Cacosmia and Cacogeusia in Patients with Persistent Anosmia and Ageusia due to COVID-19

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Abstract

Objective: The most frequent symptoms in COVID-19 infection are fever, cough, and fatigue. Also, olfactory and gustatory disorders can be seen with the infection. Despite an abundance of studies reporting anosmia and ageusia, there are limited studies on the development of cacosmia and cacogeusia. This study aimed to contribute to the literature on this novel disease by reporting and evaluating cacosmia and cacogeusia patients.

Methods: One hundred and twenty patients presenting to our clinic with loss of taste and smell after COVID-19 infection without subsequent improvement were examined in this study. Cacosmia and cacogeusia subsequently developed in 17 of these patients. Patients' demographic characteristics such as age and gender, history of chronic disease, and smoking status were investigated. Laboratory tests and magnetic resonance imaging of the brain were performed.

Results: Cacosmia and cacogeusia developed in 17 (14.1%) patients out of 120 patients who had persistent anosmia and ageusia after COVID-19. No significant difference was observed in terms of gender, but mean age was statistically significantly lower in the group developing cacosmia. Decreased olfactory bulb volume was observed in two patients, interpreted as secondary to the infection.

Conclusion: Cacosmia and cacogeusia can develop in late COVID-19 and can significantly impair the quality of life of patients. There is no correlation between the severity of the disease and the rate of these symptoms. Currently, there is no efficient treatment for these patients. Further studies are required to reveal the underlying sensorineural pathology for the development of cacosmia and cacogeusia and treatment of these symptoms.

Keywords: Ageusia, anosmia, cacogeusia, cacosmia, COVID-19

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INTRODUCTION

COVID-19 is a severe, highly infectious, acute respiratory disease caused by the novel coronavirus (SARS-CoV-2). It began in the Chinese city of Wuhan in December 2019 and rapidly spread across the world, being declared as a pandemic in March 2020.[1]

Coronaviruses are enveloped, single-stranded large RNA viruses capable of infecting both humans and animals. The virus is transmitted through direct contact with respiratory droplets from the an infected individual or by contact with surfaces contaminated by the virus. The mean incubation period is 14 days, although a clinical COVID-19 manifestation develops within 4-5 days in most patients.[2]

Seven types of coronavirus causing disease in humans have been described. SARS-CoV-2 (a new type of coronavirus) causes COVID-19 infection. The S1 domain of SARS-CoV-2 spike protein binds to the angiotensin converting enzyme 2 receptors of the host cell. The nasal cavity is a vital region susceptible to the SARS-CoV-2 virus and is one of the sites through which the virus enters the body.[3] SARS-CoV-2 may bind to Goblet and ciliated cells in the nasal mucosa. The viral load in the nasal cavity is high at the beginning of the infection.[4]

The most frequently seen symptoms in COVID-19 are fever, cough, diffuse muscle pain, and fatigue. Lymphocytopenia and a ground-glass appearance associated with pulmonary involvement at computed tomography are frequently encountered in COVID-19 pneumonia.[5] Neurological and cardiovascular diseases and acute cerebrovascular events

Table 1. Patients' Gender Distributions

		Gender		
		Female	Male	Total
Anosmia	Ageusia count	59	44	103
	%within group	57.28	42.72	100.0
Cacosmia	Cacogeusia count	10	7	17
	%within group	58.82	41.18	100.0
Total	Count	69	51	120
	%within group	57.5	42.5	100.0

Table 2. Patients' Age Distributions

Group	N	Mean	Std. Deviation	Median	Minimum	Maximum
Anosmia-Ageusia	103	37.83	10.856	37.00	15	66
Cacosmia-Cacogeusia	17	28.35	10.446	25.00	15	44
Total	120	36.45	11.264	36.00	15	66

can also accompany the severe COVID-19.[6] Upper respiratory tract disease symptoms such as odynophagia, sore throat, nasal discharge, and nasal congestion can be seen.[7] The incidence of gustatory and olfactory disorders such as anosmia, hyposmia, and ageusia is also high in COVID-19 disease. Loss of taste and smell may be seen during days 2-14 of COVID-19 infection and may appear as the first disease symptoms.[8]

Anosmia is defined as olfactory dysfunction and may frequently be seen following upper respiratory tract infections such as COVID-19. Nasal cavity infection may derive from damage associated with obstruction of the nasal passage or viral involvement of the olfactory epithelium or olfactory nerve.[9]

