



Taste Dysfunction In COVID-19 Patients; A Cross-Sectional Observational Study

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ABSTRACT

Introduction

It has been observed that olfactory dysfunction (anosmia, hyposmia and parosmia) and gustatory (taste) dysfunction (ageusia, hypogeusia and dysgeusia) are one of the classical presentations of COVID-19. Gustatory (taste) dysfunction attributable partly to loss of retro-nasal olfaction (which adds to the flavour, a component of taste sensation) while eating or drinking food.

Materials and Methods

It is a cross sectional observational study involving COVID-19 patients aged between 18 to 100 years. Taste dysfunction was analysed and compared with various inflammatory markers and sino-nasal symptoms.

Results

In this time bound study, 61.88 % of the study participants were male and 38.13 % were females. Majority of the participants were in the age group between 20 and 60 years. Fifty four (33.75%) developed gustatory dysfunction in the form of ageusia/hypogeusia. Among the individuals with ageusia/hypogeusia, majority of the patients (n=26) (48.15%) complained of 50-75% loss of taste sensation followed by 50-75% loss of taste sensation in fourteen (25.93%) patients. Mean duration of ageusia/hypogeusia among 54 patients was 9.33 ± 4.13 days. There was no statistically significant association between gustatory or taste dysfunction with serum inflammatory markers except serum ferritin levels. There was significant relationship between presence sino-nasal symptoms and development of taste dysfunction.

Conclusion

Ageusia (hypogeusia) was found in significant proportion of patients with COVID-19. These symptoms also contribute to significant proportion of depression and low confidence and results in poor nutrition and subsequent nutritional deficiencies which may lead to long Covid syndrome.

Keywords

Taste disorders; Ageusia; Coronavirus; Smell

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly infectious novel coronavirus leading to Coronavirus disease 2019 (COVID-19).^{1, 2} The disease was first detected in December 2019 in Wuhan seafood market, China. Being

highly infectious, this virus caused the deadly pandemic leading to millions of individuals being infected and has killed lakhs of people across the globe. Fever, cough and breathlessness along with constitutional symptoms like fever and myalgia are the classical symptoms of COVID-19.^{3, 4, 5}

It has been observed that olfactory dysfunction (anosmia, hyposmia and parosmia) and taste dysfunction (ageusia, hypogeusia and dysgeusia) are one of the classical presentations of COVID-19. It has been observed that anosmia coincides with the occurrence of taste dysfunction (TD) manifesting as ageusia or

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hypogeusia and is attributed to loss of retro-nasal olfaction (which adds to the flavour, a component of taste sensation) while eating or drinking food.⁶ Although the exact mechanism is not known it is found now that there are ACE-2 (Angiotensin Converting Enzyme-2) receptors present on the gustatory epithelium which may act as the receptors for SARS-CoV-2.⁷

The need for the study: Taste dysfunction is one of the early symptoms of COVID-19 and has been considered not only troublesome for oral nutrition but also a contributor of the significant proportion of depression in COVID-19. However, the prevalence of taste dysfunction varies widely as reflected by the results of various studies. It is important to recognize these symptoms early so that the infected person can be diagnosed, isolated and treated early. Hence, this study was undertaken to know the prevalence of taste dysfunction in patients admitted to tertiary care hospital.

Primary objective of the study was to find the prevalence of taste dysfunction and sino-nasal symptoms in patients with COVID-19.

Secondary objectives of the study was to (i) find the

relationship between classical symptoms of upper respiratory viral infection (rhinorrhea, nose block and headache) with the occurrence of taste dysfunction (ii) find the relationship between taste dysfunction and markers of inflammation in COVID-19.

Materials and Methods

This was a cross-sectional study involving all admitted patients with COVID-19. The diagnosis of COVID-19 was made by either of the following

- Presence of SARS-CoV-2 RNA detected by reverse transcription polymerase chain reaction (RT-PCR) in the nasopharyngeal or oropharyngeal swab specimens&/or
- Positive Rapid Antigen Test for SARS-CoV-2.

The diagnosis was made based on the interim guidelines issued by the ministry of health and family welfare (MOHFW), Government of India.

Patients with COVID-19 were classified based on the severity into 3 categories as per Indian Council of Medical Research (ICMR) (Table I).

