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## Serotypes of *Aggregatibacter actinomycetemcomitans* in relation to periodontal status and geographic origin of individuals-a review of the literature

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### Abstract

**Objectives:** Several studies have focused on the relationship among serotype distribution, ethnical status and geographic populations, and periodontal conditions. Studies that have investigated the prevalence and the distribution of *A. actinomycetemcomitans* serotypes and the relation between the different serotypes of the bacterium and periodontal status were reviewed.

**Material and Methods:** A systematic literature search for publications regarding the distribution of *A. actinomycetemcomitans* serotypes in subgingival samples of periodontitis patients and periodontally healthy subjects by employing polymerase chain reaction (PCR) was conducted.

**Results:** From the 85 studies identified in the first analysis, only 12 met all inclusion and exclusion criteria. Clinical isolates from diverse geographic populations with different periodontal conditions were evaluated. Serotypes a, b and c were largely found, and serotype c was the most prevalent. They were isolated from various periodontal conditions, including aggressive periodontitis.

**Conclusions:** The available literature suggests that serotypes a, b, and c are globally dominant, serotypes d and e are rare, and the prevalence of the most recently identified serotype f is still unknown. It is widely accepted that distribution patterns of *A. actinomycetemcomitans* vary among subjects of different ethnicity and geographic regions. The correlation of different serotypes with various periodontal conditions remains unclear.

**Key words:** *Aggregatibacter actinomycetemcomitans*, serotypes, periodontal disease, prevalence.

## Introduction

Periodontitis is a collective term for inflammatory conditions affecting supporting tissues of the teeth induced by microbial deposits (1). Progressive loss of tooth attachment in periodontitis may eventually culminate in loss of affected teeth. As a consequence, periodontal disease is one of the most important concerns for dentists, patients and the public dental healthcare system.

Epidemiological studies have shown that periodontal disease occurs predominantly in a slowly progressing form, chronic periodontitis, which in the majority of patients involves a limited number of teeth and rarely interferes with tooth function before adulthood (2). Periodontitis also occurs in a severe and rapidly progressing form, denoted aggressive periodontitis, which most often starts at an early age (2,3).

Clinical and microbiological studies have identified only a few bacterial species associated with periodontal disease in adults (4). *Aggregatibacter actinomycetemcomitans* is a Gram-negative, nonmotile, facultative anaerobic coccobacillus bacterium that colonizes the human oral cavity, associated with the etiology of aggressive periodontitis (5-7), and can also be detected in the oral cavity of chronic periodontitis patients and periodontally healthy subjects (8,9). This microorganism produces a variety of virulence factors, such as lipopolysaccharide, leukotoxin and cytotoxic distending toxin (CDT) (10).

Development of techniques to detect the genetic variability of microorganisms has allowed for the observation of genetic differences in the leukotoxin promoter region between various *A. actinomycetemcomitans* strains, which are directly correlated with their leukotoxicity (11). Strains that are highly leukotoxic have a deletion of 530 base pairs in the leukotoxin promoter region, while those that are minimally leukotoxic present contain the complete leukotoxin promoter region. Thus, the highly leukotoxic strains (designated the JP2 clone) can produce 10 to 20-fold more toxin than the others, providing them with the potential to interfere with the host's innate immune defense (12).

*A. actinomycetemcomitans* can be grouped into six serotypes (a-f) based on the polysaccharide antigen on the cell surface (13). Numerous studies have examined the relationship of *A. actinomycetemcomitans* serotype, ethnical status and geographic populations, and periodontal disease status, but with conflicting results (14-17). Subjects are usually colonized by a single serotype, which can persist for life (18), and the frequency distribution of *A. actinomycetemcomitans* serotypes differs among various populations (19). There are no epidemiological studies on the distribution of *A. actinomycetemcomitans* serotypes, but the available literature suggests that serotypes a, b, and c occur much more frequently among oral isolates than serotypes d, e, and f (13,20-22). Differences in serotype distribution have been shown

among African, Asian, Europeans, and North and South American populations (21-25).

The different studies describe different microbiological identification techniques. Detection methods for *A. actinomycetemcomitans* currently used include bacterial culture, DNA probe hybridization (20), specific antibody immunofluorescence (21), gene amplification via PCR methodology (22), including multiplex, nested multiplex and quantitative PCR. Each methodology varies with regard to detection time, the minimum number of cells that can be detected, and the ability to quantify the numbers of *A. actinomycetemcomitans* present in samples. PCR-based methods are not only suitable for the confirmation of strains, but have also been shown to have high sensitivity and specificity for the detection of *A. actinomycetemcomitans* from clinical samples of supragingival and subgingival plaque, and allow rapid detection of *A. actinomycetemcomitans* from clinical samples.

