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Jul 02 2021 02:28AM Date:

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Submission Confirmation for PONE-D-21-21595 Subject:

PONE-D-21-21595

Clinical characteristics and outcomes of COVID-19 patients in Bali, Indonesia PLOS ONE

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From: "PLOS ONE" plosone@plos.org

Notification of Formal Acceptance for PONE-D-21-21595R2 Subject:

PONE-D-21-21595R2

Clinical characteristics and outcomes of COVID-19 patients in Bali. Indonesia

Dear Dr. Nelwan

I'm pleased to inform you that your manuscript has been deemed suitable for publication in PLOS ONE. Congratulations! Your manuscript is now with our production department.

If your institution or institutions have a press office, please let them know about your upcoming paper now to help maximize its impact. If they'll be preparing press materials, please inform our press team within the next 48 hours. Your manuscript will remain under strict press embargo until 2 pm Eastern Time on the date of publication. For more information please contact onepress@plos.org.

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on behalf of Dr. Nguyen Tien Huy Academic Editor PLOS ONE

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Within one week, you'll receive an e-mail detailing the required amendments. When these have been addressed, you'll receive a formal acceptance letter and your manuscript will be scheduled for publication. An invoice for payment will follow shortly after the formal acceptance. To ensure an efficient process, please log into Editorial Manager at http://www.editorialmanager.com/pone/, click the 'Update My Information' link at the top of the page, and double check that your user information is up-to-date. If you have any billing related questions, please contact our Author Billing department directly at authorbilling@plos.org. If your institution or institutions have a press office, please notify them about your upcoming paper to help maximize its impact. If they'll be preparing press materials, please inform our press team as soon as possible -- no later than 48 hours after receiving the formal acceptance. 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The manuscript must describe a technically sound piece of scientific research with data that supports the conclusions. Experiments must have been conducted rigorously, with appropriate controls, replication, and sample sizes. The conclusions must be drawn appropriately based on the data presented. Reviewer #2: Yes Reviewer #3: Partly 3. Has the statistical analysis been performed appropriately and rigorously? Reviewer #1: Yes Reviewer #2: Yes Reviewer #3: Yes 4. Have the authors made all data underlying the findings in their manuscript fully available? The PLOS Data policy requires authors to make all data underlying the findings described in their manuscript fully available without restriction, with rare exception (please refer to the Data Availability Statement in the manuscript PDF file). The data should be provided as part of the manuscript or its supporting information, or deposited to a public repository. For example, in addition to summary statistics, the data points behind means, medians and variance measures should be available. If there are restrictions on publicly sharing data—e.g. participant privacy or use of data from a third party—those must be specified. Reviewer #1: Yes Reviewer #2: Yes Reviewer #3: Yes 5. Is the manuscript presented in an intelligible fashion and written in standard English? PLOS ONE does not copyedit accepted manuscripts, so the language in submitted articles must be clear, correct, and unambiguous. Any typographical or grammatical errors should be corrected at revision, so please note any specific er Reviewer #1: Yes Reviewer #2: Yes Reviewer #3: No Please use the space provided to explain your answers to the questions above. You may also include additional comments for

Paviawar #2: Thank you for addressing the comments. I baliave the manuscript is fit for publication after the edits. Good

Reviewer #1: This article can be accepted by the journal. The author has addressed all my comments

Thank you for your great work!

the author, including concerns about dual publication, research ethics, or publication ethics. (Please upload your review as an attachment if it exceeds 20,000 characters)

luck to the authors.

Reviewer #3: Authors did a great job revising the manuscript but still there are certain considerations for example:
- In the heading- Study setting Line no. 95-100 authors have defined the classification of groups. This was repeated again from line 108 to 110.
- Line no: 162- "pneumonia non-COVID-19" could be written as pneumonia (non-COVID)

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Reviewer #1: Yes: Van Phu Tran

Reviewer #2: Yes: Abdelrahman M Makram

Reviewer #3: Yes: Zeeshan Ali Khan

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From: "PLOS ONE" plosone@plos.org

PLOS ONE Decision: Revision required [PONE-D-21-21595R1] Subject:

PONE-D-21-21595R1

Clinical characteristics and outcomes of COVID-19 patients in Bali, Indonesia PLOS ONE

Thank you for submitting your manuscript to PLOS ONE. After careful consideration, we feel that it has merit but does not fully meet PLOS ONE's publication criteria as it currently stands. Therefore, we invite you to submit a revised version of the manuscript that addresses the points raised during the review process, especially on the data analysis. Please describe more in detail the methods of multivariable regression analysis. How did the authors include factors in the model?

