DANISH MEDICAL JOURNAL

Original Article

Dan Med J 2020;67(9):A05200370

Acute loss of smell and taste among patients with symptoms compatible with COVID-19

Nadia Calvo Bodnia[1] & Terese L. Katzenstein[2]

1) ENT Clinic, Herlev, 2) Department of Infection Medicine, Rigshospitalet, Denmark

Dan Med J 2020;67(9):A05200370

ABSTRACT

INTRODUCTION:
The aim of this study was to describe the clinical symptoms, including affection of sense of smell and taste, among participants in a party held in Copenhagen after which many participants reported symptoms compatible with coronavirus disease 2019 (COVID-19).

METHODS:
A 37-item questionnaire was sent electronically to all 95 participants seven weeks after the party. The questionnaire included questions about the type, timing and duration of COVID-19 symptoms.

RESULTS:
In total, 65 of 95 (68%) participants responded, among whom 51/65 (78%) had symptoms compatible with COVID-19; 53% (27/51) had affection of their sense of smell and taste; 70% (19/27) reported a total loss of taste. These symptoms continued for 1-3 weeks for 78% and 3-6 weeks for 22% (6/27). Interestingly, 11/27 (41%) reported that they had not fully regained their sense of taste and 3/27(11%) were still very affected by this symptom. Moreover, 44% of the respondents who had lost their sense of taste perceived this symptom as moderate to severe. Eighty-one percent (22/27) reported a total loss of smell. This symptom continued for 1-3 and > 3 weeks in 74% and 26%, respectively. At the time of the investigation, 48% had not fully regained their sense of smell and 7% were still very affected. More than half of the respondents who lost their sense of smell perceived this symptom as moderate to severe.

CONCLUSIONS:
Many patients with clinically diagnosed COVID-19 report an affected sense of smell and taste. The duration of these symptoms currently remains unknown.

FUNDING: none.

TRIAL REGISTRATION: not relevant.

In December 2019, a sudden increase in the number of patients with an unusual and severe pneumonia was reported from the city of Wuhan, Hubei Province, China. Soon after the pathogenic agent was identified as a new coronavirus that was named severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) due to similarity in the clinical picture and phylogenetic relatedness with SARS [1]. The first reported death from SARS CoV-2 occurred in January 2020. The SARS CoV-2-induced illness was named COVID-19. The virus has subsequently spread to more than 188 countries & regions (assessed 17 May 2020), and the WHO has declared it a pandemic. The first case of COVID in Denmark was reported on 26 February 2020. Whereas respiratory symptoms along with signs of severe inflammation (cytokine storm) and complications hereof were the main symptoms initially described [2], a steady awareness of affection of sense of smell and taste is surfacing [3-7].

Affection of the sense of smell and taste was not initially described. However, by mid-March 2020, the German virologist Henrik Streeck described that almost a third of COVID-19 patients reported a loss of smell and taste lasting several days. This was among COVID-19 patients in the district of Heinsberg in North Rhine-Westphalia, an area highly affected by COVID-19 following a carnival in February. More than four million people worldwide have tested positive for SARS CoV-2, with the infection most likely being highly underdiagnosed.

Post-infectious olfactory dysfunction is well known and anosmia (loss of smell), though a rare symptom, has also been reported in the course of other coronavirus infections [4, 7]. The high proportion of people in our study and in many recent studies [6, 8] reporting affection of their sense of smell and taste due to COVID-19 is very unusual [9]. Which course will these symptoms follow? Will patients regain their sense of smell and taste or may we expect an overflow of patients with anosmia and ageusia referrals to ear- nose and throat (ENT) offices in the future?

We describe COVID-19 symptoms among participants in a dinner and dance party held in Copenhagen in March 2020, just prior to the implementation of the “corona lock-down” in Denmark. The study focuses on the disturbance of the sense of smell and taste and on the course of these symptoms.

METHODS

For the purpose of this study, we developed a questionnaire, with a special focus on smell and taste symptoms (**see supplementary material**). The questionnaire with 37 questions was sent electronically to all 95 participants seven weeks after the party. The guests were given two weeks to answer the questionnaire. The questions focused on symptoms compatible with COVID-19 with a special focus on impairment of sense of smell and taste and the progression of these symptoms. Furthermore, information about other family members developing symptoms compatible with COVID-19 was collected in the questionnaire **(see**

supplementary material).

Percentages of affected people were calculated based on the number of respondents.

We classified respondents < 16 years as children.

A total of 47 people answered the question about the onset of their symptoms relative to their participation in the party. The timing of debut was calculated based on those who responded to this question.

