Prevalence and progression of untreated periodontal disease in a young Indonesian population
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SUMMARY AND CONCLUSIONS

CHAPTER 8

During the last decades, epidemiological cross-sectional studies have shown that periodontal diseases start early in life and increase in severity with age. The fact that, in some individuals, gingivitis develops into periodontitis, several possible risk factors have been identified, e.g. gender, plaque, calculus, existing attachment loss and the like.

In CHAPTER 1 the perspective of the last decades in relation to this concept of risk is described. Although cross-sectional studies of clinical and microbiological factors can be meaningful, longitudinal studies are needed to study the natural history of a disease and its determinants. Knowledge of the natural history allows analysis of potential factors and conditions that may have an impact on the disease process, possibly resulting in the development of effective control measures.

Such knowledge will facilitate in the identification of individuals for whom periodontal disease will become a serious oral health problem prior to the development of irreversible periodontal damage, and in the application of effective preventive measures.

In order to establish possible clinical and microbiological risk factors, a longitudinal study was initiated in a young population deprived of regular dental care in 1987. All inhabitants in the age range 15–25 years, living in a village with approximately 2000 inhabitants at a rest estate on Western Java, Indonesia, were examined clinically and microbiologically.

Clinical and microbiological baseline data (CHAPTER 2). In CHAPTER 1 the baseline cross-sectional data obtained in 1987 in terms of the clinical periodontal condition and prevalence of periodontal diseases in the oral cavity are described. In total, 255 adolescents, comprising 130 males and 125 females, participated in the study. Samples for bacteriological examination were taken from the gingiva, the mucosa of the tongue, and the saliva. Plaque index, bleeding upon probing, pocket depth, and attachment loss (AL) were recorded on the approximal surfaces from the vestibular aspect of all teeth as
CHAPTER 8

SUMMARY AND CONCLUSIONS
During the last decades, epidemiological cross-sectional studies have shown that periodontitis is universal, that this disease starts early in life and increases in serenity with age. The fact that in some individuals, gingivitis develops into periodontitis, is still a matter of extensive research. At present, several possible risk factors for the initiation and progression of periodontitis have been identified: age, gender, plaque, calculus, existing attachment loss and the presence of certain periodontal bacteria. In CHAPTER 1 the perspective of the research over the last decades in relation to this concept of risk is described. Although cross-sectional studies of clinical and microbiological factors can be meaningful, longitudinal studies are needed to study the natural history of a disease and its determinants. Knowledge of the natural history allows analysis of potential factors and conditions that may have an impact on the disease process, possibly resulting in the development of effective control measures. Such knowledge will facilitate (i) the identification of individuals for whom periodontal disease will become a serious oral health problem, prior to the development of irreversible periodontal damage, and (ii) the application of effective preventive measures.

In order to establish possible clinical and microbiological risk factors, a longitudinal study was initiated in a young population deprived of regular dental care. In 1987 all inhabitants in the age range 15 - 25 years, living in a village with approximately 2000 inhabitants at a tea estate on Western Java, Indonesia, were examined clinically and microbiologically.

Clinical and microbiological baseline data (CHAPTER 2)

In CHAPTER 2 the baseline cross-sectional data obtained in 1987 in terms of the clinical periodontal condition and prevalence of periodontal bacteria in the oral cavity are described. In total 255 adolescents, comprising 130 males and 125 females, participated in the study. Samples for bacteriological examination were taken from the gingiva, the dorsum of the tongue, and the saliva. Plaque index, bleeding upon probing, pocket depth, and attachment loss (AL) were recorded on the approximal surfaces from the vestibular aspect of all teeth as
well as the mid-vestibular and mid-lingual aspects of the Ramfjord teeth. Calculus was scored only on the four surfaces of the Ramfjord teeth. Following the clinical measurements the deepest bleeding pocket with no clinical loss of attachment was sampled for microbiological examination. In addition, in 37 subjects a deep bleeding pocket (≥4 mm) with at least 4 mm of attachment loss was sampled. The microbiological analysis included phase-contrast microscopy for evaluation of the presence of cocci, rods, motile rods and spirochetes as well as immunofluorescent evaluation of the presence of *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis* and *Prevotella intermedia*. Moderate periodontitis (max. AL 3 or 4 mm) was found in 26% of the population, advanced periodontitis (max. AL ≥5 mm) in 8%, whereas 66% of the population showed no or minor periodontitis (max. AL ≤2 mm). *A. actinomycetemcomitans* was found in 57% of the population, *P. gingivalis* in 87%, *P. intermedia* and motile rods in all cases and spirochetes in 89%. Of all the sampled sites of the oral cavity *P. gingivalis* (66%), *A. actinomycetemcomitans* (37%) and spirochetes (63%) were most frequently detected in the sampled pockets without attachment loss. Motile rods were most prevalent on the tongue and in the saliva (92% and 89% respectively). *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia*, motile rods, and spirochetes were observed in abundance in the saliva, on the dorsum of the tongue and gingiva as well as in the pocket, both in sites with and without attachment loss. No significant association between the clinical periodontal parameters and the prevalence of the micro-organisms was observed at a patient level. At a site level both *P. gingivalis* and spirochetes were more prevalent in sites with attachment loss.

