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ORIGINAL ARTICLE

## Periodontitis in psoriasis patients. A blinded, case-controlled study

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### Abstract

**Objective.** Destructive periodontitis is one of the most frequent and widespread bacterial infections in humans. Psoriasis is a common condition in the general population. Since both psoriasis and periodontal diseases are characterized by an exaggerated response of the immune system to the epithelial surface microbiota, there may possibly be an association between these two conditions. The aim of the present pilot study was to investigate the prevalence of periodontal disease in psoriasis patients compared to healthy controls. **Material and methods.** Dental bite-wing X-rays were obtained from 155 psoriasis patients aged 45–60 years, as well as from 155 age- and gender-matched controls. All X-rays were examined by the same investigator for accumulated destructive periodontitis using bone level and loss of teeth as endpoints. **Results.** A significantly lower radiographic bone level ( $p < 0.001$ ) and a significantly higher number of missing teeth ( $p < 0.001$ ) were observed in the psoriasis cases compared to the controls. **Conclusion.** Our study indicates that psoriasis patients experience more bone loss than age- and gender-matched controls.

**Key Words:** Dermatological conditions, periodontal diseases, periodontal diseases and systemic disorders

### Introduction

Psoriasis is a chronic, inflammatory, multi-system disease characterized predominantly by skin and joint manifestations affecting  $\approx 2\%$  of the general population [1–4]. The autoimmune-type inflammation of the skin has a strong genetic background, but is also influenced by environmental factors. Streptococcal infections may precipitate psoriasis [5]. Other disease-modifying factors may be trauma, drugs, sunlight and metabolic and psychogenic factors, as well as alcohol and smoking [6,7]. Psoriasis is reported to be associated with cardiovascular disease [8], metabolic syndrome [9], inflammatory bowel diseases, rheumatoid arthritis, sero-negative spondyloarthropathies, malignancy, streptococcal tonsillitis, smoking, alcohol abuse, psychiatric disorders and stress [10–13].

Chronic destructive periodontal disease is a family of bacterial infections characterized by immunologically motivated destruction of periodontal supporting tissues [14]. The disease affects  $> 50\%$  of adults in the USA, and 5%–10% are so severely affected that they

may consequently lose their teeth [15]. The bacterial flora at the diseased sites is complex, totaling 500–700 different microbial species in the sub-gingival dental biofilm [16]. The main pathogens are thought to be a group of Gram-negative, anaerobic microorganisms. However, Gram-positive bacteria, including beta-hemolytic *Streptococci*, also constitute a significant proportion of this biofilm [16]. The ensuing inflammatory reaction is responsible for the progression of loss of periodontal ligament and bone. If left untreated and allowed to progress, teeth become mobile and may eventually be lost. In addition to local responses, periodontitis patients have systemic responses, such as elevated levels of C-reactive protein, von Willebrand's factor and thrombin, as well as increased leukocyte counts [17,18]. Periodontal diseases have been described as being coexistent with coronary heart disease and cerebrovascular diseases, respiratory diseases, diabetes, premature birth and low birth weight, osteoporosis, rheumatoid arthritis [19], emotional stress [20] and hyperkeratosis palmo-plantaris of the Papillon-Lefèvre syndrome [21].

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Both psoriasis and periodontal diseases are characterized by an exaggerated immune response to the microbiota residing on epithelial surfaces. Dendritic cells (DCs) play an important role in driving an exaggerated immune response [22,23], and are for example crucial to the initiation and regulation of both innate and adaptive immunity, inasmuch as they form a bridge between the two immune systems by trafficking from the epithelial barriers to the regional lymph nodes.

