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Research Article

Anosmia in Covid-19 Patients: Prognosis, Symptom Associations, and Recovery Follow-up

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I N F O

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A B S T R A C T

Background: Anosmia and loss of taste are among the cardinal symptoms of active COVID-19 infection. Fever, respiratory symptoms, and varying degrees of gastrointestinal symptoms were common clinical manifestations of this viral infection. The study aimed to describe anosmia in confirmed COVID-19 patients and its association with other systemic symptoms and recovery patterns.

Methods: A cross-sectional study was conducted at Al-Imamain Al-Kadimain Teaching Hospital in Baghdad, Iraq, in 2021. Two hundred and eighteen COVID-19 patients who attended the ENT outpatient clinic at this hospital were confirmed positive for COVID-19 by RT-PCR.

Results: Of 218 positive cases, 130 patients (59.6%) had anosmia. The most common symptoms among patients were fever (64.7%), headache (49.5%), fatigue (46.8%), dizziness ((41.3) and myalgia (38.1%). It was observed that 54 (41%) anosmic patients recovered within 3 months, and 40 (31%) within 3–6 months. There was a significant association between the onset and recovery time of anosmia and the age and gender of patients.

Conclusion: This study concluded that anosmia is the most often reported symptom in COVID-19 patients.

Keywords: Anosmia, Covid-19, Olfactory Dysfunction, Diarrhoea

Introduction

Since the onset of the coronavirus disease 2019 (COVID-19) pandemic, reports from around the world have indicated that anosmia and loss of taste are prominent signs of an active infection. Coronaviruses were first grown by Tyrell and Bynoe in 1966. It has been seen that alpha coronaviruses typically cause asymptomatic or mild symptoms.[1] Beta coronaviruses (including SARS-CoV-2) cause serious pulmonary disease and deaths. The disease caused by the novel coronavirus that emerged in China in 2019 was called COVID-19.[2] The increased frequency of persisting symptoms among those who did not get the COVID-19 vaccine highlights the possible preventive impact of immunisation.[3]

Both fever and respiratory symptoms, which have varying fatality rates, are often observed the clinical signs of this

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viral infection. The clinical features often associated with SARS-CoV-2 include respiratory symptoms, fever, cough, and shortness of breath.[4] Typically, they require testing before a COVID-19 diagnosis can be made or ruled out. Both upper airway symptoms and gastrointestinal symptoms may be present in a patient, but these are insufficient clues for a conclusive diagnosis.[5] Reports of olfactory dysfunction in otherwise asymptomatic individuals have generated interest in this symptom as a possible early indicator of COVID-19 infection. In addition, because of the high viral load inside the nasal cavity, olfactory neurons can have a particularly high risk of injury.[6] Therefore, it is crucial to assess the prevalence of the disease's prognostic indicators. The majority of the infected cases and patients who were in close contact with sufferers were the focus of worry internationally. Due to shortage of test kits, even in developed nations with robust healthcare systems, all suspicious cases were not examined for asymptomatic carriers.[7] The aim of this study is to provide a detailed description of anosmia in individuals who tested positive for COVID-19, examine its correlation with other systemic symptoms, and assess the olfactory dysfunction recovery patterns of COVID-19 patients who recovered, in a sample of patients attending the Al-Imamain Al-Kadimain Teaching Hospital in Baghdad, Iraq.

Materials and Methods

Study Design, Study Setting, and Study Population

A cross-sectional study was conducted at Al-Imamain Al-Kadimain Teaching Hospital, Al-Karkh Health Directorate in Baghdad, Iraq, from May 1, 2021, to November 1, 2021. It included COVID-19 patients who attended the ENT outpatient clinic at this hospital and were confirmed by RT-PCR testing.

