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OPEN PEER REVIEW

Spatio-temporal Analysis of COVID-19: A Global Study

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About this report

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1 Original submission

4 comments · 15 Sep 2022 – 26 Sep 2022

Referee 1 Reviewer

MINOR REVISION 15 Sep 2022

Dear Associate-Editor

I have reviewed the manuscript titled "Spatio-temporal analysis of covid 19: a global study". This is an interesting study. The manuscript requires minor revision before publication. I will upload my comments for revising the manuscript.

The manuscript should be revised by a native English speaker.

Kind regards.

Referee 2 Reviewer

MAJOR REVISION 21 Sep 2022

Dear Authors
The manuscript needs Major Revision.
Your manuscript is very well designed; however, please address the following comments to increase the quality of your manuscript.

Abstract:
Please explain the mixed exploratory study in the methodology section.
Also describe how to calculate the cumulative incidence rate (CIR), case fatality rate (CFR), and case recovery rate (CRR) in the methodology section.
Mention the software used for data analysis in this manuscript.
Please write the keywords according to MeSH.

Introduction:
In the introduction, describe the spatial analysis and Simpson's paradox in ecological studies.
Please write out acronyms in full the first time you use them, for example, OHSA.

Methodology:
Describe a mixed exploratory study.
Explain more about the three main types of data sources in this study.
Are the data from the World Bank website valid? What year were the data from?
What are the dependent and independent variables in Joinpoint regression analysis?
What is the Grid search method?
Please provide interpretations of the different indices used for data analysis, such as Global Moran's I, Getis-Ord Gi*, and Anselin Local Moran's I.
Please write out acronyms in full the first time you use them, for example, OHSA.
Mention the software used for data analysis in this manuscript.

Results:
Please mention the titles and captions of graphs and tables in the text.
Please indicate the population denominator used to calculate CIR, CFR, and CRR.
Which areas had the highest and lowest CIR, CFR, and CRR?
Where were the high-risk and low-risk cluster areas for CIR, CFR, and CRR?
What is meant by this sentence: “The optimal value of bandwidth estimated to be 2411.332 Kilometers based on

OHSA method”?
Please report the values of the average annual percentage change (AAPC) and the annual percentage change (APC) along with their confidence intervals for different time trends.
What was your purpose in presenting Table 1?
Please review and modify the results.

Discussion:
Please discuss each of the results obtained.
Good luck

Associate Editor

MAJOR REVISION 24 Sep 2022

Dear authors
According to the reviewer's comments, the manuscript needs to be revised to address all comments clearly. Also, provide the link for your ethics code. For example: "This study is approved under the ethical approval code of .... IC-23456 (webpage of ethical approval code is: http://www.URL.com/IC-23456)."
In the conflict of interest section, what do you mean by "The authors declare no conflicts of interest."? One of the authors is a member of the editorial board. For example: "We declared that one of our authors ([AUTHOR NAME], [ROLE IN JOURNAL]) is on the editorial board. The journal confirmed that the mentioned author with CoI was completely excluded from all review processes. We also introduced this author with CoI during the submission as an opposed reviewer."
Best regards.

Editor-in-Chief

MAJOR REVISION 26 Sep 2022

Dear Authors
According to the reviewers’ and associate editor’s comments, your article needs major revision. When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully: please outline every change made in response to their comments and submit the required files.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewer 1

Dear Associate-Editor

I have reviewed the manuscript titled "Spatio-temporal analysis of Covid-19: a global study". This is an interesting study. The manuscript should be revised minor before publication. I will upload my comments for revising the manuscript. The manuscript should be revised by a native English speaker.

Reply to comments reviewer number 1

Dear Reviewer. Thank you for your valuable comment. The all of your valuable comment has applied. Corrections were highlighted in yellow.

Also, all your comments have been answered in the word file of the article. See our answers in the section below your comments.

Dear Reviewer, Thank you for taking the time to review our manuscript.

Reviewer 2

Dear Authors

The manuscript needs Major Revision. Your manuscript is very well designed, however, apply the following comments to increase the quality of your manuscript.

Reply to comments reviewer number 2

Dear Reviewer. Thank you for your valuable comment. The all of your valuable comment has applied. Corrections were highlighted in yellow.

Abstract:

Please explain about mixed exploratory study in the methodology section.

