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Letter to the Editor

Low prevalence of post-COVID-19 syndrome in patients with asthma

To the Editor,

A significant number of patients suffering from COVID-19 infection refers illness-related symptoms several weeks or months after the acute episode. The so-called post-COVID syndrome or long COVID syndrome includes persistent symptoms that could be the result of residual inflammation, organ damage, non-specific effects from the hospitalization or prolonged ventilation, social isolation or impact on pre-existing health conditions.^{1–3} Very recently, Moreno-Perez et al² published in *Journal of Infection* a large prospective series of 277 patients (66% of them hospitalized) in a mediterranean population the post-COVID syndrome at about 3 months after diagnosis was detected in 141 individuals (51%), 59% of hospitalized patients and 37% of outpatients.² Several series with different follow-up periods have reported the incidence of persistent symptoms ranging from about one third in outpatients and up to 90% in hospitalized patients.^{1–6} However, our clinical experience led us to suspect that patients with asthma had post-covid syndrome less frequently. In fact, in patients with preexisting asthma, a lower COVID-19 susceptibility has been reported.^{7,8} It is possible that this lower susceptibility also affects the long-term persistence of disease symptoms. For this reason, we evaluated the persistence of symptoms attributed to COVID-19 three months after infection in a series of patients with asthma under follow-up in our department.

In the period between March 3 and December 11, 2020, a total of 2995 patients over 14 years of age tested positive for SARS-CoV-2 (determined by RT-PCR technique) in our health department, 77 of them with asthma (2.6%). Three of these 77 patients were excluded for this study (two of them due to death and one due to lack of follow-up). A total of 74 patients with asthma were periodically surveyed by telephone about their clinical evolution. Symptoms referred at three months were recorded for evaluation. The study was approved by the local institutional ethics board, that authorized the study without written individual patient consent statement due to the characteristics of the disease. Severity of asthma was established according to the prescribed therapy following international GINA recommendations (<https://ginasthma.org/>): mild (step 1 and 2 of GINA), moderate (step 3 and 4) or severe (step 5). Asthma was classified as allergic, eosinophilic and non-T2. The allergic group included patients with elevated IgE, a positive prick test to pneumo-allergens or seasonal asthma associated with rhinitis. Eosinophilic patients included those who were non-allergic with a blood eosinophil count of more than 300 per millilitre. Patients who did not meet these criteria were classified as non-T2 phenotype.

Of the 74 patients with asthma, 42 were females (57%). The median age was 49 years (interquartile range 34–60). Asthma was mild in 17 (23%) patients, moderate in 52 (70%) and severe in five (7%) (four receiving omalizumab and one benralizumab). Twenty-five patients with asthma (34%) were asymptomatic during SARS-CoV-2 infection, 34 (46%) developed symptoms but did not require hospital admission, and 15 (20%) were hospitalised. Forty-six patients were classified as having allergic asthma, seven as eosinophilic asthma, and 21 as non-T2 asthma. Admitted patients were five allergic, three eosinophil and seven non-T2 phenotypes.

Seven of the 74 (9.5%) patients with asthma infected by SARS-CoV-2 that were followed-up reported post-COVID syndrome at 3 months; none of the 25 asymptomatic patients, 3 of the 34 patients (8.8%) with COVID-19 that not required hospitalization (2 fatigue and one hyposmia), and 4 (27%) of hospitalized patients (cough 2 of them, and dyspnoea and fatigue one patient each symptom). If we only consider symptomatic patients at diagnosis, the prevalence of post-COVID syndrome was 14% (7 of 49). All but one of the 7 patients with post-COVID syndrome were receiving inhaled corticosteroids. Only one patient with post-COVID syndrome was classified as non-T phenotype asthma. Two patients with post-COVID syndrome had mild asthma, 4 moderate and 1 severe.

In our experience, patients with preexisting asthma have a lower prevalence of post-COVID syndrome than that reported among the totality of COVID-19 patients. In addition to the mentioned series by Moreno-Perez et al² other experiences with general COVID-19 population reported consistent results. In a series of 110 patients hospitalised with COVID-19, at 8–12 weeks postadmission most (74%) had persistent symptoms (notably breathlessness and excessive fatigue),⁴ almost three times as many of our hospitalized asthmatic patients. (27%). In another series with 177 patients with less severe disease (6% asymptomatic, 85% with mild disease and 9% requiring hospitalization) with a median follow-up of 5.6 months after illness onset, one third reported at least one symptom (8.8% in our moderate cases), the most common, fatigue.⁶

The reason for this lower prevalence of post-COVID syndrome in asthma could theoretically be related to immune characteristics of the patients or to treatment. In fact, in-vitro studies have shown that inhaled glucocorticoids reduce the replication of SARS-CoV-2 in airway epithelial.⁹ However, almost all our symptomatic patients were receiving this drug.

Our study has several limitations. Patients, of one single centre, were followed up by telephone and no face-to-face interview was conducted. In addition, it is possible that the patients did not report mild symptoms or psychological disturbances. This implies that it is an exploratory study that needs to be confirmed.

In conclusion, we have found that our patients with asthma have a low prevalence of persistent symptoms at three months of

onset of COVID-19. It seems of interest to confirm this finding in other centres and with larger samples and to analyse its possible causes.

Declaration of Competing Interest

The authors declare no conflict of interest

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