The effect of sibling relationship on the periodontal condition (CHAPTER 3)

Since the study population described in CHAPTER 2 was derived from 1 village, it included relatively many siblings. This opened up the possibility for investigating the effect of sibship on the periodontal condition. Because family units consisting of 2 siblings are, from a statistical point of view, not adequate for a proper analysis, only family units consisting of 3 or more subjects were included in the present study. Consequently, for this study 23 family units
consisting of 3 or more siblings could be selected, including a total of 78 subjects. In this population the effect of sibship on the periodontal condition and oral microflora was studied. The mean approximal loss of attachment was 0.29 mm. The individual mean ranged from 0 to 1.27 mm. To quantify the extent of periodontal involvement in the individual dentition, the number of sites with a probing depth of ≥5 mm in conjunction with attachment loss ≥2 mm was determined for each subject. In an ANCOVA-model, the within-family variance was compared to the between-family variance. When the within-family variance was significantly smaller than the between-family variance an effect of sibship was considered to be present. Such an effect was observed for several microbiological parameters, however with no relationship to the periodontal condition. Clinically a significant effect of sibship was found for plaque, calculus and loss of attachment. These results support the hypothesis that periodontitis aggregates in families.

Longitudinal clinical data and prospective clinical and microbiological risk assessment (CHAPTER 4)

CHAPTER 4 describes the clinical periodontal condition at baseline (1987) and at follow-up (1994), 7 years later, in the 167 subjects that could be re-evaluated. In 1994 the same clinical procedure was carried out as in 1987. The purpose of this study was to investigate the relationship between progression of the disease and baseline clinical and microbiological data. Mean values at baseline and at follow-up were plaque index (PI): 1.01 and 1.15, bleeding on probing (BOP): 0.80 and 1.16, pocket depth (PD): 3.26 mm and 3.32 mm, attachment loss (AL): 0.33 mm and 0.73 mm, respectively. All parameters except PD showed a statistically significant increase over the 7-year period. In the 160 subjects, the prevalence of the studied bacteria irrespective of the sample site was: A. actinomycetemcomitans 53%, P. gingivalis 88%, P. intermedia 100%, spirochetes 89% and motile micro-organisms 100%. At the full mouth level, logistic regression showed significant odds ratios for progressive disease with age (1.15), subgingival calculus (1.20) and subgingival presence of A. actinomycetemcomitans (4.61). Presence of any of the selected micro-organisms on the mucous membranes was not related with progressive
disease. In order to study local factors to explain local disease activity, each subject was characterized using the sampled pocket, which was the deepest bleeding pocket without AL at baseline, as a single response site per patient. In this constrained design, the main statistical factors associated with progressive disease were presence of motile micro-organisms and the plaque score. At the full mouth level, 3 main risk markers for disease progression were identified: age, amount of subgingival calculus and subgingival presence of A. actinomycetemcomitans.

Subgingival microbiota in relation to experienced progression of periodontitis (CHAPTER 5)
In CHAPTER 5 the experienced progression of disease between baseline (1987) and follow-up (1994) is investigated in relation to the composition of the subgingival microbiota at follow-up. In 1994 the same clinical procedure was carried out as in 1987. At this time, the microbiological procedure included only the analysis of the subgingival microbiota. For this purpose, a pooled sample of the deepest pocket in each quadrant was obtained and analyzed, using microbiological culture techniques. Full, clinical and microbiological evaluation was completed in 158 of the 167 subjects available at follow-up. At baseline the mean values of the clinical parameters were AL = 0.35 mm, PI = 1.01, BOP = 0.80, PD = 3.25 mm and number of sites with subgingival calculus (NSC) = 6.04 and at follow-up AL = 0.75 mm, PI = 1.16, BOP = 1.19, PD = 3.34 mm and NSC = 5.85. All parameters except PD and NSC showed a statistically significant increase. At follow-up the prevalence of A. actinomycetemcomitans was 40%, of P. gingivalis 67%, of P. intermedia 66%, of Fusobacterium nucleatum 79%, of Bacteroides forsythus 16%, of Campylobacter rectus 4%, and of P. micros 6%. No differences in clinical parameters were found between groups with or without these micro-organisms. In 129 subjects AL of ≥2 mm at ≥1 site was found. Logistic regression showed three significant odds-ratio’s for experienced progressive periodontitis: Plaque index (12.2), gender (3.4) and A. actinomycetemcomitans (2.9). This means, that more plaque increases the odds for progression of periodontitis to a large extend. Females have lower odds for progression of disease. Presence of A. actinomycetemcomitans may increase
the odds for progression of disease. It is feasible to suggest, that in addition to aiming for low levels of plaque, one of the goals of periodontal treatment may be the eradication of *Actinobacillus actinomycetemcomitans* from the subgingival microbiota of periodontitis patients, especially when considering the present findings, the prospective data in CHAPTER 4 and both the past and current literature.