The authors established the COVID-19 diagnosis based on the participants' self-reported symptoms, the timing hereof and positive SARS CoV-2 testing among some of the participants. Similar criteria have been used in other COVID-19 studies published in high-impact journals [6].

Trial registration: not relevant.

RESULTS

In total, 65 of the 95 participants responded (producing a 68% response rate). The cohort consisted of 22 women (mean age 45 years (range: 16-62 years)), 15 men (mean age 45 years (range: 20-66 years) and 28 children, 14 girls and 14 boys (mean age 13 years).

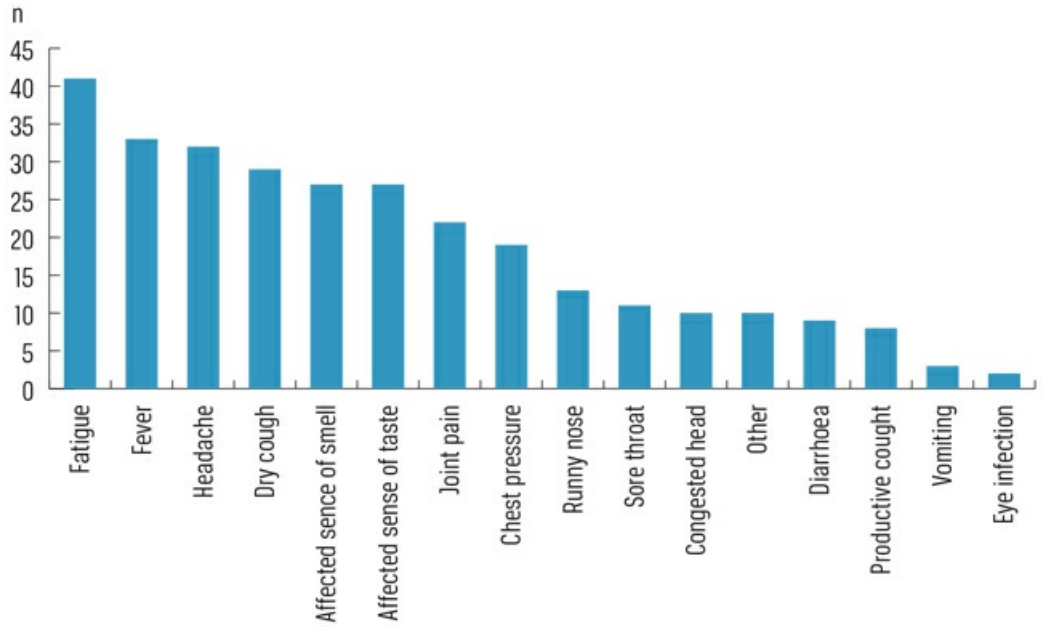
The sex distribution among the non-responders was similar to that among the respondents. However, the age distribution was slightly different as the percentages of children were 43% and 30% among respondents and non-respondents, respectively.

Only four patients had been tested for SARS CoV-2, all of whom tested positive.

One of the non-responders, a woman (approximately 70 years old) was hospitalised with severe confirmed COVID-19. Another non-responder, a woman with mild symptoms, also tested positive. Two of the responders with a positive COVID-19 test had spouses and children who developed symptoms as well, but who were not tested.

Most of the respondents (78% (52/65)) developed symptoms compatible with COVID-19. Fatigue, headache, fever, dry cough and disturbance of the sense of smell and taste were among the most frequent symptoms (**Figure 1**).

FIGURE 1 / Symptoms compatible with coronavirus disease 2019.



Among the responders, an equal share of men and women (86%) developed symptoms, whereas this was reported from 79% of the boys and 64% of the girls. Most of the guests (60%) who developed symptoms compatible with COVID-19 developed symptoms 3-5 days after the party, whereas 23% of the guests answered that their symptoms had presented 6-9 days after the party; and in 13% of the cases, symptoms presented after 10-14 days. One person developed symptoms after 17 days and one only after four weeks. She was the last person to fall sick in a family of four. One person tested positive for COVID-19, but never developed any symptoms. For most of the guests, the duration of symptoms compatible with COVID-19 was less than three weeks (**Table 1**).

TABLE 1 / Duration of symptoms compatible with coronavirus disease 2019. The values are n.

