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Viral suppression and immune recovery after antiretroviral therapy initiation in a Moroccan human immunodeficiency virus type 1-infected cohort: A retrospective analysis

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Abstract

Introduction: Morocco has made substantial progress in expanding human immunodeficiency virus (HIV) testing and treatment, yet longitudinal data on immuno-virologic outcomes remain limited.

Objective: We sought to define the clinical profile at presentation and analyze long-term immuno-virologic outcomes under expanding integrase inhibitor-based treatment.

Methods: We performed a retrospective analysis of patients with confirmed HIV-1 infection who initiated antiretroviral therapy at the Center of Virology, Infectious, and Tropical Diseases at the Military Training Hospital between 2017 and 2025. Demographic, clinical, immunological, and virological data were collected at baseline and throughout follow-up. Statistical analyses were conducted using the Statistical Package for Social Sciences software.

Results: Late presentation was common: 35.7% presented with Centers for Disease Control and Prevention stage C, and 41.5% had CD4 < 200 cells/μL. Women had higher baseline cluster of differentiation 4 (CD4) counts than men (416 vs. 250 cells/μL; $p = 0.001$), whereas men displayed higher viral loads (1.19×10^5 vs. 5.51×10^4 copies/mL; $p = 0.005$). Opportunistic infections remained substantial, including cytomegalovirus (16.5%), tuberculosis (12.5%), and toxoplasmosis (5.8%). First-line therapy was initially non-nucleoside reverse transcriptase inhibitor-based in half of the patients, but rapid national adoption of updated guidelines led to 93.8% receiving dolutegravir plus two nucleoside reverse transcriptase inhibitors at the last follow-up. Viral loads declined sharply within the first month, with most patients achieving and maintaining suppression from months 6–12 onward. CD4 counts rose from a median of 279 cells/μL at baseline to 560 at year 3, peaking at 610 at year 5 before stabilizing.

Conclusion: Morocco's transition to dolutegravir-based antiretroviral therapy has produced durable virologic control and robust immune recovery. Persistent late diagnosis, sex-based disparities, and limited access to genotyping remain major

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obstacles. Strengthening early testing, expanding molecular monitoring, and enhancing differentiated care services will be essential to sustain national progress.

Keywords: Human immunodeficiency virus type 1; Epidemiology; Immuno-virologic surveillance; Clinical characteristics; Antiretroviral therapy; Morocco

1. Introduction

Four decades after its discovery, human immunodeficiency virus (HIV) still remains a major global health challenge. Despite advancements in HIV prevention and treatment, the global response to the epidemic remains insufficient, with progress toward the 2030 Joint United Nations Programme on HIV/AIDS (UNAIDS)' targets being off track even before the emergence of COVID-19. As of 2024, an estimated 1.3 million new infections continue to occur annually, with sub-Saharan Africa bearing the highest burden.[1,2] Antiretroviral therapy (ART) has transformed HIV from a fatal disease into a chronic condition, reducing morbidity and mortality. Yet a cure remains elusive, with only a few exceptional cases, such as the Berlin, London, and Düsseldorf patients, achieving long-term viral eradication.[3] While ART achieves viral suppression in the majority of patients, clinical outcomes are heterogeneous. Between 15% and 30% of patients globally fail to achieve full immune reconstitution despite virologic suppression, and others experience regimen modifications within the first two years due to toxicity, intolerance, or virologic failure.[4]

Morocco represents a unique setting within the Middle East and North Africa (MENA) region, where the epidemic is concentrated but sustained by key populations at risk. Though classified as a low-prevalence country (0.08%), Morocco faces a concentrated epidemic, with approximately 23,500 people living with HIV. The country's National HIV Testing and Confirmation Strategy (2021–2026) has prioritized expanding community-based and self-testing initiatives, particularly among key populations, reaching over 1 million tests performed in 2024. The country operates 47 HIV referral centers, including 16 pediatric units, facilitating early linkage to care and ensuring integration of HIV testing into primary healthcare services. These initiatives have translated into substantial public health gains, with ART coverage increasing from 55% in 2016 to 95% in 2024.[5,6] Notably, 95% of individuals receiving ART have achieved viral suppression, positioning Morocco on track to meet two of the UNAIDS' 95–95–95 targets and underscoring the effectiveness of its national HIV strategy.[5,7]

Despite these achievements, challenges persist in sustaining long-term immuno-virologic success. Data on the longitudinal evolution of viral load and cluster of differentiation 4 (CD4) counts, the burden of co-infections, and the frequency and causes of regimen changes remain scarce in Morocco and across the MENA region. The absence of routine baseline genotyping and drug-resistance surveillance further limits the ability to anticipate or explain treatment failure.

This study provides a comprehensive epidemiological and virological analysis of HIV-1 in Morocco, assessing viral load dynamics, immune function, treatment responses, and adherence patterns across diverse populations. By contextualizing these findings within demographic and clinical variations, this research aims to generate critical insights into HIV-1 progression and resistance trends. These data will inform national HIV management strategies, optimize patient care, and guide future public health interventions in Morocco's evolving epidemic.

2. Materials and methods

2.1. Study design and patients

We conducted a retrospective study on HIV-infected patients diagnosed between January 2017 and January 2025, using data from the Center of Virology, Infectious, and Tropical Diseases (CVMIT) at Mohamed V Military Training Hospital in Rabat, Morocco. This database included demographic, clinical, immunologic, and virologic information up to January 2025. To ensure confidentiality, all data was retrieved using coded identifiers.

