

A clinical observation of otorhinolaryngological manifestations in post covid-19 patients

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Abstract

Background & objective: COVID-19 disease caused by the Novel severe acute respiratory syndrome corona virus-2 (SARS-CoV2) is causing a World-wide health crisis since 2020. Nose, nasopharynx, oropharynx are the major sites where SARS-CoV2 virus harbours and act as the source of transmission, various ENT related post-COVID manifestations are being observed every now and then. We conducted this study with the aim of observing ear, nose, throat manifestations in post-COVID patients. **method:** We conducted an Observational study on 136 patients, who came to our outpatient department, Department of otorhinolaryngology & Head and neck surgery, Rajendra Institute of Medical Sciences, Ranchi fulfilling the inclusion and exclusion criteria. They were observed for the period of 6 months. For all the patients, detailed history taking and physical examination done. All the patients were investigated according to their presenting complaint and they were analysed. **Results:** In our study males (88, 65%) were the most common to develop post-ENT manifestations. The most common affected age group was 41-50 years (48, 35%). Among these 136 patients, 20(15%), 51(37%), 33(24%) and 32(24%) patients developed Ear, Nose, Throat and multiple manifestations respectively. The most common symptom was Headache seen in 22(16%) patients while least common was the Tinnitus noted in 1(1%) patient. Ear manifestations include Sensorineural hearing loss (11, 8%), conductive hearing loss (4, 3%), otitis media with effusion (4, 3%) and tinnitus (1, 1%). The nose & paranasal sinus manifestations include Headache (22, 16%), dryness of nose (14, 10%), olfactory dysfunction (12, 9%) and epistaxis (3, 2%). The larynx and pharyngeal manifestation include dryness of mouth (11, 8%), Sore throat (5, 4%), Gustatory dysfunction (5, 4%), LPR (4, 3%), Vocal cord palsy (3, 2%), Aphthous ulcer (3, 2%) and oral candidiasis (2, 1%). **Conclusion:** In our study observed that nose and paranasal sinuses manifestation were the most common ENT manifestation among post-COVID-19 infected patients. It is being observed in our day-to-day practice post-COVID ENT manifestations are increasing. Hence, further detailed study on this subject is necessary for better understanding of these manifestations and their management.

Keywords: Post-COVID manifestations, ENT manifestations, COVID-19, SARS-CoV2 virus, ACE2 receptors.

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Introduction

COVID-19 disease caused by the Novel severe acute respiratory syndrome corona virus-2 (SARS-CoV2) is causing a World-wide health crisis since 2020. SARS-CoV2 viruses are single stranded RNA virus which comes the family of *coronaviridae* [1]. This virus has great affinity for Angiotensin-converting enzyme 2 (ACE2) receptors which is seen on different human organs. They enter the human body mainly via nose where the virus activating ACE2 receptors & TMPRSS2 Protease are found abundantly in nasal goblet and ciliated cells [2]. Most of the COVID-19 patients presented with the lower respiratory tract symptoms (cough, shortness of breath) as they are transmitted by droplets. Due to its tropism towards ACE2 receptors multiple organs are involved such as Cardiovascular system (acute MI, Heart failure, endotheliopathy), Nervous system (cytokine-mediated brain damage, cerebrovascular disease), haematological manifestation (lymphopenia, blood hypercoagulopathy), Gastrointestinal system (diarrhoea, vomiting), endocrine system (cortisol insufficiency) and Skeletal system

(myalgia) [3]. ENT manifestations have also been noted during infection such as sore throat, headache, loss of smell, tonsillar enlargement, pharyngeal oedema, nasal congestion [4]. Not only during infection, many individuals have experienced persistent symptoms and a decline in health-related quality of life during post-COVID recovery period [5] for more than three weeks after the diagnosis which is known as Post-COVID syndrome. Numerous studies on post-COVID manifestation such as thromboembolic event leading to stroke, myocardial infarction and myalgia, cognitive impairment, worsening on diabetes etc are available. As nose, nasopharynx, oropharynx are the major sites where SARS-CoV2 virus harbours and act as the source of transmission, various ENT related post-COVID manifestations are being observed every now and then. Only very few literatures on post-COVID ENT manifestations are subject available. Thus, we conducted this study with the aim of observing ear, nose, throat manifestations in post-COVID patients.

