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### Java project on periodontal disease. Periodontal condition in relation to vitamin C, systemic conditions and tooth loss

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**Publication date**

2014

**Document Version**

Final published version

[Link to publication](#)

**Citation for published version (APA):**

Amaliya, A. (2014). *Java project on periodontal disease. Periodontal condition in relation to vitamin C, systemic conditions and tooth loss*. [Thesis, externally prepared, Universiteit van Amsterdam].

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## Chapter 7

### Summary and conclusions

Numerous studies have shown an association between periodontal disease and a number of putative periodontal pathogenic bacteria. However, the host response, which may be of decisive importance for the disease, is influenced by genetic predisposition, systemic and environmental conditions as well as life style factors. In this respect an increasing number of studies have shown an association between periodontal disease and several predisposing factors such as smoking, diet and diabetes mellitus type 2. In 1987 a longitudinal prospective study was initiated to investigate the natural history of periodontal disease in an Indonesian rural population deprived from regular dental care (Van der Velden et al. 2006). Fifteen years later, in 2002, the participating subjects were examined for the third time. For that examination 128 subjects could be retrieved of the original group of 255 subjects. Clinical measurements included evaluation of plaque, bleeding on probing, pocket depth and attachment loss. The results showed that 20% of the population developed severe periodontitis. Unfortunately a number of the above mentioned predisposing factors were not included in this study. Therefore, additional studies of this population were initiated to further elaborate on possible factors that might have contributed to the variation in the severity of the disease.

In CHAPTER 2 research is described that studied the relationship between plasma vitamin C levels and the severity of periodontitis in the above mentioned study population. In 2005, 123 out of 128 subjects could be retrieved who were present in the examination of 2002. In these 123 subjects plasma vitamin C levels were assessed from non-fasting venous blood samples. Information about the subject's dietary habits during the last month was obtained by means of a personal interview guided by a questionnaire. Results showed that plasma vitamin C levels ranged from 0.02 to 34.45 mg/l with a mean of 7.90 mg/l. Analysis showed a statistical significant inverse relationship between plasma vitamin C levels and periodontal attachment loss, as assessed in 2002. Subjects with vitamin C deficiency (14.7% of the study population) had more attachment loss compared to those with depletion or normal plasma vitamin C values. The negative association between plasma vitamin C levels and periodontal attachment loss suggested that vitamin C deficiency may contribute to the severity of periodontal breakdown.

As discussed above it may be suggested that, in addition to vitamin C, the amount of periodontal destruction in this population may have been influenced by other environmental factors and systemic conditions. This was investigated in a study conducted in 2011 (CHAPTER 3), in 98 of the 123 subjects who had participated in the 2005 survey. A full set of dental radiographs was obtained of each subject and amount of alveolar bone loss was

assessed. In addition, the following parameters were evaluated: plasma vitamin C, vitamin D, HbA1c and CRP, the haptoglobin phenotype, the presence of putative periodontopathic bacteria and viruses, dietary habits, smoking and anthropometrics. Results showed that in this population 45% showed vitamin C depletion/deficiency, 82% had vitamin D insufficiency/deficiency, 70% were in a pre-diabetic state, 6% had untreated diabetes, 21% had relatively high CRP values ranging from 3.1-16.1mg/l. Analysis showed no relationship between amount of alveolar bone loss and the plasma levels of vitamin C, vitamin D, HbA1c as well as haptoglobin phenotype. However, the BMI, numbers of subgingival *P. gingivalis* cells, plasma CRP values and number of guava fruit servings were significant predictors, explaining 19.8% of the variance of alveolar bone loss. *P. gingivalis* and CRP showed a positive relationship with the amount of bone loss whereas BMI and guava fruit were negatively related. Post hoc analysis regarding the relationship between BMI and bone loss showed that the lower decile of this population, having a BMI  $\leq 19$ , had significantly more bone loss than the remaining part of the population. In contrast to the results of described in chapter 2 in this study no relationship was found between plasma vitamin C values and periodontal breakdown. This discrepancy is most likely due to the fact that in this study fasting blood samples were taken whereas the results in chapter 2 were obtained from non-fasting blood samples. In conclusion, results of this study suggest that elevated levels of *P. gingivalis* may be indicative for the risk of periodontitis progression whereas increased consumption of guava fruit, containing relatively high amounts of vitamin C, may play a protective role in periodontitis of a malnourished population.