**Longitudinal evaluation of the development of periodontal destruction in spouses (CHAPTER 6)**

It has been suggested that putative periodontal pathogenic bacteria can be transmitted from one subject to another. The latter may consequently develop periodontitis. Since the study population described in CHAPTER 5 included in 1987 32 married couples, it was possible to study longitudinally the influence of being married on the development of periodontal destruction in spouses. In 1994, 23 of these couples could be retrieved. The mean age of this group of subjects was 29.1 years and the couples were married on average for 10 years. For each couple, the partner with the highest mean score for mean loss of attachment in 1994 was classified as the affected proband. The other partner was classified as the spouse. The microbiological culture revealed a relatively high prevalence of *A. actinomycetemcomitans* (50%), *P. gingivalis* (67%), and *P. intermedia* (61%). Analysis showed no differences in composition of the microflora between diseased probands and spouses. Among the 23 *A. actinomycetemcomitans* positive subjects, 2 positive couples were present. Furthermore, among the 31 *P. gingivalis* and 28 *P. intermedia* positive subjects, 9 and 7 positive couples were found, respectively. The clinical data showed that: (1) in 1987, the affected probands already had a worse periodontal condition as compared to that of the spouses; (2) in both probands and spouses the mean attachment loss increased during the 7-year period; (3) the difference in mean attachment loss between affected probands and spouses, as observed in 1987, increased in the period up until 1994. Therefore, 10 years of cohabitation showed no influence of the periodontal condition of the proband on the periodontal condition of the spouse.
Relation of data from deepest pocket per quadrant to full-mouth scores (CHAPTER 7)

When the subgingival presence of periodontal pathogens is studied in groups of patients or populations, mostly a number of the deepest sites is sampled. The mean clinical parameters of these deep sites are also frequently used as a descriptor of the clinical situation of these subjects. CHAPTER 7 describes to what extent the natural progression of periodontitis as measured in the deepest approximal pocket in each quadrant reflects the disease progression at the approximal sites on a full-mouth level. Therefore, the deepest pocket in each quadrant was determined at follow-up. The changes in clinical parameters PI, PD and AL between baseline (1987) and follow-up (1994) were calculated both as full-mouth mean scores and means for these 4 deepest sites. A regression analysis was used to evaluate the relationship between full-mouth score and the 4 test sites. For disease progression between baseline and follow-up, significant correlation coefficients were observed between the 4-site and full-mouth mean changes (PD: $r = 0.80$, AL: $r = 0.70$, PI: $r = 0.77$). Regression coefficients were 0.51 for PD, 0.35 for AL and 0.55 for PI. The precision of the estimate for the full-mouth mean, as predicted by the 4-site mean, is determined by the residual standard deviation: for PD 0.31 mm, for AL 0.31 mm for PI 0.29. In the present population, a reasonable to good correlation between full-mouth and 4-sites data was observed. However, the high residual standard deviation in the regression analysis illustrates the inaccuracy for the 4-site data, when used as a descriptive for changes in the periodontal condition on a full-mouth level. Data evaluating progression of periodontitis based on a limited number of diseased sites should be interpreted cautiously.

In conclusion, the results of the research, which is described in this thesis, elucidate the rôle of a number of risk factors in the natural history of progressive periodontal disease. At least 10 years of cohabitation showed no influence of periodontal condition of the affected proband on the periodontal condition in spouses. Furthermore, in this population, it was found that loss of attachment was associated with sibship. This confirms the assumption, that there is a genetic background to periodontal disease. These results question the
rôle of a periodontally diseased subject as a source for the spread of periodontitis merely through infection. Both in CHAPTER 4 and 6 it is clear that the main influence on the risk of progression of periodontal disease is the amount of plaque. The amount of subgingival calculus was a prospective risk marker in this untreated population. Comparison of CHAPTER 4 and CHAPTER 6 learned that there is an effect of age on the odds for progression of periodontitis. This, however, might be explained by the finding that older subjects tend have more plaque than younger subjects. In agreement with the current literature, females were less prone to periodontal disease. Another risk marker for progression of periodontal disease appeared to be the subgingival presence of *A. actinomycetemcomitans*. In addition the numbers of *P. gingivalis* related to the amount of attachment loss, when this micro-organism was present in the subgingival plaque.

Overall, the findings in this thesis suggest, that subgingival presence of *Actinobacillus actinomycetemcomitans*, the amount of subgingival calculus and, above all, the amount of plaque are the most important risk factors in the progression of untreated periodontitis. The influence of plaque is to such an extent, that analysis of risk should always take this factor into account, by including plaque scores as co-factor into the analysis.
in conclusion, the results of the research, which is described in this thesis, elucidate the role of a number of risk factors in the natural history of progressive periodontal disease. At least 10 years of consultation showed no influence of periodontal condition of the affected proband on the periodontal condition in spouses. Furthermore, in this population, it was found that loss of attachment was associated with age. This confirms the assumption that there is a genetic background association with disease. These results question the