In addition, the authors need to follow the reporting STROBE guidelines published in this link: https://www.equator-network.org/wp-content/uploads/2015/10/STROBE_checklist_v4_combined.pdf A checklist should be submitted as a supplemental file.

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We look forward to receiving your revised manuscript.

Nguyen Tien Huy, Ph.D., M.D. Academic Editor PLOS ONE

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Reviewers' comments:

deviewer's Responses to Questions

Comments to the Author

1. If the authors have adequately addressed your comments raised in a previous round of review and you feel that this manuscript is now acceptable for publication, you may indicate that here to bypass the "Comments to the Author" section, enter your conflict of interest statement in the "Confidential to Editor" section, and submit your "Accept" recommendation.

Reviewer #1: All comments have been addressed

Reviewer #2: All comments have been addressed

Reviewer #3: (No Response)

2. Is the manuscript technically sound, and do the data support the conclusions?

The manuscript must describe a technically sound piece of scientific research with data that supports the conclusions experiments must have been conducted rigorously, with appropriate controls, replication, and sample sizes. The consust be drawn appropriately based on the data presented.

Reviewer #2: Partly

Reviewer #3: Partly

3. Has the statistical analysis been performed appropriately and rigorously?

Reviewer #1: Yes

Reviewer #2: Yes

Reviewer #3: Yes

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Reviewer #1: Yes

Reviewer #2: Yes

Reviewer #3: Yes

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Reviewer #1: Yes

Reviewer #3: No

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Reviewer #1: Thank you for your great effort. Your team edited and clarified the comments of the reviewers and editors very well, but some points must be defined or fixed.

- Please clarify the aim of the study with the specific study population in that sentence: "This study aimed to compare clinical and laboratory manifestations 77 disparity between COVID-19 and non-COVID-19 patients."
 Please check for grammatical errors and ensure that all manuscripts are written in standard English.

- Please indicate a number of participants with missing data for each variable of interest.
 Please check carefully the STROBE checklist for the cross-sectional study and fill in the missing parts.

Reviewer #2: Thanks for sending the manuscript back after the revision. The authors have done a great job in addressing the comments. There are still some major proofreading errors. I will give some examples here (please note that all line numbers are from the non-clean version):

- 1. Line 34: it should be "may vary" instead of "might be varied".
 2. Line 41: it should be "compared".
 4. Line 44: it's better to be like this: COVID-19 patients (45 non-severe and 6 severe). Because is not appropriate here.
 5. Line 47: "found". This should be pointed out that the methods and results should be written in the past time. This mistake is done throughout the manuscript. Please check the manuscript for this (e.g., line 74 for "increased", line 75 for "had", line 77 for "described").
- 6. Line 66: What does "Older patients or comorbidities" mean? It was right the first time.

Other major considerations:

- Other major considerations:

 1. Please cite the sample size calculation formula. The reader should be able to replicate what was done. I was not able to replicate it as the information is deficient.

 2. With small sample size, I can't actually see how the distribution for the continuous data like age would be conforming winormal distribution. Please see if the distribution is normal. If not, I recommend presenting the median and IQR as well.

 3. Please also include in the limitations that this study has not accounted for the different COVID-19 variants.

 4. The conclusion in lines 403-406 does not actually apply to the gap and aim of the study. In my opinion, it should be replaced with clinical recommendations or at least merged with it.

Reviewer #3: Authors did a great job in revising their manuscript. However there are certain grammatical and punctuation

- errors that needs to be addressed For example:

- errors that needs to be addressed for example:
 Line 35: "Feports the"
 Line 73: "- COVID-19", please remove the dash.
 Line 77: value "values"
 Line 140: every symptom and sign- "every sign and symptom"
 Line 216: "Details"- "detailed". And many more.
 Authors needs to use active voice sentences and should extensively proofread the manuscript with respect to sentence formation, grammar as well as punctuations in order to make it more readable.
 Resides to make it impactiful, authors should specify and compare the symptoms of COVID-19 that occur in ball use.

