

COVID-19 associated Mucormycosis (CAM) of head and neck region: A systematic review

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Handling editor:

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Ref.: Ms. No. JCTRes-D-21-00141

COVID-19 associated Mucormycosis (CAM) of Head and Neck region; A Systematic Review
Journal of Clinical and Translational Research

Dear Dr Kamat,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Oct 06, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: This timeous review deals with the occurrence, risk factors and treatment of COVID-19-associated mucormycosis (CAM).

The following important issues should be addressed:

The language of the manuscript needs to be improved. Although one is able to follow the authors' arguments, the significant number of editing and grammatical errors, does distract and will need to be corrected before it can be accepted for publication.

Introduction

In 35-36: I am not sure waht the authors meant by the phrase "quality of life and disease of death". Please revise to make it clear.

In 36-50: The same ideas are repeated in two sentences regarding the aim of the review. It is suggested that the authors consolidate this section to avoid repetition..

In addition, it is unclear waht is meant by a "guideline for CAM". Should this be a guideline for the management or prevention of CAM or the treatment of CAM?

Results

Page 6, ln 3. It is unclear what the authors meant with "3rd to 7th decades" -is it the age of the patients? Please rephrase to make this clearer.

Line 13-15. Always refer to COVID as COVID-19

Discussion

Page 7, ln 25-27. Are the risk factors in figure 2 specific to COVID-19?

Page 8, ln 5-13. The authors speculate about the reason for the rise in CAM cases. Do they consider climate change as a possible contributing factor?

Page 8, ln 28 and P12, ln 7. The authors mention oxygen supplementation as part of the treatment regimen that may cause adverse effects, leading to CAM. Is it the provision of O2 specifically or the intubation associated with ventilation that would contribute? This is important to clarify as the authors later suggest hyperbaric O2 treatment as a possible alternative antifungal option.

Page 9, ln 24-30. The argument that the development of DKA during treatment, indicates the effect of the virus on the pancreas is unclear.

Page 10, ln 28-29. The authors state that the mentioned eplanations for the association between obesity and COVID-19 are also known risk factors for mucormycosis. This argument is unclear and a reference for this statement should be supplied

Page 10, ln 42. Please define the abbreviation HCQ

Page 11, ln 20 and fig 2. On page 7 the authors refer to figure two as an indication of the risk factors for mucormycosis, however here they refer to is as a depiction of the pathogenesis.

These are two very different concepts and the authors should make sure what they mean to show with this figure

Page 13, table 2. Regarding the COVID-19 related recommendations the following amendment is suggested:

"Avoid unnecessary use of broad-spectrum antibiotics, antivirals"

"Closely monitor co-morbidities, especially obesity and diabetes, during....treatment"

Regarding the mucormycosis related recommendations the following amendment is suggested:

The statement "encourage proper hygiene practises" is very vague and it is unclear which practices, except for wearing clean masks, the authors refer to in this context.

Reviewer #2: The good review article of data on Covid associated Rhino- orbital- cerebral Mucormycosis .

Reviewer #3: The authors present a case of covid associated invasive fungal sinusitis and perform a systematic review of the the literature. The review is helpful to readers and there is a need to consolidate the burgeoning literature on this disease. The manuscript would be improved with grammatical editing and refinement of the systematic search terms. Specific comments are included:

Methods

page 4 line 34 Please describe the consensus - was a third expert polled?

Please provide additional details regarding the inclusion and exclusion criteria for studies.

The search term mucormycosis was used, but aspergillus is a significant pathogen in immunocompromised hosts with similar albeit typically less aggressive disease. Indeed, most reviews on the topic of invasive rhino-orbital sinusitis include both Mucorales as well as Ascomycetes infections. For example, a brief literature search with that term and COVID-19 identified the 3 cases below, one of which was a coinfection of aspergillus and rhizopus. I would suggest broadening the systematic review to include terms such as invasive fungal sinusitis and invasive fungal infection, invasive fungal orbital cellulitis, etc in order to ensure that the review is truly sampling the literature appropriately. I would also consider changing nomenclature to "invasive fungal sinusitis", which is a more broadly descriptive term. If the authors have a specific reason to evaluate only mucormycosis, this should be stated. However, I would still advise broadening the search terms and only reporting the mucorales cases if so, because as shown below the term mucormycosis does not identify all relevant articles.

