Prevalence and characteristics of taste disorders in cases of COVID-19

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Prevalence and characteristics of taste disorders in cases of COVID-19: a meta-analysis of 29,349 patients

Running Header Title: **Taste disorders in COVID-19: Meta-analysis**

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Abstract

Background: The purpose of this meta-analysis is to assess the overall pooled prevalence of taste disorders and their subtypes in COVID-19 patients.

Methods: We conducted a systematic review and meta-analysis.

Results: 59 studies (n=29349, 64.4% female) were included. Overall, the pooled prevalence of taste disorders in COVID-19 patients was 48.1% [95% CI: 41.3-54.8]. The prevalence of taste disorders in studies with objective assessments was higher compared to subjective assessments (59.2% vs 47.3%). The disorders were observed in 55.2% European, 61.0% North American, 27.1% Asian, 29.5% South American, and 25.0% Australian patients. Ageusia, hypogeusia, and dysgeusia were detected in 28.0%, 33.5%, and 41.3% of COVID-19 patients. We identified 91.5% of the included studies as high-quality.

Conclusions: The prevalence of taste disorders in COVID-19 patients is 48.1%. Objective assessments tend to show higher prevalence than subjective assessments of the disorders. Dysgeusia is the most common subtype followed by ageusia and hypogeusia.

KEYWORDS: Coronavirus; COVID-19; taste; gustatory; meta-analysis

1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) infection caused by the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was first reported in Hubei Province in Wuhan, China in December 2019 and since then had spread globally. As of 16 August 2020, globally, 21.2 million laboratory-confirmed human cases and over 760,000 deaths have been alerted to the World Health Organization.[1] The rapidly evolving nature of the SARS-CoV-2 infection has steered bafflement amongst physicians, worldwide. Heterogeneity of clinical manifestations, in addition to the severity of the disease, adds on to the burden in managing this deadly virus.

Atypical presentations including olfactory dysfunction (*i.e.* anosmia, hyposmia, and dysosmia) and gustatory or taste disorder (*i.e.* ageusia, hypogeusia, and dysgeusia) were initially trivialized, however, have now become sine qua non. Centers for Disease Control has recently added new onset of loss of smell and taste to its chief symptoms which may suggest SARS-CoV-2 infection, besides cough, shortness of breath, fever, chills, muscle pain, and sore throat.[2]

Interestingly, only meagre number of cases involving olfactory and gustatory dysfunction has been reported amongst the Asian population, particularly China. An earlier report by Mao et al.[3] revealed hypogeusia in 5.6% and hyposmia in 5.1% cases, whereas, a multicenter European study revealed a 88.0% of the patients with gustatory dysfunction and 85.6% of the COVID-19 patients with olfactory dysfunction.[4]

Researchers have unveiled that the variation in clinical manifestation across different populations worldwide is attributed to the mutation found on genome on virus sequences.[5] As we all know, Coronaviruses are single-stranded RNA virus well-known for their expeditious nature of mutation as well as recombination.[6] Thorough molecular epidemiological study and analysis will aid in understanding the behavior as well as the potential capacity of this novel virus.

A recent meta-analysis by Aziz et al.[7] demonstrated the prevalence of taste disorder in 49.8% of COVID-19 patients. Their meta-analysis is based on five included studies. Due to the limited data available, the authors cautioned that their results have a high heterogeneity rate and might have some degree of bias. Furthermore, the situation is rapidly evolving and there are new available studies which can be appraised together with the previous ones. Considering this, a better design and robust meta-analysis is essential to reassess and depict the association of taste disorders with COVID-19 infection.

Olfactory dysfunction has become the current key symptom ensuing the increasing evidence of its association with SARS-CoV-2 infection.[8-10] Interestingly, taste disorder has been related to retronasal olfactory dysfunction rather than diminished gustation itself.[11] Recent data, however, has suggested that gustatory dysfunction is an independent manifestation rather than ensuing retronasal trajectory.[12] The SARS-CoV-2 distinctive tendency to cause selective neurological impairment may explain the different presentation of gustatory and olfactory dysfunction,[4] but it is entirely possible that there are different rates of chemosensory disturbance which varies from study to study. We performed a comprehensive systematic review and meta-analysis of the currently available literature to outline the prevalence of taste disorders in patients with COVID-19.

2. MATERIALS AND METHODS

2.1 Systematic Review Protocol

We conducted a systematic review and meta-analysis of the literature in accordance with the PRISMA guideline to identify studies that presented the prevalence of taste disorders in patients with COVID-19, worldwide.[13] The protocol of this study was registered with the International Prospective Register of Systematic Reviews (PROSPERO) database, registration number: CRD42020188384.

