

Dear reviewers and editorial board,

Below you will find the issues raised by the reviews and our comments accordingly.

Reviewer:

This manuscript offers new evidence to support the hygiene hypothesis, an interesting topic which has drawn increasing attention in recent years considering this potential role in the development of Crohn's disease. This case-control study was well carried out, especially the well-designed questionnaire containing most of interested environmental factors, making the data analysis reliable and convincing. The relationship between several important variables supporting the hygiene hypothesis and CD development has been clearly demonstrated in the discussion section, even taking into consideration the extreme geographical differences in Brazil. Meanwhile, the structure of this manuscript is complete and the language is perfect.

Authors' reply:

The authors thank the reviewer for the time dedicated to our manuscript and for his/her kind comments.

Reviewer:

However, there are two questions remaining to be explained. The first question is about the sample size. The sample of CD patients and healthy people in this study was 145 and 163 respectively. Given the multivariate analysis in this case-control study aiming at finding the predictive factors of CD development, the determination of the sample size is supposed to be explained so that the conclusion will be more convincing.

Authors' reply:

No sample size calculation was performed. The sample size was based on a convenience sample according to the number of patients diagnosed with CD recorded in our outpatient clinic (**information added to the manuscript**).

Reviewer:

The other question refers to one of the predictive variables, the age. Under age of 40 was considered to be a predictive factor in this study, as a comparable evidence of the predominance of CD in young individuals, but survey of age was the age when patients filled the questionnaire in this manuscript, and how about the age when patients were first diagnosed as Crohn's disease? According to the Montreal classification of CD, as well as plenty of previous studies, the age of initial diagnosis may play prior role in the development of CD.

Authors' reply:

We considered the age when patients filled the questionnaire, being under 40 years of age a predictive factor for CD in this study. As this was a case-control study comparing CD with healthy controls, the results did not consider the age of initial diagnosis of CD

by the Montreal classification. Since the controls were healthy individuals, we could not compare this variable between the two study groups.