



July 30, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12243-review.doc).

**Title:** Does a biological link exist between Periodontitis and Rheumatoid arthritis?"

**Author:** Dr. Rosamma Joseph, Dr. MG Jose Raj, Dr. Shobha Sundareswaran, Dr. Priyanka Chand Kaushik, Dr. Nagrale Amol Vijay, Dr. Susan Jose and Dr. Sreeraj Rajappan

**Name of Journal:** *World Journal of Rheumatology*

**ESPS Manuscript NO:** 12243

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(A) **Reviewer 00632011-**

**Reviewer comment**

1. **Typo.** *There are so many typos throughout the manuscript, even in the title (exist: exit). The authors should check typos carefully. p-10, -4: Kobiyashi et al.: Kobayashi p-12: ANTIDODY: ANTIBODY, RANLK: RANKL*

**Author response:-** Appropriate changes have been made in the manuscript.

**Reviewer comment**

2. **pro- and anti-inflammatory cytokines** *In the introduction (p-5, 3rd paragraph), the authors mentioned about pro- and anti-inflammatory cytokines. They wrote the examples of anti-inflammatory cytokines though with no example of pro-inflammatory cytokines. The authors should write the examples of pro-inflammatory cytokines, such as IL-1 and TNF-alpha, as well*

**Author response:-** Appropriate changes have been made in the manuscript.

**3. Reviewer comment**

**Th1, Th2 type cytokines** *(p-5, 3rd paragraph) Same as mentioned above, the authors should write example of Th1 and Th2 type cytokines*

**Author response:-** Appropriate changes have been made in the manuscript.

**Reviewer comment**

4. **References** *There are some sentences that describe phenomenon without citing any references (p-5, l-6 from bottom; p-5 l-5 from bottom; p-5 l-4 from bottom). Please cite adequate references for each sentences. That's what the review article should take care.*

**Author response:-** Appropriate changes have been made in the manuscript.

**Reviewer comment**

5. *Redundancy of contents* Some parts of manuscript contain redundant sentences. For example, first and second sentences of "Similarities between RA & PD" are redundant. It is better to crop redundant sentences as much as possible.

**Author response :-** Appropriate changes have been made in the manuscript.

**Reviewer comment**

6.- *Antibodies to IL-1 alpha and IL-6 (P-9, l-9 from bottom)* The authors wrote "low titres of antibodies to IL-1 alpha and IL-6", though it should be low titres of IL-1 alpha and IL-6

**Author response :-** Appropriate changes have been made in the manuscript.

**Reviewer comment**

7. *Figure 1* This figure is confusing. It might describe RA in the left side, and PD in the right side. However, position of "RA" and "PD" were not suitable position, and that gives confusion. Please modify the figure. Also, the differences what the authors want to mention among figure and tables are quite difficult to find. The authors should clarify what the authors want to mention in figure, and the difference of each figure and tables states.

**Author response :-** Appropriate changes have been made in the manuscript.

(B) Reviewer 00742340

**Reviewer comment**

*"Does a biologic link exist between Rheumatoid arthritis and Periodontitis?"* was submitted to World Journal of Reumatology. There are several concerns related to the study. Specific comments are noted below: The English language should be adjusted. The study does not provide anything new that is no longer studied before, including background, methods, results and conclusions. The conclusions presented as known for several years. Additionally, more methodologically rigorous reviews have been recently published. Examples are cited below: Quirke AM, Lugli EB, Wegner N, Hamilton BC, Charles P, Chowdhury M, Ytterberg AJ, Zubarev RA, Potempa J, Culshaw S, Guo Y, Fisher BA, Thiele G, Mikuls TR, Venables PJ. Heightened immune response to autocitrullinated *Porphyromonas gingivalis* peptidylarginine deiminase: a potential mechanism for breaching immunologic tolerance in rheumatoid arthritis. *Ann Rheum Dis.* 2014 Jan;73(1):263-9. Kaur S, Bright R, Proudman SM, Bartold PM. Does periodontal treatment influence clinical and biochemical measures for rheumatoid arthritis? A systematic review and meta-analysis. *Semin Arthritis Rheum.* 2014 Apr 28. Agnihotri R, Gaur S. Rheumatoid arthritis in the elderly and its relationship with periodontitis: a review. *Geriatr Gerontol Int.* 2014 Jan;14(1):8-22. Scher JU, Bretz WA, Abramson SB. Periodontal disease and subgingival microbiota as contributors for rheumatoid arthritis pathogenesis: modifiable risk factors? *Curr Opin Rheumatol.* 2014 Jul;26(4):424-9. Kaur S, White S, Bartold PM. Periodontal disease and rheumatoid arthritis: a systematic review. *J Dent Res.* 2013 May;92(5):399-408. Okada M, Kobayashi T, Ito S, Yokoyama T, Abe A, Murasawa A, Yoshie H. Periodontal treatment decreases levels of antibodies to *Porphyromonas gingivalis* and citrulline in patients with rheumatoid arthritis and periodontitis. *J Periodontol.* 2013 Dec;84(12):e74-84. Scher JU, Ubeda C, Equinda M, Khanin R, Buischi Y, Viale A, Lipuma L, Attur M, Pillinger MH, Weissmann G, Littman DR, Pamer EG, Bretz WA, Abramson SB. Periodontal disease and the oral microbiota in new-onset rheumatoid arthritis. *Arthritis Rheum.* 2012 Oct;64(10):3083-94. Rutger Persson G. Rheumatoid arthritis and periodontitis - inflammatory and infectious connections. Review of the literature. *J Oral Microbiol.* 2012;4 English language should be adjusted. The study does not provide anything new that is no longer studied before, including

*background, methods, results and conclusions. The conclusions presented as known for several years. Additionally, more methodologically rigorous reviews have been recently published.*

**Author response:-** Recently published reviews have been cited and appropriate changes have been made in the manuscript.

(C) Reviewer 00742466

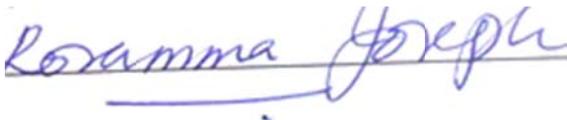
**Reviewer comment**

This is well written review. Easy to follow well organized manuscript. I assume the title is just a misprint which reads Does a biological link exit between.....It probably meant to be "exists" Nothing original but a good review article.

**Author response:-** References and type setting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Rheumatology*.

Sincerely yours,

A handwritten signature in blue ink that reads "Rosamma Joseph". The signature is written in a cursive style and is positioned above a horizontal line.

Dr. Rosamma Joseph, MDS

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