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REVIEW ARTICLE

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Gustatory dysfunction in COVID-19 patients: a rapid systematic review on 27,687 cases

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ABSTRACT

Objective: This is a rapid systematic review concerning taste alterations in 27,687 individuals infected with SARS-CoV-2, published in the worldwide literature.

Material and methods: Of the 485 articles recovered, 67 eligible studies (27,687 confirmed COVID-19 cases) were included in this analysis. We analysed the prevalence of the taste alterations in patients considering the country of origin of the studies.

Results: The results show strong important differences in the overall reported prevalence of taste alterations among the different countries (from 11% of Korea to 88.8% of Belgium).

Conclusions: These data highlight that there is a different geographical distribution of taste alterations in COVID-19 patients. Gustatory dysfunction seems to be an understudied symptom of COVID-19 and this may explain the inconsistencies of diagnostic criteria for COVID-19 case definition. Furthermore, this diagnostic underestimation can lead to an increased risk of contagion for the whole population and for the working classes most at risk, including the dental one.

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KEYWORDS
COVID-19; taste; ageusia; gustatory alteration; dysgeusia

Introduction

Starting from December 2019 in Wuhan, China, the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread all over the world causing a pandemic of coronavirus disease 2019 (COVID-19). As at September 2020, SARS-CoV-2 has caused over one million deaths [1]. The virus mainly targets the respiratory system causing cough, fever, and difficulty in breathing [2]. Most cases result in mild symptoms, but some patients evolve to severe pneumonia and multi-organ failure. Among the most common symptoms (independent or in association with other manifestations), recent literature presents ageusia (loss of taste), with or without anosmia (loss of smell) [3]. Loss of taste is now a distinguishing symptoms of COVID-19 with a high predictive value [4]. The European Centre for Disease Prevention and Control (EDCD) was one of the first public health agencies that include sudden onset of ageusia, dysgeusia or anosmia as main clinical criteria for identifying probable COVID-19 cases [5]. Anyway, until August 2020 these symptoms were not used by all clinical trials to identify COVID-19 cases and to prioritise diagnostic tests. Afterwards, in the USA, the Centres for Disease Control and Prevention (CDC) have modified the definition of COVID-19 case on 5 August, including taste disorders as a main clinical criterion for diagnosis [6]. Soon after, the World Health Organisation (WHO) COVID-19 updated the case definition of COVID-19 and included onset of ageusia as suggestive of a probable COVID-19 case [7].

The different geographical distribution of the prevalence of these symptoms may show differences in the method used to identify cases of national or local public health agencies, which may in turn affect the inclusion of taste assessment in COVID research. For this reason, we carried out a rapid systematic review with the aim of collecting comprehensive data on the taste alterations prevalence worldwide and, precisely, in 16 countries. Further, we investigated the predominance of this topic in the overall COVID-19 literature.

Methods

Study design

This study was performed in compliance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines and it used a rapid review method because of time constraints [8] following the criteria for a restricted review. In this paper, were met the minimum requirements for completing a rapid systematic review [9]. Accordingly, the search was performed by three investigators (N.C., M.E.B., L.L.M.), while N.C. and M.E.B carried out the verification of a sample of full texts for accuracy of title and abstract screening and data extraction. Key terms used were (COVID or COVID-19 or SARS-CoV-2) AND (hypogeusia or

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dysgeusia or gustatory or taste or ageusia). The search was conducted in PubMed/MEDLINE and COCHRANE Library using advanced search (all fields) tool. A second search was performed in order to correlate the number of papers aboutCOVID-19 in each country with the number of papers about taste alterations due to COVID-19 in each country. For this reason, we performed a new search on PubMed/MEDLINE using the keywords COVID-19, taste and name of each country.

Study selection and data extraction

The criteria of exclusion were: duplicate publications, irrelevant articles, articles not in English language, studies that not clearly confirmed infection status, studies that did not analyse gustatory outcomes in each patient, case reports and review/systematic reviews. Studies that used telephone surveys or Apps were only included in this paper if the patients had a confirmed COVID-19 diagnosis. Studies that reported cases from two or more geographical areas were included only if information from individual countries was available. The primary outcome was to establish the gustatory alterations (ageusia, hypogeusia, dysgeusia) prevalence in confirmed COVID-19 cases worldwide and in different geographical areas; the secondary aim was to assess a pattern of taste alterations in published cases. No limits were posted on the cohorts dimension to ensure a comprehensive search and to identify the maximum amount of useful articles.

