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PRELIMINARY COMMUNICATION / ПРЕТХОДНО САОПШТЕЊЕ

# Otorhinolaryngological symptoms in hospitalized patients with COVID-19 – single-medical-center study in Serbia

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**SUMMARY**

**Introduction/Objective** The infectious condition named coronavirus disease 2019 (COVID-19) was caused by coronavirus2 (SARS-Cov-2). Patients with COVID-19 disease may have symptoms which can range from mild to severe clinical condition.

The aim of this study was to observe and analyze the presence of otorhinolaryngology symptoms in hospitalized patients with moderate to severe COVID-19 disease.

**Methods** The descriptive clinical study analyzed data from medical records in 230 hospitalized patients with moderate to severe COVID-19 pneumonia at Zvezdara Clinical Hospital Center, Belgrade, Serbia. Otorhinolaryngology symptoms as well as generalized COVID-19 related symptoms were analyzed from medical records during the year 2021. SARS-CoV-2 virus infection was previously confirmed in all patients with positive polymerase chain reaction test and/or rapid antigen test.

**Results** The mean age of 230 patients included in this study was 64 years. The most common general symptoms were cough 72%, fever 52%, dyspnea 46%, malaise 46% while to a lesser extent were observed myalgia 19%, vomitus 3%, and diarrhea 3%. The distribution of otorhinolaryngological symptoms showed that the most frequent symptom was anosmia 22%, while the throat pain was present in 20% and ageusia in 19% of patients. The otorhinolaryngological symptoms which were present in lower frequencies were headache in 16% of patients, tinnitus in 6%, vertigo in 5%, and hearing loss in 3% of patients. Comorbidities were observed more often in patients older than 50 years. Hypertension was the most common chronic disease in 60%, followed by diabetes in 23%, chronic obstructive pulmonary disease in 7%, malignancy in 7%, hypothyroidism in 6%, and renal disease in 4% of patients.

**Conclusion** Otorhinolaryngological conditions that should be the subject of further post COVID survey are prolonged anosmia, ageusia or hypogeusia, auditory dysfunction and vertiginous complaints.

**Keywords:** COVID-19; otorhinolaryngology symptoms; SARS-CoV-2 virus

## INTRODUCTION

Coronaviruses can cause respiratory and gastrointestinal mucosa dysfunction as well as neurological and hepatic dysfunction in animals and humans [1, 2]. Viral invasion of the respiratory mucosa can cause symptoms of the upper respiratory airways. Recent studies showed that SARS-CoV-2 virus infection named as COVID-19 disease could cause fever, cough, dyspnea, and fatigue but as well otorhinolaryngological symptoms as pharyngodynia, nasal congestion, rhinorrhea and headache [3, 4]. The loss of smell (anosmia) and altered function of taste (dysgeusia) or loss of taste (ageusia) were the most prominent otorhinolaryngological symptoms frequently reported with heterogenous frequencies. In mild to moderate COVID-19 infection patients reported olfactory dysfunction in more than 85% while gustatory dysfunction was reported in more than 88% of patients [4]. In recent meta-analysis the rate of gustatory dysfunctions ranged from 5.6% to 62.7% while for olfactory disfunction varied from3.2% to 98.3% [5]. American Academy of Otolaryngology-Head and Neck Surgery proposed symptoms as anosmia and dysgeusia as symptoms for screening procedure for possible COVID-19 disease [5]. Anosmia can occur as an early symptom before other COVID-19 symptoms [6]. Besides this most frequent otorhinolaryngology disorders, less frequently were reported tinnitus, vertigo, as well as hearing loss [7]. The entry mechanism of SARS-CoV-2 virus was described as binding of the viral S protein to the angiotensin-converting enzyme 2 (ACE2) receptor. Spike proteins on the surface of SARS-CoV-2 virus binds to ACE2 receptors on the surface of the target cell. The entry of the virus in the host cell is enabled by serine protease type II (TMPRSS2) which binds and cleaves the ACE2 receptors which are highly expressed in the nasal and bronchial mucosa. Recent studies suggested that olfactory dysfunction as a consequence of SARS-CoV-2 virus infection was caused by non-neuronal cell-specific mechanism operating within the olfactory epithelium [8, 9].

