

Transient Anosmia and dysgeusia in COVID-19 disease: a cross-sectional study

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Abstract

Objective: This study aims to explore the prevalence of anosmia and dysgeusia and their impact on COVID-19 patients. **Design:** This is a cross-sectional study. Patients diagnosed with COVID-19 between 1st October 2020 and 30th June 2021 were randomly selected from a national COVID-19 registry. The Anosmia Reporting Tool and a brief version of the questionnaire on olfactory disorders were used to measure the outcomes via telephone interviews. Data were analyzed using SPSS 27 statistics software. **Results:** A total of 405 COVID-19 adults were included in this study, 220 (54.3%) were males and 185 (45.8%) were females. The mean±SD age of participants was 38.2 ± 11.3 years. Alterations in the sense of smell and taste were reported by 206 (50.9%), and 195 (48.1%) of the patients respectively. Sex and nationality of participants were significantly associated with anosmia and dysgeusia (p<0.001) and (p-value=0.001) respectively. Among patients who experienced anosmia and dysgeusia, alterations in eating habits (64.2%), impact on mental wellbeing (38.9%), concerns that the alterations were permanent (35.4%), and physical implications and difficulty performing activities of daily living (34%) were reported. **Conclusion:** Anosmia and dysgeusia are prevalent symptoms of COVID-19 disease, especially among females. Neuropsychological implications of COVID-19 in the acute infection phase and prognosis of anosmia and dysgeusia in COVID-19 are areas for further exploration.

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impact on mental wellbeing (38.9%), concerns that the alterations were permanent (35.4%), and physical implications and difficulty performing activities of daily living (34%) were reported.

Conclusion: Anosmia and dysgeusia are prevalent symptoms of COVID-19 disease, especially among females. Neuropsychological implications of COVID-19 in acute infection phase and prognosis of anosmia and dysgeusia in COVID-19 are areas for further exploration.

Keywords : Anosmia, taste, smell, COVID-19, dysgeusia, gustatory, olfactory, COVID complications.

Key points

- Olfactory and taste dysfunction following Covid-19 is possibly underreported in the literature, as most studies are based on self-reports rather than a more objective assessment.
- This is a cross sectional study that included random selection of an early cohort of COVID-19 patients from a national registry.
- We used validated tool for outcome measurement.
- Short term anosmia and dysgeusia are prevalent symptoms of COVID19 disease, especially amongst females and have considerable impact on patient's life.
- Effective management strategies for anosmia and dysgeusia must be investigated.

Introduction

In December 2019, the Coronavirus Disease 2019 (COVID-19) outbreak emerged in Wuhan, Hubei Province, China and rapidly spread throughout the country and then evolved into a global pandemic (1). On February 12, 2020, The World Health Organisation (WHO) declared that the disease was caused by the novel coronavirus as COVID-19(1). Efficient screening, prompt diagnosis and isolation of the infected individuals were deemed fundamental to contain the outbreak (2).

Several signs and symptoms were observed in some patients including non-productive cough, fever, myalgia, fatigue, dyspnoea, diarrhoea, nausea and vomiting, while other patients were asymptomatic (3). The diagnosis of COVID-19 is based on the clinical suspicion, computerised tomography (CT) findings, and a reverse transcription polymerase chain reaction molecular test (RT-PCR) (3).

The incubation period of COVID-19 is presumed to be between 2 and 11 days, with a mortality rate reaching 2 to 4% (3). The most common peripheral nervous system manifestations of COVID-19 include anosmia (loss of smell) and dysgeusia (taste impairment). Although, most patients gradually regain their sense of smell and taste, the mechanism of these dysfunction is not fully understood (4). Post-infectious olfactory dysfunction is thought to be the result of involvement of the olfactory bulb and damage to the olfactory receptors cells due to the neurotrophic features associated with SARS-CoV-2 (5). Minimal data are available for the mechanism of taste disorders among patients with COVID 19, Single cell RNA-sequencing studies showed that epithelial cells of the tongue express ACE-2 receptors where buccal mucosa may play a role in entry of SARS-COV2. Additionally, indirect damage of the taste receptors through infection and inflammation of the epithelial cells are hypothesised to play a role in the pathogenesis. (6)

