

Covid-19 Impacts on People with HIV

Since its outbreak in the spring of 2020, the Covid-19 pandemic has greatly threatened human's health and lives. People living with HIV who are not taking antiretroviral treatment (ART), have a low CD4 cell count—particularly those with advanced HIV disease, and are at increased risk of opportunistic infections and AIDS related complications. However, there is evolving and conflicting evidence whether people living with HIV have an increased risk of acquisition of SARS-CoV-2 infection and/or Covid-19 clinical complications compared to the general population. Many people with HIV have one or more comorbidities—such as obesity, diabetes mellitus, cardiovascular disease, liver disease (especially cirrhosis), chronic kidney disease, pulmonary disease, cancer, smoking history, and co-infections like tuberculosis—which may put them at increased risk for Covid-19 acquisition and complications.

Several case report series and small cohort studies among hospitalized Covid-19 patients with HIV have shown comparable clinical outcomes and similar risk of SARS-CoV-2 infection when compared with general population, particularly in those with well controlled HIV infection (on ART and with a CD4 count > 200 cells/mm³ and suppressed viral load). These limited clinical data suggest the mortality risk in people with HIV is associated with known Covid-19 factors such as older age and presence of comorbidities including cardiovascular disease, diabetes, chronic respiratory disease, and obesity [1–3].

There have been several systematic and non-systematic reviews that evaluated Covid-19 outcomes among people with HIV; most have found comparable outcomes of mortality and morbidity when compared with HIV negative patients [4–8]. Methods did not always include assessment of outcomes while controlling for known Covid-19 risk factors [8]. There is also limited data in patients with advanced HIV disease (i.e., low CD4 cell count).

One systematic review, notably published as a pre-print, found of 144,795 hospitalized Covid-19 patients in North America, Europe, and Asia the pooled prevalence of HIV in Covid-19 patients was 1.22% [95% (CI): 0.61%-2.43%] translating to a 2-fold increase compared to the respective local-level pooled HIV prevalence in the general population of 0.65% (95% CI: 0.48%-0.89%) – which hinted at a potential susceptibility among people with HIV [9].

Additional data on this topic come from several cohort studies from South Africa, the USA and the UK [10–12] have reported a moderate increased risk of death directly attributed to HIV infection after adjustments for age, sex, ethnicity and presence of comorbidities; an unpublished meta-analysis including these studies found that the risk of death was almost double that of HIV-negative patients; however, confounding by comorbidities associated with increased risk of severe Covid-19 cannot be ruled out [13].

Covid-19 also brings adverse effects on the diagnosis, treatment, and vaccination of people with HIV. Due to the pandemic, an estimated 100,000 HIV tests were not performed in 2020 among the 8 EU/EEA countries (including Belgium, Bulgaria, Czech Republic, Estonia, France, Latvia, Poland, Portugal, Romania, and Slovenia) that reported data on testing. This resulted in 7,500,000 tests in 2020 down from 9,000,000 in 2019 (a 18% decrease in HIV tests). In the WHO Europe region, an estimated over 1,000,000 HIV tests were not performed last year, resulting in 57,000,000 tests in 2020 versus 70,000,000 in 2019 (18% decrease). This is because 60% of countries in WHO Europe reported < 50% decrease in HIV testing between March-May 2021 [14–17]. Impacts of Covid-19 on HIV testing has led to impacts on HIV diagnosis. In WHO Europe, an estimated 25,143 individuals living with HIV were not diagnosed in 2020 because of the pandemic. This resulted in 104,765 new diagnoses in 2020

down from 136,449 in 2019 (a 26% decrease in HIV diagnoses) [14]. In addition, up to 70% of HIV clinics were disrupted in WHO Eastern Europe countries with 60% of physicians sharing HIV and Covid-19 care duties [18]. Case studies across WHO Europe show that 4% of people living with HIV (approximately 60,000) reported an interruption of ART due to lockdowns and that 6% (around 120,000) were unable to go collect ART due to mobility restrictions. Around 30% of people living with HIV in WHO Europe had to adapt their HIV care during the pandemic, facilitating an increase in the use of telehealth services. In addition, some EU countries (including Romania, Italy, Portugal, and Ireland) experienced shortages in HIV medicines and the discontinuation of pre-exposure prophylaxis (PrEP) programmes [19–21]. Another issue is that people with HIV were not prioritised for Covid-19 vaccination in around 60% of countries in WHO Europe and only 14% had national guidelines for the vaccination of people living with HIV [22]. Covid-19 also has impacts on the mental health of people with HIV. Case studies across WHO Europe show that around 40% of people with HIV had mild to severe psychological distress since the Covid-19 outbreak and had a need for psychosocial support. Among this group, 70% reported feeling more depressed and anxious and 19% considering suicide [17,23].

Protecting people living with HIV during the Covid-19 pandemic, and ensuring they can maintain treatment, is critical. Hereby are some Covid-19 guidance for people with HIV.