2.2 Eligibility Criteria

The objective was to identify studies published during the COVID-19 outbreak that presented the prevalence of taste disorders in patients with COVID-19, worldwide. There was no restriction on the study design; therefore, observational studies, clinical trials, and case series were included. In addition to the published studies, preprints were also considered if data of interest were reported. Review articles, case reports, opinions, and perspectives were excluded. Data reported by news reports and press releases or data collected from websites or databases were not considered.

2.3 Search Strategy

PubMed, Scopus, Web of Science, Embase, and Google Scholar databases were searched to identify studies published between 1 December 21 and 23 June 2020 without language restrictions. The following key terms were searched: coronavirus, COVID-19, COVID19, nCoV, SARS-CoV-2, SARS-CoV2, taste, gustatory, ageusia, hypogeusia, dysgeusia, and parageusia. Complete details of the search strategy are in Supplementary Table S1. To ensure a robust search procedure, references of the included studies were also reviewed. Duplicate studies were excluded by using EndNote X8 software.

2.4 Study Selection

To identify eligible studies, articles of interest were screened based on the title and abstract, followed by full text by two authors (J.S. and M.A.I.) independently. Disagreements about inclusion were discussed and resolved by consensus.

2.5 Data extraction

Data extraction was done independently by two authors (J.S. and M.A.I.). From each eligible study, we extracted the following information into a predefined Excel spreadsheet: first author's last name; study design; country of the participants; data collection period; total number of COVID-19 patients; number of female COVID-19 patients; age; COVID-19 confirmation procedure; confirmatory procedure of taste disorders; investigated taste abilities and types of taste disorder.

2.6 Quality Assessment

The quality of included studies was assessed independently by two authors (J.S. and M.A.I.) using the Joanna Briggs Institute (JBI) critical appraisal tools[14] and all of the authors took part in the discussion to resolve any discrepancies. The studies were classified as low-quality (high-risk of bias) if the overall score was ≤50%. To assess publication bias, a funnel plot presenting prevalence estimate against the standard error was constructed and the asymmetry of the funnel plot was confirmed with Egger's test.

2.7 Data analyses

Random-effects model was used to obtain the pooled prevalence and 95% confidence intervals (CIs) of taste disorders in patients with COVID-19. Heterogeneity between studies was assessed using the I^2 statistic (I^2>75% indicating substantial heterogeneity) in addition to using the Cochran's Q test to identify the significance of heterogeneity, where p<0.10 was considered as statistically significant. Additionally, to identify the outlier studies and the sources of heterogeneity, a Galbraith plot was constructed. All the analyses and plots were generated by using metaprop codes in meta (version 4.11-0) and metafor (version 2.4-0) packages of R (version 3.6.3) in RStudio (version 1.2.5033).[15]

2.8 Subgroup and Sensitivity Analyses

As subgroups, the prevalence of taste disorders in COVID-19 patients from different geographical regions, in different types including ageusia, hypogeusia, and dysgeusia and assessment types of taste disorder (*i.e.* subjective or objective) were analyzed. To identify the source of heterogeneity and to check the robustness of the results, sensitivity analyses were performed through the following strategies: i) excluding small studies (n<100); ii) excluding the low-quality studies (high-risk of bias); iii) excluding studies not reporting COVID-19 confirmation assay; iv) excluding the outlier studies; and v) considering only cross-sectional studies.

3. RESULTS

3.1 Study selection

Our search initially identified 775 studies. After removing 379 studies [duplicate studies (n=318), review articles (n=47), and case reports (n=14)]; titles and abstracts of 396 studies were screened for eligibility, of which 337 studies were excluded because of lack of relevant and sufficient data on prevalence. Finally, 59 studies were included in the systematic review and meta-analysis (Figure 1).

3.2 Study characteristics

Detailed characteristics and references of the included studies are presented in Table 1. Overall, this meta-analysis reports data from 29349 COVID-19 patients (64.4% female). Ages of the COVID-19 patients included in this meta-analysis ranged from 28.0±16.4 to 66.4±14.9 years. Studies were from five continents [Europe (n=19496), Asia (n=5636), North America (n=1100), South America (n=148), and Australia (n=28)] including 23 countries - UK, Italy, Spain, Poland, Turkey, France, Belgium, Switzerland, Germany, USA, Canada, China, Korea,

Iraq, Iran, Israel, Saudi Arabia, Brazil, Argentina, Uruguay, Bolivia, Venezuela, and Australia. Among the included studies, 96.6% confirmed COVID-19 patients by using the RT-PCR method, whereas the method was not reported in two studies.

