

# Low birth weight and periodontal diseases association

Florianópolis, November 9<sup>th</sup> 2005.

## Dear Editor,

The article published in the *Revista de Saúde Pública* (Journal of Public Health) by Cruz et al<sup>1</sup> reported the association between low birth weight babies and mothers' periodontal disease. A scientific clarification of the role of the periodontal disease in pregnant women for preterm and low birth weight is important and has been widely investigated. Contrary to the findings by Cruz et al,<sup>1</sup> studies using adequate methodologies and designs do not find an association.<sup>2</sup>

What is the evidence for and against the association? There are plausible biological pathways. Prostaglandins E<sub>2</sub> (PG-E<sub>2</sub>), tumoral necrosis factor alpha (TNF- $\alpha$ ) and other cytokines are produced in periodontal disease. They trigger early labor resulting in preterm babies. In addition, such cytokines might interfere with fetal growth by inducing hypertension and secondary uterine vascular changes resulting in low birth weights. Despite having biological plausibility, some critical points must be considered before to announce conclusive results. Periodontal disease results in cytokines production. That occurs in intermittent episodes of "periodontal bursts". The episodes occur throughout life with long periods of quiescence. Second, even if during pregnancy the periodontal sites are active, a very low level of periodontal disease-related cytokines are produced.<sup>5</sup> Finally, such cytokines produced in the mouth need to migrate and achieve sufficient levels in the placenta region to accelerate labor and restrict nutrients to the fetus. Therefore, to check if the proposed mechanism is possible, it is necessary to identify before the pregnancy whether there is periodontal disease. It is imperative in studies planned to test this hypothesis, that the gestational age is correctly assessed and to analyze separately the babies delivered on term and those preterm. In addition, it is essential to obtain sound information about confounders (eg. tobacco before pregnancy), and to control for them in the analysis. In the paper by Cruz et al<sup>1</sup> the commonly recognized association between smoking and low

birth weight was not found, which suggests that this information was not adequately collected.

Although some studies found a positive association between periodontal disease and increased risk for undesirable pregnancy outcomes, the shortcomings in the methods used by them, casts serious doubts on the validity of their outcomes and conclusions.

Overall, there is not enough scientific evidence to support such an association.

There are only three published clinical trials that tested the hypothesis that periodontal treatment among pregnant women would reduce the incidence of preterm and low birth weight.\* Only one of them, showed a protective effect of periodontal treatment for gestational outcomes. Observational prospective studies did not find such an association.<sup>3,4</sup>

From a public health point of view, important questions arise from the research results like those published by Cruz et al:<sup>1</sup> should we alert pregnant women or those intending to get pregnant, to seek periodontal care to avoid preterm low birth weight babies? Is it ethical to arouse fear in women when there is no sound evidence of a relationship between periodontal disease and pregnancy outcomes? The answers to both questions are no. What is the impact of such information on the lay press and in the health services? Most importantly, in countries like Brazil, where access to dental and health services is limited, claims about an association between periodontal disease and undesirable pregnancy outcomes could create an artificial and unnecessary demand for health services that waste valuable resources.

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## AUTHORS' ANSWER

Salvador, November 18<sup>th</sup> 2005.

**Dear Editor,**

In their letter, Vettori, Sheiham and Peres raised theoretical, methodological and ethical questions regarding the article "Maternal periodontal disease as a factor associated with low birth weight".

We do understand that the building up of scientific knowledge is also marked out by debates like this. However, it is important to emphasize that the objective of the study in question was limited to verifying whether an association exists between maternal periodontal disease and low birth weight, without claiming to characterize this as causal or even to have exhausted the discussion about the matter. It can be clearly seen that at no time were the findings from our investigation presented with a "conclusive tone". The need to conduct further investigations with different methodological approaches with the aim of broadening the basis of evidence around this association was highlighted. Hypotheses of causality in epidemiology are strengthened through the existence of theories that support the biological plausibility and also the presence of strong associations between the variables studied. This is in addition to other criteria such as consistency, specificity, temporality, biological gradient, coherence, experimental evidence and analogy (Hill,<sup>2</sup> 1965).

