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Investigating smell and taste disorders in COVID-19 patients referred to public hospitals in Arak, Iran in 2020

Investigación de los trastornos del olfato y el gusto en los pacientes de COVID-19 remitidos a los hospitales públicos de Arak (Irán) en 2020

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Abstract

Introduction: The 2019 Coronavirus (COVID-19) pandemic has caused widespread disasters around the world. There is growing evidence that suggests olfactory and taste disorder is observed in COVID-19 patients. Anosmia and taste disorders can occur alone or with other symptoms of COVID-19, such as a dry cough. However, the pathogenic mechanism of anosmia and its clinical features in patients with COVID-19 is still unclear.
Methods: This retrospective cross-sectional study was conducted in Arak, Markazi province, in public hospitals in 2020. A total of 54 patients referred to Arak public hospitals were included in the study after examining their inclusion and exclusion criteria and performing PCR tests. Patients were divided into symptomatic and asymptomatic groups. In the symptomatic group, based on the severity of the disease, patients were divided into three groups: 1- Moderate patients with high fever and moderate respiratory symptoms, 2- Severe patients with shortness of breath, 3- As bad as it can be patients with respiratory failure, septic shock or dysfunction in multiple organs. Demographic information, including age, gender, recent travel experience, symptoms (fever, myalgia, cough, shortness of breath, fatigue, sore throat, anosmia, diarrhea, etc.), past nasal and paranasal diseases, smoking history, and disease severity was obtained from the positive patient. The present study data were collected through three questionnaires on approximate time of onset, the interval of symptoms, associated clinical symptoms, and severity of changes.
Results: Out of 54 patients in the study, the frequency of anosmia in asymptomatic, moderate, severe, and as bad as it can be grouped was 11% (n=6), 9% (n=5), 20% (11), and 59% (n=32), respectively. The frequency of taste disorder in these groups was 28% (n=15), 17% (9), 17% (n=9) and 39% (n=21), respectively. Productive cough (93%), constipation (98%), and confusion (93%) were the most common symptoms observed in patients with smell and taste disorders. The Chi-Square Independence T test results and Fisher exact test showed that the clinical sign of anosmia was significantly related to taste disorder. The interval between different disease severity groups with anosmia and taste disorder did not show a significant difference.
Conclusion: In the present study, the severity of the disease was associated with the manifestations of anosmia and taste disorders, so that in severe cases, a higher percentage of patients with two disorders also showed other symptoms of the disease, especially cough, constipation, and confusion. Further clinical studies are needed to determine the exact correlation, pathogenesis, prognosis, and association between the severity of the disease and smell and taste disorders worldwide.

Keywords: COVID-19, clinical signs, epidemiology, smell disorder, taste disorder.