All patients included in this study had their HIV-1 infection confirmed by the Virology Laboratory at CVMIT, one of Morocco's national referral centers for HIV diagnosis and management. Although located within a military institution, CVMIT provides care to military beneficiaries, their families, and civilians referred through the national HIV program. Referrals originate from multiple regions of the country, making the cohort geographically and socially diverse, and reflective of patients engaged in specialized HIV care at a tertiary-level reference center. According to the Ministry of Health, the diagnostic process follows a two-step confirmation method, beginning with an

enzyme-linked immunoassay screening test (ELISA HIV-1/2; 4th generation Genscreen Plus®). Until 2023, HIV-1 confirmation was performed by Western blot; since then, the country has transitioned to quantitative polymerase chain reaction using the COBAS® 4800 system (Roche Diagnostics, Switzerland) to enhance diagnostic accuracy.[5] The 8COBAS® 4800 assay used at CVMIT has a validated analytical detection limit of 20 copies/mL.

Immune status was assessed at each patient visit using $CD4^+$ T cell counts measured with the Beckman Coulter NAVIOS flow cytometer. Acquired immunodeficiency syndrome (AIDS) diagnosis was determined based on the Centers for Disease Control and Prevention (CDC) criteria.

According to the Moroccan National Guidelines, screening for opportunistic infections is performed systematically at the time of HIV diagnosis. Tuberculosis (TB) screening includes chest radiography and sputum testing, followed by Xpert *Mycobacterium tuberculosis*/rifampicin molecular confirmation when indicated. Cerebral toxoplasmosis is evaluated through neurological assessment, brain imaging, and *Toxoplasma gondii* immunoglobulin G serology. Cytomegalovirus (CMV) infection is diagnosed based on compatible clinical findings supported by CMV polymerase chain reaction. These baseline evaluations form part of routine national HIV care protocols.[8,9]

This retrospective study was conducted in accordance with the Helsinki Declaration and was approved by the Ethics Committees of the Faculty of Medicine and Pharmacy of Mohammed V University in Rabat, Morocco (Approval ID: CERB 47/23).

2.2. Data analysis

Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as medians with corresponding interquartile ranges (IQR), as appropriate. Comparisons between groups were performed using nonparametric tests such as the Mann–Whitney *U* test for continuous variables and the chi-squared or Fisher's exact test for categorical variables.

Longitudinal evolution of plasma HIV-1 viral load and $CD4^+$ T cell counts was described at predefined clinical follow-up intervals (baseline; months 1, 3, 6, 9, and 12; and annually thereafter), reflecting the real-world structure of patient monitoring in this cohort. As follow-up timing varied across individuals, longitudinal trends were summarized using medians and proportions at each time point. A standard approach for programmatic HIV cohorts with heterogeneous visit schedules.

Viral suppression was defined as a plasma HIV-1 RNA level below 200 copies/mL. Virologic rebound was defined as any HIV-1 RNA value ≥1,000 copies/mL after prior suppression <200 copies/mL. Isolated increases in the log 3–5 range were therefore classified as true virologic rebounds, reflecting significant viral activity rather than assay fluctuation. Immunological recovery was assessed using both overall median $CD4^+$ T cell counts and CD4 category distributions. Immune recovery was defined as $CD4^+$ >350 cells/mm^3, and rates at each time point were calculated from the subset of patients with available data at that specific interval. Given that patients were newly diagnosed between 2017 and 2025, not all individuals had reached each predefined follow-up interval at the time of data extraction. The progressive decrease in sample size at later time points, therefore, reflects staggered diagnosis years rather than loss to follow-up.

All statistical analyses were conducted using IBM's Statistical Package for Social Sciences software, version 25. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Demographic and epidemiological characteristics

The study population comprised 224 adults with confirmed HIV-1 infection who initiated antiretroviral therapy and had sufficient virologic and clinical data for analysis.

Most patients were male (n = 161, 71.9%), with a male-to-female ratio of 2.6:1. The overall median age was 43 years (IQR: 36.5–52.5), with 22.3% aged 18–35 years, 44.6% aged 36–50 years, and 33% over 50 years, with comparable distributions between sexes. Marital status differed significantly between sexes (p < 0.0001): nearly half of the cohort were married (48.2%), more often women (66.7% women vs. 41.0% men), while 43.3% were single. Heterosexual transmission was overwhelmingly dominant (99.1%), with only one isolated case of men who have sex with men (MSM) transmission (0.4%) and one bisexual transmission (0.4%) recorded among male participants. Most diagnoses occurred during routine medical care (78.5%); other circumstances included partner notification (13.8%), blood donation (5.4%), and voluntary testing (2.2%). Diagnosis was most often made during medical check-ups (78.5%), with fewer cases identified through partner testing (13.8%) or voluntary screening (2.2%). At diagnosis, 35.7% of the patients were classified as CDC stage C, 44.2% of patients were in CDC stage A, and 20.1% were in stage B. Women were more frequently diagnosed at earlier stages (63.5% stage A vs 36.6% in men), while men were more often diagnosed at advanced stage C (39.1% vs. 27.0% in women; p = 0.001) (Table 1).

