Factors Associated with HIV Viral Suppression in People Followed in an Outpatient Clinic in Angola During and After the COVID-19 Pandemic

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Calcagno Andrea[1], Pizzi Costanza[2], Pocongo Barbara[3], Ronzoni Niccolò[4], Alladio Francesca[1], Ngiambudulu M. Francisco[5], Kalume Alberto[6], Di Perri Giovanni[1], Gobbi Federico[4,7].

[1] Unit of Infectious Diseases, Department of Medical Sciences, University of Torino, Italy; [2] Cancer Epidemiology Unit, Department of Medical Sciences, University of Turin and CPO Piemonte, Turin, Italy; [3] Instituto Nacional de Luta Contra SIDA – MINSA, Luanda, Angola; [4] Department of Infectious - Tropical Diseases and Microbiology, IRCCS Sacro Cuore Don Calabria Hospital, Negrar (VR), Italy; [5] Grupo de Investigação Microbiana e Imunológica, Instituto Nacional de Investigação em Saúde (National Institute for Health Research), Luanda, Angola; [6] Hospital Divina Providência, Luanda, Angola; [7] Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy.

Running Title: COVID-19 and HIV viral load in Angola

Type of article: Research Letter

Word count: 1199

Figures: 1

Tables: 1

Corresponding Author:
Andrea Calcagno
Unit of Infectious Diseases
Amedeo di Savoia Hospital
C.so Svizzera 164, 10149 Torino, Italy
+390114393884
andrea.calcagno@unito.it

Keywords: Virological suppression, Adherence, COVID-19, integrase inhibitors.

Ending the acquired immunodeficiency syndrome (AIDS) epidemic is one of the most relevant health challenges the world is facing. The COVID-19 pandemic led to a severe disruption in health programs worldwide: travel restrictions, avoidance of health facilities, limitations in supply chains, and redirection of resources affected HIV preventive and treatment services.[1] As a consequence, HIV testing and new antiretroviral treatment (ART) initiation declined in 2020 and this effect was more pronounced according to the stringency of pandemic measures.[2] Despite this, HIV services showed a variable resilience, and the effect on virological suppression rates is debated. While some studies showed no decline in viral load suppression rates in ART-treated patients, some others did.[3–5] Data in African countries showed consistent service disruption (including a higher chance patients had of running out of medicine during the lockdown in Uganda) but no change in virological suppression rates.[2,6] However, the consequences of such service disruption on disease progression, selection of resistance-associated mutations, and transmission to others are mostly unknown. The study aimed to analyze factors (including COVID-19) associated with HIV virological suppression of treated PLWH in Luanda (Angola) in a large outpatient clinic.

This study was approved by the Comité de Ética do Ministério da Saúde (Ethics Committee of the Angolan Ministry of Health) with a reference number: 06/CEMS/2024. Pseudo-anonymous data were extracted from the outpatient clinic database from January 2017 until April 2022. Care for PLWH was done according to Angolan guidelines. Among those patients who had at least one visit in a given year (2017, 2018, and 2019) we calculated the proportion who had no visits in the following year or the following two years. We then analyzed the median time between each patient's visits and between each patient's HIV RNA measurement by period of visit/measurements respectively. In particular, three periods were identified: before (period 1), during (April 2020 to March 2021, period 2), and after (period 3) the tightest COVID-19 restrictions. Finally, we estimated the effect of the quarter of HIV RNA measurement on virological control. This analysis was restricted to patients with at least one measurement before and after April 2020, on antiretroviral treatment for at least 12 months, and for whom HIV RNA was measured within 3 years from the clinical visit. Two outcomes of interest were identified: virological suppression (VS, defined as HIV RNA <50 copies/mL) and virological failure (VF, defined as HIV RNA >1000 copies/mL). To account for the within-patient correlation population-averaged panel data regression models were fitted, using generalized estimating equations with binomial family, logit link, and within-patient exchangeable correlation structure. Estimates are therefore expressed as Odds Ratios (OR) and their corresponding 95% Confidence Intervals (CI). The first quarter of 2017 was used as a reference period. Gender, age, treatment type and treatment duration since the start of follow-up were treated as potential confounders. Antiretroviral therapy was analyzed at the beginning of follow-up and changes over time were also recorded.

