Are People Living With HIV at Greater Risk for COVID-19?

Two new studies come to different conclusions about the risk for severe illness and death.

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People with HIV had a higher risk for severe COVID-19 in a new analysis from the World Health Organization (WHO) that mainly looked at people in South Africa. In contrast, the largest study to date from the United States did not see a similar association. However, neither study considered the effect of CD4 T-cell levels, which may be a key risk factor for poor COVID-19 outcomes. Both studies were presented at the International AIDS Society Conference on HIV Science (IAS 2021).

In the early days of the COVID-19 pandemic, many people living with HIV were concerned about whether they were more likely to develop severe COVID-19 because immune suppression is a risk factor for worse outcomes. Early on, small studies suggested that people living with HIV were not more likely to develop severe COVID-19 or die from it. But as time went on, larger studies began to show that people with HIV and COVID-19 have a modestly increased risk for severe illness and death.

The new studies presented last week do not clear up the confusion, but they do shed more light on risk factors for poor outcomes.

WHO Analysis

Silvia Bertagnolio, MD, of the World Health Organization presented findings from a large analysis of data reported to the WHO Global Clinical Platform. Although the study included more than 15,000 people with HIV who were hospitalized with COVID-19 in two dozen countries, the vast majority (95%) were from South Africa.

The researchers looked at 15,522 people living with HIV, who made up 9.2% of the 268,412 hospitalized COVID-19 patients from 37 countries in the database through the end of April 2021. Nearly two thirds were women (792 of whom were pregnant), and the average age was approximately 46 years. Although 92% of those whose treatment status was known were on antiretroviral therapy, these data were available for only 60%. Underlying health conditions were common, including hypertension (33%), diabetes (23%) and obesity (17%).

More than a third (36%) of the HIV-positive people had severe or critical illness at the time of

hospital admission, defined as a low oxygen level; admission to an intensive care unit (ICU); treatment for shock; or receiving oxygen therapy, mechanical ventilation or extracorporeal membrane oxygenation. Among the severe cases, 90% were ages 65 or older. Overall, nearly a quarter died in the hospital (17% of those with mild to moderate illness and 35% of those with severe or critical illness).

Having HIV was independently associated with a 13% higher risk for severe or critical illness after adjusting for age, sex and comorbidities and a 30% higher risk of dying in the hospital after also adjusting for COVID-19 severity. Older age (over 65 years), male sex, hypertension and diabetes were also associated with an increased risk for severe illness and death.

“HIV infection is a significant independent risk factor for both severe/critical COVID-19 presentation at hospital admission and in-hospital mortality,” the researchers concluded. “The increased risk of poor outcomes in people living with HIV hospitalized for COVID should be considered when prioritizing SARS-CoV-2 vaccine among vulnerable groups.”

The study has some limitations, however, including lack of information about HIV treatment status for 40% of the patients, inconsistencies in how different countries reported hospitalizations and lack of data about CD4 counts and viral load. While most people in the database were from South Africa, Bertagnolio noted that a sensitivity analysis that excluded these patients showed similar results. However, when the data were divided by region, HIV remained an independent risk factor for death in Africa but not in Europe or the Americas.

United States Analysis

Matthew Durstenfeld, MD, of the University of California at San Francisco, presented findings from the largest study to date of people with HIV hospitalized with COVID-19 in the United States. The researchers hypothesized that since HIV-positive people are more likely to have cardiovascular risk factors, they also may be at higher risk for cardiovascular complications and mortality related to COVID-19.

This analysis included all adults hospitalized with COVID-19 through December 2020 at 107 hospitals participating in the American Heart Association’s COVID-19 Cardiovascular Disease Registry. Among the 21,528 patients in the database, 220 were living with HIV. People with HIV were, on average, younger than HIV-negative people (56 versus 62 years), and more likely to be men (72% versus 54%), Black (51% versus 25%), current smokers (13% versus 7%) and on Medicaid (45% versus 25%). Body mass index and rates of hypertension, diabetes and other comorbidities were similar.

