



Patterns of Otorhinolaryngological Manifestations of Covid-19: A Longitudinal Questionnaire-Based Prospective Study in a Tertiary Hospital in Saudi Arabia

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Abstract

Objective: Many studies investigated the manifestations of COVID-19, yet few described the pattern and severity of otolaryngological symptoms. We aim to describe the picture of COVID-19-associated otorhinolaryngological manifestations and recovery to explore individualized treatment, onward referral, and complications prevention. **Design:** Prospective longitudinal questionnaire-based study. **Setting:** The online questionnaire was filled 3 times through a remote interview over a period of 1 month from June 2020 to July 2020. **Participants:** Patients with confirmed COVID-19 by RT-PCR who were clinically stable. **Main Outcome Measures:** Date of diagnosis, sociodemographic data, and the presence of predictive factors, such as nasal and paranasal disease, anosmia and dysgeusia. Validated tools were used, such as Sino-nasal Outcome Test (SNOT-22), smell test (medical academy screening tool), Voice Handicap Index (VHI), and Reflux Symptoms Index (RSI). **Result:** The questionnaire was sent to 363 patients and the response rate was 70.80% (n = 257). The mean age was 34.58 years (SD = 11.22) and the rate of male participants was 60.7%. The most common otorhinolaryngological symptoms at the time of enrollment was fever (48.6%), whilst the commonest severe symptom was cough (57%). After 1 month, only 11 participants had persistent severe symptoms, especially sleep and psychological symptoms (73%), and the majority were female (63.6%). All of them had at least 1 comorbidity. There was a significant difference between the mean age of participants with severe symptoms (mean = 27.45, SD = 8.39) and without severe symptoms (mean = 34.90, SD = 2.53, $t(255) = 2.17, P = .031$). **Conclusion:** COVID-19 has a wide-ranged spectrum of presentations, with otorhinolaryngological symptoms being the commonest and most serious. Studying these symptoms is vital to advance management options.

Keywords

COVID-19, SARS-CoV-2, Sino-Nasal Outcome Test, anosmia, dysgeusia, disease progression, diagnostic tests, routine, otolaryngology

Dates received: 9 October 2021; revised: 9 February 2022; accepted: 10 February 2022.

Key Points

1. The mean duration from receiving the diagnosis of COVID-19 until the showing of the symptoms was 4.81 days.
2. Anosmia and dysgeusia were the main reasons for patients to test for COVID-19.
3. Fever was the most common otolaryngological manifestation that appears in patients with COVID-19 followed by headache.
4. Females showed higher risk of getting severe otorhinolaryngological manifestations more than males.

5. While the most severe symptom at the beginning of the study was cough, difficulty falling asleep was the most severe symptom at the end of the study.

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6. The percentage of participants who had severe symptoms at the end of the study was 4.28% and all of them had a comorbid disease.
7. This study provides a more detailed picture of the association between COVID-19 and the otolaryngology manifestations and recovery.

Introduction

Coronavirus disease (COVID-19) is caused by the single-stranded RNA severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The first case of COVID-19 was reported in December 2019 in Wuhan, Hubei province, China, which presented as a type of pneumonia of unknown cause.^{1,2} On January 30, 2020, the World Health Organization (WHO) declared COVID-19 as a pandemic and a public health emergency of international concern.¹⁻³

COVID-19 can be transmitted through both respiratory droplets and direct contact.⁴ Interestingly, the average incubation period of COVID-19 is approximately 2 to 5 days, although incubation periods of up to 14 days have been observed.⁵ The severity of a patient's condition ranges from complete absence of symptoms to life-threatening complications. Possible symptoms include fever (98%), cough (76%), myalgia or fatigue (44%), sputum production (28%), headache (8%), hemoptysis (5%), and diarrhea (3%).⁶ One study also reported olfactory symptoms, such as anosmia and hyposmia, in 76% of patients.⁷ The commonly reported complications are acute respiratory distress syndrome, respiratory failure, multiple organ failure, and even death.⁶

The main reservoir is the upper respiratory tract, from where a swab is usually collected to diagnose COVID-19 disease. Recently, many studies have been conducted to investigate the otolaryngological symptoms related to COVID-19. Cough and anosmia are among the most commonly reported symptoms. Also, there were unanimously reported symptoms, such as ageusia, sore throat, nasal congestion, postnasal discharge, otalgia, runny nose, and hoarseness.⁸⁻¹¹ However, there is a limited number of studies that focused on the following: detailed otolaryngological presentation of COVID-19 using SNOT-22 questionnaire that measures the impact of sinonasal symptoms on sleep quality and psychology of infected patients; subjective analysis of the otolaryngological symptoms over a longitudinal course; and the effect of otolaryngological-related pathologies and chronic diseases on the manifestation of otolaryngological symptoms in COVID-19 patients.

