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Assessment of Anosmia and Ageusia as Diagnostic Marker for Identifying Corona Virus Disease-2019

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Abstract: ***The objective of the present study was to detect viral infected clinical features in the naso-pharyngeal cavity with special reference to loss of smell (anosmia) and taste (ageusia) during COVID-19 pandemic. This study was a retrospective emergency department-based study. All the data were gathered among COVID-19 patients (n=4552) who visited the emergency department at IDBG & Hospital, Kolkata. The study was completed within a period of 7-months who visited this department between 01.08.2020 to 28.02.2021. All patients presenting COVID-19 related symptoms had specific clinical parameters and questions were asked regarding loss of smell (anosmia) and taste (ageusia). In the case of age (years), in higher age group, significantly (P<0.000) higher anosmia and ageusia when compared to without anosmia and ageusia. The pulse rate (bpm) was significantly (P<0.009) increased in anosmia group, both respiratory rate (per min) was significantly (p = 0.046) increased while and SpO_2 (%) was significantly (p = 0.047) decreased in anosmia group in comparison with without anosmia group. Only respiratory rate (per min) significantly (P<0.000) increased while SpO_2 (%) significantly (P<0.000) decreased in ageusia group. Systolic blood pressure (mm Hg) and temperature (^0F) were obtained significant change (P=0.018 and P=0.013) between the groups. This study helps to detect suitable markers viz. anosmia and ageusia in COVID-19 diagnosis. Moreover, in eastern India, this is first time endeavour in which prior to test of clinical parameters, these two olfactory dysfunctions confirmed the infection of corona virus.***

Keywords: SARS-COV-2, COVID-19, TMPRSS2, Anosmia, Ageusia, Oral mucocutaneus lesion, Hypogeusia

1. Introduction

In December 2019, unexplained pneumonia cases were initially reported in Wuhan, China. The pathogen, A novel corona virus named severe acute respiratory syndrome corona virus 2(SARS-COV-2), was isolated from lower respiratory tract samples of infected patients and the resultant disease was termed as corona virus disease 2019 (COVID-19).[1]

Corona viruses causes illness ranging from the common cold to SARS (severe acute respiratory syndrome) and MERS (Middle East Respiratory Syndrome) [2] corona viruses, new viruses that cause severe acute lower respiratory infection (ARI), with 10% and 35% mortality rates, respectively, and more than 50% mortality rates seen in older and immune suppressed people.[3]

The new century has been the emergence of several novel viruses that cause respiratory tract infections in humans including SARS corona virus infection mainly in China, MERS-COV in Saudi Arabia and Asia, and H7N9 influenza A viruses in Eastern China. MERS-COV and H7N9 viruses are still a mode of transmission of MERS-COV and H7N9 influenza A virus are poorly understood and their oral manifestation if any ill-defined, [4,5] There are no reliably effective antiviral agents available for these diseases. [2,6]

Viral infection typically manifests with a fever, but this is neither always present nor measured by the clinician.[7] Clinical features are often nonspecific and may include malaise, myalgia, generalized weakness, rashes, and mucosal lesions such as ulceration or bleeding. These are not always major features, not always checked by a clinician or may often be seen by non-orally trained health care workers. Thus, undiagnosed, or misdiagnosed are likely to be quite common.[8]

Suspect of Covid-19 is mainly made on clinical signs (fever, fatigue, dry cough, anorexia, rhinorrhea, dyspnea, diarrhea, abdominal pain, anosmia and ageusia),[9] On vital parameters (elevated temperature, pulse oximetry saturation)[10] and on radiological settings (x-ray, chest CT scan) lab findings [11] could often demonstrate lymphopenia, elevated LDH and c-reactive protein (CRP). Nasopharyngeal and oropharyngeal swab, allowing the virus isolation, confirms the diagnosis.[12,13] Indian Council of Medical Research (ICMR) recently included loss of taste (Ageusia) and loss of smell (Anosmia) as new covid symptoms apart from the previous sign of fever, short breath and cough.[14] It was well-known fact that loss of taste (ageusia) and loss of smell (anosmia) preceding the onset of respiratory symptoms could be one of the signs of the disease.[15-18]

In this regard, the objective of the present study was to detect viral infected clinical features in the naso-pharyngeal cavity with special reference to loss of smell (anosmia) and taste (ageusia).

