



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Scientific letter

# Viral etiology of exacerbations of patients with chronic obstructive pulmonary disease during the winter season<sup>☆</sup>

## Etiología viral de las exacerbaciones de los pacientes con enfermedad pulmonar obstructiva crónica en la época invernal

Dear Editor,

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory process that alters the patient's functional capacity. It is estimated to be the fourth leading cause of death worldwide, affecting 2.4% of the population.<sup>1</sup> COPD exacerbations (COPDE) constitute the main complications of this disease since they deteriorate lung function. These acute processes have multifactorial causes, including viral infections, especially during the winter season.<sup>1,2</sup>

Chronic inflammation caused by viral infection and stimulation of IL-8 and other cytokines appear to be the cause of COPDE and lung lesions.<sup>3</sup> The viral impact in these processes has been underestimated until now due to the detection techniques used; the current use of molecular techniques has demonstrated the leading role of viruses in these episodes. With this technology, different studies have demonstrated viral infection in between 30 and 40% of COPDE cases, primarily involving rhinovirus, influenza and respiratory syncytial virus (RSV).<sup>3,4</sup>

The incorporation of molecular techniques in the diagnosis of viral infections has allowed us to study their participation in acute COPDE cases.

We report a prospective study conducted during the period with the highest prevalence of this type of infection (from October 2018 to February 2019). One hundred and eighty-seven patients (79% men) who came to the emergency department with an exacerbation (cough, expectoration and respiratory distress) of their previously diagnosed COPD were analysed during the study period.

A single throat swab culture was performed in each patient to detect bacteria and viruses. The viruses were studied using a commercial real-time RT-PCR (Allplex Respiratory Assay, Seegen, South Korea) that simultaneously and differentially detected 16 different viruses.

One hundred and four (104) positive samples (55.6%) were detected in the 187 patients, of which 78 (41.7%) corresponded to viruses alone, 19 (10.1%) to bacteria alone, and 7 (3.7%) to viruses and bacteria together. That is, viruses represented 45.4% (85 cases) of all respiratory processes in these patients. Differences in viral aetiology were observed in each of the months studied: with 36.6% in November and 69.7% in December. Similarly, the percentage of

viral infections as the sole cause of COPDE has also fluctuated: it was 60% in October and 94.4% in February.

The main viruses detected have been rhinovirus (30.5%), influenza A (H3N2) (28.2%), RSV-B (22.3%), coronavirus (16.4%), adenovirus (1.1%) and metapneumovirus (1.1%). The bacteria detected were mainly *P. aeruginosa* and *H. influenzae* and, of the 7 virus–bacteria associations, rhinovirus represented the majority of them (57%). Five patients (5.8%) with influenza A (H3N2) infection required admission to the ICU; no patient died as a result of viral infection.

A recent meta-analysis on the prevalence of viral infections in COPDE showed that a virus can be detected in up to 50% of cases if molecular techniques are used.<sup>1–4</sup> In our study, positive results for viruses reached a total of 45.4%, a value that is within the range reported. Our study simultaneously analysed the presence of bacteria, although they have represented only 10.1% of the cases. Whether they are simple colonizers or true pathogens cannot be determined.<sup>2,5</sup>

Rhinoviruses have been the most commonly detected viruses, which coincides with other studies that estimate them at up to 58%,<sup>1,2</sup> although in the winter season there is a high circulation of these viruses associated with the common cold. As expected, influenza viruses, in this case circulating A (H3N2), and RSV have been the cause of 50.5% of COPDE cases. Viral aetiology distribution data similar to ours have already been described, although with variations depending on the type of influenza circulating in a given winter epidemic.<sup>1–4</sup>

Rapid identification of the viral aetiology of COPDE cases avoids the unnecessary administration of antibiotics and anticipates a good prognosis. Of the main viruses involved, only influenza could be prevented by systematically vaccinating these patients each season.

### Conflict of interest

The authors have no conflict of interest.

### References

- Jafarinejad H, Moghooei M, Mostafaei S, Salimian J, Jamalkandi SA, Ahmadi A. Worldwide prevalence of viral infection in AECOPD patients: a meta-analysis. *Microbial Path.* 2017;115:190–6, <http://dx.doi.org/10.1016/j.micpath.2017.10.021>.
- Wedzicha JA, Singh R, Mackay AJ. Acute COPD exacerbations. *Clin Chest Med.* 2014;35:157–63, <http://dx.doi.org/10.1016/j.ccm.2013.11.001>.
- Almansa R, Socías D, Andaluz-Ojeda I, Martín-Loeches F, Bobillo J, Blanco J, et al. Viral infection is associated with an increased proinflammatory response in chronic obstructive pulmonary disease. *Viral Immunol.* 2012;25:249–53, <http://dx.doi.org/10.1089/vim.2011.0095>.
- Britto CJ, Brady V, Lee S, de la Cruz CS. Respiratory viral infections in chronic lung diseases. *Clin Chest Med.* 2017;38:87–96, <http://dx.doi.org/10.1016/j.ccm.2016.11.014>.
- Jankauskaite L, Miseviciene V, Vaideliene L, Kevalas R. Lower airway virology in health and disease. From invaders to symbionts. *Medicina.* 2018;54:72, <http://dx.doi.org/10.3390/medicina54050072>.

<sup>☆</sup> Please cite this article as: Reina J, Sala E, Fraile P. Etiología viral de las exacerbaciones de los pacientes con enfermedad pulmonar obstructiva crónica en la época invernal. *Med Clin (Barc).* 2020. <https://doi.org/10.1016/j.medcli.2019.05.025>

Jordi Reina<sup>a,\*</sup>, Ernest Sala<sup>b</sup>, Pablo Fraile<sup>a</sup>

\* Corresponding author.

E-mail address: [jorge.reina@ssib.es](mailto:jorge.reina@ssib.es) (J. Reina).

<sup>a</sup> Unidad de Virología, Servicio de Microbiología, Hospital  
Universitario Son Espases, Palma de Mallorca, Spain

<sup>b</sup> Servicio de Neumología, Hospital Universitario Son Espases, Palma  
de Mallorca, Spain