Archives of Pediatric Infectious Diseases
Volume 12 · Issue 2 · e141584

OPEN PEER REVIEW

# Patient-Reported Outcomes and Healthcare Practices: A Retrospective Analysis of Cystic Fibrosis Management During the COVID-19 Pandemic

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| SUBMITTED | REVISED | ACCEPTED | DOI |
| --- | --- | --- | --- |
| 2 Oct 2023 | 4 Dec 2023 | 28 Dec 2023 | 10.5812/apid-141584 |

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## 1 Original submission

5 comments · 4 Nov 2023 – 23 Nov 2023

### Referee 1 Reviewer

MAJOR REVISION 4 Nov 2023

Dear Editor
I would like to inform you that the authors have conducted a descriptive study and described some outcome endpoints of CF patients based on medical records and data collection. It would be better if they changed the title and objective of the study according to their approach.
Moreover, the authors have used a researcher-developed tool and scale to assess the effect of COVID-19 on CF patients without considering the confounders and period effect.
My decision is a major revision.
Reviewer,

### Referee 2 Reviewer

MAJOR REVISION 10 Nov 2023

Dear Author
Thank you for submitting this article.
Overall, the article needs English editing; for example, please do not use the future tense in the statistical analysis section.
Abstract
1- Please decrease the total word count to 250.
Introduction:
1- Please describe the complications of COVID-19 infection in CF patients in Iran and other countries.
Material and Method:
1- What was the definition of CF cases? How did you confirm the disease in your patients?
2- What method did you use to reduce bias in questionnaire completion by physicians? How many physicians completed the questionnaire, and did they receive any instructions for this task?
3- How were patients with COVID-19 identified? What were the criteria for infection?
4- What was the sampling method?
Result:
1- Please give the percentage of positive cases as a single value, not both positive and negative rates.
Discussion:
1- Please check that all results are discussed in this section, for example, clinical findings in COVID-19 cases.
Conclusion:
1- This section is very long and presents the results of the study. Please shorten it and give the most important finding of the study.
2- Best regards

### Referee 3 Reviewer

MINOR REVISION 12 Nov 2023

Hi dear authors
Please answer these questions:
1-What is your explanation for the higher rate of COVID-19 among patients with a history of COVID-19 vaccination (55.9%) compared with those with no vaccination history (36.6%)?

2- Do you know what percentage of your patients who wore face masks at all times became infected with COVID-19?
3- Can you give examples of the various foods that patients added to their diets to prevent COVID-19, given that 57.6% of them became infected?

**Saeed Sadr** Reviewer

MINOR REVISION 16 Nov 2023

This article can be accepted with minor changes.
According to the reference provided for this sentence ("Due to fear of infection and mismanagement of the disease in Iran, many individuals have lost their lives during several waves of COVID-19 outbreaks.")—reference 6—it cannot be inferred from this article that fear and mismanagement in Iran are specifically higher than in other countries and have caused an increase in patient deaths. It is recommended that this sentence be corrected.

**Associate Editor**

MINOR REVISION 23 Nov 2023

Reviewer 1:
Dear Editor
I would like to inform you that the authors have conducted a descriptive study and described some outcome endpoints in CF patients based on medical records and data collection. It would be better if they changed the title and objective of the study according to their approach.
Moreover, the authors have used a researcher-developed tool and scale to assess the effect of COVID-19 on CF patients without considering the confounders and period effect.
My decision is a major revision.

Reviewer 2:
Dear Author
Thank you for submitting this article.
Overall, the article needs English editing. For example, in the statistical analysis part, please don't use future-tense verbs.
Abstract
1- Please decrease the total word count to 250.
Introduction:
1- Please describe the complications of COVID-19 infection in CF patients in Iran and other countries.
Material and Method:
1- What was the definition of CF cases? How did you confirm the disease in your patients?
2- What method did you use to reduce bias in questionnaire completion by physicians? How many physicians were completing the questionnaire, and did they receive any instructions for this task?
3- How were patients with COVID-19 identified? What were the criteria for infection?
4- What was the sampling method?
Result:
1- Please give the percentage of positive cases as a single value, rather than both positive and negative rates.
Discussion:
1- Please check that all results are discussed in this part, for example, clinical findings in COVID-19 cases.
Conclusion:
1- This part is very long and presents the results of the study. Please shorten it and give the main finding of the

