

# Clinical otorhinolaryngological presentation of COVID-19 patients in Saudi Arabia

## A multicenter study

Laila M. Telmesani, MD, FRCSEd, Danah H. Althomaly, MD, Lamia A. Buobliqah, MD, Roa T. Halawani, MD, Mona M. Ashoor, MD, Marwan J. Alwazzeah, MD, Suad A. Al Mubarak, MD, Maha A. AlHarbi, MD, Rana F. AlMuslem, MD, Sahal S. Arabi, MD, Waleed E. Saleh, MD, Amal Y. ALYosif, MD, Mohammad R. Al Eid, MD, Lena S. Telmesani, MD, Abdulaziz S. AlEnazi, MD.

### ABSTRACT

**الأهداف:** لتقييم سمات أمراض الأنف والأذن والحنجرة، بما في ذلك الانتشار، والشدة، والأعراض المبكرة بين المرضى المصابين بفيروس كورونا في المملكة العربية السعودية.

**المنهجية:** أجريت دراسة استقصائية متعددة المراكز في 3 مراكز طبية (مستشفى جامعة الملك فهد، الخبر، مستشفى القطيف المركزي، القطيف، ومستشفى أحد، المدينة المنورة) من مناطق جغرافية مختلفة في المملكة العربية السعودية على المرضى المصابين بفيروس كورونا والأعراض المصاحبة، وتمت المصادقة على الدراسة من قسم الأخلاقيات البحثية من جامعة الإمام عبدالرحمن بن فيصل، وتم جمع بيانات اجتماعية ديموغرافية وأعراض كورونا العامة وأعراض الأنف والأذن والحنجرة لدى المرضى المؤكد أصابهم بفيروس كورونا.

**النتائج:** شملت الدراسة على 1734 مريضاً إيجابياً بفيروس كورونا متوسط العمر كان  $37.7 \pm 11.6$  سنوات. والسبب الرئيسي للإصابة هو الاتصال الوثيق بحالة معروفة. وكانت غالبية الحالات خفيفة (51.8%)، تليها حالات متوسطة (45.6%) وحادة (2.6%). ومع ذلك، فإن 33.7% من المرضى لم تكن لديهم أعراض. ارتبطت شدة فيروس كورونا ارتباطاً كبيراً بنوع الجنس الذكور ( $p=0.017$ ) والفتحة العمرية الأعلى ( $p=0.04$ ) والتدخين ( $p<0.001$ ). كانت الأعراض العامة الأكثر شيوعاً لدى مرضى فيروس كورونا. هي الحلق الحاد (20.9%)، وفقدان الشم (15.5%)، وضعف الشم (10%)، وفقدان حاسة التذوق (11.4%). وكان أكثر الأعراض العامة شيوعاً هو الحمى (20.9%) السعال (6.8%)، والصداع (2.7%)، وقصور التنفس (1.7%). دون اختلافات ذات دلالة إحصائية. بشكل عام، أظهر 79.5% أعراض ORL كأعراض أولية للإصابة بفيروس كورونا، وفقر الدم والتهاب الحلق من أكثر الأعراض شيوعاً.

**الخلاصة:** تُعد أعراض الأنف والأذن والحنجرة أعراضاً سريرية مبكرة لدى مرضى فيروس كورونا وتقدم هذه الدراسة دليلاً واضحاً على أنها منتشرة بين المرضى. يجب النظر لهذه الأعراض للكشف الأولي عن العدوى لأنها قد تظهر قبل أعراض أخرى.

**Objectives:** To assess the otorhinolaryngological (ORL) symptoms, including their prevalence, severity, and early presentations among coronavirus disease-19 (COVID-19) patients in the Saudi population.

**Methods:** This was a multicentric, cross-sectional study carried out on severe acute respiratory syndrome coronavirus-2 positive patients at 3 COVID-19 centres; Imam Abdulrahman Bin Faisal University, King Fahd Hospital of the University, AlKhubar, Qatif Central Hospital, AlQatif, and Ohud Hospital, Al Madinah Al Munawarah, Saudi Arabia. The validated survey consisted of sociodemographic data, general symptoms of COVID-19, and ORL manifestations.

**Results:** A total of 1734 COVID-19 positive patients were included in the study (mean age:  $37.7 \pm 11.6$  years). Most of the cases were mild (51.8%), followed by moderate (45.6%), and severe (2.6%) cases. Approximately 33.7% were asymptomatic. Severity of symptoms was significantly associated with male gender ( $p=0.017$ ), higher age-group ( $p=0.04$ ), and smoking ( $p<0.001$ ). The most common initial ORL presentations were sore throat (20.9%), anosmia (15.5%), hyposmia (10%), and loss of taste (11.4%). Overall, 79.5% showed ORL symptoms as the initial presenting symptoms for COVID-19, with anosmia and sore throat being the most common symptoms.