Duration	Children	Women	Men	Total
1-7 days	14	1	3	18
1-2 wks	5	7	4	16
2-3 wks	0	9	4	13
3-4 wks	0	2	1	3
Other	1	0	1	2

Fifty-three percent of the persons with COVID-19 symptoms experienced affection of their sense of taste and smell. The majority (77%) were women (17/22). These symptoms were rarely reported by children (14% (4/28)) and only by 40% of the men. The majority (70%; 19/27) described a total loss of taste and 81% of smell (22/27). Of those who reported smell and/or taste disturbance, 4% (2/52) reported this as their sole COVID-19 symptom. About 50% reported a disturbed sense of smell and/or taste in the middle of the course of the disease, 25% at the beginning and 25% at the end of the course of the disease. The disturbance of taste continued between 1-3 weeks for 78% and between 3-6 weeks for 22% (6/27) (**Table 2**). Interestingly, 11/27 (41%) reported that they had not fully regained their sense of taste when completing the questionnaire with 3/27 (11%) still reporting to be very anxious because of this symptom. Among the respondents who lost their sense of taste, 44% (12/27) perceived this symptom as moderate to very severe. The duration of a disturbance of smell continued for 1-3 weeks for 74% (20/27) and for more than three weeks for 26% (7/27) (Table 2). It was reported by 48% that they had not fully regained their sense of smell at the time of questionnaire completion and 7% were still very affected hereof. Among respondents who lost their sense of smell, 56% perceived this symptom as moderate to very severe.

TABLE 2 / Duration of the affected sense of taste or smell. The values are n.

	1-7 days	7-14 days	14-21 days	21-28 days	5 wks	6 wks
Taste	7	10	4	2	2	2
Smell	8	7	5	3	2	2

DISCUSSION

Following a party held in Denmark shortly after the introduction-of SARS CoV-2 into the country, the majority (78%) of those completing a COVID-19 questionnaire reported COVID-19-related symptoms. Only four of the respondents had been tested for SARS CoV-2, but 100% of those tested positive. At the time, access to testing in Denmark was restricted to a limited number of patient categories, mainly persons with severe respiratory symptoms and healthcare personnel.

Due to the timing and the type of symptoms that the affected participants described, it was assumed that all had COVID-19. Furthermore, two of the responders with a positive SARS CoV-2 test had spouses and children who also developed symptoms, but who were not tested. All this strengthens the likelihood that all the guests with symptoms actually had

COVID-19. Among the non-respondents, two tested SARS CoV-2-positive.

Assuming that all non-respondents, except for the two with a positive SARS CoV-2 test, were without COVID-19 symptoms and maybe therefore had little incentive to complete the questionnaire, the rate of (mainly) clinically diagnosed COVID-19 was still high at 57% (54/95).

Both children and adults reported COVID-19 symptoms (Table 1). As many of the children participating in the party attend the same school, and many of the adults are parents to the children, the party might not have been the only possible source of spreading of the virus within this cohort. However, only five days after the party, Denmark implemented a corona lock-down including school closures, limiting the other sources of infection.

The percentage of children who reported symptoms in our study was high at 71%. Relative to the literature, this seems a very high percentage which might be explained by the fact that the children in this cohort were mostly teenagers [10]. As shown in Table 1, the duration of the symptoms was shorter among children than among adults.

Olfactory and/or gustatory disturbance was reported by 53% of the respondents, underlining the importance of awareness of these symptoms. The literature suggests a higher prevalence of anosmia in mild-moderate COVID-19 disease versus severe disease, and in younger age groups [6] . In our study, anosmia and ageusia were more frequently reported by women than by men, and more often by adults than by children. Maybe women are more aware of changes in their senses of smell and taste. Our findings are in line with those of previous publications reporting that people under the age of 60 years and women are affected more frequently [3, 6, 11].

Though loss of smell and taste is not life threatening, it may have an impact on quality of life. There is increasing evidence that olfactory impairment can affect quality of life through environmental and social anxiety, food and weight disturbances and depression [11]. In our study, about 50% of the responders with an affected sense of smell or taste reported that they perceived these symptoms as moderate to very severe.

Since the release of the statement by Prof C. Hopkins, President of the British Rhinological Society, [9] that anosmia/ageusia can be the only symptom of COVID-19, it has been emphasised for ENT doctors around the world to encourage use of personal protective equipment in such cases to prevent the doctors from getting infected [4]. In the study by Hopkins et al [6], 3.4% of the respondents reported a loss of sense of smell or taste as the sole symptomatology, which matches our findings of 4%. Olfactory and gustatory dysfunction has been shown to be a stronger predictor of SARS CoV-2 infection than self-reported fever [6].