Material & methodology

This observational study was conducted on patient attending the ENT OPD who were fulfilling mentioned criteria over a period of 6 months started from October 1st 2020 to March 31st 2021. During this 6 months, 136 post-COVID patients were observed. The following data were collected on the patient presenting complaint, past history, treatment history related to the COVID-19 infection and ear, nose, throat examination will be done. According to the presenting

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complaint, patient was evaluated. For patient with ear symptoms, examination with otoscope, microscope done. In case of hearing loss Pure tone audiometry and Impedance audiometry was done. For patient with nose and PNS symptoms, Anterior rhinoscopy, DNE and

imaging study of PNS were done. Oral cavity examination, direct and indirect laryngoscopic examination were done for patient with throat complaints. Then all the data were analysed.

Table 1: Inclusion and exclusion criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
✓ Age ≥ 18 yr ≤ 70 yr	✓ Age < 18 yr > 70 yr
✓ ≥ 2 weeks from turning negative on RT-PCR for COVID-19 infection	✓ < 2 weeks on turning negative on RTPCR for COVID-19 infection
✓ Patient willing to give consent for study	✓ Patient symptoms persisting in the past before the COVID-19 infection
	✓ Patient refuses to give consent

Results

In our study 136 patients had ENT symptoms during their post-COVID period. Among the 136 patients 88(65%) and 48(35%) patients are male and female respectively which is depicted in the Fig 1. Most age group to get affected was between 41-50 years. The age distribution was tabulated in the Table 1.

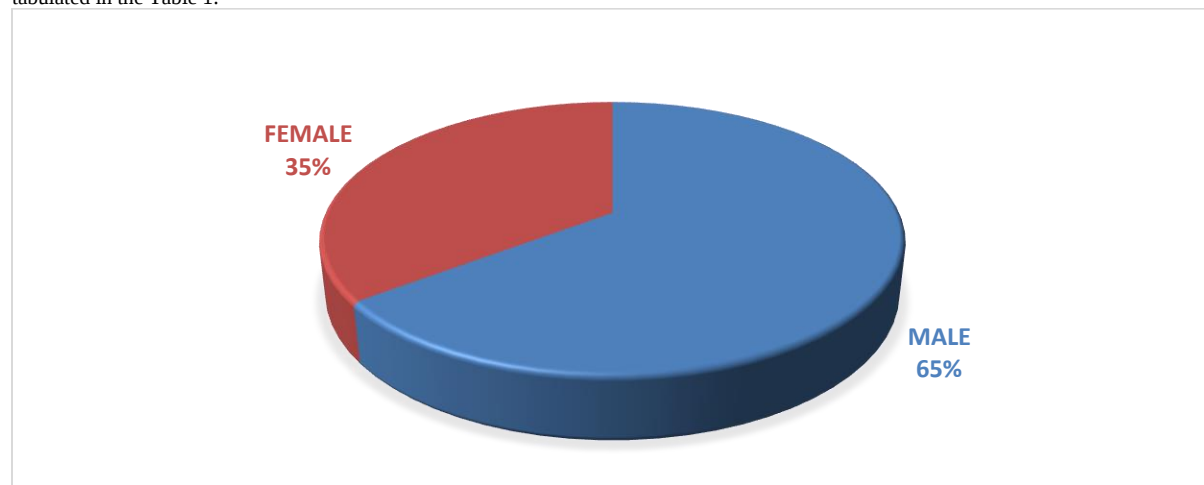


Fig 1: Gender distribution

Table 1: Age Distribution of patients

AGE GROUP	No. OF PATIENTS(n)	PERCENTAGE (%)
18-30	12	9
31-40	27	20
41-50	48	35
51-60	35	26
>60	14	10

Among the ENT manifestations which are tabulated in Table 2, Nose and paranasal sinuses manifestations were most common ones observed in 51(37%) patients. The most symptom was the headache seen in 22(16%) patients. Second most common was the dryness of nose which was observed in 14(10%). The least common was the Tinnitus seen in 1(1%) patient followed by oral candidiasis in 2(1%) patients. About 32(24%) patients had multiple ENT complaints. Fig 2 showing the Ear, nose, throat manifestation distribution.

