

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 corona virus 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, 2 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 al⁴ and Antje Haehner et al⁹ 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

reported in 209 patients. 158 patients complained of post nasal drip and 152 patients presented with facial pain. Dysphagia was reported by 42 patients and 61 patients had ear pain. Mucus production was one of the presenting symptoms in 36 patients. Table 2.

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 than 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. Rhinorrhoea 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, rhinorrhoea, 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	DRAWBA STUDY
1	Yonghyun Lee et al ¹	Prospective	Korean	3191	36.5 years(24.5-54)	Females 2030(68.9%) Males 1161(31.1%)	Anosmia and aguesia 254(8%) Anosmia only 135(4.2%) Aguesia only 99(3.1%)	Study inc asymptomatic disease study was anosmia
2	Jerome R. Lechien et al ²	Prospective	European	417	36.9±11.4 years (19-77)	Females 263 (63.1%) Males 154(36.9%)	Out of 417, patients 357 (85.6%) olfactory dysfunction. 284 (79.6%) patients were anosmic, 73 (20.4%) were hyposmic, phantosmia(12.6%) and parosmia(32.4%). Out of 417 patients ,342 patients (88.8%) reported gustatory disorders, reduced /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 inc to-moderate patients >18yrs. The otorhinolaryngological symptom graded or related to infection. present in patients with otorhinolaryngological symptom to COVID not included
3	Carol H. Yan et al ³	cross-sectional study	Americans	59	18-79 Years	Females 29(49.2%) Males 29 (49.2%) Transgender 1(1.6%)	Ageusia 42 (71%), Anosmia 40(68%) Nasal obstruction 28(47.5%), sore throat 19(32.2%), Rhinorrhea 18(30.5%)	Short survey at a single point in time as well as subjective assessment determine impairment. Further surveying after COVID risk of poor interpretation of smell and taste through t knowledge diagnosis recall bias in the comprehensive reports of related are cannot be
4	Lauren T. Roland et al ⁴	cross-sectional study	Americans	145	40±13 years	Females 94(64.8%) Males 51(35.2%)	Change in smell/taste 95(66%),sore throat 59(41%),nasal congestion 68(47%), Rhinorrhoea 52(36%),Dyspnoea 50(34%)	Study inc patients <18 years and question based (risk interpretation smell and taste through t knowledge diagnosis ruled out)
5	Carol H. Yan et al ⁵	Retrospective study	Americans	128(26 admitted and 102 ambulatory)	53.5 years (40-65) admitted 43 years (34-54) ambulatory	Admitted patients Females 17(65.4%) Males 9(34.6%) Ambulatory patients Females 50(49%) Males 52(51%)	Anosmia/hyposmia 7(26.9%)admitted vs 68 (66.7%)ambulatory and dysgeusia 6(23.1%)admitted vs 64(62.7%)ambulatory Sore throat 9(34.6%) admitted vs 46(45.1%)ambulatory	Focuses on moderate patients. studies a better detection extent to anosmia overall trajectory

6	Valeria Dell'Era et al ⁶	cross-sectional study	Italians	355	Olfactory symptoms 49 years (40-60) Taste symptoms 51 years (51-60)	Females 163(45.9%) Males 192(54.1) Olfactory dysfunction Females 115(48.5%) Males 122(51.5%) Taste Dysfunction Females 122(52.6%) Males 110(47.4%)	Olfactory symptoms 234(66%), taste disorders 232(65.4%)	The olfactory and gustatory symptoms were subjects of a study that was not performed by endoscopy/specific anosmia over the period in center.	
7	Mustafa et al ⁷	Prospective study	Egypt	20	20-50 years			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	Study was conducted on a small number of COVID positive asymptomatic patients.
8	Marlene M. Speth et al ⁸	Prospective, cross-sectional	Americans	103	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%).	Studied symptoms reports in patient demographic data related to COVID-19 infection with infection to apply to olfactory	
9	Antje Haehner et al ⁹	Prospective, cross-sectional	German	34				Sudden smell and taste loss 22(64.7%)	URTI patient study of a testing center which 32 positive (76%) details are described in symptom patients & described
10	Radoslaw sierpinski et al ¹⁰	Cross sectional survey	Poland	1942	50 years	Females 1169(60.2%) Males 773(39.8%)	Olfactory disorder 956(49.2%) Taste disorder 923(47.5%)	Questionnaire (risk of poor interpretation smell and taste through the knowledge diagnosis ruled out)	
11	Jerome R. Lechien et al ¹¹	Prospective	Europeans	86	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 questionnaire (risk of poor interpretation smell and taste through the knowledge diagnosis ruled out)	
12	Luigi Angelo Vaira et al ¹²	Prospective	Italians	345	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 hypogeusia 78 (22.6%) Moderate hypogeusia 25 (7.2%), Severe hypogeusia 16 (4.6%) Ageusia 36 (10.4%)	Part of the reported symptoms were not recorded in the hospital records of the personnel	

Table 2: Number of patients with various otorhinolaryngological symptoms from the included studies.

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			Anosmia/Ageusia 22		-	-	-	-	-	-
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

Supplementary Files

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- [PRISMA2009FlowDiagram.doc](#)