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Original Research Article

Clinical and immunological outcomes in HIV-2 and HIV-1 and 2 co-infections at a tertiary care centre in Maharashtra

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ABSTRACT

Background: HIV-2 and HIV-1 and 2 co-infections are rare but clinically significant subtypes with varying response to treatment and progression of disease exist. Not much data from central India especially Maharashtra is available regarding their immunologic courses. The objective was to examine the sociodemographic characteristics, baseline and follow-up CD4 trends, and antiretroviral therapy (ART) outcomes in HIV-2 and HIV-1 and 2 dually infected patients.
Methods: Retrospective analysis was conducted among 27 patients co-infected with HIV-2 or HIV-1 and 2 who were attending a tertiary ART centre in Maharashtra. Baseline and most recent CD4 counts and ART regimen were analysed. Demographic data, and treatment outcomes like alive on ART, died, transfer out, stopped, and opted out were described using descriptive statistics.
Results: Tenofovir-lamivudine-dolutegravir (TLD) was prescribed in the majority of patients. Mean CD4 baseline count of survivors on ART was 352.3 cells/µl, and recent CD4 improved to 519.3. High mortality was observed in those on protease inhibitor-based regimens (ZL+LPV/r, TL+LPV/r).
Conclusion: TLD-based ART produced better immunological outcome. Protease inhibitor-containing regimens needed in HIV-2, could be associated with poor prognosis in patient on ART.

Keywords: HIV-2, Co-infection, ART, NNRTIs

INTRODUCTION

Human immunodeficiency virus type 2 (HIV 2), less prevalent globally than HIV 1. It is endemic in West Africa and increasingly being detected elsewhere, including India, particularly in Maharashtra and surrounding states.[1] HIV 2 prevalence in Indian research varies from 0.3 to 0.8%, with rates of coinfection of HIV 1 and 2 at ~0.35% in Mumbai.[2]

HIV 2 differs from HIV 1 on the clinical level: it develops more slowly, has lower plasma viral titers, and is much less likely to be transmitted by sexual, vertical, and needle exposure.[3] The genealogical distinction between HIV 2 and HIV 1 is ~55%, giving rise to diagnostic challenge and suggesting that standard HIV 1 testing may miss HIV 2 infections.[4]

Interestingly, HIV 2 is inherently resistant to all non-nucleoside reverse transcriptase inhibitors (NNRTIs) due to natural polymorphisms in the gene of reverse transcriptase and requires integrase strand transfer inhibitor (INSTI-) or PI-based regimens to treat.[5-11] Non-nucleoside reverse transcriptase inhibitor (NNRTI) based regimens, which are common in most first-line HIV 1 treatments are ineffective and lead to treatment failure in HIV 2/dual infections.[12] Management is also complicated by limited access to HIV 2 viral load tests and drug resistance testing; most resource-limited settings can only employ CD4 monitoring in isolation. Meanwhile, World Health Organization (WHO), Department of Health and Human Services (DHHS), British HIV Association (BHIVA), and others highly recommend early initiation of ART, most prominently INSTI-based regimens for HIV 2 and HIV 1/2 coinfected patients.[13]

Given these unique virological and therapeutic challenges, evaluation of real-world immunological outcomes specifically, CD4 trends and ART regimen effect in HIV 2 and dual-infected patients on India's national ART program is needed. This study aims to bridge this evidence gap from a Nagpur-based tertiary ART Centre.

METHODS

This was a retrospective observational study conducted at the antiretroviral therapy (ART) Centre, Government Medical College and Hospital, Nagpur, Maharashtra. The data collected from January 2018 to December 2024 and involved individuals living with HIV (PLHIV) diagnosed with HIV-2 infection or HIV-1 and 2 coinfections under the national HIV testing algorithm.

Selection criteria

Inclusion criteria

Patients were included if they had a verified diagnosis and a minimum of one recorded baseline and follow-up CD4 count.

Exclusion criteria

Incomplete demographic, clinical, or CD4 records were excluded.

Data collection and procedure

Programmatic ART centre records were analyzed using a structured format. Extracted variables were sociodemographic factors, ART regimen, baseline and most recent CD4 counts, and treatment outcomes categorized by national guidelines as alive on ART, died, transferred out, stopped, or opted out.[14] As there are few randomized clinical trials for HIV-2, treatment at the centre conformed to expert guidelines that advised two NRTIs with either an integrase strand transfer inhibitor (INSTI, e.g., dolutegravir) or a boosted protease inhibitor (lopinavir/ritonavir, darunavir/ritonavir).[15] CD4 count was employed as the surrogate immunologic marker since HIV-2 viral load and drug resistance assay were not routinely available in the national AIDS control program.[15,16]

Ethical approval

Institutional Ethics Committee of Government Medical College and Hospital, Nagpur reviewed and approved the study protocol (No-EC/Pharmac/GMC/NGP/3819, Dated 28/08/2025). Patient identifiers were not made during data abstraction to protect confidentiality.

