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ORIGINAL ARTICLE

Contemporary Analysis of Olfactory Dysfunction in Mild to Moderate Covid 19 Patients in A Tertiary Health Care Centre

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Abstract Introduction: The World Health Organization declared COVID-19 a pandemic on March 11, 2020. The virus that causes COVID-19 was designated as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). Several studies have reported chemosensory dysfunction, such as anosmia and ageusia, as common findings in COVID-19 positive patients. To date, qualitative olfactory testing has been performed only in a very few cohort studies on COVID-19 patients. However, objective testing is necessary to verify or determine the true magnitude of their deficits. Moreover, the proportion of COVID-19 patients exhibiting true olfactory disturbances is unknown. Aim of the Study: To determine the true prevalence of olfactory dysfunction in COVID-19 patients by objective assessment in mild to moderate symptomatic patients. Materials & Methodology: This was a prospective cross-sectional analytical study. All patients who were COVID-19 positive and having mild to moderate symptoms and not admitted in ICU formed part of the study group. Objective evaluation of smell function was done. Results: Self-reported smell dysfunction was present in 26.9% patients (n=62) and taste dysfunction was seen in 10.9% (n=25) of patients. On quantitative assessment of smell dysfunction, it was noted that 41.3% (n=95) of patients had some form of smell dysfunction out of which 70.5% patients (n=67) had hyposmia and 29.5% patients (n=28) had anosmia. Conclusion: Incidence was found to be more by objective assessment when compared to self-reported symptoms.

Keywords · Olfactory disturbance · Self-reported · Objective · Subjective · Incidence · Covid-19

Introduction

Corona viruses are important human pathogens now but earlier detected mostly in animals. At the end of 2019, a novel corona virus was identified as the cause of a cluster of pneumonia cases in Wuhan city, China. The disease rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world. In February 2020, the World Health Organization designated the disease as COVID-19, which stands for corona virus disease 2019 [1]. The World Health Organization declared COVID-19 a pandemic on March 11, 2020 [2]. The virus that causes COVID-19 was designated as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).

The most common symptoms of COVID-19 include fever, fatigue, cough and shortness of breath [3, 4]. Also, several studies have reported chemosensory dysfunction, such as anosmia and ageusia, as common findings in COVID-19 positive patients [5–7]. In general, hyposmia occurs most commonly in upper respiratory tract infections [8], but in COVID-19 patients, these symptoms can be present in the absence of other nasal symptoms such as nasal obstruction and nasal discharge thus suggesting that there could be a direct relationship between COVID-19 infection and damage to the chemosensory system [5, 9]. Olfactory dysfunction impairs quality of life, because this loss affects food enjoyment, social interaction and associated with increased incidence of depression [10–12].

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To date, qualitative olfactory testing has been performed only in a very few cohort studies on COVID-19 patients. However, objective testing is necessary to verify or determine the true magnitude of their deficits. Moreover, the proportion of COVID-19 patients exhibiting true olfactory disturbances is unknown.

Aim of the Study

To investigate the effects of COVID-19 in mild to moderate symptomatic patients admitted in our tertiary care centre and to determine the true prevalence of olfactory dysfunction in COVID-19 patients by objective assessment.

Materials and Methodology

This was a prospective cross-sectional analytical study performed in our tertiary care centre which was involved in treating COVID-19 cases. Institutional ethical committee clearance was obtained. All patients who were COVID-19 positive and having mild to moderate symptoms and not admitted in ICU formed part of the study group.

In our institute, patients were divided into 3 categories based on the severity of disease and associated co-morbid conditions [TABLE 1]. A written informed consent was taken from all the patients to be part of this study. All patients who satisfied study criteria were enrolled.

Inclusion Criteria

1. Mild to moderate COVID-19 patients.
2. Age 18–60 years.
3. Nasopharyngeal or oropharyngeal swab positive for SARS-CoV-2 infection by Reverse Transcriptase – Polymerase Chain Reaction (RT-PCR) technique.

Exclusion Criteria

1. Patients with previous history of nasal surgery
2. Known case of allergic rhinitis, sinusitis, nasal polyposis, major head injury
3. Pre-existing manifestation of smell dysfunctions
4. Psychiatric or neurological disorders or any chronic nasal disease

A total of 230 patients tested positive for COVID-19 infection between 6 and 12th July 2020 were included in the study. All patients irrespective of olfactory symptoms underwent a simple smell identification test where 10 commonly used items were used as odorants. These test kits were given to the patient right at the time of admission along with the customised COVID-19 medication kits issued by the hospital. The odorants were chosen to represent the familiarity in day to day life and they were presented in 10 mL air tight, chromatic bottles commercially available so that patient visually does not identify the content. With eyes closed, the subject was asked to sniff and identify the smell of each odorant. First response was taken and scored 1 for correct and 0 for wrong/no response. There was an interval of at least 30 s between successive presentations to prevent olfactory desensitization.