- Besides to make it impactfull, authors should specify and compare the symptoms of COVID-19 that occur in bali vs symptoms that occurs at another place, was there any significant difference.

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Reviewer #1: Yes: Van-Phu Tran

Reviewer #2: Yes: Abdelrahman M Makram

Reviewer #3: Yes: Zeeshan Ali Khan

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PONE-D-21-21595 Clinical characteristics and outcomes of COVID-19 patients in Bali, Indonesia PLOS ONE

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- An unmarked version of your revised paper without tracked changes. You should upload this as a separate file labeled

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We look forward to receiving your revised manuscript.

Nguyen Tien Huy, Ph.D., M.D. Academic Editor PLOS ONE

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5. We note you have included a table to which you do not refer in the text of your manuscript. Please ensure that you refer to Tables 6. 7 and 8 in your text: if accented, production will need this reference to link the reader to the Table.

[Note: HTML markup is below. Please do not edit.] Reviewers' comments Comments to the Autho 1. Is the manuscript technically sound, and do the data support the conclusions? The manuscript must describe a technically sound piece of scientific research with data that supports the conclusions. Experiments must have been conducted rigorously, with appropriate controls, replication, and sample sizes. The conclusions must be drawn appropriately based on the data presented. Reviewer #2: Partly Reviewer #3: Partly 2. Has the statistical analysis been performed appropriately and rigorously? Reviewer #1: Yes Reviewer #3: Yes 3. Have the authors made all data underlying the findings in their manuscript fully available? The PLOS Data policy requires authors to make all data underlying the findings described in their manuscript fully available without restriction, with rare exception (please refer to the Data Availability Statement in the manuscript PDF file). The data should be provided as part of the manuscript or its supporting information, or deposited to a public repository. For example, in addition to summary statistics, the data points behind means, medians and variance measures should be available. If there are restrictions on publicly sharing data-e.g. participant privacy or use of data from a third party-those must be Reviewer #1: Yes Reviewer #2: Yes Reviewer #3: Yes 4. Is the manuscript presented in an intelligible fashion and written in standard English? PLOS ONE does not copyedit accepted manuscripts, so the language in submitted articles must be clear, correct, and unambiguous. Any typographical or grammatical errors should be corrected at revision, so please note any specific errors Reviewer #1: Yes Reviewer #2: Yes Reviewer #3: No 5. Review Comments to the Author Please use the space provided to explain your answers to the questions above. You may also include additional comments for the author, including concerns about dual publication, research ethics, or publication ethics. (Please upload your review as an attachment if it exceeds 20,000 characters) Reviewer #1: Firstly, the manuscript describes the deeper knowledge about clinical characteristics and outcomes of COVID-Reviewer #1: Pirsty, the manuscript describes the deeper knowledge about clinical characteristics and outcomes of COVID-19 patients in Bali. The conclusion is interesting, it provides evidence to the physicians the diversity of clinical characteristics to detect the key signs and symptoms in COVID-19 patients as it compares COVID-19, non-COVID-19 patients and the control group. This manuscript has led the way to further studies in the future to investigate the coinfection between COVID-19 and dengue fever in Indonesia.

Overall, the study is well-conducted and the authors clearly explained the findings meticulously. The title is 10-word in length, which is good and well-addressed for the research aim.

MAJOR CONSIDERATION

1. The study conclusion was not calculated. MAJOK CONSIDERATION

1. The satudy population was not calculated.

2. Please note whether the outcome assessor is "blind". Sometimes the person measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome assessor would most likely not be blinded to exposure status conducting the outcome assessment. In this case, the outcome assessor would most likely not be bilinded to exposure statt because they also took measurements of exposures. (Remove).

4. The authors should specifically mention how many healthy participants were in the control group, how did they define a healthy group? Were they tested with negative RT-PCF?

5. The study designs and patients (in the Methods section) is not well-organized, it should be divided into smaller subheadings to make it more clear, such as study population, study settings, ethical consideration.

