Journal of
Periodontology
&
Implant Dentistry

Research Article

Chronic Plaque Psoriasis and Plaque-induced Chronic Periodontitis; Is There Any Association: A Cross-sectional Study

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Received: 23 February 2011; Accepted: 19 April 2011
J Periodontol Implant Dent 2011; 3(1): 13-20
This article is available from: http://dentistry.tbzmed.ac.ir/jpid

Abstract

Background and aims. Psoriasis and periodontitis are characterized by an exaggerated host immune response to epithelial cell surface microbiota. Thus, mediators produced as part of host response orchestrate the inflammatory cascade and cause tissue destruction. The aim this study was to investigate the prevalence of periodontitis in psoriasis patients, and to find whether any correlation exists between them.

Materials and methods. This hospital-based cross-sectional study included 100 age- and gender-matched subjects divided into two groups: group 1: psoriasis (test) and group 2: chronic periodontitis (CP) (control). Both groups were evaluated for periodontal clinical parameters (gingival index (GI), plaque index (PI), probing depth (PD), periodontal attachment level (PAL) and tooth loss (1-3 or ≥4). Furthermore, subgingival microbial analysis of dental plaque was carried out to estimate the levels of periodontopathic organisms, using polymerase chain reaction (PCR). ANOVA, independent sample t-test and chi-square test were used for statistical analysis.

Results. Psoriasis patients showed significantly higher GI, PI, PD, PAL and tooth loss (≥4) compared to controls. Furthermore, their microbiological analysis showed significantly greater number of *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* positive samples. However, no difference was found in *Tannerella forsythia* positive samples.

Conclusions. The prevalence of periodontitis is higher in psoriasis subjects as compared to age- and gender-matched periodontitis controls. We hypothesized that this assumption is valid as periodontitis shares several important common pathways with psoriasis. Further studies with larger sample sizes are warranted to substantiate this association.

Key words: **Psoriasis, chronic periodontitis, skin diseases, papulosquamous, dental plaque.**

Introduction

Chronic plaque psoriasis (Psoriasis Vulgaris) is a papulosquamous disease defined by erythematous plaques with a silvery scale. It is a common, relapsing, inflammatory multi-system disease with skin and joint manifestations. It is characterized by predominantly red skin patches, and inflamed, swollen

skin lesions covered with silver-white scales affecting >2% of the general population.[1,2] It can affect individuals of any race. However, epidemiologic studies have shown a higher prevalence in western European and Scandinavian populations. It is slightly more common in men[3] and has two peaks of incidence, the first in young adults (aged 16-22) and the second in older (aged 57-60) individuals.[4] Genetic and environmental factors influence this disease strongly and streptococcal infections may also 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, inflammatory bowel diseases, rheumatoid arthritis, sero-negative spondyloarthropathies, malignancy, streptococcal tonsillitis, smoking, alcohol abuse, psychiatric disorders and stress.[9] To date many possible hypotheses regarding its etiology have been proposed, but the exact nature of its etiopathogenesis is yet unknown. However, hightened immune response seems to be most likely.

Chronic destructive periodontal disease is a family of bacterial infections characterized by immunologically motivated destruction of periodontal supporting tissues.[10] The disease affects >50% of adults in the USA.[11] It has a multi-factorial origin, and its course might be transient, undergoing cycles of exacerbations and spontaneous remissions.[12] The bacterial flora at the diseased sites is complex, totalling 500–700 different microbial species in the sub-gingival dental biofilm.[13] The main pathogens are thought to be a group of Gram-negative, anaerobic microorganisms. However, Gram-positive bacteria, including beta-haemolytic *Streptococci* (also implicated in the aetiology of psoriasis), constitute a significant proportion of this biofilm.[13] Its activity is influenced by bacterial attack and host responses.[10] The host responds to periodontal infections with an array of events involving both innate and adaptive immunity. In response to endotoxins derived from periodontal pathogens, mediators target the destruction of alveolar bone and supporting connective tissues.[10] The periodontal infection, in its early stages, may permit injurious agents derived from bacteria, or bacteria themselves to gain access to the connective tissue.[14,15] It also appears that systemic manifestations arise due to many oral bacteria and are significantly increased in periodontitis.[16] This potentially results from transient access of oral bacteria to the circulation.[14] Periodontal diseases have been described as being coexistent with coronary heart disease, cerebrovascular diseases, respiratory diseases, diabetes, osteoporosis, rheumatoid arthritis,[17] premature birth and low birth weight, hyperkeratosis palmoplantaris of the Papillon–Lefèvre syndrome,[18] and chronic kidney diseases.[19]

