



PEER-REVIEW REPORT

Name of journal: *World Journal of Virology*

Manuscript NO: 77072

Title: Anatomophysiological relationships of tasting and smelling loss in patients with COVID-19

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05426937

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Brazil

Manuscript submission date: 2022-04-13

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-05-22 09:34

Reviewer performed review: 2022-05-30 12:10

Review time: 8 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

No.

Response to the Reviewer:

Thank you for accepting our manuscript



PEER-REVIEW REPORT

Name of journal: *World Journal of Virology*

Manuscript NO: 77072

Title: Anatomophysiological relationships of tasting and smelling loss in patients with COVID-19

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05352073

Position: Peer Reviewer

Academic degree: MD

Professional title: Director, Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Brazil

Manuscript submission date: 2022-04-13

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-06-01 13:38

Reviewer performed review: 2022-06-12 08:42

Review time: 10 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

To the author This manuscript discussed the anatomical and physiological considerations about two of the symptoms reported by patients: the loss or reduction of smell and taste. As a review, 17 articles were included and analyzed. The review suggests that viral mechanisms of action may be related to lesions both at the local level and at the level of the central nervous system. At present, SARS-CoV-2 is in the state of pandemic, this manuscript has special clinical significance. However, some limitations and shortcomings should be addressed. Firstly, the title of the manuscript is not reasonable enough. In the discussion and conclusion part, apart from the considerations about anatomophysiological relationships, the author also discussed the treatment, prevention, and prognosis of the disease and the two complications with considerable length. In addition, for the article the review included, only a few of them explored the anatomical and physiological relationships. Majority of them merely speculated the possible pathological mechanisms in the discussion part, which was a routine component for a manuscript. Therefore, I recommend to replace the title with "Anatomophysiological relationships and clinical considerations of tasting and smelling loss in patients with COVID-19". Secondly, for clinical significance, temporary taste and smelling lost is common and insignificant. Only persistent tasting and smelling lost is a severe complication for COVID-19 infection. It was recommended that the prevalence rate and prognosis of persistent tasting and smelling lost was added in the introduction part and discussion part. Furthermore, as the virus has been mutated, the omicron strain is the main virus strain at present. The clinical features and physiological considerations of this strain should be discussed. Thirdly, Minor language polishing is needed. I



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recommend the author to replace long sentences into several short sentences, so as to make sentences more comprehensible. It's better that one sentence contains only one idea. For example: "Regarding preventive measures against COVID-19 and its symptoms, such as loss of smell and taste, the importance of using PPE (personal protective equipment) is found in the literature, as in the study by Kim et al.[34], that limited access to this equipment (mask, lab coat, new gloves and face shield) was significantly associated with a higher risk of developing symptoms of COVID-19, in addition to being associated with more severe disease, with moderate or severe symptoms[34]." This sentence is too length and better to be divided into two sentences. Fourthly, in the method part, the eligible criteria and exclusion criteria should be clearly expressed. Fifthly, in the table of the included articles, the study type was recommended to be listed. Lastly, in the discussion part, the preventive measures were discussed. What is the role of vaccination for the prevention of the disease and the two complications? It would be better to add these contents into the manuscript.

Response to the reviewer:

Dear Reviewer,

A new version of the revised article is also attached to the submission system according to the standards required by the World Journal of Virology. All suggestions were accepted and the changes included in the article. We believe that these changes have significantly improved our manuscript.

Sincerely,

The authors

1) First: Title changed to: **Anatomophysiological relationships and clinical**

considerations of tasting and smelling loss in patients with COVID-19

- 2) Second: In Discussion, added:

There are difficulties in quantifying the prevalence and incidence of gustatory and olfactory dysfunction in the general population, due to causes such as analysis and evaluation methods, sample size and area, and the correct definitions of dysfunctions[40]. Multicentric research from Europe, in the year 2020, showed interesting data such as that 85.6% of patients with COVID-19 reported olfactory loss. It was also one of the pioneering studies in the identification of taste loss, which at the time was 88.0% in patients with COVID-19. In addition, the manuscript described that infected patients could experience this loss without the presence of other significant symptoms[40].

- 3) Third: In Discussion, changed to:

Regarding preventive measures against COVID-19 and its symptoms, such as loss of smell and taste, the importance of using PPE (personal protective equipment) is found in the literature, as in the study by Kim *et al.*[34], that limited access to this equipment (mask, lab coat, new gloves and face shield) was significantly associated with a higher risk of developing symptoms of COVID-19, in addition to being associated with more severe disease, with moderate or severe symptoms[34].

Adequate access to PPE by health professionals, especially those on the front line, is associated with a lower chance of contracting the disease, and even if PPE fails, there is an association with less severe and shorter forms[34].

- 4) Fourth: In Method, added:

- Eligibility criteria:

The inclusion criteria were:

- Description of changes in smell and taste due to COVID-19;
- Human studies;
- Publications in English only;
- Publications that allow full access to the text.

- The exclusion criteria were:

- Articles that have been duplicated;
- Animal studies;
- When the title was not related to the objective;
- There was no loss of taste;
- There was no loss of smell;
- Other languages (except English);
- When access to the full text has not been obtained;
- Brief communications, letters to the editor, editorials, reviews, comments and conference abstracts.

5) Fifth: In Results, added study type (Table 1)

6) Last: In Discussion, added:

With the emergence of coronavirus variants, infections caused by Omicron can currently be highlighted, which resulted in mild disease, mainly due to the discovery and use of vaccines. Compared to other strains such as Delta, Omicron infections were more often associated with symptomatology and upper respiratory tract infections, have lower viral loads, less dysregulated immune cell profiles, and lower levels of pro-inflammatory cytokines[41].

A study, through questionnaires, evaluated the clinical profile of patients who

developed COVID-19 after full vaccination, in symptomatic patients. The most frequent symptoms were: asthenia (82.4%), chemosensory dysfunction (63.4%), headache (59.5%), coryza (58.2%), muscle pain (54.9%), loss of appetite (54.3%) and nasal obstruction (51.6%). However, 62.3% and 53.6% of survey participants reported olfactory and gustatory dysfunction, respectively. Symptom severity was mild or moderate in almost all cases. Chemosensory dysfunction is still a frequent symptom, even in people who contracted the infection after full vaccination. In this way, the sudden loss of smell and taste may continue to represent a useful and specific diagnostic aid in suspected COVID-19, even in vaccinated individuals[42].

In References, added:

40. **Lechien JR**, Chiesa-Estomba CM, De Siaty DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *Eur Arch Otorhinolaryngol* 2020; **277**, 2251-2261. doi: 10.1007/s00405-020-05965-1. PMID: 32253535; PMCID: PMC7134551.
41. **Young B**, Fong SW, Chang Z, Tan KS, Rouers A, Goh YS, Tay DJW, Ong SWX, Hao Y, Chua SL et al. Comparison of the Clinical Features, viral Shedding and Immune Response in Vaccine Breakthrough Infection by the Omicron and Delta Variants. *Research Square* 2022, EuropePMC, ID: ppcovidwho-328680.
42. **Vaira LA**, De Vito A, Lechien JR, Chiesa-Estomba CM, Mayo-Yañez M, Calvo-Henriquez C, Saussez S, Madeddu G, Babudieri S, Boscolo-Rizzo P, Hopkins C, De Riu G. New Onset of Smell and Taste Loss Are Common Findings Also in Patients With Symptomatic



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COVID-19 After Complete Vaccination. *Laryngoscope* 2022; 132: 419-421. doi:
10.1002/lary.29964. PMID: 34812498; PMCID: PMC9011575.