Original article

The prevalence of olfactory dysfunction and its associated factors in patients with COVID-19 infection: A Hospital-based study

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Abstract

Background:The coronavirus disease of 2019 (COVID-19) is a global viral pandemic that originated in East Asia (China) and is quickly spreading to every corner of the globe. In Bangladesh, no research has been conducted on olfactory dysfunction in COVID-19 infected patients and its associated factors. We aimed to determine the correlation between olfactory dysfunction (OD), particularly anosmia and COVID-19 infected patients' demographic and clinical characteristics. ***Methods:*** We conducted a hospital-based prospective observational study. We collected patients' information, including laboratory-confirmed COVID-19 test results from a COVID dedicated hospital, Square Hospitals Ltd., Dhaka, Bangladesh. We used the Pearson Chi-square test and logistic regression model to assess the associations between demographic and clinical characteristics and OD (i.e. anosmia). ***Results:*** Out of 600 COVID-19 positive patients, 38.7% were diagnosed with OD. We found that patients' age, smoking status, cough, dyspnea, sore throat, asthenia, and nausea or vomiting were significantly associated with anosmia. We observed smoking patients were 1.73 times more likely to experience anosmia than non-smoking patients Odd ratio (OR)=1.73, 95% confidence interval (CI) = 1.01-2.98]. Interestingly, our data showed that the risk of developing anosmia was greater in younger patients than in older patients, and this risk decreased as age increased (OR) range for different age groups: 1.26 to 1.08]. In addition, patients who complained of asthenia had a significantly double risk of developing anosmia [OR = 1.96, CI = 1.23-3.06]. ***Conclusions:*** Our study shows that 38.7% of patients diagnosed with OD. Patients' age, smoking status, and asthenia are significantly positively associated with anosmia. Since anosmia can be a significant marker for the diagnosis of COVID-19, we suggest regular screening of OD in patients with early symptoms of COVID-19, particularly younger patients, smokers, and who complained of asthenia.

Keywords: COVID-19; Anosmia; Olfactory Dysfunction; Factors; Bangladesh

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Introduction

The 2019 coronavirus illness, also known as COVID-19, is an ongoing viral pandemic that originated in East Asia (China) and has since rapidly spread to every region and nation in the world.[1-3] On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic. On March 8, 2020, the first verified case of COVID-19 was discovered in Bangladesh, and the disease is still active.[4-7]

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The virus transmitted from person to person by being exposed to virus-containing droplets, aerosols, and surfaces and contracting them through the oral cavity, nasal cavity, or eyes.[9]Fever, dry cough, sore throat, weariness, dyspnea, and other symptoms are typical in COVID-19 patients.[10]Furthermore, olfactory or gustatory dysfunction (e.g., anosmia-loss of sense of smell) is sometimes seen as a sign of COVID-19.[10-13]Several studies have also found a significant incidence of olfactory impairment (OD), particularly anosmia, in COVID-19 individuals, which is sometimes thought to be the initial symptom.[11,14-21]Anosmia is a loss of olfactory sense that can be caused by allergies, nasal polyps, viral diseases, upper respiratory tract infections, and other factors.[22,23]Brann et al. further emphasized that COVID-19 patients' anosmia might be caused by inflammation of non-neuronal support cells in the nose and forebrain.[24]They also said that in this scenario, nasal obstruction is unrelated to anosmia; consequently, such individuals may suffer anosmia without complaining of a stuffy nose. However, it is unknown which sorts of COVID-19 patients are most likely to experience this symptom.

As far as we know, no studies on OD for COVID-19 infected individuals have been conducted in Bangladesh. We aimed to see if there was a link between OD, namely anosmia, and the demographic and clinical features of COVID-19 infected patients.

Materials and Methods

Ethical statement and inform consent

Informed consent was taken from the patient or legal guardian of the patient. Moreover, the aims and objectives of the study, along with its procedure, risk and benefit were explained to the patients.

Ethics committee approval

The ethical clearance was taken from the ethical committee at SQUARE Hospital Ltd.

