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SCREENING OF SMELL AND TASTE SENSATION IN MILD TO MODERATE COVID 19 CASES: AN EMERGING SYMPTOM?: A PROSPECTIVE STUDY

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ABSTRACT

Background: WHO declared COVID 19 viral infection as PHEIC followed by pandemic. And it was a catastrophe to world economy. Anosmia and dysgeusia were of the symptoms of discussion. Nations were earnestly looking for Cost effective management. **Objective:** To describe correlation between clinical , epidemiological , laboratorial and radiological , finding of COVID 19 infected patient and their relation to anosmia and dysgeusia **Methods:** Prospective study carried out in tertiary care hospital, AKOLA from a period of November 2020 to Feb. 2021, Conducted on Patient with RTPCR positive COVID 19 admitted to ward are interviewed using questionnaire in Google form and data collected from medical records after obtaining verbal informed consent. Questionnaires are developed by a team of qualified doctors. All data analyses are completed with SPSS version 25. **Results:** 52% of patients were having either anosmia or dysgeusia, in which 65 % patient had developed these symptoms before diagnosis COVID 19. These symptoms were more significant in age group of 40 to 60 ($p < 0.05$) **Conclusion:** Use of anosmia or dysgeusia as early screening tool of COVI D- 19 is add-on for diagnosis and abate morbidity and mortality. Neurotropic virus has less impact on pulmonary function because majority of anosmia and dysgeusia patient had mild or absent HRCT thorax changes. There was no relation between Anosmia and any other nasal symptoms.

KEYWORDS

Anosmia, Dysgeusia, COVID 19, PHEIC-public health of international concern, OD-olfactory dysfunction, GD-gustatory dysfunction, SARS-CoV- sever acute respiratory syndrome-corona, ICMR, CORAD score, screening tool.

INTRODUCTION

Mysterious viral pneumonia of unknown origin started from Wuhan city, China. It is identified as enveloped RNABetacoronavirus that is currently named SARS-CoV-2 (phylogenetic similar to SARS–Cov). WHO declared this pandemic as Public Health Emergency of International Concern (PHEIC). It drastically hit India and presented as a catastrophe to our economy and health system due to population and low literacy rate in India.

The world started following safety measures, like international travel restrictions, social distancing, masks and hand hygiene etc. Internationally, the WHO provides various guidelines. Similarly, the Indian Council of Medical Research (ICMR) has provided guidelines in India for prevention, diagnosis, management, psychosocial support etc. Till Aug2021 in India, the total cases of COVID-19 reported more than 3.23 crore with the death toll of 4.32 lakh. The human-to-human transmission was well known and the mode of transmission is mostly air born through respiratory droplets or direct contact.

Covid-19 has varied symptomatic presentation, the most common prodromal symptoms of COVID 19 are Fever, cough, fatigue, running nose, and less abundant symptoms are anosmia, hypogeusia, diarrhea, headache[3]. A large group people are asymptomatic carriers who can be potential source for disease transmission. Post-viral olfactory disorders usually occur after an upper respiratory tract infection (URTI) associated with a common cold or influenza[2]. Women are more often affected than men and post URTI disorders usually occur between the fourth and eighth decade of life[3:] In the general population, 2-3% are affected by lifelong olfactory disorders (from hyposmia to anosmia)[2] and two of the most frequent etiologies are the common cold and flu[2].

There are two most common conditions those are associated with anosmia i.e. Olfactory Cleft Syndrome with Mucosal Obstruction and Post-Viral Anosmia Syndrome. Olfactory cleft syndrome with mucosal obstruction of the olfactory cleft is a" conductive “loss. Contrary to this post-viral anosmia syndrome happened direct infection of the olfactory mucosa and destruction of the olfactory sensory neurons through receptors on sustentacular cells (TMPRSS2)[18] . These syndrome has different outcomes .It is quite complicated due to multiple neural system in human nose, Includes main olfactory system , vomeronasal system ,CN V somatosensory system and nervus terminalis[11].