2. Materials and Methods

Study Design
This study was a retrospective emergency department-based study.

Study design
The data were gathered among COVID-19 patients who visited the emergency department at IDBG & Hospital, Kolkata.

Place of study
Emergency department, IDBG & Hospital, Kolkata.

Period of study
The study was completed within a period of 7-months who visited the emergency department between 01.08.2020 to 28.02.2021.

Study population
The data of studied patients (n = 4552). No sample size calculation was required. This is a retrospective study who visited the emergency department with COVID-19 infection.

Sample size
During the study period of 7-months, the data were gathered among 4552 patients

Study parameters
All patients presenting COVID-19 related symptoms had physical examination as per the clinical parameters viz. pulse rate (bpm), respiratory rate (per min), oxygen saturation (SpO_2 as %), systolic blood pressure (SBP as mm Hg) and temperature (^0F) along with age (years) and onset from (days), data were collected. Besides these clinical features, questions were asked regarding loss of smell (anosmia) and taste (ageusia), which were also noted.

Statistical analysis
Statistical analysis was performed by using the SPSS program for Windows, version 20.0. Continuous variables were presented as mean ± SD and the data used compared between present (Yes) and absent (No) of anosmia (smell) as well as ageusia (detaste) group related to age, and clinical features by using Mann-Whitney U test. $P<0.05$ was considered significant.

3. Results

Table 1 describes comparative analysis between anosmia (yes and no) related to age, and clinical parameters. In the case of age (years), in higher age group, significantly ($P<0.000$) higher anosmia when compared to without anosmia. The pulse rate (bpm) was significantly ($P<0.009$) increased in anosmia group in comparison with without anosmia group. Both respiratory rate (per min) was significantly ($p = 0.046$) increased while and SpO_2 (%) was significantly ($p = 0.047$) decreased in anosmia group when compared to without anosmia group. Rest parameters such as onset from (days), systolic blood pressure (mm Hg) and temperature (^0F) were obtained non-significant between the groups.

Table 1: Comparative analysis between anosmia (yes and no) related to age, length of stay, clinical features

Anosmia		Age (Year)	Onset From (Days)	Pulse rate (bpm)	Respiratory rate (per min)	SpO_2 (%)	Systolic Blood Pressure (mm Hg)	Temperature (^0F)
Absent	M ± SD	54.41 ± 16.99	10.87 ± 7.62	86.88 ± 14.67	19.30 ± 3.32	96.22 ± 5.22	126.69 ± 17.60	98.41 ± 0.35
Present	M ± SD	56.42 ± 16.02	11.26 ± 11.53	87.61 ± 14.49	19.43 ± 3.50	96.06 ± 5.99	126.22 ± 26.32	98.38 ± 0.58
P-value		0.000	0.311	0.009	0.046	0.047	0.115	0.192

Table 2 describes comparative analysis between ageusia (yes and no) related to age, and clinical parameters. In the case of age (years), in higher age group, significantly ($P<0.000$) observed ageusia when compared to without ageusia. The respiratory rate (per min) significantly ($P<0.000$) increased while SpO_2 (%) significantly ($P<0.000$) decreased in ageusia group when compared to without ageusia group. Systolic blood pressure (mm Hg) and temperature (^0F) were obtained significant change ($P = 0.018$ and $P = 0.013$) among ageusia group in comparison with non-ageusia group. Rest parameters such as onset from (days), and pulse rate (bpm), were obtained non-significant between the groups.