The significance of otorhinolaryngological symptoms in COVID-19 patients calls for more thorough investigations.⁶ First of all, this information can help determine the appropriateness of the available drugs and referral guidelines for patients with COVID-19-related otorhinolaryngology symptoms. However, there are no sufficient

randomized controlled studies examining the available drugs that has potential benefits in COVID-19 management. Secondly, it can help prevent the progression of the disease and facilitate monitoring of high-risk patients who are more likely to develop severe disease and the associated complications.⁷

In this study, we aimed to evaluate the patterns of otorhinolaryngological manifestations in patients with mild to severe COVID-19 infection who are medically stable.

Methods

Ethical Considerations

This study was approved by the Institutional Review Board of Imam Abdulrahman bin Faisal University (IRB No. 2020-01-127). After study approval, an informed consent at the beginning of each interview was taken from each patient in the study. Patients who refused to accept enrollment were excluded.

Setting and Design

This longitudinal questionnaire-based prospective study was conducted over a 1-month period. The questionnaire was distributed to all COVID-19 patients whose diagnosis was confirmed by reverse transcription polymerase chain reaction. They were selected randomly from our hospital and the temporary medical quarantines outside the hospital based on their severity of symptoms (mild to severe) from June 2020 to July 2020.

Participants

About 363 patients who were diagnosed positive for COVID-19 and had mild to moderate symptoms were approached to be included in this study. Patients on mechanical ventilation, admitted to the intensive care unit (ICU) and those who were critically unstable were excluded. The questionnaire included questions on the date of diagnosis (the date of symptom onset), sociodemographic data such as sex, age, nationality, height, weight, level of education (bachelor, diploma, secondary school, middle school, elementary school, none), occupation (health worker, employee, student, retired, unemployed), smoking history (smoker vs non-smoker), medication for COVID-19, and presence of chronic diseases including diabetes (DM), hypertension (HTN), cardiac disease, and renal disease. Additionally, data on predictive factors that might influence the presentation of COVID-19 symptoms in patient whom they have these pathologies, such as nasal and paranasal disease, allergic rhinitis (AR), nasal polyps, nasal and paranasal tumors, and chronic sinusitis were collected.

Main Outcome Measures

All patients completed the following tests 3 times: once at the beginning of the study, again after 2 weeks, and then again at the end of the study period, which was at 1 month. Each patient completed the Arabic version of the Sino-nasal Outcome Test-22 (SNOT-22) questionnaire, which is a disease-specific health-related quality of life assessment tool used for assessing rhinology and extra-rhinology symptoms.^{12,13} The SNOT-22 questionnaire consists of 22 items that reflect the health burden of chronic rhinosinusitis symptoms. The items are categorized into 5 main domains: rhinological symptoms, extra-nasal rhinological symptoms, ear and facial symptoms, sleep dysfunction, and psychological disease. Moreover, otolaryngological manifestations were further evaluated using the Smell test (medical academy screening tool), the Voice Handicap Index, and the Reflux Symptom Index.^{14,15}

A unified medication protocol, which included hypertonic saline nasal irrigation and intranasal administration of corticosteroids and antibiotics, if indicated, was prescribed for all patients.

Analysis

The analysis was done using the StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC. Chi-square tests were used to compare the distribution of otolaryngology symptoms among participants with different characteristics. In addition, the *t*-tests were used to compare the mean score of the SNOT-22 questionnaire as well as other continuous variables amongst several study participants groups. Furthermore, to estimate the odds of developing a severe COVID-19 symptoms, various logistic regression models were used. In these models, the dependent variables were absence versus presence of the severe COVID-19 symptoms whilst the independent variables were the various sociodemographic features and health indicators. The adjustment of these models were done with the following 2 variables; age and gender.

Results

A total of 363 participants were approached, and 257 patients agreed to participate in the study (70.80%). The mean age of the patients was 34.58 years (standard deviation [SD]=11.22, min=16, max=79), and almost 60% (n=156) were male. Thirty-five percent of the patients had completed a bachelor's degree or higher (n=90), 6.23% (n=16) were former smokers, and 19.07% (n=49) were current smokers. Around one-quarter of the patients had a chronic disease (DM, 38.71% [n=24]; HTN, 25.81% [n=16]). Additionally, 55.64% (n=143) reported taking analgesic medication before visiting the hospital to control

COVID-19 symptoms. Approximately 30% (n=79) of the patients reported nasal and/or paranasal problems, 72.15% (n=57) reported AR, 13.92% (n=11) reported nasal polyps, 29.11% (n=23) reported chronic rhinitis, and 2.53% (n=2) reported nasal tumors. Table 1 summarizes the patients' sociodemographic features in relation to the severity of otolaryngological symptoms measured using the SNOT-22 questionnaire.

The mean duration from symptom onset to COVID 19 diagnosis was 4.81 days (SD=3.84, min=0, max=15). Approximately half of the patients (54.86%, n=141) contracted the infection from traveling outside the kingdom, while the remaining (45.14%, n=116) contracted it from socializing with a confirmed case of COVID-19. At the beginning of the study, severe rhinology symptoms were reported in 44 (17.12%) patients, severe extra-rhinology symptoms in 62 (24.12%), severe ear and facial symptoms in 30 (11.67%), and severe psychological or sleep symptoms in 96 (37.35%). Women reported a higher rate of severe otolaryngological symptoms than men, and female sex was associated with severe rhinology symptoms (odds ratio [OR]=2.37, 95% confidence interval [CI]=1.23-4.58), severe extra-rhinology symptoms (OR=1.94, 95% CI=1.09-3.47), severe ear and facial symptoms (OR=5.15, 95% CI=2.19-12.01), and severe psychological or sleep problems (OR=2.70, 95% CI=1.60-4.56). Severe rhinology symptoms were more common in patients with a history of AR (OR=2.40, 95% CI=1.19-4.84). DM increased the risk of developing severe ear and facial manifestations of COVID-19 (OR=2.90, 95% CI=1.05-8.02) (Table 2).

