

Original Research Article

ENT SYMPTOMATOLOGY IN PATIENTS SUFFERING FROM COVID-19 INFECTION

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ABSTRACT

Background: To study the spectrum of ear, nose and throat manifestations in patients diagnosed with COVID-19 infection over 1-month duration.

Materials and Methods: It is observational prospective study (January to June 2021) conducted in 200 COVID -19 positive patients for a period of 6 months. All patients who tested COVID antigen (RAT/RT-PCR) positive admitted at Northern Railway Central Hospital or advised home isolation in follow-up of COVID-OPD, were taken in this study.

Results: Majority (83.5%) of patients were treated as out-patients i.e. had mild COVID-19 infection (home isolated). The most common presenting symptom in patients with covid-19 was found to be fever (76%) followed by shortness of breath (22.5%). 13.5% patients were asymptomatic. The most common ENT manifestation as the presenting symptom of covid-19 was found to be dry cough (8%) followed by anosmia & ageusia (6.5%) each. Majority of patients (56%) had at least one ENT symptom during COVID-19 illness. The commonest ENT symptom on follow-up over a period of 4 weeks was found to be ageusia (33%) followed by anosmia (28%) and dry cough (27%). It was found that the inflammatory markers in covid-19 patients with positive ENT symptoms were elevated in the first 2 weeks and normalized by the 4th week in majority of patients. Elevated levels of inflammatory markers were found to be significantly associated with ENT symptoms like odynophagia, dry cough, sore throat, hyposmia and headache.

Conclusion: We conclude that the Otorhinolaryngological manifestations are not rare symptoms of COVID- 19 disease, especially in mild or moderate form of the disease. ENT symptoms usually appear initially and may precede the development of severe COVID- 19 disease.

Keywords: COVID-19, Anosmia, Ageusia, Inflammatory markers, SARS COV-2, Olfactory Dysfunction.

INTRODUCTION

In the month of December 2019, sudden rise in pneumonia cases of unidentified cause was seen in the city of Wuhan in Hubei province of China.^[1] Throat swabs of these patients were taken for bacterial & fungal culture and sent to Chinese Center for Disease Control and prevention (CCDC) on 07/01/2020. The causative microorganism for the disease was identified and was named as severe acute respiratory syndrome, Corona virus-2 (SARSCoV-2) by the International Committee on Taxonomy of viruses. Severe acute respiratory

syndrome Corona virus-2 (SARSCoV-2) is a new Corona virus that was highly contagious and was responsible for the pandemic disease called Corona virus Disease (COVID-19). It was earlier also called as the 2019 novel Corona virus (2019-nCoV). It was found to be highly contagious and soon spread to rest of the world. WHO (World Health Organization) named the disease caused by the novel Corona virus as COVID-19 on February 12, 2020.^[2]

The World Health Organization declared COVID-19 infection as pandemic on 11th March 2020.^[3] As on 16 July 2021, 188.^[3] million people were affected

and 4 million deaths had been recorded worldwide. In India, 30.9 million people had been affected and 4,12,000 deaths had been recorded due to COVID-19 infection. Corona viruses mainly target epithelial cells.^[4] It also directly affects the endothelial cells lining the blood vessels. Other novel pathologic features of the virus are hypercoagulability, excessive multi-organ immune response & long term sequelae. Transmission of Corona virus is through aerosols, fomite or feco-oral route depending on the species. Incubation period of Covid-19 is between 2-14 days, however people develop symptoms as early as 4-5 days post exposure, the average being taken as 5 days.^[4] Covid-19 remains contagious even during latency period, thus the patient without any covid-19 presenting complaints can transmit the disease. COVID-19 infection has multi-organ manifestations. Individuals infected with SARS-CoV-2 may be asymptomatic or the disease may present as a mild upper respiratory tract illness, However, about 5% patients experience severe viral pneumonia that leads to respiratory failure and in many cases death.^[5] These patients require intensive hospital care and treatment.

