Author's response to reviews

Title: Epidemiology of episodic adenolymphangitis: a longitudinal prospective surveillance among a rural community endemic for bancroftian filariasis in coastal Orissa, India

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Author's response to reviews: see over
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To
The Editor
BMC Public Health

Sub.: Ms: 1066802644484799 - Submission of REVISED manuscript for consideration of publication in the BMC Public Health

Sir,

Thank you very much for your letter and considering our manuscript positively. Also, I thank for the comments of the reviewers for refinement of the manuscript.

Please find herewith submitting the REVISED VERSION of the manuscript entitled, “Episodic adenolymphangitis due to bancroftian lymphatic filariasis: a longitudinal prospective surveillance in rural coastal Orissa, India”. The revised title of the manuscript, as per the suggestion of the reviewer is “Epidemiology of episodic adenolymphangitis: a longitudinal prospective surveillance among a rural community endemic for bancroftian filariasis in coastal Orissa, India”.

The paper has been revised as per the comments of the reviewers. I am herewith provided the point-to-point information to indicate where and how the revision has been made.

Reviewer 1 (Dr. James Kazura)

1. The points required clarification have been addressed in the revised manuscript as follows:
   a. The two villages are close together by less than two kilometers. And no data on mf rates, specifically for these two villages are available. This information has been incorporated in the revised manuscript (page: 3, paragraph: 2, lines: 2-3 and 10-11).
   b. Before this study, the district experienced once in 1997, the mass drug administration of diethylcarbamazine. This information has been incorporated under STUDY AREA in the revised manuscript (page: 3, paragraph: 2, lines: 8-10).
   c. The method of determining the duration of ADL episode is explained in the revised manuscript (page: 3, paragraph: 3, lines: 5-16).
   d. The fever means raise of temperature. It is noted along with other symptoms by recall method as well as by observing the medical/prescription records as adjuncts. This information was
e. Some ADL episodes cluster in members of the same household. It has been mentioned in the revised manuscript (page: 4, paragraph: 1, line: 1).

f. As some data such as mean episodes per individual are in small number, they are presented to the second decimal point.

2. With regard to association of ADL with mf status, we agree that, in the present study an insensitive detection method was used, i.e., finger prick blood sample in stead of nucleopore filtration of venous blood. This limitation has been mentioned under DISCUSSION in the revised manuscript (page: 7, paragraph: 1, lines: 9-11).

3. The data on overall prevalence of infection based on circulating filarial antigenemia is available for the study district. The data, along with the reference has been incorporated under STUDY AREA in the revised manuscript (page: 3, paragraph: 2, lines: 7-8).

4. As suggested by the reviewer, comments regarding the use of footwear and other footcare practices are incorporated under DISCUSSION in the revised manuscript (page: 4, paragraph: 2, lines: 18-22).

5. As suggested, the manuscript is rechecked to improve syntax and clarity.

Reviewer 2 (Dr. Pradeep Kumar Das)

1. It is a general comment and no modification is suggested.

2. As reviewer commented, this study do not address understanding the natural history and progression of the disease. It deals only with epidemiological aspects of adenolymphangitis and this information may be useful to deal the above issues. Accordingly changes have been made under BACKGROUND in revised manuscript.

3. In Results and Conclusions of ABSTRACT, the statement regarding the influence of gender on average number of episodes has been rewritten, as reviewer opined that it is confusing. (page: 2, paragraph: 3, lines: 4-5).

   In the second part of this point, reviewer opined that the statements regarding difference between males and females in ABSTRACT and RESULTS AND DISCUSSION are contradictory. However, it is cleared that the statement in ABSTRACT is about the average number of episodes per individual, where as the statement in RESULTS AND DISCUSSION is about the incidence of ADL episodes. These are now clear in revised manuscript.

4. The reviewer pointed out that the definition of ADL given in the BACKGROUND is different from the definition used for this study. It is true that these two definitions differ slightly. The first once is mentioned during giving the background with its reference. The second once is working definition with all associated symptoms.

5. With regards to methods of investigations, reviewer suggested to indicate who conducted the surveillance and who confirmed the cases, etc. As suggested by the reviewer, these details are incorporated under DATA COLLECTION in the revised manuscript (page: 3, paragraph: 3, lines: 8-13).

