Disturbances of lung function in HIV positive patients

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Received: 2022-09-12 - Accepted: 2022-11-26 - Published: 2022-12-01

How to Cite: Agostini M. Disturbances of lung function in HIV positive patients. Interam. J. Health Sci. [Internet]. 2022;(2):120. Available from: https://ijhsc.com/journal/article/view/120

ABSTRACT

The presence of disturbances in the respiratory function on HIV positive patients, derive from multiple causes. The principal mechanism of injury is the inflammation that triggers a flood of biomarkers, which leads to a respiratory function decline. Within the causes, we find modifiable factors such as tobacco and drugs use, and non-modifiable factors like gender, age, CD4 recount, viral burden, HIV itself, ART, co-infections such us HCV and the presence of breathing infections like *Pneumocystis Jiroveci* pneumonia and *Tuberculosis*. Facing a chronic pathology requires to control obstructive alterations so, it results convenient to request spirometry and diffusion tests.

KEYWORD

HIV, Chronic obstructive pulmonary disease (COPD), Antiretroviral treatment.

INTRODUCTION

It is estimated that since the beginning of the global epidemic, 77.3 million people have contracted the HIV infection. In 2018, the total number of 37.9 million people who live with VIH (PL WH) has been received in the whole world[1].

According to December 2021 epidemiologic reports, 140000 people live with HIV in Argentina, of which a 17% serology is unknown. An 83% of infected people is in antiretroviral treatment. They received assistance from public effectors and received a 6,7/10 treatment. Related with gender, there is 2.4 masculine cisgender for each feminine cisgender. Generally, at the diagnosis moment, the average age of this people is between 28 and 35 years old. The way of transmission is predominantly sexual conforming the 98% due to the lack of condom use and the prevention measures that promote not only the State but also the different national organizations which work to assist people with HIV and the hole population, in general[2].

That is the reason why in 2020, aims have been set to reach at global level, which are called: 90-90-90. These consists in achieve the 90% of people be diagnosed, the 90% people from that group receive treatment and, the 90% from that last group, be with adhesion.

Despite the arrival of antiretroviral therapy (ART), the epidemic of the human immunodeficiency virus is still a global health crisis with a high burden of respiratory disease among infected people. While the first complications of the epidemic were fundamentally opportunistic infections, the improve of survival showed the appearance of non-infectious diseases that are associated with chronic respiratory symptoms and lung impairment.[3]

DEVELOPMENT

Obstructive ventilator defects and reduced diffusion capacity are common findings in adults, and the association between HIV and chronic obstructive pulmonary disease is increasingly recognized. There is synergy between viral factors, opportunistic infections, conventional influences such as tobacco smoke and exposure to biomass fuel, and potentially, the immunological effects of art in the development of chronic obstructive pulmonary disease associated with HIV.[4-5-6]

Lung chronic illnesses in HIV patients are less recognized than other events not AIDS such us cardiovascular, liver and kidney manifestations or neoplasms. However, EPOC is frequent among people infected with HIV and it is significantly associated with the weakness, the altered physical function and the risk of hospitalization of people who live with HIV [7-8].

In a pulmonary sub study of the START study, 1026 patients from eighty different sites from twenty countries have been evaluated. They investigated the association between de lung function and biomarkers, to which total bilirubin and albumin was added. Elevated D-dimer dosages and IL-6 were associated with a larger obstruction of air flow (lower FEV1 / FVC). The commonly available biomarkers, particularly the systemic inflammation ones, are related to a worse transversal lung function, but they are not related to the subsequent decline of the lung function among HIV positive people with an early infection and basal T CD4 cells count with more than 500 cells/µl. They found that the systemic inflammation markers are associated with a transversal lung function lower than [10] (Table 1).

A study done in Uganda in 2018, was the first to report that the biomarkers of macrophage activation (Scd163) and systemic inflammation markers (hsCRP –IL-6) are related to decreased lung function in elderly people living with VIH (PLWV), on ART. This is highly important because the lung is a storage of HIV.[10]

TABLE 1: BIOMARKERS AND INFLAMATION IN HIV

SMART STUDY	**BIOMARKERS**
	D-Dimer
	High-sensitivity C-reactive protein (hsCRP)
	Interleukin-6 – IL-27
	Serum amyloid A
	Soluble intercellular adhesion molecule (sICAM)
	Soluble cell adhesion molecule (sVCAM).

Source: MacDonald, D. M., Zanotto, A. D., Collins, G., Baker, J. V., Czarnecki, M., Loiza, E., & Kunisaki, K. M. Associations between baseline biomarkers and lung function in HIV-positive individuals. *AIDS*. 2019:*33*(4), 655-664.