As above, would consider changing CAM to CA-IFS - COVID associated Invasive Fungal Sinusitis.

Sebastian SK, Kumar VB, Gupta M, Sharma Y. Covid Assosiated Invasive Fungal Sinusitis [published online ahead of print, 2021 Feb 25]. Indian J Otolaryngol Head Neck Surg. 2021;1-4. doi:10.1007/s12070-021-02471-6

31% of IFS in Covid 19 patients was aspergillus

El-Kholy NA, El-Fattah AMA, Khafagy YW. Invasive Fungal Sinusitis in Post COVID-19 Patients: A New Clinical Entity. *Laryngoscope*. 2021 May 19:10.1002/lary.29632. doi: 10.1002/lary.29632. Epub ahead of print. PMID: 34009676; PMCID: PMC8242424.

Results:

Percentages would be helpful here (e.g. % mortality)

Could table 1 be modified to also provide summary statistics? E.g. % male, % diabetes % mortality. Currently a few of the columns are summated in the footnote but % would be useful and data such as mortality would be important to present. Perhaps the final row of the table could provide a summary for each column?

More data on treatment would be helpful for readers. For example, did patients require exenteration more often than is reported in the literature prior to covid? Did patients require more debridements of the sinus -- or perhaps did they receive fewer debridements because of the severity of illness? Were minimally invasive measures such as retrobulbar amphotericin injection or post-operative amphotericin irrigation used?

What were relevant risk factors for IFS among patients without diabetes? Did they have other causes of immunosuppression? This is an important question - does COVID and/or covid therapy alone predispose to IFS, or does it merely increase the risk for an already at risk population (such as organ transplant recipients, hematologic malignancy, etc) It is alluded in the discussion that some patients had no comorbidities, but it would be helpful to provide readers with this information in the results section (e.g. the table may have a column for "other risk factors")

Would the authors be able to explore risk factors for mortality? For example, does diabetes have increased mortality versus no diabetes? O2 therapy? etc. A logistic regression can provide an OR, and the authors may consider controlling for confounders in these analyses.

Discussion

Would be helpful to expand more on differences between CA-IFS/M and historical IFS. For example, to review the % of comorbidities reported elsewhere versus those observed in this review. Certainly it seems diabetes plays an outsized role (generally it is reported in around 50-60% but seems to be much higher here)

The authors should identify published data on supplement use in the Indian population. The current discussion is largely speculative.

Is there evidence for statements regarding supplemental oxygen and prolonged ICU stay linking to mucor? page 8 Line 38-40. I do not see references

page 8 line 43 - The authors may consider also reviewing literature regarding the suppression of fungal immunity during covid infection (e.g. Moser D, Biere K, Han B, et al. COVID-19 Impairs Immune Response to *Candida albicans*. *Front Immunol*. 2021;12:640644. Published 2021 Feb 26. doi:10.3389/fimmu.2021.640644)

Table 2 - As this is a systematic review, can the authors provide levels of evidence for each of these measures, for example per Oxford standards? I recognize that evidence may be limited for this fairly novel disease, but it is important that readers know what backs these recommendations. If it is simply level 5 (expert opinion) that is acceptable but should be stated. (<https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009>)

Authors' response

To,

Michal Heger, PhD

Editor-in-Chief

Journal of Clinical and Transitional Research

Re: revision JCTR-D-21-00141

Respected Sir,

Thank You for giving us an opportunity to resubmit a revised version of our manuscript entitled "COVID-19 associated Mucormycosis (CAM) of Head and Neck region: A Systematic Review". We have addressed all comments of the reviewers using the track changes function in Word (attached as supplementary material not for publication). Moreover, every modification or rebuttal of the reviewer's comments is detailed per comment below in red italics. The changes have been highlighted in the text. Grammar and language also has been improved as suggested. We are grateful for the useful comments of the reviewers, as a result of which the paper has been considerably improved. The authors also would definitely do necessary corrections if suggested further.