The objective of the present study was to review the studies that have investigated the prevalence and the distribution of *A. actinomycetemcomitans* serotypes in subgingival samples of periodontitis patients and periodontally healthy subjects by employing polymerase chain reaction (PCR) and to examine the possible association between periodontal conditions and serotypes.

## Material and methods

### Data sources and search strategy

The electronic database PubMed was searched systematically for studies published between January 2002 and December 2012. No language restrictions were applied. Both Mesh and Major terms were used in the search and Boolean operators (OR, AND) were used to combine the searches. The bibliographies of all potentially relevant studies and review articles were also searched. The search terms included "serotypes" AND "*Aggregatibacter actinomycetemcomitans*" OR "*Actinobacillus actinomycetemcomitans*" AND "periodontal disease" OR "periodontitis". The search was carried out twice by two different people.

### Study selection

Eligibility criteria applied to all studies retrieved by the search were established. Duplicate records or double-published studies and articles published before 2002 were excluded. No limitations were placed on the geographical location. Studies involving the distribution of *A. actinomycetemcomitans* serotypes in subgingival samples of periodontitis patients and periodontally healthy subjects by employing PCR were eligible for inclusion in this review. All abstracts were reviewed in order to identify any studies of interest. Two reviewers independently assessed the full-text articles for eligibility. Only studies which met all the eligibility criteria were finally included. Relevant data were abstracted from all studies meeting the eligibility criteria. The fol-

lowing data were extracted from each study: (1) the first author and year of publication; (2) the country where the study was conducted; (3) searched serotypes; (4) Aim of study; (5) Principal findings and (6) possible association between periodontal conditions and serotypes.

**Results**

Eighty-five articles were identified, of which 66 were excluded based on their titles and abstracts. The full text of each of the 19 remaining papers was reviewed, and seven were excluded because they did not match the inclusion criteria for this review. The remaining 12 stud-

ies were included in the review, nine cross-sectional studies and three longitudinal studies.

The study selection is presented in **table 1**. The publication dates ranged from 2003 to 2012. The study sample sizes ranged from 49 to 486 individuals and the number of participants positive for *A. actinomycetemcomitans* ranged from 13 to 204 individuals. Participants' ages ranged from 4 to 82 years. Definition of periodontal disease varied greatly between the studies. Although majority of the studies defined periodontitis based on probing pocket depth (PPD) and/or clinical attachment level (CAL) measurements, their definitions varied in