Sampling

Convenience sampling was carried out; all patients who consulted the outpatient clinic of the ENT department for 6 consecutive months, 5 days/week, 5 hours/day were included in the study. A questionnaire was administered by the researcher through direct interviews. It included sociodemographic characteristics (age, gender, and personal phone number), and clinical features (fever, myalgia, cough, dyspnoea, fatigability, sore throat, anosmia, diarrhoea, chest pain or compression, nasal burning sensation, sneezing, and headache), along with the onset, type and time of recovery from anosmia, and history of chronic diseases.

Two hundred and fifty COVID-19-positive patients were interviewed during the study period, of whom only 218 responded to our follow-up calls and were included in this study.

Inclusion Criteria

All adult patients (> 18 years of age) diagnosed with COVID-19 using RT-PCR in the outpatient setting

Exclusion Criteria

Patients with severe critical illnesses, or those who were lost to follow-up (not responding to 3 telephone calls)

Statistical Analysis

Data input, management, and analysis were performed using Microsoft Excel 2010 and IBM SPSS version 24. Descriptive analyses of the variables were reported as frequencies and percentages for categorical data, which were visually depicted in figures and tables. To compare qualitative variables, the chi-square test or Fisher's exact test was used. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to assess risk factors. A significance level of $p \leq 0.05$ was used to evaluate statistical significance.

Ethical Considerations

The study received approval from the Ministry of Health, the Al-Karkh Health Directorate, Baghdad, Iraq, and the ethics committee of Al-Imamain Al-Kadimain Teaching Hospital. The study was purely observational, and patients provided verbal consent.

Results

This study included 218 COVID-19 patients. Among them, 78.9% were aged below 50 years, 21.1% were aged 50 years or more, 39.4% were male, and 60.6% were female. Of all patients, 130 (59.6%) had anosmia (Figure 1), and 85.8% had other symptoms (Figure 2). The most common symptom among patients was fever (64.7%), followed by headache (49.5%), fatigue (46.8%), dizziness (41.3%), and myalgia (38.1%). About 81 (37.2%) patients had chronic diseases (Table 1).

Table 2 shows that 108 (62.8%) anosmic patients were below 50 years of age, 52 (60.5%) were male, and 78 (59.1%) were female. Symptoms such as runny nose, sneezing, and nasal burning sensation were significantly associated with anosmia ($p < 0.05$). Absence of fever, headache, fatigue, gastric upset, shortness of breath, cough, chest pain, and diarrhoea was found to be significantly associated with the presence of anosmia ($p < 0.01$).The presence of chronic diseases was also significantly associated with anosmia ($p < 0.01$; Table 2 and Figure 2).

Of all anosmic patients, 104 had complete anosmia and 26 had partial anosmia (Figure 3).

Figure 4 shows the time of recovery of anosmia among the participants; 54 anosmic patients recovered their olfactory sensation within three months, 40 recovered within 3–6 months, and 36 anosmic patients still had anosmia.

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Anosmia was associated with other symptoms among 99 (76%) anosmic patients (Figure 5).

Table 3 shows the distribution of anosmic patients according to their age groups. The onset and recovery time of anosmia were significantly associated with the age of anosmic patients (p = 0.004 and p = 0.001, respectively).

Table 4 shows the distribution of anosmic patients by gender. There was a significant association between the onset of anosmia and gender (p = 0.023). Another significant association was shown between time recovery and type of anosmia with gender (p = 0.031 and p = 0.012, respectively).

There was a significant association between time of recovery (less than 3 months) and between anosmic patients with sneezing, headache, myalgia, and fatigue ($p < 0.05$); while absence of cough, chest pain or pressure, pharyngitis, and diarrhoea were found to be significant with short time of recovery (< 3 months) ($p < 0.001$) (Table 5).

