



Investigating the relationship between the severity of periodontitis and rheumatoid arthritis: a cross-sectional study

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Abstract

Objectives This paper evaluates the prevalence and severity of periodontitis (PD) in patients with rheumatoid arthritis (RA), focusing on the link between the severity of PD with RA disease activity/disability scores, the influence of RA treatment on PD, and levels of vitamin D.

Methods A total of 93 RA patients were enrolled in the cross-sectional study and analyzed accordingly as RA-PD ($N = 63$, 67.8%) and RA-only ($N = 30$, 32.2%) groups. A number of associations between rheumatological clinical data, i.e., Disease Activity Score (DAS28 CRP), health assessment questionnaires, and PD severity (measured by periodontal outcome parameters) with regard to serum levels of vitamin D were assessed. The outcome variables were compared by parametric and non-parametric tests.

Results A total of 29% of RA patients were diagnosed with severe PD. The RA-PD group presented a higher mean DAS28 CRP score in moderate–severe PD compared to periodontally healthy-initial stage PD subjects (4.49 ± 1.22 vs. 3.86 ± 1.58 , $p = 0.033$). RA patients treated with biologic disease-modifying antirheumatic drugs (bDMARDs) were less likely to be diagnosed with PD ($p = 0.022$) and revealed significantly lower PD outcome parameters, i.e., bleeding on probing (%) and bone loss (%) ($p < 0.05$). Vitamin D concentration was significantly lower in RA-PD group with diagnosed advanced severe PD (IV stage) compared to moderate PD (II stage) (39.61 ± 17.12 vs. 52.07 ± 18.23 nmol/l, $p = 0.031$).

Conclusions The study revealed a high prevalence of severe PD in RA patients, being significantly associated with higher RA disease activity and lower vitamin D level in RA-PD group, while bDMARD treatment was related to lower PD outcome parameters.

Key Points

- Severe PD is prevalent amongst RA patients and is associated with RA disease activity. The higher RA DAS28 CRP score is associated with moderate-severe PD compared to periodontally healthy-initial stage PD in RA patients.
- Biologic DMARDs treatment used for RA is linked to lower PD rates and PD outcome parameters.
- Significantly lower vitamin D level is found in advanced severe PD compared to moderate PD stage in RA-PD subjects.

Keywords Disease activity · Periodontitis · Rheumatoid arthritis · Vitamin D

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Introduction

Rheumatoid arthritis (RA) and periodontitis (PD) are both chronic inflammatory diseases with shared genetic, environmental risk factors and pathogenesis mechanisms; however, the prevalence markedly differs [1]. PD affects approximately 50% of adults and 60% of people over 65 years of age and varies according to the severity of the disease [2]. RA occurs in 0.5–1% of whole population [3]. Epidemiological studies focusing on association between RA and PD show different results with a large interval of PD present from 28 to 85% of RA subjects, of which 11–14% are diagnosed with severe PD [4–6].

Immune mechanisms resulting as the progressive destruction of connective tissue and bone loss are pathognomonic in RA and also common in PD. The latter is an infectious disease caused by periodontal pathogens (predominantly by *Porphyromonas gingivalis* (*P. gingivalis*)), *Aggregatibacter actinomycetem-comitans* (*A. a actinomycetem-comitans*), *Tannerella forsythia*, *Treponema denticola*, and other infectious pathogens that may trigger a local and systemic immune response [7]. Furthermore, oral bacteria DNA and their antibodies are also found in serum and the synovial fluid of RA patients suggesting a plausible role for PD in RA etiopathogenesis [8]. In fact, the linkage between both diseases shows PD to be more prevalent in active RA compared to a healthy population, and also a higher RA incidence in individuals with PD [6, 9, 10]. A recently published meta-analysis comprising thirteen case-control studies revealed an increased risk of RA in patients with PD compared to healthy controls [11]. However, the published data is heterogeneous, and the population-based Epidemiological Investigation of Rheumatoid Arthritis case-control study undertaken in Sweden shows the development of PD to be independent from RA [12].

