



The Association of Smell and Taste Dysfunction with COVID19, And Their Functional Impacts

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Abstract The novel coronavirus disease 2019 (COVID-19), which caused Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), was appeared at the end of 2019 in wuhan city in china. Covid-19 has high ability of transmission from human to another human, and due to its fast spread globally, the World Health Organization (WHO) announced that Covid-19 is pandemic disease on March 11, 2020. Several articles have reported many common ENT-related symptoms as an early sign of COVID19. To measure the prevalence of insomnia and dysgeusia in COVID19 patients in Saudi Arabia and investigate their functional and psychological effects on patients. This study evaluated the impact of insomnia and dysgeusia on COVID-19 patients' quality of life using the short version of the Olfactory Disorders-Negative Statements (sQODNS) Questionnaire. It was done from 5 June to 30 July 2020, in the Eastern region of Saudi Arabia. A total of 274 laboratory-confirmed COVID-19 patients were participated. The most common ENT-related symptoms were headache 69%, insomnia 65.3%, and dysgeusia 64.6%. Interestingly, insomnia can greatly affect patients' daily life, as around 37.6% of our patients had problems with taking part in daily activities, 42% felt isolated, 68.1%

had changes in appetite, 51.4% had more stress, and 28.2% had increased anger secondary to loss of smell. In Addition, 62% (110) of patients who lost their taste declared that their daily activities were affected. ENT-related symptoms are one of the most COVID19 manifestations. The duration of both insomnia and dysgeusia is an important contributing factor on the patients' functional & psychological state as it may prolong their isolation period. Therefore, Otolaryngologists considered the first-line physicians for many of Covid-19 patients, which makes us at higher risk to be infected with Covid-19 too. It is also particularly important for Otolaryngologists to develop a management guideline to reduce the duration and severity of all ENT-related features.

Introduction

In December of 2019, a novel member of Coronavirus family is identified as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which causes the Coronavirus disease 2019 (Covid-19) Wuhan city, Hubei province in China was the first place where was identified, as it had become an epidemic. Covid-19 is a highly contagious transmission human-to-human, which caused it's spreading all over the world. the World Health Organization (WHO) In March 2020 stated that COVID-19 is a pandemic disease [1–3].

Covid-19 patients are mainly presented with fever, cough, fatigue, muscle pain, arthralgia, and shortness of breath. palpitations, abdominal pain, diarrhea, headache, and dizziness are non-repertory symptoms that could be presented before respiratory symptoms or come in isolation in Covid-19 patients [4].

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Anosmia, ageusia, and dysgeusia have been reported as symptoms of Covid-19 disease as it is affecting many Covid-19 patients as it is confirmed by The American Academy of Otolaryngology-Head and Neck Surgery and by British Rhinology Society [4, 5]. The Covid-19 disease is recommended to be screened in people who suffer from anosmia and dysgeusia as the first or the only manifestation [5]. Many viral infections such as rhinovirus, parainfluenza Epstein–Barr virus, and some types of coronavirus, are known to cause anosmia by causing nasal mucosa inflammation leading to rhinorrhea and thus smell dysfunction. Interestingly, Covid-19 patients can suffer from anosmia without rhinorrhea or nasal congestion [6].

This study aims to measure the prevalence of insomnia and dysgeusia in COVID19 patients in Saudi Arabia and investigate their functional and psychological effects on patients.

Methodology

This study evaluated the impact of insomnia and dysgeusia on the quality of life of COVID-19 patients using the short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQODNS) which consists of 6 questions. The study was done from 5 June to 30 July 2020, in the Eastern region of Saudi Arabia. The following inclusion criteria have been considered: laboratory-confirmed COVID-19 infection (RT-PCR, reverse transcription polymerase chain reaction); patients clinically able to fulfill the questionnaire, and native speaker patients. The following exclusion criteria have been considered: patients without a laboratory-confirmed COVID-19 infection diagnosis; patients with olfactory or gustatory dysfunctions before the epidemic; patients who were in the intensive-care unit at the time of the study (due to their health status). Thus, we mainly included mild-to-moderate COVID-19 patients, defined as patients without need of intensive care. Clinical data have been prospectively collected during clinical consultation; in the patient's room; or online for housebound patients. The online questionnaire was created with Google Questionnaire.

Results

274 laboratory-confirmed COVID-19 patients were participated. Female participants (55%) were more than male participant (45%). Most of our participant were Saudi with only (3%) of participant were non-Saudi. The majority of our patients were between the age of 18–50 years (78.1%), which can be attributed to the various social activities like

going to the workplace or social gathering. Only 2 cases out of 274 were above the age of 65 years. (Table 1).