Both psoriasis and periodontal diseases are characterized by an exaggerated immune response to the epithelial cell surface microbiota. The immune system further induces T cells to produce cytokines and these cytokines stimulate proliferation of keratinocytes and production of antigenic adhesion molecules in the dermal blood vessels. These adhesion molecules further stimulate T cells to produce cytokines, thus perpetuating the response.[20] Dendritic cells (DCs) have been implicated as important mechanism in driving the heightened immune responses,[21,22] and have been found crucial in the initiation and regulation of both innate and adaptive immunity. Moreover, they are thought to bridge between the two immune systems by migrating from the epithelial barriers to regional lymph nodes. We determined various common mechanisms possibly heightening immune responses as implicated in the etiopathogenesis of both psoriasis and periodontitis. Hence we hypothesized there might be a possible association in the pathogenesis of these disease entities. The aim of the study was to find out the prevalence of periodontitis in psoriasis patients and to hypothesize various possible mechanisms relating these diseases for further investigations. Very few published studies have shown an association between psoriasis and chronic periodontitis. To the best of our knowledge, this is the first study to report the prevalence of periodontitis in psoriasis patients as estimated by the clinical and microbiological outcomes using PCR technology.

Material and Methods

The study population consisted of 2 groups: group 1: psoriasis; group 2: chronic periodontitis (CP). The subjects in group 1 were selected from the Outpatient section, Department of Dermatology & Venereology,

Victoria Hospital, Bangalore, and those of group 2 were recruited from the Outpatient section, Department of Periodontology, Government Dental College and Research Institute, Bangalore, India. Written informed consent was obtained from those who agreed to participate voluntarily. Ethical clearances were obtained from the institution's ethical committee and review boards. The study was conducted from March 2010 to November 2010.

In the periodontitis group, subjects with any autoimmune diseases or any other systemic diseases which can alter the course of periodontal disease, a history of smoking or use of tobacco in any forms, medication like antibiotics or a history of periodontal therapy in the preceding 6 months, pregnant/lactating women and subjects unwilling to participate in the study, were excluded. In the psoriasis group, subjects with any autoimmune disease, immunocompromised patients, smoking habits or any other diseases, which have an influence on periodontal status and patients with periodontal treatment in the preceding 6 months or medications which influence its status, were excluded.

Study population

Patients completed a health history questionnaire to ensure that they were medically qualified for participation in the study. After the patients were screened and determined to be eligible for participation, a total of 100 subjects with an age range of 25-55 years were recruited based on convenient sampling method. Group 1 consisted of 50 patients (34 males and 16 females) and group 2 consisted of 50 CP patients (35 males and 15 females) with probing depths (PD) of ≥5 mm and periodontal attachment level (PAL) of ≥3 mm in at least 30% sites with radiographic assessment of bone loss. The inclusion and various dropouts have been presented in Table 1. As psoriasis has a low incidence in India,[23] a sample size of n=50 was considered statistically significant based on its power.

Data collection

Each subject underwent a full-mouth periodontal probing and charting (UCLA University of California Los Angelis, USA); the gingival index (GI),[24] plaque index (PI),[24] pocket depth (PD), periodontal attachment level (PAL), tooth loss and microbial plaque analysis were evaluated. The PD and PAL were measured considering a fixed reference point on the occlusal surface of the teeth and cementoenamel junction.

A previously calibrated examiner (RK) performed all the clinical assessments using University of North Carolina (UNC)-15 periodontal probes UNC-15 (Hu-Friedy, Inc. Chicago, Illinois (IL), USA) to ensure adequate intra-examiner reproducibility. The examiner was considered calibrated once statistically significant correlation and statistically non-significant difference between duplicate measurements were obtained (r = 0.89 for PD and r = 0.91 for PAL). The PD and PAL values were rounded to their nearest millimeter.