Despite the somewhat controversial results obtained in several epidemiological, clinical, and serological studies, there are evident links and similarities that connect these two diseases which point to a shared immunopathological pathway. For instance, periodontal pathogen *P. gingivalis* expresses the peptidylarginine deiminase (PPAD) enzyme which leads to the citrullination of peptides and the production of autoantibodies in RA [13]. Furthermore, another pathogenic PD bacteria, *A. Actinomycetem-comitans*, secretes leukotoxin A that induces hypercitrullination of host proteins, changes the function of neutrophils, and maintains autoantigen citrullination in RA [14]. Microbial dysbiosis and subsequent inflammatory processes stimulate immune cells to overproduce pro-inflammatory cytokines such as interleukin (IL)-6, IL-1 β , IL-17, tumor necrosis factor- α (TNF- α), and matrix-degrading enzymes (metalloproteinases (MMPs)). An increased activation of the receptor activator of the nuclear factor kappa B ligand (RANKL), and the cascade of immune

responses are implicated in RA and PD pathogenesis that culminates in cartilage and bone destruction in RA and loss of tooth-supporting tissues in PD [13].

Overlapping pathogenesis mechanisms of both diseases disclose a possible association of RA treatment with disease modifying anti-rheumatic drugs (DMARDs) on periodontal inflammation, mostly focusing on biologic DMARDs (bDMARDs) [15]. Another potential immunomodulatory and anti-inflammatory agent in RA and PD is the biologically active form of vitamin D 1.25(OH) $_2$ D $_3$ [16]. Reduced serum vitamin D level and lower vitamin D intake is associated with increased RA disease activity and severity, as well as gingival inflammation, a higher bleeding index, severe PD, and alveolar bone loss [16, 17]. To date, there are very few scientific articles that have assessed the effect of vitamin D in both diseases together.

Thus, the aim of this study was to evaluate the prevalence and severity of PD in RA patients, with a particular focus on PD severity association with RA disease activity/disability scores, RA treatment influence on PD, and vitamin D level as a modifiable factor possibly interacting with the clinical course of both diseases.

Materials and methods

Study population This cross-sectional study enrolled 93 participants with diagnosed RA, which met the ACR/EULAR 2010 rheumatoid arthritis classification criteria (or 1987 ACR classification criteria if diagnosed before year 2010) [18, 19]. All of the eligible subjects were recruited from Vilnius University Hospital Santaros Clinics (VUHSC) Rheumatology Centre, having first signed a written informed consent previously approved by the Vilnius Regional Biomedical Research Ethics Committee (Approval No. 158200-18-922-500). The research was carried out in accordance with the principles of the Declaration of Helsinki of 1975, revised in 2013.

A wide range of data was collected from all subjects by a rheumatologist researcher at VUHSC Rheumatology Centre. Data included sociodemographic, clinical/medical data (e.g., current RA treatment), behavioral habits (e.g., smoking, alcohol consumption, etc.), as well as oral health-related behavior. A Health Assessment Questionnaire (HAQ) and Rheumatoid Arthritis Impact of Disease score (RAID) were collected [20, 21]. HAQ was used to quantify disability in activities of daily living and RAID-the impact of disease. RA activity was measured by the disease activity score 28 (DAS28), counted by 28 tender and 28 swollen joints, the patient's global assessment of disease activity based on visual analogue scale (VAS, 100 mm), and the concentration of C-reactive protein (CRP, mg/l). The latter was recorded from patients' medical data. RA disease activity was categorized by DAS28 CRP score as

follows: high disease activity (≥ 5.1), moderate (> 3.2 to 5.1), low (2.6 to ≤ 3.2), and remission (< 2.6) [22].

All recruited subjects were adults (≥ 18 years). Certain subjects were excluded from the study, i.e., those diagnosed with other autoimmune comorbidities (e.g., diabetes mellitus, etc.), cancer (< 5 years), pregnancy, having less than 8 teeth remaining, or taking medications known to affect periodontal tissues (calcium channel blockers, etc.).