Common symptoms among patients with COVID-19 infection include sore throat, fever, dry cough, shortness of breath (dyspnea), headache, muscle ache (myalgia), confusion, rhinorrhea, chest pain, diarrhea, nausea/vomiting, conjunctival congestion, nasal congestion, fatigue (malaise), hemoptysis, and chills. Interestingly most expressions of COVID-19 infection are non-specific. Anosmia (loss of smell) and ageusia (loss of taste) have also been reported in multiple studies. Reports of olfactory dysfunction and ageusia in otherwise asymptomatic persons had led to interest in this sign as a potential early indicator of SARS-CoV-2 infection. Furthermore, olfactory neurons could be at especially high risk of injury because of the high viral load within the nasal cavity.^[6]

In literature, studies held in China and Europe show presence of anosmia and ageusia in covid-19 patients. In this study we looked for all ear, nose, and throat related symptoms and tried to find if there were any other symptoms seen commonly in covid-19 infection, which appears earlier and which could help in early diagnosis of the infection. Early diagnosis is important for the control of COVID-19 infection. Recognition of early signs such as anosmia, ageusia or any other ENT symptoms might be very helpful for the diagnosis of COVID-19 infection and isolation of the patients as high transmissibility of COVID-19 infection before and immediately after symptom onset was reported in a recent epidemic study.

As the pandemic continued to expand, early detection and screening for suspicious cases, based on broader clinical findings, was found to be a useful aid to diagnosis, besides RT-PCR confirmation. Thus in this study we looked forward to find various ENT symptoms which could lead to screening and

early diagnosis of COVID-19 infection. We had also studied if; ENT symptoms were the presenting symptoms of the infection. All patients tested covid-19 positive and having positive ENT symptoms were tested for levels of inflammatory markers (CBC, CRP, D-DIMER, LDH, S. FERRITIN) to find out if there was any association between ENT symptoms and levels of inflammatory markers in covid-19 infection.

MATERIALS AND METHODS

It was an observational prospective study conducted in all patients tested COVID antigen (RAT/RT-PCR) positive at our Northern Railway Central Hospital (NRCH) New Delhi for a period of 6 months (January 2021 to June 2021)

Inclusion Criteria: All patients who tested COVID antigen (RAT/RT-PCR) positive admitted at NRCH or advised home isolation in the follow-up of COVID-Out patient department from January 2021 to June 2021 were taken in this study.

Exclusion Criteria: Patients with history of same / similar ENT symptoms prior to COVID-19 infection.

The study was conducted after taking an informed consent of the patients in a language understood by them. Patient's demographic data including name, age, sex, address, date of onset of symptoms, duration, history of contact with covid-19 positive patient, date of getting tested covid-19 positive was entered into the proforma.

Patient were asked for history of sudden onset ENT specific symptoms like earache, ear discharge, ear blockage, ear bleed, tinnitus, vertigo, decreased hearing, nasal blockage, rhinorrhea, hyposmia, anosmia, epistaxis, headache, facial heaviness, sore throat, odynophagia, dysphagia, ageusia, dry cough, hoarseness of voice. All positive symptoms were noted in the proforma. Patient's SPO2 level and respiratory rate were checked and depending on that, patients were classified as mild, moderate or severe as per the guidelines provided by Ministry of Health and Family Welfare, Government of India.

Mild- fever and/or uncomplicated URTI without dyspnea or hypoxemia SPO2 >94% on Room air(RA) or RR<24/min.

Moderate- Pneumonia with no signs of severe disease SPO2 90-93% on RA or RR 24-30/min.

Severe- Respiratory distress requiring mechanical ventilation. SPO2 <90% on RA or RR>30/min.

Mild cases were noted and sent for home isolation as per our hospital protocol. Moderate and severe cases were admitted to the ward/ICU as per our hospital protocol.

Weekly update was taken from these patients for the next 4 weeks regarding improvement or worsening of symptoms and was noted in the proforma. This was done via telephonic conversation even if the patient was admitted in the ward to avoid direct contact and exposure of the examiner to the virus.

Those patients who did not report any ENT symptoms in the 1st interview were followed up on 2nd, 3rd, 4th week to check for development of any ENT symptoms.

