

The Sungai Buloh experience: A retrospective study in olfactory and gustatory disturbance in COVID-19

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Abstract

Introduction: Olfactory and gustatory disturbance has been recognized as one of the COVID-19 symptoms. The prevalence of the symptoms may vary between region globally and multiple factors may have contributed to the development of the symptoms.

Objective: To identify the prevalence of olfactory and gustatory disturbance in patients with COVID-19 in Sungai Buloh centres.

Methods: This retrospective study, conducted for a month – April/May 2020, recruited 201 COVID-19 patients from Hospital Sungai Buloh (HSB), National Leprosy Control Centre (NLCC), and Institut Latihan Kejururawatan Kebangsaan Malaysia (ILKKM) who met the inclusion criteria. Socio-clinical data were collected from 'ehis' electronic system database and anosmia clerking sheet, designed for the study. Statistical analyses were performed using IBM-SPSS statistical software version 26.

Results: This study reported 14.9% of patients diagnosed with COVID-19 experienced olfactory and/or gustatory disturbances, where the mean age is 33 years, and patients predominantly male (70%) and asymptomatic of COVID-19 symptoms (70%). Some patients (4.5%) had olfactory and/or gustatory disturbance in the absence of other symptoms, and 10.4% reported olfactory and/or gustatory disturbances with other COVID-19 symptoms. Logistic regression showed an association between developments of olfactory and/or gustatory disturbances with symptomatic of COVID-19 symptoms, smoking status, and nationality.

Conclusion: New onset of olfactory and/or gustatory disturbances during the COVID-19 pandemic is a good screening tool for early detection of COVID-19 in the absence of other symptoms. Patients who are symptomatic of COVID-19 symptoms, smoker and Malaysian may have a higher risk of developing olfactory and/or gustatory disturbances in COVID-19.

Keywords: COVID-19, Sg Buloh, olfactory, gustatory, nasal, smell, taste

Introduction

A novel member of human RNA coronavirus, also known as severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) was newly identified in Wuhan, Hubei Province, China, at the end of 2019 [1]. In February 2020, World Health Organization, (WHO) has renamed the disease as "COVID-19" [2]. As of 16th August 2020, WHO has reported 21,294,845 cases with 761 779 deaths globally [3].

The most common clinical manifestations are mainly like those of influenza [4] which are fever, cough myalgias, and fatigue. But the patient may also have presented with dyspnea, sore throat, rhinorrhea, arthralgia [5].

Recently there is literature especially from European countries mentioning that olfactory disturbance may be one important feature in these patients [6,7]. It is said that Coronavirus is known to cause loss of smell or loss of taste along with symptoms of common cold [8]. This may due to direct damage of the virus on the olfactory and gustatory receptors [9].

An olfactory disorder which includes anosmia and hyposmia is defined as a loss in the ability to smell or a change in the way odors are perceived [10]. On the other hands, taste disorders can be described as ageusia (complete loss of taste), hypogeusia (diminished sense of taste), hypergeusia (enhanced gustatory sensitivity) or dysgeusia (a qualitative gustatory disturbance

relating to a distorted taste perception or a persistent taste sensation in the absence of stimulation) [11]. There is a close association between olfactory and gustatory function as loss of taste usually reflects a loss of smell function as a result of a retronasal olfactory function [12]. The gustatory system (transmitted via the glossopharyngeal, facial, and vagal nerves) only recognizes the basic tastes (sweet, sour, salty, bitter, and umami), but most of the culinary experiences are recognized by the olfactory nerve [13]. Given the close association between olfactory and gustatory dysfunction, we have assumed that olfactory disturbance will also present in a patient with gustatory disturbance.

The first confirmed case reported in Malaysia was on 24th January 2020 [3]. The Ministry of Health (MoH) Malaysia first defined COVID-19 case as an acute respiratory infection with or without fever, and has traveled to or resided in a foreign country within 14 days before the onset of illness or close contact in 14 days before illness onset with a confirmed case of COVID-19 or attended an occasion related to COVID-19 outbreak. They have recently added anosmia and ageusia as part of the case definition of COVID-19 [14].