Table 1. Baseline demographic, clinical, and immuno-virologic characteristics of a human immunodeficiency virus type 1-infected Moroccan cohort

Parameters	Female (*n* = 63)	Male (*n* = 161)	Total (*n* = 224)	*p*-value
Age (years)				0.927
Median (interquartile range)	43 (36.5–52.5)	43 (37–54)	43 (36.7–54)	
18–35	15 (6.7%)	35 (15.6%)	50 (22.3%)	
36–50	27 (12.1%)	73 (32.6%)	100 (44.6%)	
>50	21 (9.4%)	53 (23.7%)	74 (33.0%)	
Marital status				<0.001
Single	11 (4.9%)	86 (38.3%)	97 (43.3%)	
Married	42 (18.8%)	66 (29.5%)	108 (48.2%)	
Divorced/Widow(er)	10 (4.4%)	9 (4.0%)	19 (8.5%)	
Sexual orientation				0.005
Heterosexual	63 (28.1%)	159 (71.0%)	222 (99.1%)	
Bisexual	0	1 (0.4%)	1 (0.4%)	
MSM	–	1 (0.4%)	1 (0.4%)	
Circumstances of discovery				<0.001
Medical check-ups	39 (17.4%)	137 (61.1%)	176 (78.5%)	
HIV positive partner	23 (10.3%)	8 (3.6%)	31 (13.8%)	
Voluntary testing	1 (0.4%)	4 (1.8%)	5 (2.2%)	
Blood donation	0	12 (5.4%)	12 (5.4%)	
CDC stage				0.001
A	40 (17.9%)	59 (26.3%)	99 (44.2%)	
B	6 (2.7%)	39 (17.4%)	45 (20.1%)	
C	17 (7.6%)	63 (28.1%)	80 (35.7%)	
Opportunistic infections and co-infections				
Cytomegalovirus infection	6 (2.7%)	31 (13.8%)	37 (16.5%)	-
Tuberculosis	5 (2.2%)	23 (10.3%)	28 (12.5%)	-
Toxoplasmosis	2 (0.9%)	11 (4.9%)	13 (5.8%)	-
Other	2 (0.9%)	4 (1.8%)	6 (2.7%)	-
Median initial CD4 cell count at diagnosis (interquartile range) (cells/mm^3)	416 (126–626)	250 (52–400)	279 (75.25–473.75)	-
CD4 cell count category at diagnosis (cells/mm^3)				0.001
0–49	8 (3.6%)	36 (16.1%)	44 (19.6%)	
50–199	12 (5.4%)	37 (16.5%)	49 (21.9%)	
200–349	5 (2.2%)	35 (15.6%)	40 (17.9%)	
350–499	14 (6.3%)	27 (12.1%)	41(18.3%)	
>500	24 (10.7%)	26 (11.6%)	50 (22.3%)	
Median plasma initial viral load at diagnostic (copies/mL)	5.51×10^4 (8.22×10^3–2.97×10^5)	1.19×10^5 (3.46×10^4–4.13×10^5)	1.10×10^5 (1.68×10^4–4.08×10^5)	-

(*cont'd...*)

Table 1. Baseline demographic, clinical, and immuno-virologic characteristics of a human immunodeficiency virus type 1-infected Moroccan cohort

Parameters	Female (*n* = 63)	Male (*n* = 161)	Total (*n* = 224)	*p*-value
Plasma viral load category at diagnosis (copies/mL)				
20–999	5 (2.20%)	17 (7.6%)	22 (9.8%)	
1,000–9,999	13 (5.80%)	9 (4%)	22 (9.8%)	0.005
10,000–99,999	20 (9.00%)	47 (21%)	67 (29.9%)	
>100,000	25 (11.2%)	88 (39.3%)	113 (50.40%)	

Note: Data presented as *n* (%), unless stated otherwise. Percentages were calculated using the total cohort (*n* = 224)
Abbreviations: CDC: Centers for Disease Control and Prevention; HIV: Human immunodeficiency virus; MSM: Men who have sex with men.

3.2. Opportunistic infections and comorbidities

Opportunistic infections were reported in several patients within the cohort. CMV was the most frequently observed, affecting 16.5% (*n* = 37) of individuals, with a higher prevalence among males (13.8%) than females (2.7%). The second most common co-infection was TB, reported in 12.5% of cases, with 10.3% in males and 2.2% in females. Toxoplasmosis was diagnosed in 5.8% of patients, with a higher proportion among males (4.9%) compared to females (0.9%). Other opportunistic infections were less frequent, affecting 2.7% of the cohort (Table 1). Additionally, five patients (2.2%) died during follow-up. All deaths were AIDS-related and included *Pneumocystis jirovecii* pneumonia (*n* = 2), diffuse cerebral toxoplasmosis (*n* = 1), and CMV pneumonitis (*n* = 2).

3.3. Baseline immuno-virologic characteristics

At diagnosis, the cohort exhibited heterogeneous immunological and virological profiles. The median CD4 cell count was 279 cells/mm^3 (IQR: 75–474), significantly higher among women (median: 416 cells/mm^3, IQR: 126–626) than men (median: 250 cells/mm^3, IQR: 52–400; p = 0.001). Severe immunosuppression was common: 19.6% of patients had CD4 counts below 50 cells/mm^3 and 21.9% between 50 and 199 cells/μL, while 17.9% had 200–349 cells/mm^3, 18.3% had 350–499 cells/μL, and only 22.3% had ≥500 cells/mm^3 at diagnosis (Table 1).

Baseline plasma HIV RNA levels also showed wide variation. The overall median viral load was 1.10 × 10^5 copies/mL (IQR: 1.68 × 10^4–4.08 × 10^5), with men presenting higher levels (1.19 × 10^5, IQR: 3.46 × 10^4–4.13 × 10^5) than women (5.51 × 10^4, IQR: 8.22 × 10^3–2.97 × 10^5, p = 0.005). Half of the cohort (50.4%) had viral loads exceeding 100,000 copies/mL, while 29.9% had values between 10,000 and 99,999 copies/mL, 9.8% between 1,000 and 9,999, and 9.8% fewer than 1,000 copies/mL (Table 1).