6. Demographic information should also be identified in detail. Which variables in demographic data and how are they measured?
7. Although the strengths and limitations of the study were mentioned in the manuscript, they should be written in separate sections.
MINOR CONSIDERATION MINOR CONSIDERATION
- Line 62: caused by -> which is caused by
- Line 63: [the] Middle
- Line 63: [the] Middle
- Line 65: add "globally" -> have been reported globally.
- Line 71: spread -> spreads. and difficult to trace -> which is difficult to trace
- Line 72:
- "illness" -> illnesses
+ "other disease" -> "another disease" or "other diseases"
+ "other disease" -> "another disease" or "other diseases"
- The authors need to write a full world for the first time it appears. CMV in line 73, RT-PCR in line 99
Line 77: Ball -> COVID-19 pandemic
- Line 80: non-COVID-19 pandemic Line 77: Ball -> COVID-19 pandemic
- Line 80: non-COVID patients -> non-COVID-19 patients
- Line 85: a cross sectional -> A cross-sectional
- Line 86: ...many hospitals and involving -> ...many hospitals, which involved
- Line 87: [the] Indonesian
- Line 94: [the] Ethical
- Line 99: according to the WHO criteria -> please insert a citation. Line 100: included -> categorized Line 110: remove "a" from "A mild illness", individual -> individuals Line 112: patient -> patients
Line 113: individual -> individuals
Line 113: individual -> individual has -> critical individual h - Line 119: outcome -> outcomes, the authors should describe which sources parametricollected.
 - Line 130: Real-Time
 - Line 137: negative RT-PCR with symptom -> negative RT-PCR with positive symptom Line 149: outcome -> outcomes
Line 166: COVID-like -> COVID-19-like. Non-covid -> non-COVID-19
Line 167: non-CoV -> non-COVID-19
Line 188: covid-19 should be written in uppercase. Line 188: covid-19 should be written in uppercase.
 Line 264: jlay -> plays
 Line 303: COVID-19 like illness -> COVID-19-like-illness. appeared the most -> appeared the most frequently
 Line 315: study -> studies
 Line 348: effort -> efforts
 Line 348: improve -> improving
 Line 108: This sentence should be rewritten by similarity with other documents. Source: Davici.biohub.solutions
- Line 139: This sentence should be rewritten by similarity with other documents. Source: www.kumi.com.np Many commas mistakes can be easily edited by using free proofreading software like Grammarly and Microsoft proofing tools.
-Recommendation: Minor revision

Reviewer #2: To begin with, this is an interesting article that describes the clinical course of COVID-19 in Bali, Indonesia. However, there are some major considerations that may hinder the publication of this article:

1. Although the journal does not put an emphasis on the novelty, this article does not have any implications on the current medical practice against COVID-19. The authors need to be more specific about their aim and how their findings will translate into the clinical practice.

2. The authors have not identified the gap in the literature that they intend to fill. For example, is there something that should be distinguished about COVID-19 in Bali that has not been evaluated in other places around the world? Do physicians in Ball follows other certain criteria for the diagnosis that need some revision? in Bali follow other certain criteria for the diagnosis that need some revision?

The has been no sample size calculation prior to data collection

4. The non-COVID-19 group had many diagnoses like "non-COVID-19 pneumonia, dengue hemorrhagic fever, and upper

respiratory tract infections". This should be further discussed in a table. The clinical features should also be compared. However, this only depends on the gap that the authors are willing to fill. In that case, the gap would be that the differentiation between different diseases that manifest like COVID-19 in Ball. But is that really apa? Contrastingly, I consider this a flaw in the design that the authors have included non-healthy individuals in the non-COVID-19 group. 5. Having a mere association between LDH and ICU admission has already been established in the literature. It would be also hard for a cross-sectional study to study the prognostic value of LDH, although also discussed in the literature. So, there is also no value added to that kind of link between these two variables.

Some minor considerations:

- 3.1. Are there any clinical recommendations that can be added to the abstract?
 2. Line 99: please cite the WHO criteria.
 3. Line 107: the severity classification should be cited.
 4. Line 248: Why is little known about the clinical features of COVID-19 in Indonesia? Are the authors speaking about a
- Consistently use COVID-19 instead of Covid-19.

Recommendation: Major Revision

Reviewer #3: Thank You for giving me a great opportunity to review this article.

I have reviewed this article with scrutiny. This cross sectional gives a good insight about Covid-19 in Bali Indonesia but there are certain major and minor aspects that authors need to take into consideration.

- In Abstract is compsed of 725 words, according to Plos One author guidelines, the abstract should not exceed more than 300 words. Please review the author guidelines.

 2. The aim is not specific. (For example if it is specific for people of Bali or any specific symptom only prevalent in covid-19 strain of Bali).
- strain or Ball).

 3. Are the authors talking about "alpha, beta, delta, delta plus or Mu". Please review the recent literature.

 4. Cross sectional study cannot infer temporality and it does not contain controls.

 5. Please determine the literature gaps.

 6. Eligibility criteria should be written in separate sub-heading.

- 7. Sample size should be written in separate sub-heading
 8. Please write settings into a separate sub-heading, eg: the day of admission into the hospital because symptoms varies day
- The age write settings into a separate sub-heading, egr. the day of admission into the hospital because symptoms varies day to day.
 The authors didn't described any efforts to address potential sources of bias.
 a) Selection bias: In this study 19 imported cases out of 51(37%) which are not representative of Ball-Indonesia(selection bias). This does not match with the conclusion as it states that "The findings of this study could enrich the current knowledge about COVID-19 in particular in Indonesia with limited data."
- about COVID-19 in particular in Indonesia with initiate data.

 b) Those who didn't gave consent they might have some variability in symptoms and the patients those are not hospitalized.

 9. 137-138 false negative and false positive definitions are wrong.

 10. Most important concept in severe COVID-19 is disseminated intravascular coagulation(DIC) one of the etiological factor
- 10. Most important concept in severe COVID-19 is disseminated intravascular coagulation(DIC) one of the etiological factor of thrombocytopenia in Covid-19. Please refer to this article https://ehoonline.biomedcentral.com/.../\$40164-020-00172-4. https://lournals.sagepub.com/doi/10.1177/1076029620987629

 11. D-dimer assay is the most important blood parameter which defines severity of COVID-19, it is not mentioned. Please refer to this article https://pubmed.ncbi.nlm.nih.gov/33926262/ https://www.frontiersin.org/.../10.../fpubh.2020.00432/full Lack of novelty or gap of knowledge a) Disseminated intravascular coagulation is one the most serious complication of serious Covid-19. It should be considered a process of the contract of the contrac
- b) D-dimer assay is the most important parameter to check the severity of Covid-19.
- c) CMV pneumonitis(differentials) is quite rare, can add influenza, streptococcal pneumonia, etc.,

- c) CMV pneumonitis (differentials) is quite rare, can add influenza, streptococcal pneumonia, etc.,
 d) Headache is one of the most common symptoms of covid-19, it should be considered too
 https://pubmed.ncbi.nim.nih.gov/33329305/
 Minor Considerations:

 1. The words Covid-19, non-Covid-19, non severe-Covid-19, severe covid-19 are used very harshly which creates confusion
 to readers. My suggestion is use it only in initial sentences and replace it with "patients", "disease", "mild-moderate disease"
 "severe disease", Normal individuals.

 2. In addition there are a lot of grammatical, punctuations, word selection mistakes. This could be corrected by using free
- proofreading tool like Grammarly.

 3. The tables in this article are Effective, Readable, Informative and Tidy. There are some minor considerations

- The tables in this affice are inective, readule, informative and may, there are some finite finite formations a) Table; I p-value for females is not given.
 Table in C. 6 and Table no. 8 comma is used in decimals instead of using point, (eg: sensitivity of fever is written as "45,19" rather than 45.19.

Note: This paper can have a good impact on covid-19 literature, but authors need to review the recent literature and make necessary changes in order to make it exceptional, credible, enlightening and instructional paper for clinicians as well as researchers.

6. PLOS authors have the option to publish the peer review history of their article (what does this mean?). If published, this will include your full peer review and any attached files.

If you choose "no", your identity will remain anonymous but your review may still be made public.

Do you want your identity to be public for this peer review? For information about this choice, including consent

Reviewer #1: Yes: Tran Van Phu

Reviewer #2: Yes: Abdelrahman M Makram

Reviewer #3: Yes: ZEESHAN ALI KHAN

[NOTE: If reviewer comments were submitted as an attachment file, they will be attached to this email and accessible via the submission site. Please log into your account, locate the manuscript record, and check for the action link "View Attachments". If this link does not appear, there are no attachment files.]

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