Ok, your valuable comment has been applied.

Also describe how to calculate cumulative incidence rate (CIR), case fatality rate (CFR), and case recovery rate (CRR) in the methodology section.

Ok, your valuable comment has been applied.

Mention to the software used for data analysis in this manuscript.

Ok, your valuable comment has been applied.

Please write Keywords according MeSH.

Ok, your valuable comment has been applied.

Introduction:

In the introduction, describe spatial analysis and Simpson's paradox in ecological studies.

Please write the full word for acronyms when that the first time you use them for example OHSA.

Ok, your valuable comment has been applied.

Methodology:

Describe mixed exploratory study.

Ok, your valuable comment has been applied.

Explain more about three main' types of data sources in this study.

Ok, your valuable comment has been applied.

Is the World Bank website data valid? What year was the data used?

Yes, World Bank website are valid date. We use of 2022 data for populations.

What is the dependent and independent variable in Joinpoint regression analysis?

Ok, your valuable comment has been applied.

In this study, CIR, CFR, and CRR were dependent variables and months and countries were independent variables

What is Grid search method?

Ok, your valuable comment has been applied.

The Grid search method was used to calculate the joint points where the incidence rate changes drastically.

Please write the interpretations of different indices used for data analysis such as Global Moran's I, Getis-Ord Gi* and Anselin Local Moran's I.

Ok, your valuable comment has been applied. We write the interpretations of different indices used for data analysis.

Please write the full word for acronyms when that the first time you use them for example OHSA.

Ok, your valuable comment has been applied.

Mention to the software used for data analysis in this manuscript.

Ok, your valuable comment has been applied.

Results:

Please mention the titles and captions of graphs and tables in the text.

Ok, your valuable comment has been applied.

Please indicate CIR, CFR, and CRR per how many person were calculated?

Ok, your valuable comment has been applied. CIR, CFR, and CRR per 100,000 person were calculated

Where were highest and lowest area for CIR, CFR, CRR?

Ok, your valuable comment has been applied. We mentioned in the text.

Where were the high-risk and low-risk cluster areas for CIR, CFR, and CRR?

Ok, your valuable comment has been applied. We mentioned in the text.

What is meant by this sentence "The optimal value of bandwidth estimated to be 2411.332 Kilometers based on OHSA method "

Ok, your valuable comment has been applied. We mentioned in the text.We mean optimal value of bandwidth to distinguish high and low risk areas in the best possible case when the spatial autocorrelation is at its highest value. Using incremental spatial correlation, OHSA automatically selects the optimal bandwidth value at which spatial autocorrelation and clustering intensity is maximum and then uses it as an analytical scale for the Getis-Ord Gi * statistic

Please report the values of average annual percentage change (AAPC) and the annual percentage change (APC) along with their confidence intervals for different time trends.

Ok, your valuable comment has been applied.

What was your purpose in presenting Table 1?

Ok, your valuable comment has been applied. In table 1was shown more details of temporal analysis with joinpoint regression models fitted to New Cases, Case Recovery Rate and Case Fatality Rate of Covid-19.

Please review and modify the results.

Ok, your valuable comment has been applied.

Discussion:

Please discuss each of the results obtained.

Ok, your valuable comment has been applied.

Good luck

Dear Reviewer, Thank you for taking the time to review our manuscript.

Reviewer 3

Dear Authors

This study entitled “Spatio-temporal analysis of covid-19: a global study” is a great topic that has been used by Joinpoint and ArcGIS software to examine the spatiotemporal pattern of COVID-19. This manuscript is an interesting and hot topic if it is possible to reach a correct conclusion or
test a hypothesis. There are a few points that can be improved in the article.

Reply to comments reviewer number 3

Dear Reviewer. Thank you for your valuable comment. The all of your valuable comment has applied. Corrections were highlighted in yellow.

1- Since time plays an important role in this study, the time period considered for the analysis (January 1, 2020, until September 30, 2021) should be up to date.

For obtaining the number of COVID-19 patients during October 1, 2019 until June 30, 2021 by each country we used of CDC and WORDOMETER websites. Only until June 30, 2021, the data has been reported monthly and daily on the CDC and WORDOMETER websites. After this date, the data of COVID-19 were irregular and reported every day, every week, every month, or every three months. So the data reporting intervals were not the same, and depending on high and low the incidence and prevalence of COVID-19 disease, therefore, the time trend and changes of CFR, CRR, CIR will not be valid and reliable due to the fact that the time unit is not the same. Also, access to CDC and WORDOMETER country data was only possible until June 30, 2021.