Resumen

Introducción: La pandemia de Coronavirus (COVID-19) de 2019 ha causado desastres generalizados en todo el mundo. Cada vez hay más pruebas que sugieren que se observan trastornos olfativos y gustativos en los pacientes con COVID-19. La anosmia y los trastornos del gusto pueden ocurrir solos o con otros síntomas de COVID-19, como la tos seca. Sin embargo, el mecanismo patogénico de la anosmia y sus características clínicas en los pacientes con COVID-19 aún no está claro.
Métodos: Este estudio transversal retrospectivo se realizó en Arak, provincia de Markazi, en hospitales públicos en 2020. Un total de 54 pacientes remitidos a los hospitales públicos de Arak fueron incluidos en el estudio tras examinar sus criterios de inclusión y exclusión y realizar pruebas de PCR. Los pacientes se dividieron en grupos sintomáticos y asintomáticos. En el grupo sintomático, en función de la gravedad de la enfermedad, los pacientes se dividieron en tres grupos: 1- Pacientes moderados con fiebre alta y síntomas respiratorios moderados, 2- Pacientes graves con dificultad respiratoria, 3- Pacientes graves con insuficiencia respiratoria, shock séptico o disfunción en múltiples órganos. Se obtuvo información demográfica, como la edad, el sexo, la experiencia de viaje reciente, los síntomas (fiebre, mialgia, tos, disnea, fatiga, dolor de garganta, anosmia, diarrea, etc.), las enfermedades nasales y paranasales anteriores, los antecedentes de tabaquismo y la gravedad de la enfermedad del paciente positivo. Los datos del presente estudio se recogieron mediante tres cuestionarios sobre el momento aproximado de inicio, el intervalo de los síntomas, los síntomas clínicos asociados y la gravedad de los cambios.
Resultados: De los 54 pacientes del estudio, la frecuencia de anosmia en los grupos asintomático, moderado, severo y tan malo como se puede agrupar fue del 11% (n=6), 9% (n=5), 20% (11) y 59% (n=32), respectivamente. La frecuencia del trastorno del gusto en estos grupos fue del 28% (n=15), 17% (9), 17% (n=9) y 39% (n=21), respectivamente. La tos productiva (93%), el estreñimiento (98%) y la confusión (93%) fueron los síntomas más comunes observados en los pacientes con trastornos del olfato y del gusto. Los resultados de la prueba T de independencia de Chi-cuadrado y la prueba exacta de Fisher mostraron que el signo clínico de la anosmia estaba significativamente relacionado con el trastorno del gusto. El intervalo entre los distintos grupos de gravedad de la enfermedad con anosmia y trastorno del gusto no mostró una diferencia significativa.
Conclusiones: En el presente estudio, la gravedad de la enfermedad se asoció con las manifestaciones de la anosmia y los trastornos del gusto, de modo que en los casos graves, un mayor porcentaje de pacientes con dos trastornos mostraba también otros síntomas de la enfermedad, especialmente tos, estreñimiento y confusión. Se necesitan más estudios clínicos para determinar la correlación exacta, la patogénesis, el pronóstico y la asociación entre la gravedad de la enfermedad y los trastornos del olfato y el gusto en todo el mundo..

Palabras clave: Coronavirus, conocimiento, práctica, profesionales dentales, control de la infección, creencias.

Introduction

In December 2019, a pneumonia-like viral disease first emerged in Wuhan, China. Then, it spread rapidly to more than 200 countries worldwide, resulting in more than 178 million confirmed cases and 3 million deaths worldwide, based on a report of the World Health Organization in June 2021[1]. The World Health Organization named this new virus severe acute respiratory syndrome coronavirus (SARS-CoV-2), and it named the disease caused by coronavirus disease COVID-19 in 2019. The COVID-19 pandemic is considered the most severe global health crisis since the outbreak of the flu in 1918[2]. On February 19, 2020, two patients were diagnosed with COVID-19 in Qom, Iran, and after a short time, the disease spread rapidly to neighboring provinces, such as Tehran, Markazi, Isfahan, and Khorasan Razavi, and later to 31 provinces of Iran[3]. People infected with SARS-CoV-2 have a wide range of clinical symptoms, from asymptomatic to severe disease. The disease's signs and symptoms include fever, cough, fatigue, sore throat, chest pain, shortness of breath, myalgia, headache, abdominal pain, and diarrhea. In more severe cases, the infection can cause pneumonia, acute respiratory syndrome, kidney failure, and even death[4]. One of the most important unknown characteristics of COVID-19 is the duration of clinical symptoms. In the early stages of the disease, experts believe that the recovery time in mild cases is 1-2 weeks, but in many patients, symptoms of 8 to 10 weeks or even more have been reported.

In some cases, early symptoms are replaced with long-term complications such as lung or heart damages[5]. Observational studies have reported that the elderly and people with underlying respiratory and cardiovascular diseases are at greater risk for the disease, and most patients with the disease have underlying diseases such as hypertension and cardiovascular disorders, diabetes, cancer, and chronic kidney disease and mortality rate in these people is higher than that of other patients. However, severe forms of the disease are observed in younger adults with no previous history of the disease[6]. One of the extrapulmonary symptoms of COVID-19 is smell disorder, including anosmia and hypoxemia, which is more common in adults with up to 40% infection with viruses infecting the upper respiratory tract.