Most patients reported that fever (n=125, 49.8%) was the first symptom to appear during the disease (Table 3), followed by headache (n=59, 23.5%). Regarding anosmia and dysgeusia, they were the first symptoms to appear in 8.17% (n=21) of patients, although they were commonly observed in 68.09% (n=175) of patients during the disease course, which led them to get tested for COVID-19. In addition, anosmia and dysgeusia were significantly more common in women (n=81, 80.20%) than in men, with a 2-fold increased risk of developing anosmia (OR=2.67, 95% CI=1.49-4.80).

Figures 1 and 2 summarize the prevalence of otolaryngological symptoms in COVID-19 as measured using SNOT-22. In the first few days of the study, the most common symptom was a loss of smell and taste (n=175, 68.09%), followed by cough (n=169, 65.76%), whereas at the end of the study, the most common symptom that remained was a runny nose (n=33, 12.84%). Additionally, voice hoarseness was common in 17.90% (n=46) of patients, and 17.39% (n=8) had severe hoarseness symptoms. Breathing difficulty was reported in 29.96% (n=77) of patients, and 18.18% (n=14) described it as severe. At the end of the study, however, breathing difficulty was reported by 5.06% (n=13) of patients, and only 1 patient had severe breathing

Table 1. Distribution of Sociodemographic Features in Relation to Severity of Otorhinolaryngology Symptoms as Measured Using SNOT-22.

	Total	Severe rhinology symptoms		Severe extra-rhinology symptoms		Severe ear and facial symptoms		Severe psychological or sleep symptoms		
		No	Yes	No	Yes	No	Yes	No	Yes	
	N=257	213 (82.88%)	44 (17.12%)	195 (75.88%)	62 (24.12%)	227 (88.33%)	30 (11.67%)	161 (62.65%)	96 (37.35%)	
Age										
<20	22	16 (72.73)	6 (27.27)	17 (77.27)	5 (22.73)	17 (77.27)	5 (22.73)	14 (63.64)	8 (36.36)	
20-29	65	52 (80.00)	13 (20.00)	46 (70.77)	19 (22.09)	59 (90.77)	6 (9.23)	48 (73.85)	17 (26.15)	
30-39	86	72 (83.72)	14 (16.28)	67 (77.91)	19 (22.09)	75 (87.21)	11 (12.79)	50 (58.14)	36 (41.86)	
40-49	60	51 (85.00)	9 (15.00)	44 (73.33)	16 (26.76)	54 (90.00)	6 (10.00)	33 (55.00)	27 (45.00)	
50-59	15	13 (86.67)	2 (13.33)	13 (86.67)	2 (13.33)	13 (86.67)	2 (13.33)	10 (66.67)	5 (33.33)	
≥60	9	9 (100.00)	0 (0.00)	8 (88.89)	1 (11.11)	9 (100.00)	0 (0.00)	6 (66.67)	3 (33.33)	
Gender										
Male	156	137 (87.82)*	19 (12.18)*	126 (80.77)*	30 (19.23)*	148 (94.87)*	8 (5.13)*	112 (71.79)*	44 (28.21)*	
Female	101	76 (75.75)*	25 (24.75)*	69 (68.32)*	32 (31.68)*	79 (78.22)*	22 (21.78)*	49 (48.51)*	52 (51.49)*	
Smoking										
No	208	176 (84.62)	32 (15.38)	159 (76.44)	49 (23.56)	184 (88.46)	24 (11.54)	127 (61.06)	81 (38.94)	
Yes	49	37 (75.51)	12 (24.49)	36 (73.47)	13 (26.53)	43 (87.76)	6 (12.24)	34 (69.39)	15 (30.61)	
Chronic disease										
Without	62	52 (83.87)	10 (16.13)	47 (75.81)	15 (24.19)	54 (87.10)	8 (12.90)	37 (59.68)	25 (40.32)	
With	195	161 (82.56)	34 (17.44)	148 (75.90)	47 (24.10)	173 (88.72)	22 (11.28)	124 (63.59)	71 (36.41)	
Diabetes										
No	233	193 (82.83)	40 (17.17)	177 (75.97)	56 (24.03)	209 (89.70)*	24 (10.30)*	147 (63.09)	86 (36.91)	
Yes	24	20 (83.33)	4 (16.67)	18 (75.00)	6 (25.00)	18 (75.00)*	6 (25.00)*	14 (58.33)	10 (41.67)	
Nasal/paranasal disease										
Without	178	62 (78.48)	17 (21.52)	63 (79.75)	16 (20.25)	66 (83.54)	13 (16.46)	46 (58.23)	33 (41.77)	
With	79	151 (84.83)	27 (15.17)	132 (74.16)	46 (25.84)	161 (90.45)	17 (9.55)	115 (64.61)	63 (35.39)	
Allergic rhinitis										
Without	200	172 (86.00)*	28 (14.00)*	151 (75.50)	49 (24.50)	179 (89.50)	21 (10.50)	129 (64.50)	71 (35.50)	
With	57	41 (71.93)*	16 (28.07)*	44 (77.19)	13 (22.81)	48 (84.21)	9 (15.79)	32 (56.14)	25 (43.86)	
Obesity										
No	182	151 (82.97)	31 (17.03)	138 (75.82)	44 (24.18)	161 (88.46)	21 (11.54)	118 (64.84)	64 (35.16)	
Yes	75	62 (82.67)	13 (17.33)	57 (76.00)	18 (24.00)	66 (88.00)	9 (12.00)	43 (57.33)	32 (42.67)	