**Table 1.** Description of the studies included in the review.

Study	Searched serotypes / Type of study	Aim of study	Participants number(s), Aa-positive individuals, Age	Periodontal status/ Clinical Parameters examined
Yoshida et al., 2003 (26)	a-e Cross-sectional study	To examine the frequency of mono- or poly-infection by Aa serotypes and the relationship between the detection of Pg and the distribution of Aa serotypes.	Aa was detected in 64 (19.5%) of 328 subjects (190 males aged 25–64 years and 138 females aged 22–59 years).	Minimal periodontal disease or periodontally healthy/ PPD.
Teixeira et al., 2006 (22)	a-f Cross-sectional study	To evaluate the distribution of Aa serotypes in subjects with and without periodontitis and whether there is an association between serotype and periodontal status.	Aa strains isolated from subgingival specimens of 49 Brazilian subjects (from 4 to 58 years).	Healthy periodontium; AgP; CP (AAP, 1999 [3]) / PPD; attachment loss; bleeding or exudation on deep sites; radiographic evidence of alveolar bone loss.
Thiha et al., 2007 (27)	a-e Cross-sectional study	To identify periodontopathic bacteria in diseased gingival tissue of periodontitis patients. The distribution of Aa serotypes in tissue samples was also examined.	56 subjects consisting of 32 CP (mean age 55.13 ± 7.46), 16 GAgP (mean age 35.07 ± 8.23) and 8 LAgP (mean age 31.29 ± 5.56). Prevalence of Aa was higher in the LAgP (63%) group.	CP; GAgP; LAgP (AAP, 1999 [3]) / PPD; CAL; BOP.
Fine et al., 2007 (6)	a-e Longitudinal Cohort Study	To study the prevalence of LAP, the prevalence of Aa carriage, the relationship of Aa carriage to disease initiation.	A cohort of 96 students was established that included a test group of 38 Aa-positive students and 58 healthy Aa-negative controls (from 11 to 17 years – initial).	Healthy; LAP / One 4- or 5-mm pocket; At least two 5-mm pockets; At least one 6-mm pocket with 2 mm of attachment loss.
van der Reijden et al., 2008 (28)	a-f Longitudinal Cohort Study	To investigate the serotype distribution and stability of Aa over an 8-year period in untreated Indonesian subjects.	From the total number of 158 patients in 1994, 65 (41.1%) were positive for Aa (mean age 29.4 years). In 2002, 53 (49.5%) subjects out of a total of 107 subjects were Aa positive (mean age 38.2 years).	Untreated periodontal disease / PI; bleeding index; PPD; CAL.
Hoglund Aberg et al., 2009 (29)	a-f Longitudinal study	To look for clinical signs of periodontal disease in young adults who exhibited bone loss and detectable numbers of Aa in their primary dentition.	13 subjects who all exhibited bone loss and were colonized by Aa 16 years ago (aged 7–9 years). Aa was recovered from six of these subjects (aged 23–25 years).	Detection of bone loss and Aa in primary dentition / PPD; BOP; ABL, alveolar bone loss; PI.
Kim et al., 2009 (30)	a-f Cross-sectional study	Compared serotypes of Aa in two groups of periodontal patients with different ethnic backgrounds.	194 samples of subgingival plaque from periodontal patients (98 Koreans and 96 Germans) were analyzed (ages ranged between 27 and 63 years). 45 (23.2%) tested positive for Aa.	Generalized severe periodontitis (≥ 30% sites with CAL > 4 mm, more than two teeth with >50% periodontal bone loss in relation to the total root length) / PI; GBI; PPD; CAL.

**Table 1.** Continue.

Roman-Torres et al., 2010 (31)	a-f Cross-sectional study	To elucidate the prevalence of Aa and the distribution of Aa serotypes in Brazilian subjects with CP.	Out of 486 subjects examined, Aa was isolated in 85 (17.5%) individuals (mean age 33.41 ± 9.76 years).	CP (slight [1–2mm CAL], moderate [3–4mm CAL] or severe [≥5 mm CAL]) / PPD; CAL; GI; PI.
C. Chen et al., 2010 (32)	a-f Cross-sectional study	Examined the distribution pattern of Aa serotypes in the subgingival plaque of subjects residing in the United States.	Aa was examined in 256 subgingival plaque samples from 161 subjects. A total of 82 distinct Aa strains were identified (from 11 to 32 years).	No periodontitis; LAP (with at least two teeth, either central incisors and/or first molars, CAL ≥ 2 mm, and with fewer than other four teeth with AL); GAgP (with at least two teeth with ≥ 2 mm of AL in each of the four quadrants) / PPD; Attachment loss (AL).
Sakellari et al., 2011 (33)	a-e Cross-sectional study	To investigate the distribution of Aa serotypes and the prevalence of the JP2 clone in subgingival samples of Greek subjects.	228 subjects examined for Aa. 40 subjects were positive for Aa (from 29 to 82 years).	Non-periodontitis; Untreated periodontitis Periodontitis patients receiving supportive treatment (CP or AgP - AAP, 1999 [3]) / PPD; BOP.
Bandhaya et al., 2012 (34)	a-f Cross-sectional study	To examine Aa serotypes, the ltx promoter and the presence of cdtABC genes in a group of Thai adults.	Subgingival plaque samples from 453 subjects were analysed for Aa. Eighty six subjects (19%) were positive for Aa (aged 38–59 years).	Mean PD; % sites with PD ≥ 5 mm; Mean CAL; % sites with CAL ≥ 4 mm / PPD; recession; CAL.
Cortelli et al., 2012 (35)	a-f Cross-sectional study	Investigated a large population of individuals positive for Aa and performed a two way analysis assessing the relation between the different serotypes of the bacterium and periodontal conditions.	204 individuals (mean age 33.54 ± 11.11) positive for Aa.	Non-periodontitis; AgP (PPD > 5 mm and CAL ≥ 4 mm at first molars and incisors); Mild CP (PPD > 3 mm in at least four teeth and mean periodontal CAL > 3 mm); Moderate/severe CP (PPD > 3 mm in at least four teeth and mean periodontal CAL ≥ 5 mm) / PPD; CAL; GI; PI.