Table I : COVID-19 disease category based on severity according to ICMR

CATEGORY	CRITERIA
GROUP A	<ul style="list-style-type: none"> ● Asymptomatic or patients with mild symptoms. ● Respiratory rate less than 24 per minute and ● Oxygen saturation (SpO₂) more than 94% in room air.
GROUP B	<ul style="list-style-type: none"> ● Symptomatic patient with mild to moderate pneumonia with no signs of severe disease. ● Respiratory rate 24 to 30 per minute and SpO₂ 90% - 94% in room air.
GROUP C	<ul style="list-style-type: none"> ● Symptomatic patient with severe pneumonia with any of the following <ul style="list-style-type: none"> ■ Respiratory rate more than 30 per minute ■ SpO₂ less than 90% in room air or less than 94% with oxygen ■ Acute respiratory distress syndrome (ARDS) ■ Septic shock

All patients admitted were screened for sino-nasal symptoms and taste dysfunction at the time of admission after obtaining the written informed consent. The duration of each symptom was recorded. Patients were followed up until their discharge from the hospital or until death due to COVID-19. Time taken for recovery from TD was recorded.

This was a cross sectional study with universal sampling technique adopted to all the consecutive COVID-19 patients admitted between 25/08/2020 to 25/11/2020. There were no interventions or drug trial involved in this study. Institutional ethical committee clearance was obtained.

Inclusion criteria was all patients with COVID-19 aged between 18 to 100 years admitted to KVG medical college and hospital. Exclusion criteria were (i) patients who did not give consent to participate in the study (ii) patients with pre-existing taste abnormality (due to any etiology).

Following history were recorded to assess sino-nasal symptoms: Running nose/nasal discharge, nose block, headache/facial pain, excessive sneezing, nasal itching, post-nasal drip.

Following definitions were used in the assessment of taste dysfunction (TD): (a) Ageusia: total loss of taste sensation (b) Hypogeusia: reduced but intact taste sensation (c) Parageusia: altered taste sensation. No objective taste measurement tools were used and all the above symptoms were based on the subjective reporting by study participants. However, severity of loss or reduction of taste sensation was graded as less than 25% loss, 25 to 50% loss, 50 to 75% loss and more than 75% loss of taste sensation as reported by study participants. Similarly, no objective measurement scales were used for quantification of loss of smell or alteration of smell.

Following data were collected: (i) Demographic details: Age, gender (ii) Comorbid medical conditions (iii) Sinonasal symptoms related to COVID-19 (iv) Taste symptoms (as mentioned above) (v) Investigations- Haematological parameters like Complete blood count, Renal function tests (serum creatinine, blood urea), liver function tests (serum bilirubin, serum albumin, total protein, transaminases), blood sugars [Random blood sugar (RBS), glycosylated hemoglobin percent (HbA1c)], inflammatory

markers [C-reactive protein (CRP), serum ferritin, Lactate dehydrogenase (LDH), D-dimer].

For statistical analysis, the data was entered in Microsoft office Excel 2007 and SPSS version 21 was used for analysis of data. The prevalence of sino-nasal dysfunction and taste dysfunction was calculated. The relationship of these symptoms was correlated with the disease inflammatory markers. The data was shown in the form of percentages and means. Chi-square test & t test was used for analysis.

Results

This cross sectional study included 160 patients diagnosed with COVID-19. In this time bound study, 61.88 % of the study participants were male and 38.13 % were females. Majority of the participants were in the age group between 20 and 60 years. The mean age of male study participants was 44.96 ± 16.28 years, and that of female study participants was 43.75 ± 16.78 years. The mean age of the whole study population was 44.50 ± 16.43 years (Fig. 1).

Hypertension and Diabetes mellitus were the most common comorbid conditions in the study accounting for 25% and 20.62% respectively. 80 (50%) of the study participants did not have any identifiable comorbid conditions (Table II).

In this study we categorized the Covid-19 patients in 3 disease severity category as per ICMR protocol (category A, B & C). This categorization is based on the in-hospital follow up. The participants who were initially in category A and later progressed to category B were included in category B for the analysis. We, observed that majority of the patients (n=107) belonged to category B, accounting for 66.87%. Forty three (26.87%) and ten (6.25%) of patients belonged to category A and C respectively (Fig. 2).

The baseline hematological and biochemical parameters are analysed. The mean vitamin D3 levels in the study was 16.38 ± 9.12 ng/mL which is the deficiency range. The mean CRP level was 19.31 ± 43.88 mg/L which is more than the normal upper limit (10mg/L). The mean LDH level was 406.42 ± 127.55 IU/L which is also