Different possible hypotheses have been proposed to justify this clinical sign, including damage caused by SARS-CoV-2 to the surface of the olfactory neuroepithelium in the roof of the nasal cavity or the central olfactory pathways[7]. COVID-19 patients can develop sudden anosmia without any other symptoms or, more commonly, other mild symptoms before the onset of anosmia, such as a dry cough. In a retrospective study conducted by Klopenstein et al., 54 (47%) out of 114 COVID-19-approved patients showed anosmia. This study also revealed that patients generally develop anosmia 4.4 days after the onset of SARS-CoV-2 infection with a duration of 8.96 days, and 98% of patients can recover within 28 days[8]. Since smell affects the sense of taste, people with COVID-19 may also experience a loss of sense of taste[9]. Sudden, severe, and isolated loss of sense of smell or taste, in the absence of other inflammatory manifestations of the upper airways such as allergic rhinitis, chronic rhinosinusitis, nasal polyposis, inform physicians on the possibility of developing COVID-19. Evaluation of smell and taste disorders with analog visual scale or smell or taste test in hospital or telemedicine to prevent infection facilitates early diagnosis of infected patients and reduces SARS-CoV-2 transmission[10]. Thus, given the high prevalence and importance of this emerging disease that has become a global crisis and its unknown dimensions and effects on body organs and considering the importance of two clinical findings of taste and smell disorders, the present study was conducted to evaluate smell and taste disorders in COVID-19 patients referred to public hospitals in Arak in 2020 to better understand this disease and contribute to achieving diagnostic and therapeutic goals.

Materials and methods

Study design

This retrospective cross-sectional study was conducted in public hospitals in Arak, Markazi province, Iran, in 2020. Patients with COVID-19 infection approved by PCR (polymerase chain reaction) pharyngeal swabs were included in the study. PCR swabs were tested for coronavirus in the pathology laboratory of Arak. This study was a retrospective analysis of anosmia and taste disorder in COVID-19 patients. PCR of pharyngeal swabs for the diagnosis of COVID-19 is routinely performed at this center and worldwide, so no ethical consideration is made in this study.

Study group

Individuals with incomplete data, previous anosmia or taste disorder, psychological disorders, and inaccessible subjects were excluded. Patients were divided into symptomatic and asymptomatic groups, and patients in the symptomatic group were divided into three groups based on the severity of the disease: 1- Moderate patients complained of fever with high temperature and moderate respiratory symptoms. Pneumonia findings were observed in chest radiography. Two severe patients with shortness of breath, the respiration rate of 30 per minute, blood oxygen saturation of 93%, CT scan findings with at least 50% increase in penetration volume.

Three critical patients with respiratory failure, septic shock, or dysfunction in multiple organs. Demographic data, including age, gender, recent travel experience, symptoms (fever, myalgia, cough, shortness of breath, fatigue, sore throat, anosmia, diarrhea, etc.), past nasal

and paranasal diseases, smoking history, and disease severity was taken from a positive patient. The research data were obtained through three questionnaires on approximate time of onset and interval of symptoms, the associated clinical symptoms, and severity of changes.

Statistical analysis

The Shapiro-Wilk test was used to determine whether the data follow the normal distribution. Student-t and Mann-Whitney U tests were used for parametric and non-parametric data, respectively. For classification of variables, chi-square, Fisher exact test, and Fisher-Freeman Halton tests were used. Spearman test was used for correlation. IBM-SPSS version 22 statistical software was used for data analysis. If P-value is less than 0.05, a statistically significant difference was considered.

Results

Frequency of patients in different groups of disease severity

The results of the Chi-Square test (Goodness of fit test) show that for anosmia patients, the frequencies of patients in different groups of disease severity are significantly different (P-value 0.000 <0.05). However, for the taste change patients, this difference does not show a difference at the significance level of 0.05. In general, the results show that anosmia patients are more in the as bad as it can be severe group. **Table I** shows the frequency of anosmia and taste change in patients in different disease severity groups.

The severity of disease in patients with anosmia and taste disorders

The results of Chi-Square, Independence Test, and Fisher exact test show that anosmia disease has a significant relationship with taste change disease, so that Spearman correlation coefficient with a value of 0.451 indicates that as the severity of anosmia increases and goes toward as bad as it can be, the severity of taste change will also increase and will go towards as bad as it can be. As shown in the table, out of 32 anosmia patients with severity of as bad as possible, 20 patients had taste change with severity of as bad as it can be. **Table II** shows the frequency of taste change in patients in different disease severity groups based on the severity of anosmia disease groups.