All patients giving positive history of ENT symptoms were checked for level of inflammatory markers like CBC, CRP, D-Dimer, LDH, S.Ferritin. In patients with raised levels of inflammatory markers, the levels were rechecked after 7 days interval along with the improvement of symptoms. At the end of the study (6 months), all the data was compiled together and analyzed to find the incidence of ENT symptoms as the presenting and subsequent symptoms of covid-19 infection and how long it had taken for the symptoms to disappear. It helped us find the ENT symptoms that occur in covid-19 infection for early diagnosis of the disease. It also helped us study if there was any association between ENT symptoms and levels of inflammatory markers in covid-19 infection.

Sample Size

All patients tested COVID-19 positive at NRCH from January 2021 to June 2021 were to be taken for the study. Based on the records of past OPD & admissions, it was expected that approximately 200 patients would be included in the study.

The study of Xiangming Meng, et al⁷ observed that incidence rate of olfactory dysfunction (ENT symptom) in COVID-19 patients varies from 33.9–68%. Taking this value as reference, the minimum required sample size with 7% margin of error and 5% level of significance is 176 patients. To reduce margin of error, total sample size taken was 200.

Formula used was:- $N \geq (i(1 - i))/(ME/z\alpha)^2$

Where $Z\alpha$ is value of Z at two sided alpha error of 5%, ME is margin of error and i is incidence rate.

Calculations

1) $n \geq ((.339*(1-.339))/(.07/1.96)^2) = 175.68 = 176$ (approx.) 2) $n \geq ((.68*(1-.68))/(.07/1.96)^2) = 170.60 = 171$ (approx.)

Statistical Analysis

The presentation of the Categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means \pm SD and as median with 25th and 75th percentiles (interquartile range). The association of the variables which were qualitative in nature was analyzed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0.

For statistical significance, p value of less than 0.05 was considered statistically significant.

Ethical Considerations

The objective and procedure of the study were explained to all patients. An informed consent was obtained from the participants before enrolling them into the study. The option to opt out of the study

was kept open for all patients without any clause. The decision of the patient not to participate in the research study did not affect the medical care or the relationship with the investigator and the institution. The privacy and confidentiality of the research participants was protected through all stages of the study. Subjects included in the study did not pay any extra money. Patients not participating in the study or withdrawing from the study at any later stage were not shown any kind of discrimination in the line of management.

RESULTS

Patient's demographic data, chief complaints, ENT specific symptoms, past history of ENT symptoms and levels of inflammatory markers in covid-19 infection on 1st, 2nd, 3rd, 4th week were recorded.

Mean value of age (years) of study subjects was 46.18 ± 17.2 with median (25th-75th percentile) of 48 (30-58).

In the present study, 65.50% of patients were males and 34.50% of patients were females. Hospital admission was required in only 33 out of 200 patients (16.50%). In 18.50% of patients, diabetes mellitus was present followed by hypertension (16.50%). Hypothyroidism was present in only 6 out of 200 patients (3%).

In the present study, in majority (67.00%) of patients, fever was present followed by shortness of breath (22.50%) and dry cough (17.00%).

In the present study, ENT symptom as presenting symptom was dry cough in 8.00% of patients. In the present study, out of 200 patients, majority (56%) of patients had at least one ENT symptom during COVID-19 illness. [Table 2]

Distribution of other ENT symptoms was comparable between CBC (NLR) (Normal and elevated). (Nasal blockage:- 6.32% vs 11.76% respectively (p value = 0.349), Hyposmia:- 16.84% vs 29.41% respectively (p value = 0.221), Anosmia:- 52.63% vs 35.29% respectively (p value = 0.188), Headache:- 17.89% vs 23.53% respectively (p value = 0.521), Rhinorrhea:- 12.63% vs 23.53% respectively (p value = 0.261), Loss of taste (Ageusia):- 57.89% vs 64.71% respectively (p value = 0.599), Hoarseness of voice:- 10.53% vs 5.88% respectively (p value = 1).