Vitamin D evaluation Blood samples collected using BD Vacutainer Serum Separator Tubes (5 ml) (BD Biosciences, NJ, USA) from all enrolled subjects were prepared by standard procedures, coded and labelled as required. Blood samples were analyzed for vitamin D serum level in VUHSC Centre of Laboratory Medicine using chemiluminescent microplate immunoassay (Architect ci8200, Abbott Laboratories, IL, USA) according to the manufacturer's protocol. Due to known seasonal 25(OH)D serum level variations, vitamin D measurements were performed from late October until mid-May to avoid possible bias. The fact of vitamin D supplementation use was also recorded in the database. The evaluated vitamin D concentration was classified by the clinical practice guidelines published by the Endocrine Society, and fell within the range of normal (≥ 75 nmol/l), or insufficient (≥ 50 to 75 nmol/l), or deficient (< 50 nmol/l) [23].

Oral examination A full mouth periodontal examination (probing at six-points and X-ray examination) was performed by a periodontist at the Vilnius University Hospital Zalgiris Clinic in order to assess the presence and severity of periodontal disease in all included RA subjects. PD diagnosis was approved according to the 2018 American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) classification of periodontal diseases guidelines [24], and categorized as follows: stage I, initial; stage II, moderate; stage III, severe; stage IV, advanced severe PD. Patients who were not diagnosed PD acted as the control group (RA-only) and recorded when the criteria for severe, moderate, or initial disease were not fulfilled, while all others grouped as RA-PD. The periodontal status of the RA patient was evaluated using the following variables: bleeding on probing (BOP, %), probing pocket depth (PPD, mm), alveolar bone loss (BL, %), clinical attachment loss (CAL, mm), and missing teeth. Third molars and dental implants were not evaluated.

Statistical analysis Statistical analysis was performed using the SPSS Statistics software, V.22.0 (IBM, Armonk, NY, USA). Firstly, a descriptive analysis of categorical and metric variables was performed. Continuous variables were checked for normal distribution using the Shapiro-Wilk normality test and means compared by Student *t*-test for normally distributed variables, or by the Mann-Whitney *U* test when the

distribution of data was not normal. Following Levene's test for equality of variances, the ANOVA or non-parametric Kruskal-Wallis test was applied to compare more than two groups. The Pearson or Spearman rank correlation coefficients were applied to assess the association between normally and not normally distributed variables, respectively. For categorical variables Pearson chi-square test was used. Graphs were presented using GraphPad Prism v5.03 (San Diego, CA, USA). Statistically significant results were set at $p < 0.05$.

Results

Demographic and behavioral study population characteristics

Ninety-three RA patients (84 females and 9 males with a mean age of 54.01 ± 11.01 ranging from 29 to 75 years) were enrolled in the study. To distinguish differences between RA patients with diagnosed periodontitis and periodontally healthy subjects, RA-PD ($N = 63$, 67.8%) and RA-only ($N = 30$, 32.2%) groups were analyzed. RA-PD diagnosis was significantly associated with sex, with males showing higher PD rates than females ($p = 0.029$). It is worth noting that all periodontally healthy RA subjects were non-smokers and used dental floss more frequently compared to the RA-PD group ($p < 0.05$). A more detailed sociodemographic data analysis of RA-PD and RA-only groups is provided in Table 1.

Comparison of RA disease status in RA-PD and RA-only groups

The average RA disease duration was 12.65 ± 10.38 years. In the total study group, the moderate disease activity (DAS28 CRP score) of most RA patients was present in 47 (50.5%) of subjects, whereas 25 (26.9%) presented high disease activity, and 7 (7.5%) had low, with 14 (15.1%) being on RA remission. Patients with active RA demonstrated significantly higher disease related clinical and biochemical parameters compared with those in RA remission ($p < 0.001$). More than one half of patients were older than 54 years ($N = 55$, 59.14%) and had higher RAID and HAQ scores ($p < 0.05$).

