SHORT COMMUNICATION

Evaluating virological outcomes in people with HIV on stable antiretroviral therapy with reduced frequency of HIV viral load monitoring during the COVID-19 pandemic

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Abstract

Objectives: In response to the COVID-19 pandemic, HIV outpatient attendances were restricted from March 2020, resulting in reduced frequency of HIV viral load (VL) monitoring (previously 6-monthly) in clinically stable and virologically suppressed people living with HIV (PLWH). We investigated virological outcomes during this period of reduced monitoring and compared with the previous year, prior to the COVID-19 pandemic.

Methods: People living with HIV with undetectable VL (<200 HIV RNA copies /mL) on antiretroviral therapy (ART) were identified from March 2018 to February 2019. We determined VL outcomes during the pre-COVD-19 period (March 2019–February 2020) and the COVID-19 period (March 2020–February 2021) when monitoring was restricted. Frequency and longest durations between VL tests in each period were evaluated, and virological sequelae in those with detectable VL were determined.

Results: Of 2677 PLWH virologically suppressed on ART (March 2018–February 2019), VLs were measured and undetectable in 2571 (96.0%) and 2003 (77.9%) in the pre-COVID and COVID periods, respectively. Mean (SD) numbers of VL tests were 2.3 (1.08) and 1.1 (0.83) and mean longest duration between VL tests was 29.5 weeks (SD 8.25, 3.1% were ≥12 months) and 43.7 weeks (12.64, 28.4% were ≥12 months), in the pre-COVID and COVID periods, respectively. Of 45 individuals with one or more detectable VL during the COVID-19 period, two developed new drug resistance mutations.

Conclusion: Reduced VL monitoring was not associated with poorer virological outcomes in the majority of stable individuals receiving ART. One in 20 individuals had not returned for VL testing after ≥31 months and the risk of harm in these individuals is unknown.

INTRODUCTION

Since 2016, the World Health Organization (WHO) and national guidelines have recommended the initiation of anti-retroviral treatment (ART) for all adults living with HIV regardless of WHO HIV clinical stage or CD4 T-cell count [1]. Although routine HIV viral load (VL) monitoring is recommended by the WHO [1] and many national HIV guidelines [2–4], there is a lack of consensus on the optimal interval between routine HIV VL tests for people living with HIV who are virologically suppressed on ART. The British HIV Association (BHIVA) recommends that HIV VL testing should be performed routinely every 6 months, with intervals of up to 12 months for people established on ART regimens that include a protease inhibitor (PI) [2].

Preliminary observational studies suggest that reduced frequency of HIV VL monitoring is not associated with an increased rate of ART failure [5, 6], whereas a modelling study from Uganda suggests that an adaptive approach to HIV VL monitoring frequency based on previous VL measurements may be optimal for maintaining good care while reducing costs [7].

In the UK, people living with HIV (PLWH) can access HIV care and ART free at the point of care, provided by the National Health Service. Individuals can register at any HIV centre in the UK and are not required to access HIV care from their local HIV service. Once registered at a HIV centre, individuals are generally seen at the same centre for their HIV care, monitoring and provision of antiretroviral medication. When an individual does not attend for HIV care at the HIV centre they are registered with after a period of time, usually >12 months, the HIV centre will attempt to make contact with the patient, inviting them to reattend for HIV care. In response to the COVID-19 pandemic, non-essential in-person outpatient attendances across the UK were restricted from March 2020, with gradual resumption over the following 2 years. Such clinic attendances were also encouraged to be delayed during periods of COVID-19 infection surges. This resulted in an enforced reduced frequency of HIV VL monitoring from national recommendations in people accessing HIV care who were virologically suppressed on ART across the UK.

The primary aim of our study was to investigate virological outcomes in clinically stable people who were virologically suppressed on ART and who were advised to defer their routine HIV outpatient attendance during the COVID-19 pandemic, compared with virological outcomes during the previous year, when routine monitoring was taking place.

METHODS

Study setting and ethical considerations

We conducted a retrospective case note review of people on ART accessing care at a HIV tertiary care centre based at Imperial College Healthcare NHS Trust, London, UK. All data were obtained as part of clinical care, anonymized and then collated for analysis. As per the National Research Ethics Service guidelines, additional patient consent and ethical approval were not required.