study.
2- Best regards
Decision:
Major revision
Reviewer 3:
This article can be accepted with minor changes.
According to the reference provided for this sentence: (Due to fear of infection and mismanagement of the disease in Iran, many individuals have lost their lives during several waves of COVID-19 outbreaks.) - reference 6 - it cannot be inferred from this article that fear and mismanagement in Iran are specifically greater than in other countries and have caused an increase in patient deaths. It is recommended that this be corrected.
Decision: Minor revision
Reviewer 4:
Hi dear authors
Please answer these questions:
1- What is your explanation for the higher rate of corona disease in patients with a positive corona vaccination history (55.9%) compared with those with a negative vaccination history (36.6%)?
2- Do you know what percentage of your patients who consistently wore face masks became infected with COVID-19?
3- Can you give examples of the various foods that were added to their diet to prevent COVID-19, given that 57.6% of them became infected?
Decision:
Minor revision

2

# 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.

**Dear Editors,**

We would like to thank you for the email dated 25-November-2023, and the opportunity to resubmit a revised version of the manuscript, entitled “Impact of Covid-19 on children who suffer from Cystic Fibrosis” (Manuscript ID: 141584). We would also like to take this opportunity to express our thanks to the reviewers for the positive feedback and helpful comments for correction or modification, which led to a major revision of the work and helped its improvement. We have addressed each of the reviewer’s comments as outlined below. All corrections are highlighted in the main text in yellow.

**Reviewer Comments:**

*Reviewer 1:*
*This article can be accepted with minor changes*
*According to the reference provided for this sentence: (Due to fear of infection and mismanagement of the disease in Iran, many individuals have lost their lives during several waves of COVID-19 outbreaks.) - reference 6- it is not inferred from this article that the fear and mismanagement in Iran is specifically higher than other countries and has caused the increase in the death of patients. It is recommended to correct it.*

Response: The reference is corrected.

Additionally, the COVID-19 pandemic has placed a significant burden on both national and international healthcare systems (6). Due to fear of infectious by cronovairus in Iran caused our country to several huge COVID-19 waves thus; we experienced significant mortality and morbidity (7, 8).

7. Sahlan RN, Kinkel-Ram SS, Uzoegwu K, Smith A. Fear of COVID-19, insomnia, and eating disorder symptoms among Iranian college students. Journal of affective disorders reports. 2023;13:100601.
8. Cenk M, Yegit CY, Ergenekon A, Aksoy AT, Bilicen G, Gokdemir Y, et al. Effect of COVID-19 Pandemic on Anxiety Levels of Children with Cystic Fibrosis and Healthy Children. Authorea Preprints. 2020.

*Reviewer 2:*
*Dear Editor*
*I would like to inform you that the authors have done a descriptive study and described some outcome endpoints of CF patients based on medical records and data collection. It would be better if they changed the title and objective of the study according to their approach. Moreover, the authors have used a researcher-developed tool and scale to assess the effect of*

*COVID-19 on CF patients without considering the confounders and period effect.*
*My decision is a major revision.*

Response: The title was revised according to your valuable comment, as follows:

**Patient-Reported Outcomes and Healthcare Practices: A Retrospective Analysis of Cystic Fibrosis Management during the COVID-19 Pandemic**

*Reviewer 3:*

*Dear Author*
*Thank you for submission of this article.*
*Totally the article needs English edition for example in statistical analysis part pls don't use future verbs.*

Response: The manuscript was revised for English style, grammar, and spelling mistakes.

**2.2 Statistical Analysis:**

All data was entered into Microsoft Excel software and then analyzed using IBM SPSS Statistics for Windows (Released 2012, Version 21.0, Armonk, NY: IBM Corp). Qualitative variables are presented as frequency and percentage, and quantitative variables are expressed as the mean. Inferential statistics involved calculating differences between study variables using the Chi-square test for categorical variables and the independent two-sample t-test for quantitative variables. Additionally, normality of quantitative data assessed using the Shapiro-Wilk test. It's important to note that any p-values less than 0.05 are considered statistically significant.

*Abstract*
*1- Pls decrease the total word count to 250*

Response: Thanks for your comment. The total word counts decrease to 243 words.

**Method & participants:** A descriptive retrospective study was performed at Mofid Children's Hospital to determine the effect of the COVID-19 pandemic on CF patients. Physician completed 128 valid and reliable questionnaires. Moreover, hospital medical records were also used to revalidate the data and complete the rest part of the questionnaire. The information collected for this study included demographic data, patients' height, patients' weight, Body Mass Index (BMI), past and current positive history of COVID-19-like symptoms, socially determined condition, and influence of COVID-19 on routine therapeutic measurements in CF. The data were analyzed by SPSS software version 21.