Post-infectious olfactory dysfunction is a well-described entity. A variety of pathogens may cause post-infectious olfactory dysfunction including viruses, bacteria, fungi and rare organisms such as microfilaria [11] with viral infection being the most common. Between

18% and 45% of the patients referred to the Olfactory and Gustatory Research Department (the Flavour Clinic), Holstebro, Denmark, with anosmia (2018) were diagnosed as being post-infection. The onset of post-infection olfactory dysfunction is usually sudden. Typically, women are affected more frequently than men, and they are middle-aged or older at presentation [11, 12]. This matches our findings; 77% of the women with symptoms compatible with COVID-19 lost their sense of smell, compared with 40% of the men and 14% of the children. The men and the women were middle-aged, with a mean age of 45 years. The pathophysiology of post-infectious olfactory loss remains poorly delineated but is thought to involve either damage to the olfactory neuroepithelium or central olfactory processing pathways (mediated via direct transmission of pathogens to the brain through the olfactory nerve) [11] .

The human angiotensin-converting enzyme 2 (ACE2) is the main host cell receptor of SARS CoV-2. Nasal respiratory epithelial cells and olfactory epithelial support cells have been shown to express high levels of ACE2. Furthermore, ACE2 is expressed in the oral cavity. The expression is higher in the tongue than in buccal and gingival tissues [13]. Damage to mucosal epithelial cells of the oral cavity may explain the pathogenic mechanism underlying ageusia in COVID-19, in addition to ageusia secondary to olfactory dysfunction [3].

In our study, 53% of the people with COVID-19-compatible symptoms experienced impaired sense of smell and taste. Most people (about 75%) reported recovery within a period of < 3 weeks. Even so, at the time of reporting, 41% and 48% of the persons with taste and smell impairment, respectively, had not yet fully regained these senses. Approximately 10% were very anxious about these dysfunctions. How many of these patients will attend their ENT doctor in the future? Will this create a capacity issue? How may we help these patients? Long-term studies are needed to learn about the recovery rate and choice of treatment.

Strengths and limitations

We collected thorough information about disturbances of smell and taste. The study was conducted at a time when the knowledge about the affection of these senses due to COVID-19 had yet to be established, thus limiting the risk of reporting bias. At the time of the study, access to testing by either PCR or antibody test was very restricted. The COVID-19 diagnosis was therefore based mainly on clinical symptoms.

CONCLUSIONS

We report an outbreak of clinically diagnosed COVID-19 in conjunction with a party held in Denmark in early March 2020 with a very high hit rate. Acute loss of smell and taste was reported by 53% of the affected people, more often by adults than by children. Mild olfactory and/or gustatory disturbances persisted even after the other COVID-19 symptoms had resolved.

CORRESPONDENCE: *Nadia Calvo Bodnia*. E-mail: Nadia_calvo@hotmail.com

ACCEPTED: 14 July 2020

CONFLICTS OF INTEREST: none. Disclosure forms provided by the authors are available with the full text of this article at Ugeskriftet.dk/dmj

LITERATURE

1. WHO. Naming the coronavirus disease (COVID-19) and the virus that causes it. www who int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it 2020 (1 May 2020).
2. Yang X, Yu Y, Xu J et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475-81.
3. Lee Y, Min P, Lee S et al. Prevalence and duration of acute loss of smell or taste in COVID-19 patients. J Korean Med Sci 2020;35:e174.
4. Vaira LA, Salzano G, Deiana G et al. Anosmia and ageusia: common findings in COVID-19 patients. Laryngoscope 2020;130:1787.
5. Gilani S, Roditi R, Naraghi M. COVID-19 and anosmia in Tehran, Iran. Med Hypotheses 2020;141:109757.
6. Hopkins C, Surda P, Whitehead E et al. Early recovery following new onset anosmia during the COVID-19 pandemic - an observational cohort study. J Otolaryngol Head Neck Surg 2020;49:26.
7. Suzuki M, Saito K, Min WP et al. Identification of viruses in patients with postviral olfactory dysfunction. Laryngoscope 2007;117:272-7.
8. Lechien JR, Chiesa-Estomba CM, De Siati DR 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; 277:2251-61.
9. Hopkins C, Kumar N. Loss of sense of smell as marker of COVID-19 infection. www.entuk.org/sites/default/files/files/Loss%20of%20sense%20of%20smell%20as%20marker%20of%20COVID.pdf (1 May 2020).
10. Walger P, Heininger U, Knuf M et al. Children and adolescents in the CoVid-19 pandemic: Schools and daycare centers are to be opened again without restrictions. The protection of teachers, educators, carers and parents and the general hygiene rules do not conflict with this. GMS Hyg Infect Control 2020;15:Doc11.
11. Hummel T, Whitcroft KL, Andrews P et al. Position paper on olfactory dysfunction. Rhinol Suppl 2017;54:1-30.
12. Jafek BW, Murrow B, Michaels R et al. Biopsies of human olfactory epithelium. Chem Senses 2002;27:623-8.
13. Xu H, Zhong L, Deng J et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12:8.