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Otorhinolaryngologic Manifestations of Long COVID-19 Infection Among Patients at the Quezon City General Hospital

ABSTRACT

Objective: To determine the otorhinolaryngologic manifestations of long COVID-19 infection among patients consulting at the Quezon City General Hospital.

Methods:

Design: Cross-Sectional Study

Setting: Tertiary Government Training Hospital

Participants: Patients aged 18 years old and above, who previously tested positive for the SARS-COV-2 Test, and consulted with otorhinolaryngologic problems at the Outpatient department, Emergency Room, or were admitted, or referred from other services to the Department of Otorhinolaryngology-Head and Neck Surgery, from October 2022 to January 2023 were considered for inclusion.

Results: Out of 150 participants, 127 (84.67%) reported having otorhinolaryngologic symptoms. Five percent (5%) had ongoing symptomatic COVID-19 (4 to 12 weeks) and 11% had post-COVID-19 syndrome (>12 weeks). Patients with long COVID-19 had rhinorrhea (54.51%), hyposmia (51.47%), dysgeusia (48.9%), anosmia (48.53%), sore throat (47.8%), ageusia (29.78%), tinnitus (23.53%), ear pain (23.53%), phantosmia (21.33%), and dizziness (11.76%). Out of 25 patients with long COVID, only 2 had pneumonia and 1 was hospitalized and eventually recovered.

Conclusion: This study showed a prevalence rate of 16% of long COVID-19 with rhinorrhea as the most prominent symptom. Long-term monitoring is essential and patients who had COVID should be advised to report any lingering illness which may subsequently develop. Physicians should be vigilant and aware of the clinical manifestations of long COVID in order to institute proper intervention.

Keywords: COVID-19; SARS-COV-2; long COVID; post-acute COVID-19; long haul COVID-19; ongoing symptomatic COVID-19; post-COVID-19; otorhinolaryngologic symptoms; rhinorrhea



The COVID-19 pandemic affected millions worldwide. It has a wide clinical spectrum from mild, moderate, to severe¹ manifested by respiratory tract symptoms that could progress rapidly to acute respiratory distress syndrome (ARDS).^{2,3} Acute COVID-19 also manifests different upper respiratory tract-related symptoms including nasal congestion, sore throat and smell dysfunction.² Recent studies showed that the evolution of COVID's systemic pathology has long-term degenerative effects and sequelae.^{4,6}

Long COVID can be severely disabling and the mechanisms by which the infection develops are not yet fully understood.⁵ Predictors of long COVID infection include increasing age, presence of comorbidities and the number of symptoms during the acute phase.⁵ It is a clinical diagnosis based on a history of COVID-19 infection characterized by failure to fully recover and subsequent development of symptoms⁵ which may affect multiple organs and body systems.⁴ Long COVID has been classified at different time periods due to the absence of consensus and internationally accepted definitions.³ Recently used definitions were based on National Institute for Health and Care Excellence (NICE) guidelines: ongoing symptomatic COVID-19 and post-COVID-19 syndrome³ which were utilized in our study.

Since COVID-19 has become endemic, investigative studies to determine the otorhinolaryngologic symptoms emerging in the clinical course are therefore relevant and necessary. This current undertaking aims to gather data regarding the different symptoms and long-term effects of COVID-19 specifically regarding otolaryngologic manifestations of patients in the local setting.

METHODS

This cross-sectional study was approved by the Institutional Ethics Review Board of the Quezon City General Hospital. Patients aged 18 years old and above, diagnosed by a physician with COVID-19 infection after they tested positive using Severe Acute Respiratory Syndrome Coronavirus-2 Reverse Transcription Polymerase Chain Reaction (SARS-CoV-2 RT-PCR) or rapid antigen tests, who had face-to-face consults with otorhinolaryngologic problems at the outpatient department, emergency room, or were admitted or referred from other services to the Department of Otorhinolaryngology-Head and Neck Surgery of the Quezon City General Hospital from October 2022 to January 2023 were considered for inclusion. Non-probability convenience sampling was used, wherein participants were recruited as they consulted in the department.

Following hospital protocols in October 2022 during the study period, rapid antigen tests were initially done on all patients. A positive rapid antigen test result was considered confirmatory while a negative result for symptomatic patients required an RT-PCR test. Patients with a

history of previous trauma, surgery, or radiotherapy in the oral or nasal cavities, allergic rhinitis, olfactory or gustatory dysfunction, and those with psychiatric or neurological disorders before acquiring COVID-19 infection were excluded.