Subjects and setting

We conducted a hospital-based prospective observational study. We collected clinical data of patients with laboratory-confirmed COVID-19 infection from a tertiary level COVID dedicated hospital, name: Square Hospitals Ltd., Dhaka, Bangladesh.

We considered several inclusion and exclusion criteria. The inclusion criteria were: laboratory-confirmed COVID-19 infection (reverse transcription-polymerase chain reaction, RT-PCR); adult (> 18 years old); both male and female; and patients clinically stable to answer the questionnaire. Moreover, the exclusion criteria were: patients with OD before study period; patients without a finding of laboratory-confirmed COVID-19 infection; patients who did not want to participate;patients in the intensive-care unit (ICU) at the time of the study (due to the restrictions from the hospital & their clinical condition). Accordingly, we mostly included mild-to-moderate COVID-19 patients without the need for ICU.

Clinical outcomes

Clinical data have been recorded during the ear, nose, and throat (ENT) consultation prospectively; in the patients' room who were admitted in the hospital; or over the phone for infected health professionals. The questionnaire consisted of some general questions, such as age, sex, education, smoking or other drug addiction; three general clinical questions (e.g., comorbidities such as diabetes, hypertension, chronic kidney disease (CKD), Ischemic heart disease (IHD), asthma, thyroid, dyslipidemia, and cancer; general symptoms like fever, asthenia, diarrhoea, apnea, loss of appetite etc.and ENT symptomsespecially nasal obstruction, nasal cold, anosmiaetcrelated with COVID-19 infection); and one question about the treatment of the COVID-19 infection. All patients were requested to complete the questionnaire in the presence of the investigator.

Questionnaires about the olfactory sense

We asked questions about the olfactory sense. The questions have been selected to illustrate the timing and accompanying symptoms of OD. The patients who lost their sense of smell during COVID-19 were considered patients with COVID-19 induced anosmia. These anosmic patients had no previous history of OD or any surgery or trauma within two months before COVID-19. We asked questions to determine the mean recovery time. Duration until recovery was classified into 1-4 days, 5-8 days, 9-14 days, 15-20 days, and 21+ days. Studies have shown that the viral load was significantly decreased after 14 days and could recover within 28 days.[23] Finally, a binary variable either anosmia present or absent was created.

Statistical analysis

In the analysis stage, partial or unfinished responses were excluded from the analysis. Several descriptive and inferential statistical methods were applied to analyze the data. First, a cross-tabulation with Pearson

Chi-square test was used to assess the marginal contribution of each variable's on anosmia. Second, to identify factors that were associated the anosmia, a binary multivariable logistic regression model was applied. To obtain a better-fitting model, we only included clinically relevant variables in the logistic regression analyses. A level of $p < 0.05$ was used to determine statistical significance. Statistical Package for the Social Sciences for Windows (SPSS version 25) was used to perform the statistical analyses.

Results

A total of 600 COVID-19 infected patients participated in the study, and 232 (38.7%) patients were diagnosed with OD (Figure 1). Of the OD patients, 34% had this symptom for 5 to 8 days, followed by 30% for 11 to 14 days (Figure 2).