A review of the literature showed that the prevalence of anosmia ranged between 22% to 68% (7). Regionally, a study conducted in the Kingdom of Saudi Arabia, reported that the prevalence of olfactory dysfunction, anosmia and hyposmia was 53%, 32.7% and 20.3% respectively. Patients aged 15–39-year-old were mostly affected, and the prevalence of olfactory dysfunction was higher among females (60.3%) compared to males (56.5%) (8). In the same study, the prevalence of ageusia was determined at 51.4% (4). The loss of taste and smell senses is mostly transient lasting between one and two weeks. However, few chronic cases lasting more than one year after diagnosis have been reported.

Few studies explored the impact of anosmia and dysgeusia on patients with COVID-19 and reported negative impact of these symptoms, interference with daily activities and deterioration in well-being (4,9,10). A study conducted in the Eastern region of Saudi Arabia reported that 23% of participants felt isolated, 12.6%

reported having problems with taking part in daily activities, anger in 28.2%, difficulty in relaxing in 21% of participants, and worrying about their ability to cope with their changes in sense of smell in 22% (4).

In view of their predominance as signs and symptoms of the disease and in light of their substantial impact on quality of life, there is a need to study the frequency of these two symptoms, establish their association with COVID-19 diagnosis, and whether they are prognostic factors for COVID-19 outcomes.

Objectives : This study aims to estimate the prevalence and risk factors of olfactory and gustatory dysfunction in patients infected with Covid-19 and to investigate their impact on patient's life.

Methods

Study design and setting

This is a cross sectional study that explores olfactory and gustatory dysfunction of COVID-19 infection in adult patients who were previously infected with coronavirus in Bahrain. The *inclusion criteria* were people aged 18 years and more who contracted COVID-19 between October 2020 and June 2021. We excluded patients who had pre-existing histories of olfactory or taste dysfunction.

Participants and procedure

We estimated that 385 participants are needed to measure the prevalence of smell and taste dysfunction using this formula:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

where n = Sample size,
 Z = Z statistic for a level of confidence,
 P = Expected prevalence or proportion
 (If the expected prevalence is 20%, then $P = 0.2$), and
 d = Precision (If the precision is 5%, then $d = 0.05$).

Patients who contracted COVID-19 between October 2020 and June 2021 were randomly selected using a computer-generated randomisation system from the national database of COVID-19. A total of 578 COVID-19 patients were contacted, to account for non-response rate of 30%. Data collection was conducted between June 2021 and August 2021 using telephone-based questionnaires.

Ethics considerations

Prior to data collection, patients were informed about the purpose of the research and consent was obtained. Ethics approval was obtained from two Ethics Committee.

Study instrument

The questionnaire's questions were adopted from two validated tools. The first tool is the "Anosmia Reporting Tool", which was developed by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) (11), is used to study the prevalence and pattern of anosmia and dysgeusia in COVID patients as well as the associated risk factors. The second is the "brief version of the questionnaire of olfactory disorders" (12), which is used to study the impact of anosmia and dysgeusia during COVID infections on patients. The questionnaire includes four sections: patients' socio-demographics and clinical characteristics, an assessment of the sense of smell, assessment of the sense of taste, and the impact of anosmia and ageusia on patients' life.

Statistical analysis

The data was entered into the SPSS 27 statistics software (IBM Corp., Chicago, IL, USA) for statistical analysis. Descriptive analysis was performed to present categorical variables as frequencies and percentages, whereas continuous variables were presented as means (SD), median and range. Inferential analysis was performed to test the associations between patients' socio-demographics, risk factors (including smoking status, vaccination status, and comorbidities) and the status of their senses of smell and taste using ANOVA, t-test or Chi square as appropriate. Statistical significance was deduced if p-values were 0.05 or less. Binomial regression analysis was utilised to determine significant predictors of alterations in taste and smell.