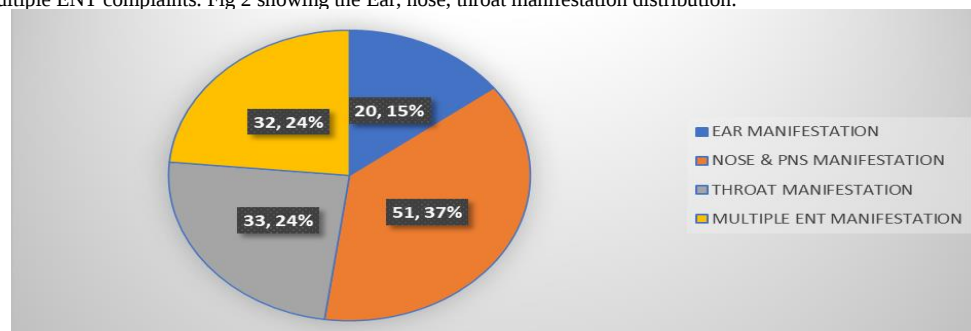


Fig 2: ENT Manifestation distribution

Table 2: ENT Manifestations

ENT MANIFESTATION	NO OF PATIENTS (PERCENTAGE)
EAR:	20(15%)
Sensorineural hearing loss	11(8%)
Conductive hearing loss	4(3%)
Otitis media with effusion	4(3%)
Tinnitus	1(1%)
NOSE & PARANASAL SINUSES:	51(37%)
Headache	22(16%)
Dryness of nose	14(10%)
Olfactory dysfunction	12(9%)
Epistaxis	3(2%)
PHARYNX, LARYNX & ORAL CAVITY:	33(24%)
Dryness of mouth	11(8%)
Gustatory dysfunction	5(4%)
Sore throat	5(4%)
Foreign body sensation in throat	4(3%)
Aphthous ulcer	3(2%)
Vocal cord palsy	3(2%)
Oral candidiasis	2(1%)
MULTIPLE ENT MANIFESTATION	32(24%)

Ear manifestations: The most common ear manifestation was the hearing loss seen in about 15 patients. Among them 11 (8%) patient had sensorineural hearing loss and 4(3%) patient had conductive hearing loss secondary to the middle ear infection. Then 4(3%) patients had otitis media with effusion. 1 (1%) patient had tinnitus. The aural manifestations were represented in the Fig 3.

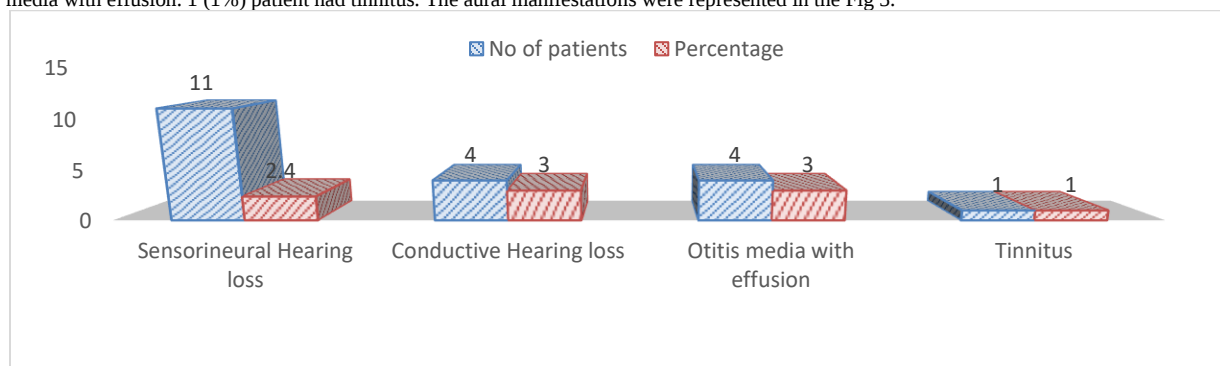


Fig 3: Ear manifestations

Nose & paranasal sinuses manifestations: 22(16%) patients presented with headache to us. Among these 22 patients, 16(73%) patients diagnosed to have Sinusitis, 3(14%) diagnosed with hypertension, 2(9%) had headache due to neurological and remaining 1(4%) cause couldn't be ruled out. The most sinus to get involved was Maxillary sinus in patients with sinusitis. About 14(10%) patients presented with dryness of Nose. About 12(9%) patients had olfactory dysfunction of hyposmia and anosmia. Epistaxis was also noted in 3(2%) patients. The nose and paranasal sinus manifestation are depicted in the Fig 4.