Fever, fatigue, and cough were the most frequent Non-ENT symptoms (66.1%, 59.1%, 58%) respectively. Joint pain, Gastrointestinal (GI) symptoms, and dyspnea were less common in our participants. The most common ENT-related symptoms were headache 69%, loss of smell 65.3%, and loss of taste 64.6%. However, Nasal congestion, sore throat, and dizziness were presented in 38–42% of our patients, which considered fairly common. (Figure 1).

Out of 274 participants, around two third of them (179 participants) reported that they lost their sense of smell after getting infected with the coronavirus. Regarding the impact of olfactory dysfunction on the quality of life of COVID-19 patients, 23% agreed, and 19.9% partially agreed that insomnia caused them to feel isolated. 12.6% of our participants agreed, 25.1% partially agreed of having problems with taking part in daily activities secondary to loss of smell. Loss of smell identified as a trigger for anger for about 28.2% of our participants. Insomnia affected the patient's appetite either positively or negatively in about 68.1%. The fifth item covered stress related to anosmia, 21% agreed that it was harder to relax, 30.4% partially agreed, 30.4% partially disagreed, and 18.2% disagreed with the statement. The sixth and final item was to explore patient's worry about their possible inability to get used to the changes in their sense of smell. 22% agreed that they were worried, 22.5% partially agreed, 24.1% partially disagreed, and 31.4% disagreed. (Table 2).

Out of 274 participants, 64.6% (177 participants) reported that they lost their sense of taste once got infected with the coronavirus. Dysgeusia caused clear imbalance in the daily life of 62.1% (110) of COVID19 patients. 74.6% of our patients have regain their sense of taste. Most patients regain their taste after 2 weeks–1 month of their infection (53.8%, 34.1%) respectively. However, only one patient had dysgeusia for more than 2 months (Table 3).

Discussion

Coronavirus disease 2019 (COVID-19) is a respiratory infection caused by the novel virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On the 11th of March 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic that emerged from East Asia and quickly spreads to the rest of the world as it is responsible for more than 350,000 deaths worldwide [3, 6].

The clinical symptoms of coronavirus disease 2019 have shown an obvious variability from asymptomatic carriers to patients with acute respiratory distress syndrome

Table 1 Personal characteristics of Covid19 patients in Eastern region, Saudi Arabia

Personal data		No	%
Gender	Male	124	45
	Female	150	55
Nationality	Saudi	266	97
	Non-Saudi	8	3
Age	Less than 18	10	3.6
	From 18–50	214	78.1
	From 50–65	48	17.5
	Older than 65	2	0.7
Severity of symptoms	Mild	93	33.9
	Moderate	150	54.7
	Severe	31	11.3

(ARDS) that could lead to death. However, most patients experience mild to moderate manifestations, such as fever, cough, dyspnea, myalgia, fatigue, sputum production, arthralgia, headache, diarrhea, rhinorrhea, and sore throat. The spread of the COVID-19 infection in Europe has shown new symptoms of the disease where patients presented with olfactory and gustatory dysfunctions [7, 8].

This study showed that female patients (55%) were more than male patients (45%). there are no studies that

show a clear relationship between infection likelihood and gender. However, when it comes to disease severity and risk of mortality, both gender and age have shown a clear impact. Female patients have a higher probability to develop a mild to moderate form of infection, as 90.7% of female patients had a mild to moderate form in this study. Another related study showed that olfactory and gustatory dysfunctions are associated with the moderate COVID-19 infection, which is more common in females due to the gender-related differences in the inflammatory pathway [8]. Whereas males are more likely to have the severe form, as 13.7% of male patients in this study had a severe infection. Two meta-analysis studies were done to show that males have a higher risk to develop a severe infection and a higher mortality rate than females [9, 10].

Regarding the relationship between the infection likelihood and age, this study shows that 95.6% of the patients were from 18 to 65-year-old, which reflects a low infection rate among age extremities. However, when it comes to the disease severity, older patients aged 50-year-old and above counted for 81.3% of all severe cases. As another study showed that patients below 40 years of age are mostly predisposed to develop a moderate form of COVID-19 [11].