Based on the sample size computation, a total of 132 participants were required based on average annual census of 566 COVID-19 patients since 2020 at 95% confidence interval and 7.5% margin of error. Informed consent was obtained before inclusion in the study. Demographic and clinical data which included sex, age, comorbidities, otolaryngologic problems, hospitalization, and presence of pneumonia were gathered using a questionnaire. Physical examination with emphasis on the ear, nose, throat, head and neck was performed.

Based on the World Health Organization (WHO) classification, long COVID includes 2 conditions, ongoing symptomatic COVID-19 and Post-COVID-19 syndrome. Patients were asked about presence of symptoms such as rhinorrhea, sore throat, anosmia, hyposmia, phantosmia, ageusia, dysgeusia, ear pain, headache, dizziness, tinnitus and hearing loss. Symptoms were classified into those with: 1) symptom duration of fewer than 4 weeks (*acute COVID-19*); 2) long COVID were further subdivided into (a) those who had symptoms from 4 to 12 weeks (*ongoing symptomatic COVID-19*); and (b) those that persisted for more than 12 weeks (*Post-COVID-19 syndrome*).⁵

Responses were tabulated and collated using MS Excel for Mac version 14.4.2 (Microsoft Corporation, Redmond, WA, USA). Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequencies and proportions were used for categorical variables, median and interquartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. STATA version 14 (STATA Corp LP, College Station, TX, USA) was used for data analysis and a p-value of < .05 was considered significant.

RESULTS

A total of 150 patients diagnosed with COVID-19 were included in the study; 52 males (34.67%) and 98 females (65.33%). Their ages ranged between 18 and 64 years old, with a mean (SD) of 32 ± 9. There was no significant age difference between asymptomatic, acute, and long COVID patients. Two (1.33%) participants had hypertension, 2 (1.33%) had asthma, and 146 (97.33%) had no comorbidities. Rapid antigen tests and COVID-19 RT-PCR test were performed on 102 (68%) and 48 participants (32%) respectively.

Out of 150 patients, 127 (84.67%) had otorhinolaryngologic symptoms, while 23 (16%) were asymptomatic. Among those who had COVID symptoms, 102 (80%) had symptoms for less than 4 weeks, and 22 (20%) had long COVID for more than 4 weeks. Majority of the

asymptomatic patients were those who were exposed to COVID-19 patients and those who had routine testing prior to a procedure, or watchers who stayed in the hospital with a patient. Eight patients (5.33%) were diagnosed to have pneumonia while 142 (94.67%) had none. One hundred thirty (130) or 86.67% of patients were isolated at home, 14 (9.33%) in COVID facilities, and 6 (4%) were admitted in the hospital. Out of 25 patients with long COVID, only two had pneumonia and one was hospitalized and eventually recovered.

Otorhinolaryngologic problems were reported by 127 symptomatic patients such as rhinorrhea (70.87%), sore throat (69.29%), anosmia (38.58%), ageusia (29.13%), headache (28.35%), hyposmia (27.56%), dysgeusia (27.56%), dizziness (15.75%), phantosmia (7.09%), tinnitus (7.09%), ear pain (5.51%) and hearing loss (1.57%).

Among patients with symptoms less than 4 weeks (*acute COVID*), the most commonly reported symptoms were rhinorrhea (74.51%) and sore throat (72.55%). Other symptoms are summarized in *Table 1*. Majority of initial symptoms resolved in a week for 102 patients (68%).

This study showed a 16% prevalence rate for long COVID. Among those diagnosed with long COVID, eight had ongoing symptomatic COVID-19 while 17 had post-COVID-19 syndrome. Among those with long COVID-19 with symptoms between 4 to 12 weeks (ongoing symptomatic), the most commonly reported symptoms were dysgeusia (62.5%), rhinorrhea (50%) and hyposmia (50%). Meanwhile, out of the seventeen participants who had post-COVID-19 symptoms (more than 12 weeks), rhinorrhea (58.82%) and hyposmia (52.94%) were common. Other long COVID symptoms are summarized in *Table 1*.

During the time of infection, 129 (86%) patients were fully vaccinated, 4 (2.67%) partially vaccinated (1 dose) and 17 (11.33%) were not vaccinated. Among patients with long COVID, seven (87.5%) with ongoing symptomatic COVID and 14 (82.35%) with post-COVID-19 were fully vaccinated.