3.3 Quality Assessment

Detailed quality assessment of the included studies is shown in the supplementary materials (Supplementary Table S2, Supplementary Table S3). Briefly, 91.5% of the included studies were of high-quality (low-risk of bias). Visual inspection of the funnel plot and Egger's test results showed that there was no significant publication bias (p=0.68) (Figure 2).

3.4 Outcomes

Overall, the pooled prevalence of taste disorders in COVID-19 patients was 48.1% [95% CI: 41.3-54.8] (Figure 3). From the subgroup analyses, we observed taste disorders in 55.2% European, 61.0% North American, 27.1% Asian, 29.5% South American, and 25.0% Australian patients with COVID-19 (Table 2, Supplementary Figure S1). Additionally, ageusia, hypogeusia, and dysgeusia were observed in 28.0%, 33.5%, and 41.3% of COVID-19 patients, respectively (Table 2, Supplementary Figure S2). Interestingly, the prevalence of taste disorder in studies with objective assessment was higher compared to subjective assessment (59.2% vs 47.3%) (Table 2, Supplementary Figure S3). Overall, very high levels of heterogeneity (ranging from 71% to 99%) were observed during the estimation of taste disorders in the main analysis as well as in different subgroup analyses. From the Galbraith plot, four studies were identified as the potential sources of heterogeneity (Figure 4).

3.5 Sensitivity analyses

Sensitivity analyses on assessing taste disorders in COVID-19 patients excluding small studies, low-quality studies, studies where COVID-19 confirmation test was not reported, excluding the outlier studies and considering only cross-sectional studies showed very marginal differences (2.5% lower to 3.8% higher) in overall pooled prevalence compared to the main findings (Table 3, Supplementary Figure S4). Overall, our sensitivity analyses indicated that the results of the prevalence of taste disorders in COVID-19 patients are robust and reliable.

4. DISCUSSION

New onset of taste dysfunction has been described as a potential early symptom of COVID-19 infection. It may present concomitantly with an olfactory dysfunction or as an isolated symptom.[8,16] Oral cavity is one of the possible routes of entry for COVID-19 infection corroborated by the discovery of SARS-COV-2 in saliva and damage of epithelial cells in the oral cavity among infected patients.[17-19] Gustation is related to sensory input perceived from taste receptors located mainly in the oral cavity following oral intake and any alteration in its settings will cause taste dysfunction.[20] There are growing evidences that taste dysfunctions are more frequent then olfactory disturbances disputing the close correlation between the two dysfunctions and create a new hypothesis of other factors responsible for the taste disorders in COVID-19 patients.[4,21]

In our meta-analysis, a high prevalence of taste disorder in patients with COVID-19 was noted across all 59 included studies. Underreporting and underestimation may explain the difference in prevalence across the world. There is a tendency for underreporting for patients in the Asia continent while underestimation may occur from the observational nature of the included studies such as medical report review. It is interesting to note that, according to the preliminary data from Wuhan, the epicenter of SARS-CoV-2 fails to disclose gustatory dysfunction as one of the manifestations of SARS-Co-V infection.[22,23] There might be fewer

otolaryngologic complaints in Chinese patients or it could have been overlooked as the assessment was more focused on the critical region such as the lower respiratory tract. There are differences between the two major types of SARS-CoV-2, S and L types owing to its single-nucleotide polymorphisms. Early cases in Wuhan, China revealed L type of SARS-Co-V to be more widespread which subsequently reduced in numbers.[24] Rapidly evolving SARS-CoV-2 notably its spike glycoprotein which binds to cell receptors governs host tropism which elucidates various disease manifestations across the population.[5,25] Angiotensin converting enzyme 2 (ACE2), the receptor of SARS-CoV-2, has variable expression level among different populations.[26] This distinction is another possible explanation for the different manifestations across populations worldwide.

