

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Dental caries and preterm birth: A systematic review and meta-analysis
AUTHORS	Wagle, Madhu; D'Antonio, Francesco; Reierth, Eirik; Basnet, Purusotam; Trovik, Tordis; Orsini, Giovanna; Manzoli, Lamberto; Acharya, G

VERSION 1 – REVIEW

REVIEWER	Associate Professor Ajesh George Western Sydney University, Australia
REVIEW RETURNED	01-Aug-2017

GENERAL COMMENTS	<p>I would like to commend the authors for undertaking this review. The area being explored is under-researched and this piece of work will make a valuable contribution. The paper is generally well written but I have provided some comments below to further refine the manuscript:</p> <p>Abstract Please include design</p> <p>Introduction Pg 3, line 34 It might be good to provide the potential pathophysiology on how dental caries may affect pregnancy outcomes. You have mentioned a few points in the discussion but I feel this is needed in the introduction to provide the reader a better understanding of the topic and further justify the review.</p> <p>Pg 3, line 36 You mention several studies but only have 2 references. You should provide a few more references that provide conflicting results</p> <p>Methodology Pg 4, line 21- You have provided the search strategy for Medline only – what about the other databases? You could include these in the supplementary files</p> <p>Pg 5, line 42- rather than outlining in detail the individual components of the NOS scale you could just highlight the 3 broad perspectives and actually include the tool in the supplementary files. That way the reader will be able to better understand Table 2 . You don't have to then repeat the scoring criteria's again in Table 2- you can just refer to the tool for this.</p>
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	<p>Pg 7, line 14 “Most of the included studies showed an overall good rate about the selection and comparability of the study groups, and for the ascertainment of the outcome of interest”- what do you mean by good- a bit more explanation here (scored at least 1 star in each of the categories?)</p> <p>Results Pg 7, line 25- Five studies explored the risk of PTB in women who compared to those who did not have caries- are there words missing ??? “who had caries”- does not make sense</p> <p>For your secondary outcomes I think you should mention in text how many studies were included in the analysis for DMFT and DMFS.</p> <p>Discussion My main concern is with this section. Your discussion is very short while your implication for clinical practice is very long. Many of the points discussed in implications needs to be moved to the discussion section.</p> <p>Pg 9, line 46: You should also strengthen the implication section with the following points:</p> <p>Even though you have found no relationship it is still important that health professionals promote oral health among pregnant women. This is because they are prone to dental problems and have limited knowledge and awareness about the importance of oral health and its potential impact on pregnancy outcomes. Further, having dental decay during pregnancy increases the risk of caries transmission after birth through certain feeding practices (you have touched on this but can be strengthened). This can lead to early childhood caries which is the most common chronic childhood disease.</p> <p>There are numerous references to support the above points</p>
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REVIEWER	Emmanuel Bujold Université Laval, Canada
REVIEW RETURNED	02-Aug-2017

GENERAL COMMENTS	<p>Abstract</p> <p>It should be more representative of the manuscript, including: (methods) appropriate dates of searches -march 2017 or Dec 2016- (results) Heterogeneity between trials, which is quite important and significant- absence of data for early PTB; and (conclusion) lack of good scientific evidences limiting the conclusions.</p> <p>Introduction Very well written. Good references.</p> <p>Methods. Excellent. Again please verify the date of searches: December 2016 (abstract march 2027).</p> <p>Results: Please provide more details about the absence of results (none of the studies provided data on early PTB??)</p>
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	<p>Discussion:</p> <p>Please discuss the fact that most studies evaluated women after deliveries, which could strongly influence the results. Please provide a better discuss about the heterogeneity observed between the studies. Please provide more details about the impact of not having data for early PTB that are typically associated with a greater risk of amniotic infection/inflammation.</p> <p>From my point of view, this is a well designed meta-analysis, which demonstrates an evident lack of good evidences in order to conclude about the association between dental caries and PTB.</p>
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REVIEWER	Elizabeth Thom George Washington University USA
REVIEW RETURNED	05-Oct-2017