On the other hand, we know that controversial topics must be worked up and put before our peers through

the channels for scientific communication (periodicals, congresses, seminars, etc.), since this procedure has been shown by the history of science to be an effective tool for enabling the emergence and establishment of new paradigms. Therefore, it is necessary and ethical to investigate the question of maternal periodontal disease as a factor associated with low birth weight and, especially, to discuss this within scientific forums set up for such purposes, even if the research findings available do not allow the hypothesis of causality to be categorically accepted or refuted.

We agree that it would be temerity to extract research techniques and inconclusive debates for application in public healthcare, without intermediation. But this has not been our practice as researchers, sanitarians and dental professionals.

Since 1996, renowned scientific periodicals have been publishing articles regarding the association between this oral infection and gestational complications. The majority of these articles have presented evidence of an association (Offenbacher et al,<sup>8</sup> 1996; Jeffcoat et al,<sup>3</sup> 2001; Lopez et al,<sup>6</sup> 2002a e 2002b). Up to July 2004 (when the manuscript of our article was first sent to this Journal), we had access to only three interventional studies testing the hypothesis that periodontal treatment in pregnant women would reduce the incidence of prematurity and low birth weight, published in the format of complete articles, namely: Mitchell-Lewis et al<sup>7</sup> (2001); Lopez et al<sup>6</sup> (2002); and Jeffcoat et al<sup>4</sup> (2003). Only the first of these did not find any evidence of an association. That study was not included in the limited list of references presented in our study because it had insufficient sample size and did not investigate the possible effect of intervening and confounding covariables on the association,

i.e. the covariables that would have the greatest possibility of presenting potentially fallacious results. We also chose not to refer to the article by Jeffcoat et al<sup>4</sup> (2003), even though it was favorable towards the association, since the authors themselves classified their work as a pilot study.

With regard to the questioning about the effect of smoking on this association, we suggest attentive reading of the discussion of our article, particularly in relation to the following excerpt:

“Another point suggestive of limitations [*to the quality of self-reported information*] was the absence of statistically significant differences between the groups, for important risk factors for low birth weight such as smoking during pregnancy and low height of the mother (Solla et al,<sup>20</sup> 1997). Widespread knowledge among the population regarding the damaging effects of smoking during pregnancy may have led to the denial of this habit by the pregnant or puerperal women.”

It can be seen through this that we understood and, in particular, accepted the limitations of the instrument for measuring the smoking habit. Nonetheless, we believe that the use of an imperfect measure, in a general manner, compromises the results of the study less than would a strategy of not investigating the effects of smoking as a coadjuvant for the occurrence of low birth weight.

Another pertinent question was in relation to the absence from the analysis of the variable of gestational age. However, the outcome was defined only as low birth weight because we agreed with the statement by Kramer<sup>5</sup> (1987) that the pattern for this complication is determined by the duration of the gestation and/or by fetal growth. In other words, the total number of infants with low birth weight will, in a general manner, include wrongly classified preterm newborns. This is far from rare, given the lack of complementary obstetric examinations, particularly in retrospective studies.

Finally, we highlight the fact that, since 2002, investigators from the Center for Research, Integrated Practice and Multidisciplinary Investigation of the Universidade de Feira de Santana, together with the Instituto de Saúde Pública and Faculdade de Odontologia da Universidade Federal da Bahia, and supported by the Research Support Foundation of the State of Bahia, have been discussing the hypothesis of this association, in a very responsible manner, in periodical seminars under the title of “Periodontia em Saúde Coletiva” [Periodontics in Public Health] (Anais<sup>1</sup>), which have had the participation of experienced researchers from Brazilian research centers, in the fields of both epidemiology and periodontics. Within our Center, studies on the association in question are in progress, with different types of delineation, in an attempt to adequately test the hypothesis of causality between maternal periodontal disease and low birth weight.

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