Of the 6023 patients (whose characteristics are shown in Table 1), we assessed 26044 visits. Among patients who had at least one visit in 2017, 16.5% did not visit in 2018, and 12.3% did not visit in

either 2018 or 2019. The percentages for individuals who had at least one visit in 2018 were slightly higher, at 18.6% (no visits in 2019) and 14.7% (no visits in 2019 or 2020). However, the proportion of those who were lost to care was much higher among the patients who had at least one visit in 2019, with 45.8% of patients with no visits in 2020 and 26.5% having no visits in either 2020 or 2021. The median time between visits differed across periods being higher in period 2 [9.9 months (IQR 1.1-16)] and 3 [8.5 months (IQR 1.2-17.2)] than in period 1 [4.9 months (IQR 1.1-9.2) (p-value from non-parametric test on the equality of the medians <0.001). For the virological efficacy analysis, we included 3505 patients (whose features are described in Table 1) who contributed to 7801 visits with measured HIV RNA during the study period. Also, the median time between viral loads measurements was observed to be higher in period 2 [17.4 months (IQR 13.1-25)] and 3 [22.2 months (IQR 16.9-29.1)] as compared to period 1 [12.8 months (IQR 8.8-17.3)] (p-value from the non-parametric test on the equality of the medians <0.001). VS and VF are depicted in Figure 1. Male patients showed lower rates of virological control (71.2% vs. 75.5% <50 copies/mL and 83.8% vs. 86.1% <1000 copies/mL, p values <0.001). Participants on second-line treatments had lower rates of VS (51.3% <50 copies/mL and 72.1% <1000 copies/mL, p values <0.001). At multivariable analysis care during the third quarter of 2020 is associated with the highest increase in the odds of VF (OR 1.93, 95%CI 1.06-3.53, p=0.03) and of non-VS (OR 2.77, 95%CI 1.52-5.03, p=0.001).

The COVID-19 pandemic had a substantial impact on HIV services with a potentially relevant effect on HIV prevention and care. Despite this, the impact on VS, selection of resistant strains, and HIV transmission in PLWH was less clear.[4,7] Data on the impact of anti-COVID-19 measures on HIV services have not been reported for Angola and the prevalence of PLWH with a suppressed viral load was missing in UNAIDS reports in 2021 and 2022.[8] We sought to examine the time between visits and the percentage of virological suppression in an HIV program in Luanda, Angola's capital. In the large population studied at the Hopital Divina Providência outpatient HIV clinic, we find that the interval between visits was much longer in 2020 and 2021, and numerous patients were lost to follow-up following the COVID-19 lockdown. This was also reported in other studies in African countries and implemented strategies seemed effective for service resilience.[4,9] In our population of mostly female PLWH treated with NNRTIs (with an increase over time in dolutegravir use paralleling the national transition to dolutegravir-based regimens), 87.5% had an HIV RNA <1000 copies/mL with 12.1% of participants presenting a low-level viremia. Our multivariate analysis suggested that the third quarter of 2020 was the period with the highest odds of VF (1.93) and HIV viremia (2.77). After 2020 we confirm the trend observed in other studies of a risk that was comparable to pre-pandemic periods. Despite not being the primary objective of our analysis, we observed a lower rate of virological control in males (83.8%) and in participants on protease inhibitor-based second-line treatment (71.1%). These may be due to the target population for increased adherence interventions and for assessing the reasons for poor virological control. Data on HIV drug resistance-associated mutations in Angola are lacking in the WHO report. Among the study limitations, we should

acknowledge the observational design, the lack of detailed information on drug resistance, and the potential follow-up of patients at other HIV services in Luanda.

In conclusion, we found a shift in HIV care during the COVID-19 crisis, with a higher likelihood of virological failure and HIV viremia peaking in the third quarter of 2020. Afterward, the risk was significantly lower with 87.5% of patients in care having an HIV RNA below 1000 copies/mL. Male patients and those on second-line treatments showed lower rates of virological control, indicating a need for customized evaluation and intervention.

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Figure and Table Legends

Table 1. Demographic, clinical and virological features of the included participants. Data are expressed as number (percentage) or mean (± standard deviation)

Figure 1. Prevalence of HIV RNA measurements <50 (white), 50-999 (orange) and >1000 copies/mL (red) according to the month and year samples were tested.