Our study aim is to identify the prevalence of olfactory and gustatory disturbances in COVID-19 patients who were admitted to our centre, and the study the association of the development of these symptoms with multiple socio-clinical factors.

Methodology

This is a retrospective study on COVID-19 positive patients admitted to Hospital Sungai Buloh (HSB), National Leprosy Control Centre (NLCC), and Institut Latihan Kejururawatan Kebangsaan Malaysia (ILKKM) from 22nd April 2020 to 22nd May 2020. Hospital Sungai Buloh has been designated as the dedicated admitting hospital for confirmed COVID-19 cases by the Ministry of Health of Malaysia (MoH). Both NLCC and ILKKM are the step-down centre for stable COVID-19 patients. The study has been approved by MoH Research and Ethics Committee (MREC) and NMRR ID obtained.

All COVID-19 patients in HSB, NLCC, and ILKKM that fulfilled the study criteria were included in this study. A total of 201 patients participated after consent obtained. Patients were identified through a search from the 'ehis' (electronic system database) and patients manual clerking sheet which includes anosmia clerking sheet. We accessed the records of patients, which contain all information relating to the patient's history and laboratory investigations.

Patients' clerking information and review notes that include the history of olfactory or taste disturbances were included in the

study. Other data from the records, including age, gender, smoking history, past medical history, medication history, and symptoms relating to the onset of COVID-19 were also recorded.

Only patients with olfactory and/or taste disturbances were asked regarding the previous history of nasal or oral surgery, previous chronic nasal problems, any associated taste disorder, parosmia, and phantosmia. Age was defined as the age when COVID-19 was diagnosed, and patients were classified as smokers if they have any history of smoking or vaping. Olfactory and taste disturbances that presented both before or after COVID-19 diagnosis was made, and durations of the symptoms were recorded and included in the study. The study was approved by the ethics committee Ministry of Health Malaysia (NMRR-20-932-54938).

Statistical analyses

Statistical analyses were performed using IBM-SPSS statistical software version 26. The results are shown in the text and tables. The patients' age, gender, nationality, medications, nasal symptoms, and duration of disease were obtained. Logistic regression correlation was used to analyse the association between multiple factors with the development of olfactory and gustatory disturbances and p-value < 0.05 is considered statistically significant..

Table 1. Age distributions of patient with olfactory and/or gustatory disturbance in COVID-19

	Total, n = 201	With Anosmia, n = 30
Mean	34.4	33.1
Median	32	31
Mode	23	24
Std. Deviation	12.42	12.17
Minimum	18	19
Maximum	70	67

Table 2. The relationship between socio-clinical characteristics and olfactory and/or gustatory disturbance of 201 patients with COVID-19.

Variables	Total n (%)	With olfactory and/or gustatory disturbance, n (%)	Without olfactory and/or gustatory disturbance, n (%)	Overall percentage having olfactory and/or gustatory disturbance
Gender				
Male	155 (77.1)	21 (70)	134 (78.4)	13.50%
Female	46 (22.9)	9 (30)	37 (21.6)	19.60%
Total	201 (100)	30 (100)	171 (100)	
Nationality				
Malaysian	132 (65.7)	28 (93.3)	104 (60.8)	13.90%
Non-Malaysian	69 (34.3)	2 (6.7)	67 (39.2)	1%
Total	201 (100)	30 (100)	171 (100)	
Symptomatic of COVID-19 symptoms				
Symptomatic	67 (33.3)	21 (30)	46 (26.9)	10.40%
Asymptomatic	134 (66.7)	9 (70)	125 (73.1)	4.50%
Total	201 (100)	30 (100)	171 (100)	
Chronic nasal symptoms				
Yes		4 (13.3)	26 (86.7)	14.90%
No		-	-	

Results

The study was conducted between 22nd April 2020 and 22nd May 2020 (1-month duration). A total of 201 patients who were admitted to HSB, NLCC, and ILKKM Sungai Buloh and diagnosed as COVID-19 positive which fulfilled the inclusion criteria were included in the study. Table 1 showed the age distribution of patients involved in the study. The mean age of patients involved in this study is 34.4 (± 12.423). Of 201 patients involved in the study, male predominant with 155 patients (77.1%) while only 46 (22.9%) patients were female. 132 (65.7%) patients were Malaysian while the remaining 34.3% were non- Malaysians.