Proportion of patients with sore throat, odynophagia and dry cough was significantly higher in patients with elevated CBC(NLR) as compared to normal CBC(NLR). (Sore throat:- 58.82% vs 31.58% respectively (p value = 0.031), Odynophagia:- 52.94% vs 6.32% respectively (p value <0.0001) and Dry cough:- 76.47% vs 43.16% respectively (p value = 0.016). [Table 3]

Distribution of ENT symptoms was comparable between CRP (Normal and elevated). (Nasal blockage:- 5.56% vs 8.62% respectively (p value = 0.718), Anosmia:- 57.41% vs 43.10% respectively (p value = 0.13), Rhinorrhea:- 16.67% vs 12.07%

respectively (p value = 0.487), Sore throat:- 27.78% vs 43.10% respectively (p value = 0.091), Loss of taste(Ageusia):- 51.85% vs 65.52% respectively (p value = 0.142), Hoarseness of voice:- 5.56% vs 13.79% respectively (p value =0.206)).

Proportion of patients with hyposmia, headache, odynophagia and dry cough was significantly higher in patients with elevated CRP as compared to normal CRP. (Hyposmia: 25.86% vs 11.11% respectively (p value = 0.046), Headache: 25.86% vs 11.11% respectively (p value = 0.046), Odynophagia:- 24.14% vs 1.85% respectively (p value = 0.0005) and Dry cough:- 60.34% vs 35.19% respectively (p value=0.008). [Table 4]

Distribution of ENT symptoms was comparable between normal and elevated D-Dimer. (Nasal blockage:- 4.71% vs 14.81% respectively (p value = 0.094), Hyposmia:- 16.47% vs 25.93% respectively (p value = 0.273), Headache:- 16.47% vs 25.93% respectively (p value = 0.273), Rhinorrhea:- 15.29% vs 11.11% respectively (p value = 0.757), Sore throat:- 34.12% vs 40.74% respectively (p value = 0.532), Loss of taste(Ageusia):- 57.65% vs 62.96% respectively (p value = 0.625), Hoarseness of voice:- 7.06% vs 18.52% respectively (p value = 0.081), Dry cough:- 44.71% vs 59.26% respectively (p value = 0.187)).

Proportion of patients with odynophagia was significantly higher in patients with elevated D-Dimer as compared to normal D-Dimer. (Odynophagia: 25.93% vs 9.41% respectively (p value = 0.028)) Proportion of patients with anosmia was significantly lower in patients with elevated D-Dimer as compared to normal D-Dimer. (Anosmia:- 33.33% vs 55.29% respectively (p value = 0.047)). [Table 5]

Distribution of ENT symptoms was comparable between normal and elevated LDH. (Nasal

blockage:- 6.58% vs 8.33% respectively (p value = 0.71), Hyposmia:- 17.11% vs 22.22% respectively (p value = 0.517), Anosmia:- 55.26% vs 38.89% respectively (p value = 0.106), Headache:- 15.79% vs 25% respectively (p value = 0.243), Rhinorrhea:- 14.47% vs 13.89% respectively (p value = 0.934), Loss of taste (Ageusia):- 56.58% vs 63.89% respectively (p value = 0.463), Hoarseness of voice:- 9.21% vs 11.11% respectively (p value = 0.743)).

Proportion of patients with sore throat, odynophagia and dry cough was significantly higher in patients with elevated LDH as compared to normal LDH. (Sore throat:-50% vs 28.95% respectively (p value = 0.03), Odynophagia:-33.33% vs 3.95% respectively (p value <0.0001) and Dry cough:-75% vs 35.53% respectively (p value <0.0001)). [Table 6]

Distribution of ENT symptoms was comparable between normal and elevated serum ferritin. (Nasal blockage:- 6.74% vs 8.70% respectively (p value = 0.667), Hyposmia:- 19.10% vs 17.39% respectively (p value = 1), Headache:- 15.73% vs 30.43% respectively (p value = 0.107), Rhinorrhea:- 14.61% vs 13.04% respectively (p value = 1), Loss of taste(Ageusia):- 62.92% vs 43.48% respectively (p value = 0.091), Hoarseness of voice:- 7.87% vs 17.39% respectively (p value = 0.232). Proportion of patients with sore throat, odynophagia and dry cough was significantly higher in patients with elevated S.Ferritin as compared to normal S.Ferritin. (Sore throat:-56.52% vs 30.34% respectively (p value = 0.019), Odynophagia:-26.09% vs 10.11% respectively (p value = 0.045) and Dry cough:- 69.57% vs 42.70% respectively (p value = 0.022). Proportion of patients with anosmia was significantly lower in patients with elevated S.Ferritin as compared to normal S.Ferritin. (Anosmia:-30.43% vs 55.06% respectively (p value = 0.035)). [Table 7]

