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Do HIV-Infected Patients Die of Chronic Obstructive Pulmonary Disease in Western Countries?

¿En los países occidentales, los pacientes infectados con el VIH mueren de enfermedad pulmonar obstructiva crónica?

Dear Editor:

According to Global Burden of Disease estimates, at least 65 million people worldwide have moderate to severe chronic obstructive pulmonary disease (COPD). In addition to being globally prevalent, COPD was responsible for more than three million deaths in 2015 (5% of all deaths globally),[1] and from 1990 to 2015, the mortality rate increased 11.6%.[2] Furthermore, chronic respiratory diseases in the United States account for more than 155,000 deaths annually and are the third leading cause of death, surpassed only by heart disease and cancer.[3]

Recent systematic reviews report that up to 11% of people living with HIV (PLWH) have spirometric test results compatible with those for COPD.[4] Furthermore, although PLWH smoke tobacco and other products at higher rates than other groups at risk for COPD, they are relatively younger, and the frequency of COPD appears higher than would be expected from smoking only.[5] Proposed hypotheses have suggested that this increase in COPD prevalence could be due to several associated factors such as local inflammation, increased susceptibility to apoptosis and an altered antioxidant–oxidant balance.[6]

Currently, the presence of HIV infection is considered a risk factor for developing COPD, a finding just recently included in the latest GOLD document.[7] This increased prevalence of COPD among PLWH, consistently observed in several studies performed in western countries, would suggest that mortality due to COPD among PLWH could be at least similar to the rate observed in the general population, especially considering that recent studies from the same geographical environment have stated that COPD in PLWH can result in higher mortality rates than in the HIV-uninfected population.[8] Surprisingly, however, published data from current cohorts of HIV-infected patients report low rates of death attributed to COPD, even less than 1% in some nationwide studies.[9]

This observation could be explained by different factors. First, with regard to death certificate coding, it is worth remembering that the immediate cause of death in COPD patients is usually due to exacerbations (half of which are infectious) and cardiovascular events.[10] In both situations, actual codification systems, such as CoDe,[11] classify the events correctly as the immediate cause of death in HIV-infected patients, but probably tend to underestimate COPD as the underlying cause. Thus, when reporting causes of death in PLWH cohorts, COPD is usually not even reported to be within the top 10 causes. This misclassification phenomenon has previously been reported in the general population,[12] but some authors have suggested that it could be even more manifested in the HIV-infected population. The trend among practitioners who are not used to caring for PLWH is to codify infectious diseases as the cause of death, related or unrelated to HIV. As a consequence, could the number of deaths caused by infections unrelated to AIDS and cardiovascular disease be systematically reported more frequently in AIDS cohort studies?

Several examples might support this hypothesis. Recent data published from the Swiss HIV Cohort Study (SHCS) reported 1.7% of deaths due to COPD in 2005–2009, whereas the reported rates for non-AIDS-related infections and heart disease were 9.2% and 6.5%, respectively.[13] Similarly, Croxford et al. reported that 0.75% of

deaths were caused by COPD (1.78% after excluding AIDS-defining illnesses) while deaths by cardiovascular disease (including stroke) and non-AIDS-defining infections accounted for 7.86% and 7.45%, respectively, of the total deaths (19% and 18% after excluding AIDS-defining illnesses).[9]

Another possible explanation, independent of the coding systems, could be that although PLWH frequently visit doctors and are linked to care, their lungs tend to be less tested and therefore less diagnosed with COPD. COPD underdiagnosis is a universal phenomenon, both in general and hospital-based populations.[14] Spirometry is not actually implemented in most hospitals as a routine test for PLWH, despite guidelines having begun to include algorithms regarding this comorbidity.[15] This underdiagnosis would then lead to an underreporting of deaths.

Both of these possible explanations, if true, may reflect a worrisome problem: COPD is not yet perceived as a relevant concern in PLWH care. This potential issue may also have caused collateral effects, as few research groups are presently addressing this particular comorbidity. In the last 10 years (2008–2017), only 191 articles indexed in Medline and related to HIV mention in their title, abstract, or keywords the term "COPD", while in the same period, 931 articles and 8437 articles mention "cardiovascular" and "cancer", respectively.

It is important to note that the scientific community still possesses an astonishing lack of knowledge in how COPD and HIV relate to each other. We do not yet have enough evidence regarding the effects of chronic HIV infection in the lungs; how these affect the local immunity, even in the presence of effective antiretroviral treatment; and how to optimize the management of COPD in PLWH, apart from implementing smoking cessation and programs to identify individuals with COPD. Further lung research in HIV is needed, and most, if not all, PLWH might be recommended to perform a baseline spirometry to aid in tracking their general and HIV-related health.

As a conclusion, we consider that the impact of COPD in terms of PLWH mortality could have been systematically and grossly underestimated in western countries. This misclassification phenomenon could have lead physicians to minimize COPD role as a comorbidity in this population.

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