Risk estimation was done using OR and 95% CI. Risk factors associated with the time of recovery were sneezing, headache, myalgia, and fatigue ((OR: 2.6; 95% CI: 1.1–6.3), (OR: 5.5; 95% CI: 2–15), (OR: 5.70; 95% CI: 2–17), (OR: 4.2; 95% CI: 1.6–11.0), respectively), while protective factors were found to be cough, chest pain or pressure, pharyngitis, and diarrhoea ((OR: 0.1; 95% CI: 0.03–0.24), (OR: 0.2; 95% CI: 0.05–0.5), (OR: 0.08; 95% CI: 0.03–0.24), (OR: 0.9; 95% CI: 0.03–0.25) respectively) (Table 5).

Table 1.Demography and Clinical Presentation of COVID-19 Patients

Demographic Variables and Clinical Features		n	%
Age group (years)	< 50	172	78.9
	≥ 50	46	21.1
Gender	Male	86	39.4
	Female	132	60.6
Anosmia	Yes	130	59.6
	No	88	40.4
Clinical symptoms	Yes	187	85.8
	No	31	14.2
Fever	Yes	141	64.7
	No	77	35.3
Runny nose	Yes	55	25.2
	No	163	74.8
Sneezing	Yes	62	28.4
	No	156	71.6
Headache	Yes	108	49.5
	No	110	50.5
Myalgia	Yes	83	38.1
	No	135	61.9
Fatigue	Yes	102	46.8
	No	116	53.2
Dizziness	Yes	90	41.3
	No	128	58.7
Gastric upset	Yes	64	29.4
	No	154	70.6
Nasal burning sensation	Yes	35	16.1
	No	183	83.9
Shortness of breath	Yes	55	25.2
	No	163	74.8
Cough	Yes	64	29.4
	No	154	70.6
Chest pain or pressure	Yes	39	17.9
	No	179	82.1
Pharyngitis	Yes	43	19.7
	No	175	80.3
Diarrhoea	Yes	53	24.3
	No	165	75.7
Chronic diseases	Yes	81	37.2
	No	137	62.8
	Total	218	100.0

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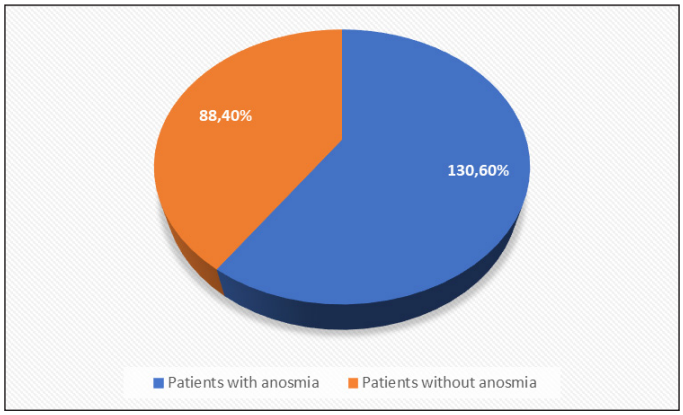

Figure 1.Distribution of Patients With and Without Anosmia

Table 2.Distribution of COVID-19 Patients Based on Anosmia

Demographic Variables and Clinical Features		Anosmia				p Value
		Yes		No		
		n	%	n	%	
Age group (years)	< 50	108	62.8	64	37.2	0.066
	≥50	22	47.8	24	52.2	
Gender	Male	52	60.5	34	39.5	0.840
	Female	78	59.1	54	40.9	
Fever	Yes	73	51.8	68	48.2	0.001
	No	57	74.0	20	26.0	
Runny nose	Yes	42	76.4	13	23.6	0.003
	No	88	54.0	75	46.0	
Sneezing	Yes	48	77.4	14	22.6	0.001
	No	82	52.6	74	47.4	
Headache	Yes	49	45.4	59	54.6	< 0.001
	No	81	73.6	29	26.4	
Myalgia	Yes	43	51.8	40	48.2	0.065
	No	87	64.4	48	35.6	
Fatigue	Yes	49	48.0	53	52.0	0.001
	No	81	69.8	35	30.2	
Dizziness	Yes	48	53.3	42	46.7	0.110
	No	82	64.1	46	35.9	
GI upset	Yes	30	46.9	34	53.1	0.013
	No	100	64.9	54	35.1	
Nasal burning sensation	Yes	30	85.7	5	14.3	0.001
	No	100	54.6	83	45.4	
Shortness of breath	Yes	25	45.5	30	54.5	0.013
	No	105	64.4	58	35.6	
Cough	Yes	26	40.6	38	59.4	< 0.001
	No	104	67.5	50	32.5	
Chest pain or pressure	Yes	17	43.6	22	56.4	0.024
	No	113	63.1	66	36.9	
Pharyngitis	Yes	22	51.2	21	48.8	0.210
	No	108	61.7	67	38.3	
Diarrhoea	Yes	22	41.5	31	58.5	0.002
	No	108	65.5	57	34.5	
Chronic diseases	Yes	60	74.1	21	25.9	0.001
	No	70	51.1	67	48.9	

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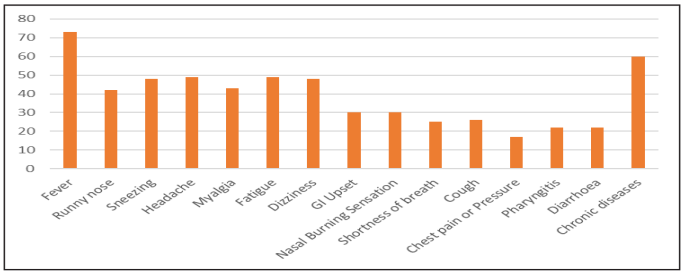

