Shiraz E-Medical Journal
Volume 23 · Issue 1 · e113670

OPEN PEER REVIEW

Differential Diagnostic Utility of Clinical Laboratory Data in Patients with Severe and Non-severe COVID-19

Ali Hosseinzadeh, Mohammad Hassan Emamian, Marzieh Rohani-Rasaf, Ahmad Khosravi, Fariba Zare, Hossein Sheibani, Ehsan Binesh, Amir Atashi, Shirin Mahmoudi, Reza Chaman

SUBMITTED	REVISED	ACCEPTED	DOI
14 Feb 2021	13 Jun 2021	17 Jun 2021	10.5812/semj.113670

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.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Maysam Rezapour, Referee 1, Referee 2 2
2 **Revision 1** 4
Authors' reply to reviewers 5
Reviewer and editor comments 10

1 Original submission

3 comments · 15 Apr 2021 – 19 May 2021

Maysam Rezapour Reviewer

MINOR REVISION 15 Apr 2021

Thanks for the opportunity to review this manuscript.
In general, this manuscript can be accepted after the following comments are addressed.
Introduction:
Please note the different methods used to classify the severity of COVID-19 in various other studies.
Methods:
1. What was the approach to reducing the variables to reach the final model?
2. With regard to the very large variation in units (measurements) related to the variables entered in the model, in my opinion, there is a need to standardize the variables and enter them in standardized form in the regression model.
Results:
1. The full model for multivariate analysis is not presented.
2. Also show the correlations among the independent variables in the descriptive statistics table.
Discussion:
1. The use of the term "risk factor" for INR, NLR, and LDH in cross-sectional studies is not appropriate.
2. At the end of the discussion, provide a general and practical conclusion.

Referee 1 Reviewer

MINOR REVISION 22 Apr 2021

1- The manuscript needs English editing.
2- Please describe which changes in the significant variables mentioned are related to disease severity in the results and abstract. For example, high or low NLR.
3- Age, gender, and body index are not laboratory data!!!
4- My decision is acceptance with minor revision.

Referee 2 Reviewer

MINOR REVISION 19 May 2021

For the manuscript Differential diagnostic utility of clinical laboratory data in patients with severe and non-severe COVID-19, I suggest accepting this manuscript after revision, and the authors should consider the suggestions described below:
1. Compare the traditional methods of analysis with the methods based on this subject. Maybe a table could help.
2. The perspectives section must address the use of this work for COVID-19, according to your proposal.

3. The text is written in very poor English, with issues such as 1: incorrect spelling, 2: incorrect use of tenses, and 3: incorrect sentence structure.

4. Some parts of the introduction on COVID-19 and … need to refer to the papers below, so these papers should be added to the manuscript:
1: Covid-19 treatment by plant compounds ,S Mazraedoost, G Behbudi, SM Mousavi, SA Hashemi .Advances in Applied NanoBio-Technologies 2 (1), 23-33
2; Ultra-sensitive viral glycoprotein detection NanoSystem toward accurate tracing SARS-CoV-2 in

biological/non-biological media
SA Hashemi, NGG Behbahan, S Bahrani, SM Mousavi, A Gholami, ...N.Omidifar
Biosensors and Bioelectronics 171, 112731
3; Recent Biotechnological Approaches for Treatment of Novel COVID-19: From Bench to Clinical Trial,SM Seyyed Mojtaba Mousavi, Seyyed Alireza Hashemi, Najmeh Parvin, Drug Metabolism Reviews
4: Effect of silver nanoparticles disinfectant on covid-19,G Behbudi Advances in Applied NanoBio-Technologies 2 (2), 63-67

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.

June 6, 2021
Dr. Kamran Bagheri Lankarani
Managing Editor
Shiraz E-Medical Journal

Dear Dr. Lankarani

Thank you very much for reviewing our manuscript entitled “Differential diagnostic utility of clinical laboratory data in patients with severe and non-severe COVID-19”. We also greatly appreciate the reviewers for their helpful and thoughtful comments. We agreed with all comments and tried to address them accordingly. The reviewers’ comments and the authors’ replies are as follows:

Response to Reviewer 1

Comment 1: Compare the traditional methods of analysis with the methods based on this subject. Maybe a table could help

Response: In traditional analysis methods, usually dichotomous logistic regression, ordinal logistic regression, or multi-nominal logistic regression are used to assess the factors related to the severity of the disease (according to the different levels of dependent variables). But in our method, in addition to investigating the factors associated with disease severity, we can understand the accuracy of classifying patients into different classes based on the severity of the disease. Moreover, we can evaluate the sensitivity and specificity of each variables in distinguishing severe cases. In this study, both methods have been used (Table 2 and Figure 2).

Comment 2: The perspectives section must address the use of this work for covid 19, according to your proposal.

Response: The text has been revised as suggested by the reviewer. (Background- last paragraph- 4th sentence and conclusion section added)

Comment 3: The Text is too Poor language such as 1: grammar overall is not being able to spell words correctly,2: Not using tenses correctly,3: not structuring sentences correctly.