Table 1: Distribution of socio-demographic characteristics of study subjects

Socio-demographic characteristics	Frequency	Percentage
Gender		
Female	69	34.50%
Male	131	65.50%
Hospital admission		
No	167	83.50%
Yes	33	16.50%
Co-morbidities		
Hypertension	33	16.50%
Diabetes mellitus	37	18.50%
Hypothyroid	6	3%
Chief complaints		
Asymptomatic	27	13.50%
Loose motions	1	0.50%
Vomiting	1	0.50%
Headache	1	0.50%
Odynophagia	2	1.00%
Chest pain	5	2.50%
Anosmia	17	8.50%
Ageusia	14	7.00%
Sore throat	10	5.00%

Rhinorrhea	8	4.00%
Myalgia	30	15.00%
Cold	1	0.50%
Fever	134	67.00%
Dry cough	34	17.00%
Shortness of breath	45	22.50%

Table 2: Distribution of ENT symptoms as presenting symptoms of study subjects

ENT symptoms as presenting symptoms	Frequency	Percentage
Anosmia	13	6.50%
Headache	1	0.50%
Ageusia	13	6.50%
Sore throat	9	4.50%
Rhinorrhea	6	3.00%
Dry cough	16	8.00%
Odynophagia	2	1.00%

Table 3: Association of ENT symptoms with CBC (NLR)

ENT symptoms	Normal(n=95)	Elevated(n=17)	Total	P value
Nasal blockage	6 (6.32%)	2 (11.76%)	8 (7.14%)	0.349*
Hyposmia	16 (16.84%)	5 (29.41%)	21 (18.75%)	0.221†
Anosmia	50 (52.63%)	6 (35.29%)	56 (50%)	0.188†
Headache	17 (17.89%)	4 (23.53%)	21 (18.75%)	0.521*
Rhinorrhea	12 (12.63%)	4 (23.53%)	16 (14.29%)	0.261*
Sore throat	30 (31.58%)	10 (58.82%)	40 (35.71%)	0.031†
Odynophagia	6 (6.32%)	9 (52.94%)	15 (13.39%)	<.0001†
Loss of taste(Ageusia)	55 (57.89%)	11 (64.71%)	66 (58.93%)	0.599†
Hoarseness of voice	10 (10.53%)	1 (5.88%)	11 (9.82%)	1*
Dry cough	41 (43.16%)	13 (76.47%)	54 (48.21%)	0.016*

* Fisher's exact test, † Chi square test

Table 4: Association of ENT symptoms with CRP

ENT symptoms	Normal(n=54)	Elevated(n=58)	Total	P value
Nasal blockage	3 (5.56%)	5 (8.62%)	8 (7.14%)	0.718*
Hyposmia	6 (11.11%)	15 (25.86%)	21 (18.75%)	0.046†
Anosmia	31 (57.41%)	25 (43.10%)	56 (50%)	0.13†
Headache	6 (11.11%)	15 (25.86%)	21 (18.75%)	0.046†
Rhinorrhea	9 (16.67%)	7 (12.07%)	16 (14.29%)	0.487†
Sore throat	15 (27.78%)	25 (43.10%)	40 (35.71%)	0.091†
Odynophagia	1 (1.85%)	14 (24.14%)	15 (13.39%)	0.0005*
Loss of taste(Ageusia)	28 (51.85%)	38 (65.52%)	66 (58.93%)	0.142†
Hoarseness of voice	3 (5.56%)	8 (13.79%)	11 (9.82%)	0.206*
Dry cough	19 (35.19%)	35 (60.34%)	54 (48.21%)	0.008†

