

## Subjective and Objective Analysis of Prevalence of Anosmia and Hyposmia in Covid 19 Infected Patients in a Tertiary Care Centre - A Cross-sectional Study

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### Abstract

The new coronavirus disease 2019 (Covid-19) is a highly contagious viral infection resulting from the SARS-CoV-2 (severe acute respiratory syndrome - covid virus - 2) infection, which is transmitted from human to human by respiratory secretions. This virus, belonging to the coronavirus family, can result in various clinical presentations of the disease, from common rhinorrhoea to severe acute respiratory syndrome.

This study was conducted in covid positive patients admitted in Sakra World Hospital, Bangalore, a tertiary care centre. This paper reviews the olfactory physiology and summarizes the clinical reports of anosmia and hyposmia in this current viral outbreak, specifically aimed at identifying if anosmia/hyposmia is one of the major indicating symptom of covid infection and to examine the possible role of olfactory disturbances as a screening diagnostic tool in mildly symptomatic patients.

The study was conducted on 200 patients with a positive RTPCR (Reverse transcriptase polymerase chain reaction) for Covid and admitted in our hospital, each patient was assessed with a subjective DynaCHRON questionnaire and then underwent objective Indian smell identification test to identify odor discrimination and odor threshold. The data regards the prevalence of hyposmia and anosmia along with the prevalence of isolated olfactory dysfunction and was found that hyposmia [58.50%] was more prevalent than anosmia [7.50%]. Olfactory dysfunction is severe in grade [28.50] and isolated olfactory dysfunction was seen in 20.50%, which is statistically significant with p value  $p < 0.0001$ .

We conclude that the olfactory dysfunction is one of the common symptom in Covid 19 infected patients with moderate to severe degree of loss and the objective smell test can be a helpful screening tool in diagnosing the early phase of the disease.

**Keywords:** COVID 19; Olfactory Dysfunction; Hyposmia; Anosmia

## Abbreviations

COVID 19: Corona Virus Disease; SARS-CoV: Severe Acute Respiratory Syndrome - Corona Virus; RTPCR: Reverse Transcriptase Polymerase Chain Reaction; DynaCHRON : Dysfonctionnement Nasal Chronique; ACE 2 : Angiotensin - Converting Enzyme 2; Ors: Odorant Receptors; OSNs: Olfactory Sensory Neurons; SuC: Sustentacular Cell; TMPRSS 2: Transmembrane Protease, Serine 2 Enzyme; INSIT: Indian Smell Identification Test

## Introduction

The pandemic of Coronavirus Disease (COVID-19) has caused a major health disaster throughout the world. It is highly contagious viral infection resulting from the SARS-CoV-2 infection, which is known to cause infection from human to human by respiratory droplets. Nasal respiratory epithelial cells and olfactory epithelial support cells have shown to express high levels of ACE2 proteins and is seen that it is in turn used by the SARS-Cov2 virus, which causes the COVID-19 syndrome [1].

There is increasing evidence that olfactory dysfunction can present in COVID-19 patients. Olfactory dysfunction can occur alone or can present along with other symptoms of COVID-19. However, the pathogenic mechanism of olfactory dysfunction and its clinical characteristics in patients with COVID-19 remains unclear [2].

As the molecules of substances are transported via the nasal cavity, the quality and intensity of smell perception depends on the state of the nasal epithelium and the status of the peripheral and central nervous system. Initially, odorants enter the nasal cavity, and will reach the olfactory cleft area. The odorants are detected by the odorant receptors (ORs) on the cilia of the OSNs. This leads to the opening of the chloride channels and in turn causes the efflux of chloride ions, resulting in action potential [3].

Anosmia is defined as the inability to detect olfactory sensations (i.e., absence of smell function). Hyposmia or microsmia refers to decreased sensitivity to odours [4].

There are several known aetiologies for olfactory disturbances, few cases with permanent anosmia or hyposmia might be due to prior upper respiratory infections, head trauma, and nose and paranasal sinus diseases, of these most causes usually reflect a permanent damage to the olfactory neuroepithelium. Despite of

detailed evaluations in substantial proportion of cases the cause remains idiopathic [4].

Factors that predispose individuals to post viral olfactory dysfunction and the mechanisms underlying it remain unclear, although direct insult to an already compromised neuroepithelium is one of the possibilities and in rare cases, central structures may also become involved [4].

Coronavirus enters the hosts olfactory neuroepithelium and further accumulates in the sustentacular cells (SuC) which abundantly express ACE2 and TMPRSS2 protein. SuCs normally involved in the processing of the odorants by endocytosis of the odorant-binding protein complex [5].