On behalf of the authors,

Kindest regards,

Dr. Mamata Kamat

Note: as the search terms were broadened as suggested by the reviewer 2, the table has been updated accordingly. Additionally, table 2 is added. The abstract, methods, results and discussion are updated according to the data of articles included (obtained after refined search terms).

REVIEWER # 1:

This timeous review deals with the occurrence, risk factors and treatment of COVID-19-associated mucormycosis (CAM).

The following important issues should be addressed:

The language of the manuscript needs to be improved. Although one is able to follow the authors' arguments, the significant number of editing and grammatical errors, does distract and will need to be corrected before it can be accepted for publication.

We are grateful for your commentary and suggestions, which we have addressed to the fullest extent as indicated below for every one of your comments. The language and terminology have been further polished in accordance with your suggestions.

Introduction

In 35-36: I am not sure what the authors meant by the phrase "quality of life and disease of death". Please revise to make it clear.

The phrase has been revised as follows;

“The incidence of CAM is increasing drastically affecting the quality of life to an extent that it has become the cause of death”

In 36-50: The same ideas are repeated in two sentences regarding the aim of the review. It is suggested that the authors consolidate this section to avoid repetition..

The repeated text has been deleted.

In addition, it is unclear what is meant by a "guideline for CAM". Should this be a guideline for the management or prevention of CAM or the treatment of CAM?

It has been corrected as suggested.

Results

Page 6, ln 3. It is unclear what the authors meant with "3rd to 7th decades" -is it the age of the patients? Please rephrase to make this clearer.

The following text has been revised as suggested.

“A total of 261 patients were affected by CAM, between 3rd to 7th decades of life”

Line 13-15. Always refer to COVID as COVID-19

Revised as suggested. Thank You

Discussion

Page 7, ln 25-27. Are the risk factors in figure 2 specific to COVID-19?

No, the risk factors are not specific to COVID-19. Here the phrase has been omitted and added in discussion section.

Page 8, ln 5-13. The authors speculate about the reason for the rise in CAM cases. Do they consider climate change as a possible contributing factor?

Yes, the following text regarding the same has been added.

“Additionally, seasonal climatic changes have been known to affect the prevalence of fungal spores. Hot and dry summer conditions in tropical countries like India are conducive for the small sporangiospores of Mucorales to aerosolize and scatter in the environment.[41]

Page 8, ln 28 and P12, ln 7. The authors mention oxygen supplementation as part of the treatment regimen that may cause adverse effects, leading to CAM. Is it the provision of O₂ specifically or the intubation associated with ventilation that would contribute? This is important to clarify as the authors later suggest hyperbaric O₂ treatment as a possible alternative antifungal option.

The phrase is modified as “oxygen supplement with ventilator support”. Thank You

Page 9, ln 24-30. The argument that the development of DKA during treatment, indicates the effect of the virus on the pancreas is unclear.

The role of SARS-CoV-2 on the pancreas is described. The following phrase has been added.

Studies have shown that SARS-CoV-2 attaches to the angiotensin-converting enzyme 2 (ACE 2) receptors which are abundantly found in high levels in the endocrine pancreas. This leads to beta cell dysfunction and insulin resistance leading to hyperglycaemia [48].

Page 10, ln 28-29. The authors state that the mentioned explanations for the association between obesity and COVID-19 are also known risk factors for mucormycosis. This argument is unclear and a reference for this statement should be supplied.

More relevant text has been added with the reference as follows.

“Additionally, it has been observed that obese people are physically inactive, more insulin resistant and show gut dysbiosis, that elevates the inflammatory response to SARS-CoV-2 infection [6].”

Page 10, ln 42. Please define the abbreviation HCQ

Provided the abbreviation; Hydrochloroquine (HCQ). Thank You

Page 11, ln 20 and fig 2. On page 7 the authors refer to figure two as an indication of the risk factors for mucormycosis, however here they refer to is as a depiction of the pathogenesis. These are two very different concepts and the authors should make sure what they mean to show with this figure

The following necessary changes are done indicating the risk factors of CAM.