* Fisher's exact test, † Chi square test

Table 5: Association of ENT symptoms with D-Dimer

ENT symptoms	Normal(n=85)	Elevated(n=27)	Total	P value
Nasal blockage	4 (4.71%)	4 (14.81%)	8 (7.14%)	0.094*
Hyposmia	14 (16.47%)	7 (25.93%)	21 (18.75%)	0.273†
Anosmia	47 (55.29%)	9 (33.33%)	56 (50%)	0.047†
Headache	14 (16.47%)	7 (25.93%)	21 (18.75%)	0.273†
Rhinorrhea	13 (15.29%)	3 (11.11%)	16 (14.29%)	0.757*
Sore throat	29 (34.12%)	11 (40.74%)	40 (35.71%)	0.532†
Odynophagia	8 (9.41%)	7 (25.93%)	15 (13.39%)	0.028†
Loss of taste(Ageusia)	49 (57.65%)	17 (62.96%)	66 (58.93%)	0.625†
Hoarseness of voice	6 (7.06%)	5 (18.52%)	11 (9.82%)	0.081†
Dry cough	38 (44.71%)	16 (59.26%)	54 (48.21%)	0.187†

* Fisher's exact test, † Chi square test

Table 6: Association of ENT symptoms with LDH

ENT symptoms	Normal(n=76)	Elevated(n=36)	Total	P value
Nasal blockage	5 (6.58%)	3 (8.33%)	8 (7.14%)	0.71*
Hyposmia	13 (17.11%)	8 (22.22%)	21 (18.75%)	0.517†
Anosmia	42 (55.26%)	14 (38.89%)	56 (50%)	0.106†
Headache	12 (15.79%)	9 (25%)	21 (18.75%)	0.243†
Rhinorrhea	11 (14.47%)	5 (13.89%)	16 (14.29%)	0.934†
Sore throat	22 (28.95%)	18 (50%)	40 (35.71%)	0.03†
Odynophagia	3 (3.95%)	12 (33.33%)	15 (13.39%)	<.0001*
Loss of taste(Ageusia)	43 (56.58%)	23 (63.89%)	66 (58.93%)	0.463†
Hoarseness of voice	7 (9.21%)	4 (11.11%)	11 (9.82%)	0.743*
Dry cough	27 (35.53%)	27 (75%)	54 (48.21%)	<.0001†

* Fisher's exact test, † Chi square test

Table 7: Association of ENT symptoms with Serum Ferritin

ENT symptoms	Normal(n=89)	Elevated(n=23)	Total	P value
Nasal blockage	6 (6.74%)	2 (8.70%)	8 (7.14%)	0.667*
Hyposmia	17 (19.10%)	4 (17.39%)	21 (18.75%)	1*
Anosmia	49 (55.06%)	7 (30.43%)	56 (50%)	0.035†
Headache	14 (15.73%)	7 (30.43%)	21 (18.75%)	0.107†
Rhinorrhea	13 (14.61%)	3 (13.04%)	16 (14.29%)	1*
Sore throat	27 (30.34%)	13 (56.52%)	40 (35.71%)	0.019†
Odynophagia	9 (10.11%)	6 (26.09%)	15 (13.39%)	0.045†
Loss of taste(Ageusia)	56 (62.92%)	10 (43.48%)	66 (58.93%)	0.091†
Hoarseness of voice	7 (7.87%)	4 (17.39%)	11 (9.82%)	0.232*
Dry cough	38 (42.70%)	16 (69.57%)	54 (48.21%)	0.022†

* Fisher's exact test, † Chi square test

DISCUSSION

In December 2019, a novel Corona virus epidemic, caused by the severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) emerged from China. Due to its widespread and infection, COVID-19 is an important health hazard and was soon declared a pandemic. According to studies conducted previously⁸ it was found that non-ENT manifestations like fever, cough, shortness of breath and myalgia are more common in COVID patients than ENT manifestations. It is not uncommon to see the ENT manifestations in these patients. ENT symptoms are more commonly seen during the early stages of the disease. The identification of these symptoms may help in isolating the paucisymptomatic patients.

During the outbreak, many authors reported an increase in the presence of anosmia in COVID-19 subjects. After initial reports, a few studies indicated that anosmia presenting in COVID-19 subjects is more frequent than expected for a routine upper respiratory tract infection. Multiple studies from China and Europe show presence of anosmia and ageusia in covid-19 patients. In a study by Mishra P et al.⁹ on comparison with world literature reported that, the prevalence of anosmia is higher in European population as compared to Indian population. Also the symptom of anosmia improved when the patient recovered from the disease.

