Reviewer's report

Title: Relationship of birth and first month of life in children and developmental defects of enamel

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Reviewer: peter arrow

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Review of “Relationship of birth and first month of life in children and developmental defects of enamel".

Authors: Mermarpour M, Golkari A, Ahmadian R.

The study is a cross-sectional study of children 9-11 years attending public and private schools in the city of Shiraz. Information on exposure factors were collected via parent completed questionnaire and derived from a mandatory “Health Status Evaluation Form”. The outcome of interest was determined by clinical assessment by two calibrated senior dental students. Exclusion criteria were applied. Data were analysed for associations between exposure and outcome factors using chi-square, logistic regression and Spearman’s correlation.

This reviewer has a few comments and a number of queries to the authors regarding the manuscript.

Abstract — The authors stated in the background section that, “the aim of the study was to identify …… conditions during the first month of life that can lead to DDE in permanent teeth. Lead implies a causal relationship, which the design of this study (cross-sectional study) is unable to do and the sentence should be rephrased accordingly.

Background — The authors have presented and reviewed the literature outlining what is known of the condition of interest. It would have been useful to delineate in some manner the different types of enamel defects that are discussed in the literature because the causal factors for different types of defects are likely to be different; for example some of the studies refers to molar incisor hypomineralisations, while others refer to hypoplasias. And also to focus on studies which discussed DDE in permanent teeth, if the focus of this study is to be on DDE in permanent teeth, as suggested by the background comments in the abstract.

Methods —

• The authors reported that 1000 children were sampled; this is a result and should be reported in that section.
• The authors selected girls’ school and boys’ school, some context for the reader to explain this is warranted, such as, are there only separate schools for girls and boys and no co-educational primary schools in Shiraz?

• From the description provided; 4 schools (2 boys’ and two girls’ schools) were selected from each of the 4 zones, which equates to 16 schools, and each school had 80 children sampled, which equates to 1280 children being sampled, which does not agree with the 1000 reported by the authors. An explanation is required for this difference.

• The reason/s for separation into the 4 geographic zones should also be provided.

• Sample size estimation (how determined) and the estimated number should be reported.

• The reasoning behind the criteria applied to exclude some children should be explained more fully, especially when some of the criteria may be associated with the occurrence of the outcome of interest, such as atypical restorations or fissure sealant applications, which are likely to be associated with the occurrence of severe hypomineralisations.

• The authors mentioned that fluoride level was the same throughout the city, the level should be reported, and clarified that it was the same across the geographical zones.

• The authors reported institutional ethical approval, and information on whether informed consent was sought and/or obtained by parents/carers of the children should also be reported.

• The section on collection of exposure factors needs clearer explanation. For example, were all information provided by the parent; as it is written, it seems to suggest that the information contained on the mandatorily completed “Health Status Evaluation Form” was obtained by the researchers “derived”, Line 129.

• Line 130, and “the parents were asked to refer to their children’s birth card when answering these questions”, further explanation of what questions and what the birth card is should be included. What information was sought by the questionnaire, how many questions and who was to complete the questionnaire should be included in the explanation of data collection methods. Do parents and carers have information relating to APGAR scores?

• The information on examiner training should be reported in a separate section and more information should be provided including how the training was undertaken. The authors reported an “alpha” of 0.73, this is unclear and given that there were 2 examiners both between and within examiner reliabilities should be reported.

• The authors reported using the modified DDE index. The modified DDE index used index teeth, and the age range of this study’s participants may not have all the index teeth present (an explanation what the index was, how it was scored etc. should be included). The authors need to explain how this was handled.

• On line 155, the authors mentioned that “each of the characteristics of birth
chi-squared test." What the characteristics are should be reported.

- On line 157 the authors mentioned “seven factors ……”, these seven factors should be reported.

Results —

- The authors reported the number who presumably consented (1000) in the methods section, some information on consent rate as well as number of returned questionnaires, how many were used etc. should also be provided. There should also be report on the number of teeth by type of teeth present, given that the age groups of children selected would have both primary and permanent teeth present (refer to comments in methods section regarding the DDE index used).

- The age distribution of the study participants should be reported.

- Table 1 as presented, showing the proportion with DDE with the factors as measured, is a bit confusing and the authors should reconsider presenting the information in an alternative form. Similar to Table 2, with the factors in one column and the outcome in the other two columns and then the statistical test findings in another column, but with minimal amount of borders to enable an uncluttered view of the table. Also in general it is preferable to present as n and %.