COVID-19, has the neuroinvasive propensity, with olfactory neurons being currently discussed as a portal of entry for neuroinvasion and the spread of CoVs after infection of neural cells from CNS to the periphery via transneuronal route [10]. The olfactory neuroepithelium has the ability to regenerate, but in few cases where there is significant amount of damage to the basement membrane, regeneration can be incomplete [6].

Early in infection, SARS-CoV-2 targets cells, such as nasal and bronchial epithelial cells and pneumocytes, through the spike (S) protein that binds to the angiotensin-converting enzyme 2 (ACE2) receptor. The type 2 transmembrane serine protease (TMPRSS2), present in the host cell, promotes viral uptake by cleaving ACE2 by endocytosis and activates the S protein of the virus, which in turn mediates coronavirus entry into host cells [7-10].

The progression and severity of olfactory dysfunction in Covid-19 is still not well - known. Usually in post-viral anosmia, around 30 to 50% of the patients reported complete recovery of their olfaction, while 50% show permanent anosmia [10,11].

## Materials and Methods

In this study 200 patients admitted in Sakra World Hospital, Bengaluru with positive RTPCR for covid 19 and who are clinically stable and not on prolonged and high oxygen requirement and with no previous history of nasal surgeries or smell disturbances were assessed. Each Patient was subjected to subjective DynaCHRON Questionnaire and objective smell identification test after taking written informed consent. Patients were evaluated by a single

investigator and within the stipulated time specified for the study from December 2020 to May 2021.

### Subjective test: Translated DyNaCHRON Questionnaire

The DyNaChron (Dysfonctionnement Nasal Chronique) self-reporting questionnaire, a subjective instrument, should be compared with objective measurement instrument.

Olfaction loss self-assessment grid (extracted from the DyNaCHRON questionnaire first 10 questions). DyNaCHRON is a validated questionnaire for global assessment of rhinologic functions. We used a short version of DyNaCHRON including only the first few questions concerning nasal symptoms, smell perception and taste abilities [12].

Based on various Subjective scales references the Questionnaire results will be analysed: 1 to 4 indicate mild symptom, scores of 5 - 6 indicate moderate symptom, and ratings of 7 to 10 indicate severe symptom (Serlin., et al. 1995).

commercially available were used. Cotton buds dipped in the essence, used as test material and placed 1 cm in front of the nostril with the other nostril closed and repeated in the other. The subject was asked to sniff and identify the smell from the answer card containing four choices for each odorant [4].

### Interpretation

The response was scored 1 for the correct and 0 for the wrong response and the cut-off value of 4 is considered (values ≤4 - Hyposmia; Value 0 - Anosmia).

### Results

In the current study, identification of olfactory dysfunction, odor identification and odor threshold were assessed. Olfactory threshold was considered for grading the severity of loss of smell and it was compared with the subjective DynaCHRON questionnaire.

Out of 200 patients included in the study, 114[57.00%] and 86[43.00%] were females and majority of age group was between 31-40 years [34%] and 57[28.50] had severe infection, 30[15%] had moderate infection and 33[16.50%] had mild disease and the rest 80[40%] [Figure 1] had no smell disturbances based on DynaCHRON questionnaire and 41[20.50%] had Isolated olfactory dysfunction [Figure 2] which was statistically significant with p value of 0.0001 and it was not associated with age or gender of the patient.

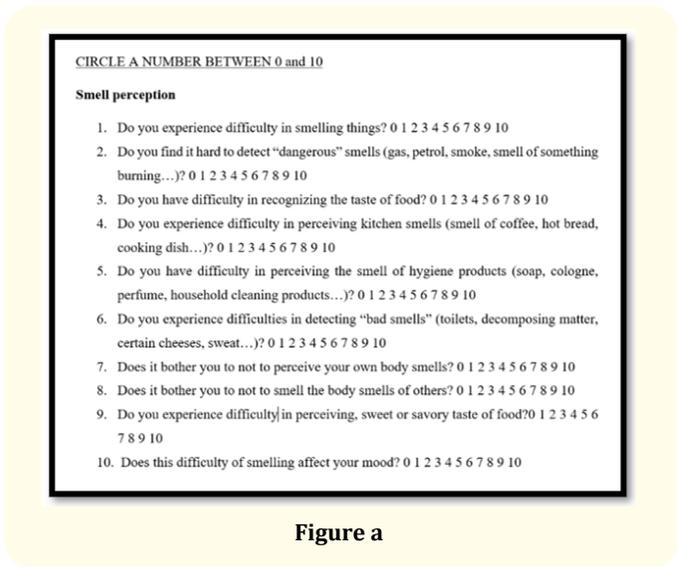


Figure a

### Objective test

Essence of 10 commonly used items were used as odorants.