Prevalence of new onset anosmia in Indian population with COVID-19 was found to be 14.8%. Reports of olfactory dysfunction and ageusia in otherwise asymptomatic persons have led to interest in this sign as a potential early indicator of SARS-CoV-2 infection.

We conducted an observational prospective study at Northern Railway Central Hospital (NRCH), New Delhi from January 2021 to June 2021 to study spectrum of ear, nose and throat manifestations in patients diagnosed with COVID-19. 200 patients who tested COVID antigen (RAT/RT-PCR) positive, admitted at NRCH or advised home isolation in follow up of NRCH COVID OPD from January 2021 to June 2021 were included in this study. Out of 200 patients only 33 patients (16.5%) were hospitalized and 167 patients (83.5%) were home isolated. Patient's demographic data, chief complaints, ENT specific symptoms, past history of ENT symptoms and levels of inflammatory markers in covid-19 infection on 1st, 2nd, 3rd, 4th week were recorded.

The maximum numbers of patients in our study were in the 30-58 years age group which was consistent with the studies by Panda S et al¹⁰, Shaik A et al¹¹ and Mishra P et al⁹. Mean age in our study was 46.18 ± 17.2 which is slightly higher than in other studies. In the present study out of total 200 COVID-19 positive patients, 131(65.5%) were males while 69(34.5%) were females. The Male:

Female ratio was 1.89:1, which was comparable to other studies.

In the present study 18.5% patients had HTN, 16.5% had DM and 3% had thyroid disorder, rest of the patients did not have any co-morbidities.

In the present study the most common presenting symptom in Covid-19 patients was fever (67%) followed by SOB (22.5%), dry cough (17%) which was comparable to the other studies.

In the present study, ENT manifestations as the presenting symptom was dry cough (8%) followed by anosmia (6.50%), ageusia (6.50%), sore throat (4.50%), rhinorrhea (3.00%) and odynophagia (1.00%). ENT symptom as presenting symptom was headache in only 1 out of 200 patients (0.50%). There were no similar studies to compare this.

In the present study overall 10.5% and 28% patients had hyposmia and anosmia respectively. The incidence of hyposmia was lower as compared to the study by Sayin I et al¹⁴, whereas the incidence of anosmia was higher as compared to the above studies. All patients recovered the sense of smell within 4-22days which was found similar to the above studies. [Table 8]

In the present study 33% patients had loss of taste (ageusia) which was similar to the study by Borah H et al¹². Most of the patients in the present study regained the sense of taste within 5-24 days.

In the present study 4%, 8% & 10.5% patients had nasal blockage, rhinorrhea & headache respectively, which was lesser as compared to the other studies.

The recovery time of these symptoms in our study was less than 15 days.

In the present study 20% and 27% patients had sore throat & dry cough respectively which was comparable to the other studies. The overall time to recover was 3-22days. [Table 9]

In the present study 7.5% patients had odynophagia which was comparable to the other studies. 5.5% patients had hoarseness in the present study; there were no studies available to compare this. Levels of inflammatory markers in COVID-19 patients with ENT symptoms. Literature review did not reveal any studies that showed association between inflammatory markers & ENT symptoms in COVID-19 positive patients.

In the present study all the COVID positive patients with ENT symptoms underwent evaluation for levels of inflammatory markers {CBC (NLR), CRP, D-Dimer, LDH, S.Ferritin}. It was observed that COVID-19 positive patients with ENT symptoms had significantly elevated levels of inflammatory markers in the 1st and 2nd week of illness, most of which gradually came within normal limits by the 4th week. [Table 10]

In the present study, elevated levels of inflammatory markers were found to be significantly associated (p value <0.05) with the ENT symptoms like odynophagia, dry cough, sore throat, hyposmia & headache in COVID-19 positive patients. Anosmia was found to be significantly lower (p value< 0.05) in patients with elevated D-Dimer & S.Ferritin levels. [Table 11]