Chandra et al.,[11] accomplished a study at The United States evaluating spirometries, diffusion tests, biomarkers and the presence of calcium in the coronary arteries. They found an association between de decline of DLCO with a higher level of calcium in the coronary artery and mortality increase. The presence of endothelin-1, biomarker of endothelial diffusion was associated with

the decrease of DCLO and increase of calcium at coronary level. In the same year, 25509 patients were studied by Clother and col[12] in The United States. 423 of them compatible with the EPOC definition. They found a relation with a risk significantly higher to myocardial infarction, particularly type 2 (T2), in the sepsis or bacteremia context.

Kunisaki[13] did an investigation job during the period 2017-2018, that included the participation of the MACKS cohort, (Multicenter AIDS Cohort Study) and a cohort formed by gay and bisexual men, and other ones who practice sex with men with or without HIV (GBHSH). The HIV negative participants were younger, from black ethnicity, and they also consumed marijuana, tobacco and presented co-infection with HCV. The group conformed with HIV positive patients, had an average age of 57 years old, they consumed marijuana and tobacco and they were under ART, with a CD4 count higher than 674 cell/mm^3 and undetectable viral burden. They were studied with spirometries and DLCO diffusion tests. The most relevant findings related to the spirometry consisted in VEF1 results that revealed similarities in both groups. However, this fact changed when they set the results to confusion factors. VEF1 was about 2.2% lower in HIV positive patients, a difference without statistic relevance. High levels of CD4 nadir was associated to an increase in DLCO levels, what is related to a better aptitude to transport oxygen from air to blood.

A British study has developed that elderly people who suffer from HIV would have worse respiratory health than those who do not suffer from it, at similar ages. POPPY cohort patient's data have been analyzed, an observational and transversal study that count on three groups of participants: HIV positive people older than 50 years old, HIV positive people younger than 50 years old and people who do not suffer from HIV also older than 50 years old. Breathing symptoms were evaluated by St. Georges´ questionnaire. The obtained score was of 17.7 points in older HIV positive patients, 17.5 in younger HIV positive people, and a score of 9 years in older people without HIV. In order to understand the questionnaire and its findings, we say that healthy men have a score of 7.6, 22.5 for EPOC diagnosed patients and 32.4 for patients who suffer from asthma. The investigation found out a strong relationship between the respiratory function, age, mental health and life quality. [14]

An investigation presented at EACS european conference in 2021, has demonstrated that VIH positive people with low ART, present a faster rate of lung function decline than HIV negative patients. Smoking tobacco as a habit, interacts with HIV contributing to lung function decline, reason why smoking cessation must be a priority for people who live with HIV. 2 HIV positive cohorts have been studied: COCOMO/INSIGT-SMART and Danish negative people. Patients have been studied with spirometry and DLCO diffusion tests at two moments: basal state and 24 months later. Annual rate of FEV_1 lung function decline was faster in people who live with HIV than at controls, having the first ones a 8.5ml annual decrease. The most outstanding difference presented was the fact that HIV people who actively smoke, showed an annual decrease of 16.8ml in lung function. [15]

An investigation put into practice in Rosario city, Argentina, studied lung function on HIV positive patients under ART or elite control, non-smokers, with undetectable viral burden, CD4 higher than 600 cell/mm^3, without comorbidities neither history of respiratory infectious pathologies. They were studied in laboratory, C reactive protein dosage and lung function tests: spirometry, TC6M and diffusion test in two moments: basal state and 24 months later. Significantly differences have been found in this parameters in CVF, VEF_1, in the group under ART and at TC6M, in both groups. They built a work and follow-up algorithm for patients, taking into account the exposure to inflammation, positive serology and ART in one group (Figure 2). [16]