Results

Our first search detected 485 studies and 101 full text articles, that meet the inclusion criteria, were evaluated. Of these 91 papers, 67 were included in the data synthesis (Figure 1). Studies derived from 16 different countries and from multi-national cooperations. Most studies were from Europe ($n = 45$), followed by Middle East ($n = 8$), North America and South America ($n = 9$), East Asia ($n = 6$) and Africa ($n = 1$). Precisely: 1 study is from Belgium, 9 from France (of which 1 studying France, Germany and China), 4 from Germany, 22 from Italy, 1 from Poland, 7 from Spain, 2 from UK (of which 1 studying USA too), 1 from Brazil, 2 from Canada, 6 from USA, 2 from Israel, 1 from Qatar, 5 from Turkey, 3 from China, 1 from Hong Kong, 2 from Korea and 1 from Somalia.

The prevalence of gustatory dysfunction in COVID-19 positive patients differed in different countries. Study from Belgium reported a prevalence of 88.8% [10]; in France the prevalence reported ranges between 24% [11] and 65% [12] and in Germany between 14% [13] and 69.4% [14]; in Italy it varies from 25.4% to 96%; a polish study reported 47.5% [15] of prevalence; in Spain and UK the prevalence respectively ranges from 6.2% [16] to 70% [17] and from 63.1% [18] to 64.8% [19]. Therefore, in Europe the prevalence reported is 48% (10033 out of 20859 patients with GD). The only one study from Brazil reported a prevalence of 76.2%, the two studies from Canada showed a prevalence range from 57.1% [20] to 63.4% [21] while studies from USA reported values from 10% [22] to 71% [23]. Thus, in America the GD is found

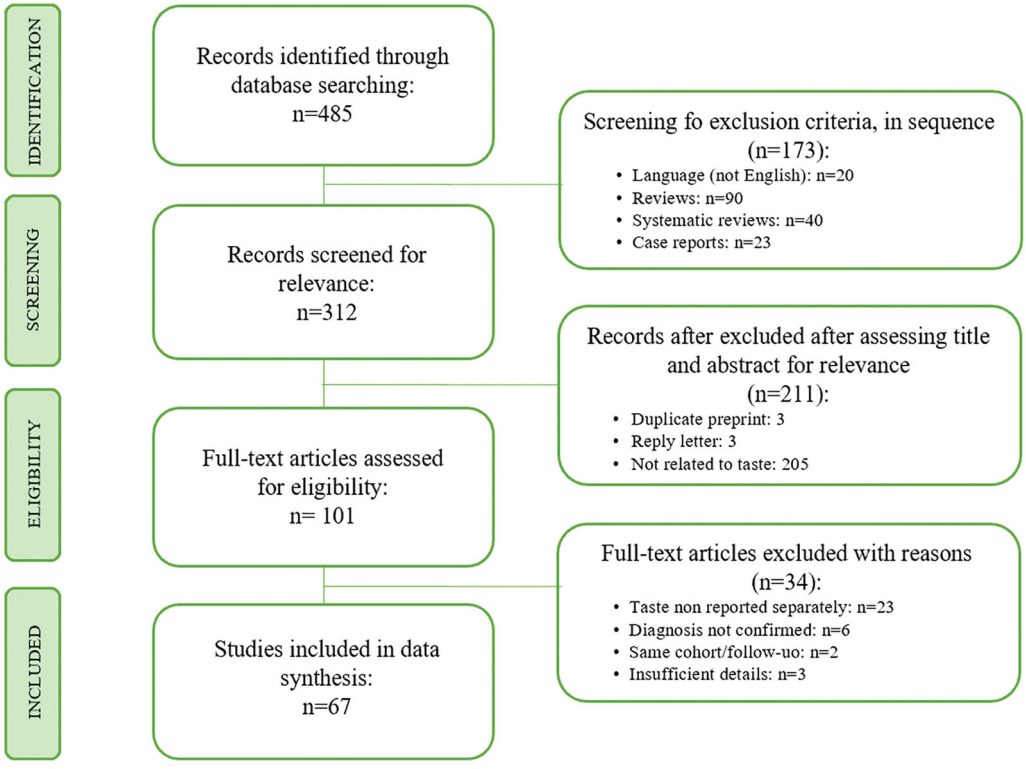

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart of study selection process.