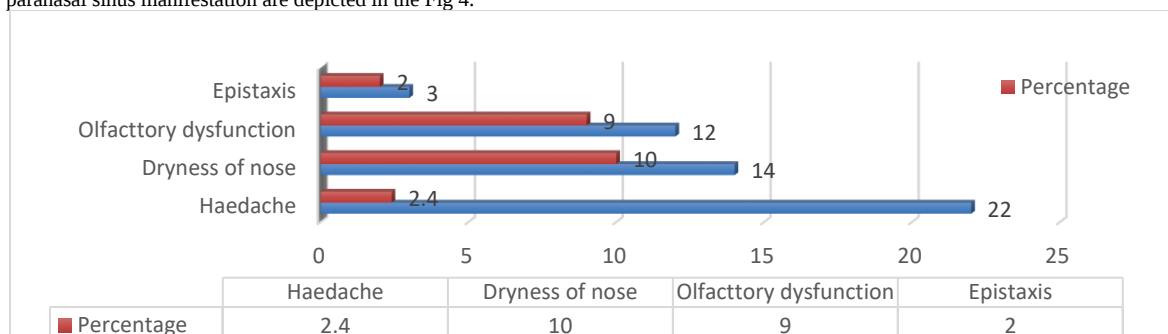


Fig 4: Nose and paranasal sinuses manifestations

Larynx, pharynx & oral cavity manifestations: Among the 33(24%) patients with laryngeal and pharyngeal manifestation represented in Fig 5, dryness of mouth(11, 8%) was the most common symptom. Gustatory dysfunction and Sore throat were noted on 5(4%) patients each. 4(3%) patients presented with foreign body sensation in throat were found to have Laryngo-pharyngeal reflux disease(LPRD). Vocal cord palsy was noted on 3(2%) patients. Painful oral ulcer (aphthous ulcer) was noted on 3(2%) patients and 2(1%) patients had Oral Candidiasis.