Eligibility criteria

Inclusion criteria were all people with an undetectable HIV VL (defined as <200 HIV RNA copies/mL) between 1 March 2018 and 28 February 2019. People were excluded if they had one or more detectable HIV VL measurements during this time period, were not on ART for ≥6 months or had interrupted ART.

Data collection

Clinical data collected included baseline demographics, date of ART start, HIV-specific parameters (most recent and nadir CD4 T-cell count and all sequential HIV VL results and dates of measurements) and clinical outcomes including new HIV drug resistance mutations during the study period. Individuals who did not have a HIV VL measurement during the COVID-19 period were followed up until the 22 September 2022 to establish whether they returned for a HIV VL test.

Outcome measures

HIV VL outcomes in people on ART for ≥6 months with undetectable HIV VL between 1 March 2018 and 28 February 2019 were determined for the pre-COVID-19 period (1 March 2019–29 February 2020) when routine HIV VL monitoring was being carried out. These were then compared with the VL outcomes in the COVID-19

period (1 March 2020–28 February 2021) when reduced HIV VL monitoring was being carried out in the subset who were suppressed on ART during the pre-COVID-19 period.

Secondary outcomes were frequency of HIV VL testing and longest duration between consecutive HIV VL tests in each period and virological sequelae, including emergent HIV drug resistance mutations, in those with detectable HIV VL during the COVID-19 period.

Statistical analyses

Descriptive statistics summarized variables using median (interquartile range, IQR), mean (SD) and total (percentage), as appropriate. All statistical analyses were conducted using Excel version 2206 (Microsoft Corporation, Redmond, WA, USA).

RESULTS

Of 3264 people registered at the centre between 1 March 2018 and 28 February 2019, 3231 had been taking ART for ≥6 months. Of these, 3006 had at least one plasma HIV VL measurement between 1 March 2018 and 28 February 2019; 2677 of these were virologically suppressed and formed the study population. Among this population, median (IQR) age was 51 years (42–58), 2042 (76.3%) self-identified as male or transgender male, 633 (23.6%) self-identified as female or transgender female and gender was unknown in two (0.1%) individuals. The majority of individuals were of white [1329 (49.6%)] or Black African/Caribbean [713 (26.6%)] ethnicities, 102 (3.8%) individuals were of Asian ethnicity and 330 (12.3%) individuals were of mixed ethnicity; ethnicity was not documented in 203 (7.7%) individuals. Overall, 1603 (59.9%) of individuals identified sex between men and 857 (32.0%) identified heterosexual intercourse as their main routes of HIV acquisition. In total, 115 (4.3%) acquired HIV perinatally, six (0.2%) via injecting drug use, three (0.1%) via blood transfusion and it was not documented in 93 (3.5%) individuals. Median most recent and nadir CD4 counts were 697 and 240 cells/μL, respectively.

Primary outcome

Among study participants, plasma HIV VLs were measured during the pre-COVID-19 period in 2661 (99.4%) individuals, of whom 2571 (96.6%) remained virologically suppressed over this time (Figure 1).

Of this latter group, plasma HIV VLs were measured during the COVID-19 period in 2048 (79.7%) individuals, with 2003 (97.8%) remaining virologically suppressed and 45 (2.2%) having at least one plasma VL measurement > 200 copies/mL (Figure 1). The remaining 523 (20.3%) individuals did not return for a plasma HIV VL measurement during the COVID-19 period (Figure 1).

Secondary outcomes

Mean (SD) numbers of VL tests per year were 2.3 (1.08) and 1.1 (0.83) for the pre-COVID-19 and COVID-19 periods, respectively. The mean (SD) longest durations between VL tests were 29.5 weeks (8.25) and 43.7 weeks (12.64) for the pre-COVID-19 and COVID-19 periods, respectively. The longest duration between VL tests was ≥12 months in 3.1% and 28.4% of individuals during the pre-COVID-19 and COVID-19 periods, respectively (Table 1).