*Introduction:*
*1- Pls give the covid19 infection complication in Cf patients in Iran and other countries*

Response: Owing to Mathew HR et al meta-analysis, the COVID-19 complications in CF individuals are quite the same in many countries. As well, as complications added to the manuscript.

Also, Mathew H.R. et al in their meta-analysis depicted more CF individuals during COVID-19 presented with high-grade fever, fatigue and needed supplemental oxygen therapy due to a decrease in oxygen saturation (2).

*Material and Method:*
*1- What was the definition of CF cases? How did you confirm the disease in your patients?*

Response: CF cases are equal to CF individuals or CF patients. As well, we indicated the "CF patients" phrase in the Material and Method part of the manuscript. In addition, Mofid Hospital is the tertiary hospital center in Tehran, Iran, and many CF patients registered in the HIS system of Mofid Hospital previously. Also, we confirmed the patients' disease by the sweat chloride test.

*2- What way you used to decrease the bias of questionnaire filling by physicians. How many physicians were filling the questionnaire and did they have any instruction for this job?*

Response: As we mentioned in the manuscript "A valid and reliable questionnaire was completed by physicians via CF patients' parents after a verbal informed consent by a phone call. As well, hospital medical records were also used to revalidate the data and complete the rest part of the questionnaire.". Moreover, physicians asked neutral-worded questions, made sure participants answered questions that were not leading, and so on.

Furthermore, a nurse practitioner and a pediatric pulmonary fellowship physician who had previous knowledge and experiments of filling out questionnaire participated in the current study data collection.

questionnaire were completed by a single nurse practitioner and a pediatric pulmonary fellowship physician via CF patients …

and reviewed by expert single nurse practitioner and a pediatric pulmonary fellowship physician. The …

*3- How did patients with COVID19 were found? What was the criteria for infection?*

Response: Owing to Mofid Hospital is the tertiary hospital center in Tehran, Iran, many patients who suffered from COVID-19 infections are referred here. Additionally, the COVID-19 criteria that we used are World Health Organizations (WHO) criteria such as PCR test, chest CT scan, serological tests or the presence of common cold-like symptoms.

Furthermore, we used the World Health Organization (WHO) COVID-19 criteria (guideline) for patient confirmation.

… the results of PCR test, chest CT scan, serological tests or the presence of common cold-like symptoms in the patient …

*4- What was the sampling method?*

Response: As we mentioned previously in the manuscript “we recruited all confirmed CF patients who referred to Mofid hospital between March 2020 and May 2022 in our study”.

*Result:*
*1- Pls give the percentage in cases who are positive in one value, not both positive and negative rates*

Response: Thanks for your comment. The changes were made.

Additionally, 36.6% of the patients who did not inject the COVID-19 vaccine had a history of COVID-19. On the other hand, 55.9% of the patients who were fully vaccinated (history of injecting at least two doses of vaccine) had a history of infection with COVID-19.

Also, 42.6% of patients whose family members were vaccinated were infected with COVID-19 without any significant relationship ($p > 0.05$).

… Half of the patients who were underweight in terms of BMI, Z score were infected with COVID-19. Moreover …

patients, 30.8% were infected with COVID-19.

Also, 33.3% of obese patients had a history of COVID-19 infection.

*Discussion:*
*1- Pls check that all results are discussed in this part for example clinical findings in COVID19 cases.*

Response: The manuscript was revised to discussing all results.

… non-vaccinated patients. Furthermore, as the same as many previous studies (5, 7-9, 12), the coronavirus clinical findings of the current study; for instance, Fever, cough, sore throat, body pain, and gastrointestinal symptoms were the same. However, in various COVID-19 waves, several symptoms were highlighted.

… It seems that since in the studies of other countries during the pandemic, physiotherapy was performed unchanged or more than before (17). This difference may be attributed to cultural variations in Iran and inadequate patient education on the importance of physiotherapy. However, we found no significant relationship between the frequency of chest physiotherapy and COVID-19 infection in our study.