COVID-19 patients in this study showed different manifestations, the most common clinical manifestations

Fig. 1 The incidence of ENT vs non- ENT manifestation in COVID 19 patients

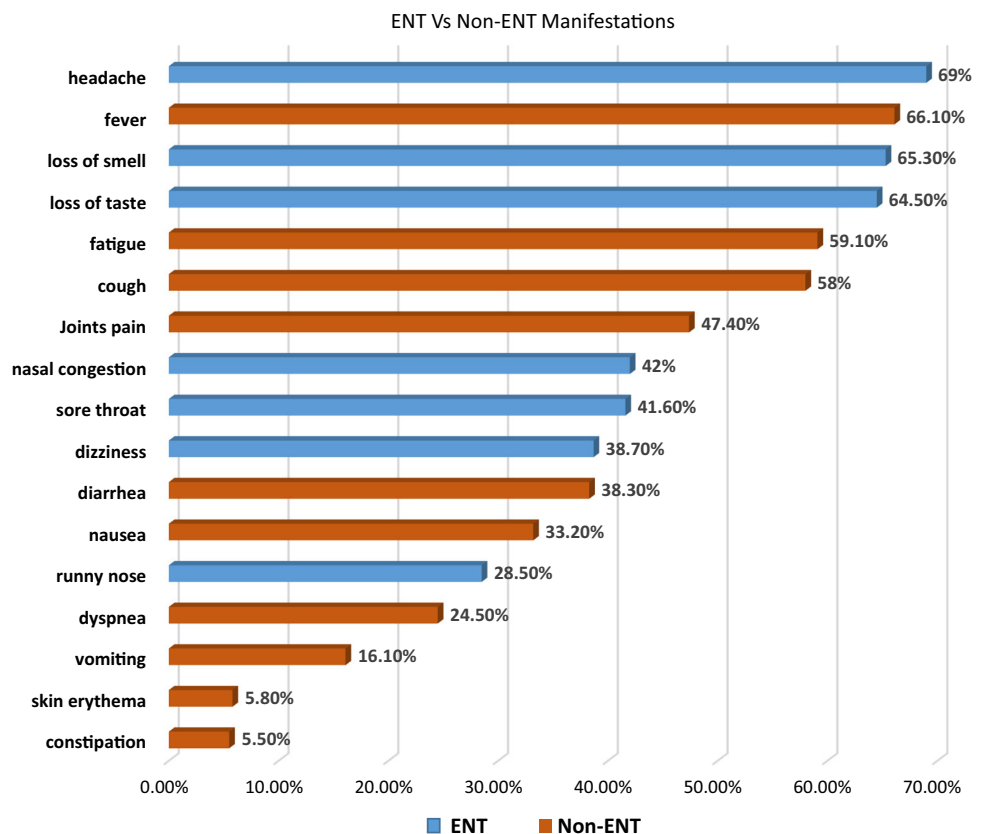


Table 2 The Short version of Questionnaire of Olfactory Disorders-Negative Statements Among COVID19 patients in Saudi Arabia

Domain	Items	Agree (%)	Partly agree (%)	Partly disagree (%)	Disagree
Loss of smell	The changes in my sense of smell make me feel isolated	23	19.9	28.3	28.8%
	Because of the changes in my sense of smell, I have problems with taking part in activities of daily life	12.6	25.1	33.5	28.8%
	The changes in my sense of smell make me feel angry	9.9	18.3	26.8	45%
	Because of the changes in my sense of smell, I eat less than I used to or more than I used to	33	35.1	24.1	7.8%
	Because of the changes in my sense of smell, I try harder to relax	21	30.4	30.4	18.2%
	I am worried that I will never get used to the changes in my sense of smell	22	22.5	24.1	31.4

were headache (69%), fever (66.10%), loss of smell (65.3%), and loss of taste (60.6%). As three of those most common symptoms are ENT symptoms, along with other common ENT presentations such as; nasal congestion (42%), sore throat (42.6%), dizziness (38.7%), and runny nose (28.5%). Therefore, otolaryngologists considered the first-line physicians for many of Covid-19 patients (Fig. 1) [4]. That makes Otolaryngologists at higher risk to be infected with Covid-19 than other specialties [12].

Even though olfactory and gustatory dysfunctions in the Covid-19 patients are common, the pathophysiological pathway is still not clear. Moreover, there is no significant relationship between the development of olfactory or gustatory dysfunction and comorbidities. However, it is known that coronavirus targets cells with Angiotensin 2 Converting Enzyme (ACE2) receptors. ACE2 receptors can be found in the lung, heart, blood vessels, kidney, intestine. Moreover, it can be found in the brain which explains the neurotropism of SARS-COV-2 by the central nervous system. However, the liver could be affected too even though there are no ACE2 receptors, which means there is another possible pathophysiology. Moreover, many studies have shown the ability of coronavirus to invade the olfactory bulb to reach the central nervous system. However, the exact pathophysiological mechanism that leads to different clinical manifestations is still not known [5].