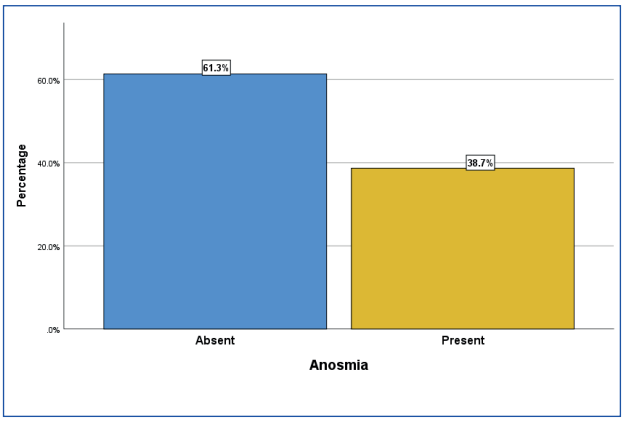

Figure 1. Percentage of COVID-19 patients with or without anosmia

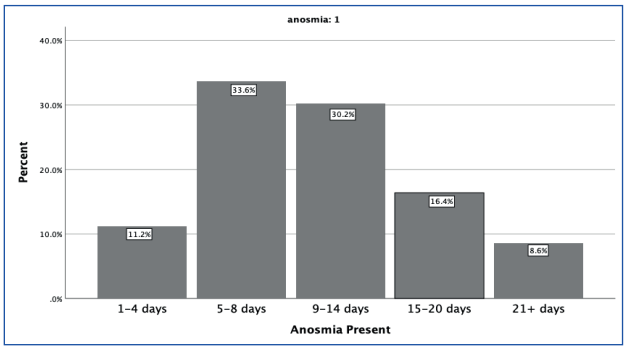

Figure 2. Percentage of COVID-19 patients with duration anosmia present

There were 383 (64%) males and 217 (36%) females. Also, among the patients with anosmia, 62.1% were male. The mean age of patients was 50.20 ± 14.81 years (range: 22-88 years). The highest percentage (33.6%) of anosmia patients belong to the age group 30-39 years. 75.4% were from the urban area, 62.9% completed a university degree. Among all patients, 62% had comorbidities, and out of anosmia patients, 51.3% had comorbidity where the most prevalent comorbidities of patients were diabetes and hypertension. As expected, the highest percentage (75%) of patients had a fever, and the lowest parentage (3.9%) of patients had nausea or vomiting. From bivariate analyses, we observed that age (P<0.001), education (P<0.001), diabetes (P=0.001), hypertension (P<0.001), and CKD (ESRD) (P=0.025) were significantly associated with the anosmia. We also showed that most of the symptoms were also significantly related to anosmia (Table-1).

Table 1. Distribution of patients' socio-demographic and clinical characteristics across the outcome variable (anosmia) including p-value from Pearson Chi-Square Tests.

Factors		Anosmia				P-value
		No		Yes		
		Count	Column %	Count	Column %	
Gender	Female	129	35.1	88	37.9	0.475
	Male	239	64.9	144	62.1	
Age (in years)	20-29	16	4.3	17	7.3	<0.001
	30-39	69	18.8	78	33.6	
	40-49	62	16.8	46	19.8	
	50-59	90	24.5	32	13.8	
	60+	131	35.6	59	25.4	
Area	Rural	81	22.0	57	24.6	0.468
	Urban	287	78.0	175	75.4	

Factors		Anosmia				P-value
		No		Yes		
		Count	Column %	Count	Column %	
Education	Post-graduation	34	9.2	34	14.7	<0.001
	Graduation	186	50.5	146	62.9	
	Higher Secondary	83	22.6	39	16.8	
	Secondary School	44	12.0	8	3.4	
	Primary	21	5.7	5	2.2	
Diabetic	No	187	50.8	150	64.7	<0.001
	Yes	181	49.2	82	35.3	
Hypertension	No	177	48.1	154	66.4	<0.001
	Yes	191	51.9	78	33.6	
Asthma	No	324	88.0	212	91.4	0.197
	Yes	44	12.0	20	8.6	
Thyroid	No	350	95.1	221	95.3	0.934
	Yes	18	4.9	11	4.7	
Dyslipidemic	No	344	93.5	225	97.0	0.059
	Yes	24	6.5	7	3.0	
Depression	No	365	99.2	231	99.6	0.059
	Yes	3	0.8	1	0.4	
Chronic Kidney Disease	No	332	90.2	221	95.3	0.025
	Yes	36	9.8	11	4.7	
IHD	No	322	87.5	213	91.8	0.098
	Yes	46	12.5	19	8.2	
Neurological Disease	No	357	97.0	231	99.6	0.029
	Yes	11	3.0	1	0.4	
Allergic Rhinitis	No	366	99.5	230	99.1	0.640
	Yes	2	0.5	2	0.9	
Cancer	No	360	97.8	230	99.1	0.222
	Yes	8	2.2	2	0.9	
Comorbidity	No	115	31.3	113	48.7	<0.001
	Yes	253	68.8	119	51.3	
Smoking or Other Addiction	No	308	83.7	186	80.2	0.270
	Yes	60	16.3	46	19.8	
Fever	No	56	15.2	58	25.0	0.003
	Yes	312	84.8	174	75.0	
Cough	No	155	42.1	137	59.1	<0.001
	Yes	213	57.9	95	40.9	
Dyspnea	No	216	58.7	166	71.6	0.001
	Yes	152	41.3	66	28.4	

