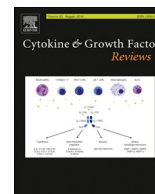




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Letter to the Editor

Letter to the Editor on “Bonafè M, Prattichizzo F, Giuliani A, Storci G, Sabbatinelli J, Olivieri F. Inflamm-aging: Why older men are the most susceptible to SARS-CoV-2 complicated outcomes. Cytokine Growth Factor Rev”


Dear Editor,

We read with great interest the review article by Bonafè F et al. in *Cytokine & Growth Factor Reviews* [1], which describes the main features typical of aging (inflamm-aging, immune-senescence and age-related diseases) as a partial explanation of the disproportionate COVID-19 mortality suffered by elderly men. Patients of older age (> 60 years) and with other co-morbidities such as hypertension, respiratory disease, cardiovascular disease, diabetes and chronic kidney disease are indeed found to present with more severe SARS-CoV-2 infection and have adverse outcomes.

Systemic immune activation and inflammation are also recognized as essential components in the pathogenesis of HIV infection. Despite antiretroviral therapy (ART)-related benefits on health and quality of life of HIV-infected patients, an increase in common age-related conditions occurs that may represent an accelerated aging phenotype, whereby the increased rate of complications occurs earlier than in a control group of the same age [2,3]. The pathogenesis of these non-communicable diseases is complex but is also attributable to persistent immune activation and inflammation. This accelerated aging during HIV disease is supported by studies on DNA-methylation level, telomere length and immune-senescence while chronic immune activation is found in HIV-infected patients and is characterized by an increase in proinflammatory mediators, dysfunctional Tregs and a pattern of T-cell-senescent phenotypes, similar to those observed in the elderly.

During SARS-CoV-2 pandemic, there have been few case published reports of COVID-19 in HIV-infected persons but, surprisingly, the vast majority of cases were mild or moderate and the risk of death or admission to an intensive care unit seems lower than in general population [4]. Well-treated HIV patients who reach normal CD4⁺ cell level and suppressed HIV viremia may not have an increased risk for severe COVID-19, but in this population, some of the conditions cited by Bonafè et al. coexist that could increase their overall risk. In the large majority of European HIV cohorts, more than half of the patients are males, aged > 50 years (although HIV infection can add nearly 10 years to chronologic age due to premature aging [5]), most are smokers and with cardiovascular diseases, hypertension and/or metabolic syndrome. Despite these well-established characteristics of HIV-infected patients, the COVID-19 pandemic seems not to particularly affect this population. Further, antiretroviral therapy (protease inhibitors or tenofovir) seems to have no significant clinical benefit for SARS-Cov-2 infection *in vivo*. Therefore, a panel of biomarkers of immunological/biological age may not be enough to effectively assess individual susceptibility to the adverse outcome of Sars-Cov-2 infection in HIV-infected individuals.

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