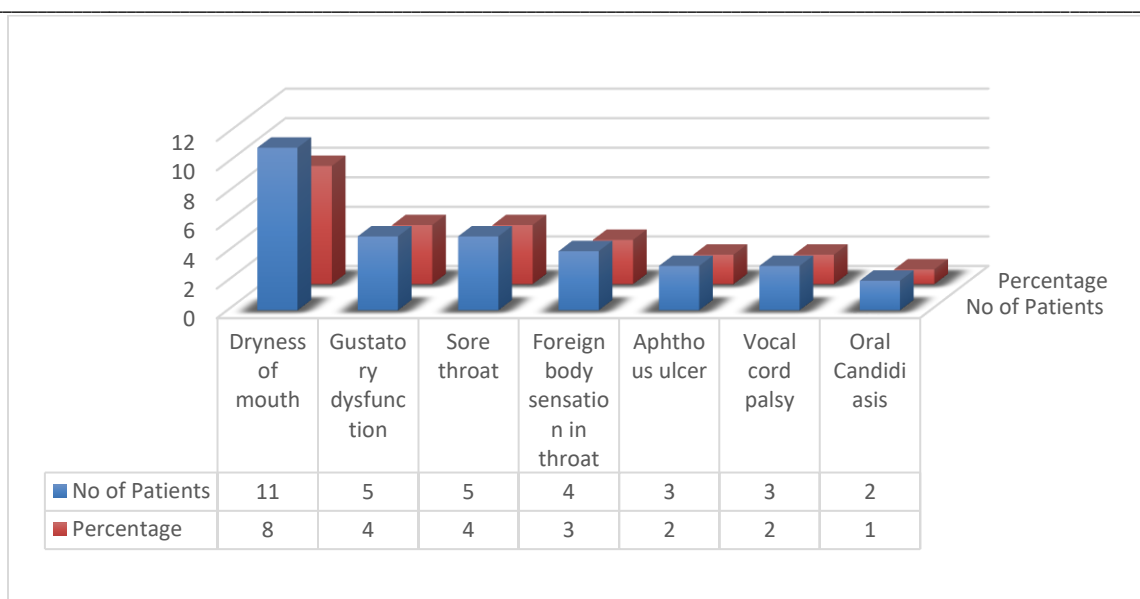


Fig 5: Larynx, pharynx and oral manifestations

Discussion

Novel coronavirus (2019-nCoV) outbreak started by the end of 2019. It belonged to the class of SARS-related coronavirus as they are highly contagious and enter via the ACE-2 (Angiotensin-converting enzyme 2) receptors [6]. This ACE2 receptors are expressed in most of the human organs. But they are strongly expressed in Type II alveolar epithelial cells while weakly in the oral, nasal mucosa and nasopharynx [7]. Due to this most of COVID-19 infected patients present with lower respiratory tract symptoms than the upper respiratory symptoms. In this study we discussing about the ENT manifestation among post-COVID-19 infected patients. In our study, male (88, 65%) were common to have ENT manifestation than Female (48, 35%). This might be because of the reason that the prevalence of COVID-19 infection had male predominance [8] as they have higher plasma level of ACE2 than female [9]. Age group between 41-50 years were common age group to be involved in our study with 48 (35%) patients. In our study group, hearing loss (15, 11%) is the most common ear manifestation. Sensorineural hearing loss (11, 8%) was the most type of hearing loss and 4 (3%) patients had conductive hearing loss secondary to middle ear infection. The probable pathogenesis of hearing loss could be virus induced, immune-complex mediated, cellular stress response or vascular occlusion [10]. Other postulated etiopathogenesis for SARS-CoV2 virus were inflammatory response on Cochlear hair cell and hearing centres such as medulla oblongata, temporal lobe due to the presence of ACE2 receptors [11]. Likely cause for conductive hearing loss secondary to Otitis media with effusion is ascending nasopharyngeal infection to middle ear [12]. This ascending nasopharyngeal infection also explains the otitis media with effusion which was noted on 4 (3%) patients. In a study conducted by Chirakkal et al, stated that COVID-19 had deleterious effect on Cochlear outer hair cells [13]. This could have led to the symptom of tinnitus in COVID-19 infected patients. Tinnitus was observed in 1 (1%) patient which was least common manifestation among our study group. Among the nose and Paranasal sinuses related symptoms, most common symptom during the post-COVID infection was headache (22, 16%). Out of these 22 patients 16 (73%) patients diagnosed have Sinusitis. Sinusitis possibly because of secondary upper respiratory congestion leading to the impaired muco-ciliary clearance, secondary sinus ostium obstruction [14]. Maxillary sinus was found to be the most common affected sinus among our study population. Olfactory dysfunction

was noted on 12 (9%) patients might be secondary to the damage of olfactory receptor. The mechanism behind the olfactory receptor neuron damage is ACE2- independent virus transfer via olfactory ensheathing glial cell by exosomes [15]. Most of the patient have temporary olfactory dysfunction as olfactory epithelium can regenerate over time if stem cell layer is not damaged [16].

About 14 (10%) patients, had complaint of dryness of nose. This might be because of the presence of ACE2 membrane protein on the secretory nasal goblet cells [17, 18]. SARS-CoV2 virus on binding with these cells disrupt the mucus production which might lead to the dryness of nose [19]. Due to this change in mucus density and production, chemical odorant molecules unable to bind to odorant receptors causing olfactory dysfunction [20]. Epistaxis was noted in patients 3 (2%) who had history of dryness of nose.

Around 5 (4%) patients had sore throat. Throat irritation due to the postnasal discharge secondary to the sinusitis was the common cause observed in our study. 5 (4%) patients came to us with dysgeusia (both hypo and ageusia). The postulated mechanism for dysgeusia is direct damage to ACE2- expressing cells of taste buds and peripheral chemoreceptors [21], inflammatory response of oral mucosa during virus entry via ACE2 receptors [22] and impairment of olfactory-gustatory interactions as a result of damage to neuroepithelium [23]. Aphthous ulcer were observed in about 3 (2%) patients. The most probable aetiology for them might be due to Virus or physiological stress [24]. About 2 (1%) of our patients had oral candidiasis, might be secondary to the immune dysregulation caused by the COVID-19 infection [25].

Dryness of mouth in 11 (8%) probably due to the muco-tropic and neuropathic effects of virus on salivary gland led to dryness of mouth [26]. Muco-tropic effect is due to the presence of ACE2 and TMPRSS2 receptors expression on salivary gland epithelial cells [27] and on ACE2 receptor on neural cells affecting autonomic function of salivary gland [28].

3 (2%) patients presented to us with the Vocal cord palsy. The possible theory for this is because of ACE2 receptors on nerve cells [29] causing neurological complication of both peripheral and central nervous system. 4 (3%) of our patients had foreign body sensation in throat who were diagnosed have Laryngopharyngeal reflux disease (LPRD). LPRD, which is a subtype of gastro-oesophageal reflux disease. In this due to the impairment of the upper oesophageal sphincter (UES) action, gastric contents reflux into the larynx and

pharynx. The aetiology for this disease is that stress and diet habits. In COVID-19 patient, it is hypothesised that SARS-CoV2 virus causing damage of UES [30] which enters via the pharyngeal epithelial cells which contains ACE2 receptors.

Conclusion

In our study observed that nose and paranasal sinuses manifestation were the most common ENT manifestation among post-COVID-19 infected patients. It is being observed in our day-to-day practice post-COVID ENT manifestations are increasing. Hence, further detailed study on this subject is necessary for better understanding of these manifestations and their management. Limitation of our study was that conducted on a small sample size for a shorter period of time.

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