Of the 45 people with one or more detectable plasma HIV VL measurements during the COVID-19 period, two (4.4%) developed new major HIV drug resistance mutations. Both these individuals had a history of intermittent adherence to ART and engagement with HIV care in the years prior to 2018. As a comparison, of the 90 individuals with one or more detectable plasma HIV VL measurements during the pre-COVID-19 period, six (6.7%) developed new major HIV drug resistance mutations. Of the 523 individuals without HIV VL testing during the COVID-19 period, 369 (70.6%) individuals subsequently had one or more undetectable plasma HIV VL measurements consistently, 14 (2.7%) individuals had one or more detectable plasma HIV VL measurements and 140 (26.7%) still had not returned for HIV VL measurement, as of the 22 September 2022. Among the 523 individuals who did not have a HIV VL test performed at our centre during the COVID-19 period, median (IQR) age was 51 years (43–59), 423 (80.9%) self-identified as male or transgender male, 99 (18.9%) self-identified as female or transgender female on 1 (0.2%) was of unknown gender. Median most recent and nadir CD4 counts were 710 and 250 cells/μL, respectively. Of the 14 individuals with detectable plasma HIV VLs and the 140 individuals who had not returned for HIV VL measurement, median (interquartile) ages were 49 (43–54) and 49 (40–57), respectively, nine (64%) and 120 (86%) self-identified as male or transgender male, median most recent CD4 counts were 648 and 729 cells/μL, respectively, and median nadir CD4 counts were 170 and 280 cells/μL, respectively. Of these 14 individuals with one or more detectable plasma HIV VL measurements, six subsequently resuppressed, four developed new major HIV drug resistance mutations and four disengaged from HIV care with our centre.
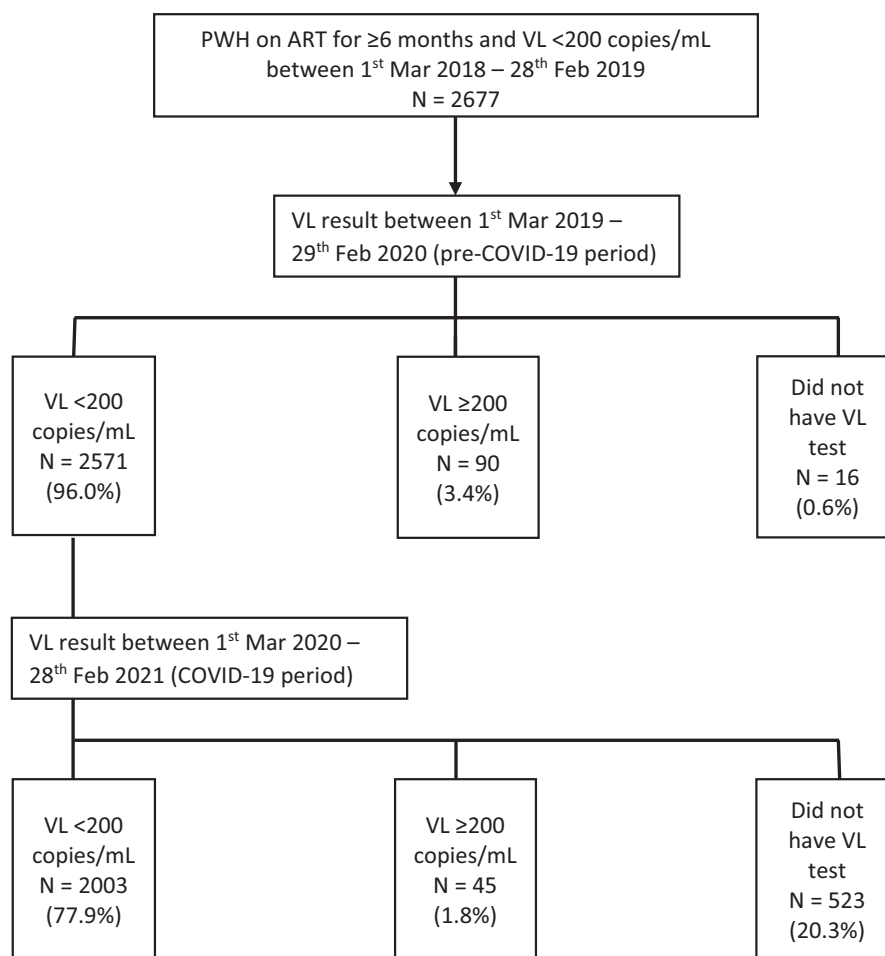
Abbreviations: PWH = people with HIV, ART = antiretroviral treatment, VL = plasma viral load (HIV RNA copies/mL)

FIGURE 1 Flowchart of virological outcomes in people living with HIV (PLWH) who were previously stable on antiretroviral treatment (ART), between 1 March 2018 and 28 February 2021.