Apart from anosmia, taste disorders (dysgeusia) are known to be related to a wide variety of viral illnesses[7]. The suggested mechanism of SARS-CoV-2 causing altered taste is its ability to bind to angiotensin-converting enzyme-2 receptor, which is readily expressed on multiple organ systems, including the surface of the tongue and oral cavity[18]. Another mechanism is due to failure of retro nasal air flow from nasopharynx while swallowing . This route is vital for adding flavor to food[11]

In current pandemic of Covid-19, in spite of huge number of cases we had in India, clinical data available to us is insufficient. Symptoms like taste and smell impairment emerged as potential symptoms and signs which helped for early diagnosis of Covid-19. The aim of this study to correlating clinical, epidemiological, laboratorial and radiological finding of patient and there relation to anosmia and dysgeusia.

MATERIALS AND METHODS

Study Site, Study Population and Sample

The present cross sectional prospective study was conducted at tertiary care hospital which cater health care services to more than a district. For current study, patients were enrolled from September 2020 to mid of the February 2021. During this duration, a total of 134 study subjects were appeared in total; 117 gave their consent for the study, and 17 patients were drop out of the study, so a total of 100 patients were enrolled for the study. They belong to the category of mild to moderate COVID 19 infections.

Selection Of Patients

Inclusion Criteria

- RTPCR positive Covid-19 patients with age more than 18 years who comes under mild to moderate
- Patient those who were able to give their formal verbal consent for study

Exclusion Criteria

- Serious ill patients, admitted to ICU due to any reason were excluded
- Known case of any anosmia and chronic disease of nose

Development Of Data Collection Tool

A questionnaire was prepared by a ENT experts. It semi structured, semi opened ended, Google form based questionnaire. Which were pilot tested on 7 patients, to check understandability of tool. Few modification were done after initial pilot testing in terms of language

and also, few areas questions were added related to history and symptoms.

Data Collection

The data is collected only after informed and verbal consent from selected patients who were admitted with mild to moderate COVID 19. All the data collected by junior residents and senior residents, data collection guided and monitored by unit head.

Data Collection

Data was gathered about disease by asking verbal question directly to patient about socio demographic details, anosmia and dysgeusia, associated clinical symptoms , duration and related question. Other data included demographic data, past medical history, symptoms, laboratory values, chest X-rays, CT scans and vitals, Laboratory values included complete blood counts, biomarkers for organ function, and analysis of immunological responses. Severities of cases were classified based on the ICMR guideline[12].Those who were asymptomatic or with Mild clinical symptoms with no signs of pneumonia in imaging were classified as “Mild” and those with signs of pneumonia on imaging and fever or clinical respiratory tract manifestations without hypoxemia were classified as “Moderate". The therapeutic principles comprised of general supportive therapy, active control over high fever, oxygen therapy if necessary, antiviral treatments, monitoring of liver, kidney, myocardial, and lung functions and management of any other symptoms or complication related to disease. Anonymity of data was maintained.

Statistical Analysis

Continuous variables were presented as mean (± SD) and categorical variables were written as number (%). We compared proportions for categorical variables between groups using Chi-square test. We evaluated a p-value less than 0.05 as statistically significant. All data analyses were completed with SPSS version 25.

RESULTS AND DISCUSSION

Table1: Distribution Of RT-PCR Positive Symptomatic And Asymptomatic Patients (for Anosmia And Dysgeusia) As Per Various Factors (n=100)