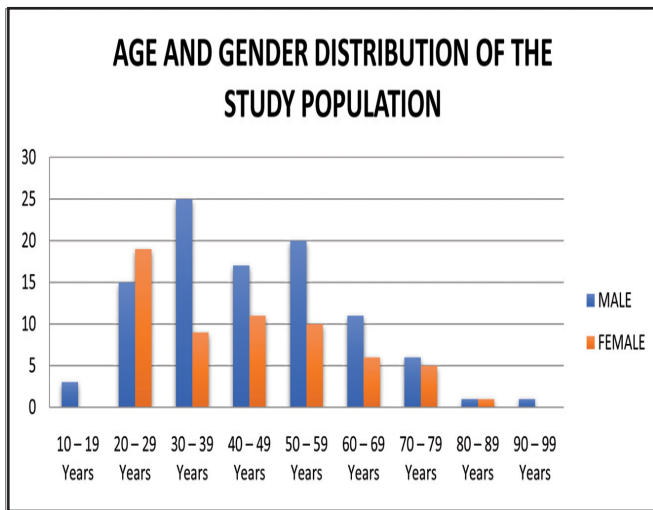


Fig. 1. Bar diagram of age and gender distribution of study population

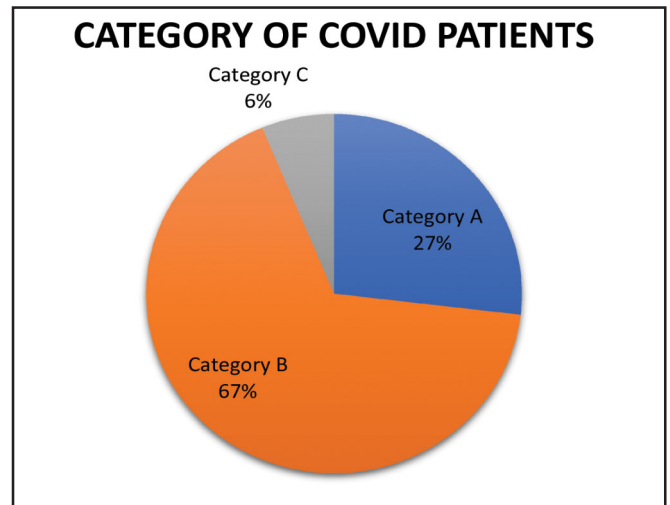


Fig. 2. Distribution of patients among category A, B and C severity group

Table II: Comorbidities in the study population

SL. NO.	COMORBIDITIES	NO. OF PATIENTS NO. (%)
1	Hypertension	40 (25%)
2	Diabetes Mellitus	33 (20.62%)
3	Hypothyroidism	4 (2.5%)
4	Ischemic heart disease (IHD)	1 (0.62%)
5	Maturity onset diabetes of young (MODY)	1 (0.62%)
6	Supraventricular tachycardia (SVT)	1 (0.62%)
7	No Comorbidities	80 (50%)

beyond the normal range (105-333 IU/L). The mean D-dimer level was 0.59 ± 1.03 g/L which is slightly above the normal upper limit (0.5 g/L). These observations suggest that there is significant inflammation in patients with Covid-19 across all categories of severity.

In this study, we collected serial values of CRP, serum ferritin levels, serum LDH 1 levels and D-dimer levels (which were done as per protocol of the ministry of health

and family welfare). At least 3 values of the above mentioned parameters were collected. It was observed that there was improvement in the serial CRP levels as compared to D-dimer and serum ferritin levels. However, there was no significant change in the serial LDH 1 levels.

Among the sino-nasal symptoms headache was the most common symptom which was seen in twenty three (14.37%) study participants. The mean duration of headache was 7 ± 3.68 days. Thirteen (8.12%) patients had running nose and five (3.12%) had nose block. The mean duration of running nose and nose block was 5.69 ± 2.56 days and 9.4 ± 5.94 days respectively.

Fifty four (n=54) (33.75%) developed gustatory dysfunction in the form of ageusia or hypogeusia. Among the individuals with ageusia/hypogeusia, majority of the patients (n=26) (48.15%) complained of more than 75% loss of taste sensation followed by 50-75% loss of taste sensation in fourteen (25.93%) patients. Mean duration of ageusia/hypogeusia among 54 patients was 9.33 ± 4.13 days (Table III).

The mean CRP level among patients with TD is 20.49 ± 52.65 mg/L as compared to 18.70 ± 38.92 mg/L among patients without TD. This was not statistically significant (p=0.8081) (Table IV).

The mean ferritin level among patients with TD is

Table III: Severity of symptoms in patients with COVID-19

SNO.	SEVERITY OF SYMPTOMS (% of loss of taste sensation)	AGEUSIA/HYPOGEUSIA NO. (%)	MEAN DURATION OF SYMPTOMS (in days)
1	< 25 %	6 (11.11 %)	6.83 ± 2.31
2	25 – 50%	8 (14.81%)	8.37 ± 6.02
3	50 – 75 %	14 (25.93%)	10.21 ± 3.35
4	> 75%	26 (48.15%)	9.73 ± 4.09

Table IV: Taste dysfunction in COVID-19 patients belonging to different categories