Considering the route of SARS-CoV-2 virus transmission, otorhinolaryngology examination was not a part of clinical routine for hospitalized patients, first of all because of the high

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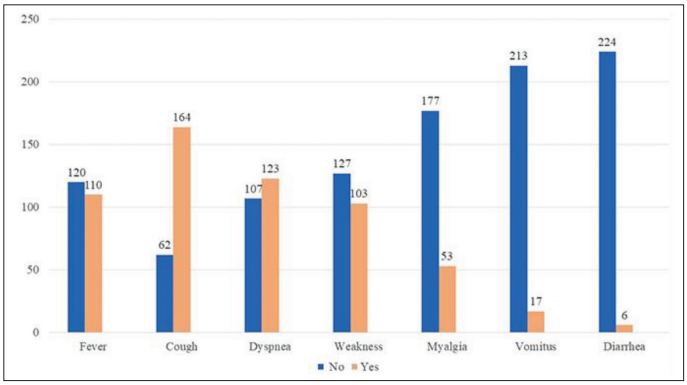


**Figure 1.** Distribution of the general symptoms in COVID-19 hospitalized patients

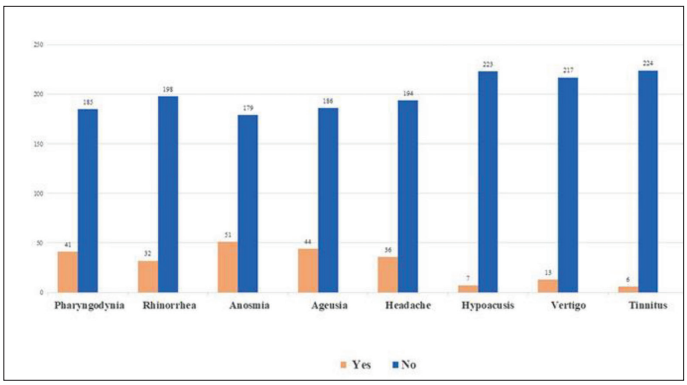


**Figure 2.** Distribution of otorhinolaryngology symptoms in hospitalized COVID-19 patients

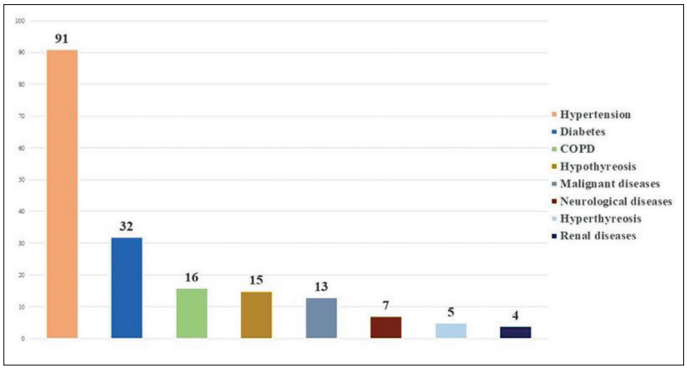


**Figure 3.** Comorbid diseases present in hospitalized patients with COVID-19 pneumonia

risk for transmission of the infection to health-care providers. Obtaining otorhinolaryngology symptoms data in hospitalized patients with COVID-19 disease can be useful for follow up of the patients with otorhinolaryngology dysfunction during the post-COVID period.

The aim of this descriptive clinical study was to analyse the occurrence of otorhinolaryngology symptoms in hospitalized patients with moderate to severe COVID-19 disease. The patients were hospitalized at Zvezdara Clinical Hospital Center, Belgrade, Serbia.

## METHODS

This clinical observational study analyzed medical data in 230 hospitalized patients with previously confirmed SARS-CoV-2 virus infection. This study was approved by institutional ethics committee (6206/1/2022). The demographic data (sex, age), as well as the frequency of general and otorhinolaryngological symptoms were analyzed. Patients were hospitalized at Zvezdara Clinical Hospital Center, Belgrade, Serbia during the year 2021. All of them had positive polymerase chain reaction test and/or rapid antigen test for COVID-19 and had moderate to severe pneumonia which was diagnosed according to the COVID-19 clinical protocol [10]. Otorhinolaryngology symptoms as well as generalized COVID-19 related symptoms were analyzed from medical records.