RA-PD group subjects presented a higher mean DAS28 score (4.37 ± 1.28 vs. 3.82 ± 1.65) and CRP level (13.82 ± 24.44 vs. 8.44 ± 12.99 mg/l); however, this was not statistically significant ($p > 0.05$). However, a significantly higher RA DAS28 CRP score was revealed in moderate-severe PD compared to the periodontally healthy-initial stage PD group (4.49 ± 1.22 vs. 3.86 ± 1.58 , $p = 0.033$) (Fig. 1), indicating that PD severity could be associated with elevated RA activity and its consequences. Moreover, RA-PD diagnosed subjects

Table 1 Demographic and behavioral characteristics of RA-PD and RA-only group

	Total <i>N</i> = 93	RA-PD group <i>N</i> = 63 (67.8%)	RA-only group <i>N</i> = 30 (32.2%)	<i>p</i> value
Age (years)	54.01 ± 11.01	55.33 ± 9.5	51.23 ± 13.37	0.168
BMI (kg/m ²)	24.96 ± 4.34	25.24 ± 4.39	24.38 ± 4.26	0.539
Sex				0.029*
Female	84 (90.32%)	54 (85.71%)	30 (100%)	
Male	9 (9.68%)	9 (14.29%)	0	
Smoking status				0.005*
Never smokers	54 (58%)	36 (57.1%)	18 (60%)	
Current smokers	15 (16.2%)	15 (23.8%)	0	
Former smokers	24 (25.8%)	12 (16.3%)	12 (40%)	
Alcohol consumption				0.505
Never	49 (52.7%)	31 (49.2%)	18 (60%)	
Once per week	5 (5.3%)	3 (4.8%)	2 (6.7%)	
Once per month	39 (42%)	29 (46%)	10 (33.3%)	
Annual dental prophylaxis/year	0.333			
< Once	16 (17.2%)	12 (10.8%)	4 (13.3%)	
Once	54 (58%)	38 (60.3%)	16 (53.3%)	
Two and more times	23 (24.8%)	13 (20.6%)	10 (33.4%)	
Dental floss				0.016*
Yes	69 (74.2%)	42 (66.7%)	27 (90%)	
No	24 (25.8%)	21 (33.3%)	3 (10%)	
Tooth brushing/day				0.155
Once	24 (25.8%)	20 (31.7%)	4 (13.3%)	
Two and more times	69 (74.2%)	43 (68.3%)	26 (86.7%)	

Values represent the mean ± SD, standard deviation or *N*, %

BMI body mass index, *RA* rheumatoid arthritis, *PD* periodontitis

**p* < 0.05

showed higher VAS (45.81 ± 20.11 vs. 40.83 ± 21.75 mm) and RAID scores (4.68 ± 2.17 vs. 3.94 ± 2.44), although these differences were not statistically significant. Detailed analysis of RA-PD and RA-only group clinical characteristics is presented in Table 2.

Periodontitis analysis in RA-PD group

Almost one third of RA patients (*N* = 27, 29.0%) had severe periodontitis (stage III+IV) (Fig. 2). The RA-PD group signalled significantly higher BOP, BL, CAL, and PPD

Table 2 RA disease parameters in RA-PD and RA-only group

	Total, <i>N</i> = 93	RA-PD group, <i>N</i> = 63(67.8%)	RA-only group, <i>N</i> = 30(32.2%)	<i>p</i> value
RA data (mean, SD)				
RA duration (years)	12.16 ± 9.44	11.17 ± 8.3	14.23 ± 11.32	0.25
DAS 28 (score)	4.19 ± 1.43	4.37 ± 1.28	3.82 ± 1.65	0.08
VAS (mm)	44.2 ± 20.67	45.81 ± 20.11	40.83 ± 21.75	0.28
HAQ (score)	0.85 ± 0.62	0.84 ± 0.64	0.86 ± 0.57	0.71
RAID (score)	4.44 ± 2.27	4.68 ± 2.17	3.94 ± 2.44	0.14
Biochemical parameter (mean, SD)				
CRP (mg/l)	12.08 ± 21.5	13.82 ± 24.44	8.44 ± 12.99	0.98

CRP C-reactive protein, *DAS 28* disease activity score 28, *HAQ* health assessment questionnaire, *PD* periodontitis, *RA* rheumatoid arthritis, *RAID* rheumatoid arthritis impact of disease, *SD* standard deviation, *VAS* visual analogue scale