There are three types of taste dysfunction observed in our meta-analysis (Table 2). Comparison for the type of taste dysfunction revealed dysgeusia has a higher prevalence (41.3%) than both ageusia (28.0%) and hypogeusia (33.5%). Though, the exact mechanisms underlying the different presentation of taste dysfunction among patients with COVID-19 infection remain unclear, there are several possible explanations. All the three types of taste dysfunction may occur as a result of damage along the central taste pathway, including the brainstem, thalamus, cranial nerves, or cerebral cortex. Earlier evidence has shown that cerebral involvement in COVID-19 patients might ensue during the early and late phase of infection.[27] Ageusia (complete loss of taste) and hypogeusia (reduce taste sensation) may occur due to disturbance of the composition and volume of saliva as well as the compromised epithelial cells of the tongue.

Dysgeusia which is a state of altered or distorted perception of taste, may arise from isolated injury to any one of the major nerve pathways. Taste perception may also be altered when there is olfactory dysfunction which affects the central multisensory input as the overall taste perception is the culmination process of the integrated central multisensory system with

the primary taste sensation.[28] On the other hand, it cannot be excluded that the self-reported questionnaire may be confusing to patients. Rather than evaluating the ability to identify the primary taste, it may instead evaluate perception of flavour.[29]

Even though, earlier meta-analysis[30-32] acknowledged that dysgeusia is the most common impairment among COVID-19 patients, they did not perform any subgroup analysis for the different type of taste dysfunction and this highlights the new contribution of our meta-analysis. Female predominance was noted in our meta-analysis with 64.4% of patients. Females can more readily recognize changes in chemosensory dysfunction as compared to their male counterparts and this sensitivity may explain the differences in their prevalence. Another explanation is the gender differences in inflammatory cytokine production,[33] but more studies are required to prove the causality.

There are four objective studies included in our meta-analysis. Remarkably all of them showed a higher prevalence rate of taste dysfunction (59.2%) than the prevalence from the subjective studies (47.3%). Adamczyk et al.[34] showed self-reported questionnaire has a sensitivity of 77% and specificity of 86% of detecting taste disorder but when objective taste test was performed the sensitivity increases to 94% and the specificity to 100%. In a single center study in Italy with 72 patients, Vaira et al.[35] disclosed taste test was able to establish 47% of patients with taste dysfunction. Their result contradicts earlier studies in Europe-based on self-reported questionnaire which resulted in a lower prevalence rate. A multicenter cohort study evaluating objective chemosensitive dysfunction of three hundred and forty five COVID-19 patients comprising two groups of patients, one group consisted of home quarantine patients and the other group hospitalized patients,[36] found under-reporting of chemosensitive disorders among their patients from both groups. As the hospitalized group represents the severe COVID-19 infection, their result refutes the view that the presence of chemosensitive dysfunction signals a mild to moderate infection and construes that those with severe disease

tend to neglect such symptoms. The use of objective taste test revealed 44.9% of their patients had taste dysfunction.

To overcome the hurdles of performing an objective taste test which most of the time is a hospital-centric procedure with its inherent risk of transmission of infection to health care providers and other patients, a home-based taste test is suggested as an alternative. Vaira et al.[37] assessed a home-based objective taste test self-performed by patients and demonstrated that it was reliable in detecting taste dysfunction. Out of the thirty-three quarantined patients with COVID-19 infection, 51.5% was confirmed to have taste dysfunction. The authors proposed that a home-based objective taste test may form a good public health strategy for early detection of paucisymptomatic COVID-19 cases which may break the chain of transmission by isolation of the infected patients.

The result of our meta-analysis is in line with the finding of an earlier meta-analysis by Borsetto et al.[31] that discovered subjective assessment with self-reported questionnaires appears to underestimate the prevalence of taste dysfunction. Conversely, Hintschich et al.[38] demonstrated patients with self-reported taste dysfunction did not exhibit a genuine impaired taste when confirmed by objective taste test alluding to impaired retronasal olfaction as the cause of the altered taste. This could be explained by the intimate relationship between olfaction and the perception of flavor, giving rise to the subjective taste dysfunction.

Understanding a common phenomenon in any condition when the focus is more on life-threatening organ damage;[39] in COVID-19 infection the focus is on pulmonary failure and death. As proper recognition of a disorder entails its ensuing proper treatment, this simply cannot be overlooked. Recovery of patients depends not only on the treatment but also on the resumption of an appropriately composed diet which may assist body innate immunity to fight against infection and the repairing process of damaged cells. Dietary composition and nutrition especially those known as antioxidants have been proposed as the determinants behind the

variable death rate of different European countries which highlighted their critical roles as a protective mechanism against infection.[40] As taste is one of the five senses, when it is ignored and underestimating the effect of gustatory dysfunction on the quality of life of patients, means rendering suboptimal treatment and thus delivering inferior quality of care.

