



# Prevalence of Post-COVID-19 Cough One Year After SARS-CoV-2 Infection: A Multicenter Study

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## Abstract

This multicenter study presents prevalence data and associated risk factors of post-COVID-19 cough one year after hospital discharge in COVID-19 survivors. Individuals recovered from COVID-19 at three public hospitals in Madrid (Spain) were scheduled for a telephonic interview. They were systematically asked about the presence of respiratory symptoms, e.g., fatigue, dyspnea, chest pain, and cough after hospital discharge. Clinical and hospitalization data were collected from hospital records. Overall, 1,950 patients (47% women, mean age:61, SD:16 years) were assessed at 11.2 months (SD 0.5) after hospital discharge. Just 367 (18.8%) were completely free of any respiratory post-COVID-19 symptom. The prevalence of long-term cough, chest pain, dyspnea, and fatigue was 2.5%, 6.5%, 23.3%, and 61.2%, respectively. Clinical and hospitalization factors were not associated with long-term post-COVID-19 cough. In conclusion, the prevalence of post-COVID-19 cough one year after SARS-CoV-2 infection was 2.5% in subjects who had survived hospitalization for COVID-19. No clear risk factor associated to long-term post-COVID-19 cough was identified.

**Keywords** COVID-19 · Cough · Persistent · Symptoms · Risk factors

## Introduction

The world is confronting a catastrophic pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible of the coronavirus disease 2019 (COVID-19) [1]. Although clinical manifestations of COVID-19 are heterogeneous; fever, cough, fatigue, and dyspnea are the most prevalent symptoms at the acute phase [2, 3]. Cough is present in 60% of patients as an onset symptom of acute COVID-19 [2, 3]; however, it is also present in other acute viral upper respiratory tract infections. Although cough is not usually considered one of the most bothersome symptoms by COVID-19 patients, as compared with other related symptoms such as dyspnea, fever or chest pain, it is highly relevant since it increases the risk of community transmission by respiratory droplets [4].

Healthcare professionals are also in front of a second pandemic related to SARS-CoV-2, the “long-haulers”, that is, people experiencing post-COVID-19 symptoms after the acute phase longer than it would be expected [5]. A preprint meta-analysis has found that almost 80% of COVID-19 survivors exhibit at least one post-COVID-19 symptom, being fatigue, headache, attention disorders, hair loss, and dyspnea

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the most prevalent [6]. In an Editorial published in *Lung*, Dicipinigitis and Canning advised about the relevance of cough as a persistent post-COVID-19 symptom [7]. Lopez-Leon et al. [6] reported an prevalence of post-COVID-19 cough of 19% (95%CI 7–34%,  $n=7$  studies). Another meta-analysis focusing on respiratory post-COVID-19 symptoms found a pooled prevalence of post-COVID-19 cough of 14% (95%CI 6–24%,  $n=8$  studies) [8]. Similarly, Song et al. also reported a prevalence of 18% (95%CI 12–24%,  $n=14$  studies) for post-COVID-19 cough in previously hospitalized survivors [9]. All studies included in these meta-analyses had follow-up periods ranging from 3 to 12 weeks [6, 8, 9]. Our research group proposed an integrative model defining time reference points where persistent post-COVID-19 symptoms are those lasting longer than 24 weeks after the infection [10]. This multicenter study presents prevalence data and associated risk factors of post-COVID-19 cough one year after hospital discharge in a sample of subjects who had survived hospitalization for COVID-19.

## Methods

The current multicenter cohort study included patients hospitalized for SARS-CoV-2 infection (ICD-10 code) during the first wave of the pandemic (from March 1 to May 31, 2020) at three public hospitals of Madrid (Spain). From all hospitalized patients with a positive diagnosis of SARS-CoV-2 by real-time reverse transcription-polymerase chain reaction (RT-PCR) and radiological findings, a randomized sample of 700 patients from each hospital was selected. The study was approved by Local Ethics Committee of all the hospitals (HUIL/092-20, HUF/EC1517, HSO25112020). Participants provided informed consent before collecting data.

Clinical (age, gender, height, weight, pre-existing comorbidities) and hospitalization [symptoms at hospitalization, days at hospital, intensive care unit (ICU) admission] data were collected from hospital medical records. Participants were scheduled for a structured telephonic interview by trained healthcare professionals. They were systematically asked about the presence of respiratory symptoms such as fatigue, dyspnea, chest pain, and cough after hospitalization and if symptoms persisted at the time of the study. We asked for the following questions: Do you suffer from...*specific post-COVID-19 symptom*...at this moment? Had this...*specific post-COVID-19 symptom*...started after hospitalization due to COVID-19 or did you suffer from it before?