Reporting guidelines

STROBE guidelines for reporting cross sectional studies were followed in this study.

Results

Characteristics of participants

A total of 578 COVID-19 patients were contacted; of these, 405 adult patients consented to participation and 173 patients were excluded. Reasons for exclusion were: 54 had missing contact details, 45 had invalid contact numbers, 27 did not respond to phone calls, 20 refused to participate, 26 due to language barriers, and 1 person died. Out of 405 participants, 220 were males (54.3%) and 185 were females (45.8%). The mean age of participants was 38.2 years \pm 11.3 years. (median age: 36 years). The majority of patients were Bahrainis (n=270, 66.7%). The non-Bahrainis were from South Asia (n=104, 25.7%), East Asia (n=13, 3.2%), Arabic countries outside the Gulf Cooperation Council (GCC) (n=11, 2.7%), the GCC (n=5, 1.2%), and from other nationalities (n=2, 0.5%). Seventy-eight percent of the participants were married (n=309), 19.4% were single (n=77), 2% were divorced (n=8), and 0.5% were widowed (n=2). Further, 56.2% of participants had received COVID vaccines (n=223), while 43.8% were not vaccinated (n=174) [Table 1]

Close contact with COVID positive individuals was reported by 67.4% of the participants (n=273). Twenty percent of participants were smokers (n=81). Other comorbidities were sinusitis or allergies (15.3%), diabetes mellitus (13.1%), hypertension (12.8%), and chronic respiratory conditions (3.5%). [Table 1]

Table 1. The sociodemographic and clinical data of participants

Characteristic	Description	Count
Sex	Male	220
	female	185
Age	38.2 (18- 64, SD= 11.3, Median= 36)	38.2 (18- 64, SD= 11.3, Median= 36)
Nationality	Bahraini	270
	GCC Arab	5
	Non-GCC Arab	11
	East Asia	13
	South Asia	104
	Others	2
	Hospitalised	88
Hospitalisation status	Not Hospitalised	317
	Vaccinated	223
Vaccination status	No vaccine	174
	Single	77
Marital status	Married	309
	Divorced	8
	Widowed	2
	None	105
Treatment requirement	Symptomatic only	249
	Other medical treatment	51
Clinical characteristics	Yes	Cumulative %

Are you a healthcare worker?	22 (5.4%)	5.4
Were you a close contact of a confirmed COVID-19 positive case?	273 (67.4%)	67.4
Travel to known area with widespread community transmission	29 (7.2%)	100
Smoking	81 (20.3%)	100
Sinusitis/ allergy	28 (15.3%)	15.3
Chronic respiratory disease / asthma	14 (3.5%)	3.5
DM	53 (13.1%)	13.1
Hypertension	52 (12.8%)	12.8
Immunocompromised	10 (2.5%)	2.5

Clinical presentation of COVID-19 and the treatment course

Regarding the clinical presentation of COVID-19, the most prevalent symptoms were malaise (73.8%), fever (64%), cough (54.3%), headache (51.6%), anosmia (50.9%), and dysgeusia (48.1%). On the other hand, 22.4% of COVID patients were asymptomatic. [The frequencies and percentages of other symptoms are outlined in Table 1]. The treatment requirements were: symptomatic treatment (61.5%), no treatment (25.9%), and more invasive forms of treatment (12.6%). Hospitalisation was required in 21.7% of patients (n=88) and 5.5% of participants were admitted to the Intensive Care Unit (ICU) (n=22). [Table 2]