Table 1. Studies included for the evaluation of gustatory dysfunction (GD).

Reference	GD	COVID+	Prevalence (%)	Country
Lechien et al. 2020 [10]	342	385	88.8	Belgium
	342	**385**	**88.8**	**TOTAL BELGIUM**
Zayet et al. 2020 [12]	62	95	65	France
Lapostolle et al. 2020 [35]	757	1487	50.9	France
Zayet et al. 2020 [36]	34	70	48.6	France
Tudrej et al. 2020 [37]	92	198	46.5	France
Poncet-Megemont et al. 2020 [38]	81	139	58.3	France
Chary et al. 2020 [39]	64	115	55.6	France
Klopfenstein et al. 2020 [40]	34	70	48	France
Qiu C et al. 2020 [41]	50	116	43.1	France (Germany and China)
Bènèzit et al. 2020 [11]	63	452	24	France
	1237	**2742**	**45.1**	**TOTAL FRANCE**
Qiu C et al. 2020 [41]	20	39	51.3	Germany (France and China)
Luers et al. 2020 [14]	50	72	69.4	Germany
Fistera et al. 2020 [13]	6	43	14	Germany
Hintschich et al. 2020 2020 [42]	18	41	44	Germany
	94	**195**	**48.2**	**TOTAL GERMANY**
Paderno et al. 2020 [43]	320	508	63	Italy
Vaira et al. 2020 [44]	39	72	54.2	Italy
Petrocelli et al. 2020 [45]	184	300	61.3	Italy
Giacomelli et al. 2020 [46]	17	59	28.8	Italy
Vaira et al. 2020 [47]	76	106	71.7	Italy
Mercante et al. 2020 [48]	113	204	55.4	Italy
Liguori et al. 2020 [49]	48	103	46.6	Italy
Dell'Era et al. 2020 [50]	232	355	65.4	Italy
Magnavita et al. 2020 [51]	31	82	37.8	Italy
Meini et al. 2020 [52]	69	100	69	Italy
Vaira et al. 2020 [53]	234	340	67.8	Italy
Gelardi et al. 2020 [54]	52	72	72.2	Italy
Vacchiano et al. 2020 [55]	66	108	61	Italy
De Maria et al. 2020 [56]	48	95	50.5	Italy
Vaira et al. 2020 [57]	91	138	65.9	Italy
La Torre et al, 2020 [58]	70	105	66.7	Italy
Paderno et al. 2020 [59]	135	151	89	Italy
Cazzolla et al. 2020 [60]	17	67	25.4	Italy
Freni et al. 2020 [61]	35	50	70	Italy
Vaira et al. 2020 [62]	4	33	12.1	Italy
Barillari et al. 2020 [63]	174	294	59.2	Italy
Lovato et al. 2020 [64]	116	121	96	Italy
	2171	**3463**	**62.7**	**TOTAL ITALY**
Sierpinski et al. 2020 [15]	923	1942	47.5	Poland
	923	**1942**	**47.5**	**TOTAL POLAND**
Romero-Sanchez et al, 2020 [16]	52	841	6.2	Spain
Martin-Sanz et al. 2020 [65]	114	215	53	Spain
Villarreal et al. 2020 [17]	161	230	70	Spain
Abalo-Lojo et al. 2020 [66]	74	131	56.5	Spain
Izquierdo-Dominguez et al. 2020 [67]	442	846	52.2	Spain
Rojas-Lechuga et al. 2020 [68]	128	197	65	Spain
Beltrán-Corbellini et al, 2020 [69]	28	79	35.4	Spain
	999	**2539**	**39.3**	**TOTAL SPAIN**
Patel et al. 2020 [18]	89	141	63.1	UK
Menni et al. 2020 [19]	4178	6452	64.8	UK (and USA)
	4267	**6593**	**64.7**	**TOTAL UK**
	10,033	**20,859**	**48**	**TOTAL EUROPE**
Brandao Neto et al. 2020 [70]	499	655	76.2	Brazil
	499	**655**	**76.2**	**TOTAL BRAZIL**
Carignan et al. 2020 [21]	85	134	63.4	Canada
Lee et al. 2020 [20]	32	56	57.1	Canada
	117	**190**	**61.6**	**TOTAL CANADA**
Yan et al. 2020 [23]	42	59	71	USA
Pinna et al. 2020 [22]	10	50	10	USA
Kempker et al. 2020 [71]	27	51	52.9	USA
Menni et al. 2020 [19]	490	726	67.5	USA (and UK)
Aggarwal et al. 2020 [72]	3	16	19	USA
Dawson et al. 2020 [4]	24	42	57	USA
	596	**944**	**63.1**	**TOTAL USA**
	1212	**1789**	**67.8**	**TOTAL AMERICA**
Biadsee et al. 2020 [25]	67	128	52	Israel
Levinson et al. 2020 [24]	14	42	33.3	Israel
	81	**170**	**47.6**	**TOTAL ISRAEL**
Al-Ani and Acharya, 2020 [26]	28	141	19.8	Qatar
	28	**141**	**19.8**	**TOTAL QATAR**
Sayin et al. 2020 [28]	46	64	71.9	Turkey
Altin et al. 2020 [27]	22	81	27.2	Turkey