Table 3. Commonly reported COVID-19 symptoms in studied centres

	Frequency	Percentage (%)
Asymptomatic	126	62.7
Fever only	10	5.0
Respiratory symptoms only	26	12.9
Gastrointestinal symptoms only	1	.5
Fever with respiratory symptoms	21	10.4
Fever with gastrointestinal symptoms	1	.5
Skin rashes with or without other symptoms	2	1.0
Fever with nonspecific systemic symptoms	2	1.0
Non-specific systemic symptoms without a fever	1	.5
Gastrointestinal with respiratory symptoms	1	.5
Anosmia/ageusia only	9	4.5
Fever with anosmia	1	.5
Total	201	100.0

Table 4. Development of olfactory and/or gustatory disturbance compared to COVID-19 symptoms in days

Days	Frequency	Percentage (%)
-23	1	4.8
-10	2	9.5
-3	1	4.8
-1	1	4.8
0	10	47.6
1	1	4.8
2	1	4.8
3	1	4.8
5	1	4.8
7	1	4.8
8	1	4.8
Total	21	100.0

Table 5. Types of olfactory and/or gustatory disturbance

Types of disturbances	Frequency	Percentage, %
Olfactory only	13	43.3
Gustatory only	7	23.3
Both	10	33.3
Total	30	100.0

Of the 201 patients, 125 patients (62.2%) were asymptomatic, 9 patients (4.5%) had olfactory and/or gustatory disturbance in the absence of other symptoms, 46 patients (22.9%) had other symptoms apart from olfactory and/or gustatory symptoms and 21 patients (10.4%) reported olfactory and/or gustatory disturbances with other COVID-19 symptoms.

When comparing nasal symptoms with olfactory and/or gustatory disturbance, out of 10 subjects only 1 (3.3%) subject had nasal congestion with rhinorrhea, while the other 9 (30%) subjects with olfactory and or gustatory disturbance had concurrent rhinorrhea only. However, we found that all patients that had nasal symptoms (nasal congestion or rhinorrhea) in this study had concurrent olfactory and/or gustatory disturbance. There are 191 (95%) patients without nasal symptoms in this study and only 20 (10.5%) of them had olfactory and/or gustatory disturbances (Table 2).

Among 30 patients (14.9%) who reported olfactory and/or gustatory disturbances; 13 patients reported only anosmia or hyposmia, 7 reported the only ageusia while the remaining 10 patients reported both symptoms. (Table 3) shows the common covid-19 symptoms reported in this study. No patients reported pre-existing anosmia or hyposmia or chronic nasal symptoms which include frequent sneezing, nasal congestion, or rhinorrhea. 4 (13.3%) of these patients did mention having allergy but the type of allergy was not specified.

The onset of olfactory and/or gustatory symptoms was compared in patient with other COVID-19 symptoms. Of the 21 patients who were symptomatic and having olfactory and/or gustatory symptoms, the onset ranged from day 23 before COVID-19 symptoms to day 8 after developing symptoms. 10 (47.6%) patients developed olfactory symptoms on the same day as COVID-19 symptoms, 5 (23.8%) patients before, and 6 (28.6%) patients had olfactory symptoms after developing other COVID-10 symptoms (Table 4).

Of 30 patients with olfactory disturbances, only 3 (10%) patients reported no improvements in their symptoms while the other 27 (90%) patients reported improvements in their ability to smell and taste. All of these 3 patients were asymptomatic of other COVID-19 symptoms.

