

Lian-Sheng Ma
Editorial Office Director, Company Editor-in-Chief, Editorial Office
World Journal of Gastroenterology

Dear Dr. Ma

Thank you very much for your letter dated April 10, 2022, and for the careful review of our manuscript, which we have amended following the reviewers' suggestions. A copy of the revised manuscript with the changes highlighted in red font has been uploaded to the submission system. Also, please find below an itemized point-by-point response to the reviewers' comments.

We look forward to hearing from you about the status of this manuscript, which we hope is now acceptable for publication in World Journal of Gastroenterology. Please feel free to contact me if you require any additional information.

Sincerely,

Ornella Cassol
cassol.ornella@gmail.com
Phone: +55-54-96601987

Reviewer #1

- Abstract. Some errors: Please delete Both entities have the same characteristics of progression and similar therapeutic responses but should be considered 2 different diseases. This is incorrect.

Response: The sentence was deleted from the abstract.

What is meant by analytic study?

Response: An analytic study attempts to determine whether there is a relationship between two factors, that is, the effect of an exposure or intervention on an outcome (a disease or health-related condition). An example is a cross-sectional study.

Please delete: Findings with $P \leq 0.05$ were considered statistically significant. P Value has not been used in abstract. 57.5% were female and 42.5% were female

Response: The sentence was deleted from the abstract. The result was corrected to "... and 42.5% were male."

Check Change conclusion to one which only talks about the present report and not 'other publication'

Response: The conclusion was changed to: "Our results demonstrated an IBD prevalence of 9.51% and incidence of 1.61% per 100,000 population. The patients were predominantly female, and CD was more prevalent than UC."

Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes, Briefly mention in which part of Brazil is this state

Response: The background was amended accordingly: "This is the first study on the epidemiology of inflammatory bowel diseases (IBD) in Rio Grande do Sul, the southernmost state of Brazil with the country's fifth largest population."

Results.: The gender figures in results do not match with abstract and is >100% Since the pharmacy covers 70% of population, how was prevalence calculated The results are minimalistic

Response: The gender figures were corrected. We also corrected in the Materials and Methods section that the pharmacy within the Brazilian Unified Health System covers 78% of the state population. Rio Grande do Sul is among the 5 Brazilian states with the largest number of people who have private health insurance, after São Paulo, Rio de Janeiro, Minas Gerais, and Paraná states. That is, 2,592,412 people have private health insurance (22.78% of the state population) and only occasionally use the public health system. Therefore, it is estimated that approximately 78% of the population obtain their

medications through the FME, which is the government specialty pharmacy program within the Brazilian public health system. Based on that, we decided to carry out our epidemiological study using data from the FME of the Rio Grande do Sul state.

Discussion. is very long and unfocused. This has to be shortened and the focus should only be to compare with other sites in Brazil and with developed world. The discussion about gender is not needed.

Response: The Discussion section has been shortened and adjusted as requested.

Biostatistics. Does the manuscript meet the requirements of biostatistics? Unclear. Must explain the calculations

Response: The text has been adjusted as requested, with the assistance of statistician Dr. Mario Wagner, and is presented now as a 'Data analysis' subsection.

Reviewer #2:

I have reviewed the manuscript submission No.75184 entitled “Epidemiology of inflammatory bowel diseases in the state of Rio Grande do Sul, Brazil” with interest.

In this article, the authors stated that this is the first study with estimated incidence and prevalence rates of inflammatory bowel diseases in the state of RS between 2014 to 2019. I found that the value of this study is important. Besides, there are some concerns given to the authors as follows:

1. Overall, this article firstly reported epidemiological studies of IBD in the state of RS. However, there are still some possible bias in the results, since the authors regarded the age that the patients begin to receiving the free specialty drugs (from Farmácia de Medicamentos Especializados, FME) as their onset age. In fact, some patients may not afford the treatment. This limitation should be emphasized in the discussion.

Response: As suggested, the limitation about the patients’ onset age was emphasized in the Discussion. Regarding the comment “*In fact, some patients may not afford the treatment,*” all patients included in the study are users of the Brazilian Unified Health System, that is, they are the ones eligible to receive the free specialty medications. In Brazil, access to care is provided through private health insurance or the Unified Health System, which is a universal health care system funded by federal taxes and operated by state or municipal governments that includes the public provision of core physician and hospital services without copayments or patient charges. Approximately 22% of the population in the state of RS have private health insurance and only occasionally use the public health system. Therefore, because the FME is a government program within the Brazilian Unified Health System, it is responsible for supplying specialty medications to approximately 78% of the state population, all of them users of the public health system. A brief explanation about the Brazilian Unified Health System was added to the Materials and Methods section.