Statistical analysis

Data were analysed with MedCalc® version 10.1.2.0. Descriptive statistics including mean, standard deviation, median, interquartile range (IQR), and range were computed for baseline and latest CD4 counts within outcome groups. CD4 count distributions were plotted with box-and-whisker plots to show central tendency and variability. Distribution of ART regimens by treatment outcome was shown using stacked bar charts for visual comparison.

RESULTS

Demographic features

Twenty-seven patients with HIV-2 or HIV-1 and 2 coinfections were enrolled in the study. The average age at registration was 46.8±10.7 years, ranging from 27–70 years, which reflects that the majority of participants were middle-aged adults. Most patients were men (n=19, 70.4%), and females represented 29.6% (n=8); no transgender patients were recorded within the cohort. Geographically, 85.2% (n=23) of patients were from Nagpur district (urban and rural together), and the rest, 14.8% (n=4), were from other surrounding districts, such as Yavatmal, Gondia, and Chhindwada. Education-wise, 12 patients (44.4%) had reached the college level, 9 (33.3%) had reached the secondary level, 4 (14.8%) had primary education, and 2 (7.4%) were illiterate (Table 1). These results suggest that the cohort was largely urban, male, and well to moderately educated.

Table 1: Demographic characteristics of patients with HIV-2 and HIV-1 and 2 coinfections (n=27).

Variables	N	%
Age (years)		
Mean±SD	46.8±10.7	NA
Range	27-70	NA
Sex		
Male	19	70.4
Female	8	29.6
Transgender	0	0.0
District		
Nagpur (urban + rural)	23	85.2
Other districts	4	14.8
Education level		
Illiterate	2	7.4
Primary	4	14.8
Secondary	9	33.3
College	12	44.4

CD4 count trends

In the present study baseline and recent CD4 counts were compared by treatment outcome categories. Those patients still alive on ART (n=12) had a mean baseline CD4 count of 352.3 cells/µl, which significantly increased to 519.3 cells/µl at most recent follow-up, indicating an optimal immunological response. In contrast, patients who died within the follow-up time (n=7) had a reduced mean baseline CD4 count of 239.4 cells/µl, and their most recent

CD4 count increased only slightly to 289.1 cells/µl, reflecting poor immune recovery. Opt-out/transfer-out individuals (n=2 and n=5, respectively) had intermediate baseline CD4 counts (mean 362.0 and 321.0 cells/µl, respectively), with modest increases at follow-up. One of the patients who discontinued ART had a constant CD4 level of 488 cells/µl. Survival and retention on ART were in general linked with larger baseline CD4 counts and greater gains over time (Table 2 and Figure 1). Table 2 presents the descriptive statistics of CD4 counts (both baseline and latest) across different ART status categories. Values include sample size (count), mean, standard deviation (SD), minimum (min), 25th percentile (25%), median, 75th percentile (75%), and maximum (max). Due to limited sample sizes in some categories (e.g., "stopped" and "opted out"), certain quartile statistics (25%, 75%) are not computed and denoted as "—". These values provide insight into CD4 progression and variability among patients with different treatment outcomes.

Regimen analysis

The most common regimen used was Tenofovir + Lamivudine + Dolutegravir (TLD), taken by 13 patients (48.1%). This regimen was also linked to the best immunological response, with the majority of patients on TLD staying alive and still under care with robust CD4 recovery. However, treatment with protease inhibitor (PI)-based regimens such as Tenofovir + Lamivudine + Lopinavir/ritonavir (TL+LPV/r) and Zidovudine + Lamivudine + Lopinavir/ritonavir (ZL+LPV/r) had poorer outcomes in terms of increased mortality and program transfers. Among those on TL+LPV/r (n=6), two patients died, one stopped treatment, one opted out, and three were transferred out. Similarly, both patients on ZL+LPV/r died during follow-up. A small proportion of patients received other regimens, including ZLN, ALD, and ZL+ATV/r, but outcomes were variable and limited by small numbers. Table 3 displays the distribution of ART outcomes across different antiretroviral therapy (ART) regimens. Regimens are abbreviated as follows: TLD (Tenofovir + Lamivudine + Dolutegravir), TL+LPV/r (Tenofovir + Lamivudine + Lopinavir/ritonavir), ZLN (Zidovudine + Lamivudine + Nevirapine), ALD (Abacavir + Lamivudine + Dolutegravir), ZL+ATV/r (Zidovudine + Lamivudine + Atazanavir/ritonavir), and others. Outcome categories include "alive on ART," "Died," "opted out," "stopped," and "transfer out." The data indicates better retention on TLD, while regimens involving LPV/r show higher proportions of adverse outcomes such as death or transfer. Considering together in present study, the findings reveal that younger patients, male patients, and those with higher baseline CD4 counts retained more effectively on ART and experienced better immunological recovery. TLD regimens based on dolutegravir were characterized by better outcomes, while PI-based regimens, although needed for HIV-2 control, were related to higher mortality and program attrition.