6. The reviewer suggested to provide more details from data analysis. As suggested by the reviewer data is reanalyzed and necessary information is provided as follows:
a. The data is analyzed to assess the differences in annual incidence, duration and clinical presentation between individuals with and without chronic disease. The results are shown in RESULTS in revised manuscript (page: 5, paragraph: 1, lines: 1-2; page: 5, paragraph: 2, lines: 9-12; page: 6, paragraph: 1, lines: 1-6).

b. As opined by the reviewer, time series analysis could not be done as data is insufficient.

c. The analysis for co-existence of more than one symptom is analyzed and results are given in brief, as these results are not remarkable (page: 5, paragraph: 4, lines: 5-6).

d. The relation between ADL incidence and different pathological groups is analyzed and shown in RESULTS in revised manuscript (page: 4, paragraph: 3, lines: 5-7).

e. As suggested by the reviewer, it is examined to see whether any symptom is specific for any age group or gender. The results are shown under RESULTS in revised manuscript (page: 6, paragraph: 1, lines: 1-6).

7. As suggested by the reviewer, the actual period of survey and geographical coordinates of the villages are provided under METHODS (page: 3, paragraph: 2, line: 4; page: 3, paragraph: 3, line: 2).

8. The reviewer suggested to limit the DISCUSSION. Accordingly DISCUSSION part is limited to epidemiological aspects of ADL only. However, a few lines on management of ADL are given as one of the reviewers suggested to add some lines on foot care and other practices related to control of bacterial infections.

9. As per the comment of the reviewer on the title, the title of the paper has been modified as “Epidemiology of episodic adenolymphangitis: a longitudinal prospective surveillance among a rural community endemic for bancroftian filariasis in coastal Orissa, India”

10. The results in ABSTRACT are corrected and the values of standard deviation are provided where ever appropriate.

Reviewer 3 (Dr. Kapa D Ramaiah)

**Major compulsory revisions**

1. As reviewer suggested, the name of each test and its purpose is given under DATA ANALYSIS (page: 4, paragraph: 2, lines: 2-8).

2. The reviewer suggested to delete the results pertaining to univariate analysis when results of multivariate analysis are given. Accordingly the the results of univariate analysis are deleted and only the results of multivariate analysis are kept (page: 5, paragraph: 2, lines: 6-9; page: 5, paragraph: 3, lines: 4-6).

3. As suggested by the reviewer, ANOVA for incidence and duration of ADL episodes is carried out separately for lymphoedema patients and hydrocele patients. The effect of age and gender (only age in hydrocele patients) among these patients is examined and the results are shown under RESULTS (page: 5, paragraph: 2, lines: 9-12; (page: 5, paragraph: 3, lines: 6-8). Where ever, individual F values are available they are given along with probability. For Multivariate ANOVA by regression, combined F for entire model is available and is given (table 1).

4. As suggested by the reviewer, the DISCUSSION part is shortened and made precise. The repetition of points is avoided.
Minor essential revisions

1. The statistical significance of the difference in the incidence of ADL between males and females is given (page: 2, paragraph: 3, line: 2).
2. The average number of episodes per year is per affected person. It is mentioned in the revised manuscript (page: 2, paragraph: 3, line: 5).
3. The standard deviation for the mean duration of days is given (page: 2, paragraph: 3, line: 6).
4. As commented by the reviewer, it is not correct to say inflammation of the lymphoedema, it is inflammation of the lymph nodes. It is corrected in the revised manuscript (page: 2, paragraph: 4, line: 4).
5. The typographic error pointed out by the reviewer is corrected.

Discretionary revisions

1. In page 2 (ABSTRACT), the reviewer opined that it is difficult to interpret the statement on association between ADL and microfilaraemia. Hence this statement is deleted from ABSTRACT.
2. The Reviewer suggested to give more details of study area. Accordingly, the occupation of study population and other details are included (page: 3, paragraph: 2).
3. The reviewer commented on justification for use of method of diagnosing ADL from African study. As no other study reported the specificity and sensitivity of this method, the African study has been referred.
4. The incidence of ADL is high in bancroftian filariasis than in brugian filariasis. This statement is supported by studies. The earlier statement indicating that the ADL incidence is higher in brugian filariasis. The study do not follow the procedure as other studies followed. Hence that statement is deleted.
5. The reviewer pointed out that one should cautious that disability and economic loss caused by chronic disease is life long and much higher. It has been incorporated under DISCUSSION in the revised manuscript (page: 7, paragraph: 2, lines: 12-13).
6. The reviewer commented that the finding on association between ADL and mf is not new, and suggested to make only one point that the absence of microfilaraemia in a vast majority of ADL patients is in conformity with earlier studies. Accordingly modifications are made in revised manuscript under DISCUSSION (page: 7, paragraph: 1, lines: 8-9).

Please let me know if we need to do further. And I request you to consider this revised paper for publication in *BMC Public Health*.

With regards,

Sincerely

(B. V. Babu)