New-Onset Ageusia among COVID-19 Patients - The Trend in the Indian Population

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ABSTRACT

Introduction
The COVID-19 virus has already caused a pandemic and needs no fresh introduction. Many studies in western literature have described the prevalence of anosmia and ageusia as symptoms of COVID-19. However, to our knowledge, there is no study describing the trend of new onset ageusia amongst covid positive patients in the Indian population. The objective of this study is to analyze the trend of new onset ageusia in COVID-19 affected individuals in the Indian population.

Materials And Methods
This is a retrospective observational study conducted in a treatment facility set up in Eastern part of India. The data was collected from Sep 2020 to Dec 2020. The study included 422 patients who were laboratory confirmed COVID-19 positive cases. Clinical data was extracted from the medical records of the patients. All the patients were treated as inpatients. The data was collected by Critical care specialist and Physician. All patients were classified as asymptomatic and symptomatic. The presence or absence of new onset ageusia was documented and statistically analyzed.

Result
Of 422 cases studied, 401 (95.0%) were male and 21 (5.0%) were female with the mean age of 37.9 ± 8.3 years. 147 (34.8%) were symptomatic and 275 (65.2%) were asymptomatic with 18 % (76/422) patients having ageusia in the study population.

Conclusion
The prevalence of ageusia amongst covid positive patients in Indian population is lesser as compared to reports in the western literature. The cause of this difference in prevalence of ageusia in different ethnicities is unknown. Apparently healthy individuals with new onset ageusia should be considered as asymptomatic covid carriers and should be treated accordingly.

Keywords
Ageusia; COVID-19; Indian; Prevalence; SARS-CoV-2; Taste

The COVID-19 or SARS-CoV-2 virus had already caused a pandemic and needs no fresh introduction. When the first case of COVID-19 infection emerged in Wuhan province of China, no one ever thought that this infection is going to baffle the scientists and researchers to unimaginable extents.¹² Today, millions of lives have been lost due to this virus and yet it continues to be a diagnostic challenge as far as clinical symptomatology is concerned.³ Apart from the usual and common symptoms of fever, malaise, and cough, there is nothing specific and unique which can be attributed to COVID-19 infection with infallible certainty. Moreover, more than 80% of individuals who are infected with this virus, are asymptomatic carriers of this virus.⁴

Many studies worldwide have tried to describe symptoms that could help in the early detection of COVID-19 infection. Two of these symptoms are anosmia and ageusia.⁵⁶ Anosmia has been explained by the neurotropic and neuroinvasive potential of the
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The invasion of the olfactory neuroepithelium leads to a sensorineural type of anosmia without the traditional manifestations of an upper respiratory tract infection i.e. nasal congestion and rhinorrhea. The pathophysiology of new-onset ageusia, however, is still unexplained among the covid positive patients. It has been postulated that angiotensin-converting enzyme 2 receptor, which is used by SARS-CoV-2 to bind and penetrate the cell, is widely expressed on the epithelial cells of the mucosa of the oral cavity. The prevalence of ageusia amongst the covid positive patients in western literature is 38-40 percent. However, in our hospital setup, we found that the number of COVID positive patients presenting with ageusia is lesser as compared to what has been described in the literature.

This study was conducted to analyze the trend of new-onset ageusia in the covid positive patients in the Indian population. To the best of the authors’ knowledge, this is the largest study so far in the Indian setup assessing the prevalence of new-onset ageusia amongst the patients infected with COVID-19.

Materials and Methods

This is a retrospective observational study conducted at a covid treatment facility set up in the Eastern part of India. We retrospectively analyzed patients from Sep 2020 to Dec 2020 who had been diagnosed as having COVID-19 infection according to the WHO technical guidance for laboratory diagnosis of COVID-19. A confirmed case was defined as a positive result on real-time reverse transcription polymerase chain reaction (RT-PCR) analysis of the nasopharyngeal specimen. Nasopharyngeal specimens were collected and placed in a viral transport media as per the laid down guidelines by the WHO. COVID-19 infection was confirmed by RT-PCR assay using a SARS-CoV-2 nucleic acid detection kit. Radiological assessment and laboratory testing including complete blood count, liver function test, and renal function test were done as per the clinical need of the patients.

