

Persistence of Olfactory Dysfunction in Post CoVid-19 Patients Using Sniffin Sticks - A Prospective Study

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ABSTRACT

Introduction

This study is conducted to assess the Olfactory dysfunction (OD) of CoVid-19 recovered patients using ODOFIN Sniffin 'Sticks and to analyze the demographic features, duration of recovery, co-morbidities/metabolic disorders associated with persistence of OD in Post CoVid-19 patients.

Materials and Methods

This prospective observational study was conducted at our tertiary care hospital on 40 CoVid-19 recovered patients with persistent OD. The olfaction was assessed qualitatively using ODOFIN Sniffin 'sticks at 6th, 10th, 12th weeks Post CoVid and the results documented and analysed.

Results

Total 40 eligible patients were selected. 50% of study participants were males and 60% aged 18-38 years. 3 patients were diabetic and 3 were hypertensive. 37 had OD of which 26 had hyposmia and 11 had anosmia 6 weeks Post CoVid. 22 had OD of which 14 had hyposmia and 8 had anosmia 10 weeks Post CoVid. 10 had persistent OD 12 weeks Post CoVid. There was no association found between age, co-morbidities and OD at 6, 10 and 12 weeks Post CoVid ($p > 0.05$). Hyposmia was common among females at 10 weeks Post CoVid which was found to be statistically significant ($p < 0.05$).

Conclusions

Knowledge about time pattern on the recovery of OD in Post CoVid patients will be essential in counselling and treating them.

Keywords

Olfactory dysfunction; Post CoVid; Odofin Sniffin 'Sticks

Altered taste and smell sensations were common symptoms of the CoVid-19 disease, Olfactory Dysfunction (OD) in CoVid-19 patients was found to be 47.85%.¹ Post CoVid OD lasting for a prolonged period of time might impact quality of life (QOL) and can result in psychological illnesses such as depression, anxiety, anorexia and its nutritional effects, social interaction issues, and cognitive impairment.² OD following a respiratory infection is not unique to CoVid-19, viruses such as adenovirus, rhinovirus, corona virus and influenza are already known etiological factors for Post Viral Olfactory Dysfunction (PVOD).³ However, prevalence of post CoVid OD varies between studies, and several factors have been reported to be associated with the prognosis of smell loss in CoVid-19 cases.⁴ Studies on duration of post CoVid OD is still unclear as most of the data's were based on questionnaires or

telephone interviews. Olfaction being an important sense in human life, knowing the recovery rate and factors associated with persistence of OD in post CoVid patients is crucial. In India mostly a subjective evaluation of CoVid-19 induced OD is carried out and limited studies are available on objective assessment of OD in post CoVid patients. Using established olfactory tests will help to characterize OD in more detail.⁵

The Sniffin Sticks Test (SST) is a semi-objective and

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validated olfactory test used for objective assessment of OD.⁶ The objective of the study is to assess the OD of CoVid-19 recovered patients using SST and to observe the duration of recovery and to analyze the demographic features, co-morbidities/metabolic disorders associated with persistence of OD in post CoVid-19 patients.

Materials and Methods

This is a prospective observational study conducted at our tertiary care hospital from July 2021 to December 2021. After getting Institutional Ethical Clearance, reverse transcriptase polymerase chain reaction/ rapid antigen test (RT-PCR/RAT) positive CoVid patients with OD were identified through inpatient medical records/OPD basis. This study included 40 CoVid-19 recovered patients (RT-PCR/RAT negative) with persistent OD (more than 6 weeks from the time of onset of smell loss). Participants under 18 years of age, with known olfactory disorder before the CoVid-19 disease, previous histories of nasal disorders and nasal/sinus surgeries, history of nasal tobacco (snuff) abuse, with psychological / psychiatric disorders, neurological disease known to be associated with OD were excluded from the study. Sample size was calculated using Cochran's formula taking a prevalence of 14.8%,⁷ and precision of 10%, the sample size was calculated to be 40. Informed written consent from the patients meeting the inclusion and exclusion criteria was obtained. At 6th week post CoVid, after complete ENT examination and investigations, olfactory dysfunction was assessed with Questionnaire for Olfactory Dysfunction (QOD)⁸ and SST and results documented. All the patients were reviewed at 10th and 12th week post CoVid and olfactory assessment was repeated with SST and results were documented. Olfactory training was encouraged in all the study participants. At the end of 12th week post CoVid, in patients with persistent OD, demographic features and associated co-morbidities and recovery rate of OD were assessed. The results were statistically analysed and presented. The study methodology is shown in (Fig. 1).