3.4. Antiretroviral therapy regimens and treatment outcomes

3.4.1. Distribution of antiretroviral therapy regimens

At treatment initiation, the most frequently prescribed regimen was two nucleoside reverse transcriptase inhibitors (NRTIs) plus a non-NRTI (NNRTI), accounting for half of patients (50.0%), predominantly efavirenz (EFV) + emtricitabine (FTC) + tenofovir disoproxil fumarate (TDF) (30.8%) and lamivudine (3TC) + zidovudine (ZDV) + EFV (19.2%). Two NRTIs plus an integrase inhibitor (INSTI) accounted for 47.3% of first-line regimens, almost exclusively 3TC+TDF+dolutegravir (DTG) (46.0%), with only two patients (0.9%) receiving 3TC+ZDV+DTG. Protease inhibitor (PI)-based combinations were rarely used at baseline (2.2%), mostly lopinavir/ritonavir + TDF + FTC (1.8%). By the end of follow-up, the treatment landscape had shifted decisively toward DTG-based regimens. Nearly all patients (93.8%) were receiving a 2NRTI+INSTI combination, with 3TC+TDF+DTG as the predominant regimen. NNRTI-based regimens had almost disappeared (1.8%), while PI-based regimens persisted only in selected cases (1.8%), and dual PI+INSTI therapy was prescribed in 2.2% of patients. The median duration of ART exposure was 48 months (IQR: 3–99), with no significant difference between sexes (p = 0.494) (Table 2).

3.4.2. Viral load evolution over time

Longitudinal assessment of plasma HIV-1 RNA demonstrated a rapid and sustained virologic response to ART. Viral load declined steeply within the first month of therapy, with the majority of patients approaching suppression by 6–12 months. Thereafter, levels remained durably controlled throughout follow-up, extending to seven years in some individuals. There were isolated episodes of viral rebound, also referred to as isolated high-level rebounds, typically ranging between 3 and

Table 2. Antiretroviral therapy distribution among the 224 patients

Treatment	Female (*n* = 63)	Male (*n* = 161)	Total (*n* = 224)	*p*-value
First ART regimen				
2 NRTI + NNRTI	31 (13.8%)	81 (36.2%)	112 (50%)	
EFV+FTC+TDF[a]	20 (8.9%)	49 (21.9%)	69 (30.8%)	
3TC+ZDV+EFV[b]	11(4.9%)	32 (14.3%)	43 (19.2%)	
2 NRTI + INSTI	30 (13.4%)	75 (33.5%)	105 (47.3%)	
3TC+TDF+DTG[c]	30 (13.4%)	73 (32.6%)	103 (46%)	0.794
3TC+ZDV+DTG	0	2 (0.9%)	2 (0.9%)	
2 NRTI + PI	2 (0.90%)	3 (1.3%)	5 (2.2%)	
LOP/r+TDF+FTC	2 (0.9%)	2 (0.9%)	4 (1.8%)	
3TC+ZDV+LOP[b]	0	1 (0.4%)	1 (0.4%)	
PI + INSTI (LOP+DTG)	0	2 (0.90%)	2 (0.9%)	
Last ART regimen				
2 NRTI + NNRTI (EFV+FTC+TDF)	0	4 (1.8%)	4 (1.8%)	
2 NRTI + INSTI (3TC+TDF+DTG)	60 (26.8%)	150 (67%)	210 (93.8%)	0.543
2 NRTI+PI (LOP/r+TDF+FTC)	2 (0.9%)	2 (0.9%)	4 (1.8%)	
2 PI + INSTI (DRV+RTV+DTG)	1 (0.4%)	4 (1.8%)	5 (2.2%)	
PI + INSTI (LOP+DTG)	0	1 (0.4%)	1 (0.4%)	
Median duration of ART (months) (interquartile range)	58 (36–88)	51 (28–88)	48 (3–99)	0.494

Note: [a]Atenef: EFV+FTC+TDF, [b]Avocomb: 3TC+ZDV, and [c]DLT: DTG+3TC+TDF. Percentages were calculated using the total cohort (*n* = 224).
Abbreviations: 3TC: Lamivudine; ART: Antiretroviral therapy; DRV: Darunavir; DTG: Dolutegravir; EFV: Efavirenz; FTC: Emtricitabine; INSTI: Integrase strand transfer inhibitor; LOP: Lopinavir; NNRTI: Non-nucleoside reverse transcriptase inhibitor; NRTI: Nucleoside reverse transcriptase inhibitor; PI: Protease inhibitor; RTV: Ritonavir; TDF: Tenofovir disoproxil fumarate; ZDV: Zidovudine.

5 $\log_{10}$ copies/mL. These events were most frequently observed between two and four years after treatment initiation. However, these episodes were usually followed by re-suppression, suggesting that the gaps in adherence or regimen modifications were temporary rather than indicative of persistent therapeutic failure. These findings collectively highlight the significant efficiency of ART in attaining sustained virologic suppression in this Moroccan cohort (Figure 1A). Using a stricter virological threshold (<200 copies/mL), population-level suppression rose steadily in the early phases of treatment and remained consistently high thereafter. As shown in Figure 1B, 49% of patients were suppressed at month 1, increasing to 62% by month 3 and surpassing 80% by month 6. From the first year onward, suppression stabilized at 85%–90% across all subsequent time points.