GUSTATORY DYSFUNCTION	MEAN CRP (mg/L)	MEAN FERRITIN (mcg/L)	MEAN LDH (IU/L)	MEAN D DIMER (g/L)
Category A				
Gustatory dysfunction	19.34 ± 70.41	199.47 ± 260.24	403.95 ± 93.78	0.29 ± 0.19
No Gustatory dysfunction	17.02 ± 41.71	164.57 ± 163.72	403.32 ± 162.89	0.59 ± 1.60
T Value	0.1349	0.5372	0.0150	0.8243
p Value	0.8933	0.5940	0.9881	0.4145
Category B				
Gustatory dysfunction	22.34 ± 42.86	240.72 ± 304.66	416.62 ± 99.11	0.45 ± 0.35
No Gustatory dysfunction	14.10 ± 24.48	152.54 ± 165.13	393.08 ± 129.27	0.45 ± 0.44
T Value	1.2570	1.9341	0.9204	0.0117
p Value	0.2115	0.0558	0.3595	0.9907
Category C				
Gustatory dysfunction	8.01 ± 7.82	731.87 ± 562.81	592 ± 151.63	0.7 ± 0.79
No Gustatory dysfunction	73.81 ± 92.90	223.16 ± 204.60	440.57 ± 130.79	3.53 ± 2.05
T Value	1.1837	2.2168	1.6100	2.2470
p Value	0.2705	0.0575	0.1461	0.0548

253.49 ± 321.47 mcg/L as compared to 159.93 ± 166.71 mcg/L among patients without TD. This was statistically significant (p=0.0163) (Table IV).

The mean LDH-1 level among patients with TD is 421.90 ± 106.63 IU/L as compared to 398.53 ± 136.79 IU/L among patients without TD. This was statistically not significant (p=0.2744) (Table IV).

The mean D-dimer level among patients with TD is 0.41 ± 0.34 g/L as compared to 0.69 ± 1.23 g/L among patients without OD. This was statistically not significant (p=0.1043) (Table IV).

We compared the inflammatory markers like CRP, serum ferritin, serum LDH-1 and D-dimer in patients with and without taste dysfunction across all three disease category (category A, B & C). There was no statistically significant association between gustatory or taste dysfunction with any of the above serum inflammatory markers (Table IV).

A total of 54 patients (prevalence = 33.75%) developed taste dysfunction. 10.62% of the patients with sino-nasal symptoms developed taste dysfunction and there was significant relationship between presence sino-nasal symptoms and development of taste dysfunction.

Discussion

In a meta-analysis of 3563 patients with COVID-19 infection, it was found that the mean prevalence of self-reported loss of smell to be 47%.⁸ Moein *et al.* demonstrated that 98% of the hospitalized study participants (n=60) had some degree of OD on formal testing, whereas only 35% had self-reported loss of smell or taste. Hence, formal testing for OD and TD is more accurate than just relying on self-reporting of the symptoms.⁹

In a metaanalysis, 32,918 patients out of 138,785 patients had TD.¹⁰ Taste dysfunction may last for months with very little improvement after about two months.^{11,12} Hence, TD has considered as one of the harbinger of long COVID syndrome.

One of the proposed mechanism of TD is the binding

of SARS-CoV-2 to angiotensin converting enzyme-2 receptors in the salivary glands leading to impaired salivary flow.¹³ There is limited literature available on the correlation between TD and the COVID-19 disease severity.

In a metanalysis, it was found that 78.8% of patients had taste recovery at 30 days, 87.7% at 60 days, 90.3% at 90 days, and 98.0% at 180 days, with median recovery time of 12.4 days.¹⁴

In our study, mean duration of ageusia/hypogeusia among 54 patients was 9.33 ± 4.13 days. As mentioned earlier we could not follow up the patients until complete recovery of the taste perception.

ACE2 receptors are expressed highly over tongue than other parts of oral cavity and this may be the likely reason for taste dysfunction. ACE2 receptors are also expressed on various cells of the body (glial cells and neurons in the brain, alveolar epithelial cells, gut, kidney and myocardium).^{15, 16}

There is no data on the pharmacological or non-pharmacological interventions to improve the taste dysfunction.

Following are the limitations of the study:

1. The assessment of TD was subjective.
2. Objective examination to detect specific modality of taste dysfunction was not carried out.
3. Long term follow up of the patients is not done to know the average time taken for complete recovery from TD.
4. Effect of these symptoms on the quality of life and mental health is not evaluated.
5. The effect of medications on the occurrence and severity of TD is not evaluated.

Conclusion

Ageusia (or hypogeusia) was found in significant proportion of patients with covid-19. These symptoms also contribute to significant proportion of depression and low confidence and results in poor nutrition and subsequent

nutritional deficiencies which may lead to long Covid syndrome.

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