Logistic regression was performed to study the association of age, gender, presence of chronic illness, presence of COVID-19 symptoms, smoking status, the nationality of patients, clusters, and whether the origin of a case from western or eastern on the likelihood of patients having olfactory and/or gustatory disturbance. Results show that symptomatic of COVID-19 ($p < 0.001$), smoking status ($p = 0.003$), and nationality ($p = 0.009$) are statistically significant factors for causing the development of olfactory and/or gustatory disturbance. Symptomatic patients of COVID-19 are 6.34 times more likely to developed olfactory and/or gustatory disturbance compared to asymptomatic patients. While smokers are 2.50 times more likely to developed olfactory and/or gustatory disturbance compared to a non-smoker. This study also revealed that Malaysians are 9.02 more odds of developed olfactory and/or gustatory disturbance compared to non-Malaysians.

Table 6. Multivariate analysis of factors with development of olfactory and/or gustatory disturbance

Characteristics	Olfactory Disturbances				Simple Logistic Regression			Multiple Logistic Regression		
	Yes		No		Crude OR	95% CI	p-value	Adjusted OR	95% CI	p-value
	n	%	n	%						
Age										
< 55	27	-14.5	162	-85.7	ref	(0.51,7.86)	0.321			
≥ 55	3	-25	9	-75	2					
Gender										
Male	21	-13.5	134	-86.5	ref	(0.27,1.53)	0.317			
Female	9	-19.6	37	-80.4	0.64					
Presence of Chronic illness										
Yes	2	-6.5	29	-93.5	ref	(0.65,12.68)	0.167	ref		0.096
No	28	-16.5	142	-83.5	2.86			3.93	(0.78,19.72)	
Symptomatic of Covid -19										
Symptomatic	21	-31.3	46	-68.7	6.34	(2.71,14.85)	<0.001	7.12	(2.67,19.04)	<0.001*
Asymptomatic	9	-6.7	125	-93.3	ref			ref		
Smoking Status										
No	17	-11.5	131	-88.5	ref	(1.12,5.60)	0.025	ref		0.003*
Yes	13	-24.5	40	-75.5	2.5			4.52	(1.67,12.24)	
Nationality										
Malaysian	28	-21.2	104	-78.8	9.02	(2.08, 39.11)	0.003	8.01	(1.68,38.30)	0.009*
Non-Malaysian	2	-2.9	67	-97.1	ref			ref		
Clusters										
Local	20	-14.3	120	-85.7	ref	(0.52,2.69)	0.7			
Overseas	10	-16.4	51	-83.6	1.18					
Imported case										
Eastern	25	-14.1	152	-85.9	Ref	(0.42,6.39)	0.482			
Western	5	-20.8	19	-79.2	1.63					

Results shown from multivariate logistic regression; models include the following covariates: age at presentation, gender of patients, underlying chronic illness, presence or absence of Covid-19 symptoms, smoking status, nationality, clusters of case and possible source of infection; either Eastern (including local case) or Western.

* Significant at p-value <0.05

It was not statistically significant when age, gender, presence of chronic illness, a different cluster of infection; whether western versus eastern, or local versus overseas clusters were compared. The results are tabulated in (Table 6).

Discussion

This study reports 14.9% of patients diagnosed with COVID-19 experienced olfactory and/or gustatory disturbances. Post viral olfactory disturbance is commonly seen in women and typically over 50 years [15]. In our study, the upper age limit is 70 years old. Studies had shown that the number of functioning olfactory receptor neurons decreases with age. This explains the reason for the elderly being more vulnerable to infections with a decrease in recovery of post-viral olfactory disturbances. [16]

Our mean age of patients having olfactory disturbances is 33.07 ($\pm$ 12.157), and more women are affected (19.6%). Other studies conducted looking at COVID-19 and olfactory disturbances also showed that the incidence is higher in females than males [17–19]. Twenty (66.7%) of our patients with olfactory and/or gustatory

disturbance did not have concurrent nasal symptoms (rhinorrhea or nasal congestion) but all of our patients with nasal symptoms had concurrent olfactory disturbance.