To our knowledge, no published study has shown an association between psoriasis and chronic destructive periodontal disease. Cases of desquamate gingivitis associated with psoriasis [24] and psoriasis-like lesions on the oral mucosa and gingiva have been reported [25]. Moreover, comorbidity seems evident between hyperkeratosis palmo-plantaris and rapidly destructive periodontal disease in the Papillon-Lefèvre syndrome [21]. Relationships between the onset of palmoplantar pustulosis, periodontitis and bacterial heat-shock proteins [26], and regression of palmoplantar pustulosis by periodontal treatment in a subject with severe periodontitis [27] have also been reported. However, none of these studies relate to chronic, destructive periodontal disease. The aim of the present pilot study was to investigate the prevalence of periodontal disease in psoriasis (test) patients and age- and gender-matched non-psoriasis controls.

## Material and methods

### Study design

In 2007 the membership lists of the Norwegian Psoriasis Association (NPA) comprised  $\approx$  5000 names. The data collection was conducted during 2007, within the time frame granted by the Privacy Ombudsman for the Norwegian universities (NSD). All registered NPA members aged 45–60 years ( $n = 866$ ) received an information letter describing the background and aim of the study. A questionnaire, which was mailed twice to all 866 persons with a 2-month interval, followed the information letter and asked if their diagnosis of psoriasis had been confirmed by a physician, if they had psoriasis arthritis or if they had any other general diseases/conditions. Also, they were asked if they suffered from bleeding

gums, if they thought they had periodontitis or if a dentist had actually diagnosed them with chronic destructive periodontal disease. The questionnaires ended with a request for the name and telephone number of their dentist and consent to obtain their latest bite-wing X-rays from their dentist's files. The questionnaire was accompanied by an informed consent form and information that the Regional Committee for Medical Research Ethics (Southern-Norway, Oslo, Norway) approved the study. The respondents were granted anonymity and informed that the records would be destroyed following the data collection and handling, within the time frame granted by the NSD, and that the X-rays would be promptly returned to their respective dentists.

### Final population

A total of 339 patients responded (39.15%). Eighty of these respondents were excluded from the study due to incomplete response (Table I). A total of 259 dentists were contacted by letter and telephone, and asked to participate by providing the identified bite-wing X-rays. All dentists responded positively to the study, but X-rays were not received from 94 dentists within the time frame of the study. Ten patient or control X-rays were excluded due to poor quality. This left 155 pairs of double bite-wing X-rays to be included in the study. The mean age of the participants was 51 years, and 43.2% were male. Reasons for non-inclusion of patients in the study are shown in Table I.

### Data collection

All dentists who had been named by the respondents received a letter containing all relevant information about the study. In this letter they were instructed to identify the latest pair of bite-wing X-rays of their included psoriasis patients. The letter was followed by a telephone conversation in which all details were explained again, and the dentists were asked if they had understood the instructions. The dentists were also carefully instructed to select the last pair of bite-wing X-rays of the first 'healthy' (i.e. no history of skin disease) age- and gender-matched patient seen following the psoriasis patient in their recall archives.

Table I. Reasons for non-inclusion of patients in the study. Values shown represent numbers of patients, with percentages in parentheses.

Total no. of patients	No response	No written consent or insufficient answers	No name or telephone no. of dentist	No response from dentist in time	Insufficient quality of X-rays	Total no. of lost patients	No. of included patients
866 (100)	527 (61)	68 (8)	12 (1)	94 (11)	10 (1)	711 (82)	155 (18)

Both sets of X-ray bite-wings were then mailed to the project leader (H. P.). Approximately 80% of Norwegians consult their dentist regularly [28] for dental maintenance and repair. The population described here (both cases and controls) were regular visitors to the dentist and had bite-wing radiographs taken annually or bi-annually. The patients' responses to the questions about diagnosed or perceived periodontal disease indicated that the psoriasis groups were not skewed compared to other regular dental visitors.

Upon receipt, the pairs of X-rays were labeled with random numbers in order to blind their origin for the person reading the X-rays. Reliability tests were performed before and during the reading procedure. The identity of the subjects was not revealed to the investigators.