Factors		Anosmia				P-value
		No		Yes		
		Count	Column %	Count	Column %	
Sore Throat	No	241	65.5	182	78.4	0.001
	Yes	127	34.5	50	21.6	
Asthenia	No	299	81.3	152	65.5	<0.001
	Yes	69	18.8	80	34.5	
Myalgia	No	307	83.4	196	84.5	0.732
	Yes	61	16.6	36	15.5	
Loss Appetite	No	319	86.7	180	77.6	0.004
	Yes	49	13.3	52	22.4	
Loose Motion	No	315	85.6	203	87.5	0.509
	Yes	53	14.4	29	12.5	
Headache	No	326	88.6	216	93.1	0.068
	Yes	42	11.4	16	6.9	
Nausea or Vomiting	No	334	90.8	223	96.1	0.013
	Yes	34	9.2	9	3.9	
Nasal Cold	No	336	91.3	219	94.4	0.161
	Yes	32	8.7	13	5.6	
Facial Pain	No	346	94.0	215	92.7	0.514
	Yes	22	6.0	17	7.3	
Abdominal Pain	No	346	94.0	223	96.1	0.258
	Yes	22	6.0	9	3.9	
Chest Pain	No	353	95.9	221	95.3	0.697
	Yes	15	4.1	11	4.7	
Nasal Obstruction	No	340	92.4	218	94.0	0.462
	Yes	28	7.6	14	6.0	

Table-2 shows the association between patients' characteristics and anosmia from the multivariable binary logistic regression model. We found that patients' age, smoking status, cough, dyspnea, sore throat, asthenia, and nausea vomiting were significantly associated with the anosmia. The risk of developing anosmia for younger patients was higher than the older patients, and this risk decreased with the increasing age [OR 1.26 to 1.08]. Patients with smoking or other addiction had a 1.73 times higher chance to develop anosmia than non-smoker [OR=1.73, 95% confidence interval (CI) = 1.01-2.98]. Besides, patients complained asthenia had significantly double risk to develop the anosmia [OR = 1.96, CI = 1.23-3.06, p =0.001]. All other statistically significant variables showed negative relation with the anosmia.

Table 2. Association between patients' characteristics and Anosmia from the multivariable binary logistic regression model.

Factors	Categories	Estimate	Odds ratio (OR)	95% C.I. for OR		P-value
				Lower	Upper	
Gender	Female	0.16	1.17	0.77	1.80	0.46
	Male (Ref)					
Age (in years)	20-29	0.23	1.26	0.52	3.06	0.61
	30-39	0.24	1.27	0.70	2.32	0.43
	40-49	0.08	1.08	0.60	1.96	0.79
	50-59	-0.59	0.55	0.31	0.99	0.05
	60+ (Ref)					
Diabetic	Yes	0.11	1.12	0.69	1.80	0.65
	No (Ref)					
Hypertension	Yes	-0.40	0.67	0.41	1.09	0.10
	No (Ref)					
Asthma	Yes	-0.25	0.78	0.41	1.46	0.43
	No (Ref)					
Thyroid	Yes	0.44	1.56	0.64	3.80	0.33
	No (Ref)					
Dyslipidemic	Yes	-0.39	0.68	0.26	1.77	0.43
	No (Ref)					
CKD-ESRD	Yes	-0.28	0.76	0.35	1.66	0.49
	No (Ref)					
IHD	Yes	-0.17	0.84	0.44	1.61	0.60
	No (Ref)					
Neurological disease	Yes	-2.00	0.14	0.01	1.24	0.08
	No (Ref)					
Cancer	Yes	-1.28	0.28	0.05	1.51	0.14
	No (Ref)					
Smoking or other addiction	Yes	0.55	1.73	1.01	2.98	0.05
	No (Ref)					
Fever	Yes	-0.28	0.76	0.46	1.24	0.27
	No (Ref)					
Cough	Yes	-0.71	0.49	0.32	0.76	<0.001
	No (Ref)					
Dyspnea	Yes	-0.51	0.60	0.39	0.93	0.02
	No (Ref)					
Sore throat	Yes	-0.79	0.45	0.29	0.70	<0.001
	No (Ref)					
Asthenia	Yes	0.67	1.96	1.26	3.06	<0.001

