

14 Mar 2019

Dear Dr. José Derraik,

We sincerely thank the reviewers for their generous comments on our manuscript.

In response to the reviewers' comments and suggestions, we have reanalyzed our data and rewritten most parts of our manuscript. Here are the major revisions:

- English language improvement, in response to Reviewer 1 and 3.
- Utilization of the Zero-Inflated Beta Random Effect model to illustrate the longitudinal natures of our data, in response to Reviewer 1; utilization of appropriate statistical tests (including two way RM ANOVA) and reported all p-values, in response to Reviewer 3.
- Because the disease onset time for each patient was not the same, we reset the analysis time intervals as: early post-partum, early pre-onset, late pre-onset, early disease, middle disease, late disease, and post disease, to better reflect the condition of the patients.
- In response to Reviewer 1,2, and 3, we updated all figures plotted by R to show explicit results.

On behalf of all the authors, I am submitting our new version of the manuscript for your assessment.

Enclosed please find our point-to-point responses to previous reviews. We believe our manuscript has been substantially improved and would be appropriate to publish in PeerJ.

Thank you very much again for your considerations.

Yours Sincerely,  
Li Hong



On behalf of all authors.