A total of 422 patients were included in the study who were confirmed cases of COVID-19. All the patients were treated as inpatients in a separate treatment facility manned permanently by a Critical care specialist and a Physician. On admission, a detailed history was taken from the patient, and subsequently, every following day patients were asked about the development of any new symptom. It was specifically taken care of that no leading questions were asked to the patients regarding the loss of taste. The patients were discharged once the RT PCR for COVID-19 was negative. The sampling schedule was as per the laid down guidelines by the WHO, Indian Council of Medical Research (ICMR), and Ministry of Health and Family Welfare (MOHFW). All these patients were followed up for one month from the date of discharge. All of them reported complete recovery of taste. Only verbal consent was taken from the patients. Written informed consent was waived off keeping in view the high infectivity of the disease and urgent need to collect data.

Exclusion criteria included patients who had a history of middle ear surgery, tongue surgery, comorbidities like Hypertension and diabetes mellitus, and patients who required mechanical ventilation.

We reviewed the medical records of the laboratory-confirmed COVID-19 positive patients admitted to our covid treatment facility and collected data on age, sex, and presence or absence of symptoms. Patients were classified into two groups viz. asymptomatic and symptomatic. Asymptomatic patients were the ones who did not have had any symptom but were COVID positive when tested as contacts of lab-confirmed covid positive individuals. Symptomatic patients were the ones who presented with any symptom suggestive of COVID infection as described earlier and were tested positive thereafter.

All the symptoms were documented by the Critical Care specialist and the Physician. To minimize the risk of cross-infection no objective testing for the taste sensation was done.

The data on categorical variables is shown as n (% of cases). The inter-group statistical comparison of distribution of categorical variables is done using the Chi-Square test or Fisher’s exact probability test if more than 20% of cells have expected frequency less than five.

In the entire study, the p-value less than 0.05 is
statistically significant. All the hypotheses were formulated using two-tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data was statistically analyzed using Statistical Package for Social Sciences (SPSS ver 21.0, IBM Corporation, USA) for MS Windows.

Results

A total of 422 hospitalized patients with confirmed SARS CoV-2 infection were included in the analysis.

Age distribution:

Of 422 cases studied, 71 (16.8%) had an age between 24-28 years, 73 (17.3%) had an age between 29-33 years, 73 (17.3%) had an age between 34-38 years, 76 (18.0%) had an age between 39-43 years, 75 (17.8%) had an age between 44-48 years and 54 (12.8%) had age between 49-52 years.

The distribution of mean ± SD of age in the entire study group was 37.9±8.3 years and the minimum-maximum age range was 24-52 years.

Sex distribution:

Of 422 cases studied, 401 (95.0%) were male and 21 (5.0%) were female. The male to female sex ratio was 19:1 in the study group. This apparent disproportion in the gender distribution is because the covid treatment facility was set up for the soldiers and dependents of the Armed Forces. Later on, it was made exclusively for the soldiers and the dependents were kept in home isolation.

Distribution of symptomatic status of COVID-19:

Of 422 cases studied, 147 (34.8%) were symptomatic
and 275 (65.2%) were asymptomatic in the study group depicted by Fig 3.

Prevalence of ageusia:
Of 422 cases studied, 346 (82.0%) did not have ageusia and 76 (18.0%) had ageusia in the study group as depicted by Fig 4.

Prevalence of ageusia according to the symptomatic status of COVID-19 disease:
Of 147 symptomatic cases of COVID-19 disease, 71 (48.3%) did not have ageusia and 76 (51.7%) had ageusia. Of 275 asymptomatic cases of COVID-19 disease, none had ageusia.

The prevalence of ageusia is significantly higher in the group of symptomatic cases compared to a group of asymptomatic cases in the study group (P-value<0.001). The data is depicted in Table I.