The interval between different groups of disease severity

Table III shows the interval comparison results using the Kruskal-Wallis test for anosmia and taste change. The interval between different disease severity groups for anosmia and taste change did not show a significant difference.

Clinical symptoms in different groups of disease severity

Out of 37 patients with fever and anosmia, 24 were in the "as bad as it can be" group, and 11 were in the severe group. **Table IV** shows the frequency of symptoms in different groups of disease severity. Significant results of the Chi-Square Independence Test, Fisher exact test, have been presented. Significance at the level of 0.05 indicates the relationship between symptoms and different severities of the disease.

Discussion

Several infectious diseases have been treated the human health (10-15). SARS-COVID disease caused higher morbidity and mortality in the last century[16-19].

Smell and taste disorders are associated with a wide range of viral infections. These sensory disorders are a

Table I:

	Severity					
	None	Moderate	Severe	As bad as it can be	Total	P value
Anosmia; n (%)	6 (11%)	5 (9%)	11 (20%)	32 (59%)	54	0.000
Taste change; n (%)	15 (28%)	9 (17%)	9 (17%)	21 (39%)	54	0.067

Table I:

	Severity				
	None	Moderate	Severe	As bad as it can be	P value
Taste change; median interval (IQR)	-	7 (7-14)	17 (16-17)	17 (7-20)	0.211
Taste change; median interval (IQR)	-	14 (14-14)	17 (9-17)	15.5 (7-20.5)	0.725

IQR = interquartile range

Table I:

		Anosmia severity				Total	P value	Correlation (Spearman)
		None	Moderate	Severe	As bad as it can be			
Taste change severity; (within Anosmia severity, n (%)	None Moderate Severe As bad as it can be	4 (66.7%) 0 (0.0%) 2 (33.3%) 0 (0.0%)	0 (0.0%) 4 (80.0%) 0 (0.0%) 1 (20.0%)	3 (27.3%) 5 (45.5%) 3 (27.3%) 0 (0.0%)	8 (25.0%) 0 (0.0%) 4 (12.5%) 20 (62.5%)	15 (27.8%) 9 (16.7%) 9 (16.7%) 21 (38.9%)	0.000	.451**
Total		6 (100.0%)	5 (100.0%)	11 (100.0%)	32 (100.0%)	54 (100.0%)		

**. Correlation is significant at the 0.01 level (2-tailed).

Table I:

		Anosmia severity					
		None, (n= 6; 11%)	Moderate, (n= 5; 9%)	Severe, (n=11; 20%)	As bad as it can be, (n= 32; 59%)	Total	P value
Nasal_congestion	No	6 (100%)	5 (100%)	5 (45%)	26 (81%)	42 (78%)	0.027
	Yes			6 (55%)	6 (19%)	12 (22%)	
Fatigue	No	4 (67%)			13 (41%)	17 (31%)	0.004
	Yes	2 (33%)	5 (100%)	11 (100%)	19 (59%)	37 (69%)	
Dry_caugh	No		5 (100%)	3 (27%)	19 (59%)	27 (50%)	0.001
	Yes	6 (100%)		8 (73%)	13 (41%)	27 (50%)	
Productive_caugh	No	6 (100%)	5 (100%)	8 (73%)	31 (97%)	50 (93%)	0.100
	Yes			3 (27%)	1 (3%)	4 (7%)	
Fever	No	4 (67%)	5 (100%)		8 (25%)	17 (31%)	0.000
	Yes	2 (33%)		11 (100%)	24 (75%)	37 (65%)	
Dyspnea	No	2 (33%)	4 (80%)	8 (73%)	11 (34%)	25 (46%)	0.062
	Yes	4 (67%)	1 (20%)	3 (27%)	21 (66%)	29 (54%)	
Headeche	No	4 (67%)	1 (20%)	5 (45%)	12 (38%)	22 (41%)	0.447
	Yes	2 (33%)	4 (80%)	6 (55%)	20 (63%)	32 (59%)	
Chest_pain	No	6 (100%)		11 (100%)	23 (72%)	40 (74%)	0.000
	Yes		5 (100%)		9 (28%)	14 (26%)	
Sore_throat	No	6 (100%)	5 (100%)	6 (55%)	20 (63%)	37 (69%)	0.086
	Yes			5 (45%)	12 (38%)	17 (31%)	
Body_pain	No	6 (100%)	5 (100%)		15 (47%)	26 (48%)	0.000
	Yes			11 (100%)	17 (53%)	28 (52%)	
Low_appetite	No	6 (100%)	5 (100%)	8 (73%)	7 (22%)	26 (48%)	0.000
	Yes			3 (27%)	25 (78%)	28 (52%)	
NandV	No	6 (100%)	5 (100%)	8 (73%)	24 (75%)	43 (80%)	0.429
	Yes			3 (27%)	8 (25%)	11 (20%)	
Diarrhea	No	6 (100%)	5 (100%)	11 (100%)	13 (41%)	35 (65%)	0.000
	Yes				19 (59%)	19 (35%)	
Constipation	No	6 (100%)	5 (100%)	11 (100%)	31 (97%)	53 (98%)	1.000
	Yes				1 (3%)	1 (2%)	
Confusion	No	6 (100%)	5 (100%)	8 (73%)	31 (97%)	50 (93%)	0.100
	Yes			3 (27%)	1 (3%)	4 (7%)	