3.4.3. Switching of antiretroviral therapy regimens

Patterns of regimen switching are illustrated in Figure 2. At ART initiation, the most common regimen was

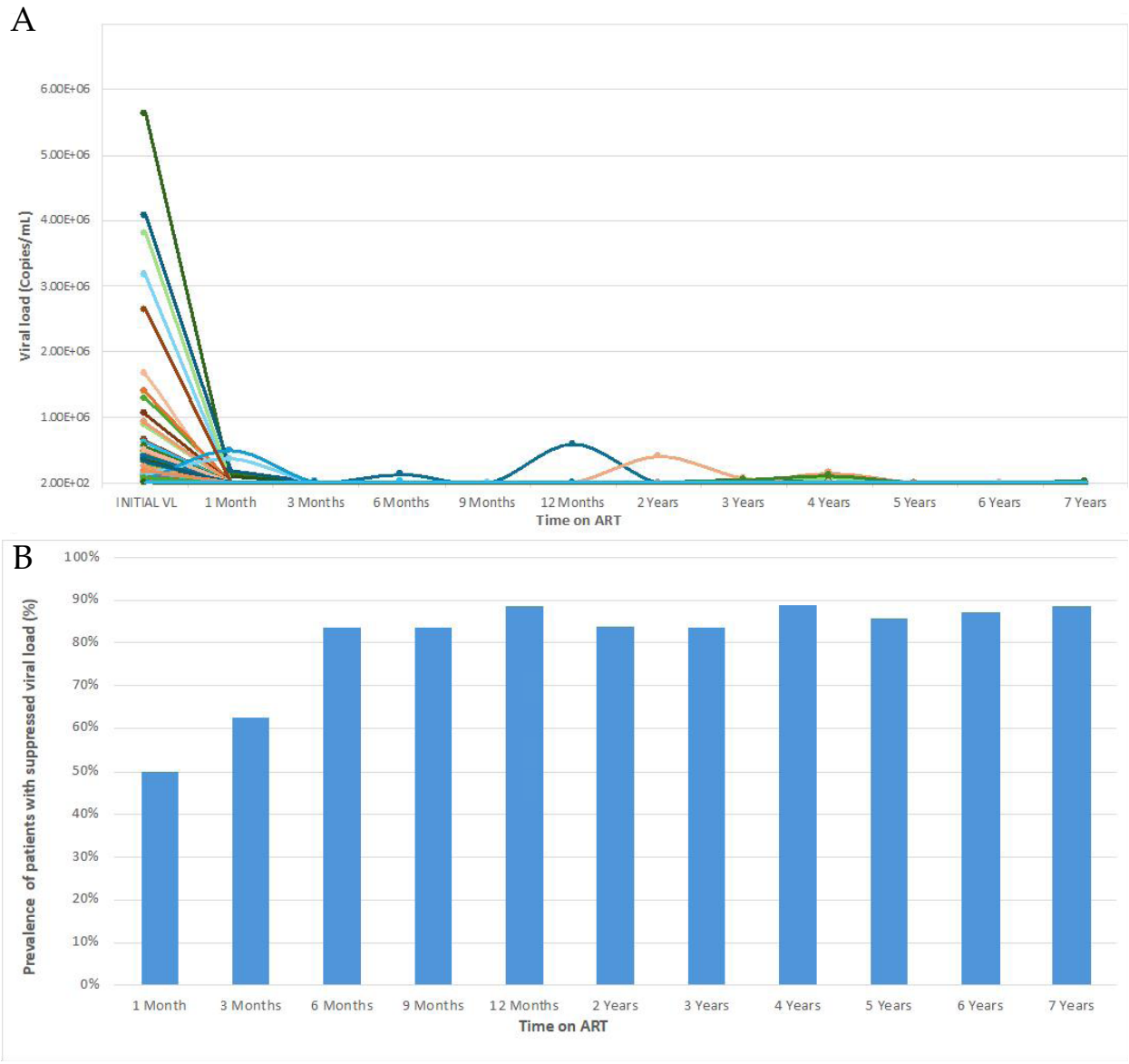

Figure 1. Longitudinal virologic response after ART initiation in the study cohort. This figure presents the longitudinal evolution of HIV-1 viral load (VL) and the proportion of patients achieving virological suppression following ART initiation. (A) Longitudinal changes in viral load among 224 patients followed for up to seven years after ART initiation. Each line represents the viral load trajectory of an individual patient. A marked reduction in viral load is observed within the first month of treatment, with the majority of patients achieving substantial suppression by six months. (B) Proportion of patients achieving HIV-1 RNA <200 copies/mL at each follow-up interval. Suppression increased steadily during the first 6 months of ART, surpassed 80% by month 6, and remained above 85% throughout years 1 to 7 of follow-up.
Abbreviations: ART: Antiretroviral therapy; HIV: Human immunodeficiency virus.

3TC+TDF+DTG (46.0%), followed by FTC+TDF+EFV (30.8%) and 3TC+ZDV+EFV (19.2%). During follow-up, a significant transition occurred, mostly from EFV-based regimens toward DTG-based therapy. Specifically, 28.1% of patients moved from FTC+TDF+EFV to 3TC+TDF+DTG, and 19.2% from 3TC+ZDV+EFV to 3TC+TDF+DTG. By the last follow-up visit, 93.8% of patients were receiving 3TC+TDF+DTG, confirming its dominance as the standard of care. Only a small minority (≤2.2%) transitioned to PI-based or DRV/RTV+DTG salvage regimens, reflecting therapeutic adjustments in complex cases (Figure 2).

3.4.4. Cluster of differentiation 4 T cell recovery over time

Cluster of differentiation 4 T cell trajectories were analyzed in 224 patients who initiated ART between 2017 and 2025, with variable follow-up lengths depending on the year of diagnosis. The median baseline CD4 count was approximately 279 cells/mm^3. A rapid increase was observed within the first month of therapy, rising to around 300 cells/mm^3. Although a slight dip occurred at month 3, the CD4 count steadily increased, reaching approximately 360 cells/mm^3 by month 6 and 420 cells/μL by month 12. Continued immune restoration was evident through year 2 (470 cells/mm^3), with a peak at year 3 (560 cells/mm^3). A minor decrease occurred in year 4, followed by a peak recovery point at year 5 (610 cells/mm^3). However, a modest decline was observed thereafter, stabilizing between 560 and 570 cells/mm^3 through years 6 and 7 (Figure 3A).