FIGURE 2: ALGORITHM FOR THE APPROACH AND TREATMENT OF RESPIRATORY DISORDERS IN PATIENTS WITH PRESERVED IMMUNITY

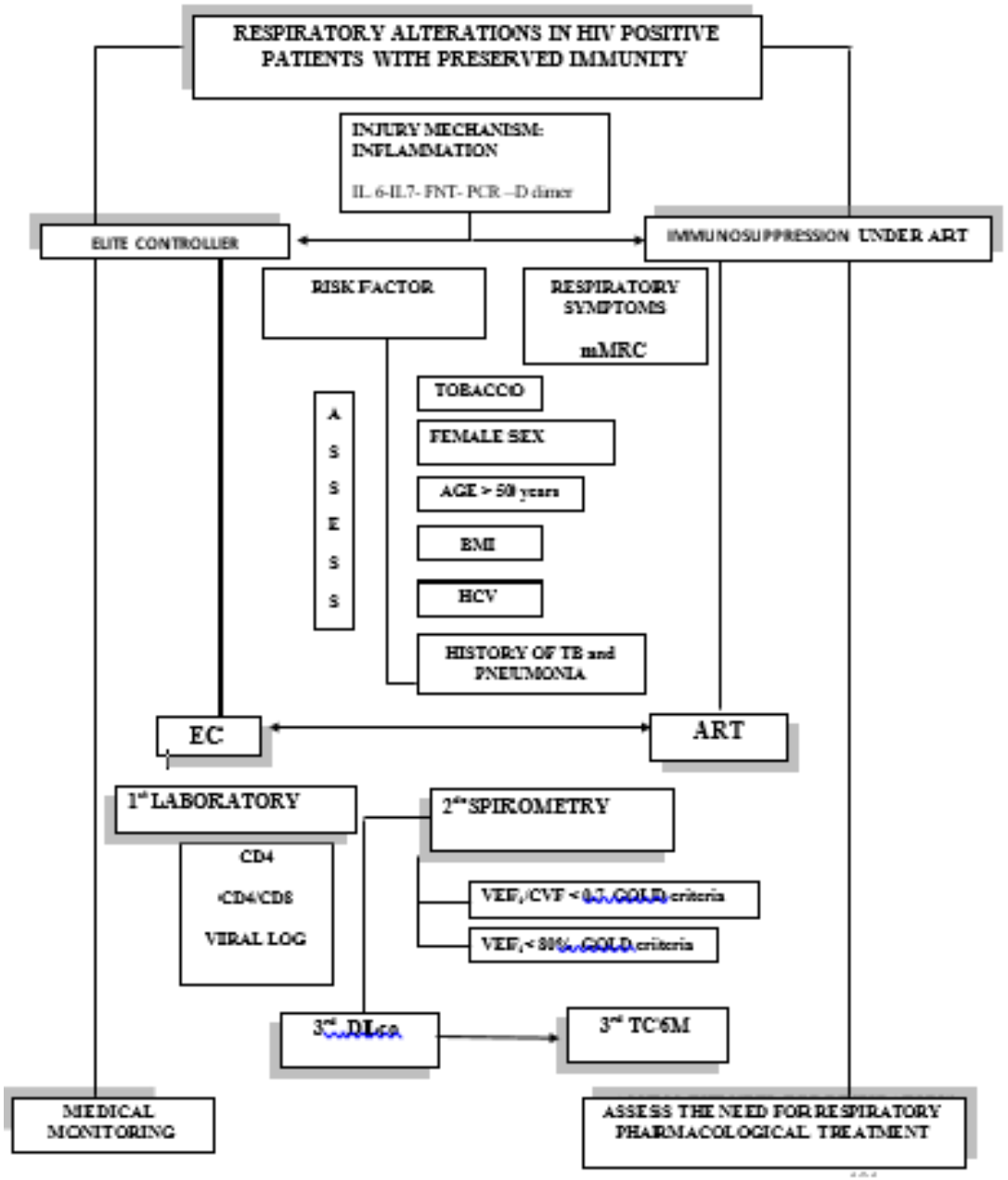

Figure 2: Agostini, M. (2022). Alteración de la función respiratoria relacionada al VIH. *PhD Thesis.* Universidad Nacional Nacional, Rosario.

Chronic obstructive pulmonary disease is a frequent, preventable, non-curable, and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation owing to airway or alveolar abnormalities, which are usually caused by substantial exposure to noxious particles of gases. The chronic

airflow limitation that characterises COPD it caused by a mixture of diseases of the small airways and parenchymal the destruction. COPD is one of the major contributors to global years of life lost, with attributable death rates ranked thirds worldwide in 2010; it is projected to be the fifth largest in terms of disease burden, and the fourth largest cause of death by 2030.[17]

Mishra & Mishra[19], in his job they tell as COPD is more prevalent in HIV positive population; 16-20% of individual with HIV infections had COPD, and poorly controlled HIV infection worsens spirometric and diffusing capacity measurements and accelerate lung function by about 55-75ml/year. Up to 21% of HIV-infected individual have obstructive ventilator defects and reduced diffusion capacity is seen in more than 50% of HIV-infected population. COPD can be viewed not exclusively as a pulmonary disease but rather as a systemic syndrome sparked and fueled by a persistent low-grade attributable inflammatory state[19].

Chronic lung disease will become the third most common cause of death by 2030 in the general population. Early detection and proper management is a priority to improve the prognosis and quality of life of patients. In turn, the diagnosis of COPD reinforces smoking cessation, involves a thorough study of pulmonary function by spirometry, carbon dioxide diffusion test (CDDT) and lung cancer screening. [20]

CONCLUSIONS

Within the not AIDS events, we must consider the chronic obstructive pulmonary illness, implement early screening methods for an early diagnosis and an accurate treatment. The flow obstruction, the declines of the diffusion aptitude like alterations in the 6 minutes walking test are findings more and more frequently among the investigated populations. At the same time, if they show risk factors such us tobacco, marijuana consumption, history of respiratory infections, a low CD4 nadir, detectable viral burden and smoke exposition, the risk of present this mentioned alterations increases. Positive serology, antiretroviral treatment and advanced age are factors that make this condition worse.

Because of the precedent words, when we diagnosis HIV, is needed to carry out an exhaustive questionnaire, physical examination, laboratory including inflammation biomarkers and request exams of respiratory function within complementary methods.

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CONFLICTS OF INTEREST

None.

FINANCING

None.

AUTHORSHIP CONTRIBUTION

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