“The summary of probable risk factors for CAM has been depicted in figure 2.”

Page 13, table 2. Regarding the COVID-19 related recommendations the following amendment is suggested:

"Avoid unnecessary use of broad-spectrum antibiotics, antivirals"

"Closely monitor co-morbidities, especially obesity and diabetes, during....treatment"

The suggestions are included in the table. Thank You.

Regarding the mucormycosis related recommendations the following amendment is suggested:

The statement "encourage proper hygiene practises" is very vague and it is unclear which practices, except for wearing clean masks, the authors refer to in this context.

Thank you. Specific practices have been mentioned as suggested.

“Encourage proper hygiene practices; frequent hand wash, respiratory hygiene, eye protection, maintain social distance etc

REVIEWER # 2:

The good review of data on Covid associated Rhino-orbital-cerebral Mucormycosis.

Thank you for your encouraging words.

REVIEWER # 3:

The authors present a case of covid associated invasive fungal sinusitis and perform a systematic review of the literature. The review is helpful to readers and there is a need to consolidate the burgeoning literature on this disease. The manuscript would be improved with grammatical editing and refinement of the systematic search terms. Specific comments are included:

Thank You for the comments, suggestions and encouraging words.

Methods

page 4 line 34 Please describe the consensus - was a third expert polled?

The difference of opinion was settled by consensus after discussion with remaining authors.

Please provide additional details regarding the inclusion and exclusion criteria for studies.

The additional inclusion and exclusion criteria are provided.

The search term mucormycosis was used, but aspergillus is a significant pathogen in immunocompromised hosts with similar albeit typically less aggressive disease. Indeed, most reviews on the topic of invasive rhino-orbital sinusitis include both Mucorales as well as Ascomycetes infections. For example, a brief literature search with that term and COVID-19 identified the 3 cases below, one of which was a coinfection of aspergillus and rhizopus. I would suggest broadening the systematic review to include terms such as invasive fungal sinusitis and invasive fungal infection, invasive fungal orbital cellulitis, etc in order to ensure that the review is truly sampling the literature appropriately. I would also consider changing nomenclature to "invasive fungal sinusitis", which is a more broadly descriptive term. If the authors have a specific reason to evaluate only mucormycosis, this should be stated. However, I would still advise broadening the search terms and only reporting the mucorales cases if so, because as shown below the term mucormycosis does not identify all relevant articles.

Thank you for your valuable suggestion.

However, Considering the sheer number of CAM cases, our prime aim was to exclusively study the risk factors and the different treatment modalities and their effects on the incidence of COVID-19 Associated Mucormycosis. Moreover, we focussed exclusively on CAMs considering the aggressiveness, morbidities and mortality.

However, the reviewer's suggestion helped to us refine our search strategy. Hence, we broadened the search terms that included “((Mucormycosis) OR (invasive fungal sinusitis)) AND (COVID-19)”, which identified 95 papers. Considering our inclusion and exclusion criteria, finally 33 full text articles were analysed in this study.

As above, would consider changing CAM to CA-IFS - COVID associated Invasive Fungal Sinusitis.

As, we have exclusively studied mucormycosis, CAM has been used.

Sebastian SK, Kumar VB, Gupta M, Sharma Y. Covid Assosiated Invasive Fungal Sinusitis [published online ahead of print, 2021 Feb 25]. Indian J Otolaryngol Head Neck Surg. 2021;1-4. doi:10.1007/s12070-021-02471-6

Thank you for the suggested reference. Our broadened search terms identified the reference and the above article is included in the revised work.

31% of IFS in Covid 19 patients was aspergillus

El-Kholy NA, El-Fattah AMA, Khafagy YW. Invasive Fungal Sinusitis in Post COVID-19 Patients: A New Clinical Entity. Laryngoscope. 2021 May 19:10.1002/lary.29632. doi: 10.1002/lary.29632. Epub ahead of print. PMID: 34009676; PMCID: PMC8242424.

Although, our revised search terms found this article, it did not meet our inclusion criteria.