The statistical analysis was conducted with STATA 16.1 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LP. USA). Data were presented as mean (standard deviation, SD) or percentages as appropriate. Multivariate Poisson regression prediction and

risk models were constructed to identify variables independently associated with the presence of cough as persistent post-COVID-19 symptom. Adjusted odd ratio (OR) with their 95% confidence intervals (95%CI) were calculated. A priori, the level of significance was set at 0.05.

## Results

A total of 2100 hospitalized patients were randomly selected and invited to participate. Forty refused to participate, 10 were not able to be contacted after three attempts, and 100 had deceased after hospital discharge. The final sample consisted of 1950 patients (47% women, mean age:61, SD:16 years). The most common symptoms at hospital admission due to SARS-CoV-2 infection were fever (75.5%), dyspnea (31.8%), myalgia (31.7%), and cough (28.1%). Eight hundred and thirty-one ( $n=831$ , 42.6%) had no comorbidities, 710 (36.4%) had one comorbidity, 275 (14.2%) had two comorbidities, and the remaining 134 (6.8%) had three comorbidities (Table 1).

Participants were assessed a mean of 11.2 months (SD 0.5) after hospital discharge. At the time of evaluation, only 367 (18.8%) were completely free of any respiratory post-COVID-19 symptom. Overall, the prevalence of post-COVID-19 respiratory symptoms such as cough, chest pain, dyspnea, and fatigue was 2.5%, 6.5%, 23.3%, and 61.2%, respectively (Table 1). No association was found between the presence of long-term post-COVID-19 cough and the remaining post-COVID-19 symptoms: fatigue (OR1.07, 95%CI 0.73–1.56  $P=0.413$ ), dyspnea (OR0.95, 95%CI 0.83–1.10,  $P=0.352$ ), or chest pain (OR1.12, 95%CI 0.83–1.51,  $P=0.251$ ).

The regression model did not reveal any clinical variable associated with the presence of post-COVID-19 cough: age (OR1.01, 95%CI 0.99–1.03,  $P=0.237$ ), female gender (OR 0.96, 95%CI 0.72–1.29,  $P=0.468$ ), height (OR0.97, 95%CI 0.82–1.14,  $P=0.681$ ), weight (OR1.037, 95%CI 0.87–1.23,  $P=0.717$ ), or number of pre-existing medical comorbidities (OR1.39, 95%CI 0.69–2.81,  $P=0.477$ ). Similarly, no significant association of long-term post-COVID-19 cough with hospitalization variables was either observed: the number of symptoms at hospital admission (OR1.26, 95%CI 0.59–2.69,  $P=0.142$ ), number of days at hospital (OR1.02, 95%CI 0.99–1.04,  $P=0.141$ ), or ICU admission (OR1.24, 95%CI 0.44–3.50,  $P=90.687$ ).

Particular attention was paid to those variables which could promote cough, e.g., smoking, obesity, and cough, and dyspnea, as onset symptoms at hospital admission. No association of being active smoker (OR1.35, 95%CI 0.52–3.52), obesity (OR0.85, 95%CI 0.15–4.78,  $P=0.861$ ), or experiencing cough as onset symptom (OR1.095, 95%CI 0.89–1.33,  $P=0.205$ ) was observed. Although a greater

**Table 1** Demographic and clinical data of the sample ( $n = 1950$ )

Age, mean (SD), years	61 (16)
Gender, male/female (%)	1035 (53.1%)/915 (46.9%)
Weight, mean (SD), kg	75 (15)
Height, mean (SD), cm	165 (17)
Smoking status, $n$ (%)	
Active	96 (8.5%)
None or former	1046 (91.5%)
Main symptoms at hospital admission, $n$ (%)	
Fever	1477 (75.7%)
Dyspnea	621 (31.8%)
Myalgia	606 (31.7%)
Cough	549 (28.1%)
Headache	336 (17.2%)
Diarrhoea	210 (10.8%)
Anosmia	169 (8.7%)
Ageusia	146 (7.5%)
Throat Pain	102 (5.2%)
Vomiting	55 (2.8%)
Medical co-morbidities	
Hypertension	515 (26.4%)
Diabetes	236 (12.1%)
Chronic heart disease—cardiovascular disease	234 (12.0%)
Asma	126 (6.5%)
Obesity	88 (4.5%)
Chronic obstructive pulmonary disease	77 (3.9%)
Stroke	38 (2.0%)
Rheumatological disease	37 (1.9%)
Stay at the hospital, mean (SD), days	11.4 (11.2)
Intensive care unit (ICU) admission	
Yes/No, $n$ (%)	130 (6.6%)/1820 (93.4%)
Stay at ICU, mean (SD), days	13 (14)
Persistent post-COVID-19 respiratory symptoms, $n$ (%)	
Fatigue	1206 (61.4%)
Dyspnea	459 (23.4%)
Chest pain	126 (6.5%)
Cough	50 (2.5%)

proportion of patients with long-term post-COVID-19 cough experienced dyspnea at onset (44%) as compared with those without persistent post-COVID-19 cough (31.1%), the difference did not reach statistical significance (OR1.63, 95%CI 0.99–2.93,  $P = 0.057$ ).