Olfactory disorders can be divided into three groups. Hyposmia and anosmia are defined as a decreased and absent sense of smell, troposmia as distorted perception of an existing smell, and phantosmia as the perception of a nonexistent smell. Cacosmia is defined as the perception of an unpleasant odor that does not actually exist. Smell disorders have an adverse effect on an individual's quality of life. The underlying cause behind these disorders is unclear, although it may be central and peripheral in origin.[10]

Cacogeusia is defined as an illusion or sensation of unpleasant taste not related to the ingestion of specific substances.[11] Despite an abundance of studies reporting anosmia and ageusia, there are limited studies on the development of cacosmia and cacogeusia.[12] This study aimed to contribute to the literature on this novel disease by reporting and evaluating cacosmia and cacogeusia patients.

METHODS

Approval for this retrospective study was granted by the Kastamonu University Clinical Research Ethical Committee (no: 2020-KAEK-143-66, date: March 11, 2021). Patients presenting to our otolaryngology clinic with anosmia and ageusia developing following COVID-19 infection between April 2020 and February 2021 were examined. One hundred and twenty patients with no improvement at follow-up were investigated retrospectively.

Patients were started on intranasal steroid therapy (twice a day) at initial presentation, and smell training was also recommended. Patients were asked to place coarse coffee, thyme oil, lavender oil, and cloves into four different containers and to smell each one for 2 minutes, first with short breaths and later inhaling deeply, and to do this morning and evening for 3 months. Patients were invited to attend monthly follow-ups.

One hundred and twenty patients whose anosmia and ageusia complaints persisted were reevaluated. Sixty-nine were female, and 51 were male, ranging in age between 15 and 66. Demographic characteristics such as age and gender, chronic diseases, drug use, allergy history, and smoking status were recorded.

Seventeen of the 120 patients who were followed-up due to persistent anosmia and ageusia have developed cacosmia and cacogeusia. The 120 patients' complete blood count values, liver function tests, kidney function tests, vitamin B12 levels, and magnetic resonance imaging (MRI) of the brain results were investigated.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS, Version 15.0, Chicago IL). Numeric variables were expressed as mean±standard deviation (SD) and median (minimum-maximum) values. Categorical variables were expressed as count and percentage values.

RESULTS

One hundred and twenty patients with anosmia and ageusia developing after COVID-19 infection and with no improvement despite treatment were examined. Sixty-nine patients (57.5%) were female, and 51 (42.5%) were male, ranging in age between 15 and 66 (Table 1). Ten patients were aged under 20, 28 were aged 20-30, 46 were aged 30-40, 24 were aged 40-50, and 12 were 50 or older. The mean age of the patients was

37.83 years (Table 2). Cacosmia and cacogeusia developed in 17 (14.1%) patients out of 120 patients who had persistent anosmia and ageusia after COVID-19 during the six months follow-up. No improvement in symptoms occurred despite medical treatment and olfactory training.

Diabetes was present in eight of the 103 patients, hypertension in 12, and allergic complaints in 18. Six of the patients with diabetes mellitus were using oral antidiabetics, and four were using insulin. Irregular antihistaminic use was present in the 18 patients with allergic complaints. Eighteen patients were smokers.

Seventeen patients had a loss of smell and taste at the initial presentation. These symptoms were subsequently replaced by perceptions of unpleasant tastes and odors within a mean of three months. Ten of these 17 patients were female, and seven were male, four being aged under 20, five aged 20-30, five aged 30-40, and three aged 40-50. The mean age of these patients was 28.35. No patients aged over 45 described unpleasant smell and taste perception. None of the patients developing cacosmia and cacogeusia required hospitalization while undergoing COVID-19 infection.

Allergic asthma was present in one of the 17 patients, hypertension in one, and arrhythmia in one. The patient with asthma was using a montelukast sodium and salbutamol. One patient was using amlodipine, another metoprolol, and one patient who had undergone thyroidectomy was using levothyroxine sodium. Iron deficiency anemia was detected in one patient at laboratory tests, and vitamin B12 in deficiency in another patient. These patients were referred to the internal diseases clinic, where treatment was initiated.

