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OPEN PEER REVIEW

Exploring Drug-Resistant Mutations in Protease Inhibitors and Subtype Distribution Among HIV-1 Positive Patients in Lorestan Province, Iran

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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Contents

1 Original submission Associate Editor 2
2 Revision 1 3
Authors' reply to reviewers 4
Reviewer and editor comments 8

1 Original submission

1 comment · 2 Mar 2024

Associate Editor

MAJOR REVISION 2 Mar 2024

According to the reviewers' comments, the manuscript needs major revision.
Sincerely

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.

To JJM Editorial Board

Date: March 2024

Subject: Detailed response to reviewers

Manuscript ID: 145562

Manuscript Title: Exploring Drug-Resistant Mutations in Protease Inhibitors and Subtype Distribution Among HIV-1 Positive Patients in Lorestan Province, Iran

Our team appreciates the reviewers for their observations and comments on the manuscript entitled ***"Exploring Drug-Resistant Mutations in Protease Inhibitors and Subtype Distribution Among HIV-1 Positive Patients in Lorestan Province, Iran***". We have fulfilled their comments and suggestions and wish to submit a revised version of the manuscript for further consideration in the ***Jundishapur Journal of Microbiology.*** We provide a point-by-point response explaining how we have addressed each of the reviewer's comments.

Sincerely yours,

To dear reviewer 1:

Comment: Based on reviewing the manuscript, it seems there are some grammatical as well as spelling errors that should be rechecked and corrected.

Reply: Thank you for your feedback. The entire manuscript has been thoroughly rechecked and any grammatical and spelling errors have been corrected.

Comment: The introduction part is very short, so need more information regarding the importance of the research

Reply: Thank you for your valuable comments. We have updated and expanded the introduction as you recommended. All changes have been highlighted in the manuscript.

Comment: In the material and method part the statistical method should be considered and included in the text.

Reply: The statistical analysis was incorporated at the end of the methods section.

Comment: References should be update since many outdated references has been used.

Reply: Thank you for your feedback. All references have been updated as per your recommendation.

To dear reviewer 2:

Comments:

Dear Authors

.Thanks for your valuable work, but some questions need your answers for clarification

Material and methods

1- Why the authors didn't use fresh samples instead of those collected between 2015 and 2016?

Reply1: Thank you for your question. The use of samples from 2015-2016 was primarily due to the limited availability of fresh samples and the challenges associated with new sample collection. These challenges include difficulties in securing patient collaboration, which can significantly hinder the collection process.

2- Why the authors collected samples which are above 16?

Reply 2: We appreciate your query regarding the age range of our study participants. The sample collection was restricted to individuals aged 16 and above, reflecting the predominant age group of patients presenting at health centers within Lorestan province. This decision was also influenced by the logistical difficulties encountered in obtaining pediatric samples, which necessitated the exclusion of younger age groups to maintain the integrity of the study's data set. We acknowledged this limitation in the study's limitations section.

3- Are there any excluded and included criteria?

Reply 3: Thank you for the feedback. The patients were included based on the following criteria: Samples were collected from patients aged above 16 years in both groups. Patients who had been on antiretroviral regimens for at least one year were included, provided that treatment information, as supplied by the physicians, was available.

4- Since the sequences data were submitted on the NCBI (GeneBank), please use the accession numbers for building the phylogenetic tree.

Reply 4: Thank you for your suggestion. The phylogenetic tree was reconstructed using the relevant accession numbers of the samples.

To dear reviewer 3:

I read carefully the manuscript titled ” Exploring Drug-Resistant Mutations in Protease Inhibitors and Subtype Distribution Among HIV-1 Positive Patients in Lorestan Province, Iran;”. The paper is written well in a scientific way and has new findings. I recommend the manuscript for publication in with following major changes.

Comment 1: I suggest the authors to use more and new published papers to expand the discussion.

Reply1 : Thank you for the valuable suggestion. The discussion section has been expanded to include new published articles and highlighted in the manuscript.

Comment 2: The used primers needs to be cited.

Reply2: Thank you for your comment. The primers used have been cited with the relevant article in the manuscript.

Comment 3: Please write a conclusion more cautiously, since several confounding factors were not assayed within the experiment.

Reply 3: Thank you for your feedback. The conclusion section has been carefully revised in light of our limitations.

The development of drug resistance mutations in HIV is predominantly driven by the pressures of antiretroviral treatment. This dynamic leads to the formation of resistant viral variants that can

be transmitted to treatment-naive individuals, resulting in expedited virological failure and a reduction in viable treatment options. It is imperative to accurately determine the prevalence, emergence, and transmission of drug resistance to effectively manage patient treatment and inform health policy decisions. In this study, we have documented a significant number of mutations in the protease gene among HIV-positive patients from Lorestan province, Iran, who have been treated with antiretrovirals. These findings underscore the critical need for a meticulous selection of antiretroviral regimens (ARVs), ongoing patient follow-up, reinforcement of adherence strategies, and comprehensive monitoring of viral load to detect early signs of treatment failure.

Comment 4: Abbreviations must be fully spelled only out at the first time.

Reply 4: Thank you for your feedback concerning the abbreviations. We have verified that all abbreviations are fully spelled out the first time they are used in the manuscript.

Comment 5: The probable limitations of study must be mentioned.

Reply 5: The limitation of the study has been included at the end of the manuscript.

It is imperative to acknowledge certain limitations within this study. The phylogenetic analysis conducted is restricted to the protease region of the viral genome. For a more holistic view of viral resistance patterns, it is crucial to also consider and sequence other significant regions, including gag and env. Furthermore, the absence of pediatric patient samples in our dataset may affect the breadth of our conclusions. Nevertheless, the data presented herein provides important insights into resistance mutations, which are valuable despite the methodological limitations. Future research with a larger cohort would be beneficial to reinforce the validity and robustness of these findings.

Comment 6: Keywords must be written based on Mesh terms

Reply 6: all keywords have been updated to align with Mesh terms.

Human immunodeficiency virus, HIV Protease, drug Resistance, Mutation, Antiretroviral agents, Iran

2 Revision 1

0 comments

No public comments in this round.