Plaque sample collection

Supragingival plaque was removed with a sterile curette (Hu-Friedy, Inc. Chicago, Illinois, USA) and subgingival plaque was then collected in a single pass with a second sterile curette, starting at the most apical extent of the deepest periodontal pocket. Collected samples were placed in airtight plastic vials with 500 µL of Tris EDTA (TE) buffer and were immediately transferred to the laboratory for microbiological analysis using PCR technology.

DNA extraction and polymerase chain reaction

The samples were stored at -20ºC to be processed immediately. The samples were thawed to room temperature and centrifuged (10,000 rpm, for 3-4 minutes); the supernatant was discarded and this process was repeated 3 times. To this end, nearly 500 µL of Lysis buffer 1 was added and centrifuged (in the same manner as mentioned above). Then, 50 µL of Lysil buffer 2 and 5 µL of proteinase K were added. This mixture was kept in a water bath at 75ºC for 2 hours.

Table 1. Outline of inclusion and exclusion of patients in the study, values shown represent number of patients

Recruitments and dropouts	Screened for eligibility		Eligible patients		Ineligible (based on inclusion & exclusion)		No. of pts unwilling/ violated inclusion		No. of pts dropped intentionally		Total no. studied	
Groups	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**
No. of Patients	218	275	62	56	156	219	12	1	0	5*	50	50

No: Number; pts: patients.
* Five patients were intentionally excluded from control group to match the number in test group.

It was then kept in a boiling water bath for 10 minutes and then stored at -20ºC for analysis.

Primers (16S rRNA genes, short DNA fragments) [(*Aa*F), 5'-ATT GGG GTT TAG CCC TGG TG-3', (*Tf*F), 5'-TAC AGG GGA ATA AAA TGA GAT ACG-3', (*Pg*F), 5'-TGT AGA TGA CTG ATG GTG AAA ACC-3', Conserved reverse primer (C11R), 5'-ACG TCA TCC CCA CCT TCC TC-3' were used for detection] containing sequences complementary to the target region along with a DNA polymerase are key components to enable selective and repeated amplification. The three major steps in PCR were repeated for 30 or 40 cycles. This was carried out on an automated cycler. Denaturation at 94°C, annealing at 54°C and extension at 72°C were performed. As PCR progressed, the DNA generated was itself used as a template for replication. The master mix contained all the necessary components to generate new strands of DNA for *Aggregatibacter actinomycetemcomitans (Aa), Tannerella forsythia (Tf)* and *Porphyromonas gingivalis (Pg)*, setting in motion a chain reaction in which the DNA template was exponentially amplified.

Limit of detection

In pure cultures, the multiplex PCR simultaneously detected as few as 10 *Aa* and *Pg* cells.

Statistical analysis

All data were analyzed using a software program (Software Analyzer, SPSS 17.1 SPSS Inc., Chicago, IL, USA). A test for the validity of the normality assumption using standardized range statistics (mean ± standard deviation) was carried out. The assumption was valid, and accordingly, parametric tests were carried out. ANOVA was carried out for demographic variables to assess if the groups differed significantly (Table 2). Further, pair-wise comparisons using the independent sample t-test were carried out (Table 3). Group comparisons for non-parametric variables were performed by chi-squared test to evaluate the hypothesis of equality of means. It was carried out to find out any association of groups with the underlying cause (Table 3). Statistical significance was defined at $p \leq 0.05$.

Results

The present study aimed at investigating the prevalence of periodontitis in psoriasis and age- and gender-matched non-psoriatic controls as estimated by the outcomes of periodontal clinical and microbiological parameters. All the values obtained were rounded off to the nearest whole number. The results of the present study indicate that mean GI, PI, PD, PAL and tooth loss (≥4) were significantly higher in the study group compared to controls. However, the difference was not significant for tooth loss (1-3) between groups 1 and 2 (Table 4).