The cerebral volumetric evaluation was performed employing volumetric cerebral MRI. An olfactory bulb volume less than 40 mm^3 with increased olfactory bulb depth was reported in one patient. It was reported that this might have been secondary to viral infection. An olfactory bulb volume of 50 mm^3 was measured in another patient, and this was also suspected to have been secondary to viral infection. No neurological pathology capable of causing smell and taste disorder was detected at cerebral MRI in the other 15 patients.

No statistically significant gender difference was determined between the 17 patients developing cacosmia and cacogeusia and the 103 patients who had persistent anosmia and ageusia. The median age of the 103 patients presenting to the clinic describing anosmia and ageusia was 37 (15-66), but was significantly lower at 25 (15-44) in the 17 patients describing cacosmia and cacogeusia ($P < .004$).

DISCUSSION

The most frequent symptoms in COVID-19 infection are fever, fatigue, body pain, and cough. Gastrointestinal symptoms, neurological complications, and neuropsychiatric symptoms may be seen during the course of the disease. Olfactory and gustatory dysfunction is also frequently seen in COVID-19 infection. The sense of smell is more affected than that of taste. A meta-analysis from 2020 reported a prevalence of olfactory dysfunction symptoms such as dysosmia, anosmia, and in COVID-19 infection of 52.7%, and a prevalence of gustatory dysfunction symptoms such as dysgeusia, hypogeusia, and ageusia of 43.9%. Olfactory dysfunction can develop in association with peripheral causes (such as nasal congestion and rhinitis) secondary to viral infection. It may also derive from central causes associated with viral involvement of olfactory neurons.[12]

Rates of anosmia development with COVID-19 infection in cross-sectional studies from Italy, Spain, the United Kingdom, France, Belgium, and the United States range between 33.9% and 68%. The majority of patients with the olfactory disorder also describe the gustatory disorder. These two symptoms are very likely interrelated.[13,14]

A study from Europe reported widespread olfactory and gustatory dysfunction (loss of taste) in COVID-19 infection, at 85–88%.[15] Another study determined olfactory dysfunction (loss of smell) and viral upper respiratory tract infection at a rate of 39%. Various factors, such as age and gender, are thought to affect improvement.[16]

In a study from France, Klopfenstein et al.[17] reported that anosmia developed in 47% of 114 patients undergoing COVID-19 infection, and that dysgeusia accompanied anosmia at a rate of 85%. Anosmia emerged in a mean 4.4 days after infection. In another study of 202 COVID-19 patents from Italy, the prevalence of anosmia was 64%.[18] Gane et al.[19] detected COVID-19 positivity in a patient developing sudden onset anosmia with no additional symptoms in their case report. Similarly, Eliezer et al.[20] determined COVID-19 positivity in a patient developing complete anosmia and ageusia with no other symptoms (such as fever, cough, or gastrointestinal complaints). They recommended that patients with smell and taste disorder alone should be evaluated in terms of COVID-19 infection.

Olfactory perception is a complex process involving various parts of the brain. While no abnormal findings are detected at cerebral MRI in the majority of cases of loss of smell, blockage of olfactory activation in the brain can be seen at evaluation with functional MRI of the brain when a pleasant scent is emitted.[20] Aziz et al.[21] reported a milder course of disease in patients with olfactory dysfunction due to COVID-19.

Anosmia, hyposmia, and ageusia frequently appear in COVID-19 patients, but few studies have investigated the emergence of cacosmia following COVID-19 infection.[22] Anosmia and ageusia were seen at the beginning of infection in our 120 patients.

Ten of these 17 patients were female, and seven were male, four being aged under 20, five aged 20-30, five aged 30-40, and three aged 40-50. The mean age of these patients was 28.35. Cacosmia and cacogeusia generally developed in young adults with COVID-19, and there was no significant gender difference.

The most important limitation of this study is the retrospective design and the relatively short period of follow-ups.

CONCLUSION

Cacosmia and cacogeusia can develop in late COVID-19 and can significantly impair the quality of life of patients. There is no correlation between the severity of the disease and rate of this symptoms. Currently, there is no efficient treatment for these patients. Further studies are required to reveal the underlying sensorineural pathology for the development of cacosmia and cacogeusia and treatment of these symptoms.

Ethics Committee Approval: Ethical committee approval was received from the Kastamonu University Clinical Research (no: 2020-KAEK-143-66, date: March 11, 2021).

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