Category	Symptomatic	Asymptomatic
Age		
<40 years	16	12
: 40 To 60 years	23	24
:> 60 years	13	12
Chi-square statistic = 0.4735 P-value is =789203 Not significant at p < .05.		
Sex		
Female	26	17
Male	25	32
Chi-square statistic = 2.7045 P-value = 100068 Not significant at p < .05.		
Risk Factor		
Allergy	04	01
Smoking	04	01
Chi-square statistic = 0 P-value = 1 Not significant at p < .05		
Co Morbidity		
DM	05	04
HTN	07	06
COPD	03	01
Others	08	08
Chi-square statistic = 0.8145 P-value = 846003 Not significant at p < .05.		
Clinical Symptoms		
Malaise	17	15
Fever	37	22
Cough	32	30
Shortness Of Breath	11	03
Headache	09	06
Chill	03	03
Nasal Obstruction	06	00
GI Symptoms	05	01
Rhinorrhea	05	02
Chi-square statistic = 10.654265714352 P-value = 0.222068760521 Not significant at p < .05.		
Spo2 At Time Of Admission		
:<=92	3	3
93 To 95	16	11
95	33	34
Pneumonia	21	24
With Out Pneumonia	30	25
Chi-square statistic = 1.416671758188 P-value = 0.841292270077 Not significant at p < .05.		
Corad Score On HRCT		
1 (Normal)	00	00
2 (Abn. Consistent With Inf. Other Than Covid19	00	00
3 Unclear Whether Covid 19 Is Present	00	00
4 Abnormality Suspicious Of Covid	0	03
5 Typical Covid	17	16
Chi-square statistic = 0.07334353199 P-value = 0.786529392119 Not significant at p < .05.		
CT Severity Score		
Mild < 7	20	07
Moderate(8 To 17)	01	10
Sever(>18)	00	02
Chi-square statistic = 15.561800123204 P-value = 0.000417636107 Significant at p < .05		
Laboratory		
D Dimer	13	13
Ferritin	03	14
LDH	07	10
N/L Ratio	3	4

Table 2 Socio Demographic Characteristics Of Study Subject

category	Symptomatic		
	Anosmia	Dysgeusia	Both
Age			
<40	6	4	6
: 40 To 60	2	8	13
:> 60	3	8	2
Chi-square statistic = 9.893958215697 P-value = 0.042252332053 Significant at p < .05			
Sex			
Female	4	8	14
Male	7	11	7
Chi-square statistic = 3.606978284873 P-value = 0.164723141871 Not Significant at p < .05			
Risk Factor			
Allergy	2	2	0
Smoking	1	0	3
Chi-square statistic = 5.333333333333 P-value = 0.069483451223 Not Significant at p < .05			
Co Morbidity			
DM	1	2	2
HTN		4	3
COPD	2	0	1
Others		1	7
Chi-square statistic = 14.421437292866 P-value = 0.025266886787 Significant at p < .05			
Clinical Symptoms			
Malaise	3	6	8
Fever	7	16	14
Cough	10	8	14
Shortness Of Breath	1	5	5
Headache	4	2	3
Chill	2	0	1
Nasal Obstruction/ Rhinorrhea	1	3	7
GI Symptoms	0	1	4
Chi-square statistic = 16.816217080183 P-value = 0.397584923392 Not Significant at p < .05			
Spo2 At Time Of Admission			
:<=92	1	1	1
93 To 95	4	5	7
95	7	10	16

Chi-square statistic = 0.387784090909 P-value = 0.983464783845 Not Significant at p < .05			
Radiology			
Pneumonia	4	7	10
With Out Pneumonia	8	12	10
Chi-square statistic = 1.094987468672 P-value = 0.578397613412 Not Significant at p < .05			
Corad Score On HRCT			
1 (Normal)	0	0	
2 (Abn. Consistent With Inf. Other Than Covid19	0	0	
3 Unclear Whether Covid 19 Is Present	0	0	
4 Abnormality Suspicious Of Covid	0	1	3
5 Typical Covid	4	6	7
Chi-square statistic = 1.822058823529 P-value = 0.402110074064 Not Significant at p < .05			
Ct Severity Score			
Mild < 7	4	7	9
Moderate(8 To 17)	0	0	1
Sever(>18)	0	0	
Chi-square statistic = 1.155 P-value = 0.561299863623 Not Significant at p < .05			
Laboratory			
D Dimer	3	6	4
Ferritin	1	1	1
LDH	1	3	3
N/L Ratio	0	1	2

Among the 100 enrolled patients, 57 were males and 43 females. Among them 55 cases were mild category and remaining were in moderate category, in which 3 were requiring oxygen, based on oxygen saturation and CT or x-ray proved pneumonia. The mean age of patients was 40 years.