Psoriasis patients in the present study had significantly greater scores ($p<0.00$*) for GI and PI (2.37 ± 0.256 and 2.426 ± 0.286, respectively) as compared to age- and gender-matched controls (2.177 ± 0.32 and 2.183 ± 0.293, respectively). In addition, the pocket depth and attachment levels (6.783 ± 0.915 and 6.705 ± 0.906, respectively) were significantly greater ($p<0.00$*) as compared to controls (5.59 ± 1.183 and 5.59 ± 1.183, respectively). Moreover, psoriasis patients had significantly fewer teeth compared to controls.

Furthermore, group comparisons for non-parametric variables were performed by chi-square test, assessing the hypothesis of equality of means between groups 1 and 2. It was shown that only *Aa and Pg* ($p = 0.00$* and $p = 0.044$*, respectively) differed significantly and *Tf* did not show any correlation ($p = 0.069$) between the test and control groups (Table 4, Figure 1).

Discussion

The magnitude of periodontal destruction in psoriasis patients indicates that there may be an association between the two diseases. We know that both psoriasis and periodontitis share many common risk factors.

Table 2. ANOVA for descriptive baseline characteristics

Parameters	N	Group 1 (Test)	Group 2 (Control)	F	P
Age (Mean ± SD)	50	41.76 ± 8.551	39.88 ± 8.778	1.177	0.281
Sex (M/F)	50	34/16	35/15	0.046	0.831

SD: Standard Deviation; M: males; F: females.

Table 3. Independent sample *t* test to find out which parameters are significant

Parameters	N	Group 1 (Test)	Group 2 (Control)	Std Error	P
GI (Mean ± SD)	50	2.37 ± 0.256	2.177 ± 0.32	0.0579	0.002*
PI (Mean ± SD)	50	2.426 ± 0.286	2.183 ± 0.293	0.0579	0.00*
PD (Mean ± SD)	50	6.783 ± 0.915	5.59 ± 1.183	0.2115	0.00*
PAL (Mean ± SD)	50	6.705 ± 0.906	5.711 ± 1.207	0.2134	0.00*

* Statistically significant

Table 4. Chi-squared and Fisher's exact tests for periodontopathic microorganism between groups 1 and 2

Parameters	Value	Diff	Pearson's chi-squared P value	Fisher (Sig)
Tooth loss (1-3)	0.679	1	0.410	0.537
Tooth loss ≥ 4	18.919	1	0.00*	0.00*
Aa	19.385	1	0.00*	0.00*
Tf	3.305	1	0.069	0.106
Pg	4.058	1	0.044*	0.069

Aa: *Aggregatibacter actinomycetemcomitans*; *Tf*: *Tannerella forsythia*; *Pg*: *Porphyromonas gingivalis;* Diff: Difference.

Genetic and environmental factors are involved in the etiologies of these inflammatory diseases.[1,25,26] Alcohol and smoking are known to be associated with psoriasis[6,7] and CP.[17] A link between psoriasis and stress,[27] and stress-induced periodontitis[28] also exists. Chronic human immunodeficiency virus infection, associated with severe psoriasis[29] and periodontal exacerbations[30] are well known. Systemic infections (CVD, metabolic syndrome, rheumatoid arthritis, malignancies),[9,16] streptococcal infections,[5] immunosupperants, various medications and many more are common to both psoriasis and periodontitis.

Despite having so many risk factors in common, there are very few studies available in the literature relating psoriasis and periodontitis.[31,32] It has been reported that psoriasis patients have significantly fewer teeth than their age- and gender-matched controls, as well as a significantly larger distance from the cementoenamel junction to the alveolar crest in the lateral segments of the dentition.[31] In addition, it has been suggested that actual periodontal breakdown may be associated with exacerbation of psoriasis and that exacerbations and remissions of psoriasis may