Descriptive statistics were calculated for demographic characteristics and other followed parameters and presented as frequencies and percentages. Statistical analysis was performed using the IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

The analyzed medical data of 230 hospitalized patients showed that 102 (44%) were males and 128 (56%) females. The mean age of the patients was 64 years.

The most common general symptoms were cough (72%), fever (52%), dyspnea (46%), and malaise (46%). Myalgia (19%), vomitus (3%), and diarrhea (3%) were observed to a lesser extent (Figure 1).

The distribution of the otorhinolaryngology symptoms showed that throat pain or pharyngodynia was present in 20% of patients, anosmia in 22%, ageusia in 19 %, headache in 16%, tinnitus in 6%, vertigo in 5%, and hearing loss in 3% of patients (Figure 2). All patients with hearing loss had hypertension, two of them had diabetes and hypertension and all patients with hearing loss had more than a three-fold increase in the value of C-reactive protein and ferritin. The similar results of biochemical analyses were present in patients with anosmia, ageusia, and vertigo.

Comorbidities were present frequently in patients older than 50 years. The hypertension was leading chronic disease in 60%. In 23% of patients with diabetes, hypertension was present at the same time. In 7% of patients was reported chronic obstructive pulmonary disease, and asthma. Hypothyroidism was present in 6%, malignant disease in 7%, and renal disease in 4% of hospitalized patients (Figure 3).

## DISSCUSION

Pharyngodynia, rhinorrhea, dysfunctions of smell and taste can be the symptoms of COVID-19 in the patients with moderate to severe acute respiratory inflammation. In this study percent of anosmia and ageusia was present in 22% and 19% of patients. Özçelik Korkmaz et al. [7] reported higher incidence of otorhinolaryngological symptoms in hospitalized patients than our study: the rate of taste dysfunction was 41.3%, smell dysfunction was

37.9%, and the rate of sore throat was 32.7%, for tinnitus 11.2%, hearing loss 5.2%, and vertigo 6.1%. Johnson et al. [11] recently published results of one of the largest single institution study conducted in Mayo Clinic. The authors reported that rate of subjective altered smell and taste in 2250 COVID-19 patients was 29.6%. The rates of most common otorhinolaryngological symptoms were reported in other study as 34.5%, for taste loss, 31.8% for smell loss and sore throat as 26% [12]. Results of a meta-analysis on otorhinolaryngological symptoms pointed out that the prevalence of olfactory dysfunction in COVID-19 patients was 52.73% after having analyzed ten studies [13]. Nine studies were analyzed for gustatory dysfunction demonstrating prevalence of 43.93%. Less frequent were rates for dizziness 2.2% and hearing loss 0.9% [13]. In this study hearing loss was present in 3% of patients. The patients pointed out that they had normal hearing function before they were infected with SARS-CoV-2 virus. Objective measurements of hearing function were not performed in this study. All patients with hearing loss had hypertension, two of them had diabetes and hypertension. KIlic et al. [14] reported that sudden hearing loss could be the only sign of a COVID-19 infection in patients with no other symptoms of disease. Recently published results of meta-analysis on hearing loss, tinnitus and vertigo in patients with COVID-19 showed that hearing loss rate was 3.1% in four analyzed studies, while in analysis of six studies on tinnitus the occurrence rate was 4.5% and analysis of nine papers on vertigo demonstrates the rate was 12.2% [15]. In this study tinnitus was present in 6%of patients and vertigo in 5%. The main remarks of the authors of meta-analytical studies were the weakness of study data collection like self-reports and medical records without the objective evaluation and control groups. According to that opinion the results of our study can be observed as results of descriptive clinical study without objective measurements for otorhinolaryngological symptoms. Milisavljevic et al. [16] published one of the latest objective study on sudden hearing loss in COVID-19 disease. The results of that study showed the rate of 40.5% for sensorineural type of hearing loss. It was confirmed by audiological assessment in 74 patients with moderate form of COVID-19 disease. All patients were treated in tertiary hospital center [16].