(*continued*)

Table 1. Continued.

Reference	GD	COVID+	Prevalence (%)	Country
Salepci et al. 2020 [73]	77	223	34.5	Turkey
Sakalli et al. 2020 [74]	81	172	47.1	Turkey
Çalıca Utku et al. 2020 [75]	51	143	35.7	Turkey
	277	**683**	**40.5**	**TOTAL TURKEY**
	386	**994**	**38.8**	**TOTAL MIDDLE EAST**
Mao et al. 2020 [29]	12	214	5.6	China
Liang et al. 2020 [30]	33	86	38.4	China
Qiu et al. 2020 [41]	30	239	12.5	China (and France, Germany)
Cho et al. 2020 [31]	36	83	43.4	Hong Kong
	111	**622**	**17.8**	**TOTAL CHINA**
Lee et al. 2020 [32]	353	3191	11	Korea
Kim et al. 2020 [33]	58	172	33.7	Korea
	411	**3363**	**12.2**	**TOTAL KOREA**
	522	**3985**	**13.1**	**TOTAL EAST ASIA**
Farah et al. 2020 [34]	17	60	28.3	Somalia
	17	**60**	**28.3**	**TOTAL SOMALIA**
	17	**60**	**28.3**	**TOTAL AFRICA**
	12,170	**27,687**	**44**	**WORLD**

The highlighted boxes show the total of cases by country and by continent.