*Indicates chi-square P value $<.05$.

difficulty. However, the risk of developing severe breathing difficulty or hoarseness was not significantly associated with sociodemographic features or health indicators.

The total number of patients with severe symptoms at the end of the study was 11 (4.28%). However, only 8 (72.73%) patients had severe symptoms at the beginning of the study. Regarding the type of severe symptoms, 8 (72.73%) patients had severe sleep or psychological symptoms, 4 (36.36%) had severe rhinological symptoms, and 3 (27.27%) had severe extra-rhinology symptoms, while none had severe ear or facial symptoms. There was a significant difference in the mean age of patients with severe symptoms at the end of the study (mean=27.45, SD=8.39, min=16, max=40) and those who did not have severe symptoms at the end of the study (mean=34.90, SD=2.53, min=16, max=79, $t(255)=2.17$, $P=.031$). Most patients

with severe symptoms after 1 month were female ($n=7$, 63.64%) and non-smokers ($n=9$, 81.82%), and had no AR ($n=7$, 63.64%). However, most reported at least 1 nasal or paranasal problem ($n=6$, 54.55%), and all of them had a comorbid disease ($n=11$, 100%).

Figure 3 summarizes the distribution of the severe otorhinolaryngological symptoms during the study period, as measured using SNOT-22. The most common severe symptom was cough, which was significantly more common in women ($n=52$, 51.49%) than in men ($n=44$, 28.21%, $\chi^2(1)=14.20$, $P<.001$), and female sex doubled the risk of developing severe cough (OR=2.70, 95% CI=1.60-4.55). In terms of COVID-19 medication, 2 patients received remdesivir, 2 received ritonavir and lopinavir, 4 received hydroxychloroquine, and 11 received azithromycin.

Table 2. Summary of Unadjusted and Adjusted Regression Models That Estimate the Risk of Developing Severe Otolaryngology COVID-19 Symptoms.

	Severe rhinology symptoms		Severe extra-rhinology symptoms		Severe ear and facial symptoms		Severe psychological or sleep symptoms	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age ^a	0.97 (0.94, 1.00)	0.97 (0.94, 1.00)	0.98 (0.96, 1.01)	0.99 (0.96, 1.01)	0.98 (0.96, 1.01)	0.98 (0.94, 1.02)	1.01 (0.99, 1.04)	1.02 (0.99, 1.04)
Gender ^b								
Male	Reference							
Female	2.37 (1.23, 4.59)*	2.23 (1.15, 4.34)*	1.95 (1.09, 3.47)*	1.89 (1.05, 3.38)*	5.15 (2.19, 12.10)*	4.93 (2.09, 11.64)*	2.70 (1.60, 4.56)*	2.88 (1.69, 4.90)*
Smoking ^c								
No	Reference							
Yes	1.78 (0.84, 3.78)	2.73 (1.14, 6.54)*	0.83 (0.46, 1.50)	0.75 (0.39, 1.42)	0.83 (0.38, 1.81)	0.52 (0.18, 1.46)	1.18 (0.69, 1.99)	0.94 (0.53, 1.67)
Chronic disease ^c								
Without	Reference							
With	1.10 (0.51, 2.37)	0.83 (0.36, 1.90)	0.99 (0.51, 1.94)	0.85 (0.42, 1.74)	0.86 (0.36, 2.04)	0.64 (0.24, 1.66)	0.85 (0.47, 1.52)	0.92 (0.48, 1.73)
Diabetes ^c								
No	Reference							
Yes	0.97 (0.31, 2.98)	1.36 (0.41, 4.56)	1.05 (0.40, 2.78)	1.26 (0.45, 3.55)	2.90 (1.05, 8.02)*	5.08 (1.51, 17.02)*	1.22 (0.52, 2.87)	1.02 (0.41, 2.58)
Nasal/paranasal disease ^c								
Without	Reference							
With	0.65 (0.33, 1.28)	0.61 (0.30, 1.22)	1.37 (0.72, 2.61)	1.36 (0.71, 2.60)	0.54 (0.25, 1.17)	0.49 (0.22, 1.11)	0.76 (0.44, 1.31)	0.77 (0.44, 1.34)
Allergic rhinitis ^c								
Without	Reference							
With	2.40 (1.19, 4.84)*	2.13 (1.09, 4.18)*	0.91 (0.45, 1.83)	0.87 (0.43, 1.77)	1.60 (0.69, 3.71)	1.49 (0.62, 3.60)	1.42 (0.78, 2.58)	1.30 (0.70, 2.43)
Obesity ^c								
No	Reference							
Yes	1.02 (0.50, 2.08)	1.36 (0.64, 2.89)	0.99 (0.53, 1.86)	1.15 (0.59, 2.23)	1.05 (0.46, 2.40)	1.53 (0.61, 3.85)	1.37 (0.79, 2.38)	1.45 (0.80, 2.61)

^aAdjusted for gender.

^bAdjusted for age.

^cAdjusted for age and gender.

*Indicates significant P value <.05.

Table 3. Distribution of COVID-19 Otorhinolaryngology Symptoms as Experienced by the Study Participants During the Course of Their Disease.

Symptoms	First symptoms to appear		Symptoms concurrent with presence of anosmia	
	N = 257	%	N = 175	%
Loss of smell and/or taste	21	8.17		
Fatigue	28	10.89	36	20.57
Headache	59	22.96	85	48.57
Runny nose/nasal congestion	36	14.01	81	46.29
Cough	42	16.34	73	41.71
Body ache	39	15.18	0	0
Fever	125	48.64	72	41.14
Sore throat	32	12.45	0	0
Sneezing	4	1.56	0	0
Diarrhea/Nausea/loss of appetite	7	2.72	34	19.43
Breathing difficulty	15	5.84	2	1.14
Dizziness	4	1.56	0	0
Nasal block	3	1.17	0	0
Voice change	1	0.39	0	0
Body rash	1	0.39	0	0
Ear pain	1	0.39	0	0
Eye symptoms	2	0.78	0	0
Sinusitis	2	0.78	0	0

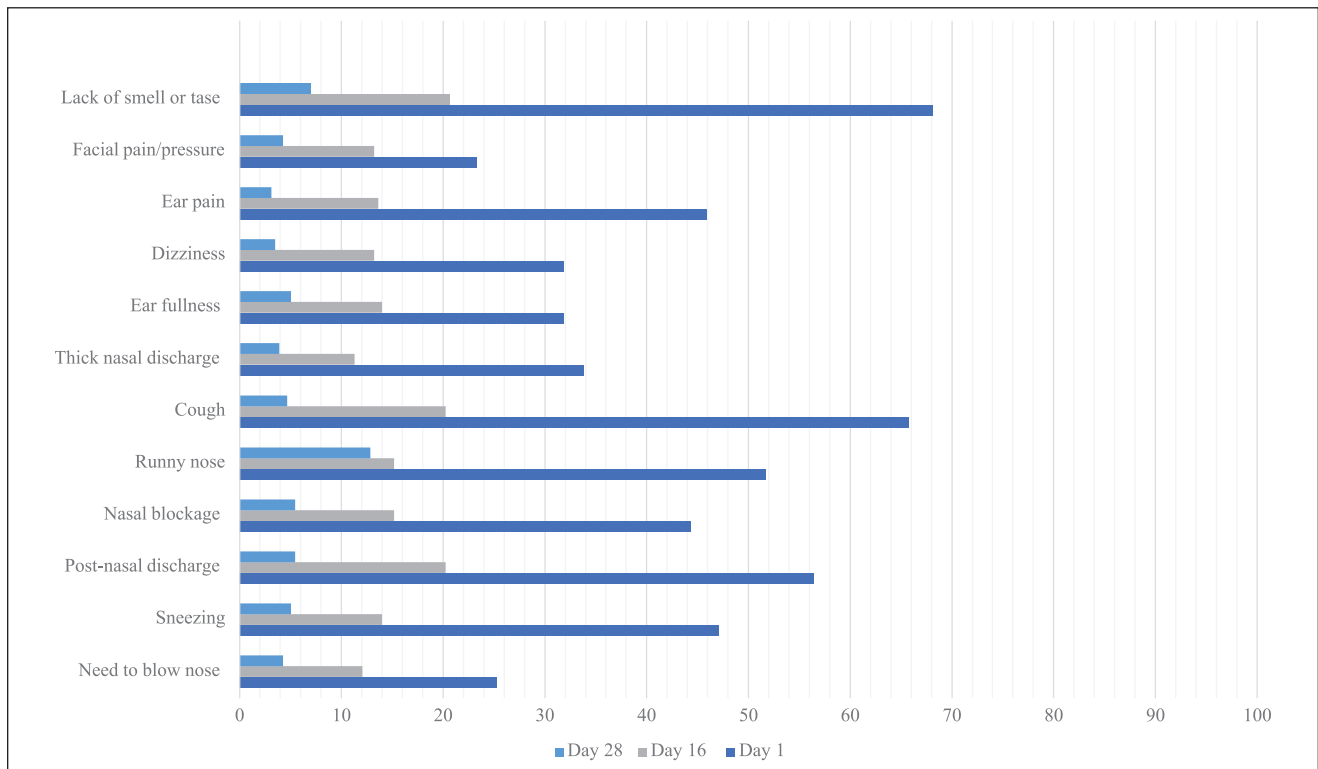


Figure 1. Bar graph that shows the rate of nasal, extra-nasal, ear and facial symptoms associated with covid-19 during the study period.