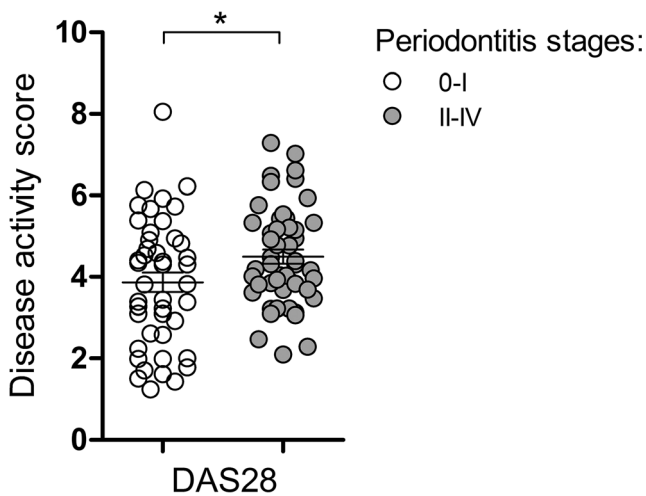


Fig. 1 DAS28 score comparison in RA-PD group by periodontitis stages. DAS 28 disease activity score 28, PD periodontitis, RA rheumatoid arthritis. * $p < 0.05$

periodontal parameters ($p < 0.001$) and a number of missing teeth ($p = 0.004$) compared with the RA-only group. No association between seropositive RA (positive rheumatoid factor (RF) and/or anti-citrullinated protein antibodies (ACPA)) and PD was observed ($p > 0.05$). Evaluating the effect of smoking on PD, ever smokers (both current and former smokers) had higher mean CAL, PPD, BOP, and BL parameters compared with those who had never smoked in RA-PD group. Similar PD outcome shifts were also observed in elderly RA patients ($p < 0.05$), their older age being associated with moderate and severe PD ($p = 0.006$).

RA treatment influence on RA and PD status

With regard to RA treatment, 48 (51.6%), patients were treated with bDMARDs (e.g., TNF- α inhibitors, IL-6 receptor antagonist, anti-CD20 monoclonal antibody), either alone or in combination with conventional synthetic DMARDs (sDMARDs, e.g., methotrexate, sulfasalazine, hydroxychloroquine, etc.). Of the rest 45, 43 (46.2%) RA patients received conventional sDMARDs monotherapy or combination of ≥ 2 sDMARDs, and 2 (2.2%) patients were not treated with any anti-rheumatic drug. The use of glucocorticoids was not assessed in the study. Patients treated with

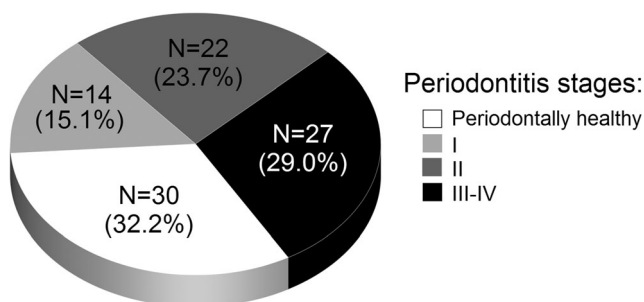


Fig. 2 Periodontitis stages in RA

bDMARDs were less likely to be diagnosed with PD ($p = 0.022$) (Fig. 3a) and revealed significantly lower DAS28 score, VAS (mm), CRP (mg/l) levels and lower PD outcome parameters – BOP (%) and BL (%) ($p < 0.05$) (Fig. 3b) compared with conventional synthetic DMARD-only treated subjects.