The chosen odorants, represent familiarity in day-to-day life. The essence of cardamom, kewra, khus, lemon, mango, orange, pineapple, rose, thinner, vanilla in 20 ml airtight bottles

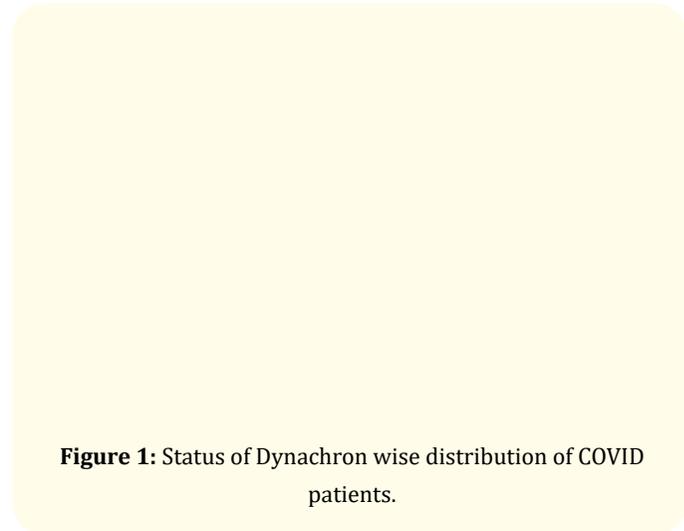
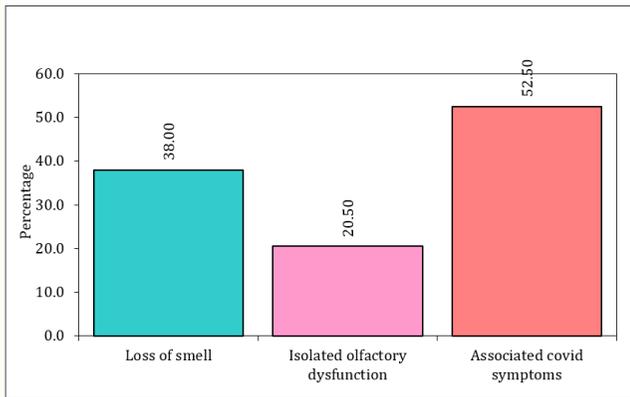


Figure 1: Status of Dynachron wise distribution of COVID patients.



**Figure 2:** Presence of Loss of smell, Isolated olfactory dysfunction and Associated covid symptoms wise distribution of COVID patients.

INSIT was used to categorise these patients with smell disturbances of Hyposmia or Anosmia, to know the prevalence of both. It was seen that hyposmia 117[58.50%] was more prevalent than anosmia 12[7.50%] [Figure 3].

The Indian smell identification test was used to detect the olfactory dysfunction by analysing both odor discrimination and odor threshold [Figure 4] objectively to correct the subjective error of DynaCHRON questionnaire.

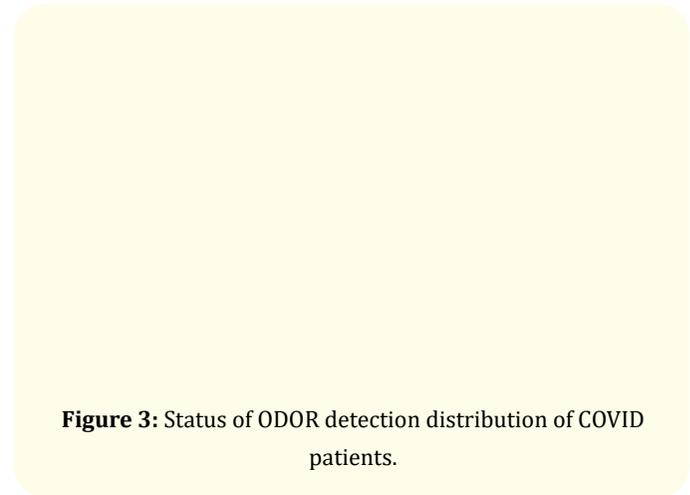
On comparing both the odor threshold and DynaCHRON it was found that most patients with smell dysfunction had severe type of disease which is also confirmed statistically by kappa agreement as seen in the table 1 below.