Table I:

		Taste change severity					
		None, (n= 15; 28%)	Moderate, (n= 9; 17%)	Severe, (n=9; 17%)	As bad as it can be, (n= 21; 39%)	Total	P value
Nasal_congestion	No	8 (53%)	9 (100%)	4 (44%)	21 (100%)	42 (78%)	0.000
	Yes	7 (47%)		5 (56%)		12 (22%)	
Fatigue	No	8 (53%)		4 (44%)	5 (24%)	17 (31%)	0.025
	Yes	7 (47%)	9 (100%)	5 (56%)	16 (76%)	37 (69%)	
Dry_caugh	No	6 (40%)	4 (44%)		17 (81%)	27 (50%)	0.000
	Yes	9 (60%)	5 (56%)	9 (100%)	4 (19%)	27 (50%)	
Productive_caugh	No	15 (100%)	9 (100%)	6 (67%)	20 (95%)	50 (93%)	0.033
	Yes			3 (33%)	1 (5%)	4 (7%)	
Fever	No	7 (47%)	4 (44%)	2 (22%)	4 (19%)	17 (31%)	0.246
	Yes	8 (53%)	5 (56%)	7 (78%)	17 (81%)	37 (69%)	
Dyspnea	No	3 (20%)	9 (100%)	4 (44%)	9 (43%)	25 (46%)	0.001
	Yes	12 (80%)		5 (56%)	12 (57%)	29 (54%)	
Headeche	No	4 (27%)	5 (56%)	2 (22%)	11 (52%)	22 (41%)	0.235
	Yes	11 (73%)	4 (44%)	7 (78%)	10 (48%)	32 (59%)	
Chest_pain	No	15 (100%)	5 (56%)	7 (78%)	13 (62%)	40 (74%)	0.016
	Yes		4 (44%)	2 (22%)	8 (38%)	14 (26%)	
Sore_throat	No	11 (73%)	4 (44%)	7 (78%)	15 (71%)	37 (69%)	0.464
	Yes	4 (27%)	5 (56%)	2 (22%)	6 (29%)	17 (31%)	
Body_pain	No	8 (53%)	4 (44%)	4 (44%)	10 (48%)	26 (48%)	1.000
	Yes	7 (47%)	5 (56%)	5 (56%)	11 (52%)	28 (52%)	
Low_appetite	No	7 (47%)	9 (100%)	6 (67%)	4 (19%)	26 (48%)	0.000
	Yes	8 (53%)		3 (33%)	17 (81%)	28 (52%)	
NandV	No	11 (73%)	9 (100%)	6 (67%)	17 (81%)	43 (80%)	0.335
	Yes	4 (27%)		3 (33%)	4 (19%)	11 (20%)	
Diarrhea	No	7 (47%)	9 (100%)	9 (100%)	10 (48%)	35 (65%)	0.001
	Yes	8 (53%)			11 (52%)	19 (35%)	
Constipation	No	15 (100%)	9 (100%)	9 (100%)	20 (95%)	53 (98%)	1.000
	Yes				1 (5%)	1 (2%)	
Confusion	No	15 (100%)	9 (100%)	6 (67%)	20 (95%)	50 (93%)	0.033
	Yes			3 (33%)	1 (5%)	4 (7%)	