Considering the significance of gustatory dysfunction in COVID-19 infection, a laboratory-confirmed COVID-19 positive and negative patient would provide more accurate information on the association. Such studies also may perform a reliable and vigorous objective testing required for its evaluation. As explanation is still lacking as to the reasons why a certain group of patients presented with either olfactory dysfunction or gustatory dysfunction, or both, a much-needed clarification may emanate from a neurological assessment of the neural pathways involved. It is acknowledged that the interaction between host and virus characteristics is responsible, but no study so far has verified it. Overall, more researches on COVID-19 and gustatory dysfunction are imperative and valuable for a future prevention strategy.

Our study has several strengths. This meta-analysis is the first, to our knowledge, to comprehensively investigate the prevalence of taste disorders in patients with COVID-19. This meta-analysis was conducted with a significant number of studies and hence including a considerable number of participants, resulting in more robust estimates. Majority of the included studies confirmed COVID-19 subjects by using the RT-PCR technique, which strengthens our findings. None of the analyses represented significant publication bias demonstrating that we were unlikely to have missed studies that could have altered the findings. All the conducted sensitivity analyses generated very similar results to the main findings indicating the robustness of the meta-analysis results. Based on the quality assessments, 86.1% of the studies were of high methodological quality (low-risk of bias), which ensured a reliable result.

Nevertheless, there are several notable limitations. Based on the search strategy and considered time period, this meta-analysis could include participants from 23 countries; therefore, the prevalence may not represent a global scale and generalization of the findings should be done cautiously. All of the analyses generated substantial degrees of heterogeneity. Even though we examined the sources of heterogeneity by subgroup, sensitivity analyses and Galbraith plot, the source of heterogeneity could not be fully explained by the factors included in the analyses. While we identified the prevalence of taste disorders from the first seven-month data of the COVID-19 outbreak, we were unable to characterize taste disorders in severe vs. non-severe and survived vs. non-survived patients with COVID-19. Therefore, in the future, the characteristics of taste disorders in these settings of COVID-19 could be interesting to explore.

5. CONCLUSIONS

Based on this meta-analysis, from the first seven-month data of the SARS-CoV-2 outbreak, taste disorders are detected in 48.1% of the COVID-19 patients; therefore, taste impairment must be recognized as an early clinical symptom of COVID-19 patients.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest.

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TABLE 1. Major characteristics of the included studies.

No.	Study ID and references	Study design	Country	Data collection period	Total number of COVID-19 patients (female)	Age (years) (mean±SD / median (IQR) / range	COVID-19 confirmation procedure	Type of assessment for taste disorders (Subjective/ Objective)	Method of assessment for taste disorders
1	Abalo-Lojo 2020[41]	Cross-sectional	Spain	NR	131 (75)	50.4±NR	RT-PCR	Subjective	Self-reported questionnaire survey
2	Adamczyk 2020[34]	Case-control	Poland	Apr to May 2020	52 (1)	20.8±NR	RT-PCR	Objective	Standardized gustatory function test
3	Aggarwal 2020[42]	Cross-sectional	USA	1 Mar to 4 Apr 2020	16 (4)	67.0 (38.0-95.0)	RT-PCR	Subjective	Medical record review
4	Alshami 2020[43]	Cross-sectional	Saudi Arabia	16 Mar to 18 Apr 2020	128 (69)	39.6±15.5	RT-PCR	Subjective	In person interview
5	Beltrán-Corbellini 2020[8]	Case-control	Spain	23 to 25 Mar 2020	79 (31)	61.6±17.4	RT-PCR	Subjective	Self-reported questionnaire survey
6	Biadsee 2020[44]	Cross-sectional	Israel	25 Mar to 15 Apr 2020	128 (70)	36.2±NR	RT-PCR	Subjective	Questionnaire through mobile phone survey
7	Carignan 2020[45]	Case-control	Canada	10 to 23 Mar 2020	134 (81)	57.2 (42.6-64.4)	RT-PCR	Subjective	Telephone interview
8	Chary 2020[46]	Cross-sectional	France	25 Mar to 18 Apr 2020	115 (81)	47.0 (20.0-83.0)	RT-PCR	Subjective	Telephone interview
9	Chiesa-Estomba 2020[47]	Cross-sectional	Spain, Uruguay, Argentina,	NR	542 (324)	34.0±11.0	RT-PCR	Subjective	Online questionnaire survey