DISCUSSION

A prevalence rate of 16% of long COVID-19 infection was observed in our study which was comparable to other studies with prevalence rates ranging from 5 to 20%.^{3,5,11} Rhinorrhea was the most prevalent symptom for acute (74.51%) and long (54.41%) COVID 19. In a 2021 meta-analysis by Siso-Almirall, rhinorrhea was also the main otorhinolaryngologic symptom of acute SARS-CoV-2 infection and long COVID in a cohort of more than 1000 patients with 28% persistence for at least 4 weeks and 12-15% persistence for more than 8 weeks.⁴ During COVID-19 infection, the virus affects the respiratory epithelium and ciliary function causing structural damage.⁸ The mucociliary escalator is disrupted contributing to nasal discharge and obstruction.⁸ Other long COVID manifestations previously described^{3,4} were sore throat, anosmia, hyposmia, dysgeusia,

Table 1. Prevalence of otolaryngologic symptoms in patients with Acute COVID-19 disease and Long COVID syndrome

Asymptomatic (N=23; 15.3%)	Group A < 4 weeks (N=102; 68%) n/102 (%)	Group B Long COVID (N=25; 16%) n/25 (%)	Group 1 Ongoing symptomatic 4 to 12 weeks (N=8; 5.3%) n/8 (%)	Group 2 Post-COVID-19 > 12 weeks (N=17; 11.3%) n/17 (%)
Rhinorrhea	76 (74.51)	14 (54.41)	4 (50)	10 (58.82)
Sore throat	74 (72.55)	14 (47.8)	2 (25)	12 (70.59)
Anosmia	37 (36.27)	12 (48.53)	4 (50)	8 (47.06)
Ageusia	28 (27.45)	9 (29.78)	1 (12.5)	8 (47.06)
Headache	29 (28.43)	7 (27.21)	2 (25)	5 (29.41)
Hyposmia	22 (21.57)	13 (51.47)	4 (50)	9 (52.94)
Dysgeusia	24 (23.53)	11 (48.9)	5 (62.5)	6 (35.29)
Dizziness	18 (17.65)	2 (11.76)	0	2 (11.76)
Phantosmia	4 (3.92)	5 (21.33)	2 (25)	3 (17.65)
Tinnitus	5 (4.9)	4 (23.53)	0	4 (23.53)
Ear pain	3 (2.94)	4 (23.53)	0	4 (23.53)
Hearing loss	2 (1.96)	0	0	0

ageusia, hearing loss, headache and dizziness. These were similar to the results of our study except for hearing loss. The 4 patients diagnosed with long COVID in our study who complained of tinnitus might have hearing problems, but audiometry was not performed to document this.

In a 2020 meta-analysis by El-Anwar, sore throat (11.3%) and headache (10.7%) were the most common otorhinolaryngologic manifestations of COVID-19.² Sore throat was reported in 48.9% as initial symptom⁷ which persists in 15% and 7-9% of patients, 4 and 8 weeks after the first symptom, respectively.³ In our study, sore throat was present in 69% of symptomatic patients and 48% of those with long COVID. It is worthwhile to consider the study by Mizrahi which warns of increased risk and sensitivity to streptococcal tonsillitis up to a year after COVID-19 infection.¹²

Alterations in smell and taste are alarming symptoms for patients affected by COVID-19.^{2,4,6} In our study, anosmia and ageusia were both observed in 48% of the patients. These symptoms have a pathological basis related to neurotrophic infection of the gustatory and olfactory systems.⁴ Alega reported anosmia as one of the first symptoms of COVID-19 seen in 51% of the subjects.¹⁰ Females were more susceptible to developing ageusia and anosmia during COVID-19 infection and for extended periods compared to males.^{7,11} A higher incidence of anosmia was reported in younger patients, especially those in the third (44%) and fourth (22.2%) decades in comparison to older age groups.^{7,11}

Olfactory dysfunction is affected by SARS-CoV-2 due to its affinity to ACE-2-expressing cells, and affects essential cellular functions.⁶ It is attributed to both cell-autonomous and non-cell-autonomous



mechanisms of the compromised olfactory epithelium.⁶ In a study by Paolo-Boscolo, 88.2% of patients with COVID-19–related smell or taste dysfunction, recovered completely within 2 years while late recovery was observed in 10.9% of patients.⁷

Acute COVID symptoms may vary from asymptomatic to multisystem life-threatening symptoms.¹¹ This is referred to when the viral load of SARS-CoV-2 is at its peak and the onset of infectious symptoms follows.⁹ In about 3 weeks, the viral load becomes undetectable,²³ and most of these resolve in less than four weeks.^{1,11} In our study, 16% were asymptomatic which poses a grave threat to physicians and the community. These individuals may be responsible for the intractable spread of COVID virus worldwide.¹ Hence, physicians should always be on guard and wear N95 masks when treating individuals with or without symptoms.

Predisposing factors for long COVID include old age over 70 years,^{5,13} presence of more than 5 symptoms during the first week of illness,^{5,13} high body mass index,⁵ presence of comorbidities,^{5,13} and female sex.^{5,13} The absolute risk of developing long COVID is relatively high with increasing age.¹³ Diabetes, hypertension, or high cholesterol were not associated with long COVID however asthma was the only specific medical condition associated with increased odds of having symptoms for more than 4 weeks.^{5,13} Most of the participants in our study were relatively young with no apparent co-morbidities, and who eventually recovered from the condition.