### *Radiographic examination*

The radiographs sent by the dentists were taken with varying techniques, but the same dentist processed pairs of test and control radiographs, making comparisons possible. All measurements were carried out by one examiner (P. K.). The analog X-rays were fixed and read using a light board (Rex-Leuchtplatte Flatline; Rex Messinstrumentgebäude, Babenhausen, Germany). A 2× magnifier was used when measuring the X-rays (X-Viewer, LIC-Scadenta, Sandvika, Norway). The paper prints of digital X-rays were read directly on the image since they were more than 2× larger than the regular, non-digital, X-rays. The radiographic bone level was recorded on each bite-wing radiograph from the mesial surface of the second molar to the distal surface of the canine at all clearly readable sites by an electronic digital sliding caliper (JOCAL; C. E. Johanson, Eskilstuna, Sweden) [29], and the mean for each individual set of radiographs was calculated.

Bone level was measured as the distance from the cemento-enamel junction to the most coronal level of the alveolar crest and recorded to the nearest millimeter. The point where the periodontal space still retained its normal radiographic width was considered the alveolar crest, and infrabony pockets were measured to the point of the most apically advanced radiolucency [29]. The number and location of missing teeth from the second molar to the canine was recorded in each set of bite-wing radiographs.

All sites on the X-rays not clearly identifiable, as well as any other sites for which there was uncertainty regarding identification of the measurement, were excluded from the study as non-readable sites. The X-rays from 10 patients were analyzed for radiographic bone level twice with a 2-week interval to assess the reproducibility of the examiner's ratings. The X-rays were numbered differently between the

first and second examinations. A total of 32 sites were included at both examinations, and the intra-class correlation test (ICC) [30] was used for reliability assessment. Among the 32 sites read twice, the ICC was 0.93. There was a 100% correlation regarding non-readable sites.

### *Statistical analysis*

SPSS 14.0 (SPSS Inc., Chicago, IL) was used for data analysis. The statistical unit was the individual patient. The average bone level for each psoriasis case was compared to that of the age- and gender-matched healthy control. The Wilcoxon signed ranks test [31] was used for assessing statistical differences. Since the electronic caliper registered the bone level to two decimal points, the tests were used for registrations with two and zero decimal points, to see if the results were of both clinical and statistical interest.

The differences in actual and mean numbers of missing teeth were tested with the  $\chi^2$  test and with Student's *t*-test, respectively, and linear regression analysis was used for testing differences in bone level in patients with and without psoriasis arthritis. Loss analyses are shown in Table I, and matching of cases and controls is described in detail in the previous section on data collection.

## **Results**

A total of 121 patients with psoriasis (78%) had a lower mean bone level than their age- and gender-matched controls, whereas 26 controls (17%) showed a lower mean bone level than their corresponding matched psoriasis patient ( $p < 0.001$ ). Eight patients/controls (5%) had the same recordings. The psoriasis patients had a significantly higher number of missing teeth ( $p < 0.001$ ) (Table II).

No age-adjusted difference in bone level was demonstrated between psoriasis patients with and without arthritis ( $p = 0.98$ ).

Twenty percent of the respondents reported periodontal disease or bleeding gums, and 25% reported other diseases or conditions (Table III).

Table II. Cases and controls according to number of missing teeth (not including third molars).

	No. of missing teeth			Total
	0	1–4	>4	
Cases (psoriasis)	76	64	15	155
Controls	114	36	5	155
Total	190	100	20	310

Significant difference in tooth loss between test and control group;  $p < 0.001$  ( $\chi^2$  test).

Table III. Concomitant diseases and conditions in the 155 respondents. Values shown represent numbers of patients, with percentages in parentheses.

Diabetes mellitus	Osteoporosis	Cardiovascular disease	Psychogenic stress and depression	Bechterew's disease and arthrosis	Fibromyalgia	Sjögren's syndrome	Chronic obstructive pulmonary disease	Total
4 (2.5)	3 (2)	16 (10)	8 (5)	4 (2.5)	3 (2)	1 (0.6)	1 (0.6)	39 (25.2)

## Discussion

All participants in the present study originated from a population of 'regular dental attendees'. In Norway, this means that these particular patients seek dental care and maintenance regularly (every 6–12 months). We do not know any more about the non-respondents since such an investigation was not granted by the NSD in this pilot study.