Fifty-two patients including mild and moderate COVID 19 disease were having symptoms of either anosmia, disguise or both. More number of patients present with both symptoms. These symptoms were more significant in age group of 40 to 60 ($p<0.05$) (Table No. 1). Only 9% patients had risk factor like smoking and allergy, in which 8 patients were symptomatic.

Forty two patients had comorbidities including DM , hypertension and COPD, 5 out of 9 diabetic patient had symptoms. , 3 out of 4 patients with COPD had symptoms. (P-value = 846003 Not significant at $p < .05$.) .

The most common signs and symptoms at the onset of illness was fever ≥ 38 °C upon admission (61%), And least common were nasal obstruction (3%). 34 patients developed either anosmia or dysgeusia as initial symptoms before diagnosing COVID 19 infection without any other nasal symptoms (table 3).

Table 3. Number Of Patient Having Either Anosmia Or Dysgeusia In Relation To Covid 19 Diagnosis

	ANOSMIA	DYSGEUSIA
Before diagnosis of COVID 19	25	30
After diagnosis of COVID 19	7	10

Abnormal laboratory findings in mild and moderate patients were raised D-dimer in 26 patient in which 13 symptomatic and 13 asymptomatic patients, raised ferritin in 17 patients in which majority are symptomatic. In addition, LDH were raised in 17 patient, in which 7 symptomatic and 10 were asymptomatic patients. (Table No.2).

Oxygen saturation in blood among mild disease were above 95 in room air. Moderate disease were above 93 except for 3 who require oxygen .in this study 64 patients had 95 and above saturation.

We have found that symptomatic (anosmia or dysgeusia) patients had mild CT scan changes and CT score of less than seven except one symptomatic patient, who had moderate CT score of 12. In addition, 10 patients with moderate and 2 patient with sever CT score doesn't experience anosmia or dysgeusia (only 40 patients were advised to have CT on their course of treatment) (Chi-square statistic = 15.561800123204 P-value = 0.000417636107 Significant at $p < .05$) (Table No.1). It signifies patient with anosmia or dysgeusia has minimal lung complication. In present study 4 patient with anosmia and 6 patient with dysgeusia and 7 patient with both symptom (total 17) had CORAD score of 5. But we cannot prove its statistical significance and It require further study to comment on this (Table No.2).

During treatment for Covid 19, anosmia were improved in 21 patient and worsen in 10 patient out of which 4 patient had fluctuation. Those patients with improvement in anosmia was on systemic steroid therapy (Table No.4). While patient with dysgeusia only 2 patient had sudden improvement.

Table 4 Effect On Anosmia And Dysgeusia During Treatment

Effect	ANOSMIA	DYSGEUSIA	Both	TOTAL
IMPROVEMENT	21	2		23
WORSEN	10	0		10
FLUCTUATE	4	3		7
PHANTAM	0	22		22
DISTORTED	0	34		34
CHEMESTASIS	0	0		0

DISCUSSION

This is an cross sectional observational study of hospitalized patients with SARS-CoV-2. There was no significant disparity in the ratio of female and male patients, which was consistent with the findings of other studies.

The mean age of our study was 40 years, However, all the age groups might have been infected. Our findings concur with previous studies, showing that patients infected with SARS-CoV-2 may present primarily with cough, fever ≥ 38 °C, dysgeusia, anosmia, malaise, shortness of breath and headache with accompanying symptoms of sputum production, rhinorrhea, diarrhea like adenoviral infection[3].

Patients with mild disease may present with only anosmia or dysgeusia in the absence of fever and signs of pneumonia, moderately infected patients usually have a fever ≥ 38 °C or respiratory symptoms, mainly shortness of breath, cough, and malaise. There are many similarities between COVID-19, SARS-CoV and new micro-organisms such as avian influenza virus H7N9. However, COVID-19 cases can vary from mild to moderate or even severe, while SARS or avian influenza virus H7N9 were more severe in general[13]. COVID-19 patients included in our study presented with anosmia and dysgeusia symptoms, low-grade fever and a long incubation period leading to a higher potential for transmission.