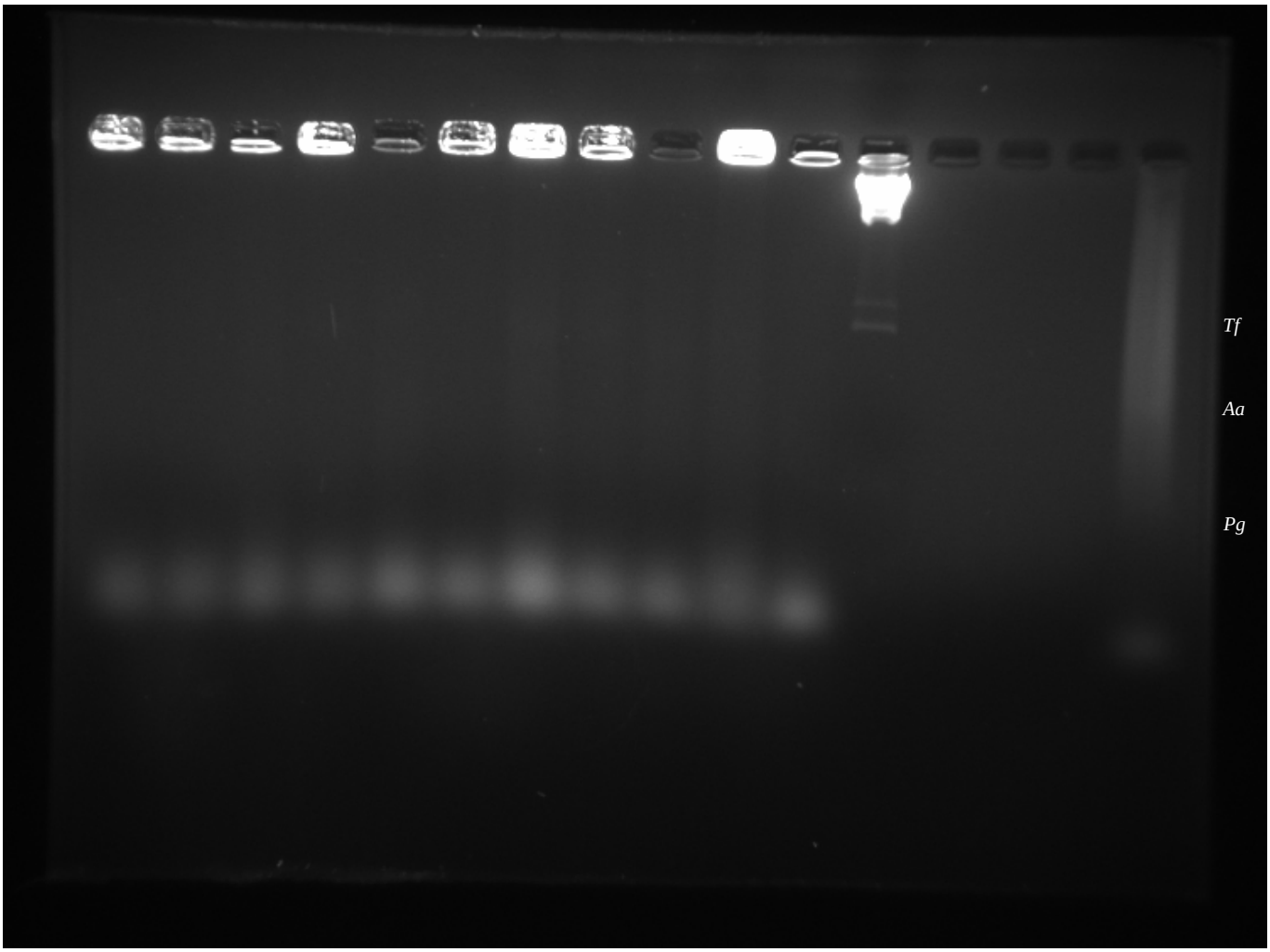

Figure 1. Specificity of multiplex PCR against American Type Culture Collection strains of oral species. Lane 1-12 16S (rDNAs) amplified from dental plaque, lane 13-15 negative controls (H2O, PBS and H2O, respectively), Lane 16 positive control size marker for *A actinomycetemcomitans* (amplicon observed at 360 bp), *T forsythus* (745 bp), and *P gingivalis* (197 bp).

correlate with bursts and remissions of periodontal breakdown.[32]

Ogorelkova et al[33] in their study stated that 'an interesting hypothesis put forward was the idea that several diseases that are classified as distinct entities, such as psoriasis, periodontitis, and others, could all be included in a general category of inflammatory barrier disorders'. One mechanism for such a claim might be that the innate immune system is directing the subsequent adaptive immune responses (T and B cell responses), important in the pathogenesis of both psoriasis and periodontitis.[34,35] Also, recent studies have demonstrated an up-regulation of Toll-like receptor (TLR)-2 in psoriatic skin,[36] and in the periodontium of periodontitis patients.[37] High expression of TLR will amplify the inflammatory reaction and subsequent T cell activation. Studies in the Yaa mouse model have shown that a two-fold increase in TLR gene dosage can dramatically induce an autoimmune pathology.[36] Thus, this might be the etiopathological basis for these disease entities.