**Conclusion:** This study confirmed the prevalence of ORL symptoms among COVID-19 patients in Saudi Arabia. Moreover, these symptoms could also be considered for early detection of COVID-19 as they might appear prior to other symptoms.

**Keywords:** COVID-19, coronavirus, otorhinolaryngology, olfactory dysfunction, presentations

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From the Department of Otolaryngology Head and Neck Surgery (L.M. Telmesani, Ashoor, L.S. Telmesani, AlEnazi); from the Department of Internal Medicine (Alwazzeah), College of Medicine, Imam Abdulrahman Bin Faisal University, King Fahd Hospital of the University, from the Department of Otolaryngology - Head and Neck Surgery (Althomaly, AlHarbi), Ministry of Health, Al-Khubar, from the Department of Otorhinolaryngology - Head and Neck Surgery (Buobliqah, Al Mubarak, AlMuslem, ALYosif, Al Eid), Qatif Center Hospital, Ministry of Health, AL Qatif, and from the Department of Otorhinolaryngology - Head and Neck Surgery (Halawani, Arabi, Saleh), Ohud General Hospital, Ministry of Health, AL Medina Al Munawarah, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Abdulaziz S. AlEnazi, Department of Otolaryngology - Head and Neck Surgery, Imam Abdul Rahman bin Faisal University, King Fahd Hospital of the University, Al Khobar, Kingdom of Saudi Arabia. E-mail: asenazi@iau.edu.sa  
ORCID ID: <https://orcid.org/0000-0001-7237-4923>

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a novel coronavirus, led to a fatal and highly infectious coronavirus disease-19 (COVID-19).<sup>1</sup> The SARS-CoV-2 first appeared in Wuhan, China in December, 2019 and rapidly transmitted among humans, leading to COVID-19 epidemic in China which was followed by a worldwide pandemic as declared by the World Health Organization (WHO) on March 11, 2020.<sup>2</sup> According to WHO reports, there have been more than 100 million confirmed cases of COVID-19, with more than 2 million deaths. The first case in Saudi Arabia was confirmed by the Ministry of Health on March 2, 2020.<sup>3,4</sup>

Clinical manifestation of COVID-19 includes wide range of clinical spectrum, ranging from no symptoms to septic shock and multi-organ dysfunctions. This variability in the clinical presentation among COVID-19 patients has also been observed in various studies carried out in Saudi Arabia.<sup>5</sup> Most of the COVID-19 studies have focused on the lower respiratory tract manifestations and sequels owing to their life-threatening nature.<sup>6</sup> In symptomatic patients, the most prevalent general symptoms reported were fever, cough, fatigue, myalgia, dyspnea, and loss of appetite.<sup>7</sup> A retrospective study with 1519 cases in Saudi Arabia reported cough (89.4%), fever (85.6%), and sore throat (81.6%) to be the most common symptoms.<sup>8</sup>

Since the virus transmission is mediated through the upper respiratory tract, encounters with otorhinolaryngological (ORL) symptoms are unavoidable.<sup>9</sup> Moreover, increasing information regarding the clinical manifestations of COVID-19 has led to a better understanding of the wide range of symptoms, including ORL symptoms.<sup>8,10</sup> Pharyngodynia, nasal congestion, rhinorrhea, olfactory, and gustatory dysfunctions are common ORL symptoms of COVID-19.<sup>10</sup> In a multicentric cohort study, it was found that all the recruited patients showed anosmia which was followed by a high percentage of patients with headache (69.1%), rhinorrhoea/nasal obstruction (40%), and cough (40%). Data from this study further emphasized the diagnostic importance of ORL symptoms for COVID-19.<sup>11</sup> Gane et al<sup>12</sup> presented a case report along with a case series where they provided evidence for isolated sudden onset anosmia as an initial presentation of COVID-19 and suggested to consider this presentation as management of the disease. A

study carried out in the Indian population showed 14.8% prevalence of anosmia in COVID-19 patients.<sup>13</sup> To assess if loss of smell and taste could be a clinical presentation, Menni et al<sup>14</sup> did a community survey via an application and found that 59% of the COVID-19 patients showed loss of smell and taste as the symptom. Their study found that loss of smell and taste along with fever, persistent cough, and fatigue were predictive symptoms of COVID-19 positive test. This correlation was observed with good specificity (0.86) and average sensitivity (0.54).<sup>14</sup> A study by Lechien et al<sup>15</sup> demonstrated a significant correlation between olfactory and gustatory dysfunctions and COVID-19 infection as the occurrence was found to be 10 times higher in COVID-19 patients compared to COVID-19 negative cases. Furthermore, the ORL symptoms were mainly presented in the mild to moderate form of the disease, and they might be the initial presenting symptoms of COVID-19.<sup>16-18</sup>

A study by Lechien et al<sup>15</sup> reported severe olfactory and gustatory dysfunctions without rhinorrhea or nasal obstruction in many COVID-19 positive patients. However, COVID-19 was not suspected at the baseline since fever, cough, or other systemic complaints were absent in these patients. As the ORL symptoms could appear before other symptoms, the physicians should consider these symptoms for the early detection of the infection.<sup>15</sup>

There is a lot of discrepancy in the prevalence of the ORL symptoms between different communities, such as the European and Asian populations, this encouraged us to evaluate the prevalence of these characteristic symptoms in the Saudi population.<sup>15,16,19-21</sup> Paucity of diagnostic tests was another major reason to understand this clinical presentation and its correlation with COVID-19, as if any early correlation is found between onset of these symptoms and COVID-19 positive cases, this could be used as an early predictor of COVID-19 cases.

We carried out this cross-sectional study and evaluated the clinical presentation, prevalence, and severity of the ORL symptoms among COVID-19 patients from different geographical areas in Saudi Arabia. Since otolaryngologists are approached first by the patients, this might aid them in identifying the suspected cases with atypical presentations.

**Methods.** A multicentric cross-sectional study carried out including SARS-CoV-2 positive patients with variable ORL symptoms and severity. Patients' information and their clinical data were collected from 3 COVID-19 centers in different regions of Saudi Arabia: Imam Abdulrahman Bin Faisal University, King Fahd

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Hospital of the University, AL Khobar, Qatif Central Hospital, AlQatif, and Ohud Hospital, Al Madinah Al Munawarah, Saudi Arabia. The study protocol was approved by the Institutional Review Board of Imam Abdulrahman Bin Faisal University, AL Khobar, Saudi Arabia on June 2020. The study was carried out according to the principles of Helsinki Declaration.

Collection of the data was between June 2020 and August 2020. Informed consent was obtained from all the patients before their participation in the study. Clinical data was collected electronically via an online survey, which consisted of 3 parts. Prior to the survey, patients were intimated over the phone.

The first part of the survey included questions addressing sociodemographic data and clinical information (medical record number, age, gender, ethnicity, occupation, time of symptoms appearance, time of laboratory diagnosis, comorbidities, smoking history, medication history, and source of the infection). The second part consisted of questions regarding the general symptoms of COVID-19, and the third part included questions specifically on the ORL presentation. A 5-point scale was used to rate the ORL symptoms (0: no symptoms, 1: almost never, 2: sometimes, 3: almost always, and 4: always). We classified the severity of the disease according to the followed measures of the Saudi Ministry of Health where mild cases are the ones who are symptom free or has mild symptoms that do not necessitate hospital admission, moderate are the ones admitted to the medical wards, while the severe-critical ones are the ones who needed intensive care unit admission.

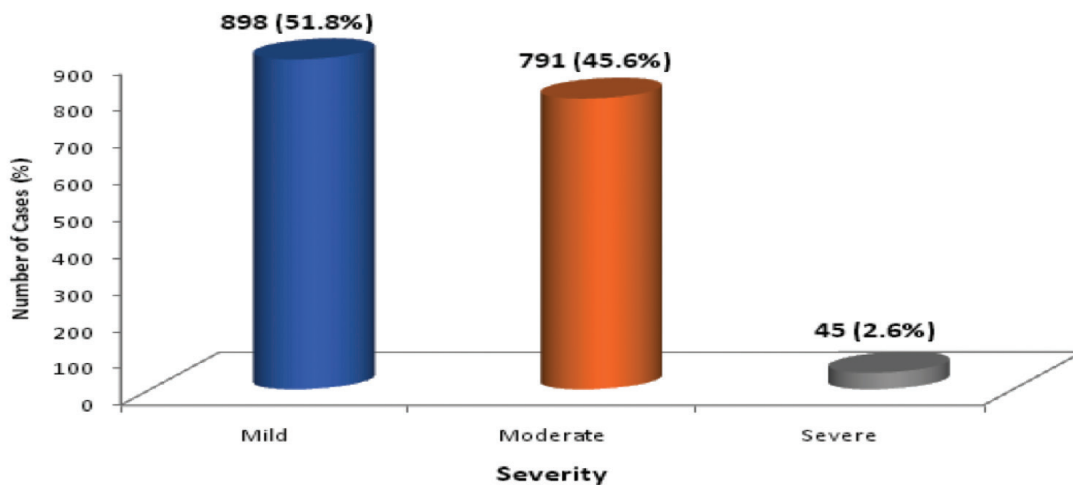
Inclusion criteria for the patients in this study included adult over 18 years of age, tested COVID

positive confirmed infection, and patients were required to be clinically available for completing the study. The study exclusion criteria were critically ill patients who were unable to fill the survey, patients less than 18 years of age, patients with previous history of smell and taste alternation, sinonasal disease, head trauma, and psychological or neurological disorders.

**Statistical analysis.** Statistical Package for the Social Sciences for Windows, version 21 (IBM Corp., Armonk, NY, USA) was used to perform the statistical analyses. All categorical variables including gender, age groups, nationality, smoking status, presence of chronic disease (yes/no), ORL symptoms, general symptoms, and severity of COVID-19 were presented as frequency and percentages. Chi-square test was used to check the association between ORL symptoms and severity of COVID-19 and other variables. A *p*-value of  $\leq 0.05$  was considered significant.

**Results.** A total of 1734 SARS-CoV-2 positive patients successfully completed the survey. Out of the 1734 patients, 51.8% were home quarantined while 33.3% were admitted in Qatif Central Hospital, Al Qatif, 8.6% in Ohud Hospital, Al Madinah Al Munawarah, and 6.3% in Imam Abdulrahman Bin Faisal University, King Fahd Hospital of the University, Al-Khobar.

Among COVID-19 patients, 926 (53.4%) were male and 898 (51.8%) were female. Approximately 51.8% had mild symptoms, 45.6% moderate, and 2.6% were severe cases (Figure 1). The percentage of moderate and severe cases was significantly higher in males compared to females ( $p=0.017$ ). The nationality of most of the patients was Saudi (90.2%), while there



**Figure 1** - Severity of coronavirus disease-19 (N=1734).

were only 9.8% non-Saudi patients. No statistically significant difference was observed between Saudis and non-Saudis ( $p=0.38$ ). Most of the patients (60.9%) belonged to the age group of 21-40 years, followed by 41-60 years (30.5%). Approximately 4.6% were  $\leq 20$  years of age, and 3.8% were  $>60$  years of age. A statistically significant correlation was observed between the severity of COVID-19 and higher age groups ( $p=0.04$ ). Among the recruited patients in this study, 291 (16.8%) were smokers and 1443 (83.2%) were non-smokers. The association between smoking and severity of COVID-19 was found to be statistically significant ( $p<0.001$ ; **Table 1**).

No significant association was found between education level and severity of COVID-19 ( $p>0.05$ ). Regarding occupation, high proportion of mild COVID-19 cases were students, healthcare workers, and unemployed respondents but the difference was insignificant ( $p>0.05$ ). On the contrary, significantly high proportion of moderate to severe COVID-19 were non-health worker employees ( $p=0.03$ ).

The initial ORL and general presenting symptoms of the patients have been listed in **Table 2**. More than one-fifth presented with sore throat (20.9%), followed by anosmia (15.5%), loss of taste (11.4%), and hyposmia (10%). Approximately 4.6% were initially asymptomatic. Among the general symptoms, majority presented with fever (20.9%), followed by cough (6.8%), and headache (2.7%). On the other hand, the

least common general symptoms were fatigue (2%), loss of appetite (1.4%), and myalgia (1.2%).

Taking into consideration the ORL symptoms and severity of COVID-19 infection, anosmia was the most frequently occurring symptom (46.2%), followed by loss of taste (45.2%), sore throat (37.7%), and hyposmia (36.3%). Other symptoms in this category included ear pain pressure (16.1%), voice change (28.4%), voice fatigue (26.3%), and breathlessness during speech (23.9%). Comparison of the ORL symptoms with the severity of COVID-19 showed no significant correlation (**Table 3**).

When ORL symptoms were compared between 2 age groups ( $\leq 40$  and  $>40$  years), it was found that nasal congestion, anosmia, hyposmia, sneezing, loss of taste, daytime sleep, and morning headache were significantly high in patients aged  $\leq 40$  years ( $p<0.05$ ). On the other hand, hearing loss, otorrhea, and loss of voice were significantly high in patients aged  $>40$  years ( $p<0.05$ ; **Table 4**).

Out of the 1734 cases, 70 patients presented with only ORL symptoms as the initial symptoms (**Table 5**). Among them, 22 (31.4%) had anosmia, while 16 (22.9%) had hyposmia, one (1.4%) had loss of taste, 11 (15.7%) had sore throat, 11 (15.7%) had rhinorrhea, 5 (7.1%) had pharyngodynia, and 4 (5.7%) had nasal congestion.

**Table 1 -** Demographics of cases with COVID-19 according to severity (N=1734).

| Characteristics        | Total<br>n | Covid-19 severity |            |          | P-value |
|------------------------|------------|-------------------|------------|----------|---------|
|                        |            | Mild              | Moderate   | Severe   |         |
| <b>Gender</b>          |            |                   |            |          |         |
| Male                   | 926        | 452 (48.8)        | 445 (48.1) | 29 (3.1) | 0.017   |
| Female                 | 808        | 446 (55.2)        | 346 (42.8) | 16 (2)   |         |
| <b>Nationality</b>     |            |                   |            |          |         |
| Saudi                  | 1564       | 808 (51.3)        | 722 (46.2) | 40 (2.6) | 0.38    |
| Non-Saudi              | 170        | 96 (56.5)         | 69 (40.6)  | 5 (2.9)  |         |
| <b>Age (years)</b>     |            |                   |            |          |         |
| >18                    | 80         | 41 (51.2)         | 36 (45)    | 3 (3.8)  | 0.04    |
| 21-40                  | 1057       | 555 (52.5)        | 480 (45.4) | 22 (2.1) |         |
| 41-60                  | 528        | 265 (50.2)        | 249 (47.2) | 14 (2.7) |         |
| >60                    | 69         | 37 (53.6)         | 26 (37.7)  | 6 (8.7)  |         |
| <b>Smoking</b>         |            |                   |            |          |         |
| Smokers                | 291        | 76 (26.1)         | 194 (66.7) | 21 (7.2) | <0.001  |
| Non-smokers            | 1443       | 822 (57)          | 597 (41.4) | 24 (1.7) |         |
| <b>Chronic disease</b> |            |                   |            |          |         |
| Yes                    | 662        | 327 (49.4)        | 313 (47.3) | 22 (3.3) | 0.134   |
| No                     | 1072       | 571 (53.3)        | 478 (44.6) | 23 (2.1) |         |

Values are presented as number and percentages (%), n: number, COVID-19: coronavirus disease-19

**Table 2 -** Initial presented symptoms in COVID-19 cases (N=1734).

| Symptoms   | n (%)      |
|--|------------|
| <b>Otorhinolaryngological symptoms</b>                                   |            |
| Anosmia  | 269 (15.5) |
| Hyposmia   | 173 (10.0) |
| Loss of taste  | 198 (11.4) |
| Nasal congestion   | 126 (7.3)  |
| Pharyngodynia  | 167 (9.6)  |
| Rhinorrhea   | 83 (4.8)   |
| Sore throat  | 363 (20.9) |
| None   | 80 (4.6)   |
| Anosmia, hyposmia and loss of taste                                      | 275 (15.9) |
| <b>General symptoms</b>  |            |
| None   | 140 (8.1)  |
| Fever  | 362 (20.9) |
| Cough  | 118 (6.8)  |
| Shortness of breath  | 29 (1.7)   |
| Headache   | 47 (2.7)   |
| Myalgia  | 20 (1.2)   |
| Arthralgia   | 8 (0.5)    |
| Fatigue  | 35 (2.0)   |
| Nausea or vomiting   | 18 (1.0)   |
| Abdominal pain   | 2 (0.1)    |
| Diarrhea   | 8 (0.5)    |
| Loss of appetite   | 25 (1.4)   |
| Fever, cough, headache, shortness of breath, muscle pain, and joint pain | 342 (19.7) |
| Headache, muscle pain, joint pain, and fatigue                           | 258 (14.9) |



**Table 3 -** Comparison of ORL symptoms according to severity of COVID-19 (N=1734).

| Symptoms                                 | Severity of COVID-19 |                                    | P-value* |
|--|----------------------|------------------------------------|----------|
|  | Mild (n=898)         | Moderate - severe (n=836)<br>n (%) |          |
| Anosmia                                  | 408 (45.4)           | 393 (47.0)                         | 0.504    |
| Loss of taste                            | 398 (44.3)           | 385 (46.1)                         | 0.451    |
| Waking up at night                       | 348 (38.8)           | 350 (41.9)                         | 0.183    |
| Excessive daytime sleep                  | 337 (37.5)           | 348 (41.6)                         | 0.081    |
| Morning headache                         | 342 (38.1)           | 336 (40.2)                         | 0.399    |
| Sore throat                              | 331 (36.9)           | 322 (38.5)                         | 0.49     |
| Hyposmia                                 | 316 (35.2)           | 313 (37.4)                         | 0.331    |
| Nasal congestion                         | 302 (33.6)           | 297 (35.5)                         | 0.405    |
| Difficulty falling asleep                | 296 (33.0)           | 283 (33.9)                         | 0.685    |
| Sneezing                                 | 255 (28.4)           | 240 (28.7)                         | 0.89     |
| Voice change                             | 260 (29.0)           | 233 (27.9)                         | 0.612    |
| Rhinorrhea                               | 253 (28.2)           | 236 (28.2)                         | 0.909    |
| Foreign body sensation in throat         | 245 (27.3)           | 227 (27.2)                         | 0.95     |
| Hoarseness of voice                      | 231 (25.7)           | 226 (27.0)                         | 0.539    |
| Voice fatigue                            | 235 (26.2)           | 221 (26.4)                         | 0.924    |
| Dizziness                                | 217 (24.2)           | 208 (24.9)                         | 0.69     |
| Breathlessness during speaking           | 215 (23.9)           | 200 (23.9)                         | 0.99     |
| Odynophagia                              | 204 (22.7)           | 197 (23.6)                         | 0.68     |
| Heart burn                               | 190 (21.2)           | 199 (23.8)                         | 0.181    |
| Facial pain/pressure                     | 166 (18.5)           | 173 (20.7)                         | 0.3      |
| Postnasal drip                           | 172 (19.2)           | 161 (19.3)                         | 0.908    |
| Abrupt awakenings accompanied by gasping | 148 (16.5)           | 159 (19.0)                         | 0.161    |
| Dysphagia                                | 145 (16.1)           | 148 (17.7)                         | 0.374    |
| Ear pain pressure                        | 137 (15.3)           | 143 (17.1)                         | 0.301    |
| Loud snoring                             | 112 (12.5)           | 133 (15.9)                         | 0.042    |
| Tinnitus                                 | 106 (11.8)           | 126 (15.1)                         | 0.041    |
| Ear fullness                             | 99 (11.0)            | 100 (12.0)                         | 0.514    |
| Epistaxis                                | 42 (4.7)             | 46 (5.5)                           | 0.39     |
| Loss of voice                            | 40 (4.5)             | 45 (5.4)                           | 0.387    |
| Hearing loss                             | 22 (2.4)             | 47 (5.6)                           | 0.001    |
| Otorrhea                                 | 22 (2.4)             | 23 (2.8)                           | 0.689    |

ORL: otorhinolaryngology, COVID-19: coronavirus disease-19, \*Chi-square test

We also assessed the mode of infection and medication among the recruited patients. It was observed that the main source of infection was close contact with the known COVID-19 infected individuals (46.7%). Other sources included occupational exposure, travel, and contact with a healthcare worker, while the source of infection was unknown for 653 (37.7%) patients.

The majority of the patients reported taking no medication (64.9%).

**Discussion.** Data regarding clinical presentations of the COVID-19 disease caused by the novel SARS-CoV-2 virus which has caused life threatening pandemic is limited. This study was carried out to record the prevalence and type of ORL symptoms of COVID-19

patients and its relation to the infection severity. We also assessed if the onset of these symptoms could be an early predictor of COVID-19. As for the transmission of this virus, the main mode of SARS-CoV-2 transmission is via airborne droplets which are produced by the cough or sneezing of the infected individuals.<sup>10</sup> Along with this, virus also transmits by touching hands to mouth, nose, or eye mucosa after contact with the droplets from the infected person. Therefore, there is high probability of clinical presentation in upper respiratory tract, or we can say that the presence of otolaryngologic symptoms is unavoidable. Approximately 25% of COVID-19 patients might have olfactory dysfunction as the first symptom, which is usually associated with taste dysfunction.<sup>10</sup> Reports from the European region were

**Table 4** - Comparison of otorhinolaryngology symptoms between different age groups (N=1734).

| Symptoms                                 | Age (years) |            | P-value* |
|--|-------------|------------|----------|
|  | ≤40         | >40        |          |
|  | n (%)       |            |          |
| Anosmia                                  | 602 (52.9)  | 199 (33.3) | <0.0001  |
| Loss of taste                            | 575 (50.6)  | 208 (34.8) | <0.0001  |
| Waking up at night                       | 455 (40.0)  | 243 (40.7) | 0.779    |
| Excessive daytime sleep                  | 491 (43.2)  | 194 (32.5) | <0.0001  |
| Morning headache                         | 476 (41.9)  | 202 (33.8) | 0.001    |
| Sore throat                              | 436 (38.3)  | 217 (36.3) | 0.407    |
| Hyposmia                                 | 445 (39.1)  | 184 (30.8) | 0.0006   |
| Nasal congestion                         | 416 (36.6)  | 183 (30.7) | 0.014    |
| Difficulty falling asleep                | 375 (33.0)  | 204 (34.2) | 0.619    |
| Sneezing                                 | 352 (31.0)  | 143 (24.0) | 0.002    |
| Voice change                             | 334 (29.4)  | 159 (26.6) | 0.195    |
| Rhinorrhea                               | 338 (29.7)  | 151 (25.3) | 0.053    |
| Foreign body sensation in throat         | 316 (27.8)  | 156 (26.1) | 0.425    |
| Hoarseness of voice                      | 310 (27.3)  | 147 (24.6) | 0.201    |
| Voice fatigue                            | 290 (25.5)  | 166 (27.8) | 0.279    |
| Dizziness                                | 287 (25.2)  | 138 (23.1) | 0.307    |
| Breathlessness during speaking           | 262 (23.0)  | 153 (25.6) | 0.207    |
| Odynophagia                              | 270 (23.7)  | 131 (21.9) | 0.401    |
| Heart burn                               | 241 (21.2)  | 148 (24.8) | 0.0749   |
| Facial pain/pressure                     | 225 (19.8)  | 114 (19.1) | 0.727    |
| Postnasal drip                           | 217 (19.1)  | 116 (19.4) | 0.88     |
| Abrupt awakenings accompanied by gasping | 193 (17.0)  | 114 (19.1) | 0.256    |
| Dysphagia                                | 189 (16.6)  | 104 (17.4) | 0.703    |
| Ear pain pressure                        | 189 (16.6)  | 91 (15.2)  | 0.426    |
| Loud snoring                             | 125 (11.0)  | 120 (20.1) | <0.0001  |
| Tinnitus                                 | 148 (13.0)  | 84 (14.1)  | 0.503    |
| Ear fullness                             | 134 (11.8)  | 65 (10.9)  | 0.555    |
| Epistaxis                                | 58 (5.1)    | 30 (5.0)   | 0.928    |
| Loss of voice                            | 46 (4.0)    | 39 (6.5)   | 0.021    |
| Hearing loss                             | 35 (3.1)    | 34 (5.7)   | 0.008    |
| Otorrhea                                 | 23 (2.0)    | 22 (3.7)   | 0.032    |

in agreement with our study, where the most common ORL symptoms were chemoreceptor disorders, ranging between 19.4-88%.<sup>12,15,19,20</sup> In contrast, these symptoms were reportedly uncommon in China.<sup>16,21</sup> A recent case series with 72,314 COVID-19 patients in Mainland, China, demonstrated pharyngodynia, nasal congestion, rhinorrhea, and anosmia to be the initial presenting symptoms of COVID-19.<sup>21</sup> Mao et al<sup>22</sup> reported loss of smell in 5.1% and loss of taste in 5.6% of the patients in their study. This clinical discrepancy might be attributed to lower screening frequency of ORL symptoms in the Chinese population, or viral mutation.<sup>15</sup>

As was seen in our study, olfactory/gustatory dysfunction and nasal obstruction were more prevalent in female patients compared to males, which could be

due to the differences in the inflammatory processes between both genders.<sup>17,23,24</sup>

However, Lovato et al<sup>24</sup> showed that the patients commonly presented with pharyngodynia (12.4%), nasal congestion (3.7%), and rhinorrhea (4%). Moreover, a multicentric European study of 417 mild-to-moderate COVID-19 patients reported face pain and nasal obstruction as the most common ORL symptoms, in addition to the olfactory and gustatory dysfunctions.<sup>15</sup>

Our study showed high prevalence of ORL symptoms among COVID-19 patients. Data showed that the ORL symptoms seemed to have direct correlation with age and gender, these symptoms were more frequently observed in young patients, whereas fever, fatigue, and anorexia were usually presented by elderly patients.

**Table 5** - Incidence of otorhinolaryngological symptoms as the only presenting symptoms of COVID-19 (n=70).

| Symptoms         | n (%)     |
|------------------|-----------|
| Anosmia          | 22 (31.4) |
| Hyposmia         | 16 (22.9) |
| Loss of taste    | 1 (1.4)   |
| Nasal congestion | 4 (5.7)   |
| Pharyngodynia    | 5 (7.1)   |
| Rhinorrhea       | 11 (15.7) |
| Sore throat      | 11 (15.7) |

The European Rhinology Society illustrated that loss of smell can be the presenting symptom before other symptoms such as cough and fever.<sup>25</sup>

Similar observations finding were also reported by Lechien et al<sup>15</sup> and Kaye et al.<sup>26</sup> The presentation of ORL symptoms, such as anosmia, hyposmia, loss of taste, and sore throat, were one of the most important findings in this study. Furthermore, in an observational study in Australia, sore throat and runny nose were found to be the most common.<sup>27</sup> Taking olfactory and gustatory dysfunctions into account, a study reported olfactory dysfunction in 68% of COVID-19 patients which was closely correlated with decreased sense of taste.<sup>12</sup> Tong et al<sup>28</sup> reported that the prevalence of olfactory dysfunctions was 52.7% and the prevalence of gustatory dysfunctions was 43.93%. While according to the European Rhinology Society, 20-60% of COVID-19 patients have a loss of smell.

Moreover, Moein et al<sup>29</sup> established that 98% of the COVID-19 patients presented with some type of smell disorders, such as hyposmia (13% mild, 27% moderate, and 33% severe) and anosmia (20%). In a study on 72 patients at the University Hospital of Sassari, hyposmia was observed in 83% and anosmia in 28%. A decreased sense of taste was observed in 46%, while 1% reported complete loss of taste.<sup>30</sup>

Lechien et al<sup>15</sup> demonstrated that olfactory dysfunction to be a crucial symptom of mild to moderate COVID-19 patients was not associated with other rhinological symptoms. While we found no significant correlation between the ORL symptoms and the severity of COVID-19 infection. Interestingly, isolated anosmia without any other symptoms has also been reported across different countries.<sup>18,31</sup> Therefore, patients with sudden anosmia should be tested for SARS-CoV-2 presence and considered as potential individuals with COVID-19.<sup>18,32</sup>

When discussing on SARS-CoV-2 infection, it is important to consider the risk factors associated with it. Females have been shown to be significantly more

affected by olfactory and gustatory dysfunctions than males, possibly due to the gender-related differences in the inflammatory reaction process.<sup>15</sup> Some of the risk factors noted to have direct correlation with severity of COVID-19 infections was age, where individuals  $\geq 65$  years of age were more vulnerable to higher morbidity and mortality. This was in agreement with our data since we found a statistically significant correlation between the severity of COVID-19 and higher age groups ( $p=0.04$ ).<sup>16</sup> Furthermore, we found significant correlation of disease severity with age, male gender, and smoking which were in coherence with data published by many studies.<sup>33,34</sup> In this study, the most frequent comorbidities were diabetes, hypertension, and blood disorders. The comorbidities associated with moderate to severe COVID-19 infection included chronic lung diseases, hypertension, and liver disease. A retrospective study carried out in China revealed hypertension, diabetes, cardiovascular diseases, and malignancy to be the most common comorbidities associated with COVID-19, while it was diabetes and hypertension in another study in Saudi Arabia, and high blood pressure, allergic rhinitis, asthma, and hypothyroidism in Europe.<sup>6,15,35</sup>

Chronic systemic diseases such as morbid obesity, diabetes, lung disease, moderate to severe asthma, kidney disease, and liver disease which have been noted to be associated with severe COVID-19 infections. According to a recent study, hypertension, obesity, and diabetes have been listed as the 3 major underlying conditions that result in particularly unfavorable outcomes in COVID-19 patients, which often led to hospitalization. We had similar findings where lung disease, hypertension, and liver disease were significantly associated with moderate to severe COVID-19 ( $p<0.05$ ). Coronavirus disease-19 can cause multi-organ dysfunction, including kidneys and liver, but mortality is mainly due to the respiratory tract infection by SARS-CoV-2 that leads to severe pneumonia. A previously published report suggested strong correlation between severity of COVID-19 infection and presence of chronic diseases in the infected individuals.<sup>36</sup> Our study showed that sore throat, anosmia, loss of taste, and hyposmia were the most common initial presenting ORL symptoms in COVID-19 patients. Physicians should consider ORL symptoms specifically olfactory dysfunction for the early detection of COVID-19 infection.

**Study limitations.** Firstly, our study has been carried out mainly on mild to moderate COVID-19 patients. So, we cannot generalize the result on all infected population including severe cases. From the

ethical prospective it was difficult to ask severe or life-threatening cases such as patients in intensive care units to fill the questionnaire. Secondly, language barrier as the questionnaire was only in Arabic and English editions so some patients who do not speak either language were unable to be included in the study. All of these weaknesses should be considered in future studies.

In conclusion, identification of patients infected with SARS-CoV-2 through specific clinical presentation is not always possible owing to the unspecific nature of the early symptoms. The present study provided clear evidence that ORL symptoms were prevalent among COVID-19 patients in Saudi Arabia and should be considered for early detection.

As anosmia and loss of taste were the most common ORL symptoms, they can be used for the screening of COVID-19 infections. In addition, physicians should give emphasis to all other ORL symptoms for early detection of the COVID-19. Future epidemiological, clinical, and basic science studies should explain the mechanisms underlying the development of these symptoms in such a specific world population.

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