This study also evaluated the impact of olfactory dysfunction on the quality of life of COVID-19 patients using the short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQODNS) which consists of 6 questions (Table 2). Part 1 contains 3 social-related questions that illustrate how olfactory dysfunction might lead to social isolation and disinterest in daily activities. That is because the sense of smell is also associated with the limbic system, and some olfactory stimuli can trigger different emotional responses and create a cortical association with other senses, such as the memory and the perception of the quality of the stimulus [13]. Part 2 consists of 1

question on how anosmia may affect eating habits since it is strongly associated with gustatory perception. That explains why patients with anosmia have difficulty in perceiving the taste of food, thus losing their appetite and pleasure when eating food. Part 3 consists of 1 question which gives insight into how olfactory impairment might increase patient's stress. Finally, part 4 which also consists of 1 question that focuses on exploring patient's worry regarding adapting to the changes in their sense of smell. The answers to all questions were either the participant agreed, partially agreed, partially disagreed, and disagreed with each statement.

The duration of insomnia is an important contributing factor on the patient's psychological state as it may prolong their isolation period. More than 42% of our patients felt isolated due to their insomnia. Interestingly, insomnia can greatly affect patients' daily life, as around 37.6% of our patients had problems with taking part in daily activities, 68.1 had change in appetite, 51.4% had more stress and 28.2% had increased anger secondary to loss of smell. In addition, 44.5% of our patients was worried about their possible inability to get used to the changes in their sense of smell. No other studies reported a detailed effect of anosmia on quality of life in COVID-19 patients. However, many studies supported the fact of olfactory dysfunction did impact the quality of life, due to the loss of food enjoyment, social interaction, and incidence of depression [14].

This study also aimed to explore the number of participants whose sense of taste was affected by COVID-19 (Table 3). Out of 274 participants, more than half of them (177 participants) reported that they lost their sense of taste once got infected with the coronavirus. Loss of taste wasn't only highlighted in this study as one of the presenting symptoms of COVID-19, but another study that was conducted in Germany also found that out of 72 patients who tested positive for COVID-19, 69% (50 patients) of them reported a reduced sense of taste [15]. A second study that

Table 3 The prevalence of dysgeusia among COVID19 patients and its impact on their daily life

Loss of taste		No			%					
Did you lose the sense of taste?	Yes	177			64.6					
	No	97			35.4					
does the lost of your taste caused a clear imbalance in your daily life?	Yes	110			62.1					
	No	67			37.9					
		The duration since symptoms start								
		Less than 1 week		2 Weeks	1 Month	2 Months	More than 2 months			
When did you regained the sense of taste?	N	%	N	%	N	%	N	%	N	%
	10	7.6	71	53.8	45	34.1	5	3.7	1	0.8

was published in June 2020 showed that 70% of their 46 patients reported having gustatory dysfunction. While this may support our finding regarding the loss of taste, Claire Hopkins's et al., in a study of 3191 COVID-19 positive patients self-isolated at home, reported that only 15.3% of patients suffered from smell or taste loss [3].

Another objective that was covered in this research is to examine the effect of gustatory dysfunction on the quality of life in Covid-19 patients (Table 3). It was found that out of the 177 who reported the loss of taste earlier, 110 of them declared that their daily activities were affected by their problem. In a different study, a significant number of patients who had smell and taste problems reported that their quality of life was affected by anosmia and subsequently, loss of taste [16].

Regarding regaining the sense of taste, we found that dysgeusia usually persists for 2 weeks to 1 month where most of the patients reported an inability to taste and improved right after. This can be attributed to the significant reduction in the viral load. The same previous European study had also observed the recovery of olfactory and gustatory functions. It was found that at least 25.5% of patients recovered both olfactory and gustatory functions throughout the 2 weeks after the resolution of general symptoms (5). Another study showed that on an initial and 1 week follow-up surveys, patients' sense of taste was reduced at the initial one, but this had fallen to 75% when they filled the second survey one week after. 60% of the whole group reported that they could still differentiate between sweet, salty, sour, and bitter tastes at the time of the first survey, improving to 88.9% in the second survey [17].

Conclusion

ENT-related symptoms are one of the most COVID19 manifestations, and the duration of both insomnia and dysgeusia is an important contributing factor on the

patient's psychological state as it may prolong their isolation period. Therefore, Otolaryngologists considered the first-line physicians for many of Covid-19 patients, which makes us at higher risk to be infected with Covid-19 too. It's also essential for Otolaryngologists to develop management guidelines to reduce the duration and severity of all ENT-related features.

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