GENERAL COMMENTS	<p>The word 'explore' is not really appropriate because the connotation is that it is not a pre-planned analysis adhering to standards. I think that 'evaluate' or 'estimate' would be better. In the abstract, the stated methodology is to estimate a summary odds ratio which is consistent with the results presented in figure 2; yet the results in the text are presented throughout as relative risks.</p> <p>The wording on page 4 “we aimed to stratify the analysis according to the type of PTB, and according to gestational age at birth...” gives the wrong impression – stratifying is usually by some covariate.</p> <p>These are really categorical secondary outcomes (e.g. the first one would be spontaneous preterm vs iatrogenic preterm vs term). The second “stratification” was a series of secondary outcomes comprising different definitions of preterm (e.g. gestational age <28 weeks). Moderate to late preterm was listed as <34 weeks – however, <34 weeks is early to moderate preterm – late preterm is usually 34-36 weeks.</p> <p>These secondary outcome data were not presented. The authors state that it was because of small numbers; however several of the studies were quite large so it is not clear why they could not at least show the numbers.</p> <p>In the following paragraph on line 51, the secondary “outcome” is not an outcome – it is a secondary “aim” or “objective”. For the NOS, the follow-up rate that was considered adequate should be specified. It is not clear why so many records were excluded (1766/1786). Is it because the search terms were so broad? It seemed that some of the outcomes searched on were irrelevant to preterm birth (eg postpartum hemorrhage).</p> <p>The authors do not state what a pre-planned interpretation of the I2 statistic might be. Nor do they comment on the observed I2.</p> <p>Minor and Wording Issues Line 9 page 3 rather than “these infants” remain at risk it would be better to say “infants born prematurely” or “preterm infants” . Line 16 page 3 – a reference is needed for the first sentence of the</p>
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	<p>second paragraph on this page Line 22 Periodontal disease has been shown... not “have been shown” Line 23 the word “assumption” is out of place – since it has just been stated that periodontal disease has been shown to carry an increased risk. Likewise “the fact that periodontitis may lead to...” sounds odd because it is a mixture of something rather certain i.e. “fact” with something very qualified i.e. “may”. The overall phrase might be better expressed as “the rationale for this association is based on the suggestion that periodontitis leads to maternal and fetal inflammation” or something similar. Line 44 page 5 “and the ascertainment outcome of interest” should be “ascertainment of the outcome of interest”. Line 46 page 5 Assessment of the selection of a study means something different than an assessment of the selection of the study groups. ...</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name

Associate Professor Ajesh George

Institution and Country

Western Sydney University, Australia

Please state any competing interests or state ‘None declared’:

None declared

Please leave your comments for the authors below

I would like to commend the authors for undertaking this review. The area being explored is under-researched and this piece of work will make a valuable contribution. The paper is generally well written but I have provided some comments below to further refine the manuscript:

Abstract

1. Please include design

Reply: Thank you for your comment. This has been done now.

Introduction

2. Pg 3, line 34 It might be good to provide the potential pathophysiology on how dental caries may affect pregnancy outcomes. You have mentioned a few points in the discussion but I feel this is needed in the introduction to provide the reader a better understanding of the topic and further justify the review.

Reply: Thank you. We have added this in the introduction section.

3. Pg 3, line 36 You mention several studies but only have 2 references. You should provide a few more references that provide conflicting results

Reply: Thank you for the comment. We have now added other references as well.

Methodology

4. Pg 4, line 21- You have provided the search strategy for Medline only – what about the other databases? You could include these in the supplementary files

Reply: Thank you for the comment. The search strategy for this study was systematic search and we have performed the same search throughout all the databases. Medline reflects the search strategy of all the databases.