			and Venezuela						
10	Dawson 2020[9]	Cross-sectional	USA	Mar to Apr 2020	42 (NR)	NR	RT-PCR	Subjective	Household survey
11	De Maria 2020[10]	Cross-sectional	Italy	NR	95 (NR)	NR	RT-PCR	Subjective	Self-reported questionnaire survey
12	Dell'Era 2020[48]	Cross-sectional	Italy	10 to 30 Mar 2020	355 (163)	50.0 (40.0-59.5)	RT-PCR	Subjective	In person interview and telephone interview
13	Gelardi 2020[49]	Cross-sectional	Italy	NR	72 (33)	49.7 (19.0-70.0)	RT-PCR	Subjective	Medical record review
14	Giacomelli 2020[50]	Cross-sectional	Italy	19 Mar 2020	59 (19)	60.0 (50.0-74.0)	NR	Subjective	In person interview
15	Izquierdo-Domínguez 2020[51]	Cross-sectional	Spain	21 Mar to 18 Apr 2020	846 (400)	56.8±15.7	RT-PCR	Subjective	Self-reported questionnaire survey
16	Kim 2020[52]	Cross-sectional	Korea	12 to 16 Mar 2020	172 (106)	26.0 (22.0-47.0)	RT-PCR	Subjective	Self-reported questionnaire survey
17	Klopfenstein 2020[53]	Cross-sectional	France	1 to 17 Mar 2020	114 (36)	47.0±16.0)	RT-PCR	Subjective	Medical record review
18	Kosugi 2020[54]	Cross-sectional	Brazil	25 Mar to 30 Apr 2020	145 (77)	36.0 (31.0-44.0)	NR	Subjective	Online questionnaire survey
19	Lagi 2020[55]	Cross-sectional	Italy	25 Feb to 26 Mar 2020	84 (29)	62.0 (51.0-72.0)	RT-PCR	Subjective	Medical record review
20	Lapostolle 2020[56]	Cross-sectional	France	24 Mar to 6 Apr 2020	1487 (752)	44.0 (32.0-57.0)	RT-PCR	Subjective	Telephone interview

21	Lechien 2020[12]	Cross-sectional	Belgium	NR	86 (56)	41.7±11.8	RT-PCR	Subjective	Self-reported questionnaire survey
22	Lechien 2020a[4]	Cross-sectional	Belgium, Italy, France, and Spain	NR	417 (263)	36.9±11.4	RT-PCR	Subjective	Self-reported questionnaire survey
23	Lechien 2020b[57]	Cross-sectional	France, Italy, Spain, Belgium, and Switzerland	22 Mar to 10 Apr 2020	1420 (962)	39.0±12.0	RT-PCR	Subjective	Self-reported questionnaire survey
24	Lechien 2020c[58]	Cross-sectional	18 European countries	22 Mar to 23 Apr 2020	2013 (1979)	39.5±12.1	RT-PCR	Subjective	Self-reported questionnaire survey
25	Lee 2020[19]	Cross-sectional	Korea	8 to 31 Mar 2020	3191 (2030)	44.0 (25.0-58.0)	RT-PCR	Subjective	Telephone interview
26	Lee 2020a[59]	Cross-sectional	Canada	16 Mar to 15 Apr 2020	56 (33)	38.0 (31.8-47.2)	RT-PCR	Subjective	Online questionnaire survey
27	Levinson 2020[60]	Cross-sectional	Israel	10 to 23 Mar 2020	42 (19)	34.0 (15.0-82.0)	RT-PCR	Subjective	Medical record review
28	Liguori 2020[61]	Cross-sectional	Italy	30 Mar to 24 Apr 2020	103 (44)	55.0±14.6	RT-PCR	Subjective	In person interview
29	Luers 2020[62]	Cross-sectional	Germany	22 to 28 Mar 2020	72 (31)	38.0±13.0	RT-PCR	Subjective	Self-reported questionnaire survey
30	Mao 2020[3]	Cross-sectional	China	16 Jan to 19 Feb 2020	214 (127)	52.7±15.5	RT-PCR	Subjective	Medical record review
31	Meini 2020[63]	Cross-sectional	Italy	NR	100 (40)	65.0±15.0	RT-PCR	Subjective	Telephone interview