Vitamin D association with RA and PD status

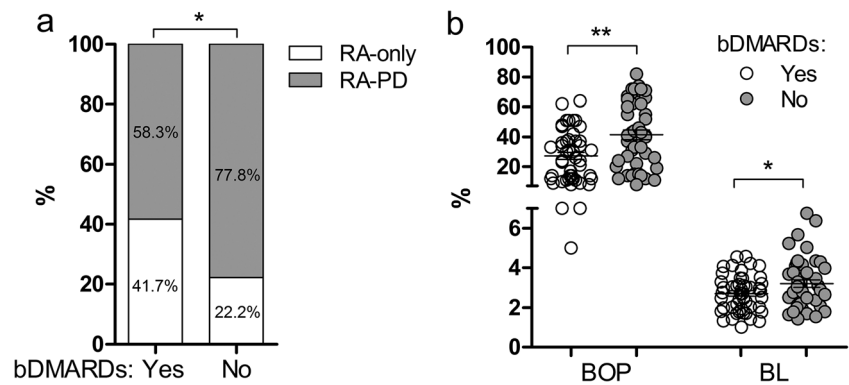
A high prevalence of vitamin D deficiency/insufficiency ($< 75\text{nmol/l}$) in RA subjects ($N = 80, 90.4\%$) was observed in this study. The average vitamin D concentration in the total group was 45.65 ± 21.33 (nmol/l). After the RA-only group was compared with then RA-PD group, a higher concentration of vitamin D tendency was found (48.13 ± 27.47 vs. $44.48 \pm 17.82\text{nmol/l}$, $p > 0.05$, respectively). A significantly lower vitamin D concentration was observed in RA-PD group with diagnosed advanced severe (IV stage) PD compared to moderate PD (II stage) (39.61 ± 17.12 vs. $52.07 \pm 18.23\text{nmol/l}$, $p = 0.031$). Of RA characteristics, a significant inverse correlation ($r 0.23, p = 0.026$) between vitamin D level and HAQ score was confirmed; however, no significant correlations between vitamin D status and PD outcome parameters were observed, apart from some weak inverse correlations with PPD, CAL, and BL ($p > 0.05$).

Discussion

The relationship between RA and PD has been investigated in numerous studies and reviews, but so far has produced inconsistent findings. This study analyzed possible associations between RA status and PD presence with regard to vitamin D and sociodemographic factors. After comparing RA-PD and RA-only groups, no significant differences in RA clinical parameters were observed. However, a more detailed analysis within the RA-PD group revealed significant associations between RA activity and PD severity, also the relation of vitamin D deficiency between RA and PD and their possible interactions. To the best of our knowledge, this is one of only a few studies that have assessed vitamin D association with both inflammatory diseases.

This study demonstrated a high prevalence of PD in RA diagnosed patients, occurring in 67.8% of subjects, with almost one third having a severe PD (III+IV stage). Consistent with our findings was a recent Finnish population follow-up study that reported nearly 80% and 85% of diagnosed PD in early and chronic RA, respectively [6]. Similar percentage of periodontal disease was present in Chinese study with PD diagnosed in 68% of RA patients and an almost 5-fold increase in odds of having PD compared to healthy controls [25]. On the contrary, a Korean National Health Insurance Service-National Sample Cohort study with a total count of

Fig. 3 bDMARD treatment association with PD in RA subjects (a) and PD outcome parameters (b). *bDMARDs* biologic disease-modifying anti-rheumatic drugs, *BL* bone loss, *BOP* bleeding on probing, *PD* periodontitis, *RA* rheumatoid arthritis. * $p < 0.05$; ** $p < 0.001$



559,280 participants revealed a much lower prevalence of PD in RA patients, present in only 20% of subjects. However, the probability of having RA was greater in patients with PD than in control group (odds ratio [OR]; 1.22, $p < 0.001$) [26]. The number of severe PD cases (29%) in our study shows a higher incidence in compare to the whole population as stated in Kassebaum et al. review and meta-regression, where the global age-standardized prevalence of severe PD was static at 11.2% [27]. Higher PD rates could be due to an impaired host immune defense in RA, which is consistent with the following results from our study.

The study revealed a significantly higher mean DAS28 CRP score in the RA-PD group with diagnosed moderate-severe PD. Moreover, RA-PD patients also appeared to have a tendency to a higher RAID score and VAS. Furthermore, the aforementioned group excelled with worse PD outcome parameters compared to the RA-only group. Other previously conducted studies [28, 29] concur with our findings, i.e., that there is a link between PD severity and a greater RA clinical activity. In contrast to our results, in a small study of 40 RA patients any association between RA activity and PD severity was not observed in terms of CRP level, DAS28 or HAQ score, although the data revealed that ACPA positivity was significantly more common in RA patients with moderate-severe PD [30]. Our study findings could be related to the fact that both active RA and severe PD are associated with increased levels of inflammatory biomarkers and mediators (especially, CRP, IL6, TNF- α , MMP's, etc.) [31]. The increase of systemic inflammation boosts PD and vice versa as it is presented in a "two-hit" theory, where periodontal dysbiotic microbial biofilm induces a first "hit" in the cascade of destructive events in chronic PD; the second "hit" provides a systemic inflammatory response fuelled by the systemic diseases, such as RA [32].