Moses and Longer[38] classified psoriasis and rapidly progressive adult and juvenile periodontitis, as angiogenic and vasoproliferative-dependent diseases. Furthermore, it is now known that persistent granulation tissue and aberrant angiogenesis contribute significantly to pathogenesis of chronic periodontitis. The activity of proteolytic enzymes (released from bacteria or bacterial products) leads to the release of pro-angiogenic cytokines from inflammatory cells. These cytokines in turn release angiogenic mediators that are sequestered in the extracellular matrix and endothelial cells lining venules. They systematically degrade their basement membrane and proximal extracellular matrix, migrate directionally, divide, and organize into new functioning capillaries. Hence angiogenesis seems to be central to the etiology and pathogenesis of psoriasis and periodontitis.[39]

Furthermore, Schamberg et al[40] conducted a carefully controlled investigation of protein metabolism in a series of patients with psoriasis. These studies led to the conclusion that individuals with psoriasis exhibit retention of nitrogen. This retention seems to be proportional to the extent and severity of the disease process. The nitrogen or the reactive nitrogen species (RNS) produced, and the impact of neopterin (secreted by activation of monocyte/macrophages in the course of host defense reactions) might cause amplification of the cytotoxic forces of RNS, which are directed against the invading pathogens. This mechanism is known to cause periodontal destruction.[41] Moreover, activation of monocytes/macrophages, which is a consequence of host defense, further initiates the production of reactive oxygen species and RNS, which might further exacerbate the destruction of periodontal tissues.

Additionally, periodontitis shares several important common pathways with psoriasis, including arachidonic acid, prostaglandin E_2 and leukotriene C4, in its pathogenesis.[42] Also, vitamin D receptor (VDR) gene polymorphisms have been reported to be associated with psoriasis[43] and periodontitis[44] and it was concluded that polymorphisms of the VDR gene might be associated with periodontal disease progression and tooth loss.

Thus, one may speculate that common risk factors and genetic traits affecting DCs, immune complexes, TLR expressions or other components of the innate immune response, angiogenetic mediators, nitrogen and RNS, several cytokines, and inflammatory mediators could predispose psoriasis patients to periodontitis or aggravate periodontal status.

Several limitations should be addressed when evaluating the relevance of our findings. Our study indicates that psoriasis patients experience more periodontal destruction. This might be attributed to the fact that psoriasis patients have high morbidity and may not be able to maintain proper hygiene. Also, as the study was carried out in a governmental institute, the patients seeking treatment here (including the ones in our study) come from lower socio-economic strata of the society. Hence, there might be a proportional co-morbidity, which could explain the higher prevalence of periodontitis. We tried to relate these diseases with various possible mechanisms but did not investigate them as they were out of the limits of this study. Any conclusions drawn at this point of time are hypothetical and should be dealt with caution.

Conclusion

In conclusion, there is a higher prevalence of periodontitis in psoriasis subjects as compared to age- and gender-matched periodontitis controls, as estimated by clinical and microbiological outcomes. Since there have been very few previous reports on such possible co-morbidity, conclusions must be drawn with caution, and large experimental studies are warranted to test the hypothetic causality between periodontal disease and psoriasis and confirm these findings.

Acknowledgements

The authors report no conflict of interests. It is a self funded research. We are thankful to Dr. Kishor Bhat, Department of Microbiology, Maratha Mandal Dental

College, Belgaum, Karnataka, India, for carrying out the required PCR for the study. We also thank, Mr. Jagannatha P. Suryanarayana for providing the necessary statistics for the study.

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