Figure 2.Associated Manifestations Among Anosmic Patients

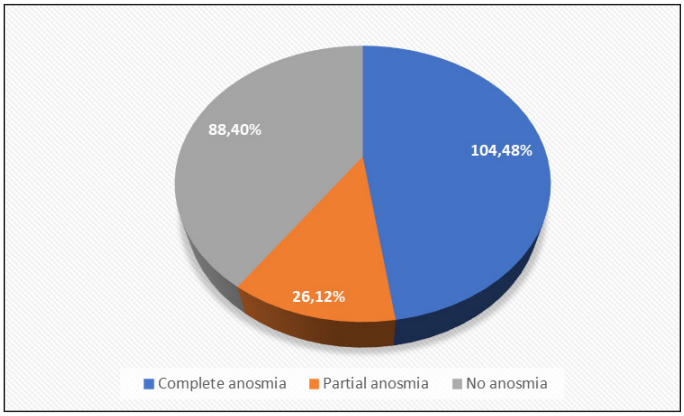

Figure 3.Degree of Anosmia Among Patients

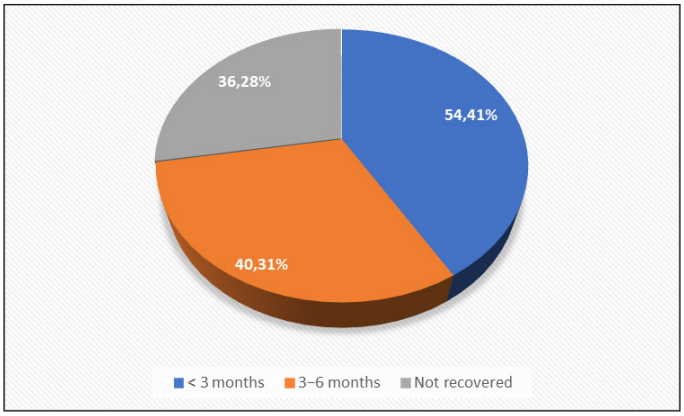

Figure 4.Time of Recovery of Anosmia

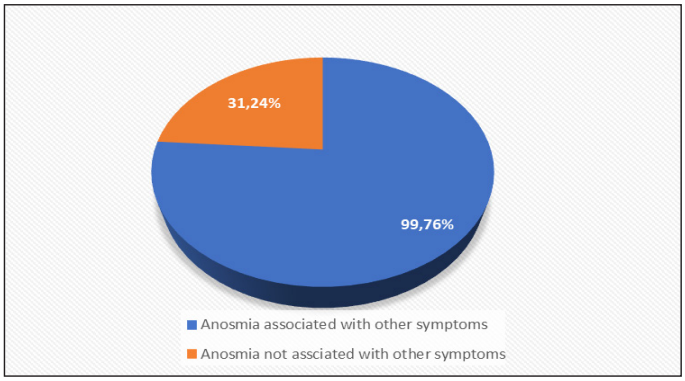

Figure 5.Association of Anosmia With Other Symptoms

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Table 3.Distribution of Anosmic Patients According to Their Age Groups (N = 130)

Anosmia Features		Age Group (Years)				p Value
		< 50		≥ 50		
		n	%	n	%	
Onset of anosmia	First week of illness	96	85.7	16	14.3	0.004
	Second week of illness	6	50.0	6	50.0	
	> 14 days of illness	6	100.0	0	0.0	
Type of anosmia	Complete anosmia	88	84.6	16	15.4	0.350
	Partial anosmia	20	76.9	6	23.1	
Time of recovery	< 3 months	38	70.4	16	29.6	0.001
	3–6 months	40	100.0	0	0.0	
	Not recovered even after 6 months	30	83.3	6	16.7	
Total		108	83.1	22	16.9	total 130

Table 4.Distribution of Anosmic Patients According to Their Gender (N = 130)

Anosmia Features		Gender				p Value
		Male		Female		
		n	%	n	%	
Onset of anosmia	First week of illness	44	39.3	68	60.7	0.023
	Second week of illness	8	66.7	4	33.3	
	> 14 days of illness	0	0.0	6	100.0	
Type of anosmia	Complete anosmia	36	34.6	68	65.4	0.012
	Partial anosmia	16	61.5	10	38.5	
Time of recovery	< 3 months	28	51.9	26	48.1	0.031
	3–6 months	10	25.0	30	75.0	
	Not recovered even after 6 months	14	38.9	22	61.1	
Total		52	40.0	78	60.0	Total 130

Table 5.Distribution of Anosmic Patients According to Recovery Time (N = 130)

Population and Clinical Features		Time of Recovery				p Value	OR	95% CI
		≤ 3 Months		> 6 Months				
		n	%	n	%			
Age group (years)	< 50	78	72.2	30	27.8	1.000	Reference	
	≥ 50	16	72.7	6	27.3		0.98	0.35–2.70
Gender	Male	38	73.1	14	26.9	0.920	Reference	
	Female	56	71.8	22	28.2		1.10	0.50–2.30
Type of anosmia	Complete	78	75.0	26	25.0	0.200	Reference	
	Partial	16	61.5	10	38.5		1.90	0.80–4.60
Fever	Yes	50	68.5	23	31.5	0.300	Reference	
	No	44	77.2	13	22.8		0.60	0.30–1.40
Runny nose	Yes	35	83.3	7	16.7	0.060	Reference	
	No	59	67.0	29	33.0		2.50	0.90–6.20
Sneezing	Yes	40	83.3	8	16.7	0.042	Reference	
	No	54	65.9	28	34.1		2.60	1.10–6.30
Headache	Yes	44	89.8	5	10.2	0.001	Reference	
	No	50	61.7	31	38.3		5.50	2.00–15.00
Myalgia	Yes	39	90.7	4	9.3	0.001	Reference	
	No	55	63.2	32	36.8		5.70	2.00–17.00