Additionally, a significant and advantageous association between bDMARDs used for RA treatment and PD outcome parameters (BOP and BL) was revealed in our study. Subjects treated with bDMARDs were less likely to be diagnosed with PD compared with conventional sDMARDs. Since RA patients tend to have higher TNF- α , IL-6 levels in oral fluids

and plasma, increased B and plasma cells infiltration is related to progressive periodontal bone loss in PD [33, 34], the association of RA bDMARD treatment with suppressed periodontal inflammation can be reasonably justified. In 2020, a published article based on previously conducted studies added weight to our understanding of the beneficial effect of TNF- α inhibitors, IL-6 receptor-inhibitors, and anti-B lymphocyte treatment on PD severity [15]. An improvement in periodontal health by anti-TNF therapy was examined in Zamri and de Vries systematic review and referred as having positive effect on BOP, PPD, CAL, and gingival index parameters over time of 6 weeks to 9 months of treatment [35]. However, some studies lack support in their findings and presume that PD may even interfere with the response to bDMARD treatment in RA [36, 37].

Regarding behavioral habits, tobacco smoking was significantly associated with RA-PD group compared to the RA-only group in the present study, as it is a common risk factor in the relationship between RA and PD [7]. Without exception, all periodontally healthy RA subjects were non-smokers, while almost a quarter of RA-PD cases were current smokers. Contributing to the fact that smoking and aging are risk factors of PD, ever smokers and older patients revealed higher CAL, PPD, BOP and BL periodontal parameters in RA-PD study group.

To maintain the essential vitamin D role in bone and calcium homeostasis and non-skeletal effects, the 25(OH)D concentration should be > 75 nmol/l [23]. Consistent with the findings in previous reports [38], about 90% of our study cohort exhibited insufficient or deficient vitamin D levels. Cross-sectional observational studies stated that vitamin D deficiency and lower 25(OH)D intake might be associated with increased RA and chronic PD risk [39, 40]. The present study demonstrated the tendency of lower vitamin D levels in the RA-PD group compared with periodontally healthy RA patients. A significantly lower vitamin D concentration was observed within the RA-PD group with diagnosed advanced severe PD (IV stage) compared to moderate (II stage) PD. This finding might be explained by the predictive cumulative systemic inflammatory effect of both diseases and support the

statement that vitamin D deficiency and co-risk factors may favor the proliferation of periodontopathic bacteria and aggravate the course of disease [40]. It is probable that the overall low vitamin D level of RA patients may explain why significant differences between RA-only and RA-PD groups, as well as PD outcome parameters are not seen.

Notwithstanding, despite the revealed significant associations this study has several weaknesses. A relatively small study population and inequality of RA-only and RA-PD groups' size may have adversely affected the statistical analysis. Still, this could be ascribed to the overall high prevalence of PD in RA population. Another limitation is low vitamin D level in the entire study cohort, probably due to the geographical latitude of Lithuania. Despite the recorded vitamin D supplementation fact no differences between groups (using supplements and not) were observed, data not shown. Hereafter, since we conducted a cross-sectional study, it was also impossible to infer the causality of exposure on RA or PD outcome, only the associations and prevalence.

To conclude, the study revealed a high prevalence of PD and vitamin D deficiency in RA patients. Moreover, the study showed that both pathologies—RA and PD—may be related to one another in bidirectional manner. Moderate–severe PD stage was significantly associated with higher RA disease activity. Furthermore, RA patients treated with bDMARDs showed significantly lower disease activity measures and PD outcome parameters—BOP and BL. However, larger cross-sectional studies are necessary to better evaluate the linkage between both diseases.

Author contribution All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Puceviciene Egle, Rovas Adomas, and Stuopelyte Kristina. The first draft of the manuscript was written by Puceviciene Egle, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Disclosures None.

Ethics approval Biomedical research is approved by Vilnius Regional Biomedical Research Ethics Committee, No. 158200-18-922-500. Informed consent was obtained from all participants. The research was carried out in accordance with the principles of the Declaration of Helsinki of 1975, revised in 2013.

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