Aa, *Aggregatibacter actinomycetemcomitans*; Pg, *Porphyromonas gingivalis*; AgP, Aggressive Periodontitis; CP, chronic periodontitis; LAgP/LAP, localized aggressive periodontitis; GAgP, generalized aggressive periodontitis; PPD, probing pocket depth; CAL, clinical attachment level; BOP, bleeding on probing; PI, plaque index; GI, gingival index; GBI, gingival bleeding index.

terms of the threshold for the extent and severity of these criteria. Various researches included a control group of periodontally healthy participants. Eight studies evaluated serotypes a-f and four studies examined serotypes a-e.

Clinical isolates from diverse geographic populations with different periodontal conditions were evaluated. The samples were obtained of the subjects from Japan, Brazil, United States, Indonesia, Sweden, Germany, Korea, Greece and Thailand.

Table 2 shows the prevalence and distribution of *A. actinomycetemcomitans* serotypes and the relationship with periodontal status of the studies included in the review. Serotypes a, b and c were largely found, and serotype c was the most prevalent. These serotypes were isolated from various periodontal conditions, including aggressive periodontitis. Serotypes d, e, and f were either not detected or were relatively infrequent.

## Discussion

There is convincing evidence of differences in serotype distribution related to geography and/or ethnic group. Available data indicate that the geographic distribution of serotypes is not uniform (6,32,33). The distribution pattern of *A. actinomycetemcomitans* serotypes varies greatly depending on the periodontal status of the allocated population and the country where the study takes place (22,26,27,32,33).

*A. actinomycetemcomitans*, an oral commensal which is also an opportunist pathogen has a distinct racial bias and a surprising range of potential virulence factors and virulence mechanisms. It is a pathogen not only in the periodontium but also in some non oral infections, possesses several virulence determinants which contribute to its ability to colonize the oral cavity, persist in the periodontal pocket, resist and evade host defenses, cause destruction to soft and hard tooth-supporting tis-

**Table 2.** Prevalence and distribution of *A. actinomycetemcomitans* serotypes and association with periodontal status.

Study / Location	Occurrence of Aa serotypes	Periodontal conditions and serotypes
Yoshida et al., 2003 (26) Japan	Aa serotype c was detected more frequently in sites that were positive for both Pg and Aa (76.9%) than in sites that were Pg-negative and Aa-positive (33.9%). The numbers of sites in which two different serotypes and three different serotypes were detected were 18 (25.0%) and 7 (9.3%), respectively.	The distribution of Aa serotypes was influenced by the presence of Pg. The findings suggest that the characteristics of serotype c may differ from those of the other serotypes.
Teixeira et al., 2006 (22) Brazil	Serotypes b and c were observed in similar frequencies, and no subject harboured d, e, or f serotype strains.	An association between serotype b and healthy periodontium and between serotype c and CP was observed.
Thiha et al., 2007 (27) Japan	Aa serotype c was detected in 50% of LAP patients.	Aa serotype c was predominantly identified in the gingival tissues of Japanese LAP patients, while the prevalence of serotype b was rather low.
Fine et al., 2007 (6) United States	Aa serotype presence in African-American students appears to be equally distributed among serotypes a, b, and c, whereas, Hispanic students show a strong association with serotype c.	The detection of Aa in periodontally healthy children can serve as a risk marker for initiation of LAP.
van der Reijden et al., 2008 (28) Indonesia	In 1994, the predominant serotype was b (53.7%), whereas a and c occurred in 17.1% and 14.6% of the subjects, respectively. In 2002, a reduction in serotypes a (7.5%) and b (30.2%) occurred. Serotypes c and e increased in prevalence from 14.6% to 35.8% and 2.4% to 9.4%, respectively.	Subgingival presence of Aa, but not a specific serotype is associated with a higher degree of inflammation. Aa serotypes distribution in Indonesian young adults shifts from predominantly serotype b to a more equal prevalence of serotypes b and c.
Hoglund Aberg et al., 2009 (29) Sweden	Serotypes a-c and e, but not d or f, were found from the fourteen 7-9-year-old subjects at the baseline examination. Among the strains isolated from the six Aa-positive young adults, serotypes a-c, and f were identified.	The presence of Aa and early bone loss in the primary dentition does not necessarily predispose the individual to periodontal attachment loss in the permanent dentition.
Kim et al., 2009 (30) Germany, Korea	In German patients, the serotypes detected most frequently were b (33.3%), c (25.0%), and a (20.8%), whereas in Korean patients, the serotype distribution was different, with serotypes c (61.9%) and d (19.0%).	Even if the percentage of patients who tested positive for Aa was identical in patients with GAgP and severe CP and different ethnic backgrounds, the distribution of Aa serotypes may exhibit marked differences.
Study / Location	Occurrence of Aa serotypes	Periodontal conditions and serotypes
Roman-Torres et al., 2010 (31) Brazil	Out of 85 positive samples, 68 were infected by at least 1 serotype, 7 by mixed, and 10 were non-serotyped. Serotypes d and f were not detected. Serotype c showed the highest prevalence (52.9%), followed by serotype a (31.8%).	The prevalence of serotype c in severe periodontitis was significantly greater than that of serotypes a and b.
C. Chen et al., 2010 (32) United States	The serotype distribution pattern of the strains was 21 (25.6%) serotype a, 12 (14.6%) b, 41 (50%) c, 6 (7.3%) e, 1 (1.2%) f, and 1 (1.2%) non-typeable.	Serotype c is the dominant serotype among Aa from subjects with periodontitis in the United States.
Sakellari et al., 2011 (33) Greece	No statistical differences were observed concerning the distribution of serotypes among groups. Serotype c was more predominant within the periodontally diseased groups.	Aa serotype b was not statistically correlated with periodontal disease in the investigated sample and the utility of microbiological testing before antimicrobial administration is emphasized.
Bandhaya et al., 2012 (34) Thailand	Serotype c was the most prevalent (57%), followed by serotypes a (33%) and b (7%).	No significant relationship between serotypes and the extent or severity of periodontal disease.
Cortelli et al., 2012 (35) Brazil	Serotypes a, b and c were largely found (98%), and serotype c was the most prevalent. Serotypes d, e, and f were either not detected or relatively rare.	Serotype c was the most prevalent in both diseased and healthy subjects. AgP subjects were not exclusively associated with Aa serotype b.

