Response to reviewers

First of all, I express my deep thanks to the reviewers who they well assessed the manuscript. The notes which were raised during the reviewing process enrich the article concerning the scientific and language issues. I took all the raising comments into consideration in the revised manuscript. I highlighted the required changes in a yellow color. I hope the changes made in the revised form are satisfactory for the reviewers and the study will be accepted for publication in the esteemed journal "World Journal of Clinical Cases".

Best regards

Professor Dr. Raid M. Al-Ani

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: I think that the Author should distinguish between the different variants of SARS-CoV-2

I added the required changes as below.

As a result of the emergence of new variants, the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) have independently developed a classification system for distinguishing various SARS-CoV-2 variants. This system divided these variants into variants of concern (VOCs) and variants of interest (VOIs) [22].

The **VOCs** are divided into five variants; **Alpha** (B.1.1.7), **Beta** (B.1.351), **Gamma** (P.1), **Delta** (B.1.617.2), and **Omicron** (B.1.1.529). All of them have mutations in the receptor-binding domain (RBD) and the N-terminal domain (NTD), of which the N501Y mutation located in the RBD is seen commonly in all variants except the Delta variant. This enhances the affinity of the spike protein to the ACE 2 receptors, increasing the viral binding and thereby entering into the host cells. Two recent preprints found that a single mutation of N501Y alone enhances the affinity of the RBD to the ACE2 receptors about ten-folds more than the ancestral strain (N501-RBD). Interestingly, the binding affinity of the Beta (B.1.351) variant and Gamma (P.1) variant with mutations N417/K848/Y501-RBD and ACE2 receptors was much

lower than that of N501Y-RBD and ACE2 receptors. Omicron was rapidly identified as a VOC due to more than 30 changes to the spike protein of the virus as well as a sharp increase in the number of cases observed in South Africa. Various mutations were reported; Q19E, A63T in the matrix, T91 in the envelope, Y505H, N501Y, Q498R, G496S, Q493R, E484A, T478K, S477N, G446S, N440K, K417N, S375F, S373P, S371L, G339D in the RBD of the spike, P13L, E31del, R32del, S33del, R203K, G204R in the nucleocapsid protein, D3G, N211del/L212I, Y145del, Y144del, Y143del, G142D, T95I, V70del, H69del, A67V in the N-terminal domain of the spike, L981F, N969K, Q954H in the heptad repeat 1 of the spike, D796Y in the fusion peptide of the spike, in addition to many other mutations in the non-structural proteins and spike protein. As a result, Omicron has 13-fold more viral infectivity and is 2.8-fold more infectious than the Delta type [22].

VOIs are a group of variants with specific genetic markers that have been linked to changes that may cause increased virulence, inhibition of antibody neutralisation as a result of an infection or vaccination, the ability to evade detection, or a decrease in the effectiveness of treatments or vaccination.. Currently, the WHO has named 8 VOIs, these are **Epsilon** (B.1.427 and B.1.429), **Lambda** (C.37), **Zeta** (P.2), **Mu** (B.1.621), **Iota** (B.1.526), **Kappa** (B.1.617.1), **Eta** (B.1.525), and **Theta** (P.3) [22].

Reviewer #2:
Scientific Quality: Grade A (Excellent)
Language Quality: Grade A (Priority publishing)
Conclusion: Accept (High priority)
Specific Comments to Authors: Good work!

Thank you.

Science Editor Comments:

The manuscript needs minor revision before publishing. Reviewer 1: I think that the Author should distinguish between the different variants of SARS-CoV-2
Language Quality: Grade B (Minor language polishing)
Scientific Quality: Grade C (Good)

The manuscript needs minor revision before publishing. Reviewer 1: I think that the Author should distinguish between the different variants of SARS-CoV-2

I added the required changes as I mentioned above.

Language Quality: Grade B (Minor language polishing)
Scientific Quality: Grade C (Good)

I did my best to submit you the revised manuscript in an excellent form. I hope Language Quality upgrade to A and Scientific Quality to A or B.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/.

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted.

Thank you very much.

I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

I received it.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns

or spaces to replace lines or vertical lines and do not segment cell content. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

I made the required changes in the Table 1.

To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/.

I visited the RCA website and I used it.