2- It is suggested to compare the trend of incidence rate (CIR), case fatality rate (CFR), and case recovery rate (CRR) before and after the extensive use of vaccines.

We examined the entire time trend from October 1, 2019 until June 30, 2021. During this time, vaccination has been done abundantly in different communities. In the discussion section, we have talked about the drastically decrease and increase of the trends that one of these cases was the injection of the vaccine. But all these drastically changes in the time process cannot be attributed to the vaccine because the disease is multifactorial and many things besides the vaccine have an effect on the increase or decrease of the incidence, such as the use of masks.

We mentioned all these subject in the discussion section fallow as:

Significant increasing progression of disease incidence during the time between Oct 2019 (10.2019) and June 2021 (6.2021) is another result of present study. It had the highest growth rate in the first months though the last ten month of evaluation demonstrated the lowest growth rate. Growth rate was some have stable in this period. High growth rate at the beginning of pandemic outbreak could be due to a dramatic increase of patients in Wuhan, China and rapid transmission to the other countries and failure to discover suitable methods to diagnose and treat the disease(1).

The drop in the speed of disease development rate may be pertained to observance of health protocols and measures such as: observation of personal hygiene, use of protective equipment such as: face mask and shield, gown, gloves, glasses, N95 respirator, especially in hospital environments, proper ventilation, hand washing with soap and water or alcoholic disinfectant after contact with any contaminated surface(2), social distancing that has affected the pattern and rate of population movement, purposeful implementation of local quarantines(3), reduction of gatherings, social events and group meetings(2), use of efficient diagnostic tools such as: rapid and large-scale tests which play an essential role in patient management and reducing the rate of disease outbreak(4) and most importantly, vaccination which is essential for infection prevention, controlling disease prevalence and reducing its recurrence rate, etc(5).

Average case recover rate had been plummeting in the first three months of epidemic outbreak significantly and after that soared until the end of time period of study. Moreover, CFR had been increasing for the first five months of epidemic though started a decreasing progression which continued until June 2021 (6.2021). This increasing process of recovery rate and reduction of case fatality rate may be due to strengthen of immune system and promotion of self-care by striving for a healthy lifestyle and consuming adequate nutrients(6, 7), paying efforts to accelerate the development of treatment for COVID-19 by reusing antiviral drugs which are previously produced and approved by the FDA or currently assessed for other viral infections and combining these drugs with new technologies. These treatments aim to reduce SARS-CoV-2 infection burden in patients, decreasing the severe symptoms and slowing down the COVID-19 improvement(8, 9). For the most part timely diagnosis and early treatment of infected cases is the first step to win this battle (10).

From the beginning of pandemic at October 2019 until the June 2021, the average case fatality rate was estimated 0.031. Although CFR only increased in the first four months of pandemic, it decreased from May2020 until Sep2021. This falling process may be due to countries access to the diagnostic tests which has been increased, recently. This theory is consistent with a study in Illinois which states that raw CFR decreases in all regions and age groups by development of diagnostic tests(11). This study also showed the increase of CRR. There has been no specific medicine for this

disease so far even though various combination of drugs and therapies are utilized, most of which are supportive and symptomatic. As for the pneumonia-like symptoms of Covid-19, early diagnosis and controlling these symptoms results in valuable findings and better soaring of improvement rate(10, 12, 13).

3- The time period considered for the analysis is different in the Methods and results in sections of the abstract from October 2019 to June 2021 OR January 1, 2020, until September 30, 2021

Ok, your valuable comment has been applied.

October 1, 2019 until June 30, 2021 is correct. Was corrected.

4- In “Data collection and data source” the population at risk is related to what year was used.

To calculate the cumulative incidence rate, case fatality rate and the case recovery rate, we needed the population at risk for the denominator. These indicators were calculated monthly for October 1, 2019 until June 30, 2021, so the population at risk as monthly in the period October 1, 2019 until June 30, 2021 was used from the World Bank website.

5- In “temporal trend” How measures were calculated for the year?