Aa, Aggregatibacter actinomycetemcomitans; Pg, Porphyromonas gingivalis; CP, chronic periodontitis; AgP, Aggressive Periodontitis; LAP, localized aggressive periodontitis; GAgP, generalized aggressive periodontitis.

sues, and interfere with host tissue repair after infection. Several studies suggest that different *A. actinomycetemcomitans* serotypes are associated with periodontal health, periodontitis, and non-oral infections (13,16,24), therefore the authors reviewed commensal with pathological *A. actinomycetemcomitans*.

It has been suggested that patients are usually infected by only one serotype and colonization is stable over time (28,30), however occasional individuals are colonized with two or three serotypes (31,33,35). Most authors reported frequencies of multiple-serotype infection up to 20% (22,27,31). There have been a few exceptions, as in a Japanese study population where two or three serotypes of *A. actinomycetemcomitans* were detected in a percentage as high as 33% of the sites tested positive (26).

In general, the serotypes a–c occur much more frequently among oral isolates than serotypes d–f. The *A. actinomycetemcomitans* serotype presence in African-American students appears to be equally distributed among serotypes a, b, and c, whereas, Hispanic students show a strong association with serotype c (6). Serotypes a, b and c are equally dominant and collectively comprise 95% or more of all *A. actinomycetemcomitans* strains in Greece (33). In Brazilian subjects, serotypes a, b and c were largely found (98%), and serotype c was the most prevalent. Serotypes d, e, and f were either not detected or relatively rare (22,31,35). The distribution pattern of *A. actinomycetemcomitans* serotypes in the subgingival plaque of subjects residing in the United States showed that serotype c is the dominant serotype, followed by serotypes a and b, and serotypes d, e, and f were either not detected or relatively rare (32).

The studies showed that Asian populations were commonly colonized with *A. actinomycetemcomitans* serotype c, but were occasionally infected with serotype b (26,27,30,34). Two studies have examined the serotype distribution patterns of *A. actinomycetemcomitans* in a Japanese population. In both studies serotype c was the dominant serotype, while serotype b was relatively rare (26,27). For 86 *A. actinomycetemcomitans* strains in Thai adults with varying degrees of periodontal disease severity the serotype c was the dominant serotype, followed by serotypes a (33%) and b (7%) (34), whereas in Korean patients, the serotype distribution was different, the serotypes detected most frequently were c (61.9%) and d (19.0%) (30). The differences between the results from these Asian populations shows that serotype distribution patterns may be affected by geographic variations, even between subjects of the same race/ethnicity. In contrast, serotype b was frequently observed in Caucasian populations (30). In German patients, the serotypes detected most frequently were b (33.3%), c (25.0%), and a (20.8%) (30).

