



## Editorial

## Impact of COVID-19 on the Most Frequent Middle and Lower Obstructive Airway Diseases/Syndromes in Adult Population



### Impacto de la COVID-19 en las enfermedades obstructivas crónicas de la vía aérea en la población adulta

The year 2020 was marked by medical and community efforts across the world to stop the coronavirus 2019 disease (COVID-19) pandemic. Caused by severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) infection, COVID-19 is associated with high morbidity and mortality (>71 million cases during the last year including 1.6 million deaths).<sup>1</sup> The clinical manifestations of COVID-19 are heterogeneous, ranging from asymptomatic to severe disease, respiratory failure and death.<sup>2</sup>

The main entrance door is the nose. The SARS-CoV-2 binds the angiotensin-converting enzyme 2 (ACE2) highly expressed in airway epithelial cells and uses it as receptor. To facilitate cell invasion, there is need for the transmembrane protease TMPRSS2 that activates the SARS-CoV-2 spike protein.<sup>2</sup> This explains why the respiratory symptoms (rhinorrhoea, anosmia, cough, dyspnoea) are predominant in COVID-19, associated or not with fever, fatigue, myalgia or diarrhoea.<sup>1</sup> The outcomes of COVID-19 are worsened by comorbidities, including malignancy, cardiovascular disease, chronic obstructive pulmonary disease (COPD), obesity, and diabetes mellitus.<sup>1,3</sup> The therapeutic management in hospitalized patients includes dexamethasone  $\pm$  antiviral therapy, supplemental oxygen, and ventilator assistance associated with prophylactic anticoagulation.<sup>1</sup>

Even though the incidence of COVID-19 in COPD patients is not different from the general population, COPD has been identified as risk factor for more severe COVID-19 and poor outcomes.<sup>4,5</sup> The prevalence of COPD in hospitalized COVID-19 patients vary considerably between 0 and 10%, respectively 4–38% in the intensive care unit (ICU) across the world and may be due to under/over-reporting of the disease.<sup>5</sup> Patients with COPD and COVID-19 are more likely to develop severe pneumonia, acute respiratory distress syndrome (ARDS), bacterial/fungal coinfection, septic shock, and have higher risk for healthcare utilization, hospitalization, admission to ICU, mechanical ventilation or death.<sup>4–6</sup> These could be partially explained by the increased ACE-2 expression found in bronchial epithelial cells from COPD patients compared to controls. Similar findings were described in current smokers versus former/never-smokers suggesting a link between ACE-2 expression and cigarette-smoke exposure.<sup>5</sup> During the pandemic, people with COPD must comply with prophylactic measures (e.g. social distancing, work from home if possible, use of masks and

hand sanitizer), stop tobacco smoking and continue their routine medications with inhaled long-acting bronchodilators  $\pm$  inhaled corticosteroids.<sup>7</sup> Exacerbations should be managed according to current recommendations. During the pandemic, clinic visits and pulmonary rehabilitation sessions have been cancelled. Healthcare systems have had to adapt to this situation by augmenting telehealth and virtual visits. Several trials assessing telehealth for COPD patients demonstrated its feasibility and non-inferiority to usual care for the management of exacerbations and in term of quality of life. Similarly, online pulmonary rehabilitation programmes seem to be as effective as in-person sessions for these patients. However, if the social distancing measures remain in place for many more months, these virtual programmes must be adapted to ensure our patients can receive optimal care.<sup>7</sup>

Increasing evidence suggests that Obstructive Sleep Apnoea (OSA) is a risk factor for COVID-19 and associated with worse outcomes. Patients with OSA have 8-fold higher risk for COVID-19 compared to a similar age population without this diagnosis. Among patients with COVID-19, OSA is associated with increased risk of hospitalization, double-risk of developing respiratory failure and triple-risk of death on day seven.<sup>8</sup> OSA induces a proinflammatory states favourable for COVID-19, intermittent blood gas disturbances increasing the risk for acute cardiovascular events and is frequently associated with obesity. Currently, it is difficult to say if OSA is an independent risk factor for COVID-19 on top of obesity or merely associated. Data showed that the compliance to continuous positive pressure therapy was improved during the COVID-19 lockdown as consequence of publicity regarding respiratory disease-related risk and spending more time at home.<sup>8</sup> In contrast, OSA management in sleep medicine departments in Europe during the first 1–2 months of pandemic was reduced by 80% because most services have been limited to phone-based follow-up and selected high-priority cases. There is medical need to develop strategies for care of patients with suspected and established OSA diagnosis during COVID-19 pandemic, possibly using more telemedicine.<sup>9</sup>

If bronchiectasis is described as radiological findings in post-COVID-19, information about the impact of COVID-19 on bronchiectasis are limited to sporadic case reports. People with cystic fibrosis (CF) frequently have bronchiectasis and were considered

at high-risk for severe COVID-19. However, early data about the impact of COVID-19 on CF patients showed a low incidence in this population and similar outcomes to the general population. More severe clinical courses were associated with low lung function and organ transplant.<sup>10</sup> However, the long-term impact of COVID-19 in people with CF is still unknown.

Among patients with COVID-19, asthma is not associated with increased risks of severe pneumonia, ARDS, hospitalization, intubation or death.<sup>3,11,12</sup> Asthma prevalence in people hospitalized with COVID-19 is similar to the general population.<sup>11,12</sup> This could be the consequence of reduced airway ACE-2 expression found in patients with type-2 inflammation or treated by inhaled corticosteroids.<sup>2</sup> Patients with asthma and COVID-19 are older, predominantly female, smoked more frequently, and had higher prevalence of diabetes, obesity, cardiovascular diseases, and dyslipidaemia than asthmatics without COVID-19.<sup>13</sup> The presence of these comorbidities, the type 2-low asthma phenotype, the use of oral corticosteroids and the severe asthma were associated with worse outcomes and higher mortality rate in patients with asthma and COVID-19 while maintenance treatment with inhaled corticosteroids and good asthma control are protective.<sup>14</sup> Most of current data suggests that biologic therapies targeting type-2 inflammation used in the treatment of severe uncontrolled asthma are not associated with an increased risk for COVID-19 infection or greater disease severity and mortality compared to the general population or asthmatics not receiving any biotherapy. In addition, no significant differences were observed when patients treated by different biologics were compared.<sup>14,15</sup> These early results on the benefits and risk of biologic asthma therapies during COVID-19 pandemic should be confirmed by future studies in largest cohorts. In contrast with other respiratory viruses, SARS-CoV-2 infection did not induce severe asthma exacerbation.<sup>12</sup> All asthmatic patients should correctly apply preventive measures, have a detailed action plan to manage exacerbations and continue their controller treatment for asthma during the COVID-19 pandemic. As for patients with OSA, there is evidence of improving medication adherence among patients with asthma during COVID-19 pandemic.<sup>16</sup>

This early data suggests that people with COPD and OSA are at risk for poor COVID-19 outcomes while the impact of COVID-19 on asthma and bronchiectasis is lower than previously predicted. However, close monitoring of patients with chronic obstructive airway diseases will be necessary to understand the medium and long-term consequences of COVID-19 pandemic.

### Conflict of interest

The author declares to have no conflict of interest directly or indirectly related to the manuscript contents.

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