Only 10.5% of patients in this study who did not have nasal symptoms had olfactory and/or olfactory disturbances. This result is conflicting with a European multi-centre study that found olfactory disturbance is commoner in COVID-19 patients without any nasal symptoms [20]. We also analysed other factors that might affect developments of olfactory and/or gustatory disturbance which include medications, related sinonasal disease, medical conditions, smoking status, and history of chemical exposure [21].

Our results showed a negative association between gender, age, medications, and medical conditions with the development of olfactory and/or gustatory disturbance. None of our patients who developed olfactory and/or gustatory disturbance has underlying sinonasal disease or history of chemical exposure. As expected, our data analysis showed smokers have an increased risk of developing olfactory disturbance compared to non-smoker owing to the alterations of the olfactory epithelium and increased apoptosis of

the olfactory sensory neurons as showed by Katotomichelakis et al [22].

Nine (30%) patients who experienced olfactory and/or gustatory disturbances are asymptomatic of other COVID-19 symptoms. From this value, 7 (23%) were screened as they had close contact with positive COVID-19 patients while the other 2 (6.7%) were screened as they had travel history. This showed none of our patients who had olfactory and/or gustatory disturbance were screened solely due to the disturbance because it is not part of screening questions for COVID-19 symptoms in our country. This explains the reason that there are fewer patients with OD symptoms in our study.

Of the 21 (70%) patients who are symptomatic of other symptoms, 15 (71%) of them developed olfactory and/or gustatory disturbance before and during the onset of other symptoms. This showed that the onset of OD in the course of COVID-19 is early and maybe a good screening question in detecting infected patients in the early course of the illness.

Recent research proposed an association between variants of SARS-CoV-2 with the development of olfactory disturbances. Three main variants of SARS-CoV-2 genomes; A, B, and C genotype which showed changes in amino acid was identified by Forster et al. through a phylogenetic network analysis [23]. The A and C genotype of SARS-Cov-2 are proposed to results in higher olfactory disturbances among Europeans and Americans and speculated to be high pathogenicity for the nasal cavity of humans as compared to the type b genotype which is found in East Asian.

In this study, we have categorized our subjects into possible clusters of the sources of infection to find a correlation between clusters and the development of olfactory and/or gustatory disturbance. Local cases and those with a history of travel to Eastern countries were grouped as one, while the remaining with travel history to Western countries were put in the same group. There is no association of this relationship in our study. Hence, we cannot conclude if a certain strain of COVID-19 is highly associated with olfactory and/or gustatory disturbance.

A post-viral OD may also manifest as dysosmia, where patients more often experience parosmia compared to phantosmia [24]. None of our subjects had any of these symptoms. Twenty-seven (90%) patients with OD reported improvements in their ability to smell and taste during their admissions, and the remaining reported no improvement during their hospital stay. All of these patients were admitted at most for 14 days. This shows that like any other post-viral olfactory disturbances, olfactory disturbances caused by SARS-Cov infection also have a good prognosis, where improvements of symptoms were seen in most of the cases [25,26].

Limitations

The study limitations include: the sample size was relatively small, patients with higher COVID-19 class of severity were not included, and no objective testing performed to verify and quantify the severity of olfactory and/or gustatory disturbance.

Conclusions

In conclusion, our study reported 14.9% of patients diagnosed with COVID-19 experienced olfactory and/or gustatory disturbances. It is a good screening tool for early detection of COVID-19. There is an association between symptomatic of COVID-19 symptoms, smoking status, and nationality with developments of olfactory and/or gustatory disturbances. However, this study failed to show the correlation between age, gender, presence of chronic illness, a different cluster of infection; whether western versus eastern, or local versus overseas clusters with the risk of developing olfactory and/or gustatory disturbances. .

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