Factors	Categories	Estimate	Odds ratio (OR)	95% C.I. for OR		P-value
				Lower	Upper	
Gender	Female	0.16	1.17	0.77	1.80	0.46
	No (Ref)					
Myalgia	Yes	-0.37	0.69	0.41	1.16	0.16
	No (Ref)					
Loss appetite	Yes	0.33	1.39	0.83	2.32	0.21
	No (Ref)					
Loose motion	Yes	-0.46	0.63	0.36	1.11	0.11
	No (Ref)					
Headache	Yes	-0.45	0.64	0.33	1.24	0.19
	No (Ref)					
Nausea vomiting	Yes	-1.24	0.29	0.13	0.66	<0.001
	No (Ref)					
Nasal cold	Yes	-0.54	0.58	0.27	1.24	0.16
	No (Ref)					
Facial pain	Yes	-0.29	0.75	0.35	1.59	0.45
	No (Ref)					
Abdominal pain	Yes	-0.50	0.61	0.25	1.48	0.27
	No (Ref)					
Chest pain	Yes	-0.20	0.82	0.32	2.08	0.68
	No (Ref)					
Nasal obstruction	Yes	-0.41	0.66	0.31	1.43	0.29
	No (Ref)					

Discussion

This study examined the relationships between ODs, namely anosmia, and the demographic and clinical parameters of COVID-19 infected individuals. To the best of our knowledge, this is Bangladesh's first hospital-based research.We discovered that around 39% of 600 patients were diagnosed with OD by COVID-19, which is consistent with a prior systematic review and meta-analysis.[24] Our findings revealed that anosmia was substantially linked with patients' age, smoking status, cough, dyspnea, sore throat, asthenia, and nausea or vomiting. The most prevalent symptoms for COVID-19 infected individuals were fever, cough, dyspnea, sore throat, myalgia, loose motion, asthenia, and appetite loss. Surprisingly, there was no gender difference in self-reported olfactory dysfunction.Agyeman et al.[24] discovered a similar conclusion in their systematic review and meta-analysis.

The likelihood of developing anosmia was greater in younger patients than in older patients, and it reduced with age. Giacomelli et al. had a similar finding, reporting that OD was more common in younger individuals.[24,25] Because older COVID-19 patients are more susceptible to other comorbidities, the anosmia issue may go undetected, and so this condition has not been observed frequently.[16] However, Dong et al.[26] found that anosmia is more common in older persons in their study. Furthermore, multiple prior research have showed that the median age for anosmia patients is about 50 years.[26-28] Again, anosmia was shown to be strongly linked with smoking or other addictions in COVID-19 patients. Specifically, during COVID-19, a smoker had double the risk of anosmia as a nonsmoker.Similar findings were obtained by Al-Ani and Acharya, who discovered