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Fatigue	Yes	43	87.8	6	12.2	0.002	Reference	
	No	51	63.0	30	37.0		4.20	1.60–11.00
Dizziness	Yes	37	77.1	11	22.9	0.400	Reference	
	No	57	69.5	25	30.5		1.50	0.60–3.00
Gastric upset	Yes	23	76.7	7	23.3	0.600	Reference	
	No	71	71.0	29	29.0		1.30	0.50–3.50
Nasal burning	Yes	23	76.7	7	23.3	0.600	Reference	
	No	71	71.0	29	29.0		1.30	0.50–3.50
Shortness of breath	Yes	15	60.0	10	40.0	0.130	Reference	
	No	79	75.2	26	24.8		0.50	0.20–1.20
Cough	Yes	8	30.8	18	69.2	< 0.001	Reference	
	No	86	82.7	18	17.3		0.10	0.03–0.24
Chest pain or pressure	Yes	6	35.3	11	64.7	< 0.001	Reference	
	No	88	77.9	25	22.1		0.20	0.05–0.50
Pharyngitis	Yes	6	27.3	16	72.7	< 0.001	Reference	
	No	88	81.5	20	18.5		0.08	0.03–0.24
Diarrhoea	Yes	6	27.3	16	72.7	< 0.001	Reference	
	No	88	81.5	20	18.5		0.90	0.03–0.25
Chronic diseases	Yes	42	70.0	18	30.0	0.690	Reference	
	No	52	74.3	18	25.7		0.81	0.40–1.70

Discussion

Worldwide devastation was brought on by the COVID-19 epidemic. There has been mounting evidence that COVID-19 patients may experience olfactory impairment. Anosmia can appear on its own or in combination with other COVID-19 symptoms such as exhaustion, dry cough, nausea, and diarrhoea. A lot of research is currently being done on the pathogenic process of olfactory impairment and associated clinical features in COVID-19 patients.[8]

This study included 218 COVID-19 patients. The majority of patients were female and under 50 years of age. More than half of the patients had anosmia. The most common associated symptoms on presentation were fever, headache, fatigue, dizziness, and myalgia. These results are in line with the research conducted by Sudre et al., who discovered that although symptom associations varied amongst individuals, anosmia, fever, coughing, and shortness of breath were the most reliable indicators of COVID-19. Testing became a cornerstone of the pandemic diagnosis and treatment, which had caused serious problems globally because other symptoms, such GI disruption, exhaustion, nasal burning, etc., were either unreliable indicators or crucial in specific situations.[9] Similar findings were reported by Moein et al., who discovered that 59 out of 60 COVID-19 patients had some degree of olfactory dysfunction. Notably, this provided evidence that anosmia is common among COVID-19-positive individuals.[10] For 23 COVID-19 patients who were under home quarantine, Vaira et al. conducted a remote olfactory evaluation using patient-self-administered olfactory tests. The patient's self-administered anosmia data assisted in the early identification and isolation of COVID-19 patients during the study's use of this complaint.[11] In contrast, Mayo Clinic deployed artificial intelligence in 2020, together with the most advanced deep neural network technology, to recognise and evaluate the clinical characteristics of COVID-19 infection. Anosmia was one of the initial symptoms of the infection, and they discovered that its incidence was 28.6 times higher in COVID-19-positive patients than in COVID-19-negative individuals.[12]

The current study found that about half of the anosmic patients had complete anosmia, 26 had partial anosmia, and the majority were male. Anosmia was significantly associated with symptoms such as a runny nose, fever, fatigue, cough, and GI symptoms. This data were documented in a European multicenter study that included 417 individuals with confirmed infection. Out of the total number of patients, 79.6% experienced complete loss of smell (anosmia) and 20.4% had a partial loss of smell (hyposmia). Anosmia was strongly correlated with fever, although nasal obstruction or rhinorrhoea did not show a significant correlation with diminished smell.[13]