- Line 170 appears to evaluate a mean score; the statistical approach adopted for that should be included in the Methods section.

- The results should also present the prevalence of DDE by types of DDE; hypomin, hypoplasia, diffuse opacities or demarcated opacities etc., and types of teeth affected with DDE; permanent/primary teeth. Along with that, consideration then should be given to undertaking appropriate analyses.

- Line 191 presumably is referring to Spearman’s correlation, this should be made clear and the rho also reported.

- Overall the authors should make clear throughout the manuscript when they are referring to primary or permanent dentition because in some sections it is unclear, for example line 188 “81 children had at least one DDE” presumably is referring to at least one tooth affected. And also the number of excluded children with permanent tooth restorations should be reported.

- In Table 2 the authors presented the results from the logistic regression analysis; it would be useful to have the estimates derived from the coefficients and their interpretation as well as the p values presented.

- The authors should more clearly explain the methodology adopted in the multiple regression and the rationale behind their model development. Usually when multiple regressions are undertaken the results from the bivariate analyses are used to consider inclusion and exclusion from the overall regression model. Then the model is fitted and variables are retained or excluded from the model based on the contribution of the variable to the overall fit of the model or some theoretical understanding of the impact of the variable to the outcome under consideration (usually a well known confounder). The authors need to explain
why they have retained the variables they have given the bivariate findings and what criteria, if any, were used in the fitting of the model to determine retention in the model. The model should be the most parsimonious, consistent with the prevailing understanding of the subject matter.

Discussion —
• There should be some discussion on response rates, and potential for bias as a result of the response rates that as well as bias from exclusion/inclusion criteria.
• The authors’ commentary in the second paragraph is unclear to this reviewer. The developmental defects are, by their very definition defects which arise at a time when enamel development is taking place and, therefore the risk factors need to be present at those critical periods of enamel development to affect the enamel. Exposure to risk factors outside of this window of critical period is unlikely to lead to developmental enamel defects. Hence, the authors’ should expand on their use of the term “direct effects” and “indirect effects” in an epidemiological context and link it more clearly to the findings of their study.
• As outlined earlier it would be more useful if the discussion involved the effects of the measured factors on the types of DDE and also in relation to the types of teeth so that biological plausibility for the critical period can be evaluated, given that health conditions around the time of birth and within the first month of birth were primary factors of interest.
• The limitations of the study, outlined in the last paragraph Line 251 (parental recall) is critical to the study’s findings and more information should be provided in the methods section on how the information was collected and what, if any, measures were used to determine reliability of parental recall.
• Table 1 also suggests possibly significant differences in DDE occurrence among boys and girls from areas 3 and 4, which should be discussed.

General Comments —
• The authors mentioned in the introduction that DDE may cause problems for children and hence the need to understand the causes of such conditions. The impact of DDE is dependent on the type and severity of the defect and the authors have not presented differentiated information on the types of defects which is necessary for the reader to form an opinion on the likely impact of the presence of enamel defects on the health of the study participants. Grouping the defects under the umbrella of DDE is insufficient.
• There are some minor typographical and syntax errors within the manuscript, which should be corrected, some of which are listed (not exhaustive). For example, Line 71 “latter group of factors cause disturbances ……”, and Line 74 , “DDE to range………”, Line 87 there should be a space after the full stop and before Apgar, and Line 89, spelling for parenteral ? or perinatal?
• Line 76 “DDE may cause problems ……… lack of oral hygiene” should be rephrased, because it seems to suggest that DDE causes lack of oral hygiene, which is not the case.
• The sentence in Line 158-159 is unclear and should be rephrased.

• Line 167 should perhaps be “at least one tooth (or permanent tooth) ………..

• Line 181, the authors used the term “rate” when referring to a proportion, which is not strictly correct and the wording should be changed.

• Line 218, the sentence is unclear; what is the consistency with other studies on the importance of the infants health in relation to what? The reference is in relation to Apgar score to enamel defects in the primary dentition and the discussion should expand on how that finding relates to the findings in this study. As indicated before, the authors also should make clear whether they are referring to DDE in permanent teeth only, primary teeth only or both.

• The authors found no significant association with birth weight while there was an association with the Apgar score. Is it possible that the Apgar score may have subsumed the birthweight relationship given the likelihood of Apgar score’s association with birthweight? Some commentary on this would be appropriate.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests.