

REKAM JEJAK DIGITAL

**Megadose Methylprednisolone for Immune Thrombocytopenia in an Infant
Positive for SARS-CoV-2: A Case Report**

AMERICAN JOURNAL OF CASE REPORTS

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Last Updated on November 16, 2021.

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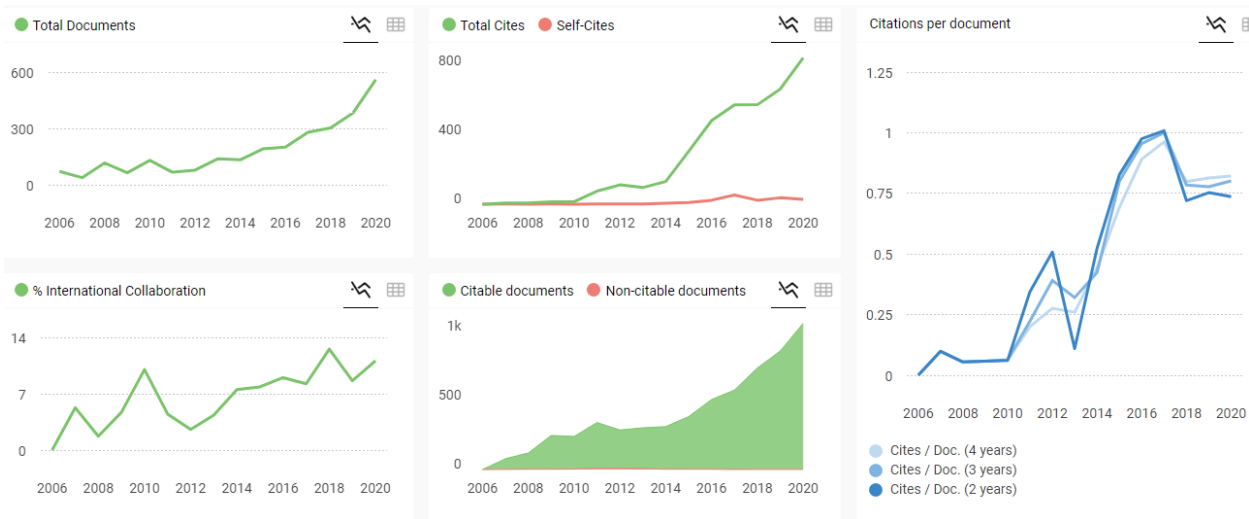
551 - 600 of 694 < >

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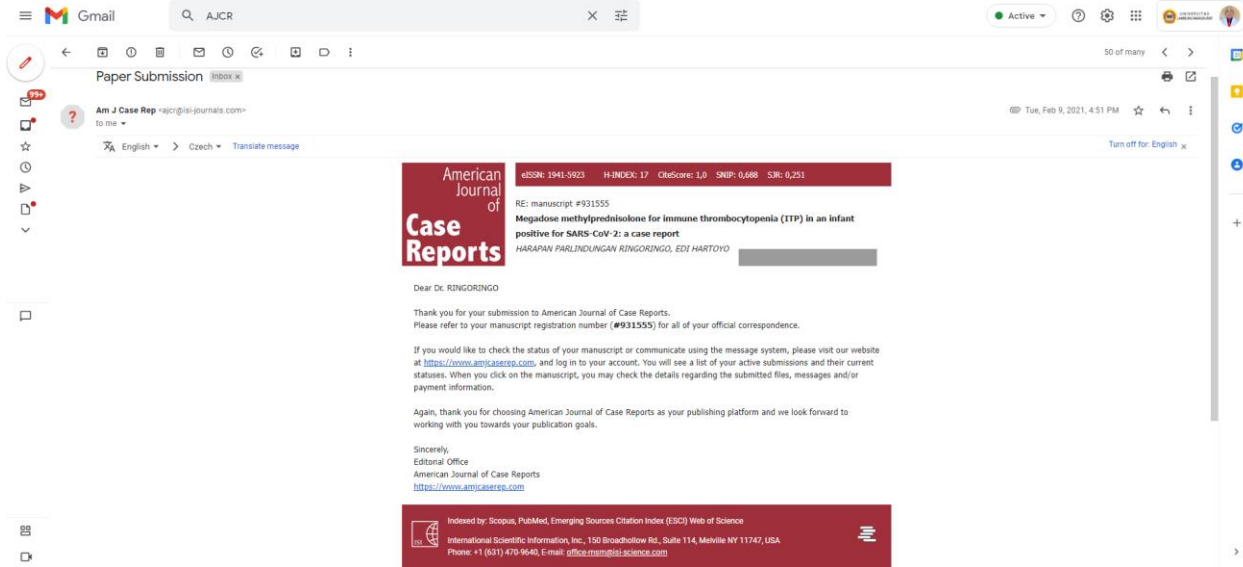
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#931517 REVISED MANUSCRIPT AND EDITED PATIENT IMAGE

From : Author (HARAPAN PARLINDUNGAN RINGORINGO) -> To : Editor 2021-03-03 15:34

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Reply

#931517 Remarks to manuscript

Dear Author,

Below, please find our reviewers' remarks regarding your manuscript. Please make the appropriate changes and upload your revised document (and revised/renamed figures, if necessary) when they are ready. Be sure to highlight the changes you have made in your documents and include a summary of the changes, as well as any responses to the reviewers' comments.

Please note that the below comments and recommendations are sent directly from our international reviewers and have not been edited or corrected.

Reviewer no. 58886329_13804DP

General comments to the Authors

The authors have presented a Case Report of immune thrombocytopenia in a 9-month-old boy, who was treated with methylprednisolone. There are several concerns with the details of the Case Report, including the confirmation of the diagnosis of SARS-CoV-2 infection and immune thrombocytopenia (ITP)

1. ITP is the most common acquired bleeding disorder during childhood, and children affected by ITP are susceptible to infectious disease.
2. The authors have not cited and discussed that thrombocytopenia is a common association with SARS-CoV-2 infection in all age groups. See, *Bhattacharjee S, Banerjee M. Immune Thrombocytopenia Secondary to COVID-19: a Systematic Review SN Compr Clin Med. 2020;1-11.
3. However, the authors have not confirmed that this infant was infected with SARS-CoV-2, on the two occasions that a RT-PCR test was performed - - 'Non-Reactive Covid-19 IgM & Reactive Covid-19 IgG Rapid Test, PCR for SARS-CoV-2 positive.'
4. The authors have not followed current clinical guidelines, and have not explained why this infant was treated with IV methylprednisolone and azithromycin and zinc and vitamin C.
5. This report does not add anything new, and it is possible that this infant was not SARS-CoV-2-positive. 5. In Figure 1, which only has the legend 'Plekie appearance,' which should be - 'The appearance of skin petechiae,' - the authors have presented a full facial image of a child, which is NOT ethically acceptable, as this image breaches the confidentiality and the identity of the child.

Attention:

All reviewers' and editors' remarks have to be addressed by changes in the corrected version of the manuscript. For example, if a reviewer inquires why a particular test is not performed, it is not sufficient to answer the question in the Response Letter. You have to provide the relevant information in the manuscript. Readers will likely have the same questions, so any explanations should also be made within the text for clarity purposes, and to improve the overall quality of the report.

All changes, including added text must be highlighted by different font color (preferably red) in the corrected manuscript file. The summary of all changes, as well as a point by point response, should be included in the Response Letter.

Sincerely yours,

American Journal of Case Reports Editorial Team

REVISE YOUR MANUSCRIPT : 25 APRIL 2021

From : Author (HARAPAN PARLINDUNGAN RINGORINGO) -> To : Editor 2021-04-25 10:23

Print

#931517 SECOND REVISED MANUSCRIPT AND EDITED PATIENT IMAGE AND CHEST-X-RAY

to Editors

The authors had amended the writing of references as details as the authors can.

To Reviewer...

The authors try to answer all of the reviewer's questions, as follow :

1. In the manuscript, the authors had changed "ptekie" to "petechiae."

2. This case is a Newly diagnosed ITP. Newly diagnosed immune thrombocytopenia (ITP) of childhood does not require an exhaustive laboratory workup for diagnosis. A history and physical examination with a review of the peripheral smear are crucial for excluding secondary causes of thrombocytopenia. The child did not appear ill-appearing, with no congenital anomaly. He was not given any drugs previously. Laboratory findings showed that only thrombocytopenia, hemoglobin, and leucocyte are within normal limits. Peripheral blood smear showed few platelets. The bleeding is petechiae. Then there was significant platelet increment after megadose MP therapy. (citation: Johnson MC, de Alarcon P. Evaluation of a child with thrombocytopenia. In: Sillis RH, Albany NY. Practical algorithms in pediatric hematology and oncology. Basel: Karger, 2003. P. 54-55.)

3. In this case, there were no symptoms and signs of Kawasaki disease. According to Kawasaki Disease Research Committee guidelines (Japanese guidelines) for diagnosis of KD (2002), the Kawasaki disease is diagnosed if five of the following six criteria :

- a. Fever persisting \geq five days
- b. Bilateral conjunctival congestion
- c. Changes of lips and oral cavity
- d. Polymorphous exanthema
- e. Changes of peripheral extremities
- f. Acute non-purulent cervical lymphadenopathy

(Citation: Singh S, Jindal AK, Pitania RK. Diagnosis of Kawasaki disease. Int J Rheum Dis. 2018;21(1):36-44. doi:10.1111/1756-185X.13224.

4. The patient's blood type was B. The patient's mother's blood type was A. The patient's father's blood type was B. The direct antiglobulin test was not performed because there were no symptoms and signs of hemolytic anemia.

5. The authors had made Table-1 to showed laboratory findings of complete blood count. The authors attached the Table-1 in separated file.

The authors had added the normal reference range in each biochemical investigation.

Blood glucose 94 mg/dL (reference range \leq 115 mg/dL), AST 64 U/L (reference range \leq 37 U/L), ALT 86 U/L (reference range \leq 43 U/L), Ureum 23 mg/dL (reference range 15-50 mg/dL), creatinine 0.6 mg/dL (reference range \leq 1.4 mg/dL).

6. The authors had changed "very rare platelets" to "few platelets."

7. The authors had added the physical examination in the manuscript. Physical examination: respiration rate 32 x/minute, heart rate 100 x/minute. Eye, ENT, and mouth, no abnormalities. Heart and Lungs within normal limits. Abdomen: there was no organomegaly—there neither lymphadenopathy nor a congenital anomaly. The upper and lower extremities were normal.

8. In the manuscript, the authors had changed the "Thorax X-ray" to "Chest X-ray."

9. The rationale or justification for continuing oral MP treatment is the authors to obey strictly as the literature of Albayrak et al. reported that no significant difference in ITP treatment to achieve normal platelet values with IVIG 0.5 g/kg body weight/day for five days or MP 50 mg/kg body weight/day for seven days or MP 30 mg/kg body weight/day for seven days. The authors choose a regimen of methylprednisolone 30 mg/kg body weight/day for seven days. (citation : Albayrak D, I-lek I, Kalayci AG, Nuran G-Irses N. Acute immune thrombocytopenic purpura' A comparative study of very high oral doses of methylprednisolone and intravenously administered immune globulin. J Pediatr 1994;125(6):1004-7.)

10. The authors had changed "rhinoroe" to "had rhinorrhea."

11. The authors' reasons to give megadose MP are :

a. In emergency cases - the platelet count of 16.000/uL- and intravenous immunoglobulin (IVIG) is expensive (the family could not afford it), MP should be given megadose, not the usual dosage.

b. Methylprednisolone is cheap.

c. According to Indonesian Covid-19 management protocol, a child with pneumonia and PCR for SARS-CoV-2 is positive, so azithromycin, corticosteroid, vitamin C and Zinc should be given. (citation: Kementerian Kesehatan RI. Protokol tata laksana covid-19. Jakarta. 2021. Edisi 2. Hal:1-99.)

That is all the authors could answer the questions of the reviewer. If there are any corrections or suggestions to make this manuscript more valuable, please do not hesitate to inform the authors.

Your sincerely,

HARAPAN PARLINDUNGAN RINGORINGO

REVISED MANUSCRIPT FROM AUTHOR : 3 MARET 2021

From : **Author** (HARAPAN PARLINDUNGAN RINGORINGO) -> To : **Editor** 2021-03-03 15:34

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#931517 REVISED MANUCRIPT AND EDITED PATIENT IMAGE

To the Reviewer and Editor

Thanks for correcting and suggesting the manuscript. The author had amended and added sentences to emphasize the case. The author makes every effort possible to answer the reviewer's questions. The author hopes this manuscript could be accepted. If there is still a correction or suggestions, do not hesitate to inform.

1. ITP is the most common acquired bleeding disorder during childhood, and children affected by ITP are susceptible to infectious disease.

Answer : ITP is indeed the most common acquired bleeding disorder during childhood. However, this disease is rarely found in infants < 1-year-old. That is why this case report is unique or a new one. This case raises awareness of ITP as a possible infant presentation of coronavirus disease.

Children affected by ITP are indeed susceptible to infectious disease. Nevertheless, in this case, the patient is febrile, rhinoroe, for three days previously till the ptekie arises in the child's skin.

2. The authors have not cited and discussed that thrombocytopenia is a common association with SARS-CoV-2 infection in all age groups. See,

*Bhattacharjee S, Banerjee M. Immune Thrombocytopenia Secondary to COVID-19: a Systematic Review SN Compr Clin Med. 2020;1-11.

Answer : The authors have cited that thrombocytopenia is very rare in children with covid-19 [23], and Kosmeri et al. stated that platelets are generally normal in children with covid-19 [22]. As you cited the ""Bhattacharjee S, Banerjee M. Immune Thrombocytopenia Secondary to COVID-19: a Systematic Review SN Compr Clin Med. 2020;1-11." In that article, from 45 patients, the majority of ITP cases (71%) were found to be elderly (>50 years), and 75% of cases had moderate-to-severe COVID-19. Only three patients (7%) were in the pediatric age group. Even the article is a systematic review, but the results can not be used for the pediatric patient.

3. However, the authors have not confirmed that this infant was infected with SARS-CoV-2, on the two occasions that a RT-PCR test was performed - - 'Non-Reactive Covid-19 IgM & Reactive Covid-19 IgG Rapid Test, PCR for SARS-CoV-2 positive.'

Answer : As the authors said in the discussion, the patient is febrile, rhinoroe for three days previously. IgG is reactive, IgM is non-reactive on the rapid test. Thorax X-ray showed pneumonia. On the 2nd day of treatment, the first PCR test for SARS-CoV-2 was positive, which means that the patient is in the late or recurrent stage of infection of Covid-19. So ITP is likely caused by Covid-19 infection. On the 4th day of treatment, to discharge the patient, the 2nd PCR test for SARS-CoV-2 was done, and the result was negative. The patient went home in good condition.

4. The authors have not followed current clinical guidelines, and have not explained why this infant was treated with of IV methylprednisolone and azithromycin and zinc and vitamin C.

Answer: As the authors said in the discussion, the authors follow the guideline according to the Indonesian Covid-19 management protocol. In this protocol, if a child with pneumonia and PCR for SARS-CoV-2 is positive, so azithromycin, corticosteroid, vitamin C and Zinc should be given [24]. Vitamin C and Zinc had been given to increase the immune system of the child [25]. Azithromycin was given to cope with pneumonia. In this case, methylprednisolone is given for ITP and covid-19. Regarding the platelet (16.000/uL) are at high risk of intracranial bleeding with covid-19 pneumonia, and IVIG is expensive (the family could not afford it), MP has given megadose, not the usual dosage. The usual dose of MP for ITP usually 2-4 mg/kg body weight/day. In this case, "a new thing" is a mega dose of MP for treatment of covid-19 with ITP in an infant.

5. This report does not add anything new, and it is possible that this infant was not SARS-CoV-2-positive. 5. In Figure 1, which only has the legend 'Ptekie appearance,' which should be - 'The appearance of skin petechiae,' - the authors have presented a full facial image of a child, which is NOT ethically acceptable, as this image breeches the confidentiality and the identity of the child.

Answer : As the authors said in answer 1 and 4, this case report is unique or a new one: immune thrombocytopenia (ITP) in an infant with positive for SARS-CoV-2. Another "new thing" is the used of a mega dose of MP in copying with Covid-19 and ITP in an infant. The mega dose is 30 mg/kg body weight/day of methylprednisolone for three days, and then 20 mg/kg body weight/day for four days in 3 divided doses.

The patient's image had edited with add a black rectangle that covered the eyes and the nose.

Here is attached the revised manuscript and the new patient's image

Attachments:

 REVISI_1-PAPER-ITP_COVID-04032021.docx [33 KB]

From : **Editor** -> To : **Author** 2021-03-03 05:22

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Reply

REVISED MANUSCRIPT FROM AUTHOR : 25 APRIL 2021

From : Author (HARAPAN PARLINDUNGAN RINGORINGO) -> To : Editor 2021-04-25 10:23

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(Citation: Singh S, Jindal AK, Pitania RK. Diagnosis of Kawasaki disease. Int J Rheum Dis. 2018;21(1):36-44. doi:10.1111/1756-185X.13224.

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Your sincerely,

HARAPAN PARLINDUNGAN RINGORINGO

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of

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Reports

eISSN: 1941-5923 IF(JCR): 2.649 H-INDEX: 17 CiteScore: 1.0 SNIP: 0.594 SJR: 0.294

RE: manuscript #931517

Megadose methylprednisolone for immune thrombocytopenia (ITP) in an infant positive for SARS-CoV-2: a case report

HARAPAN PARLINDUNGAN RINGORINGO, EDI HARTOYO

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American Journal of Case Reports
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RE: manuscript #931517
Megadose Methylprednisolone for Immune Thrombocytopenia in an Infant Positive for SARS-CoV-2: A Case Report
Harapan Parilindungan Ringoringo, Edi Hartoyo
Am J Case Rep DOI: 10.12659/AMJCR.931517

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The above-mentioned manuscript is now available online in the American Journal of Case Reports "In-Press" tab. Publication in the "In-Press" formula, aims at speeding up the public availability of the pending manuscript while waiting for the final publication date.

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Tue, Jul 27, 2021, 4:06 PM

American Journal of Case Reports
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RE: manuscript #931517 Megadose methylprednisolone for immune thrombocytopenia (ITP) in an infant positive for SARS-CoV-2: a case report HARAPAN PARLINDUNGAN RINGORINGO, EDI HARTOYO

GALLEY-PROOFS Review Request

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Corresponding Author: Harapan Parlindungan Ringoringo, e-mail: parlinringoringo@ulm.ac.id
Conflict of interest: None declared

Patient: Male, 9-month-old
Final Diagnosis: Newly diagnosed ITP
Symptoms: Petechiae on the forehead • cheeks • mouth • extremities. The patient is febrile, had rhinorrhea for three days previously. The patient is pale, weak, cannot drink
Medication: —
Clinical Procedure: The patient had immunizations of the Measles-Rubella vaccine 19 days before. Physical examination: Eye, ENT, and mouth, no abnormalities. Heart and Lungs within normal limits. Abdomen: there was no organomegaly – there neither lymphadenopathy nor a congenital anomaly
Specialty: Hematology • Infectious Diseases • Pediatrics and Neonatology

Objective: Rare coexistence of disease or pathology
Background: Immune thrombocytopenia (ITP) is rare in infants under 1 year old. Bleeding often occurs when the platelet count is <20 000/uL. The disease can progress because of accompanying COVID-19 disease.
Case Report: A 9-month-old boy, weighing 8.5 kg, came to the hospital with petechiae on the forehead, cheeks, mouth, and extremities. The patient had rhinorrhea for 3 days previously and was febrile, pale, weak, and could not drink. He had the measles-rubella vaccination 19 days prior. Physical examination showed no abnormalities of the eyes, ears, nose, throat, and mouth. Heart and lungs were within normal limits, with no organomegaly, lymphadenopathy, or congenital anomaly of the abdomen. Laboratory examination showed hemoglobin, 12.7 g/dL; leukocytes, 7420/uL; platelet count, 16 000/uL; and hematocrit, 37.9%. Erythrocyte sedimentation rate was 14 mm at 1 h and 21 mm at 2 h. Peripheral blood smear showed normal RBC morphology, normal leukocytes, and few platelets. IgG was reactive and IgM was nonreactive on rapid antibody test. RT-PCR was positive for SARS-CoV-2. Chest-X-ray showed pneumonia. The diagnosis was newly diagnosed ITP with COVID-19. Patient