We analyzed the data monthly during the period October 1, 2019 until June 30, 2021, so after 12 months, the time trend for one year will also be visible. All indicators including cumulative new cases, case fatality rate, and the case recovery rate are calculated monthly and after 12 months, the year can also be seen.

Figure 6A and Table 1 illustrates the time trend of new cases in each month and year.

The time trend of case recovery rate in each month and year is demonstrated in Table 1 and Figure6B.

Table1 and Figure 6C declare the time trend of case fatality rate in each month and year.

6- Sentence one in “temporal trend” is long and should be corrected “To evaluate the temporal trend of COVID-19, the cumulative new cases, case fatality rate, and the case recovery rate was calculated by month and year and temporal trend using Joinpoint regression analysis in Joinpoint regression program version 4.7.0.0 was plotted at alpha 5%.”

Ok, your valuable comment has been applied.

7- in “temporal trend” reference 10 has been repeated a lot

Ok, your valuable comment has been applied.

8- in order to evaluation of the seasonal trend of COVID-19 the incidence rate calculated by month?OR 3 months?

All indicators including cumulative new cases, case fatality rate, and the case recovery rate are calculated monthly and after 12 months, the year can also be seen.

Figure 6A and Table 1 illustrates the time trend of new cases in each month and year.

The time trend of case recovery rate in each month and year is demonstrated in Table 1 and Figure6B.

Table1 and Figure 6C declare the time trend of case fatality rate in each month and year.

9- Use abbreviations the cumulative incidence rate, case fatality rate, and case recovery rate in the spatial pattern analysis and cluster identification section.

Ok, your valuable comment has been applied.

In the entire text, we used abbreviations after writing the words for the first time when they were expanded.

10- Use the expanded OHSA word for the first time.

Ok, your valuable comment has been applied.

11- It’s better to report different units for CIR and, CRR, CFR in line 2 results because of high CIR.

Ok, your valuable comment has been applied.

In the present study, CIR in 10^6 individuals, CFR and CRR were calculated as percentages. The units of these indicators were mentioned in all parts of the article and line 2 results. CIR is increased because this index calculates all new cases cumulatively. In fact, in CIR, the new cases of a period are added with the new cases of previous periods. In order to compute the Cumulative incidence rate of COVID-19 the all number of newly diagnosed cases during a specific period of time was divided to total population at risk during the beginning of the period time(14). CIRs measure the risk of developing the disease

12- This sentence sequentially in the result was similar

Ok, your valuable comment has been applied. Two sentences were merged into one sentence.

13- ” Spatial patterns of Cumulative Incidence Rate, Case Recovery Rate and Case Fatality Rate which was in association with covid-19 have been declared in Figure 1-3 from the onset of epidemic Jan 2020 till the end of Sep 2021.” AND” In order to analyze the spatial pattern of COVID-19, disease CFR, CRR, CIR initially measured in all countries of the world from the start of epidemic Jan 2020 till the end of Sep 2021 and then the zoning of the disease was drawn in GIS environment (Figure 1-3).”