The distribution of CD4 immunological categories at each follow-up time point further illustrated these recovery patterns (Figure 3B). At baseline, fewer than one-third of patients had CD4 ≥350 cells/mm^3, while approximately half presented with CD4 < 200 cells/mm^3. A marked shift occurred within the first year: by month 12, nearly 60% of patients had achieved CD4 ≥350 cells/mm^3, and the proportion with CD4 < 200 cells/mm^3 had fallen below 20%. This trend continued in subsequent years, with more than 65% of patients reaching CD4 ≥ 350 cells/mm^3 by year 2 and over 80% by years 4–6. These results emphasize a significant early phase of immune recovery under ART, followed by long-term stabilization of CD4 counts, underscoring the durable benefits of ART on immune restoration.

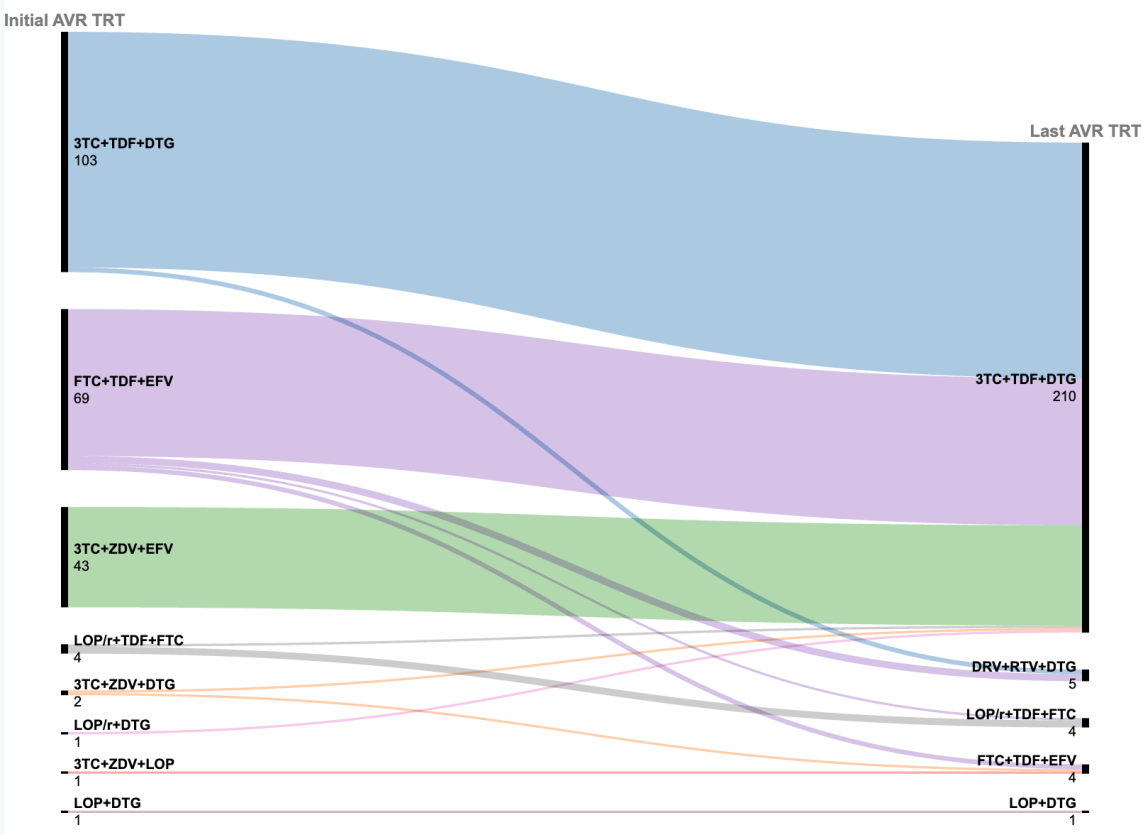

Figure 2. Switching of ART regimens for the 224 patients. Alluvial flows depict transitions from initial (left) to last ART regimens (right). Blue bands represent 3TC+TDF+DTG, prescribed in 46.0% at initiation and rising to 93.8% at last follow-up. Purple bands show FTC+TDF+EFV (30.8% initially), most of which switched to DTG-based therapy (28.1%). Green bands correspond to 3TC+ZDV+EFV (19.2% initially), with nearly all patients transitioning to 3TC+TDF+DTG. Smaller flows represent protease inhibitor-based regimens and other combinations, each accounting for <2% of patients. The width of each band is proportional to the number of patients transitioning between regimens.
Abbreviations: 3TC: Lamivudine; ART: Antiretroviral therapy; DTG: Dolutegravir; EFV: Efavirenz; FTC: Emtricitabine; LOP/r: Lopinavir/ritonavir; TDF: Tenofovir disoproxil fumarate; TRT: Treatment; ZDV: Zidovudine.

Figure 3. Longitudinal immunological response following antiretroviral therapy (ART) initiation in the study cohort. This figure illustrates changes in CD4⁺ T cell recovery and immunological status over time after initiation of antiretroviral therapy. (A) Longitudinal evolution of median CD4⁺ T cell counts. Median CD4 values (cells/mm³) are shown at baseline, months 1–12, and annually thereafter up to year 6. Median CD4 counts rose sharply during the first year and continued to increase through year 5 before reaching a plateau, consistent with sustained virological control under ART. (B) Evolution of CD4 immunological categories over time. Bars represent the proportion of patients with available CD4 measurements at each visit who fell into one of three clinically relevant strata: <200 cells/mm³, 200–349 cells/mm³, and ≥350 cells/mm³. The marked decline in severe immunosuppression and progressive increase in the proportion reaching ≥350 cells/mm³ reflect robust early immune restoration.