Some of the patients with mild disease were having only anosmia or dysgeusia. It has been propose that a CT examination should be the earliest choice in the screening and diagnosis of COVID-19. This is because the sensitivity of CT scan for SARS-CoV-2 found to be 98%[3] and it may becomes 100 % sensitive if we add anosmia and dysgeusia as screening tool. It is very important observation since routine RT-PCR sensitivity is only 71%[14]. Screening of smell and taste dysfunctions had higher sensitivity in identifying recent-onset loss of sensations in COVID-19 cases. Hence, it may be use as a simple and cost-effective screening test. This can be confirm after further studies. Patient with anosmia and dysgeusia had more of mild and well-tolerated disease (according to CT scan severity score) (Chi-square statistic = 15.561800123204 P-value = 0.000417636107 Significant at $p < .05$). In current study anosmia is not associated with any other nasal symptoms (P-value = 0.397584923392 Not Significant at $p < .05$). It suggest that COVID 19 virus is neurotropic and are directly causing injury to sensory epithelium of olfaction. The neurotropic variant are less prone for lung complication. Olfactory Dysfunction appear to be largely independent from epidemiological and clinical characteristics of the patients. The non-association with rhinitis and high prevalence as a presenting symptom makes anosmia an important symptom in the differential diagnosis between COVID 19 and common flu. Hence, using anosmia and dysgeusia as screening tool was more useful in early detection, segregation and controlling the spread of disease. This will be help for better prognosis of patients. This is a similar to the find by Luigi Angelo Viara et al[17].

In the study of Bidkar et al[2]. anosmia or hyposmia was present in 62 (81.6%) and ageusia in 64 (84.2%) of the total 76 confirmed cases. The Olfactory Dysfunction and Gustatory Dysfunction were significantly

higher among confirmed COVID-19 cases compared to negative subjects [Adj OR (95% CI): Smell 3.22 (1.77–5.88); taste 3.05 (1.61–5.76), p \0.001]. In our study, There is significant change in the presentation of sensory dysfunction when we compare with other study, it may be due to difference in study method and sample size.

The University of Pennsylvania Smell Identification Test (UPSIT) was administered to 60 confirmed COVID19 in patients by Shima T Moein et al[6]. and concluded that the Olfactory Dysfunction of the variable extent was a reliable biomarker affecting 98% of the cohort study. This gross difference is due to absence psychophysiological test in our study, in the current study we depend only on patient interview. It is due to safety protocol implemented in institution.

Rachel Kaye and colleagues[16] states that anosmia may be a critical initial symptom and it may help to alert particular individual infected with SARS-CoV2 who may unknowingly transmit the virus.

CONCLUSION

Psychophysical assessment represents a significantly more accurate assessment tool for the olfactory and taste function than questionnaire. Even in the absence of psychophysical assessment we have significant number of anosmia and dysgeusia in COVID 19 patient. Screening of smell and taste dysfunctions had higher sensitivity in identifying recent-onset loss of sensations in COVID-19 cases. Hence, it may be used as a simple and cost-effective screening tool (65 % patient developed symptoms before diagnosing COVID-19). There by early detection and reduction in mortality / morbidity. There was no relation between Anosmia and any other nasal symptoms it implies virus is neurotropic. In addition, we have observed neurotropic viruses has less impact on pulmonary function because majority of anosmia and dysgeusia patient had mild or absent HRCT thorax changes. HRCT thorax scan is the most sensitive test for diagnosing COVID 19 and its sensitivity is up to 98 %. Therefore, the presence of anosmia or dysgeusia gives an extra edge for diagnosis. Presence or absence of co morbidity does not alter the presentation of Anosmia or dysgeusia. In this we could not able to comment on exact relation of different laboratory parameters.

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