activity in dental practice, especially for patients in which bacteremia needs to be avoided (e.g. pregnancy, immunosuppression, endocarditis risk) or with a limited ability of compliance (e.g. nursing home residents).

A further focus of the current investigation was the association of aMMP-8 findings with selected potentially periodontal pathogenic bacteria. The included bacteria were defined as key players in periodontitis pathogenesis (Socransky et al. 1998). One of the major pathogens in inflamed periodontal tissue is *Pg*, which has potent virulence factors like lipopolysaccharides and gingipains. Moreover, *Pg* has the potential to colonize epithelial cells and influences the host immune reaction (Mysak et al. 2014). Considering these characteristics and their related influence on periodontal inflammation, the association to aMMP-8 findings seems plausible. In this context, a study by Salminen et al. demonstrated *Pg* and aMMP-8 in combination to be strongly correlated to periodontal disease severity (Salminen et al. 2014). Moreover, proteases derived from *Pg* and *Td* can activate proMMP-8 to aMMP-8 that is assayed by the applied test (Sorsa et al. 1992; Sorsa et al. 1995; Nieminen et al. 2018). Furthermore, *Tf* which is in the “red complex” with *Pg* and *Td* has also several virulence factors strongly related to periodontal inflammation (Sharma 2010). A previous study already showed that *Tf* would be associated with salivary aMMP-8, what is in line with the current study's finding (Yakob et al. 2012). The association between *Td* and aMMP-8 and their association to periodontal disease severity which was mentioned in previous examinations could not be confirmed by the current studies results (Yakob et al. 2012; Yakob et al. 2013; Ramseier et al. 2009). The association between aMMP-8 and highly pathogenic bacteria from “red complex” seems plausible, however these bacteria are anaerobic species which are related to more proceeded periodontitis (Socransky 1998). This seems contradictory to the association of aMMP-8 especially to early periodontitis mentioned above. For the further significantly associated bacteria, no comparable literature regarding aMMP-8 is available. Periodontitis is caused by a dysbiosis in which different potentially periodontal pathogenic bacteria are involved (Kinane et al. 2017). Accordingly, the association between aMMP-8 and *Pi*, which encourages *Pg* colonization (Socransky 1998) seems feasible. Similarly, the association of *Pm, Cr* and *En* is comprehensible, but cannot be justified otherwise.

The third aspect of the current study was the association between aMMP-8 findings and common blood parameters. The influence of periodontal inflammation on blood parameters has been discussed controversially (Kweider et al. 1993; Loos 2005; Gomes-Filho et al. 2011; Bolla et al. 2017). Regarding aMMP-8, recent studies found aMMP-8 activity in oral fluids and blood to be relevant in context of periodontal inflammation and general health, e.g. vascular diseases or rheumatoid arthritis (Rathnayake et al. 2015; Pradhan-Palikhe et al. 2010; Sorsa et al. 2011; Schmalz et al. 2017; Noack et al. 2017). In the generally healthy participants within the current study, aMMP-8 findings did not show an association to the selected blood parameters. This might suggest that the activity of periodontal inflammation visualized by salivary aMMP-8 test in healthy patients does not affect the parameters displayed in the regular differential blood count. However, this conclusion is limited by the fact that the chairside aMMP-8 test is based on one cut-off value either positive or negative and therefore does not distinguish between a moderate and/or high activity. Furthermore, aMMP-8 could be related to further, inflammation specific factors as TNF alpha or interleukins, which were shown to be related to periodontal disease and were not included in the current study (Acharya et al. 2016).

Strengths and limitations: This is the first study, which evaluates if the salivary findings of aMMP-8 are associated to periodontal disease severity, potentially periodontal pathogenic bacteria and values of regular differential blood count in a comprehensive evaluation. The recruitment of 188 generally healthy participants is a clear strength of the study. Thereby, it was aimed to include as many participants as possible within the examination period. Furthermore, the applied examinations and tests are valid and comparable to available literature. A major limitation lies within the study design: the cross-sectional examination does not allow robust causative conclusions. Further large scaled longitudinal studies would be needed to confirm the results. Another point is that the applied clinical diagnostics do not provide information on the current periodontal inflammation of the participants, because periodontitis severity was determined based on PPD and CAL. It is thereby conceivable that some of the false positive findings reflect progression of periodontal inflammation, while false negative findings might show stable periodontal conditions. As mentioned above, the used test system only differentiates between positive (>25 ng/ml) and negative aMMP-8 findings without any further categorization, what is a further limitation of the findings. Although total amount or exact concentration of aMMP-8 might be of interest, the current study aimed to evaluate the available chairside salivary aMMP-8 test. The analysis of the selected potentially periodontal pathogenic bacteria is limited by the usage of a commercially available PCR-based test system. These bacterial findings should not be considered exclusively, but only in combination with clinical findings (Untch and Schlagenhauf 2015). Thereby, the analysis of bacterial findings in relation to the clinical periodontal findings would be a promising approach. However, the resulting subgroups in the current study would be very small-sized, what strictly limits the expectable statistical power and thus the ability to draw strong conclusions. Accordingly, this analysis was renounced in the current investigation, but could be an approach for further examinations in this field. Furthermore, assessment of these bacterial species in blood samples would have been of interest and should be part of future investigations.

5. Conclusion

Chairside, saliva-based aMMP-8 test is associated to periodontitis severity and the prevalence of several selected potentially periodontal pathogenic bacteria, but not to values of regular blood count in generally healthy adults. Accordingly, salivary aMMP-8 findings could reflect periodontal disease severity as a result of an immunoreaction, especially against bacteria with high periodontal pathogenic potential.

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