Results:

Percentages would be helpful here (e.g. % mortality)

The percentage of all the variables are included in the revised table and in the text wherever applicable.

Could table 1 be modified to also provide summary statistics? E.g. % male, % diabetes % mortality. Currently a few of the columns are summated in the footnote but % would be useful and data such as mortality would be important to present. Perhaps the final row of the table could provide a summary for each column?

Thank you. Yes, the table 1 has been revised as suggested.

Additionally, a sperate table 2 has been added that depicts the summary statistics of all the parameter.

More data on treatment would be helpful for readers. For example, did patients require exenteration more often than is reported in the literature prior to covid? Did patients require more debridements of the sinus -- or perhaps did they receive fewer

debridement's because of the severity of illness? Were minimally invasive measures such as retrobulbar amphotericin injection or post-operative amphotericin irrigation used?

Yes, the necessary revision on the suggested points have been addressed in the discussion. As all the included papers did not provide individual patient data regarding the use of specific type of antifungal agents, it was out of reach for the authors to comment on the same.

What were relevant risk factors for IFS among patients without diabetes? Did they have other causes of immunosuppression? This is an important question - does COVID and/or covid therapy alone predispose to IFS, or does it merely increase the risk for an already at risk population (such as organ transplant recipients, hematologic malignancy, etc) It is alluded in the discussion that some patients had no comorbidities, but it would be helpful to provide readers with this information in the results section (e.g. the table may have a column for "other risk factors")

Thank you. Each of the suggested points are addressed and incorporated in the revised work in the discussion.

Would the authors be able to explore risk factors for mortality? For example, does diabetes have increased mortality versus no diabetes? O2 therapy? etc. A logistic regression can provide an OR, and the authors may consider controlling for confounders in these analyses.

Thank you're your valuable suggestion. However, as the some of the selected papers included quite a large number of cases, the details of individual cases were not available. Hence, the logistic regression could not be applied to the patient's data. The literature review has been described on the probable risk factors. However, the further scope has be mentioned along with the limitations.

Discussion

Would be helpful to expand more on differences between CA-IFS/M and historical IFS. For example, to review the % of comorbidities reported elsewhere versus those observed in this review. Certainly it seems diabetes plays an outsized role (generally it is reported in around 50-60% but seems to be much higher here)

Thank you. Yes, as suggested, the various co-morbidities have been compared to data of pre-covid-19 cases in the discussion

The authors should identify published data on supplement use in the Indian population. The current discussion is largely speculative.

Thank you. The published data has been identified and references have been added.

Is there evidence for statements regarding supplemental oxygen and prolonged ICU stay linking to mucor? page 8 Line 38-40. I do not see references

Thank you. References have been provided.

page 8 line 43 - The authors may consider also reviewing literature regarding the suppression of fungal immunity during covid infection (e.g. Moser D, Biere K, Han B, et al. COVID-19 Impairs Immune Response to Candida albicans. Front Immunol. 2021;12:640644. Published 2021 Feb 26. doi:10.3389/fimmu.2021.640644)

Thank you for the suggested reference. Effect of COVID-19 on fungal immunity has been described as suggested, the suggested article has been referred.

Table 2 - As this is a systematic review, can the authors provide levels of evidence for each of these measures, for example per Oxford standards? I recognize that evidence may be limited for this fairly novel disease, but it is important that readers know what backs these recommendations. If it is simply level 5 (expert opinion) that is acceptable but should be stated. (<https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009>)

Thank you for the suggestions. The recommendations fall under the category of level 5 (expert opinion). The same has been mentioned in the table.

2nd Editorial decision
3-Dec-2021

Ref.: Ms. No. JCTRes-D-21-00141R1
COVID-19 associated Mucormycosis (CAM) of Head and Neck region; A Systematic Review
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Dec 09, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #2: As the authors have revised the manuscript as per the comments , so it is acceptable

Reviewer #3: The authors have addressed many of the points raised by reviewers. Expanded search terms yielded significantly more cases, which strengthens the manuscript.