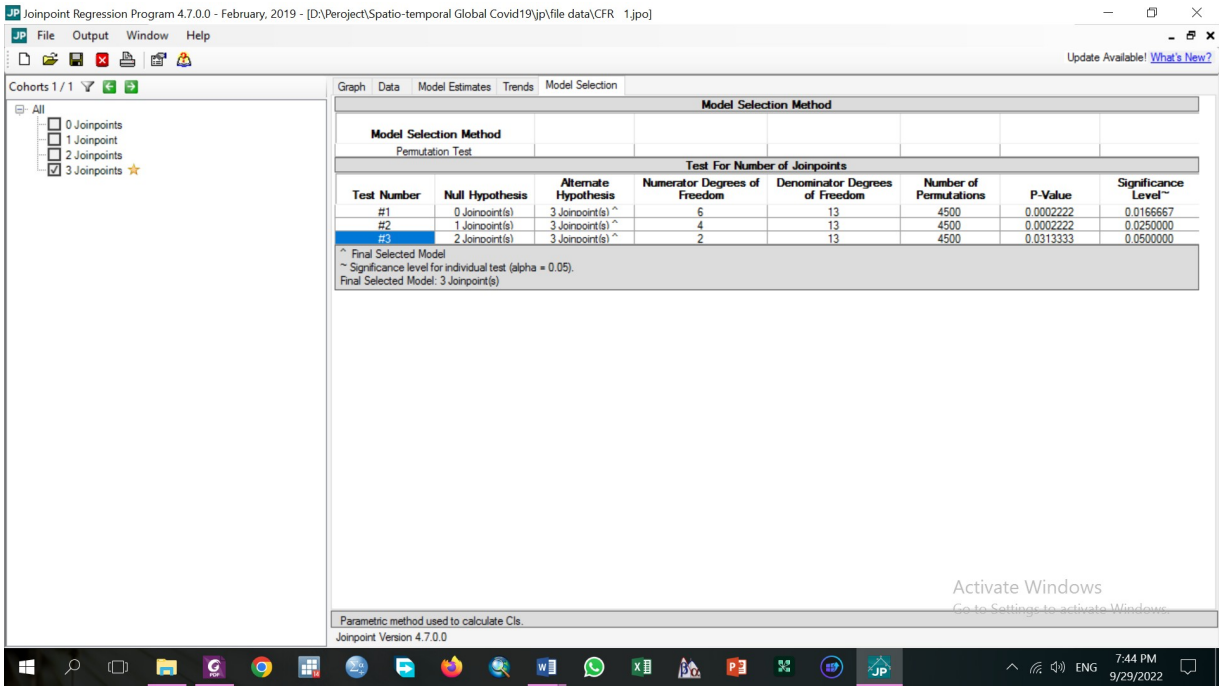
Ok, your valuable comment has been applied. Two sentences were merged into one sentence.

14- It’s better to interpret results for different waves and strains in countries.

Investigating the spatial pattern and temporal trend separately for each country is very complicated and requires a lot of budget. Also, due to the limitations in the table and Figures, we cannot show the spatio-temporal analysis for each country. Finally, the purpose of our study was to take a general look at the spatio-temporal analysis of Covid-19 in the whole world.

15- What do you mean by models in the sentence “The precision of models was examined by the sum of squared errors (SSE) and Bayesian information criterion (BIC).” In Joinpoint OR ArcGIS? BIC was not reported anywhere.

Sum of squared errors (SSE) and Bayesian information criterion (BIC) indicators are used to fit regression models and GOF (Goodness of fit). Any model that has the lowest BIS and SSE values indicates better model fit, less error, and higher explanation coefficient (R2). BIS and SSE values are not reported in the output of joinpoint software, only the best model selected based on the lowest BIS and SSE values is indicated by a yellow mark ★similar to the image below, but in the settings section, BIS and SSE indicators can be selected for model selection.



Also, check the highlighted items in the attached file and correct them.

Ok, your valuable comment has been applied. The highlighted items were reviewed and corrected.

Dear Reviewer, Thank you for taking the time to review our manuscript.

1. Al Hasan S, Saulam J, Kanda K, Hirao T. The novel coronavirus disease (COVID-19) outbreak trends in mainland China: a joinpoint regression analysis of the outbreak data from January 10 to February 11, 2020. Bull World Health Organ. 2020;17.

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14. Centers for Disease Control and Prevention. Lesson 3: Measures of Risk , [Available from: https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section2.html.
15. Binesh M, Pahlevanian A, Rahimi S, Ahmadizadeh Z. Relationship Between COVID-19-related Factors and Self-management Behaviors in People with Type-2 Diabetes: A Cross-sectional Study. Middle East Journal of Rehabilitation Health Studies. 2022;9(3).

2 Revision 1

4 comments · 7 Oct 2022 – 17 Oct 2022

Referee 2 Reviewer

ACCEPT 7 Oct 2022

Dear Editor

Responses to comments are satisfactory.

Sincerely

Referee 1 Reviewer

ACCEPT 8 Oct 2022

Dear Associate-Editor

I have reviewed the revised version of the manuscript. I think that the authors revised the manuscript appropriately and the current version of the manuscript can be published in the journal.

Kind regards

Associate Editor

ACCEPT 16 Oct 2022

Thanks to the authors for revising the manuscript. The manuscript is ready for publication now.

Editor-in-Chief

ACCEPT 17 Oct 2022

Dear Authors
We are pleased to inform you that your article is accepted for publication in the MEJRHS. We hope to receive other suitable articles from your group.