common problem during the COVID-19 epidemic crisis. SARS-CoV in a mouse model showed external infiltration through the olfactory bulb. In addition, the angiotensin-converting enzyme receptor 2, used by SARS-CoV-2 to bind to and penetrate cells, is widely expressed in oral mucosal epithelial cells[20]. These findings can explain the underlying pathogenetic mechanism of taste and smell disorders in SARS-CoV-2 infection. Smell and taste disorders are the first and only complaint in 10% of people, and 19% experience it before other classic symptoms such as fever and cough. Also, 25% of children have only smell and taste disorders at admission[21]. Therefore, these disorders are early signs of COVID-19 disease and are essential for screening and controlling the infection. The present study used a questionnaire for diagnosing patients with anosmia, taste disorder, or both. The results of this study showed that the frequency of anosmia in asymptomatic, moderate, severe, and as bad as it can be grouped were 11%, 9%, 20%, and 59%, respectively, and taste disorder in these groups were 28% and 17%, 17%, and 39%, respectively.

It has previously been reported that COVID-19-induced anosmia is associated with a mild course of the disease. One study showed that the percentage of anosmia in hospitalized patients (26.9%) was lower than in non-hospitalized patients (66.7%). In a study on 3191 patients with mild COVID-19, 15.3% had anosmia or taste disorders[22]. Leichen et al. conducted a study on 417 cases with mild to moderate disease and showed that smell disorder was present in 88% of cases and anemia was the primary symptom in 11.8% of cases[23]. A similar study conducted by Kaye et al. on 237 cases showed that anosmia was present in 73% of cases during the disease, while 26.6% of cases were initially associated with anosmia[24]. As a result, the results of this study are somewhat inconsistent with previous results. The most common symptoms of COVID-19, including fever, cough, and headache, can be observed in other non-specific viral upper respiratory tract infections. In the present study, productive cough (93%), constipation (98%), and confusion (93%) were the most common symptoms observed in patients with smell and taste disorders. Dysfunction of these two functions may begin before, after, or at the same time as these clinical signs, or it may be the only symptom. There was a significant relationship between the symptoms of the disease and different severities of the disease in patients with anosmia and taste disorders. For example, out of 37 patients with fever and anosmia, 24 were in the "as bad as it can be" group, and 11 were in the severe group. In the study conducted by Klein et al., headache, fever, dry cough, and muscle pain accounted for 38% to 43% of cases associated with taste and smell disorders.

Moreover, fatigue was the second common symptom observed in these patients. In the results of a study conducted by Klein, it manifested as a primary symptom in 80% of patients who experienced it (14% of all patients), while in previous studies, fatigue was observed at higher rates (36%-46% of patients)[25].

Conclusion

Based on the present study results, the association of headache, fever, dry cough, muscle pain, and fatigue with smell and taste disorders was 59%, 65%, 50%, 52%, 69%, respectively, which has a high percentage compared to previous studies. Anosmia or taste disorder in a patient with COVID-19 is uncomplicated in the early days, but it requires a comprehensive evaluation of central nervous system involvement. Since smell disorder may affect patients' quality of life, further clinical studies are needed to determine the exact correlation, pathogenesis, prognosis, and any association between disease severity and smell disorder worldwide. In the absence of other respiratory disorders, such as allergic rhinitis and acute rhinosinusitis or chronic rhinosinusitis, anosmia, hypoxemia, and taste disorders, physicians should be informed on the possibility of COVID-19 infection, and serious attention should be paid to isolation and testing these individuals.

Conflict of interests

The authors have no conflict of interest.

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