TABLE 1 Longest duration between HIV viral load (VL) tests in people living with HIV stable on antiretroviral treatment (ART) with HIV VL tests performed during the pre-COVID-19 period (1 March 2019 to 29th February 2020) and COVID-19 period (1 March 2020 to 28 February 2021).

Time period	Longest duration between HIV VL tests				
	<6 months	**6 to <9 months**	**9 to <12 months**	**12 to <15 months**	**≥15 months**
1 March 19–29 February 20 (pre-COVID-19 period) (N = 2661)	732 (27.5%)	1665 (62.6%)	182 (6.8%)	61 (2.3%)	21 (0.8%)
1 March 20–28 February 21 (COVID-19 period) (N = 2048)	216 (10.5%)	463 (22.6%)	788 (38.5%)	528 (25.8%)	53 (2.6%)

Note: Results are total (percentage).

DISCUSSION

The lack of consensus on the optimal interval between routine HIV VL monitoring is well recognized [6]. HIV VL monitoring is associated with significant costs, and determining the ideal balance between minimizing frequency of routine HIV VL monitoring with maximizing chances of detecting virological failure is important [8].

Using data from a cohort of >2600 clinically stable adults with HIV who were already on virologically

suppressive ART, it was reassuring the see that the enforced reduction in HIV VL monitoring during the COVID-19 pandemic was not associated with poorer virological outcomes in the majority of individuals. However, a proportion of these individuals still had not returned for HIV VL testing after more than 31 months and the risk of clinical harm in these individuals is not yet known.

Our results are in keeping with other published studies performed in HIV outpatient settings in the USA, Italy and Malawi [9–12] where, overall, the incidence of HIV VL non-suppression in people who were previously virologically suppressed on ART was similar before and during the COVID-19 pandemic. This is in contrast to a clinic serving at-risk populations in San Francisco, USA, where odds of HIV viral non-suppression increased significantly during periods of shelter-in-place ordinances [13]. An important point to note is that our analysis only included measured HIV VL and any periods of non-suppression in between HIV VL testing would not be accounted for. Our study is unique because we report on the emergence of new major HIV drug resistance mutations during this period of reduced VL monitoring with consequences on future antiretroviral drug options.

Strengths of our study include the unselected nature of the individuals from a single HIV specialist centre in London, which minimized selection bias. Ours was a longitudinal study, and the individuals served as their own controls within the study. However, this also introduces a limitation as findings from our single centre may not reflect the experiences in different populations of PLWH who may have been affected differently during the COVID-19 pandemic. Furthermore, the COVID-19 global pandemic caused significant social and psychological impact to many people, and behaviours including adherence to ART in the context of the COVID-19 pandemic may be different from adherence patterns before and after the COVID-19 pandemic. Although our findings demonstrate that reduced HIV VL monitoring was not associated with poorer virological outcomes in the majority of people who attended for HIV VL testing at some point during the COVID-19 pandemic, this may reflect survivorship bias as the outcomes of the individuals who had not returned for HIV VL testing after more than 31 months remain unknown. Reassuringly, the proportions of individuals developing HIV drug resistance mutations requiring ART adjustments were similar prior to and during the COVID pandemic. Our dataset does not permit us to understand why some individuals have not returned for HIV VL testing at our centre. It is possible that some individuals may have attended HIV centres elsewhere to receive HIV care and monitoring, as they were unable or reluctant to travel to our centre. Alternatively, whether the lack of attendance for HIV VL testing reflects lack of engagement in HIV care and poor adherence to ART is unknown.

In conclusion, our results suggest that reduced HIV VL monitoring during the COVID-19 pandemic was not associated with poorer virological outcomes in the majority of people who were virologically suppressed on ART, especially in individuals with a history of adherence to ART and engagement with HIV care. Individuals with previous poor adherence to ART may benefit from closer monitoring and enhanced support, especially during periods of uncertainty such as during a global pandemic. The overall impact of reduced HIV VL monitoring after the COVID-19 pandemic warrants further attention to monitor for longer-term harm.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL STATEMENT

All data were obtained as part of clinical care and anonymized. As per the National Research Ethics Service guidelines, additional patient consent and ethical approval were not required.

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