

June 02, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: revised manuscript no 10844).

Title: Periodontitis: Tip of the Iceberg in Chronic Kidney Disease

Author: Monchai Siribamrungwong, Pawadee Chinudomwong

Name of Journal: *World Journal of Clinical Urology*

ESPS Manuscript NO: 10844

The manuscript has been improved and revision has been made according to the suggestions of the reviewers as follows:

1. Reasonable review of a perhaps long overlooked risk factor. It might be helpful to note that microalbuminuria - a major CKD risk factor - is now appreciated to be reversible spontaneously in as many as one-half of those afflicted. It might be helpful to include the suggested features of a prospective study to fully define the risk post by Periodontitis in both CKD and ESRD. The point that attention should be paid to detect its presence is valid and helpful.
 - In the part of definition, chronic kidney disease is clearly defined that presence of albuminuria, as one of diagnostic criteria, must be there for three of more months and that the condition is believed to be irreversible spontaneously. In addition, we mentioned the effect of periodontitis and therapy on microalbuminuria in glomerular diseases and periodontitis.
 - A prospective study was added upon request. Common risk factors in periodontitis are similarly encountered among the CKD individuals, namely, DM, smoking, and age. Such characteristics were observed in different degrees along the continuum of periodontitis from no/mild, moderate and severe.
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2. Minor comments: 1.The first paragraph at definition section should be rewriting. Table 1 is redundant and could be deleted. 2. The term of "Impact" is better than the term of "effect": at page 5: "effects" of chronic renal disease on periodontal tissues.
 - Definition was rewritten and Table 1 was deleted.
 - The term "effect" was substituted by "impact" in the suggested sentence.
3. In this manuscript, the authors review the recent evidences pertaining to the association between periodontal disease and a variety of renal maladies. It is an interesting review. The reviewer has the following comments/question. 1. The authors mentioned that CKD population is increasing. It will be helpful to readers if they could provide some numbers. For example, how many CKD worldwide, how much for medical care and subsequent costs, etc. 2. Same for periodontal disease. How many worldwide, how much for medical care and subsequent costs, etc. 3. Same for the link between periodontal disease and CKD. In comparison to the general public, is the % of periodontal disease in

CKD much higher? Is it progressive depending on the CKD stages? 4. In addition to affecting inflammatory markers, will periodontal treatments affect CKD outcomes such as cardiovascular morbidity and mortality? From Fig. 1, it seems that it should. If no evidence exists to show that periodontal treatments affect CKD outcomes, then perhaps Fig. 1 and its related texts need to be modified.

- In introduction, prevalence of CKD and periodontitis were mentioned as well as the medical costs. Prevalence of periodontitis in CKD was added and comparison of prevalence with general population was illustrated.
- To date, study on effect of periodontal treatments on CKD outcomes is still not evident and requires further investigation. Hence, Figure 1 was removed.

4. WELL WRITEN REVIEW ARTICLE. DSERVES PUBLICATION. 2. TABLES 2 AND 3 COULD BE SUPPRESSED FROM THE ARTICLE.

- Both Tables 2 and 3 were deleted.

5. This is overall an intriguing topic. I found it too verbose at times and superficial in referring to the published work. It would help if some more details of suggested mechanism are presented. It is not clear whether there truly is an impact of periodontitis on CKD or vice-versa. CKD patients in general suffer from chronic inflammation which is bound to affect several systems, gums being no exception. The manuscript is too long and information is repeated over and over which is totally unnecessary. English language should be improved.

- Repetitive and redundant contents were modified as follows:
 - o Contribution of periodontitis to the inflammation was moved and integrated in the definition.
 - o Rearrangement of example in the "chronic kidney disease and periodontitis"
 - o Rearrangement of content in the "impact of chronic kidney disease on periodontal tissues"
 - o Rearrangement of content in the "effect of periodontitis on chronic kidney disease"
 - o Integration of similar examples in the "peritoneal dialysis"
- Addition of two papers was made in the "haemodialysis", mentioning significant association between PD and high CVD mortality in CKD patients. Even after adjustment of various confounders such as age, DM and smoking, hazard ratio remained notably high.
- A conclusion has been drawn that impact of periodontal intervention on cardiovascular complications remained to be further explored. Evident in this article was only intermediate outcomes such as effect on inflammatory markers.
- The manuscript was edited by the native speakers of English.

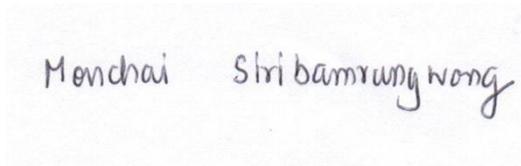
6. The article is well written and easily understandable. According to my personal opinion from a periodontal point view, the paper deserves to be published after minor polishing as follows: page 4 row 18 instead of "plaque-induced gingival disease, early onset, chronic adult and aggressive periodontitis.

Plaque-induced gingival disease (briefly called gingivitis) involve” write “plaque-induced gingivitis, chronic and aggressive periodontitis. Plaque-induced gingivitis. “page 12 row 18 instead of “in PD patients. And periodontal treatment”, write “in PD patients and periodontal treatment” page 15 CONCLUSION row 6 after “the most prevalent finding” add “due to cyclosporine mediated mechanism.” Table 4 Bone, instead of “Lytic area of bone” write “osteolytic areas”

- Correction of wording was completed as suggested.

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

Sincerely yours,

A handwritten signature in black ink on a light-colored background. The signature reads "Monchai Siribamrungwong" in a cursive script.

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