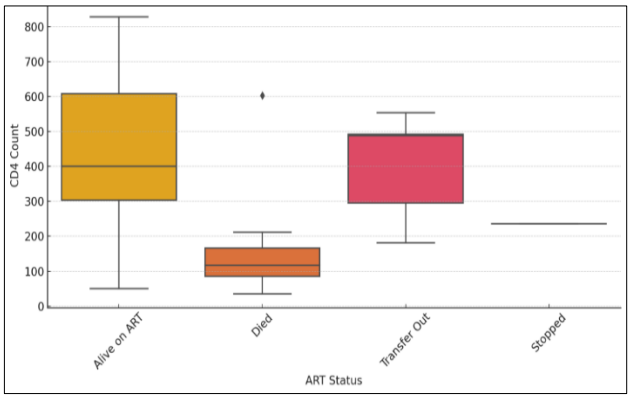

Figure 1: Summary of CD4 trends by ART outcome (n=27).

Table 2: Summary of baseline and latest CD4 counts (grouped by ART outcome) (n=27).

ART status	CD4 type	No.	Mean	SD	Min	25%	Median	75%	Max
Alive on ART	Baseline CD4	12	352.3	234.3	50	189.2	310.5	474.5	746
	Latest CD4	12	519.3	243.0	50	362.0	599.0	703.0	828
Died	Baseline CD4	7	239.4	270.3	18	69.0	199.0	390.0	851
	Latest CD4	7	289.1	248.7	35	102.0	236.0	497.0	554
Opted out	Baseline CD4	2	362.0	223.0	204.0	—	362.0	—	520
	Latest CD4	2	421.0	298.2	210.0	—	421.0	—	632
Stopped	Baseline CD4	1	488.0	—	—	—	—	—	—
	Latest CD4	1	488.0	—	—	—	—	—	—
Transfer out	Baseline CD4	5	321.0	182.2	171.0	236.0	236.0	488.0	519
	Latest CD4	5	379.2	199.5	181.0	236.0	355.0	488.0	554

Table 3: ART regimen distribution by treatment outcome (n=27).

Regimen	Alive on ART	Died	Opted out	Stopped	Transfer out
AL+LPV/r	0	1	0	0	0
ALD	1	0	0	0	0
TL+LPV/r	0	2	1	1	3

Continued.

Regimen	Alive on ART	Died	Opted out	Stopped	Transfer out
TLD	10	0	1	0	2
ZL+ATV/r	0	1	0	0	0
ZL+LPV/r	0	2	0	0	0
ZLN	0	1	0	0	1

DISCUSSION

In our series, most of the patients were middle-aged males from Nagpur district, with somewhat higher educational levels than are found in the usual HIV clinic populations. Other similar patterns of demography have been reported in other Indian series, where HIV-2 and dual infections were urban or semi-urban based with male predominance.[22]

The comparatively higher education level in our study may be partially a reflection of improved health-seeking behaviour and greater accessibility to tertiary care facilities. Such demographic characteristics may also have helped result in better retention of treatment and adherence among patients on dolutegravir-based regimens, while poorer outcomes in some patients can be attributed more to late presentation with low CD4 counts at the baseline rather than sociodemographic disadvantage.

PIs such as LPV/r and darunavir continue to be needed for management of HIV 2 because of natural NNRTI resistance but have more unpredictable potency and potential resistance, as reported in *in vitro* and cohort analyses.[15] Our dataset also demonstrated increased mortality or program dropout among those on PI based regimens, perhaps because of late start, worse adherence, or less immunological recovery.

Lower baseline CD4 levels correlated with worse outcome, highlighting the importance of early initiation of ART following HIV 2 diagnosis, a recommendation with international consensus regardless of lack of randomized trials.[18]

Systematic reviews document immunological benefits in HIV 2 groups as modest relative to HIV 1, but nonetheless clinically significant; observational studies produce analogous CD4 gains of ~70 cells/mm³ at 6–12 months.[19,20] Studies like FIT 2 (West Africa) provided endorsement for boosted lopinavir and raltegravir regimens' efficacy, with sustained immunologic and virologic suppression.[21] Our findings match these trends, demonstrating CD4 gain in TLD-treated HIV 2 patients.

Limitations

Small sample size, retrospective design, and incomplete outcome monitoring for transferred out and opted out patients in HIV 2 infection are limitations. Viral load and resistance tests were not available, which is typical of resource-limited settings treating HIV 2 cases.[18]

CONCLUSION

This study supports consistency with global HIV 2 treatment experience: TLD are linked to strong immunologic improvement, whereas PI-based regimens are more likely to result in unfavourable outcomes in program settings. Low baseline CD4 is still a significant risk factor for mortality, highlighting the need for early diagnosis and timely ART initiation.

Our data justify national policy leadership in implementing TLD for HIV 2 and dual infections, consistent with WHO and NIH expert opinion. Prospective studies and enhanced monitoring such as HIV 2–targeted viral load and resistance tests are necessary to further refine care in this underrepresented subgroup.

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