32	Menni 2020[64]	Cross-sectional	UK	24 to 29 Mar 2020	579 (400)	40.7±11.8	RT-PCR	Subjective	Smartphone-based App survey
33	Menni 2020a[65]	Cross-sectional	UK	24 Mar to 21 Apr 2020	6452 (4638)	41.2±12.1	RT-PCR	Subjective	Smartphone-based App survey
			USA		726 (567)	44.6±14.3			
34	Mercante 2020[66]	Cross-sectional	Italy	5 to 23 Mar 2020	204 (94)	52.6±14.4	RT-PCR	Subjective	Telephone interview
35	Merza 2020[67]	Cross-sectional	Iraq	18 Mar to 7 Apr 2020	15 (6)	28.0±16.4	RT-PCR	Subjective	Medical record review
36	Moein 2020[68]	Case-control	Iran	21 to 23 Mar 2020	60 (20)	46.5±12.1	RT-PCR	Subjective	Medical record review
37	Moro 2020[69]	Cross-sectional	Countries from Europe, Asia, Africa, America, and Australia.	9 to 27 Apr 2020	2343 (NR)	NR	RT-PCR	Subjective	Online questionnaire survey
38	Noh 2020[70]	Cross-sectional	Korea	NR	199 (130)	38±13.1	RT-PCR	Subjective	In person interview
39	Paderno 2020[71]	Cross-sectional	Italy	27 Mar to 1 Apr 2020	508 (223)	55.0±15.0	RT-PCR	Subjective	Self-reported questionnaire survey
40	Patel 2020[72]	Cross-sectional	UK	1 Mar to 1 Apr 2020	141 (58)	45·6 (20.0-93.0)	RT-PCR	Subjective	Telephone interview
41	Qiu 2020[73]	Cross-sectional	China, Germany, and France	15 Mar to 5 Apr 2020	394 (NR)	39.0 (NR)	RT-PCR	Subjective	Medical record review
42	Renaud 2020[74]	Cross-sectional	France	NR	97 (67)	35.0 (20.0-73.0)	RT-PCR	Subjective	Questionnaire through email survey

43	Romero-Sánchez 2020[75]	Cross-sectional	Spain	1 Mar to 1 Apr 2020	841 (368)	66.4±14.9	RT-PCR	Subjective	Medical record review
44	Sayin 2020[76]	Cross-sectional	Turkey	NR	64 (39)	37.7±11.3	RT-PCR	Subjective	Online questionnaire survey
45	Schmithausen 2020[77]	Cross-sectional	Germany	NR	41 (21)	40.0 (31.0-53.0)	RT-PCR	Subjective	In person interview
46	Sierpiński 2020[78]	Cross-sectional	Poland	17 to 18 Apr 2020	1942 (1169)	50.0 (NR)	RT-PCR	Subjective	Telephone interview
47	Song 2020[79]	Cross-sectional	China	27 Jan to 10 Mar 2020	1172 (595)	61.0 (48.0-68.0)	RT-PCR	Subjective	Telephone interview
48	Speth 2020[80]	Cross-sectional	Switzerland	3 Mar to 17 Apr 2020	103 (53)	46.8±15.9	RT-PCR	Subjective	Telephone interview
49	Trubiano 2020[81]	Cross-sectional	Australia	1 to 22 Apr 2020	28 (14)	55.0 (46.0-63.5)	RT-PCR	Subjective	Medical record review
50	Tudrej 2020[82]	Cross-sectional	Switzerland	24 Mar to 14 Apr 2020	198 (NR)	NR	RT-PCR	Subjective	Self-reported questionnaire survey
51	Vaira 2020[36]	Cross-sectional	Italy	NR	345 (199)	48.5±12.8	RT-PCR	Objective	Standardized gustatory function test
52	Vaira 2020a[35]	Cross-sectional	Italy	31 Mar to 6 Apr 2020	72 (45)	49.2±13.7	RT-PCR	Objective	Standardized gustatory function test
53	Vaira 2020b[37]	Cross-sectional	Italy	9 to 10 Apr 2020	33 (22)	47.2±10.0	RT-PCR	Objective	Standardized gustatory function test
54	Vargas-Gandica 2020[83]	Cross-sectional	Germany, USA, Bolivia, and Venezuela	NR	10 (7)	51.2±16.0	RT-PCR	Subjective	Medical record review

55	Yan 2020[21]	Cross-sectional	USA	31 Mar to 3 Apr 2020	59 (29)	18.0-80.0	RT-PCR	Subjective	Online questionnaire survey
56	Yan 2020a[84]	Cross-sectional	USA	3 Mar to 8 Apr 2020	128 (67)	53.5 (40.0-65.0)	RT-PCR	Subjective	Medical record review
57	Zayet 2020[85]	Case-control	France	30 Mar to 3 Apr 2020	95 (79)	39.8±12.2	RT-PCR	Subjective	Medical record review
58	Zayet 2020a[86]	Cross-sectional	France	26 Feb to 14 Mar 2020	70 (41)	56.7±19.3	RT-PCR	Subjective	Self-reported questionnaire survey
59	Zou 2020[87]	Cross-sectional	China	1 Feb to 3 Mar 2020	81 (43)	58.0 (50.0-68.5)	RT-PCR	Subjective	Medical record review