Table 2. The clinical presentation of COVID within the studied cohort

Clinical presentation	Present Frequency (%)	Absent Frequency (%)	Total
Asymptomatic	90 (22.4%)	312 (77.6%)	402
Malaise	299 (73.8%)	106 (26.2%)	405
Fever	259 (64.0%)	146 (36.0)	405
Cough	220 (54.3%)	185 (45.7%)	405
Headache	209 (51.6%)	185 (45.7%)	394
Experience changes in sense of smell	206 (50.9%)	199 (49.1%)	405
Experience changes in sense of taste	195(48.1%)	210 (51.9%)	405
Congestion	147 (36.4%)	257 (63.6%)	404
Chills	131 (32.3%)	274 (67.7%)	405
Rhinorrhoea	139 (34.3%)	266 (65.7%)	405
Shortness of breath	101 (24.9%)	304(75.1%)	405
Diarrhoea	92(22.7%)	313 (77.3%)	405
Chest pain	85 (21%)	320(79%)	405
Nausea / vomiting	46 (11.4%)	359 (88.6%)	405
Pneumonia	38 (9.4%)	366 (90.6%)	404

The prevalence of anosmia and dysgeusia

Out of 405 participants, changes in the sense of smell was experienced by 206 (50.9%), and changes in sense of taste was experienced by 195 (48.1%) of the patients respectively.

Associations between anosmia, dysgeusia and demographics of participants

Sex of participants and nationality were significantly associated with anosmia and dysgeusia, with higher prevalence among females (60.5%) compared to males (42.4%) ($p<0.001$) as well as among Bahrainis (p -value=0.001) compared to non-Bahrainis. [Table 3]

Age was not associated with either anosmia and dysgeusia ($P=0.133$ and $P=0.172$ respectively).

Table 3. Associations between anosmia/dysgeusia and patient characteristics

Demographic variable	Description	Loss of smell n (%)	No loss of smell n (%)	P value	Odds ratio (95% CI)	Loss of taste n (%)	No loss of taste n (%)	P value	Odds ratio (95% CI)
Sex	Male	92/217 (42.4%)	125/217 (57.6%)	<0.001	0.479 (0.321 - 0.717)	89/217 (41%)	128/217 (59%)	0.002	0.51 (0.35 - 0.74)
	Female	109/180 (60.6%)	71/180 (39.4%)			102/180 (56.7%)	78/180 (43.3%)		
Nationality	Bahraini	146/264 (55.3%)	118/264 (44.7%)	0.001	N/A	139/264 (52.7%)	125/264 (47.3%)	0.002	N/A
	GCC	4/5 (80%)	1/5 (20%)			5/5 (100%)	0/5 (0%)		
	Non GCC Arab	9/11 (81.8%)	2/11 (18.2%)			7/11 (63.6%)	4/11 (36.4%)		
	East Asia	6/13 (35.3%)	7/13 (53.8%)			5/13 (38.5%)	8/13 (61.5%)		
	South Asia	36/102 (35.3%)	66/102 (64.7%)			35/102 (34.3%)	67/102 (65.7%)		
	Other	0/2 (0%)	2/2 (100%)			0/2 (0%)	2/2 (100%)		
Marital status	Single	42/77 (54.5%)	35/77 (45.5%)	0.908		39/77 (50.6%)	38/77 (49.4%)	0.970	
	Married	154/309 (49.8%)	155/309 (50.2%)			147/309 (47.6%)	162/309 (52.4%)		
	Divorced	4/8 (50%)	4/8 (50%)			4/8 (50%)	4/8 (50%)		
Smoking status	Widowed	1/2 (50%)	1/2 (50%)	0.553	0.859 (1.42-0.520),	1/2 (50%)	1/2 (50%)	0.298	0.7 (0.1-1.2)
	Smoker	41/76 (53.9%)	35/76 (46.1%)			41/76 (53.9%)	35/76 (46.1%)		
Vaccination status	Non smoker	158/315 (50.2%)	157/315 (49.8%)	0.647	NA	149/315 (47.3%)	166/315 (52.7%)	0.160	
	Pfizer	19/201 (9.5%)	22/196 (5.5%)			20/397 (5%)	21/397 (5.3%)		
	Sinopharm	65/118 (55.1%)	53/118 (44.9%)			65/118 (55.1%)	53/118 (44.9%)		
	Sputnik	19/40 (47.5%)	21/40 (52.5%)			17/40 (42.5%)	23/40 (57.5%)		
	COVISHILD	4/9 (44.4%)	5/9 (55.6%)			5/9 (55.5%)	4/9 (44.4%)		
	No vaccine	89/174 (51.1%)	85/174 (48.9%)			81/174 (46.6%)	93/174 (53.4%)		
Medical history	No record	5/15 (33.3%)	10/15 (66.7%)	0.590	0.800 (0.355-1.80)	3/15 (20%)	12/15 (80%)	0.921	0.9 (0.2-2.1)
	Sinusitis/ allergy	12/28 (42.9%)	16/28 (57.1%)			12/28 (42.9%)	16/28 (57.1%)		
	Asthma / COPD	9/14 (64.3%)	4/14 (35.7%)			8/14 (57.1%)	5/14 (35.7%)		