The ODOFIN (BURGHART) Sniffin' Sticks Test kit (Burghart Messtechnik Denmark) consists of 16 test pens

loaded with odours such as peppermint, orange, fish, leather, rose, cloves, coffee, pineapple, liquorice, anise, lemon, banana, cinnamon, apple, turpentine, garlic. A choice card with 4 odour choices is provided for each odour pen. (Fig. 2a)

After explaining the procedure to the patient, each patient is instructed to smell each pen separately. The tip of the pen is held approximately 2 cm below one nostril, with other nostril closed with their thumb and instructed to inhale the odour for 3-4 seconds (Fig. 2 b). The procedure is repeated on the opposite side and then once again with both nostrils open and holding the test pen in the centre of the nostrils. All 16 odour pens are presented one after another, at an interval of 30 seconds. For each odour pen, a choice card with 4 odour choices is provided and the patient is asked to choose the item that best matches their olfactory perception. A correct identification is given one point. The score is a sum of all correct answers. A score less than 8 were graded as anosmia, 8-11 as hyposmia, more than 11 as normosmia and the results documented.

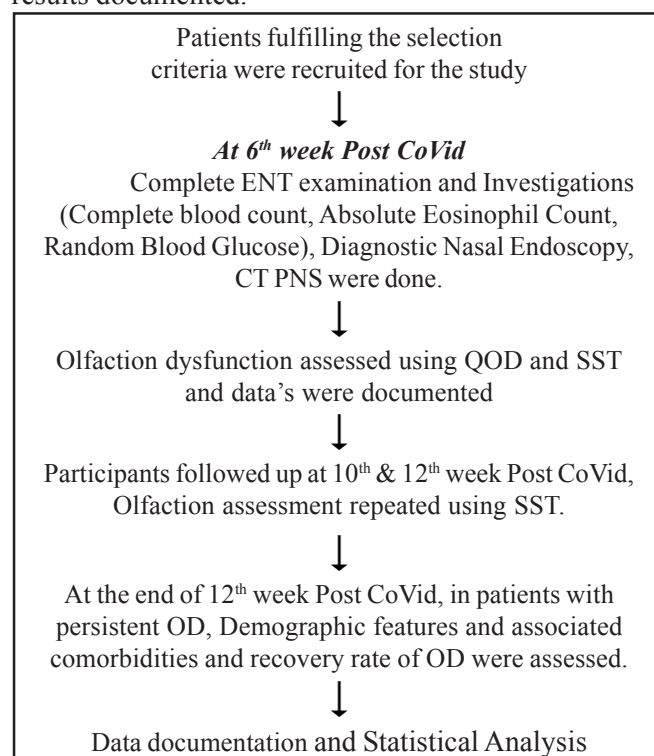


Fig. 1. Study methodology



Fig. 2a. Showing the ODOFIN Sniffin' stick test kit with 16 odour pens, choice cards and answer keys [black colour]