SD: Standard deviation; IQR: interquartile range; RT-PCR: reverse transcription polymerase chain reaction; NR: not reported

TABLE 2. Pooled prevalence of taste disorders in different subgroups of COVID-19 patients

Subgroups of COVID-19 patients	Prevalence of taste disorders [95% CIs] (%)	Number of studies analyzed	Total number of COVID-19 patients	Heterogeneity		Publication bias, Egger's test (*p*-value)
				I^2	*p*-value	
Taste disorders in different regions						
Europe	55.2 [47.4-63.0]	37	19496	99.0%	<0.001	0.19
North America	61.0 [51.9-70.0]	7	1100	82.0%	<0.001	NA
Asia	27.1 [21.0-33.2]	13	5636	96.0%	<0.001	0.22
South America	29.5 [0.0-89.7]	2	148	81.0%	0.02	NA
Australia	25.0 [9.0-41.0]	1	28	NA	NA	NA
Different types of taste disorder						
Ageusia	28.0 [20.2-35.90]	17	8856	99.0%	<0.001	0.004
Hypogeusia	33.5 [24.6-42.4]	8	1366	92.0%	<0.001	NA
Dysgeusia	41.3 [26.7-55.8]	16	3347	99.0%	<0.001	0.92
Taste disorder assessment types						
Subjective assessment	47.3 [40.4-54.3]	55	28847	99.0%	<0.001	0.72
Objective assessment	59.2 [49.0-69.3]	4	502	71.0%	0.01	NA

CIs: Confidence intervals; NA: Not applicable.

TABLE 3. Sensitivity analyses

Strategies of Sensitivity analyses	Prevalence of taste disorders [95% CIs] (%)	Difference of pooled prevalence compared to the main result	Number of studies analyzed	Total number of COVID-19 patients	Heterogeneity	
					I^2	*p*-value
Excluding small studies	46.8 [37.8-55.8]	2.5% lower	33	27862	100.0%	<0·0001
Excluding low-quality studies	48.2 [41.2-55.3]	0.4% higher	54	28993	99.0%	<0·0001
Excluding studies where COVID-19 confirmation assay was not reported	49.2 [42.4-56.0]	2.4% higher	57	29145	99.0%	<0·0001
Excluding outlier studies	49.9 [45.3-54.5]	3.8% higher	53	24563	98.0%	<0·0001
Considering only cross-sectional studies	47.9 [40.8-55.0]	0.3% lower	54	28929	99.0%	<0·0001

CIs: Confidence intervals.

FIGURE LEGENDS

FIGURE 1. PRISMA flow diagram of study selection.

FIGURE 2. Funnel plot on the prevalence of taste disorders in COVID-19 patients.

FIGURE 3. Prevalence of taste disorders in COVID-19 patients.

FIGURE 4. Galbraith plot identified four outlier studies as the potential sources of heterogeneity.

SUPPLEMENTARY MATERIALS

SUPPLEMENTARY FIGURE S1. Subgroup analyses: Prevalence of taste disorders in COVID-19 patients from (A) Europe, (B) North America, (C) Asia, (D) South America and (E) Australia.

SUPPLEMENTARY FIGURE S2. Subgroup analyses: Prevalence of (A) ageusia, (B) hypogeusia and (C) dysgeusia in COVID-19 patients.

SUPPLEMENTARY FIGURE S3. Subgroup analyses: Prevalence of taste disorder with (A) subjective assessment and (B) objective assessment in COVID-19 patients.

SUPPLEMENTARY FIGURE S4. Sensitivity analyses: Prevalence of taste disorders in COVID-19 patients (A) excluding small studies (n<100), (B) excluding low-quality studies, (C) excluding studies without COVID-19 confirmation method being reported, (D) considering only cross-sectional studies and (E) excluding outlier studies.

SUPPLEMENTARY TABLE S1. Search strategy.

SUPPLEMENTARY TABLE S2. Quality assessment of the included cross-sectional studies.

SUPPLEMENTARY TABLE S3. Quality assessment of the included case-control studies.