Substances used for odor identification were asafoetida, naphthalene balls, garlic, vicks vaporub, rose water, sandalwood oil, cardamom (elaichi), clove oil, lemon and cumin seeds (jeera). The total odor identification score was calculated by adding the number of substances correctly identified. A score of 0 (zero) was considered as anosmia; 1–8 was considered as hyposmia and more than 8 was perceived as normal olfactory function. Patients with normal olfactory function were taken as controls. In the present study, only odor identification was assessed. Other components of olfaction like odor threshold and odor discrimination were not studied.

Table 1 Categorisation of patients based on severity of disease

Category A	Category B	Category C
Pulse: 60–100/min	Pulse 100–120/min	Pulse > 120/min
SBP > 120 mm Hg	SBP 100–120 mm Hg	SBP < 100 mm Hg
DBP > 80 mm Hg	DBP 70–80 mm Hg	DBP < 70 mm Hg
RR < 18/min	RR 18–24/min	RR > 24/min
SpO2 > 94%	SpO2 88–94% without oxygen	SpO2 < 94% with oxygen
No co-morbid	Co-morbid–Diabetes, Hypertension, TB, COPD	PaO2 /FiO2 < 300
	PaO_2/FiO_2 300–500	
	Pneumonitis on CXR/Ground Glass opacities on CT Chest	

Results

The mean age of the study population was 43.56 ± 4.6 years. The male: female ratio was 1.73:1 with a male preponderance (Fig. 1). Fever being the most common complaint was present in 66.9% (n = 154) of the patients. The second most common symptom was cough which was seen in 47.8% (n = 110) of patients; followed by throat pain seen in 46.1% (n = 106) patients (Fig. 2). Self reported smell dysfunction was present in 26.9% patients (n = 62) and taste dysfunction was seen in 10.9% (n = 25) of patients. On quantitative assessment of smell dysfunction, it was noted that 41.3% (n = 95) of patients had some form of smell dysfunction out of which 70.5% patients (n = 67) had hyposmia and 29.5% patients (n = 28) had anosmia (Figs. 3, 4).

Discussion

Anosmia and ageusia are novel unique findings seen in COVID 19 and was seldom observed in SARS or MERS (Middle East Respiratory Syndrome) which are infections caused by other strains of *Coronaviridae*. The etiologies for olfactory dysfunction can broadly be mentioned under three headings: conduction, central and sensorineural disorders. In conduction disorders, there is inflammation and edema of the nasal mucosa, as observed in allergic rhinitis or rhinosinusitis thus disrupting the mechanical olfactory functions. Central olfactory dysfunction is seen in primary CNS disorders like neurodegeneration or following head injury. Sensorineural olfactory dysfunction develops due to degeneration of olfactory nerve or epithelium following an infection or drug consumption.

In our study, only 26.9% of the patients were aware of their olfactory deficit before testing whereas the incidence increased to 41.3% after the quantitative evaluation. This difference between self-reported rate and quantified smell assessment reflects that the prevalence of olfactory dysfunction related to COVID-19 would be underestimated in the epidemiological studies where the loss of smell was based on subjective reports only.

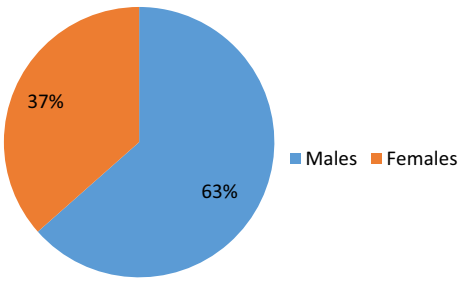

Fig. 1 Sex distribution of the study sample

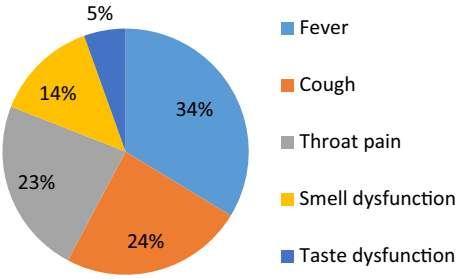

Fig. 2 Self-reported symptoms seen in COVID-19 patients

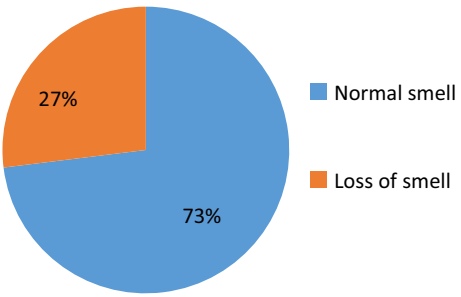

Fig. 3 Self-reported smell dysfunction in COVID-19 patients

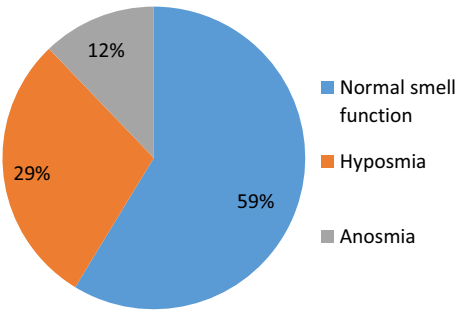

Fig. 4 Objective evaluation of smell function

Studies have demonstrated that loss of smell and taste, along with other established symptoms like fever and cough, as a strong predictor for COVID-19. Also the combination of fever, anosmia, cough, fatigue, diarrhoea, loss of appetite and abdominal pain can identify COVID-19 individuals with moderate sensitivity and high specificity [13].