4. Discussion

This study presents an extensive epidemiological and immunovirological analysis of an HIV-1-infected Moroccan cohort, providing critical insights into clinical profiles, treatment responses, and long-term outcomes within a middle-income context. Despite significant advances in ART access and the integration of HIV services into primary care, our results underscore ongoing gaps in early diagnosis, enduring sex-based disparities, and challenges in maintaining sustained virologic control.

Our cohort was predominantly male (71.9%) with a male-to-female ratio of 2.6:1, a finding aligned with broader regional trends across the MENA region, where sociocultural barriers and lower testing uptake among women restrict their representation in clinical cohorts.[9] However, national surveillance data indicate a shifting dynamic in Morocco, with women now accounting for 47% of people living with HIV in 2025, marking a steady rise in female diagnoses over the past decade.[5] This evolving trend underscores the growing epidemiological significance of

women in Morocco's HIV response. Comparatively, data from the 2023 European HIV Surveillance Report show that 72.7% of new HIV diagnoses in the European Union/European Economic Area occurred in men, corresponding to a male-to-female ratio of 2.7:1.[10] Conversely, in sub-Saharan Africa, women represent approximately 63% of HIV-positive individuals, highlighting distinct biological and socio-structural vulnerabilities that shape the regional epidemic.[1]

Age distribution analysis revealed a median age of 43 years, with 22.3% aged 18–35, 44.6% aged 36–50, and 33.0% older than 50. Age distribution was similar by sex ($p = 0.927$). This age profile reflects global trends toward an aging HIV-positive population, largely attributable to ART's success in increasing longevity. Nevertheless, aging cohorts pose new clinical challenges, particularly regarding managing comorbidities and treatment complications.[11] Morocco's national surveillance similarly emphasizes the concentration of HIV diagnoses among adults aged 25–44, a finding consistent with studies led in Morocco, which reported comparable median ages and highlighted the same age group as central to the Moroccan epidemic, underscoring the critical need for targeted prevention and early screening efforts.[5,12,13] High-income settings such as France and Spain demonstrate more effective youth-targeted and routine testing programs, underscoring the importance of enhancing HIV screening initiatives among younger Moroccans to address potential underdiagnosis in this group.[10]

Marital status contexts substantially influence HIV transmission dynamics in Morocco, with 56.7% of individuals diagnosed in our cohort being married or having ever been married, with significant differences by sex ($p < 0.0001$): women were more often married (66.7% of women vs. 41.0% of men). This pattern aligns with findings from sub-Saharan Africa, where significant transmission occurs within stable relationships, underscoring that marital status alone does not guarantee protection. Thus, couple-centered interventions, including joint HIV testing, disclosure counseling, and pre-exposure prophylaxis for serodifferent couples, become essential. While heterosexual transmission (99.1%) dominates Morocco's epidemic, other MENA countries present varied profiles; injecting drug use significantly drives infections in Iran and Libya, whereas commercial sex networks dominate in Djibouti, Somalia, and South Sudan.[14] Contrastingly, in France and the United Kingdom, MSM represent a substantial proportion (33–47%) of new HIV cases. While Morocco reports very few cases attributed to MSM or bisexual individuals, often below 1%, national surveillance data from the 2024 AIDS Report indicate that 5.3% of reported HIV cases occur among MSM.[5] This discrepancy strongly suggests substantial underreporting, driven by entrenched stigma, discrimination, and the legal criminalization of same-sex behavior, obscuring accurate epidemiological assessments and undermining targeted public health interventions.[15]

Incidental diagnoses compound Morocco's HIV challenge, with 78.5% identified during unrelated medical visits, only 2.2% via voluntary testing, and 13.8% through partner notification. This pattern reflects missed opportunities for proactive screening and argues for opt-out testing in inpatient/outpatient settings, scaled partner services, and community testing tailored to men and youth. Furthermore, incomplete sociodemographic data reflect ongoing weaknesses in health information systems, limiting accurate identification and targeted intervention for at-risk populations.

Clinical stage analysis at diagnosis revealed nearly half (48.3%) at CDC stage C (advanced immunosuppression), significantly impacting morbidity, mortality, healthcare costs, and transmission dynamics. Over 40% of male participants presented with severe immunosuppression (CD4 <200 cells/mL), emphasizing stark sex-based disparities in disease severity at entry into care. Median baseline CD4 counts were significantly lower in males (155 cells/mL) compared to females (273.5 cells/mL; $p = 0.012$), and median plasma viral loads were markedly higher in males (162,181 copies/mL) than in females (67,454 copies/mL; $p = 0.049$). These sex-based disparities underscore gendered barriers to HIV testing and healthcare access among men, including stigma, lower health-seeking behavior, and structural impediments. These findings mirror broader regional trends: in 2023, over half (52.4%) of newly diagnosed cases in the European Union/European Economic Area were classified as late diagnoses, defined as a CD4 count below 350 cells/mL.[10] Late-stage presentation has profound implications; clinically, it increases morbidity and mortality, delays initiation of ART, and often leads to greater healthcare costs, particularly in low-resource settings. From a public health perspective, individuals unaware of their status may unknowingly transmit the virus to others, perpetuating the epidemic.[16-18]

The severity of immunosuppression at diagnosis is further reflected in the frequency of opportunistic infections within this cohort. CMV was observed in 16.5% of cases, TB in 12.5%, and cerebral toxoplasmosis in 5.8%. These infections are hallmark indicators of AIDS and strongly associated with advanced disease, especially among patients classified at stage C. Of particular concern is the high prevalence of TB, which remains the leading opportunistic infection associated with HIV in Morocco

and throughout the region. National estimates from the World Health Organization in 2022 indicated that 1.2% of all TB cases and 2.7% of TB-related deaths (73 deaths) in Morocco occurred in people with HIV infection.[19] The co-epidemic of TB/HIV presents a significant clinical and public health challenge and highlights the urgent need for integrated screening and management of TB in HIV-positive individuals, particularly those presenting with low CD4 counts or clinical symptoms suggestive of TB.