Response: The manuscript has been revised by an editing service

Comment 4: Some of introduction on covid 19 and … are need using from below papers, so, below papers are add to manuscript

1: Covid-19 treatment by plant compounds ,S Mazraedoost, G Behbudi, SM Mousavi, SA Hashemi .Advances in Applied NanoBio-Technologies 2 (1), 23-33

2; Ultra-sensitive viral glycoprotein detection NanoSystem toward accurate tracing SARS-CoV-2 in biological/non-biological media

SA Hashemi, NGG Behbahan, S Bahrani, SM Mousavi, A Gholami, ...N.Omidifar

Biosensors and Bioelectronics 171, 112731

3; Recent Biotechnological Approaches for Treatment of Novel COVID-19: From Bench to Clinical Trial,SM Seyyed Mojtaba Mousavi, Seyyed Alireza Hashemi, Najmeh Parvin, Drug Metabolism Reviews

4: Effect of silver nanoparticles disinfectant on covid-19,G Behbudi Advances in Applied NanoBio-Technologies 2 (2), 63-67

Response: As suggested by the reviewer some above mentioned references were added.

Response to Reviewer 2

Comment 1: the manuscript needs English editing.

Response: The manuscript has been revised by an editing service

Comment 2: please describe what changes in mentioned significant variables are related to disease severity in the result and abstract. for example, high or low NLR.

Response: In the result and abstract section, discussion-4th- 3rd line, and also table 2 odds ratio of each variable has reported. Given that the odds ratio of all variables is above 1, that means these variables have a positive association with disease severity.

Comment 3: age, gender and body index are not laboratory data!!!

Response: The reviewer is right. But we didn't assess the diagnostic value of these variables. Actually, these variables entered to regression model as a confounder.

Comment 4: My decision is acceptation with minor revision.

Response: Thanks for your hopeful comment.

Response to Reviewer 3

Comment 1: Please do a deep English revision.

Response: The manuscript has been revised by an editing service

comment 2: you can Use the article below and cite it in the references

Prevalence of Anti-SARS-CoV-2 Antibody in Hospital Staff in Double-Center Setting: A Preliminary Report of a Cohort Study From Iran, Shiraz E-Med J. Online ahead of Print ; 22(3):e112681. doi: 10.5812/semj.112681.

Response: As suggested by the reviewer above mentioned reference was added.

2- Honarvar B, Lankarani KB, Kharmandar A, Shaygani F, Zahedroozgar M, Haghighi MRR, et al. Knowledge, attitudes, risk perceptions, and practices of adults toward

COVID-19: a population and field-based study from Iran. International journal of public health. 2020;65(6):731-9.

6- Bagheri Lankarani K, Honarvar B, Omidifar N, Pakdin M, Moghadami M, Shokripour M, et al. Prevalence of Anti-SARS-CoV-2 Antibody in Hospital Staff in Double-Center Setting: A Preliminary Report of a Cohort Study From Iran. Shiraz E-Medical Journal. 2021;22(3).

Response to Reviewer 4

Methods:

Comment 1: What was the approach of reducing the variables to reach the final model?

Response: First, univariate analysis was performed (Table 1). Variables that had a p-value<0.2 in univariate analysis were included in the regression model. Using the likelihood ratio test, variables that did not significantly increase the regression model efficacy were identified and eliminated from the regression model. Finally, only the diagnostic value of variables that were significantly associated with disease severity were evaluated using the ROC curve.

Comment 2: With regard to the very large variation of units (measurements) related to the variables entered in the model, in my opinion, there is a need to standardize the variables to enter the standardized form in the regression model.

Response: Standardization is performed to convert data distribution to normal distribution. The normality Kolmogorov-Smirnov test were used to investigate the distribution of all quantitative variables. Since all variables had normal distribution, it seems no need to standardization (Patients and Methods section- paragraph 2-line 3).

Results:

Comment 1: The full model for multivariate analysis is not presented.

Response: All variables that had a p-value< 0.2 in Table 1 were included in the logistic regression model based on the explanatory method. Since the purpose of this study was to evaluate the diagnostic value of variables that had a significant relationship with disease severity, therefore, the variables that were not significantly associated with disease severity in the multivariate logistic regression model were not shown in Table 2.

Comment 2: Also show the correlation between the independent variables with each other in the descriptive statistics table.

Response: The authors do not agree with the reviewer. According to the purpose of our study, there is no need to evaluate the correlations between variables, and actually this does not help for better understanding the results of our study. Therefore, for simplification, there is no need to express the correlation of variables.

Discussion:

Comment 1: The use of the term "risk factor" for INR, NLR, and LDH in cross-sectional studies is not appropriate.

Response: The reviewer is right. The text has been revised as suggested by the reviewer. (discussion- - 1st sentence)

Comment 2: At the end of the discussion, provide a general and practical conclusion.

Response: The conclusion section was added at the end of the discussion section.

2 Revision 1

0 comments

No public comments in this round.