… Another study depicted (21), only 1.3% of patients needed hospitalization. In Simonson et al. study (15), 8% of patients needed hospitalization, and 85% did not need any treatment. Probably,

the difference in the time of conducting the study, due to the different common variants of coronavirus explains why we reached a higher prevalence

… In fully vaccinated patients, the headache was significantly higher in COVID-19-infected patients

… Furthermore, as the same as many previous studies (5, 9-11, 14-15), the coronavirus clinical findings of the current study; for instance, Fever, cough, sore throat, body pain, and gastrointestinal symptoms were the same. However, in various COVID-19 waves, several symptoms were highlighted.

Furthermore, Simonson et al. (15) illustrated the average BMI among CF patients who were infected with COVID-19 was 22.4. In Carr et al.'s study (20), underweight patients had a more severe infection caused by Covid-19, and being overweight acted as a protective factor. The possible cause of this difference in our study with similar studies was that those studies were conducted in adults and there is a need to conduct more studies in children.

… It would related to the subtype of coronavairus infections in our patients, Omicron. The COVID-19 vaccines had typically induced immunization for previous subtypes of coronavirus. As well, in patients who not injected booster dose, the effect of vaccine nutralized. Also, some of our patients had coronavirus before the time of injection (23). …

*Conclusion:*
*1- This part is very long and gives the results of study pls brief it and give the most important and main finding of study*

Response: The conclusion part decreased to 70 words.

**Conclusion:**

A descriptive retrospective study at Mofid Children's Hospital, Tehran, Iran, to determine the impact of COVID-19 on CF patients provided valuable information about the demographic and CF patients' routine care habits during the COVID-19 pandemic. To summarize, CF patients' habits were not significantly changed during the COVID-19 pandemic. Interestingly, COVID-19 was significantly common among CF male patients. Moreover, headache as the most common symptom played a role among vaccinated patients.

*2- Best regards*

*Reviewer 4:*
*Hi dear authors*
*Please answer to these questions:*
*1-What is your explanation that patients with positive corona vaccination history (55.9%) had higher corona disease in comparison to negative vaccination history (36.6%)?*

Response: In our study, most of the patient who had corona disease was infected with the omicron subtype. On the other hand, the coronavirus vaccine injected in Iran has typically

induced immunization for older subtypes of coronavirus. Also, some of our patients had coronavirus before the time of injection.

… In our study, 79.2% of COVID-19 infections were associated with the Omicron variant …

… It would related to the subtype of coronavairus infections in our patients, Omicron. The COVID-19 vaccines had typically induced immunization for previous subtypes of coronavirus. As well, in patients who not injected booster dose, the effect of vaccine nutralized. Also, some of our patients had coronavirus before the time of injection (23).

*2- Do you know which percent of your patients that wore face mask completely infected with covid – 19 diseases?*

Response: The majority (60%) of participants wear facemasks against COVID-19 infection everywhere. Also, 28 of the patients with covid-19 wore masks in all places when leaving home, 19 wore masks only in crowded places and 6 did not wear masks at all. No significant relationship was found in this group either.

Additionally, the majority of our participant wore facemask against coronavirus in everywhere. Among CF patients, 28 of the CF participants with covid-19 wore masks in all places, 19 participants wore masks only in crowded places and 6 patients did not wear masks at all. No significant relationship was found in this group. ($p>0.05$).

In the same study, 74% of children with CF used facemasks as soon as they left home. In contrast, in the present study, the coronavirus restrictions and lockdowns were not applied with the same intensity and strictness as in other countries. Also, the lack of proper training from the media seems to be the reason for less adherence to health principles.

*3- May you example about various foods that added to their diet to prevent COVID-19 which 57.6% of them become infected?*

Response: They added mineral such as vitamins A, D, E, K, and a zinc supplement, as well, foods; for instance, tea with honey and lemon juice, garlic, ginger, and citrus fruits.

patients who added various foods such as, tea with honey and lemon juice, garlic, ginger, and citrus fruits, to their diet to prevent corona

Kind regards,

Corresponding author

## 2 Revision 1

1 comment · 27 Dec 2023

### Associate Editor

ACCEPT 27 Dec 2023

1- Please provide the relevant citation for this sentence in the methods section: "A valid and reliable questionnaire were completed by ...."
2- Authors should delete the subheadings in the results section such as 3.1, 3.2, and so on (including the Questionnaire part).
3- Please revise the following phrase in the statistical analysis section: "It's important to note that any p-values less than 0.05 are considered statistically significant."
This phrase should be replaced with "P-values less than 0.05 were considered statistically significant."