Discussion
As the COVID-19 pandemic is affecting countries across the globe with many countries witnessing the second wave of the infection, accurate knowledge of the symptoms of this deadly infection and its trend across the various population is crucial in early diagnosis and management. Fever, cough, and malaise have been the most commonly observed symptoms and consistently reported across the globe. In the initial part of the pandemic, many anecdotal reports described the presence of anosmia and ageusia in the COVID-19 affected patients. However, due to the lack of data, it was difficult to identify them, with conviction, as established symptoms of the disease. Since then multiple studies have been conducted in the western countries to study the prevalence of anosmia and ageusia among the covid patients. To the authors’ best knowledge there is no study in the Indian setup assessing the prevalence of ageusia among the covid patients.

In our study, we found that the overall prevalence of ageusia among the covid positive patients was far less as compared to the reports in the western literature. The overall prevalence of ageusia in the present study was 18%. However, the prevalence was 51.7% when the same was calculated amongst the symptomatic patients. In the systematic review and meta-analyses conducted by Tong et al the prevalence of ageusia was 43.93% with a total of 1390 participants. Similarly, the studies conducted by Yan et al and Lechien et al reported the prevalence of ageusia to be 71% and 88% respectively.

In the study by Lee et al, 488 out of 3191, i.e. 15.3% of patients reported a loss of taste. They also reported complete recovery loss of taste in 3 weeks with an average recovery duration of 7 days. The findings in the above study are consistent with our study. In our study
too, all the patients with ageusia eventually recovered with complete recovery of taste sensation. Similarly, Giacomelli et al reported a prevalence of 10.1% (6/59) for dysgeusia and ageusia.\textsuperscript{19}

The reasons for this difference in the prevalence of ageusia among the Indian population as compared to others are unclear. In the systematic review and meta-analysis conducted by Von Bartheld et al, they found that the overall chemosensory dysfunction i.e. anosmia and hyposmia was 54.8% in the Caucasians and 17.7% in the Asians. They have postulated that a virus mutation (D614G) may cause differing infectivity, while at the host level genetic, ethnicity-specific variants of the virus-binding entry proteins may facilitate virus entry in the olfactory epithelium and taste buds.\textsuperscript{20} Similarly, the prevalence of anosmia reported by Mishra et al is less in the Indian population (14.8%) as compared to the European population (47%). Since both anosmia and ageusia are part of the chemosensory dysfunction, these findings to some extent explain the observed difference in our study.

We believe that this seemingly high prevalence of ageusia in the quoted literature could be due to a few other reasons. Most of these studies were cross-sectional in design and were conducted by email/web-based questionnaires with limited accuracy. Most of these studies were conducted during the very early part of the pandemic and employed leading questions enquiring about ageusia. There could have been a tendency on the patient’s part to report pre-existing post-viral loss of taste as secondary to covid infection. This is evident by the findings of Giacomelli et al who reported that 91% of the patients reported taste alteration even before hospitalization for covid infection.\textsuperscript{19}

\textbf{Limitations}

The first limitation of our study was the lack of objective testing for the gustatory function. However, it was not done keeping in mind the high infectivity of the disease and prevent unnecessary exposure. The other limitation was that we studied ageusia in isolation without considering the effect of other symptoms. This was deliberately done to keep the study simple and legible. This also addressed the need to have data about the new-onset ageusia in the Indian population.

\textbf{Conclusion}

The prevalence of new-onset ageusia in the Indian population is 18% which is less as compared to the western population. However, it remains one of the relevant symptoms of COVID-19 infection in addition to the usual symptoms of fever cough, and malaise. This difference in the prevalence of ageusia in different ethnicities should invite further research with a larger population size to establish the trend of this important symptom. Also, despite this low prevalence, it will be utilized as an important screening tool for COVID-19 infection but with ‘heightened caution’. In an apparently healthy individual with ageusia the differential diagnosis of COVID-19 must be considered for early diagnosis and treatment, and to prevent further spread of the disease.
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