ARTICLE PUBLISHED : 3 SEPTEMBER 2021

Fri, Sep 3, 2021, 4:06 PM

Turn

American Journal of Case Reports

eISSN: 1941-5923 H-INDEX: 17 CiteScore: 1.0 SNIP: 0.594 SJR: 0.294

RE: manuscript #931517

Megadose Methylprednisolone for Immune Thrombocytopenia in an Infant Positive for SARS-CoV-2: A Case Report

Harapan Parlindungan Ringoringo, Edi Hartoyo

Am J Case Rep 2021; 22:e931517 :: DOI: 10.12659/AJCR.931517

Dear Author,

We are pleased to notify you that your manuscript #931517 titled "Megadose Methylprednisolone for Immune Thrombocytopenia in an Infant Positive for SARS-CoV-2: A Case Report", has now been **published online** at <https://www.amjcaserep.com>, along with the following Digital Object Identifier (DOI): #10.12659/AJCR.931517 . The article will be forwarded to PubMed nad PubMed Central/PMC for archive in their repository. Please note, that their publication process, which is beyond our control, usually takes approximately two weeks.

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Status History

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|------------|---|
| 2021-09-02 | Published |
| 2021-07-28 | READY for publication Note: Estimated Publication Date: Sep 12 - Sep 18, 2021 |
| 2021-07-28 | Pre-Pub plagiarism check ready |
| 2021-07-28 | Sent for Pre-Pub antiplagiarism check |
| 2021-07-27 | Ready for Pre-Pub antiplagiarism check |
| 2021-07-27 | Proofread |
| 2021-07-27 | Galley proof sent to authors |
| 2021-07-27 | Galley proof sent back for production |
| 2021-07-27 | Galley proof sent to authors |
| 2021-07-19 | Sent for production |
| 2021-07-16 | Copyediting completed |
| 2021-07-16 | In Language Quality Control |
| 2021-07-15 | Copyediting completed - waiting for authors' approval |
| 2021-07-09 | In Copyediting |
| 2021-07-09 | Paid - Extended tagging completed |
| 2021-07-08 | Paid |
| 2021-07-08 | Waiting for extended tagging Note: Please be sure that you have completed the information in the Extended Tagging tab of c proof. |
| 2021-07-08 | Accepted - invoice issued |
| 2021-07-08 | 1st Post-Rev plagiarism check ready |
| 2021-07-08 | Sent for 1st Post-Rev antiplagiarism check |
| 2021-07-08 | Ready for Post-Rev antiplagiarism check |

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|------------|---|
| 2021-07-03 | After authors corrections |
| 2021-06-30 | Sent to author(s) for corrections (2 weeks) |
| 2021-06-30 | Reconsider after revision |
| 2021-06-28 | Review 4 pending |
| 2021-06-28 | Review 4 requests sent to reviewers |
| 2021-06-20 | After authors corrections |
| 2021-06-16 | Sent to author(s) for corrections (2 weeks) |
| 2021-06-16 | Reconsider after revision |
| 2021-05-19 | Review 3 pending |
| 2021-04-27 | Review 3 requests sent to reviewers |
| 2021-04-27 | After authors corrections |
| 2021-04-06 | Sent to author(s) for corrections (3 weeks) |
| 2021-04-06 | Reconsider after revision |
| 2021-03-20 | Review 2 pending |
| 2021-03-03 | Review 2 requests sent to reviewers |
| 2021-03-03 | After authors corrections |
| 2021-03-03 | Sent to author(s) for corrections (2 weeks) |
| 2021-03-03 | Reconsider after revision |
| 2021-03-02 | Unlocked |
| | Note: Personal review recived |
| 2021-03-01 | Review pending |
| 2021-02-08 | Evaluation requests sent to reviewers |
| 2021-02-08 | Manuscript accepted for processing |
| 2021-02-08 | Plagiarism check (submission) 1 ready |
| 2021-02-08 | Sent for anti-plagiarism verification |
| 2021-02-08 | Submissions Approved |
| 2021-02-06 | Submission Received |

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