Some general comments:

Another pass through the grammar would be good. It is better but still choppy to read in some areas and there is inconsistent capitalization (e.g. Posaconazole and posaconazole. It is a generic, so lower case is correct)

I would also de-emphasize the use of "etc" to avoid a short-hand/slang style.

Please use a uniform term to describe COVID. There are references to covid, COVID, COVID-19. Selecting one and using it everywhere is best.

And specific:

p3 line 34 - capitalize March

p3 line 41-43 This sentence still does not make sense. Quality of life and mortality are different concepts. Perhaps 'drastically affecting quality of life and often leading to death'

p5 line 33 capitalize pronouns Google Scholar

p9 line 45-47 - would clarify that this was during treatment/recovery of COVID

p10-p11: it looks like there are two paragraphs discussing SARS-CoV-2 interaction with pancreatic beta cells. These should be consolidated.

p12 obesity should not be capitalized

EDITOR:

Please make sure the linguistics are in line with academic English as stipulated in our author guidelines.

Authors' response

To,

Michal Heger, PhD

Editor-in-Chief

Re: revision JCTRes-D-21-00141R1

Respected Sir,

Thank You for giving us an opportunity to resubmit a revised version of our manuscript entitled “COVID-19 associated Mucormycosis (CAM) of Head and Neck region: A Systematic Review”. We have addressed all comments of the reviewers using the track changes function in Word (attached as supplementary material not for publication). Moreover, every modification or rebuttal of the reviewer’s comments is detailed per comment below in red italics. The changes have been highlighted in the text. Grammar and language also have been improved as suggested. We are grateful for the useful comments of the reviewers, as a result of which the paper has been considerably improved.

On behalf of the authors,

Kindest regards,

Dr. Mamata Kamat

REVIEWER # 2:

As the authors have revised the manuscript as per the comments, so it is acceptable.

Thank you for the consideration and encouraging words.

REVIEWER # 3:

The authors have addressed many of the points raised by reviewers. Expanded search terms yielded significantly more cases, which strengthens the manuscript.

Thank you for the encouraging words.

Some general comments:

Another pass through the grammar would be good. It is better but still choppy to read in some areas and there is inconsistent capitalization (e.g. Posaconazole and posoconozole. It is a generic, so lower case is correct)

Thank you. The suggested changes are incorporated in the revised manuscript. Overall, the grammar and linguistics of the manuscript are refined and improved. The changes are highlighted in red.

I would also de-emphasize the use of “etc” to avoid a short-hand/slang style.

Thank you. The suggested correction is incorporated in the revised manuscript and highlighted in red.

Please use a uniform term to describe COVID. There are references to covid, COVID, COVID-19. Selecting one and using it everywhere is best.

Thank you. Uniform term COVID-19 is used throughout the revised manuscript as suggested.

And specific:

P3 line 34-capitalize March

Thank you. The suggested changes are incorporated in the revised manuscript.

P3 line 41-43. This sentence still does not make sense. Quality of life and mortality are different concepts. Perhaps ‘drastically affecting quality of life and often leading to death’

Thank you. The suggested changes are incorporated in the revised manuscript.

P5 line 33 capitalize pronouns Google Scholar

Thank you. The suggested changes are incorporated in the revised manuscript.

P9 line 45-47- would clarify that this was during treatment/recovery of COVID

Thank you. The suggested changes are incorporated in the revised manuscript.

P10-p11: it looks there are two paragraphs discussing SARS-Co-V-2 interaction with pancreatic beta cells. These should be consolidated.

Thank you. The Repeated text has been deleted and consolidated as suggested.

P12 obesity should not be capitalised.

The term Obesity is replaced with obesity as suggested.

EDITOR:

Please make sure the linguistics are in line with academic English as stipulated in our guidelines.

Thank you so much Sir for your valuable suggestions. The overall grammar and linguistics of the manuscript are refined and improved . The changes are highlighted in red.

3rd Editorial decision
03-Dec-2021

Ref.: Ms. No. JCTRes-D-21-00141R2
COVID-19 associated Mucormycosis (CAM) of Head and Neck region; A Systematic Review
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Journal of Clinical and Translational Research
Peer review process file 08.202201.003



Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: