Otorhinolaryngological manifestations of COVID-19-A systematic review

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Abstract

**Background:** In early December 2019, an outbreak of COVID-19, caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), occurred in Wuhan City, Hubei Province, China causing havoc all over the world. As clinicians, recognition of this disease is necessary to isolate these patients to prevent further human to human transmission. Due to its affinity to the respiratory tract and increased viral load in the nose and throat, we as practising otorhinolaryngologists are at increased risk of exposure to this life-threatening virus and warrants an in-depth knowledge on the symptomatology of this disease. This systematic review is intended to highlight the otorhinolaryngological manifestations of COVID-19.

**Methodology:** The literature search was performed on PubMed database using Boolean operators ‘and’, ‘or’ as “otorhinolaryngological manifestations” or “rhinology” or “otology” or “larynx” or “hearing” or “olfaction” and “covid19” or “novel corona virus” or “SARS-CoV” with filters as ‘2020’ year of study on 7/08/2020 at 11:30 Am.

**Review Results:** Total of 357 articles were obtained on search and the final 12 articles extracted based on our selection criteria were reviewed. The studies included 6825 laboratory confirmed COVID-19 patients with varying severity of disease. Olfactory dysfunction and taste dysfunction were noted in 2355 and 2224 patients respectively. Nasal obstruction was reported in 323 patients and sore throat in 261 patients. Rhinorrhoea was reported in 209 patients. 158 patients complained of post nasal drip and 152 patients presented with facial pain.

**Conclusion:** As a practising otorhinolaryngologist, a good insight into the otorhinolaryngological manifestations of COVID-19 is essential to differentiate between the prodromal symptoms of COVID-19 and non-COVID viral upper respiratory tract infection.

**Background**

Coronaviruses are enveloped positive stranded RNA viruses belonging to the family Coronaviridae and the order Nidovirales, with spikes on its surface giving it a crown like ultrastructural appearance; hence was named coronavirus. The 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as it is now called, has swiftly spread from its origin in Wuhan City of China to all around the globe. As on 14/09/2020 there has been 29 million cases with reported deaths around 9,25,000 worldwide. India ranks second in the case burden with 4.85 million cases and 79,722 deaths till then.

The incubation period for COVID-19 is believed to reach 14 days, nevertheless, most of the patients develop symptoms of COVID-19 disease after 4–5 days post infection. COVID-19 remains contagious even during the incubation period, thus patients before clinical COVID-19 presentation can spread the virus to others. Infection with 2019-nCoV presents with non-specific features such as malaise, fever, and dry cough at the prodromal phase. Symptoms of COVID-19 ranges from no symptoms, mild upper respiratory tract infection to very severe lower respiratory tract infection with bilateral lung infiltrates. Despite respiratory symptoms, COVID-19 presents with a plethora of other systemic features.

Due to its affinity to the respiratory tract, we as practising otorhinolaryngologists are at increased risk of exposure to this life-threatening virus and demands an in-depth knowledge on the symptomatology of this disease. This systematic review is intended to highlight the otorhinolaryngological manifestations of COVID-19.

**Methodology**

Search strategy and selection criteria: The literature search was performed on PubMed database using Boolean operators ‘and’, ‘or’ as “otorhinolaryngological manifestations” or “rhinology” or “otology” or “larynx” or “hearing” or “olfaction” and “covid19” or “novel corona virus” or “SARS-CoV” with filters as ‘2020’ year of study. There were no restrictions on the language of articles published. After eliminating duplicates, three investigators independently reviewed all article title: the full texts of articles considered as eligible for review were extracted for further analysis. Thereafter, eligible articles were selected for final analysis according to predefined inclusion and exclusion criteria. Difference of opinion between the authors were solved by consensus. We included only human studies and articles with clearly defined clinical outcome. The exclusion criteria included animal studies, single case reports and review articles. The search was performed at specified date and time on 7/08/2020 at 11.30 Am.

**Results**

Total of 357 studies were obtained on PubMed database search, out of which 329 studies were excluded after checking the relevance of title. Full text article of the remaining 28 articles were read thoroughly and 16 out of them were excluded due to various reasons (two studies were guidelines for otorhinolaryngological practice, seven studies were review articles, were related to anosmia in COVID era in patients not confirmed with COVID infection, one study was on recovery of anosmia post-COVID, three studies were case reports and one another study was on the pathophysiology of anosmia in COVID). Search was done strictly adhering to the PRISMA guidelines, as depicted in Chart 1.

We reviewed the final 12 articles based on our selection criteria to extract the following information from each: first author, study design, number of patients, demographic data of study population, otorhinolaryngological manifestations of COVID 19 and drawbacks of study if any. The studies included for this review collectively included 6825 laboratory confirmed COVID-19 patients with varying severity of disease. The extracted data is jotted in Table 1.

4123 females and 2647 males were included (gender distribution was not elaborated in two studies). Olfactory dysfunction and taste dysfunction was noted in 2355 and 2224 patients respectively. In the studies performed by Lauren T Roland et al and Antje Haehner et al Anosmia or ageusia were reported in 95 and 22 patients respectively. Nasal obstruction was reported in 323 patients followed by next common symptom sore throat in 261 patients. Rhinorrhoea was
Discussion

In most of the studies included in our review females were most commonly affected than males. Most of the available literature suggest a contrary observation indicating males have more susceptibility that females due to the fact that there are many differences between men and women in the immune response to Covid-19 infection. Women, compared to men, are less prone to viral infections based on a different innate immunity, steroid hormones and factors related to sex chromosomes. The presence of two X chromosomes in women emphasizes the immune system even if one is inactive. The immune regulatory genes encoded by X chromosome in female gender causes lower viral load levels, and less inflammation than in man, while CD4+ T cells are higher with better immune response. In addition, women generally produce higher levels of antibodies which remain in the circulation longer.13

COVID-19 and its relation with olfactory and gustatory dysfunction is a well-known fact and there have been abundant literature on the same. Olfactory and gustatory dysfunction are more prevalent in patients with mild to moderate disease probably due to the fact that in patients with severe disease these symptoms are commonly overlooked and less reported. In our review we noted that anosmia and ageusia are the most common otorhinolaryngological manifestation of COVID-19.

Due to the affinity of coronavirus towards upper respiratory mucosa, nasal obstruction seems to be a common symptom next only to anosmia and ageusia. Rhinorrhea and sore throat are common observations in patients with COVID-19 infection. The prodromal symptoms of COVID 19 infection and non COVID Upper respiratory viral infection include nasal obstruction and sore throat, therefore differentiating between both becomes a challenging task. Hence at our institution we have a flu OPD (with necessary safety precautions), where patients with URI and Pharyngitis (sore throat) undergo thermal screening, vitals assessment, Chest X ray and rapid antigen testing to rule out COVID-19 infection. After ruling out COVID-19 infection patient is referred to Otorhinolaryngologist for definitive management. This practise ensures safety at workplace for Otorhinolaryngologist in routine OPD and similar practise is recommended by the authors.

Facial pain and post nasal drip were recorded in 152 and 158 patients respectively, in the study performed by Jerome R. Lechien et al2 indicating that sinusitis frequently occurs in concordance with COVID-19 infection, other studies included in our review did not indicate such association. This indicates that there is a lacuna in literature regarding the incidence of sinusitis in COVID-19 patients. Sneezing was not reported in any of the included study.

Otological symptoms seems to be less common in COVID-19 patients. In the study performed by Jerome R. Lechien et al2 ear pain was documented in 61 patients. In the study performed by Mustafa et al7, they observed that the high frequency pure-tone thresholds as well as the TEOAE amplitudes were significantly worse in the test group. The results of their study showed that COVID-19 infection had deleterious effects on the hair cell of cochlea. The drawback of this particular study is the small cohort. In a case reported by Osman Kilic et al14 they noted sudden sensorineural hearing loss in a 29-year-old patient. Studies on large population is required to confirm the deleterious effect of COVID-19 infection on the hair cells of cochlea.

Conclusion

As a practising otorhinolaryngologist, a good insight into the otorhinolaryngological manifestations of COVID-19 is essential to differentiate between the prodromal symptoms of COVID-19 and non-COVID viral upper respiratory tract infection. Patients of COVID-19 tend to frequently present with anosmia and ageusia which is common in mild to moderately severe disease. Despite this, frequently they present with nasal obstruction, sore throat, rhinorrhea, postnasal drip, facial pain, nasal congestion and ear pain in decreasing order of frequency.

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Tables

Table 1: Comprehensive data obtained from the studies included
| SR.NO | FIRST AUTHOR | STUDY DESIGN | STUDY POPULATION | NUMBER OF PATIENTS | AGE | GENDER | OTORHINOLARYNGOLOGICAL MANIFESTATIONS | DRAWBACKS |
|-------|--------------|--------------|------------------|-------------------|-----|--------|--------------------------------------|-----------|
| 1     | Yonghyun Lee et al | Prospective | Korean           | 3191              | 36.5 years (24.5–54) | Females 2030 (68.9%) | Anosmia and aguesia 254 (8%) | Study included asymptomatic disease patients who did not report anosmia. |
|       |              |              |                  |                   |     | Males 1161 (31.1%) | Anosmia only 135 (4.2%) | Aguesia only 99 (3.1) |
| 2     | Jerome R. Lechien et al | Prospective | European | 417              | 36.9±11.4 years (19–77) | Females 263 (63.1%) | Out of 417, patients 357 (85.6%) of factory dysfunction. 284 (79.6%) patients were anosmic, 73 (20.4%) were hyposmic, phantosmia (12.6%) and parosmia (32.4%). | Study included patients >18 yrs. The otorhinolaryngological symptoms were graded or related to the disease. Patients were presented with various symptoms such as anosmia, hyposmia, hyperosmia, and parosmia. |
|       |              |              |                  |                   |     | Males 154 (36.9%) | Aguesia only 135 (4.2%) | Out of 417 patients, 342 patients (88.8%) reported gustatory disorders, reduced or discontinued (78.9%) or distorted ability (21.1%) to taste flavors. |
|       |              |              |                  |                   |     |                  | Nasal obstruction 194 (46.5%), Rhinorrhea 139 (33.3%), Postnasal drip 116 (27.8%), Sore throat 128 (30.7%), Face pain/heaviness 152 (36.5%), Ear pain 61 (14.6%), Dysphagia 42 (10.1%), Dyspnea 115 (27.6%) | Study included patients >18 yrs. The otorhinolaryngological symptoms were graded or related to the disease. Patients were presented with various symptoms such as anosmia, hyposmia, hyperosmia, and parosmia. |
| 3     | Carol H. Yan et al | Cross-sectional | Americans | 59              | 18–79 Years | Females 29 (49.2%) | Ageusia 42 (71%), Anosmia 40 (68%) | Short symptom at single location. The subjective assessment of smell and taste impairment was ruled out. |
|       |              |              |                  |                   |     | Males 29 (49.2%) | Nasal obstruction 28 (47.5%), sore throat 19 (32.2%), Rhinorrhea 18 (30.5%) | Further symptom surveys after COVID-19 infection were not included. |
|       |              |              |                  |                   |     | Transgender 1 (1.6%) |                  | Short symptom at single location. The subjective assessment of smell and taste impairment was ruled out. |
| 4     | Lauren T. Roland et al | Cross-sectional | Americans | 145             | 40±13 years | Females 94 (64.8%) | Change in smell/taste 95 (66.6%), Sore throat 59 (41%), Nasal congestion 69 (47%), Rhinorrhea 52 (36%), Dysphagia 50 (34%) | Study included patients >18 yrs. The subjective assessment of smell and taste impairment was ruled out. |
|       |              |              |                  |                   |     | Males 51 (35.2%) |                  | Further symptom surveys after COVID-19 infection were not included. |
| 5     | Carol H. Yan et al | Retrospective | Americans | 128 (26 admitted and 102 ambulatory) | 53.5 years (40–65) | Admitted patients | Anosmia/hyposmia 7 (26.9%) admitted vs 68 (66.7%) ambulatory and dysgeusia 6 (23.1%) admitted vs 64 (62.7%) ambulatory | Focuses on moderate patients. Studies a better extent to anosmia overall diagnosis. |
|       |              |              |                  |                   |     | 43 years (34–54) | Sore throat 9 (34.6%) admitted vs 46 (48.1%) ambulatory | Further symptom surveys after COVID-19 infection were not included. |
|       |              |              |                  |                   |     | Ambulatory patients |                  | Further symptom surveys after COVID-19 infection were not included. |
|       |              |              |                  |                   |     | Females 50 (49%) |                  | Further symptom surveys after COVID-19 infection were not included. |
|       |              |              |                  |                   |     | Males 52 (51%) |                  | Further symptom surveys after COVID-19 infection were not included. |
| Study Authors            | Study Type                      | Country | Duration | Age       | Sex Ratio (Female:Male) | Symptoms Descriptions                                                                 |
|-------------------------|---------------------------------|---------|----------|-----------|------------------------|--------------------------------------------------------------------------------------|
| Valeria Dell’Era et al  | Prospective, cross-sectional    | Italians| 51 years | 49 years  | Females:163 (45.9%) : Males:192 (54.1%) | Olfactory symptoms 49 years (40-60); Taste symptoms 51 years (51-60)                  |
| Mustafa et al           | Prospective, cross-sectional    | Egypt   | 20 years | 20-50 years| Females:163 (45.9%) : Males:192 (54.1%) | The high frequency pure-tone thresholds as well as the TEOAE amplitudes were significantly worse in the test group. The results of the current study showed that COVID-19 infection had deleterious effects on the hair cell of cochlea. |
| Marlene M. Speth et al  | Prospective, cross-sectional    | Americans| 103 years| 46.8 ± 15.9 years | Females:53 (51.5%) : Males:50 (48.5%) | Olfactory Dysfunction 63(61.2%), Gustatory Dysfunction 67(65%), Nasal Obstruction 51(49.5%), Mucus Production 36(35%). |
| Antje Haehner et al     | Prospective, cross-sectional    | German  | 34 years | 41.7 ± 11.8 years | Females:56 (65.1%) : Males:30 (34.9%) | Sudden smell and taste loss 22(64.7%). URTI patients study of which 32% positive details are reported. |
| Radoslaw Sierpinski et al| Cross sectional survey          | Poland  | 1942 years| 50 years | Females:1169 (60.2%) : Males:773 (39.8%) | Olfactory disorder 956 (49.2%), Taste disorder 923 (47.5%). Self-reported questionnaires (risk of patients to interpret smell and knowledge diagnosis ruled out). |
| Jerome R. Lechien et al | Prospective                      | Europeans| 86 years | 41.7 ± 11.8 years | Females:56 (65.1%) : Males:30 (34.9%) | Nasal Obstruction 50 (58.6%), Postnasal drip 42 (48.6%), Dysgeusia 40 (47.1%). Self-reported questionnaires (risk of patients to interpret smell and knowledge diagnosis ruled out). |
| Luigi Angelo Vaira et al| Prospective                      | Italians| 345 years| 48.5 ± 12.8 years (23-88) | Females:199 (57.7%) : Males:146 (42.3%) | Olfactory function Normal 104 (30.1%) Mild Hyposmia 76 (22%), Moderate Hyposmia 59 (17.1%), Severe Hyposmia 45 (13%), Anosmia 61 (17.7%). Gustatory function Normal 190 (55.1%) Mild Hypoguesia 78 (22.6%). Moderate Hypoguesia 25 (7.2%), Severe Hypoguesia 16 (4.6%), Ageusia 36 (10.4%). Part of the report. |
| Sr.No | First Author                          | Total number of patients | Males | Females | Olfactory dysfunction | Taste Dysfunction | Nasal obstruction | Rhinorrhea | Sore throat | Nasal congestion | Mucus production | Far pai |
|-------|--------------------------------------|--------------------------|-------|---------|-----------------------|-------------------|-------------------|------------|-------------|-------------------|------------------|--------|
| 1     | Yonghyun Lee et al\(^1\)            | 3191                     | 1161  | 2030    | 389                   | 353               | -                 | -          | -           | -                 | -                |        |
| 2     | Jerome R. Lechien et al\(^2\)      | 417                      | 154   | 263     | 357                   | 342               | 194               | 139        | 128         | -                 | -                | 15:    |
| 3     | Carol H. Yan et al\(^3\)           | 59                       | 29    | 29       | 40                    | 42                | 28                | 18         | 19          | -                 | -                |        |
| 4     | Lauren T. Roland et al\(^4\)       | 145                      | 51    | 94       | Anosmia/Ageusia 95    | -                 | 52                | 59         | 68          | -                 | -                |        |
| 5     | Carol H. Yan et al\(^5\)           | 128                      | 61    | 67       | 75                    | 70                | -                 | -          | 55          | -                 | -                |        |
| 6     | Valeria Dell’Era et al\(^6\)       | 355                      | 192   | 163     | 234                   | 232               | -                 | -          | -           | -                 | -                |        |
| 7     | Mustafa et al\(^7\)                | 20                       | -     | -        | -                     | -                 | -                 | -          | -           | -                 | -                |        |
| 8     | Marlene M. Speth et al\(^8\)       | 103                      | 50    | 53       | 63                    | 67                | 51                | -          | -           | -                 | 36               |        |
| 9     | Antje Haehner et al\(^9\)          | 34                       | -     | -        | -                     | -                 | -                 | -          | -           | -                 | -                |        |
| 10    | Radoslaw Sierpinski et al\(^10\)   | 1942                     | 773   | 1169     | 956                   | 923               | -                 | -          | -           | -                 | -                |        |
| 11    | Jerome R. Lechien et al\(^11\)     | 86                       | 30    | 56       | -                     | 40                | 50                | -          | -           | -                 | -                |        |
| 12    | Luigi Angelo Vaira et al\(^12\)    | 345                      | 146   | 199      | 241                   | 155               | -                 | -          | -           | -                 | -                |        |
|       | Total                               | 6825                     | 2647  | 4123     | 2355                  | 2224              | 323               | 209        | 261         | 68                | 36               | 15:    |

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