Since the results of the previous studies showed that a substantial part of this population has a shortage of vitamin C, a vitamin C supplementation study was initiated in the same 98 subjects of the previous study (CHAPTER 4). For vitamin C supplementation, a commercially available vitamin C supplement was chosen that contained per tablet not only 200 mg vitamin C but also 100 mg citrus flavonoids. The choice for a product that includes citrus flavonoids was based on the idea to get a supplement similar to fruit. Subjects were instructed to consume one tablet a day for 90 days. The effect of supplementation was studied on the following parameters: plasma levels of vitamin C, HbA1c, CRP and the subgingival load of putative periodontopathic bacteria and viruses in periodontal pockets. The mean plasma vitamin C value at baseline was 5.19 mg/l and included 44 subjects (45%) who showed plasma vitamin C values  $<4.0$  mg/l. After supplementation, in all individual subjects the plasma vitamin C values rose to levels above 4.0 mg/l with a mean of 12.1 mg/l, ranging from 4.1 to 21.2 mg/l. After supplementation all subjects had lower HbA1c levels than

before, interestingly 41% of the subjects in the pre-diabetic group changed to the normal group. CRP levels were also lower in all individuals after supplementation than before, decreasing from 2.16 to 0.94 mg/l. For all studied bacteria i.e. *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia*, *T. forsythia*, *P. micra*, *F. nucleatum* and *T. denticola*, and Epstein Barr virus a significant decrease in their quantity was found after supplementation. In conclusion, in this population with poor dietary conditions supplementation of vitamin C in combination citrus flavonoids resulted in a substantial improvement of the systemic condition.

As mentioned before, the 98 subjects of the above described studies also participated in a prospective longitudinal study on the natural history of periodontal disease that started in 1987. Therefore it was possible to study in these 98 subjects the relative contribution of caries and periodontal disease to tooth loss over a 24 year period (CHAPTER 5). For this purpose the full set of dental radiographs as obtained in 2011 was used in combination with the survey forms and clinical slides of the research carried out in 1987, 1994 and 2002. Results showed that 37 subjects lost no teeth whereas 61 subjects lost in total 185 teeth. In this latter group 45.9% lost 1 or 2 teeth, 32.8% lost 3 or 4 teeth and 19.7% lost  $\geq 5$  teeth. In the majority of subjects most teeth were lost due to caries. In 5 subjects tooth loss could be attributed to periodontal disease, whereas in 4 subjects teeth were lost due to both caries and periodontal disease. Analyses of the predictor variables age, gender, smoking habits and education level showed that only age and gender correlated with tooth loss. In the logistic regression analysis only age remained significant. It was concluded that in this population the majority of teeth were lost due to caries and to a minor extent due to periodontal disease.

#### Conclusions:

On the basis of the data obtained from a population deprived from regular dental care it may be concluded that:

1. Inadequate vitamin C supply contributes to a poor periodontal condition.
2. Large inter-individual differences exist regarding the capacity of vitamin C absorption.
3. Supplementation of 200 mg vitamin C daily is enough to achieve plasma vitamin C levels  $> 4.0$  mg/l, also in subjects with a poor capacity of vitamin C absorption.
4. Daily supplementation of 200 mg vitamin C in combination with 100 mg citrus flavonoids is able to reduce HbA1c and CRP levels in all subjects of this periodontally diseased population.

5. In populations with poor dietary conditions emphasis should be paid by the authorities to improve fruit intake.
6. In most subjects with severe periodontal breakdown it still takes many years before teeth are exfoliated spontaneously. Moreover, it may take more than 24 years before a root remnant is exfoliated.
7. In terms of tooth loss, caries is a bigger problem in this remote population than periodontitis
8. In populations with poor dental conditions the authorities should pay more attention to prevention of dental and periodontal diseases by means of education and preventive measures.