Table 2: Comparative analysis between ageusia (yes and no) related to age, length of stay, clinical features

Ageusia		Age (Year)	Onset From (Days)	Pulse rate (bpm)	Respiratory rate (per min)	SpO_2 (%)	Systolic Blood Pressure (mm Hg)	Temperature (^0F)
Absent	M ± SD	55.53 ± 16.02	11.15 ± 11.53	87.24 ± 14.49	19.16 ± 3.50	96.55 ± 5.22	126.26 ± 26.32	98.38 ± 0.58
Present	M ± SD	57.33 ± 17.13	11.21 ± 8.10	88.22 ± 17.18	20.41 ± 3.92	94.54± 7.99	126.60 ± 20.09	98.41 ± 0.44
P-value		0.000	0.000	0.901	0.946	0.000	0.000	0.018

In Table 3, it can be inferred that the log rank test ($P=0.292$) for the survival functions observed non-significant, indicating that there are no significant differences among the survival curves for anosmia in the patients when compared between two groups. Therefore, we can find that both absent and present of anosmia are not significantly associated with the survival rate of COVID-19 without adjusting for other covariates.

In Table 4, it can be inferred that the log rank test ($P<0.000$) for the survival functions observed significant, indicating that there are significant differences among the survival curves for ageusia in the patients when compared between two groups. Therefore, we can find that both absent and present of ageusia are significantly associated with the survival rate of COVID-19 without adjusting for other covariates.

Table 3: Kaplan-Meier: comparison of survival functions for patients with COVID-19 by with and without anosmia

Anosmia	Mean[a]				Log Rank (Mantel-Cox)	Chi-Square	df	Sig.
	Estimate	Std. Error	95% Confidence Interval					
			Lower Bound	Upper Bound				
Absent	38.376	2.750	32.986	43.765				
Present	34.377	1.714	31.017	37.737		1.112	1	0.292

Table 4: Kaplan-Meier: comparison of survival functions for patients with COVID-19 by with and without ageusia

Anosmia	Mean[a]				Log Rank (Mantel-Cox)	Chi-Square	df	Sig.
	Estimate	Std. Error	95% Confidence Interval					
			Lower Bound	Upper Bound				
Absent	23.180	1.190	20.847	25.513				
Present	39.883	1.821	36.314	43.452		63.994	1	0.000

4. Discussion

Olfactory dysfunction is a common symptom of COVID-19, but its etiology is unclear. The understanding of COVID-19 an unforeseen, pandemic situation.[13] Symptoms of COVID-19 patients range widely from fever, respiratory symptoms, to newly reported findings of ageusia and anosmia from Iran,[19] Spain,[20] Italy,[21] France,[22] UK,[23] and similar finding in the present study in West Bengal State of India. Awareness of a possible COVID-19 infection should be raised in patients with the sole presentation of ageusia, glossodynia and anosmia despite the lack of published case report or research finding on its exact mechanism of action.

However, we believe that the number may actually be too low since the studies were based on reviews of the patients' chart, which may have not noted every symptom. Earlier studies did not note this symptom and that was probably because of the severity of other symptoms like cough, fever and breathing problems. In the present study, these were beginning to note that altered or lost sense of smell and taste was also present, not just here, but in a significant proportion among higher age group of patients. These findings suggest that SARS-COV-2 infection of non neural cell types leads to anosmia and related disturbances in odor perception in covid-19 patients.[24]

Epidemiologist Henderik streak mentioned that two third of patients having anosmia and ageusia lasting several days in Germany.[25] In addition, 30% of COVID-19 confirmed cases in South Korea had the primary initial symptom of anosmia.[26] One preliminary study from China by Mao et al reported that 5.1% of the patients with COVID-19 had anosmia and 5.6% had Ageusia.[27]

In this study, the data of emergency department confirmed that majority of COVID-19 positive patients were observed anosmia and ageusia in which clinical parameters were supported. Similar findings regarding anosmia and ageusia could be suitable markers, which were evidenced from the previous international studies.

5. Conclusion

The data of anosmia and ageusia related to age, onset from and clinical parameters were observed in West Bengal state of India. This study helps to detect suitable markers viz. anosmia and ageusia of COVID-19 diagnosis. Moreover, in eastern India, this is first time endeavour in which prior to test of clinical parameters, these two olfactory dysfunctions confirmed the infection of corona virus. Although, the clinical parameters are well associated with these two markers. It is suggested further study in multicentric approach to validate this finding.

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Conflict of interest
Authors declare no conflict of interest in the study and preparation of manuscript.

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