Fig. 2b. Showing Olfactory function being assessed using ODOFIN Sniffin' sticks

Results

In present study, total of 40 patients fulfilling inclusion criteria were included. The mean age of participants was 36.8 ± 14.6 years, about 60% aged 18-38 years and 50%

were males. 3 patients were diabetic and 3 were hypertensive. The most frequent symptoms reported by patients associated with SARS-CoV-2 infection were fatigue (95%), muscle pain (87.5%), fever (65%), headache (62.5%), nasal obstruction (47.5%), diarrhea (35%), cough (30%), rhinorrhea (27.5%), dyspnoea (7.50%) (Table I). None of the study participants reported hospitalization or intensive care unit stay during the period of CoVid infection. None of the patients had undergone therapy for post CoVid OD. In this study, at 6 weeks post CoVid none of the patients had nasal complaints. The objective assessment of olfaction using the SST revealed OD in 37 (92.5%) of which 26 (65%) had hyposmia and 11 (27.5%) had anosmia 6 weeks post CoVid infection. At 10 weeks Post CoVid, 22 (55%) had OD of which 14 (35%) had hyposmia and 8 (20%) had anosmia. 10 (25%) had persistent OD 12 weeks Post CoVid (Fig. 3). None of the patients had other olfactory distortions like parosmia, cacosmia. There was no association found between age, co-morbidities and OD at 6,10 and 12 weeks Post CoVid ($p > 0.05$). Hyposmia was common among females at 10 weeks post CoVid which was found to be statistically significant ($p < 0.05$). There was improvement in SST scores at the end of 12th week post CoVid which is shown in (Table II). Majority of people with hyposmia recovered early compared to anosmics, who had longer recovery time. In this study, out of 40 patients 3 had persistent anosmia even after 6 months post CoVid infection, MRI of brain and paranasal sinus of them showed normal study and they were treated with short course of intranasal steroid therapy and found to have no improvement in olfaction.

All the patients data were collected in predesigned proforma and entered in excel sheet. All the collected data were summarized as frequency, percentage, mean and standard deviation. The summarised data were represented with the help of tables and figures. The categorical data was analysed using chi-square test, a p-value of < 0.05 was considered statistically significant and all the statistical analysis was performed using SPSSv21 operating on windows 10.

Table I : Clinical-demographic characteristics

CHARACTERISTICS	PATIENTS
Sample size	40
Age (mean ± SD)	36.8 ± 14.6
Gender	Males
	Females
	20 (50%) 20 (50%)
Comorbidities	Diabetes Mellitus - 3 Hypertensives - 3
Hospitalization	0
PRESENTING SYMPTOMS DURING COVID INFECTION	N (%)
Fever	26 (65%)
Headache	25 (62.5%)
Muscle pains	35 (87.5%)
Rhinorrhoea	11 (27.5%)
Nasal obstruction	19 (47.5%)
Diarrhoea	14 (35%)
Fatigue	38 (95%)
Dyspnoea	3 (7.5%)
Cough	12 (30%)

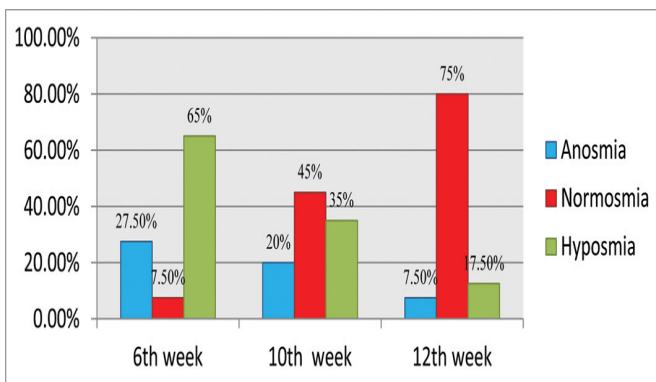
Fig. 3. Olfactory scores at 6th, 10th, 12th week Post CoVid infection assessed using SST

Table II : Sniffin stick scores

SST SCORES	(mean +SD)
At 6 weeks	8.6 + 2.7
At 10 weeks	11.3 + 2.9
At 12 weeks	12.5 + 2.986