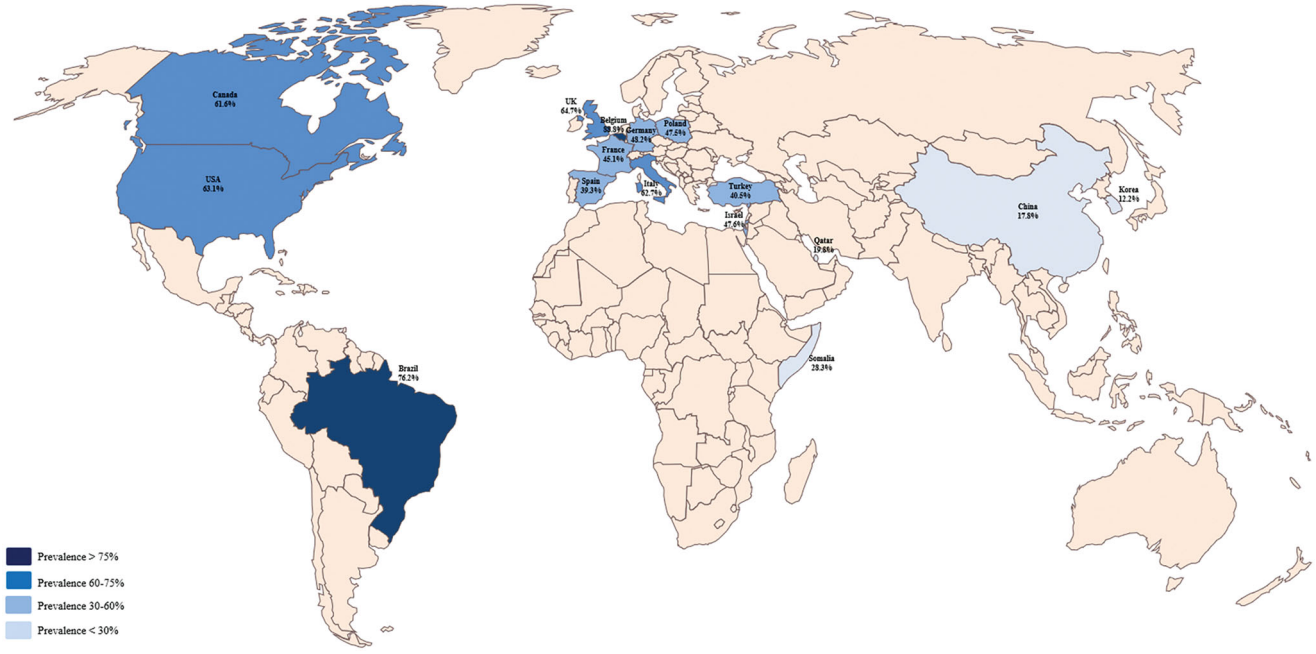

Figure 2. Worldwide prevalence of gustatory disorders (GD) in COVID-19 positive cases.

Table 2. Ratio between papers about COVID-19 and papers about taste alteration in COVID-19 confirmed cases, in each country analysed in this manuscript.

COUNTRY	PAPERS COVID-19	PAPERS COVID-19 and TASTE
Belgium	679	19
France	2019	19
Germany	1878	22
Italy	5073	48
Poland	398	5
Spain	2057	24
UK	5350	27
Brazil	1493	14
Canada	2062	9
USA	12,230	56
Israel	392	2
Qatar	113	1
Turkey	926	18
China	6087	17
Hong Kong	568	2
Korea	598	4
Somalia	7	1

in 1212 subjects on 1789 COVID-19 patients (67.8%). In Middle East, the reported average GD prevalence is 38.8% (386 out 994 patients); precisely: in Israel is between 33.3% [24] and 52% [25], in Qatar about 19.8% [26] and in Turkey from 27.2% [27] to 71.9% [28]. In the East of the Asian continent is reported an average prevalence of 13.1% (522 out of 3985 patients COVID-19 positive): in China values range is from 5.6% [29] to 38.4% [30], Hong Kong Special Administrative Region of the People's Republic of China (HKSAR) showed 43.4% [31] of prevalence while in Korea GD is reported in 11–33.7% [32,33] out of COVID-19 patients. On the African continent, the literature reported a Somali study showing a prevalence of 28.3% [34]. Therefore, worldwide 12.170 out of 27.687 confirmed COVID-19 cases (44%) reported subjective and/or objective gustatory dysfunction (GD) (Table 1).

In Figure 2, study populations and average prevalence are graphically represented.

In Table 2 we reported data concerning our second search regarding the ratio between articles concerning COVID-19 and those assessing taste alteration in COVID-19 confirmed cases, in the countries analysed in this manuscript.

Discussion

Taste alteration in COVID-19 positive patients could be an important factor in disease diagnosis [76]. The results of this pilot search on international literature shows that there are different geographical patterns of Gustatory Dysfunction in patients with confirmed SARS-CoV-2 infection. In fact, taste alteration ranges from 13.1% in East Asia to 67.8% in American continent. However, we found remarkable differences in gustatory dysfunction also among countries of the same continent. For example, in Europe the average prevalence ranges from 39.3% of Spain to 88.8% of Belgium.