It is not yet clarified weather SARS-CoV-2 virus affect peripheral neural structures and central nervous system by neural invasion or predominantly by affection of neural glial cells or neurotropism. One of proposed explanations for neural dysfunction was autoimmune neuronal damage, but this subject need further experimental investigation [17]. The genetic polymorphisms in ACE2 and TMPRSS2 could be the explanation for different values in prevalence of chemosensory defects. These variations in the binding affinity between the virus and the ACE2 receptor could cause oscillation in intensity and duration of anosmia, hyposmia, ageusia, hypogeusia or vertigo and hearing disorders [9, 18]. As observed by recent studies the rate of chemosensory dysfunction were significantly higher in Western countries than in countries in East Asia. Genetic polymorphism of ACE2, as well as mutation and variation of viral spike protein could be the cause of increased chemosensory disfunction rate [9, 18]. From otorhinolaryngology point of view, long duration of chemosensory dysfunction as well as hearing loss and vertigo are important for post-COVID follow-up of patients [18]. The dysfunction of the smell and taste resolve within weeks while in some patients last as persistent deficits. The therapies for COVID-19 associated olfactory loss are currently an object of intensive investigation [19]. Clinical protocols for accurate diagnosis and treatment of post COVID otorhinolaryngological conditions will be very important for otorhinolaryngological practice. Recent studies described that quality of life was significantly decreased in patients who suffered from post COVID-19 consequences [20].

Patients with prolonged anosmia and ageusia reported depressive behavior and deterioration in life quality. Clinical studies on life quality in post COVID hearing and balance disorders will be equally important for better analysis of otorhinolaryngological conditions in COVID-19.

## CONCLUSION

Otorhinolaryngology conditions that should be the subject of further survey in patients who were treated for COVID-19 infection are prolonged anosmia, ageusia or hypogeusia, auditory dysfunction and vertiginous complaints.

**Conflict of interest:** None declared.

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# Оториноларинголошки симптоми код хоспитализованих болесника са ковидом 19 – студија једног болничког центра у Србији

Снежана Санковић-Бабић[1,2], Владан Милутиновић[1,2], Зорана Радин[1], Неда Шапић[1], Сања Цолић[1]

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**САЖЕТАК**

**Увод/Циљ** Инфективно обољење коронавирус 2019 (ковид 19) изазвано је коронавирусом 2 (вирус *SARS-CoV*-2). Болесници са ковидом 19 могу имати клиничку слику која варира од лаке до тешке.

Циљ овог истраживања је био да се анализира присуство оториноларинголошких симптома код хоспитализованих болесника са средње тешким и тешким обликом ковида 19.

**Методе** У дескриптивној клиничкој студији анализирани су подаци из медицинске документације 230 болесника са средње тешким и тешким обликом инфекције ковид 19 који су хоспитално лечени у Клиничко-болничком центру „Звездара" у Београду, у Србији. Оториноларинголошки симптоми, као и општи симптоми везани за обољење ковид 19 анализирани су из медицинске документације за 2021. годину. Инфекција вирусом *SARS-CoV*-2 је претходно потврђена код свих болесника позитивним тестом ланчане реакције и/или брзим антигенским тестом.

**Резултати** Просечна старост 230 болесника који су били укључени у ову студију била је 64 године. Најчешћи општи симптоми су били кашаљ (72%), грозница (52%), диспнеја (46%), малаксалост (46%), док су у мањој мери примећени мијалгија (19%), повраћање (3%) и дијареја (3%). Дистрибуција оториноларинголошких симптома показала је да је најчешћи симптом аносмија (22%), док је бол у грлу присутан код 20%, а агеузија код 19% болесника. Оториноларинголошки симптоми који су били присутни у нижој фреквенцији били су главобоља код 16% болесника, тинитус код 6%, вртоглавица код 5% и губитак слуха код 3% болесника. Коморбидитети су били чешћи код болесника старијих од 50 година. Хипертензија је била најчешћа коморбидна болест код 60% болесника, дијабетес код 23%, хронична опструктивна болест плућа код 7%, малигнитети код 7%, хипотиреоза код 6% и бубрежна инсуфицијенција код 4% болесника.

**Закључак** Оториноларинголошки симптоми који треба да буду даље праћени у периоду после ковида су пролонгирана аносмија, агеузија, поремећаји слуха и равнотеже.

**Кључне речи**: ковид 19; оториноларинголошки симптоми; вирус *SARS-CoV*-2