| Between            | Agreement | Expected Agreement | Kappa  | Std. Err. | Z-value | p-value |
|--------------------|-----------|--------------------|--------|-----------|---------|---------|
| DYNACHRON and ODOR | 69.00%    | 53.20%             | 0.3376 | 0.0701    | 4.8100  | 0.0001* |

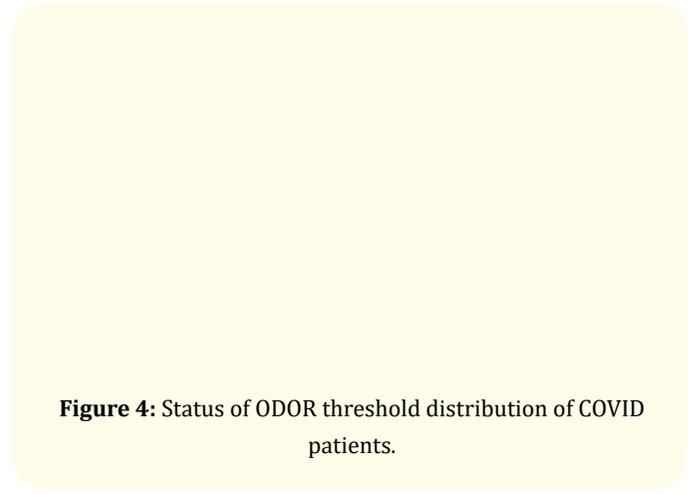
**Table 1:** Agreement between DYNACHRON and ODOR by Kappa statistics.

\*p < 0.05.

As per the statistician, minimum value of 53.20% is required to consider 2 tests reliability on each other. The statistical comparison between our subjective and objective test showed the agreement of 69%, indicating both tests are reliable and complement each other with a statistically significant p value of 0.0001.



**Figure 3:** Status of ODOR detection distribution of COVID patients.



**Figure 4:** Status of ODOR threshold distribution of COVID patients.

### Discussion

Olfaction is a primitive sense and is quite important for our day-to-day life. In the current study, the smell identification ability of our admitted patients is assessed using an Indian population specific test. INSIT is commercially available, and easy to perform. It includes 10 validated odorants, and it has been correlated with the

subjective DynaCHRON questionnaire. Significant agreement in the scores were seen among admitted patients and combined scores showed agreement of 68% with Kappa analysis with significant p value of 0.0001. This clearly shows that the olfaction is impaired in Covid 19 infected patients. Both the DynaCHRON questionnaire as well as INSIT was able to detect olfactory impairment in the tested population.

In the present study, prevalence of Isolated olfactory dysfunction was assessed along with odor identification and odor threshold was assessed. Olfactory threshold was considered for grading the severity of loss of smell and had similar results when compared to subjective DynaCHRON questionnaire.

In our study it was noted that few patients, were able to detect the odorant but were not able to identify them. This might be due to early involvement of olfactory function as a part of the disease process and not much because of unfamiliarity with the odorant as we used culturally specific Objective test.

INSIT was used to categorise these patients with smell disturbances of Hyposmia or Anosmia, to know the prevalence of both. It was seen that hyposmia 117[58.50%] was more prevalent than anosmia 12[7.50%] [Figure 3] and it was also noticed that patient who gave history of mild to moderate disease in DynaCHRON questionnaire were, able to identify most of the odorants in INSIT, indicating that these patients might be recovering from olfactory dysfunction, and this also tells us that post viral anosmia following Covid 19 might be transient olfactory dysfunction with spontaneous recovery.

## Conclusion

Based on the above-mentioned results and discussion of our study, we conclude that:

- There is a high prevalence of olfactory dysfunction in covid positive patients
- These standardized olfactory tests could be used as a screening tool in mildly symptomatic patients.
- 58.50% of hyposmia suggests, much larger prevalence of hyposmia and not anosmia with 7.50%
- Isolated olfactory dysfunction should raise a high index of suspicion in suspected covid positive patient.

Based on history and observation of the acquired data in large number of covid patients, it suggests that the patients can present to us with olfactory complains with or without other associated complains, so early objective olfactory testing could be a helpful screening tool. The severity of olfactory dysfunction in covid patients does not correlate with the disease or its progression.

To assess the disease onset, progression and sequelae, early screening for olfactory dysfunction with serial olfactory testing at graded intervals is recommended.

## Conflict of Interest

The authors declare that they have no conflict of interests.

## Informed Consent

Written informed consent was obtained from participant included in the study.

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