Table 8: Chief complaints in patients with COVID-19 in different studies in comparison to the present study

Studies	Symptoms In Descending Order Of Presentation
Borah H et al ¹²	Fever (93%)>cough(85%)>SOB(33%)>myalgia(14%)>GI(4%)
Panda S et al. ¹⁰	Fever(71%)>odynophagia(63.5%)>cough(59.3%)>SOB(20.6%)>a geusia(17.3%)>anosmia(12.8%)>GI(8.2%)
El-Anwar MW et al ¹³	Fever(73.5%)>dry cough (61%)>expectoration(22.8%)>SOB(16.8%)>sore throat(11.3%)>myalgia(10.4%)
Shaik A et al ¹¹	Cough(44%)>fever(39.3%)>SOB(32.4%)>rhinorrhea(12%)
Present study	Fever (67%)>SOB(22.5%)>dry cough(17%)> myalgia(15%)>anosmia(8%)> ageusia(7%)>sorethroat(5)>rhinorrhea(4%)

Table 9: Sore throat & dry cough with its time to resolve in different studies in comparison to the present study

Studies	Sore Throat (%)	Time To Resolve	Dry Cough (%)	Time To Resolve
Borah H et al ¹²	80%	10-20days	85	10-20days
El-Anwar MW et al ¹³	11.3%	7-30days	61%	7-30days
Shaik A et al ¹¹	9.2%	-	44%	-
Present study	20%	4-20days	27%	3-22days

Table 10: Odynophagia & hoarseness with its time to resolve in different studies in comparison to the present study

Studies	Odynophagia(%)	Time To Resolve	Hoarseness (%)	Time To Resolve
El-Anwar MW et al ¹³	5.3	-	-	-
Panda S et al. ¹⁰	63.5%	5-30days	-	-
Present study	7.50%	5-20days	5.50%	6-20days

Table 11: Association of ENT symptoms with Inflammatory markers

Inflammatory markers (Elevated levels)	Associated ENT symptoms in descending order.
CBC(NLR)	Odynophagia (p<0.0001) > dry cough (p=0.016) > sore throat (p=0.031)
CRP	Odynophagia (p=0.0005) > dry cough (p=0.008) > hyposmia /headache (p=0.046)
D-Dimer	Odynophagia (p=0.028)
LDH	Odynophagia (p,0.0001)/dry cough (p=0.0001) > sore throat (p=0.03)
S.Ferritin	Sore throat (p=0.019) > dry cough (p=0.022) > odynophagia (p=0.045)

CONCLUSION

We conclude that the Otorhinolaryngological manifestations are not rare symptoms of COVID-19 disease, especially in mild or moderate form of the disease. ENT symptoms usually appear initially and may precede the development of severe COVID-19 disease. Thus subjects who may be otherwise asymptomatic for COVID-19 symptomatology, but reporting to the treating doctor / ENT specialist with symptoms like dry cough, ageusia, anosmia or hyposmia, should alert the treating doctor of the risk of Covid infection in the patient. The treating doctor should get these otherwise asymptomatic patients tested for COVID-19, so that these patients can be timely treated & isolated. The most common ENT manifestations observed in the patients with COVID-19 are dry cough, ageusia and anosmia. Other ENT manifestations like sore throat, odynophagia, rhinorrhea, nasal blockage, hyposmia, headache and hoarseness were also present in patients with COVID-19 infection. COVID-19 may also present with sudden onset hyposmia, anosmia or ageusia not accompanied by any other symptoms. ENT symptoms may also be associated with raised levels of inflammatory markers which could lead to hypercoagulability and multi organ immune response causing further complications in COVID-19 patients.

Limitations

Limited sample size and study period. Physical examination of the patients was not possible because of practical difficulty in examining of such a huge load of patients, as ENT examination of confirmed COVID positive cases would bring the examiner under grave risk of getting a high viral load infection himself/herself. It is to be noted that ENT is one of the high risk specialties as far as COVID-19 infection is concerned. Thus the study was carried out on the bases of symptomatology. ENT symptom specific investigations like olfactory tests, taste sensation tests, pure tone audiometry etc was not done because of reasons mentioned above.

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