Several factors may be responsible for this considerable variability of prevalence in different countries. Among these, one of the most important is probably the different times in which patients were examined in the different studies and the consequent awareness of the presence of GD in COVID-19 patients.

The first study in international literature reporting a 5.6% prevalence of hypogeusia was a Chinese case series published on 10 April 2020 [29]. Contrary, a recent meta-analysis evaluating taste and smell alterations highlighted that almost half of COVID-19 positive patients had these symptoms and, above all, that 15% of patients had olfactory and gustatory dysfunctions as their initial symptoms [77]. For these reasons, most studies completed before April did not focussed on taste alterations and probably this can explain the low rate of GD prevalence in Chinese studies, the country first hit by the virus, and the high GD prevalence in countries where the pandemic has lately appeared, such as Brazil (76.2%).

Successively, the researchers started to examine GD in their patients. In fact, Aziz et al., in their evaluation, showed that about half of the COVID-19 patients (49.8%) had alteration of taste sensation [78]. Our data are according to the current and relevant literature on the worldwide prevalence of COVID-related GD: out of 27.687 confirmed COVID-19 cases, 12.170 (44%) reported GD.

Another possible problem is that most studies are retrospective, cross-sectional, and observational, so, in our analysis, recollection bias may be present. The alteration of gustatory sense may not be reported when there are other severe symptoms, such as fever, dyspnoea, and productive cough. This absence of diagnostic data could explain the lack of association between taste alterations and COVID-19 in the first studies published in the period February–March 2020. Precisely for what has just been said, the real prevalence of taste alterations (in any form) may be more significant than actually reported [78]. In fact, in the Table 2 it is evident that several reports/studies on COVID-19 and related symptoms did not examine the GD. For example, only 56 studies from US considered GD versus 12230 studies on COVID-19 or in China 17 out of 6087 studies.

The difficulty in defining and measuring the grade of GD was another important variable. In fact, the altered taste has not been validated and the term 'dysgeusia' is not universally recognised. Furthermore, the diffusion of new knowledge about it and, therefore, the recognition of taste alterations as an early symptom of COVID-19 could have led to an increase in the reporting of this symptom by patients [19]. Differently from other analyzes [79] our study evaluated the different geographic position of the papers concerning the alterations of taste, rather than the ethnicity of the same. Although this type of study fails to identify the ethnic/genetic predispositions of the onset of this particular symptom and, more generally, of the infection, we think that our analysis can be considered suitable for studying the clinical manifestations of the disease in different countries. and, consequently, to help public health surveillance bodies in implementing the right measures to contain the infectious risk.

Another probable bias could be the heterogeneity of the examined studies, due to different sampling of examined studies in this review (direct data collection from hospitalised patients, data collection by telephonic survey, retrospective studies).

Furthermore, many studies, although valid, were excluded in this review because they analysed alterations in taste and smell as a single symptom and not as separate variables.

Furthermore, most of the studies in the literature are based on subjective (self-reported) impressions of patients and only a small number of studies used structured (objective) tests to assess GD. Subsequently, a comparison was made between subjective and structured (objective) gustatory functions and no significant differences were found [80]. Hence, it can be said that self-reported alterations in taste can be considered a reliable parameter for studying the prevalence of this condition in COVID-19 patients.

Conclusion

Ageusia/hypogeusia/dysgeusia seem to be important and sometimes early symptoms inCOVID-19. For this reason, it is useful to detect the taste alterations by dentists, who can be an active part in identifying and diagnosing positive COVID-19 cases early in the near future.

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Author contributions

N.C.: Contributed to design, data acquisition and interpretation and critically revised the manuscript

M.E.B.: Contributed to design, data acquisition and interpretation, drafted and critically revised the manuscript

E.L.M: Contributed to design, drafted and critically revised the manuscript

A.P.C.: Contributed to design, drafted and critically revised the manuscript

L.L.M.: Contributed to design, data acquisition and interpretation and critically revised the manuscript

All authors have given their final approval and they agree to be accountable for all aspects of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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