Guidance for All People with HIV

- People with HIV should follow all applicable recommendations of their local centres for Disease Control and Prevention to prevent acquisition of SARS-CoV-2, such as practicing social or physical distancing, wearing masks consistently, avoiding crowded areas, and using proper hand hygiene.
- People with HIV should receive the full series of a Covid-19 vaccine (including booster doses if applicable), regardless of CD4 count or viral load, because the potential benefits outweigh potential risks. Preliminary data in people with HIV who have received Covid-19 vaccines indicate good responses in those well controlled on ART with normal CD4 counts, but diminished responses in those with advanced or untreated HIV infection [24–26].
- Influenza and pneumococcal vaccinations should be kept up to date. These vaccines, as well as other vaccines, can be administered with Covid-19 vaccines during the same health care visit.

General Management Considerations in People with HIV

Although some ART (e.g., lopinavir/ritonavir, boosted darunavir, tenofovir disoproxil fumarate/emtricitabine) have been evaluated in clinical trials to treat or prevent Covid-19, at this time, no ART have been shown to be effective in these settings [27,28]. People with HIV should not switch their ARV regimens or add ARV drugs to their regimens for the purpose of preventing or treating SARS-CoV-2 infection without prior consultations with their healthcare providers. People with HIV should also make every effort to maintain an adequate supply of ART and all other concomitant medications, which may include exploring options for alternative delivery, such as changing the delivery of medications to mail order, when possible.

Clinic or Laboratory Monitoring Visits Related to HIV Care

When there is substantial community transmission of SARS-CoV-2

- People with HIV should weigh the risks and benefits of attending versus not attending in-person HIV-related clinic appointments. Factors to consider include the extent of local Covid-19 transmission, health needs that will be addressed during the appointment, HIV status (e.g., CD4 count, HIV viral load), interval since last laboratory testing, need for vaccinations, and overall health.
- Telephone or virtual visits for routine or non-urgent care and adherence counselling may replace face-to-face encounters.

Guidance for People with HIV in Self-Isolation or Quarantine Due to SARS-CoV-2 Exposure

- Patients should contact their health care providers to report that they are self-isolating or in quarantine.
- Patients should verify that they have adequate supplies of all medications and expedite additional drug refills as needed.
- Patients should get ready for a possible transfer to a Covid-19 care facility in case they develop Covid-19 related symptoms.

Guidance for People with HIV Who Have Signs and Symptoms Consistent with or Documented SARS-CoV-2 Infection

- Patients are advised to follow their governments' recommendations regarding symptoms of Covid-19 and call their health care providers for medical advice if they develop a fever and symptoms (e.g., cough, dyspnoea). New onset or worsening dyspnoea warrants in-person evaluation.
- Patients should call their clinic in advance before presenting to the care providers.
- Patients should always use respiratory, hand hygiene, and cough etiquette when presenting to a health care facility, and they should wear a face mask.
- Upon arrival to a health care facility, patients should alert registration staff of their symptoms if they have not called in advance, so that measures can be taken to prevent Covid-19 transmission in the health care setting. Specific clinic actions include placing a mask on the patient and rapidly putting the patient in a room (if available, a negative-pressure room) or other space separated from people.

Special Considerations for Pregnancy, HIV, and Covid-19

- Currently, data on pregnancy and maternal outcomes in individuals who have Covid-19 and HIV are limited.
- Covid-19 treatment and vaccination should not be withheld from pregnant individuals with HIV.
- Pregnant individuals with HIV admitted for Covid-19 should continue their ARV regimen. Individuals not virally suppressed should consult with clinicians and/or HIV experts to check if any changes in ARV regimens are needed.

Children with HIV

Knowledge to date about Covid-19 in children and in children with HIV can be summarized as follows:

- Minimal data exist on Covid-19 among children with HIV infection. One report from South Africa of 159 children with Covid-19 included two children with HIV [29]. Although both children with HIV were hospitalized, only one was symptomatic, and neither died. HIV infection did not seem to contribute to more severe Covid-19 [30].
- Children appear less likely to become severely ill with Covid-19 than adults [31–34].
- Some subpopulations of children at higher risk for more severe Covid-19 may exist: younger age (younger than 12 months), obesity, underlying pulmonary or cardiac pathology or neurologic disease, and immunocompromising conditions are associated with more severe outcomes [35–38].
- A multisystem inflammatory syndrome in children (MIS-C) presenting with hyperinflammatory shock, with features of Kawasaki disease and toxic shock syndrome, is associated with SARS-CoV-2. The syndrome usually occurs 2 to 4 weeks or more following infection. More than 6,400 cases have been reported in the United States alone, with more than 50 MIS-C-related deaths as of January 2022. The children have serologic evidence of infection but may not have a positive nasopharyngeal reverse transcription-polymerase chain reaction test result [39–41]. Children can present with diverse signs and symptoms, including fever and gastrointestinal symptoms; significantly elevated markers of inflammation; and, in severe cases, myocarditis and cardiogenic shock. Children with MIS-C tend to be older (mean age 8–9 years) than in classic Kawasaki disease (peak incidence at age 10 months) [42–45].
- Infants and children with HIV should be current on all immunizations, including influenza and pneumococcal vaccines.
- Recommendations in the Guidance for All People with HIV section above are applicable for children with HIV.

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