Thirty-six people with HIV (16%) died in the hospital, compared with 3,290 HIV negative people (15%), which was not a statistically significant difference. After adjusting for age, sex, race and insurance status, HIV was not independently associated with in-hospital mortality, the researchers concluded. This remained the case after adding body mass index and comorbidities. Interestingly, the fully adjusted odds ratio of 1.14 in this study was similar to the 1.13 in the WHO study, but, based on the overall numbers, it reached the threshold for statistical significance in the first study

but not the second.

Having HIV was also not significantly associated with severity of illness, ICU admission (27% for HIV-positive versus 31% for HIV-negative patients), mechanical ventilation (21% versus 19%), major adverse cardiac events (19% versus 18%), COVID-19 clinical trial enrollment (9% in both groups) or length of stay (six days for both groups).

Again, this study was limited by the fact that it did not look at HIV treatment status, CD4 count or HIV viral suppression.

Spanish Risk Factor Study

But a smaller study by Daniel Kwakye Nomah, MD, and coinvestigators with the Spanish PISCIS cohort group did look at these and other risk factors for adverse COVID-19 outcomes among people living with HIV.

PISCIS is a population-based cohort of HIV-positive people (ages 16 or older) receiving care at 16 hospitals in Catalonia. The researchers collected sociodemographic and clinical data through December 2020 and linked it with a public health database to obtain information about COVID-19 diagnoses and other comorbidities.

Of the 13,142 people with HIV in the cohort, 749 (5.7%) had a confirmed diagnosis of SARS-CoV-2, the coronavirus that causes COVID-19. Most of these (83%) were men, and the median age was 44 years. Most (83%) were on antiretroviral treatment with viral suppression, and the median CD4 count was approximately 700. About two thirds had at least one underlying health condition, and nearly a quarter had three or more comorbidities.

Men who have sex with men, migrants and people with multiple comorbidities were more likely to be diagnosed with SARS-CoV-2; people who inject drugs were less likely to contract the coronavirus.

Of the 749 diagnosed individuals, 103 (14%) were hospitalized, seven (0.9%) were admitted to the ICU and 13 (1.7%) died.

People over age 75 were nearly four times more likely to have severe COVID-19 outcomes, compared with younger ones. Other risk factors for severe illness were non-Spanish origin and chronic comorbidities, including neuropsychiatric, autoimmune, respiratory and metabolic conditions. Some specific comorbidities that stood out in other studies—such as hypertension, diabetes and obesity—were not significantly associated with increased risk when considered alone. But having multiple comorbidities upped the risk: Those with four or more chronic conditions were 22 times more likely to have severe outcomes.

Most notably, lower CD4 count and detectable viral load were associated with more severe COVID-19 outcomes. However, when considering the two factors together, a CD4 count below 500 was linked to worse outcomes among people with a detectable viral load, but the difference was

not statistically significant among those with viral suppression.

Based on these findings, Nomah recommended that HIV-positive people with unsuppressed viral load, a low CD4 count and multiple comorbidities should go to the front of the line for COVID-19 vaccines.

Although concerns about increased risk remain unresolved, most experts—including WHO and the U.S. Centers for Disease Control and Prevention—agree that HIV-positive people in general should be prioritized for COVID-19 vaccination. Findings from these studies also raise the question of whether people with HIV—especially those with more advanced immune suppression—should receive an additional booster dose, which has been shown to help organ transplant patients taking immunosuppressive drugs.

Unfortunately, however, vaccine supplies remain severely limited in many of the countries that have the highest HIV burden, highlighting the need for global vaccine equity. International AIDS Society president Adeeba Kamarulzaman, MBBS, said she hoped IAS 2021 would galvanize the medical community to demand global vaccine access, just as the 2000 International AIDS Conference in Durban, South Africa, galvanized the community to ensure access to antiretroviral therapy for people in low-income countries.

“It is unacceptable that, as of today, less than 3% of the entire African continent has received a single dose of the vaccine and less than 1.5% have received both doses,” she said.

The study findings also underscore the importance of people with HIV learning their status, starting treatment, achieving viral suppression and managing comorbidities, according to Bertagnolio.

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