that smoking was substantially linked to anosmia in COVID-19 patients.[30]Furthermore, according to Katotomichelakis et al.[31]smokers had a six-fold higher chance of developing olfactory dysfunction than non-smokers. In general, cigarettes and other drugs include hazardous particles such as nicotine, tar, and so forth, or the substance itself damages the olfactory neurons. As a result, smoking is more likely to harm the olfactory neurons, resulting in olfactory dysfunction during COVID 19. Approximately 62% of the patients had comorbidity, and nearly 51% had anosmia. Surprisingly, diabetic and thyroid-related illness patients showed a little higher risk of anosmia than the other patients. Neuropathy is a typical consequence in diabetes individuals, and it is unclear if the Coronavirus also causes nervous system damage.[11,14-16]In diabetic people, this may increase the chance of COVID 19 infection. According to Klopfenstein et al. (2020), only patients with asthma had a greater risk of anosmia than patients with hypertension, diabetes, cardiovascular disease, or pulmonary illness.[32]

We discovered that individuals with asthenia also had anosmia. It has been proven that taste and scent are connected. As a result, anosmia patients develop hypogeusia, which may progress to ageusia.[9,33] Furthermore, as patients age, their desire to consume food declines, resulting in frailty. In an interview, Sandeep Robert Datta of Harvard Medical School stated that anosmia can have major psychological implications during COVID-19, which will be disastrous.[34] As a result, weakness might be linked to psychological issues such as depression. Again, individuals with nasal obstruction or rhinorrhea reported OD in the Lechien et al.[20] trial, but our investigation found a negative relationship between nasal obstruction and anosmia.[20,32] Similarly to other problems with a COVID-19 infection, reports of nasal obstruction (49.5%) and rhinorrhea (35.0%) were common, but were unrelated to OD.[31,34] Out of 232 individuals with OD, the majority (79) experienced the condition for 5 to 8 days, followed by 70 patients for nearly 2 weeks, which is comparable with prior investigations of COVID-19.[35,36] However, 20 individuals experienced anosmia for more than 2 weeks. Not unexpectedly, we discovered that roughly 3% of young patients were asymptomatic and 2% had just anosmia.

Two hypotheses can be used to treat OD: mucosal obstruction caused by local olfactory cleft inflammation causes "conductive" loss, or a post-viral anosmia syndrome caused by direct infection of the olfactory mucosa and destruction of the olfactory sensory neurons causes "neural" loss.[20, 37] These losses have different effects; in the "conductive" loss, we would expect a reasonably quick recovery of normal olfaction along with the resolution of any accompanying nasal symptoms. In the "neutral" condition, recovery would be more difficult and there would be a greater probability of lasting olfactory impairment.[33]

The study's strengths include a large sample size (n=600), PCR confirmation of COVID-19 infection, and a detailed questionnaire about health history and COVID-19 symptoms. Notably, this is the first study in Bangladesh to assess olfactory function in COVID-19 inpatients. The study did, however, have several shortcomings. First, because of the increased potential of contamination among personnel, we avoided direct smell recognition testing, and clinical data were gathered via a questionnaire. Second, because the study was conducted in a hospital, the majority of patients were older and hospitalized. Third, the olfactory function assessment was self-reported, which may have introduced bias into the study. Fourth, because this is a hospital-based study, there is a possibility of selection bias. Finally, because the study was cross-sectional, there is no information on how long after infection the olfactory function evolved and when the questionnaire was administered in connection to infection.

Conclusion

According to our findings, approximately 38.7% of patients had olfactory dysfunction. We showed that patients' age, smoking status, and asthenia are all strongly linked with anosmia. Because anosmia can be a crucial marker for the diagnosis of COVID-19, we recommend routine olfactory dysfunction screening in patients with very early COVID-19 symptoms, particularly in younger patients, smokers, and patients who have complained of asthenia.

Declaration

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Competing interests: The authors have declared

that no competing interests exist.

Conflicts of interest: The authors have no conflicts of interest.

Data Availability Statements: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors contribution:MMH: Design, collect and entry data, draft the manuscript andreview the manuscript; NAT: Organize the results, Draft the manuscript and review the manuscript; ANMJ and MNJ: Provide editorial comments and review the manuscript; and MJU: Analysis the data and review the manuscript.

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