5. Pg 5, line 42- rather than outlining in detail the individual components of the NOS scale you could just highlight the 3 broad perspectives and actually include the tool in the supplementary files. That way the reader will be able to better understand Table 2. You don't have to then repeat the scoring criteria's again in Table 2- you can just refer to the tool for this.

Reply: Thank you for the suggestion. We have now provided NOS study quality scale tool as supplementary material 2 and referred to this in the manuscript.

6. Pg 7, line 14 "Most of the included studies showed an overall good rate about the selection and comparability of the study groups, and for the ascertainment of the outcome of interest" - what do you mean by good- a bit more explanation here (scored at least 1 star in each of the categories?)

Reply: Thank you for the comment. The line has now been corrected to "Most of the included studies scored at least 1 star in each of the three categories....."

Results

7. Pg 7, line 25- Five studies explored the risk of PTB in women who compared to those who did not have caries- are there words missing ??? "who had caries"- does not make sense

Reply: Thank you. This sentence has been corrected.

8. For your secondary outcomes I think you should mention in text how many studies were included in the analysis for DMFT and DMFS.

Reply: Thank you for your suggestion. This has been done now.

Discussion

9. My main concern is with this section. Your discussion is very short while your implication for clinical practice is very long. Many of the points discussed in implications needs to be moved to the discussion section.

Reply: Thank you for your comment. Implications for clinical practice is part of the discussion which has been divided into different parts by including sub-headings.

10. Pg 9, line 46: You should also strengthen the implication section with the following points:

Even though you have found no relationship it is still important that health professionals promote oral health among pregnant women. This is because they are prone to dental problems and have limited knowledge and awareness about the importance of oral health and its potential impact on pregnancy outcomes. Further, having dental decay during pregnancy increases the risk of caries transmission after birth through certain feeding practices (you have touched on this but can be strengthened). This can lead to early childhood caries which is the most common chronic childhood disease.

There are numerous references to support the above points

Reply: Thank you for the suggestion. The above line has been added to the implication section.

Reviewer: 2

Reviewer Name
Emmanuel Bujold

Institution and Country
Université Laval, Canada

Please state any competing interests or state 'None declared':
Non declared

Please leave your comments for the authors below

Abstract

1. It should be more representative of the manuscript, including: (methods) appropriate dates of searches -march 2017 or Dec 2016- (results) Heterogeneity between trials, which is quite important and significant- absence of data for early PTB; and (conclusion) lack of good scientific evidences limiting the conclusions.
Reply: Thank you for the comment. We have now mentioned the limitations due to the heterogeneity among the included studies, lack of data on early PTB.

Introduction

2. Very well written. Good references.
Reply: Thank you.

Methods.

3. Excellent. Again please verify the date of searches: December 2016 (abstract march 2027).
Reply: Thank you. The search date has been specified in the abstract section as well as in the methods section also.

Results:

4. Please provide more details about the absence of results (none of the studies provided data on early PTB??)
Reply: Thank you for the comment. Almost all of the included studies have defined PTB as <37 weeks and not provided data on early PTB (Table 1).

Discussion:

5. Please discuss the fact that most studies evaluated women after deliveries, which could strongly influence the results.
Please provide a better discuss about the heterogeneity observed between the studies.
Please provide more details about the impact of not having data for early PTB that are typically associated with a greater risk of amniotic infection/inflammation.
Reply: Thank you for your comment. This has been done now.

From my point of view, this is a well designed meta-analysis, which demonstrates an evident lack of good evidences in order to conclude about the association between dental caries and PTB.

Reviewer: 3

Reviewer Name
Elizabeth Thom

Institution and Country
George Washington University
USA

Please state any competing interests or state 'None declared':
None declared

Please leave your comments for the authors below

1. The word 'explore' is not really appropriate because the connotation is that it is not a pre-planned analysis adhering to standards. I think that 'evaluate' or 'estimate' would be better.

Reply: Thank you for the suggestion. The word 'explore' has now been replaced with the word 'evaluate'.