In this study, less than half of anosmic patients recovered olfactory sensation within 2 weeks, and one-third recovered within a month, while the remaining still experienced anosmia 1 month after the illness. Patients in this study who developed anosmia in the first two weeks of illness had a significant association with age below 50 years and rapid recovery. This is consistent with a retrospective study conducted by Klopfenstein et al., which found that anosmia was present in 47% of confirmed COVID-19 patients. The study also found that anosmia typically developed in patients 4.4 days after the onset of infection, with a duration

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of 8.96 days. A total of 98% of patients recovered within 28 days. Additionally, they found that dysgeusia is frequently encountered in COVID-19 patients, along with anosmia.[14]

It is important to note that when the COVID-19 pandemic first appeared in China, medical professionals were underprepared, focusing exclusively on the disease's major life-threatening symptoms while ignoring the olfactory presentation. Moreover, even patients were found to be frequently ignoring symptoms like anosmia. Later, other investigations shed light on this disease, elucidated its mechanism, and confirmed its connection to infection.

A significant difference was found in our study between the onset of anosmia after 2 weeks of illness and the time for recovery in less than three months, and between anosmic patients aged below 50 years and female patients. Numerous studies have confirmed this, and the majority of them have revealed that female COVID-19 patients are more likely than men to experience smell abnormalities. This finding is consistent with other research on anosmia brought on by upper respiratory infections, particularly in patients in their forties.[15]

Another significant association was found between time of recovery and anosmic patients with sneezing, headache, myalgia, fatigue, and absence of gastrointestinal symptoms. Gastrointestinal symptoms linked to olfactory abnormalities have unusually increased in some areas during the COVID-19 pandemic. The "anosmia" and constitutional symptoms, including headache, myalgia, and diarrhoea in the United Kingdom (UK), the United States (US), and Italy, had substantial oscillations during the pandemic, with the UK showing the greatest variations.[16] Another comparable study conducted by Walker et al. looked into the loss of smell in the US, UK, Iran, France, Germany, Italy, the Netherlands, and Spain through the internet and social media. The study found a significant relationship between the number of COVID-19 patients in these nations and the daily relative search volumes for anosmia and its accompanying symptoms, such as headache, fever, and tiredness.[17] However, more studies need to be done in the future to determine the precise causes of this variation.

This study reported some risk factors associated with the time of recovery, such as sneezing, headache, myalgia, and fatigue, while protective factors included cough, chest pain or pressure, pharyngitis, and diarrhoea. Mubaraki et al. conducted a study that found a substantial association between anosmia and neurological symptoms of COVID-19 patients. Patients presenting with multiple symptoms had a higher incidence of anosmia and/or hyposmia (62.5%) than those with only one symptom. Fatigue was the most prevalent complaint, followed by myalgia and headache. The occurrence of gastrointestinal discomfort and diarrhoea in COVID-19 patients was 14%. COVID-19 participants suffering from loss of smell had a significantly greater incidence of stomach discomfort and diarrhoea compared to those who did not. This finding demonstrates a statistically significant link between gastrointestinal symptoms and anosmia in COVID-19 patients.[18,19] These results demonstrate that over a wide variety of circumstances, relationships between COVID-19 symptoms and positive test scored equally. In many settings with limited testing or benchmarking capacity, anosmia, fever, and other respiratory symptoms consistently yielded the highest impact estimates and were the most relevant and significant empirical signals.[9] It is crucial to highlight that anosmia per se should only be used as a cue for testing and prompt isolation of suspected individuals and does not necessarily indicate a confirmed COVIDinfection.[20]

Conclusion

Anosmia, in conclusion, is among the most often reported symptoms in COVID-19 patients. This indicates the need for joint syndromic surveillance, which might improve real-time epidemiological investigations worldwide and public health outcomes.

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Authors' Contribution

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

The authors declare that no generative AI or AI-assisted technologies were used in the writing, editing, or preparation of this manuscript. The authors take full responsibility for the content of the manuscript.

Source of Funding: None.

Conflict of Interest: None.

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