In the section of materials and methods, the authors said that this study assessed the population of RS including the diagnosis of disease, date of treatment initiation, sex, age, skin color, city and region of residence, and type of drug used, whereas the details of drug use are not shown anywhere.

Response: We deleted from the Materials and Methods section the variables that were not discussed in the paper (skin color, city and region of residence, and type of drug used).

As an observation study in a large scale, the objects of analysis in the part of results is too simple, more elements should be included and analyzed to improve the quality of

this study, such as the efficacy of these drugs, the outcome of disease, the incidence of complications (intestinal fistula, etc.), even the potential risk factors of IBD in RS area.

Response: The methodology of our study was focused on obtaining epidemiological data (incidence and prevalence), age and sex from the FME, which is the program supplying specialty medications to most of the state population (78%). It was not the objective of the study to analyze the efficacy of these drugs, the outcome of disease, or their complications, as these factors are not considered in the FME. The variables analyzed in the study have been corrected in the Materials and Methods section.

There are some typos and statistical errors. Firstly, in the abstract, “of which 57.5% were female and 42.5% were female” and “Crohn disease” in the key words. Secondly, in the results, “out of all patients with IBD, 622 (57.5%) were female and 460 (52.5%) were male”. Considering that this article is an observation study including some quite simple statistical analysis, the authors should confirm the accuracy and authority of these data in this paper before publishing online. Please scrutinize carefully before resubmission.

Response: In the abstract, the sentence was corrected to “... and 42.5% were male.” Also, the key word was corrected to Crohn’s disease. In the Results, the percentage for male participants was corrected to 42.5%. We apologize for this oversight. The manuscript was carefully revised for resubmission.

The resolution of these figures is low, especially annotation of Y-axis in figure 3. Authors should try to change the method of making figure.

Response: All figures have been revised for resubmission and uploaded as single PowerPoint files, as requested by the Editor-in-chief.

Science editor:

This manuscript estimated the incidence and prevalence rates of IBD in Rio Grande do Sul (RS) between 2014 and 2019.

Please describe the details of drug use in Materials and methods;

Response: The methodology of our study was focused on obtaining epidemiological data (incidence and prevalence), age and sex from the FME, which is the program supplying specialty medications to most of the state population (78%). It was not the objective of the study to analyze the efficacy of these drugs, the outcome of disease, or their complications, as these factors are not considered in the FME. The variables analyzed in the study have been corrected in the Materials and Methods section.

Some of the results are too simplistic and more elements should be included and analyzed to improve the quality of this study, such as the efficacy of these drugs, disease outcomes, incidence of complications (intestinal fistulas, etc.), and even potential risk factors for IBD in RS regions;

Response: The methodology of our study was focused on obtaining epidemiological data (incidence and prevalence), age and sex from the FME, which is the program supplying specialty medications to most of the state population (78%). It was not the objective of the study to analyze the efficacy of these drugs, the outcome of disease, or their complications, as these factors are not considered in the FME. The variables analyzed in the study have been corrected in the Materials and Methods section.

The limitation that some patients may not be able to afford treatment should be added to the discussion.

Response: All patients included in the study are users of the Brazilian Unified Health System, that is, they are the ones eligible to receive the free specialty medications. In Brazil, access to care is provided through private health insurance or the Unified Health System, which is a universal health care system funded by federal taxes and operated by state or municipal governments that includes the public provision of core physician and hospital services without copayments or patient charges. Approximately 22% of the population in the state of RS have private health insurance and only occasionally use the public health system. Therefore, because the FME is a government program within the Brazilian Unified Health System, it is responsible for supplying specialty medications to approximately 78% of the state population, all of them users of the public health system. A brief explanation about the Brazilian Unified Health System was added to the Materials and Methods section.

Figure 3 is not clear, please modify and replace.

Response: All figures have been revised for resubmission and uploaded as single PowerPoint files, as requested by the Editor-in-chief.

Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted.

I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Response: The figures were generated from statistical programs, so it was not possible to obtain images in which all components are editable.

Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Tables have been adjusted as requested.

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Response: The copyright information was added to the figures.