2. In the abstract, the stated methodology is to estimate a summary odds ratio which is consistent with the results presented in figure 2; yet the results in the text are presented throughout as relative risks.

Reply: Thank you for having spotted this mistake. This has been corrected now.

3. The wording on page 4 "we aimed to stratify the analysis according to the type of PTB, and according to gestational age at birth..." gives the wrong impression – stratifying is usually by some covariate. These are really categorical secondary outcomes (e.g. the first one would be spontaneous preterm vs iatrogenic preterm vs term). The second "stratification" was a series of secondary outcomes comprising different definitions of preterm (e.g. gestational age <28 weeks). Moderate to late preterm was listed as <34 weeks – however, <34 weeks is early to moderate preterm – late preterm is usually 34-36 weeks.

These secondary outcome data were not presented. The authors state that it was because of small numbers; however several of the studies were quite large so it is not clear why they could not at least show the numbers.

Reply: Thank you. The wording has been changed from 'stratify' to 'categories' and the correction for the sub-categories of preterm birth has been made according to the WHO.

4. In the following paragraph on line 51, the secondary "outcome" is not an outcome – it is a secondary "aim" or "objective".

Reply: Thank you. We have now corrected the line from "outcome" to "objective".

5. For the NOS, the follow-up rate that was considered adequate should be specified.

Reply: Thank you. We have removed the sentence and provided NOS study quality scale tool as supplementary material 2 and referred to this in the manuscript as per suggestion from the first reviewer.

6. It is not clear why so many records were excluded (1766/1786). Is it because the search terms were so broad? It seemed that some of the outcomes searched on were irrelevant to preterm birth (eg postpartum hemorrhage).

Reply: Thank you for your comment. Many of the initial references were excluded because they did not deal with caries in pregnancy (this was because we used broad terms when performing the search). Please refer to Figure 1 and Supplementary material 3 for a detailed explanation of the papers selected and those excluded from the present systematic review.

7. The authors do not state what a pre-planned interpretation of the I2 statistic might be. Nor do they comment on the observed I2.

Reply: Thank you for your comment. We have now mentioned this in a footnote in Table 3.

Minor and Wording Issues

Thank you so much for the detailed review on wording issues.

8. Line 9 page 3 rather than “these infants” remain at risk it would be better to say “infants born prematurely” or “preterm infants” .

Reply: The sentence has been re-written as per suggestion.

9. Line 16 page 3 – a reference is needed for the first sentence of the second paragraph on this page

Reply: Thank you. We have now added the reference for the sentence.

10. Line 22 Periodontal disease has been shown... not “have been shown”

Reply: Thank you. The correction has been made now.

11. Line 23 the word “assumption” is out of place – since it has just been stated that periodontal disease has been shown to carry an increased risk. Likewise “the fact that periodontitis may lead to...” sounds odd because it is a mixture of something rather certain i.e. “fact” with something very qualified i.e. “may”. The overall phrase might be better expressed as “the rationale for this association is based on the suggestion that periodontitis leads to maternal and fetal inflammation” or something similar.

Reply: Thank you. The sentence has been corrected according to the suggestion.

12. Line 44 page 5 “and the ascertainment outcome of interest” should be “ascertainment of the outcome of interest”.

Reply: Thank you. The sentence has been corrected.

13. Line 46 page 5 Assessment of the selection of a study means something different than an assessment of the selection of the study groups. ...

Reply: Thank you. This sentence has also been corrected as per suggestion.

VERSION 2 – REVIEW

REVIEWER	Emmanuel Bujold Université Laval, Canada
REVIEW RETURNED	21-Dec-2017

GENERAL COMMENTS	The authors answered my concerns and question. I suggest to accept this article for publication.
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REVIEWER	Elizabeth Thom George Washington University Biostatistics Center
REVIEW RETURNED	23-Dec-2017

GENERAL COMMENTS	The authors have been responsive to the reviews and the manuscript is definitely improved.
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