The vast majority of COVID symptoms do not require hospitalization and are known to be mild.¹⁵ Mild illness has various signs and symptoms of COVID with no shortness of breath, dyspnea, or abnormal chest imaging.^{1,12} In our study, the majority were isolated at home and were not afflicted with pneumonia. Many cases of long COVID have developed from milder cases despite their lower risk.⁵ Patients with mild infection have increased risk for a number of health outcomes such as significant lingering respiratory-related symptoms.¹² Hence, long-term monitoring and surveillance are essential and patients who have COVID should be advised to report any lingering illness or symptoms which may subsequently develop.

In a study by Du, long COVID-19 symptoms may vary depending on the strain acquired.¹⁴ The Omicron variant had a lower risk of developing long COVID compared to the Delta variant.⁸ Olfactory dysfunction such as anosmia is less common with the Omicron variant.⁹ General symptoms and fatigue were present among patients infected with the Alpha variant.¹⁴ Sleep difficulty was high among patients infected with the wild-type strain and the Omicron variant and was low among those infected with Delta variant.¹⁴ The Delta variant was known to cause more upper respiratory symptoms and potentially cause ear infections.¹⁴ This underscores the importance of identifying

the predominant variant in the community by the genome center and the dissemination of the inherent signs and symptoms to inform and raise awareness among the general public.

Long COVID may have a lasting impact or serious implications.¹⁵ It is related to reduced desire and ability to eat and prepare food, weight gain or weight loss and nutritional insufficiency, emotional well-being, intimacy, and social bonding, and the disruption of people's sense of reality and themselves.¹⁵ In a study by Bernarte, the majority of COVID-19 patients with anosmia had minimal or negligible impairment and only a small percentage had impaired quality of life.¹⁶ The low percentage of subjects with impaired quality of life may be due to the high number of patients who may have recovered their sense of smell along the course of the disease.¹⁶

Vaccines may not prevent long COVID-19 infection. Nonetheless, current studies support the potential protective effect of vaccination in reducing, but not eliminating long COVID risk.¹⁷ According to Greenhalgh, a triple dose of vaccine lowers rates of long COVID,¹⁸ but the prevalence of long COVID remains high for the delta and omicron variants.¹³ In our study, some patients acquired the disease even when partially or fully inoculated.

A symptom-based approach in identifying and managing long COVID is utilized in its management.⁹ Corticosteroids have been shown to resolve pneumonia and improve clinical functions. Vitamins and mineral supplements have become potential treatments for long COVID.⁹ Although it may not reduce the risk of progression to severe COVID, using Molnupiravir during the first 5 days of infection may decrease the risk of post-acute outcomes regardless of vaccination status and history of past infection.¹⁹ It is given to patients with mild to moderate COVID-19 and those at high risk of developing severe disease however, is discouraged to be given to patients less than 18 years, lactating mothers, and pregnant individuals.¹⁹ In patients with anosmia and dysgeusia, olfactory training therapy is recommended.³

There are several limitations of this study. The course of recovery of otorhinolaryngologic symptoms was not covered and specific timelines when it occurred were not determined. This cross-sectional study was conducted in a tertiary hospital and does not necessarily reflect the general population. The participants had COVID-19 infection in the past and may be prone to remote memory recall. Ideally, an RT-PCR test should be done in all patients with suspected COVID-19 infection however, a rapid antigen test was later adapted and recognized by WHO and DOH to be used to screen symptomatic patients and was utilized in some of the participants in this study.²⁰ Other than chest x-rays to rule out pneumonia, nasal endoscopy, objective olfactory tests, audiometry, and other ancillary procedures were not done in the sample studied.

Physicians should be vigilant and aware of the clinical manifestations

of long COVID and should practice protective measures when dealing with patients with or without symptoms. In the presence of lingering illness, COVID tests may be done to confirm re-infection. Long-term monitoring is essential and patients who had COVID should be advised to report any lingering illness which may subsequently unfold. Laboratory and ancillary procedures should be requested especially to those afflicted with severe and problematic symptoms to institute proper intervention.

In conclusion, this study showed a relatively low prevalence rate of long COVID-19 infection with rhinorrhea as the most prominent symptom. Other symptoms of long COVID include anosmia, hyposmia, phantosmia, dysgeusia, ageusia, sore throat, headache, dizziness, tinnitus, and ear pain. It appears that clinical manifestations of acute and long COVID infection were relatively the same except for the prolonged-time period felt and experienced by the patients.

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