Impact of anosmia and/or ageusia on patients' life

Out of those who reported anosmia and or dysgeusia, 64.2% reported alterations in eating habits, 38.9% impact on mental wellbeing, 35.4% concerns that the senses of taste and smell would not return, and about 34% had physical implications and difficulty performing activities of daily living [Table 4]. About one third found it hard to relax and 20% either felt angry or isolated.

Table 4. Impact of anosmia and/or ageusia on patients' life

Quality of life parameter	Present Frequency (%)	Absent Frequency (%)
Altered eating habits	145/226 (64.2%)	81/226 (35.8%)
Impact on mental wellbeing	88/226 (38.9%)	140/226 (61.9%)
Concerns the senses of taste and smell would not return	80/226 (35.4%)	146/226 (64.6%)
Impact on physical wellbeing	78/226 (34.5%)	148/226 (65.5%)
Difficulty performing activities of daily living	77/226 (34.1%)	149/226 (66%)
Finding it hard to relax	70/226 (31%)	156/226 (69%)
Reduced visits to restaurants	61/226 (27%)	165/226 (73%)
Feelings angry	51/226 (22.6%)	175/226 (77.4%)
Feeling isolated	48/226 (21.2%)	178/226 (78.8%)

Binomial regression model for anosmia

Table 5 shows the results of binomial regression model for loss of smell as the dependent variable and including the predictors: age, sex, smoking status, chronic respiratory disease and ICU admission as the independent variables. The predictors explained 2.6% of the variation in loss of smell ($R^2=0.026$). The only significant predictor that had an effect on loss of smell is sex of participants ($P=0.001$).

Table 5: Binomial regression Model Coefficients - Did you experience any changes in your sense of smell?

Predictor

Intercept

Age

Sex:

Female – Male

Smoking:

Yes – No

Chronic respiratory disease/Asthma:

No – Yes

ICU admission:

No – Yes

Note. Estimates represent the log odds of "Did you experience any changes in your sense of smell? = No" vs. "Did you experience any changes in your sense of smell? = Yes"

Binomial regression model for dysgeusia

Table 6 shows the results of binomial regression model for dysgeusia as the dependent variable and including the predictors: age, sex, smoking status, chronic respiratory disease and ICU admission as the independent variables. The predictors explained 2.4% of the variation in dysgeusia ($R^2=0.024$). The only significant predictor that influenced dysgeusia is sex of participants ($P=0.001$) (Table 6).

Table 6 Binomial regression Model Coefficients - Did you experience any changes in your sense of taste?