## Discussion

Identification of the phenotype of those patients at a higher risk of developing any post-COVID-19 symptoms is crucial. To the best of the author's knowledge, this is the first study investigating potential risk factors associated to the development of long-term post-COVID-19 cough

in hospitalized COVID-19 survivors. We were not able to identify any risk factor associated with long-term post-COVID-19 cough in individuals who had survived hospitalization for COVID-19.

We found that fatigue and dyspnea were the respiratory post-COVID-19 symptoms more prevalent in previously hospitalized COVID-19 survivors. Our prevalence rates for post-COVID-19 fatigue and dyspnea (61.2% and 23.3%, respectively) are in agreement with the pooled rates reported by Cares-Marambio et al. (fatigue: 52%, 95%CI 38–66%; dyspnea: 37%, 95% 28–48%) [8] and by López-León et al. (fatigue: 58%, 95%CI 42–73%; dyspnea: 24%, 95%CI 14–36) [6]. Interestingly, our study included longer follow-up periods than previous meta-analyses suggesting

that post-COVID-19 fatigue and dyspnea still persist almost one year after the infection.

We also found that chest pain (6.5%) and cough (2.5%) were much less prevalent. In fact, the prevalence of long-term post-COVID-19 cough almost one year after COVID-19 could be considered smaller than expected [7]. Previous meta-analyses reported a pooled prevalence of post-COVID-19 cough ranging from 14 to 18% at follow-ups shorter than 3 months after infection [6, 8, 9]. The prevalence of long-term post-COVID-19 cough was smaller (2.5%), suggesting that maybe post-COVID-19 cough naturally decreases during the first year after SARS-CoV-2 infection. Studies phenotyping the features and evolution of post-COVID-19 symptoms, including cough, will help for better understanding of long-COVID symptoms. An important topic to clarify in future studies is if patients newly develop a particular symptom, e.g., cough, after COVID-19, or if it is an aggravated symptom in those who already had that symptom, e.g., cough, before acute COVID-19.

We were not able to find any potential risk factor associated with the presence of post-COVID-19 cough one year after hospital admission. Probably the low prevalence rate of this symptom explains current findings. Interestingly, the presence of respiratory onset symptoms at hospital admission, e.g., dyspnea or cough, were not associated with long-term post-COVID-19 cough. So far, it is unclear if biological factors associated with the severity of the disease at the acute phase could specifically determine the presence of long-term post-COVID-19 cough, although this is unlikely due to the small prevalence rate of this symptom at a one-year follow-up.

The results of the current study should be considered according to its strengths and potential limitations. Among strengths, this is a multicenter study including a large sample of COVID-19 survivors. Our study has some limitations. First, patients were followed up by telephone and not face-to-face. Second, we only included hospitalized patients. Third, we did not collect measures of COVID-19 disease, such as inflammatory biomarkers or protein serum levels at the acute phase. Additionally, since we did not collect radiological lung findings, no data on a relationship between persistent radiological lung findings and long-term cough is yet available. Fourth, we did not collect data on severity of long-term post-COVID-19 cough. It would be needed to characterize the severity of this long-term post-COVID-19 symptom in future studies. Finally, we collected data cross-sectionally. It would be interesting to investigate the longitudinal evolution of post-COVID-19 symptoms from acute onset to one- or two-year follow-up, but at different timeframes, e.g., one, three, six, nine, and twelve months.

In conclusion, the prevalence of post-COVID-19 cough one year after SARS-CoV-2 infection was 2.5% in subjects who had survived hospitalization for COVID-19.

No risk factor associated to persistent post-COVID-19 cough was identified. Future longitudinal studies are needed to further confirm evolution of post-COVID-19 symptoms.

**Author Contributions** All authors contributed to the study concept and design. CFdIP, and VHB conducted literature review and did the statistical analysis. CG, SPC, and JTM recruited participants. JTM supervised the study. All authors collected data and contributed to interpretation of data. All authors contributed to drafting the paper, revised the text for intellectual content and have read and approved the final version of the manuscript.

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## Declarations

**Conflict of interest** The authors declare no conflict of interest.

**Ethical Approval** The study was approved by Local Ethics Committee of all the hospitals (HUIL/092–20, HUF/EC1517, HSO25112020).

**Informed Consent** Participants provided informed consent before collecting data.

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