The serotype distribution pattern of *A. actinomycetemcomitans* within a local population may change over time, as was documented in Indonesian subjects with periodontitis between 1994 and 2002. In 1994, the predominant serotype was b (53.7%), whereas a and c occurred in 17.1% and 14.6% of the subjects, respectively. In 2002, a reduction in serotypes a (7.5%) and b (30.2%) occurred. Serotypes c and e increased in prevalence from 14.6% to 35.8% and 2.4% to 9.4%, respectively (28).

Serotypes d-f were rarely detected in most populations worldwide (32,33,35). However, a high prevalence of serotype e (19–47%) was noted in Indonesian (28) and Japanese (26) individuals.

The application of molecular techniques has allowed a more detailed discrimination among different serotypes of *A. actinomycetemcomitans* and therefore the investigation of potential differences between populations of various origins as well as periodontal conditions. It has been suggested that some *A. actinomycetemcomitans* serotypes are more closely associated with periodontal disease than others.

In the United States, serotype c was the dominant serotype among *A. actinomycetemcomitans* from subjects with periodontitis (32), and in addition to the JP2 serotype b phenotype, there are other strains that are equally associated with disease initiation (6). In Japanese patients, *A. actinomycetemcomitans* serotype c was predominantly identified in the gingival tissues of localized aggressive periodontitis patients, while the prevalence of serotype b was rather low (27), and the distribution of *A. actinomycetemcomitans* serotypes was influenced by the presence of *Porphyromonas gingivalis* (26).

In Indonesian subjects was observed that the mean increase in probing pocket depth between 1994 and 2002 was significantly greater in subjects culture positive in 2002 in comparison to subjects without detectable *A. actinomycetemcomitans* in 2002 (28). This confirms that subgingival presence of *A. actinomycetemcomitans*, but not a specific serotype is associated with a higher degree of inflammation (6).

In Brazil, an association between serotype b and healthy periodontium and between serotype c and chronic periodontitis was observed (22), differing from other data, which associated serotype b strains with patients with aggressive periodontitis (35). Aggressive periodontitis subjects were not exclusively associated with *A. actinomycetemcomitans* serotype b (31,35). In general, isolates from healthy subjects belonged to serotypes a or c (35). Serotype c was the most prevalent serotype among Brazilian *A. actinomycetemcomitans*, and they were isolated from various periodontal conditions, including aggressive periodontitis (35).

In a Greek population, *A. actinomycetemcomitans* was

more prevalent in untreated periodontitis subjects, but no clear predominance of a specific *A. actinomycetemcomitans* serotype and absence of the JP2 clone were observed (33). In Sweden, the findings indicate that periodontitis affecting the primary dentition does not necessarily indicate the presence of periodontal attachment loss in the permanent dentition (29).

Population genetic studies of *A. actinomycetemcomitans* suggest that it is clonal, consisting of genetically distinct subpopulations that correlate with the known serotypes (36,37). It has been proposed that the organism can be grouped into three major phylogenetic lineages comprising serotype b strains, serotype c strains, and serotype a, d, e and f strains (38). Associations between a single serotype b clonal lineage (JP2 clone) and the aggressive form of localized periodontitis in adolescents have been the focus of much investigation (12,39). The JP2 clone shows a limited geographical and ethnic host range, predominating in subjects with an African lineage but absent from non-African populations from Northern Europe (24,40).

The studies have varied widely in periodontal disease diagnosis and status, sampling protocols, study design and microbial detection methods and serotype analysis techniques, hindering comparison of the studies.

The elimination of *A. actinomycetemcomitans* from periodontal pockets has long been considered a target of periodontal therapy, and has been correlated with stable outcomes of treatment. If *A. actinomycetemcomitans* continues to be highly associated with disease development, its detection may be used as a risk marker for disease progression.

The findings from the studies reviewed indicate that different ethnic groups are preferentially colonized by different *A. actinomycetemcomitans* serotypes and the relationship between different *A. actinomycetemcomitans* serotypes and periodontal conditions remains unclear.

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#### **Conflict of interest**

The authors declare that they have no conflict of interests related to this study.