Predictor

Intercept

Age

Sex:

Female – Male

Smoking:

Yes – No

Chronic respiratory disease/Asthma:

No – Yes

ICU admission:

No – Yes

Note. Estimates represent the log odds of "Did you experience any changes in your sense of taste? = No" vs. "Did you exp

Discussion

This cross-sectional study highlights the prevalence and associations of COVID-19 with anosmia and ageusia, and their impact on patients' life in the Kingdom of Bahrain, involving 405 patients infected between October 2020 and June 2021.

The study reported comparable rates of anosmia and dysgeusia, with almost half of the studied patients experiencing either or both symptoms. A combination of anosmia and dysgeusia was more prevalent than either of the symptoms presenting alone. Olfactory and taste dysfunction following Covid-19 is possibly underreported in the literature, as most studies are based on self-reports rather than a more objective assessment.

Our study's population had a significantly higher prevalence of anosmia/ dysgeusia amongst females in comparison with their male counterparts. Similar findings were observed in studies conducted in Saudi, Italy, and Switzerland (13,14). However, this variation between sexes was not significant in other studies (15-18). Possible reasons for this variation in results across studies are the differences in methodology, symptom definition, population studied, measurement tool and recall bias as data was mainly dependent on self-reporting of symptoms. The literature discusses potential biological differences between genders in ACE receptor expression and its location on the X-chromosome, and differences in baseline olfaction as possible explanations to the increased prevalence of these symptoms amongst females (19,20). Both human cell receptors ACE2 and TMPRSS2 are essential for the SARS-CoV-2 entrance. These receptors are mostly present in the olfactory epithelium cells. Therefore, the main hypothesis is that anosmia is caused due to damage to non-neuronal cells which, thereafter, affects the normal olfactory metabolism. A possible explanation for the higher prevalence among females would be that incomplete X chromosome inactivation would contribute to increased expression of ACE2 (21).

Symptoms related to smell and taste were generally associated with milder forms of the disease studied in the acute or initial phase (22). It is yet not clear if these symptoms have a higher impact on morbidity and mortality in the long term, especially with the possibility of neurological pathophysiology. Studies have reported significant associations of neurological burden and infection with SARS-CoV2, explaining the potential connection with entry through the olfactory bulb (23,24). In addition, recent studies demonstrated the association of microinvasive SARS-CoV2 and respiratory failure, emphasising the importance of future research on neurological impacts of COVID-19 (25,26).

In our study, smokers were more likely to experience loss of smell and taste compared to their non-smoking counterparts, although the difference was not found to be statistically significant. Other studies in the region reported significant association between smoking and both anosmia and dysgeusia (16,8). This difference could be explained by the self-reporting of smoking through a phone call, where people might be less comfortable reporting their behaviours (social acceptability bias).

Comparable rates of impact of anosmia and dysgeusia was reported by other studies (4,10,27,28). The main concerns were that the senses of taste and smell would not return, alteration of eating habits, feeling angry

and difficulty performing daily activities. While greater attention is being paid to curbing other COVID-19 related symptoms as well as rolling out the vaccines, the prognosis of Covid-19 survivors with olfactory and taste dysfunction remains an enigma which will ultimately have a huge impact on patient's quality of life especially if the loss or dysfunction is permanent.

Limitations of our study included measurement bias of some risk factors, recall bias, incomplete medical records, and missing information. Further, this study did not compare the impact of permanent vs transient loss/dysfunction of olfactory and taste. Strengths include random selection of an early cohort of COVID-19 patients from a national registry and using validated tool for outcome measurement.

Conclusion

Anosmia and dysgeusia are prevalent symptoms of COVID19 disease, especially amongst females. Further cohort or case control studies are needed to establish the association and risk factors of anosmia and dysgeusia with the disease ideally involving a control group. Definitive mechanism of action and diagnostic value of anosmia and dysgeusia remain to be verified in future studies. Effective treatment regimen for anosmia and dysgeusia post COVID should be investigated in randomised controlled trials to enhance patient's quality of life.

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