Reviewer's report

Title: Dental Health, Cardiovascular Disease Risk Factors, and Systemic Inflammation in a Pediatric Rural Community Cohort

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Reviewer: Giuseppina Campisi

Reviewer's report:

General comments:
The authors present the results of a study to investigate associations between dental health, cardiovascular disease risk factors, and systemic inflammation in children.

The topic of this study addresses current research issues in the field of paediatric community. However, a number of concerns and flaws have been raised during the evaluation and I would therefore encourage the authors to restyle the paper (highlight limitations and decrease level of statement like “relationship between dental health and hygiene and CVD risk and systemic inflammation”, since nothing is definitely proved) and or better to enrich the paper introducing in M&M objective parameters of oral health such as intra-oral examination, collection and analysis of saliva and gingival crevicular fluid samples, or measurement of the amount of volatile organic compounds in oral cavity.

At the following standard points, the answers are:

1. Is the question posed by the authors well defined? NO
2. Are the methods appropriate and well described? NO
3. Are the data sound? NO
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Quite YES
5. Are the discussion and conclusions well balanced and adequately supported by the data? NO
6. Are limitations of the work clearly stated? NO
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? YES
8. Do the title and abstract accurately convey what has been found? YES
9. Is the writing acceptable? YES A PART FROM THE TABLE

Specific Major Compulsory Revisions
The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical
Abstract:
Methods: “Screening included anthropometric assessments, blood collection, and a questionnaire about oral health and dental habits”. A questionnaire is inadequate for evaluating oral health, especially in children.
Results: “Participants ranged from 3.0-18.7 years”. Please to move this sentence in Methods.
“ In multivariable OLS regression ….”. Please not use abbreviations in the Abstract.
Conclusions: “This is the first known study of the relationship between dental health and hygiene and cardiovascular disease risk and systemic inflammation in children”; conclusions with a too strong statement for a study based on a dental questionnaire.
Please correct “counties”;
Introduction:
This section needs extensive re-writing.
The first paragraph of this section is focus solely on the tooth decay in primary teeth of children.
Several studies (Guiglia et al. 2008; Scannapieco et al. 2003; Mattila et al. 2000; Beck et al. 2001) have demonstrated that there is an association between cardiovascular disease and periodontal disease. Therefore, periodontal diseases should be also investigated. Also the authors cited the periodontal diseases in the second paragraph of the Introduction and in the Discussion. Why the authors have not include the periodontal parameters in this study?
In the third paragraph of this section, the authors did not find any cited reference regarding the association between oral health in children and risk for other chronic health conditions. The authors may cite the several relevant articles as follows:


In the third and fourth paragraphs of this section the authors have cited “robust dental hygiene” and “dental hygiene practices”. At present it is known that for evaluating dental hygiene it is necessary to effect an intraoral examination and examine at least the presence of plaque (index of plaque).

In adults, periodontal status for all teeth present, including proportional distributions for the presence of plaque (index of plaque), pocket probing depth (PPD), and bleeding on probing (BOP) are usually calculated. The number of teeth with visible signs of gingival recession, and the number of remaining teeth should be also accounted. A visual check for cavities should be performed. Oral/pharyngeal soft tissue should be also examined to detect mucosal inflammatory conditions.

In children, it is possible to effect non-invasive tests such as collection and analysis of saliva and gingival crevicular fluid samples and tests for measuring the amount of volatile organic compounds in oral cavity. In fact, gingival crevice fluid and saliva contain a large repertoire of serum proteins, inflammatory mediators, host cell degradation products and microbial metabolites, and a variety of enzymes that degrade proteins, proteoglycans, lipids and carbohydrates. Enzymes, especially proteinases, play a central part in the control of periodontal tissue turnover in health and in the tissue destruction that characterizes diseases of the periodontium. Moreover, several studies (Torresyap et al. 2003; Haffajee et al. 1994; Sculley et al. 2003, Takane et al. 2002; Haynes et al. 2003; Phillips et al. 2005, Zhou et al. 2004) have demonstrated that a focus of oral infection (e.g. gingivitis or periodontitis) generates increased oxidative stress, resulting in increased oxidation of LDL-cholesterol and accelerated atherosclerosis, thereby increasing the risk of coronary heart disease and stroke. Volatile organic compounds (VOC) (e.g. sulphur-containing compounds) (Torresyap et al. 2003), even at low concentrations, are highly toxic to tissues and may contribute to the onset of gingivitis and periodontitis (Haffajee et al. 1994).

Materials and Methods:

1. Inclusion and exclusion criteria of selection people are not described.
2. In this study, only a questionnaire has been chosen for evaluating dental health. The rationale of choosing this questionnaire is not clear and appears inadequate.

Why did authors not list the inflammatory markers considered in the methodology?

Which are the exclusion criteria for recruitment of the study population? I think that pre-existent cardiovascular condition were, certainly, excluded.

Statistical analysis section:

How did authors process data in the multivariate analysis? Were data adjusted for all cardiovascular risk factors? Please re-write this paragraph

Results section:

Which are the baseline mean values of cytokine and inflammatory variables considered in this investigation? The table should be more clear. Which is the mean BMI value? Did any child had diabetes?

Table 6: it would be important to show the results of TNF-alfa as specified in the abstract and results section?. Moreover in this table the authors listed as independent variables only Age at Screening, Gender, Parent Education, Waist Circumference, Frequency of Flossing, LDL. Why?

Why the authors did not include HDL, diabetes, blood pressure, diagnosis of metabolic syndrome in the analysis?

Which is the area under ROC curve to predict inflammatory activation in relation to dental health in the children?

Do have authors any data on IL-6 and IL-1 and fibrinogen?

Probably, it would be necessary before data processing to perform the baseline cardiovascular risk stratification of the children. Please demonstrate clearly that the association between dental health and inflammation is independent on metabolic syndrome, diabetes, blood pressure, HDL, BMI.

Discussion:

This section needs extensive re-writing.

1. The authors should compare their findings with previous publications, described above.

2. The first and second paragraph is dedicated to repeat information described in other sections.

3. In the second paragraph of this section, the authors have cited the periodontal disease but in this study any objective evaluation of the periodontal status has been made in the young patients.

4. In the third paragraph of this section, the authors have cited the flossing methods. Objectives means should be used to evaluate the correct oral hygiene of the patients. It is insufficient to use only a questionnaire.
5. In the sixth paragraph of this section, the authors have noted that “responses by parents and children were very similar”. Scientific data should demonstrated this sentence.

6. In the seventh paragraph of this section, the authors have reported only the recommendations: "The initial results reported here clearly highlight the importance of preventive dental care in overall, systemic health. The implications for preventive health care suggested by these results include reinforcing the importance of daily brushing and flossing and biannual dental cleanings…”. These conclusions are foreseen and not innovative.

This section is too far. Thus the authors must focus on the purpose of the investigation as well as the article is entitled: “Dental Health, Cardiovascular Disease Risk Factors, and Systemic Inflammation…”

For example, the authors specified, opportune, that 16.1% of participants had the metabolic syndrome, and 67.2% had at least 1 cardiovascular disease risk factor. Please comment and cite this article: Steven M. Haffner, The Metabolic Syndrome: Inflammation, Diabetes Mellitus, and Cardiovascular Disease. Am J Cardiol 2006;97[suppl]:3A–11A.

Please, discuss more clearly the relationship between dental health, systemic inflammation and cardiovascular risk also in the light of previous reports. Please discuss the clinical and future implications of these findings (the importance of preventive dental care).

Please discuss the limitation of the study.

Minor Essential Revisions

The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.

Re-write more clearly all the tables.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'