Discussion

Loss of smell is a key symptom of the corona virus disease 2019, which may be an isolated symptom or associated with other general and otolaryngological symptoms. Postviral Olfactory Loss (PVOL) is not a uncommon phenomenon. Numerous virus has been advocated to enable OD, but some studies found that rhinovirus and parainfluenza-2 to be the predominant cause of PVOL. Previous studies have shown olfactory loss following viral infection among female patients.⁹ In our study, hyposmia was common among females at 10 weeks post CoVid. Several studies suggest that a significant number of patients may have persistence of symptoms for several weeks to months after resolution of acute CoVid illness which is known as syndrome of Post-Acute Sequelae of CoVid (PASC) or long CoVid or chronic CoVid.¹⁰ Symptoms of PASC include persistent fatigue, dyspnea, anosmia, cognitive dysfunction ('brain fog'), anxiety, depression and insomnia. Several mechanisms have been proposed to explain persistence of symptoms in PASC including viral reservoirs, continued inflammation, development of autoantibodies, and/or sequelae of organ damage during acute infection.^{11,12} Exact pathophysiology behind CoVid-19 induced OD remains unclear. OD in CoVid-19 infection could be related to the involvement of the olfactory bulb or damage to the peripheral olfactory receptor cells in the nasal neuroepithelium as SARSCOV-2 is neurotrophic in nature. An emerging consensus favors a crucial role of the sustentacular cells in the olfactory epithelium as the primary mechanism of CoVid-induced anosmia.¹³ CoVid-19-related smell impairment usually does not affect patients with significant nasal symptoms, a small percentage of patients might have a component of nasal

inflammatory changes contributing to the hyposmia.¹⁴ In our study none of the patients had nasal complaints at the time of olfactory assessment and majority of the patients with hyposmia at 6 weeks from onset of smell loss recovered early compared to patients with anosmia, who had longer recovery time. In a study done by Tsivgoulis G et al showed hypothyroidism was independently ($p=0.021$) associated with higher likelihood of persistent OD among patients with CoVid-19.¹⁵ In our study none of the patient had hypothyroidism or any other metabolic disorders.

In a study done by Tsivgoulis G et al showed that CoVid-19-induced persistent (>40days) OD was associated with olfactory bulb atrophy on high-resolution brain MRI.¹⁶ A study done by Yildiz E et al¹⁷, to assess the effect of steroid nasal spray in patients with CoVid 19 related OD showed topical corticosteroids was found to be successful in the treatment of OD due to CoVid-19. In this study, out of 40 patients 3 had persistent anosmia even after 6 months post CoVid infection, MRI scan of these patients showed no such significant findings and they were treated with steroid nasal spray and found to have no improvement in olfaction.

The duration of OD in CoVid-19 disease is still unclear. Most of the studies show that anosmia in CoVid recovers within a period of 4-6 weeks, but cases of persistent anosmia lasting more than 3 months are also being reported.¹⁸ Using established smell tests will help to characterize post CoVid OD in more detail. In India mostly subjective evaluation of CoVid-19 induced OD results is carried out. Objective assessment of olfaction will be effective in identifying patients with true Post CoVid OD. The Sniffin 'Sticks Test - (SST) is a semi-objective and validated olfactory test used for assessment of OD.¹⁹ A study by Vaira et al, reported that 10.3% of patients who were found to have a disorder on objective testing had self-reported normal function.²⁰

A study by Amer et al²¹, reported an association of comorbidities with a worse olfactory recovery in patients with allergic rhinitis, smoking, and hypertension. In our study, there was no association of comorbidities with the recovery of OD following the CoVid infection.

The limitations of our study is the smaller sample size.

A study with a larger patient numbers with all levels of disease severity will be needed to determine whether there are predisposing factors for developing long term post CoVid OD.

Conclusion

Eventhough we have overcome the worst part of the initial outbreak of CoVid-19 infection, post CoVid OD has a huge negative impact on the QOL. Knowledge about time pattern on the recovery of Post CoVid OD will be essential and by objectively evaluating these patients using SST will help us to identify people with true OD and treating them. In our study most of patients with post CoVid OD recovered their olfaction at the end of 12th week post CoVid, so proper counselling and olfactory training will be essential before initiation of any treatment for post CoVid OD.

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