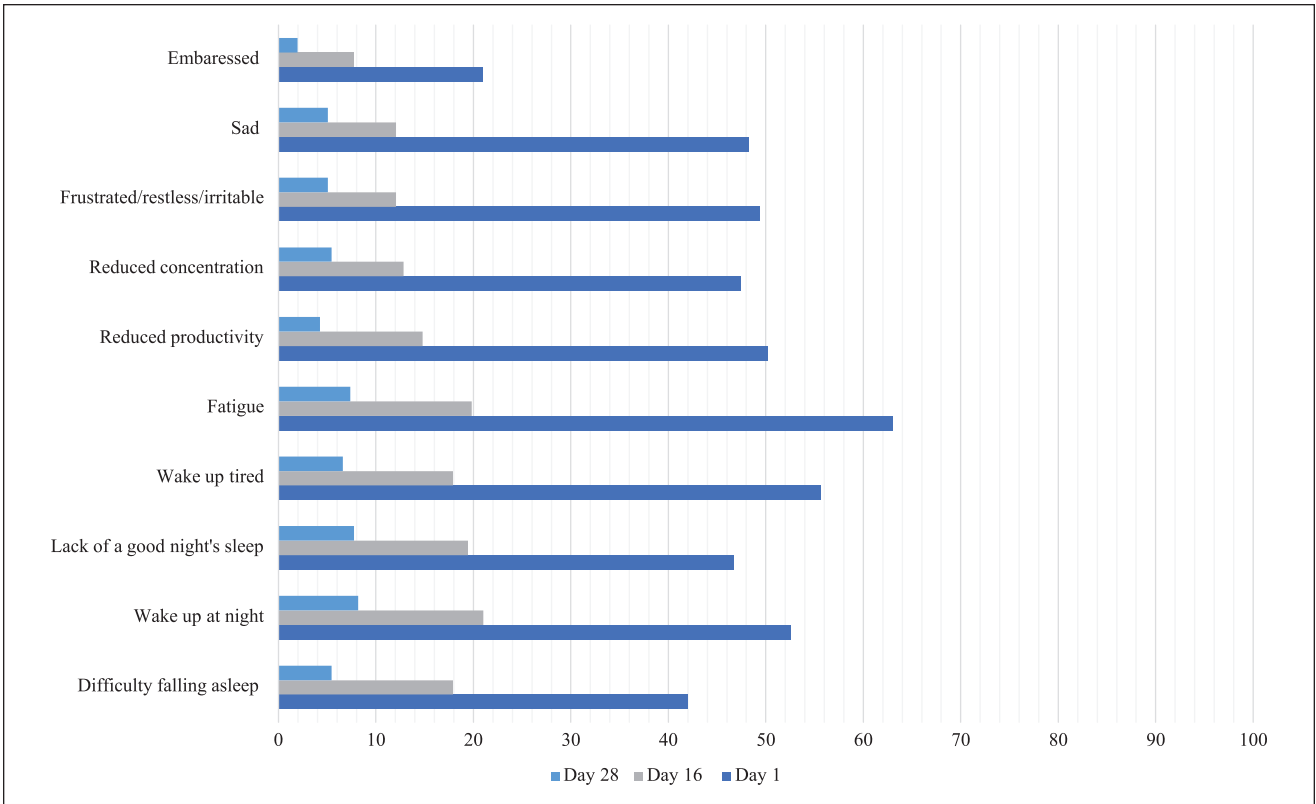


Figure 2. Rate of sleep and psychological dysfunction associated with COVID-19 during the study period.

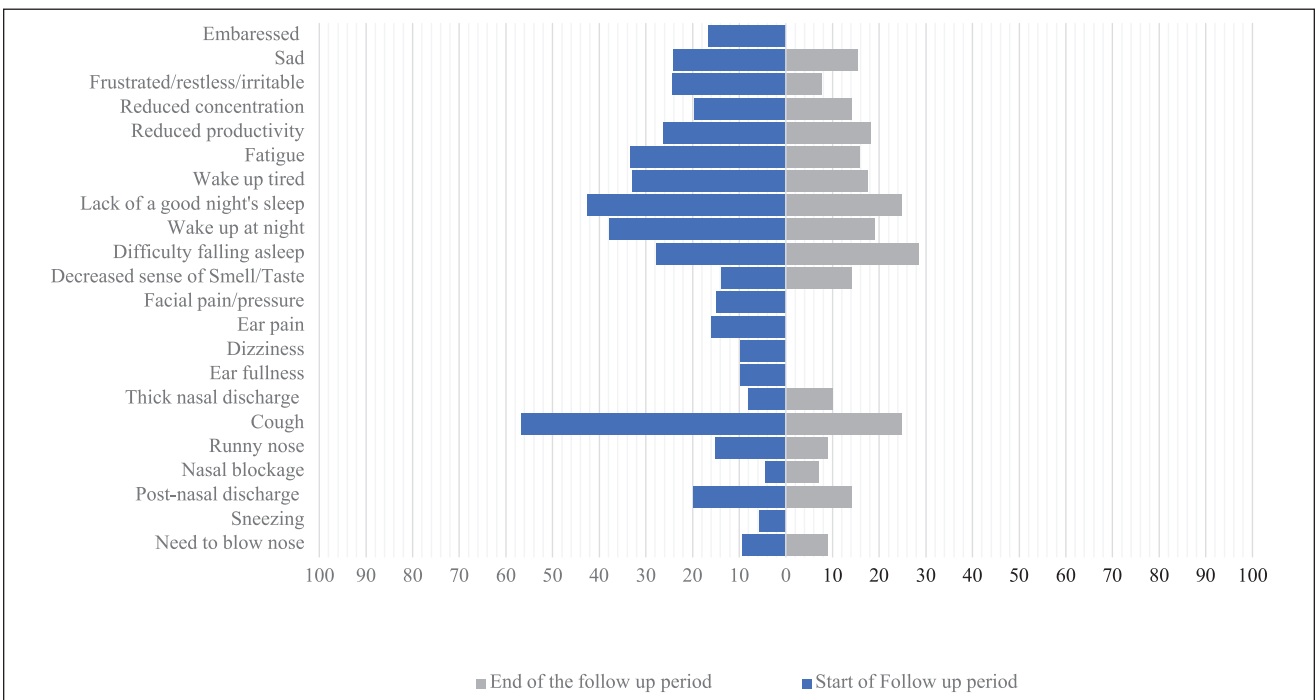


Figure 3. Bar graph that shows the distribution of severe cases amongst the symptomatic patients during the study period.

Discussion

The rapid spread of COVID-19 globally demanded urgent action aimed at improving our knowledge of the associated symptoms and their progression, including otorhinolaryngological manifestations. This will help us readily identify high-risk cases and prevent disease progression.¹⁶ Notably, the symptoms of COVID-19 are like those of other viral diseases, which makes the diagnosis difficult without appropriate SARS-CoV-2 diagnostic tests.¹⁶ We aimed to describe COVID-19-associated otorhinolaryngological manifestations and their recovery over time, to determine treatment options and better control the disease complications and outcomes.

SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2 belong to the β -coronavirus family. The clinical manifestations of these diseases are similar. The manifestations of MERS can range from an asymptomatic presentation to a life-threatening presentation that leads to death. The most common manifestations are cough, fever $>38^{\circ}\text{C}$, and shortness of breath (65%, 63%, and 52%, respectively).¹⁷ SARS is characterized by fever, chills, myalgia, malaise, dry cough, and headache.¹⁸

Comparison With Previous Literature

The patients in this study reported fever as the first symptom, followed by headache. Moreover, the clinical manifestations of COVID-19 ranged from a complete absence of symptoms to the presence of severe symptoms and even death. Per a literature review, fever, cough, and shortness of breath are the most common clinical manifestations in these 3 viral diseases. In our study, the common symptoms of COVID-19 included fever, headache, and cough, in line with the results of previous studies.^{19,20}

In the literature, there is variation in the reported otorhinolaryngology manifestations and severity.⁹ Some studies have reported that sore throat and headache are the most common otorhinolaryngology manifestations with rates of 11.3% and 10.7%, respectively. These are followed by anosmia (6%), pharyngeal erythema (5.3%), nasal congestion (4.1%), and nasal obstruction (3.4%).⁹ The most common otorhinolaryngological manifestations found by Elibol⁸ were anosmia (35.4%), ageusia (16.1%), sore throat (27%), cough (43.8%), nasal congestion (12.9%), and post-nasal discharge (6%). Our findings showed that anosmia and cough were among the most common symptoms. Therefore, anosmia is considered a clinical phenomenon of COVID-19 that requires special attention. A patient reporting anosmia and ageusia should promptly get tested to differentiate between COVID-19 and other viral diseases.

Due to the large number of infected patients and the absence of a definitive treatment, many studies have focused

on finding an effective treatment for COVID-19. Some studies have recommended the use of antiviral therapy after standard care, but no therapy has been proven to be effective.²¹

The current study, with a mean patient age of 34.58 years, revealed no relationship between symptom severity and age. Previous studies have reported that the severity of COVID-19 symptoms increases with age.²² One study conducted on 788 patients showed that older patients (age ≥ 60 years) had a significantly higher risk of developing some of the most common symptoms related to COVID-19, such as high fever and dyspnea, than younger patients (age < 60 years).²¹ Regarding sex distribution, some studies have reported that male sex is associated with more severe symptoms.^{22,23} However, we found contradictory findings for otorhinolaryngological symptoms. Furthermore, patients with DM and other comorbidities infected with COVID-19 showed rapid progression and poor prognosis, including severe ear and facial symptoms.²⁴ Although all our severely ill patients had comorbidities, none of them experienced severe ear and facial symptoms during a complete month of follow-up, as is reported in the literature.²⁵

COVID-19 symptoms should be cautiously considered and must be closely observed for guiding patient management. Several drugs are now being used to treat COVID-19. There are no sufficient randomized controlled studies examining their potential benefits in COVID-19 management. The majority of reports on the usage of these drugs in COVID-19 are based on *in vitro* or extrapolated findings.^{26,27}

There is inadequate literature regarding the prognosis of otolaryngological symptoms and their relationship with patient characteristics. At the end of the study, 11 patients had severe symptoms. These patients were further studied to determine the possible predisposing characteristics as well as long-term symptoms that could result in complications and poor prognosis. A previous study analyzed the prognostic factors of comorbid patients and concluded that these patients were more likely to experience severe symptoms. All our patients had at least 1 comorbidity (DM, HTN, cardiac disease, renal disease, etc.). Although seasonal AR was not linked to severe symptoms in this study, it is reportedly associated with anosmia.²⁶ In addition, it is worth mentioning that anosmia and ageusia are the most persistent otolaryngologic symptoms.²⁵

Clinical Applicability and Generalizability

Our study included participants who were recruited from patients in King Fahad University Hospital, 1 of the 2 main hospitals in the Eastern Province that receives cases of COVID-19. Hence, our sample can be considered representative to the Eastern Province of Saudi Arabia. Nonetheless, this cannot be confirmed because there is no statistical analysis done to compare our sample statistics to the referral population parameters.

Study Strengths

Very little details are available regarding the spectrum of otolaryngological symptoms, severity of those symptoms, and the pattern of recovery over time. This study provides a picture of the association between COVID-19, the characteristics of the manifestations and recovery. In addition, all patients were diagnosed with COVID-19 by RT-PCR from nasopharyngeal swab and have been selected randomly. Furthermore, the presence of these otorhinolaryngological manifestations can justify patients' evaluation and thus it is a great reflection of what otorhinolaryngologists may encounter in hospitals. This study evaluates important variables in the management strategies, prognosis, and diagnosis of COVID-19 patients.

Study Limitations

One of the limitations of our study was that we did not consider pregnancy as a vital variable in disease prognosis. Although adjustment was done for age and gender, our regression models were still under adjusted and there might be a remaining uncorrected confounding bias that might be resulted from unadjusted unmeasured variables. In addition, although we reported multiple statistically significant odd ratios of developing severe COVID-19 symptoms, there is a still an unexplained variability of the risk of developing severe COVID-19 symptoms that were not predicted by the included predictors as reflected by the small R^2 values of our regression models and the poor goodness of fit. Moreover, excluded severely ill patients who are medically unstable. These included those who were hemodynamically unstable, on mechanical ventilation, or required ICU admission; however, the method of data collection used in this study was impractical for these patients, especially in terms of continuous follow-up. Self-administered questionnaires have additional limitations due to their subjective nature, and this may have influenced the accuracy of the actual pattern of the disease. For example, some patients were asymptomatic despite their viral load, which objectively measures disease progression. Not comparing the similarities or the differences of the included participants is another limitation to our study. Moreover, the study sample is derived from a population living in the Eastern Province of Saudi Arabia. As a result, the generalizability of our findings may be limited. It was also difficult to ascertain whether sleep and psychological symptoms are attributed to the COVID-19 or other confounding variables, such as gender and hormonal changes. At the last date of follow-up, a limited number of patients were still symptomatic, and their complete pattern therefore remained undetected.

In terms of investigating the complete pattern of otorhinolaryngological symptoms in COVID-19 patients, we

believe that further studies that include a larger number of patients divided into 2 groups depending on the presence or absence of AR will be valuable to increase the understanding and early recognition of this emerging disease. Greater reliability and statistical strength will be achieved with a comparison of subjective questionnaires and objective clinical data, such as inflammatory markers, lymphocyte count, and viral load.

Conclusion

Otorhinolaryngological symptoms are among the most common and severe presentations of COVID-19. The commonest symptom was fever, while the most severe symptom was cough. We recommend to screen COVID-19 patients, especially females, for long lasting otolaryngological symptoms. Studying the symptoms is vital for the primary care providers and community health physicians to help in the early detection of the COVID-19 cases and identifying the spectrum of severity. Further studies are required to evaluate symptoms over a longer study period.

Acknowledgments

The authors would like to thank Aishah AlGhuneem, Mohammed AlSharit, Abdullah Abuzaid, Raghad AlGhamdi, Hassan Alkhulaif, Mohammed Al Hajji, Jumanah Jarad, Azizah Bokhari, and Remah Alzayyat for their significant contribution in data acquisition which helped in writing this research.

Author Contributions

D R, H J, A Sh, S Sh, A S, A E, A G, M B designed the work. D R, H J, A Sh, S Sh, A G, S Sh, A S acquired and analyzed data. D R, H J, A Sh drafted. S Sh, A S, A E, A G, M B revised and approved the manuscript. All authors agree to be accountable for all aspects of the work.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Data Sharing and Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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