In most of the studies, the prevalence of olfactory dysfunction ranged from 40 to 85% of the patients with COVID-19 [14–21]. The pooled prevalence of olfactory dysfunction in a systematic review that included 24 studies involving 8438 patients was found to be 41% (95% CI, 28.5%–53.9%). Also it was observed that the prevalence tended to show a decrease with increase in the mean age and that the prevalence was higher when using objective measurements compared with self-reported symptoms [22]. Similarly in a review by Passarelli et al. [23] that included 5 studies, anosmia was observed in 74.8% of the 10,818

COVID-19 positive patients. Others however have reported the prevalence of olfactory dysfunction in COVID-19 as around 15% and the median duration for spontaneous recovery of sense of smell ranged between 7 and 10 days [24, 25].

Unlike olfactory dysfunction observed in other viral infections causing common cold, no significant nasal mucosal inflammation or edema or nasal obstruction is observed in COVID-19 patients. Also olfactory dysfunction is seen even in mild and asymptomatic cases without other systemic manifestations in these patients. Several studies have established the role of ACE2 receptors in SARS-CoV-2 entry and infectivity in humans. The olfactory epithelium, in addition to the olfactory receptor neurons also contains the sustentacular cells, microvillar cells and progenitor stem cells. These supporting cells but not the olfactory receptor neurons express the ACE2 receptors. The sustentacular cells have important function including protection of the olfactory receptor neurons, providing metabolic support to them and also play a vital role in odor perception cascade. It is proposed that the olfactory dysfunction in COVID-19 is not due to direct olfactory receptor neuron dysfunction as these cells do not express the ACE 2 receptors. Instead the sustentacular cells are affected early by the viral infection which leads to impaired odor perception and secondary olfactory receptor neurons dysfunction. Involvement of the progenitor stem cells might explain the long term olfactory dysfunction experienced in some cases of COVID-19 patients [26]. In addition, disruption of the epithelial sensors in the nasal mucosa that identify chemesthesic stimuli, carried through the trigeminal nerves, is also believed to contribute to olfactory dysfunction [27].

The most widely used tests for assessing the ability to smell are those of odor threshold detection and odor identification. The more successfully used tests include the University of Pennsylvania Smell Identification Test (UPSIT), the ''Sniffin Sticks'' test, the Connecticut Chemosensory Clinical Research Center (CCCRC) test and the 12-odor Brief Smell Identification Test (BSIT), also known as the Cross-Cultural Smell Identification Test. The use of these tests in Indian population is limited by factors such as cost, differences in familiarity with the odors and difficulty in procurement of these test kits. Hence, a simple smell identification test using familiar odours for Indian population was done.

Although there are universally accepted standard tests used throughout the world for sensory systems such as hearing and vision, this is not the case for olfaction. The development of a single gold standard olfactory function test would be ideal for comparing clinical results obtained from different centers around the world. However, this may be difficult, if not impossible, owing to the cultural differences that exist for odors and fragrances used in different countries. In the absence of a gold standard test for olfactory function, identifying cultural differences and adjusting odorants used in existing smell tests may provide an alternative approach that would permit comparison of clinical data.

In a study conducted by Cain et al. [28] the identification component consistently yielded a higher frequency of anosmic scores, leading them to conclude that odor identification may be having higher sensitivity than threshold component. On the grounds of ease of use, speed of administration, and resolution between patients and controls, the identification component might seem more desirable.

Conclusion

Self-reporting of smell dysfunction is an inaccurate measure of olfactory function. Objective methods quantify smell loss and can limit any confounds because they rely on true perception of a stimuli when presented, diminishing response and measurement bias. The higher overall reported prevalence of olfactory loss in studies using objective methods compared to those using subjective methods suggests that subjective methodologies miss crucial information and might consistently underestimate true smell loss in COVID-19 patients.

Limitations of the Study

In the present study, only odor identification was assessed. Other components of olfaction like odor threshold and odor discrimination were not studied. Since different components contribute differently to olfaction loss, including other components of olfaction in the smell test will provide a more sensitive and specific way of assessing olfaction in COVID-19 patients and improve its discriminative value.

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Compliance with Ethical Standards

Conflict of interest The author declare that they have no conflict of interests.

Consent for Participation Written informed consent obtained from all participants.

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