Even if every pair of test and control X-rays were taken by the same operator (dentist), there was an obvious variation in radiographic quality between the dentists/dental clinics. Therefore, the Wilcoxon signed ranks test was used for statistical testing to overcome the difficulties with assessing bone loss accurately in millimeters and due to the test's robustness and lack of requirements with regard to the distribution of the observations [31].

Twenty-five percent of the study population reported suffering from another disease or condition, but only 5.5% of these were diseases or conditions that have previously been associated with periodontal diseases. Since we had no information about the gender- and age-matched controls other than their X-rays, confounding factors such as smoking habits were not possible to register. However, since psoriasis cases and healthy controls were obtained from the same population of regular dental visitors, and studies of Norwegian smoking habits indicate that psoriasis patients smoke the same amount as the average Norwegian [32,33], we assumed that smoking could be disregarded for the purpose of this investigation.

Psoriasis patients in this study had significantly fewer teeth ( $p < 0.001$ ) than their age- and gender-matched controls, as well as a significantly larger distance from the cemento-enamel junction to the alveolar crest in the lateral segments of the dentition ( $p < 0.001$ ). A reduced approximal bone level, using bite-wing radiographs, is regarded as the most common and valid indicator of destructive periodontal disease in all age groups. More importantly, the most common reason for tooth extraction (with the exception of third molars) in Norwegians aged  $> 45$  years is periodontal disease [34], and the most common location for reduced number of teeth, as well as reduced bone level due to periodontal disease, is the premolar and molar regions of both jaws [35]. Moreover, it has

been shown that partial recording protocols underestimate the prevalence of bone level changes [35].

Selection bias is a problem in case-controlled studies [36,37]. Key requirements for valid estimates of the 'exposure'–disease association are that the test and control groups come from the same population, and that the controls comprise a random sample of the source population associated with the disease. These requirements were honored in this pilot study. Our participation rate of 39% is low, but it must be considered that the membership lists of these types of organizations are often characterized by a significant number of dead and unreachable members (i.e. those who have moved and left no forwarding address). Moreover, the low participation rate was not connected to the factors of interest [37], which in this study were periodontitis and factors associated with the causes of periodontitis. For this particular reason the questionnaire included a question asking if the respondent thought they had, or had been diagnosed with, periodontitis. Only 20% responded positively to this question, indicating that the test population did not have specific interests in this regard.

The magnitude of tooth mortality as well as reduced bone level in psoriasis patients indicates that there may be an association between the two diseases despite the shortcomings of a pilot study design.

One may speculate as to what mechanisms might be involved in explaining this possible comorbidity, and any speculation is as possible or as farfetched as the next at this stage of the investigation. One speculation might be that the innate immune system that is directing the subsequent adaptive immune response (T- and B-cell response) is important in the pathogenesis of both psoriasis and periodontitis [38,39]. Recent studies have demonstrated an upregulation of Toll-like receptor (TLR)-2 in psoriatic skin [38], as well as in the periodontium of patients with periodontitis [40]. High expression of TLR will amplify the inflammatory reaction and subsequent T-cell activation. Studies in the Yaa mouse model have shown that a twofold increase in TLR gene dosage can dramatically induce an autoimmune pathology [41]. Thus, one may speculate that a common genetic trait affecting DCs, TLR expression or other components of the innate immune response could predispose patients to both periodontitis and psoriasis.

In conclusion, this hypothesis-generating pilot study indicates a possible association between psoriasis and chronic destructive periodontal disease. Since there have been no previous reports on such possible comorbidity, conclusions must be drawn with caution, and experimental studies are presently being designed to test the hypothetic causality between periodontal disease and psoriasis.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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