This study assessed ART regimen patterns among 224 people living with HIV, focusing on sex-based differences. No statistically significant differences were found between females and males in first-line regimen, last regimen, or median ART duration, suggesting equitable distribution of ART strategies across sexes. Similar findings have been reported in large international cohorts, such as RESPOND and OPERA, where sex was not associated with differences in ART prescription or virologic outcomes when access was uniform.[19,20]

Our data confirm the rapid dominance of INSTI-based regimens, particularly DTG plus two NRTIs, which accounted for 93.8% of current treatments at last follow-up. This shift aligns with evolving international guidelines, including those from the World Health Organization and European AIDS Clinical Society, that recommend INSTI-based combinations as first-line therapy owing to their high genetic barrier to resistance, rapid viral suppression, limited drug–drug interactions, and favorable safety profile.[21-24] The increase in INSTI use from 47.3% at ART initiation to 93.8% in current regimens underscores the rapid and widespread adoption of these agents in clinical practice in Morocco. This therapeutic transition was driven by substantial regimen switching: 28.1% of patients moved from FTC+TDF+EFV to 3TC+TDF+DTG, and 19.2% from 3TC+ZDV+EFV to 3TC+TDF+DTG. The main causes of these switches included toxicity and intolerance of earlier regimens, treatment interruptions followed by re-initiation on DTG-based therapy, improved absorption and tolerability of newer regimens, and the progressive availability and affordability of DTG at the national level. Such large-scale transitions demonstrate Morocco's responsiveness to guideline changes and its capacity to phase out older NNRTI-based regimens that were historically dominant across North Africa and much of sub-Saharan Africa.[12,13,25] By contrast, recent reviews highlight that many MENA countries still rely heavily on NNRTI-based first-line regimens due to cost and supply chain limitations, suggesting that Morocco is ahead of the regional curve.[23]

The sustained viral suppression observed over several years of follow-up underscores the clinical effectiveness and durability of INSTI-based strategies. This long-term virologic control not only reduces HIV-related morbidity and mortality but also minimizes the risk of HIV transmission, reinforcing the public health impact of successful ART rollouts. These findings are in agreement with global data showing that achieving and maintaining an undetectable viral load is central to both individual patient outcomes and population-level epidemic control.[26,27] These outcomes are in line with those reported in European and North American cohorts, where INSTI-based regimens, particularly those containing DTG or bictegravir, achieve suppression rates exceeding 85–90% at six months.[23,28] In contrast, studies from several sub-Saharan African programs have reported slightly lower suppression rates, often attributed to late presentation, intermittent drug supply, and adherence challenges.[29] However, the moderate virologic rebound observed in a minority of patients beyond the fourth year highlights the ongoing need for adherence monitoring and drug resistance surveillance, especially in settings where second-line and third-line treatment options may be limited. Factors contributing to viral rebound may include treatment fatigue, psychosocial challenges, or pharmacologic issues such as drug–drug interactions and poor absorption. Interventions such as differentiated care models, community-based ART delivery, and long-acting injectable regimens may help sustain adherence and simplify care for individuals at risk of disengagement.[30,31]

Historically, NNRTI-based regimens have been widely used in North Africa, especially in Morocco, primarily due to their availability, lower cost, and incorporation into early first-line regimens. However, growing concerns over resistance and evolving World Health Organization guidelines have triggered a shift toward DTG-based regimens, even in low- and middle-income countries.[12,13,32,33] Our findings reflect this global transition, although resource limitations and programmatic constraints continue to influence implementation timelines across different settings.

Protease inhibitor-based regimens were rarely prescribed in our cohort (<5%), consistent with data from European cohorts,[10,23] where PIs are largely reserved for patients with virologic failure or documented resistance mutations. This trend is driven by the higher pill burden, increased risk of metabolic complications, and less favorable tolerability associated with PIs compared to INSTIs. The shift away from PI use has also been facilitated by the high efficacy of DTG in both naïve and experienced patients, even in the presence of some pre-existing resistance mutations.[22] Taken together, our results position Morocco as an early adopter of DTG-based first-line

therapy in the MENA region, with regimen quality and virologic outcomes comparable to those in high-income European settings, while surpassing many regional peers still transitioning away from NNRTI-based strategies.

Despite the underrepresentation of women (28.1%) in our cohort, the analysis revealed no sex-based differences in treatment regimen or duration. This is reassuring and suggests equitable care delivery, consistent with prior analyses showing that when women have comparable access to ART, their outcomes are similar to those of men. Nevertheless, previous studies have highlighted important sex-specific considerations, including differences in drug metabolism, tolerability, and pregnancy-related ART modifications, which warrant continued attention in clinical management.[34,35]

The trajectory of CD4 T cell restoration in our cohort underscores the central importance of early ART initiation for achieving optimal immunological outcomes. At diagnosis, patients were in profound immunosuppression (median 279 cells/mm^3), with nearly 40% presenting with fewer than 200 cells/mm^3. Women had significantly higher baseline CD4 counts than men (416 vs. 250 cells/mm^3, p = 0.001), while men more frequently presented with higher viral loads (median 1.19 $\times 10^5$ vs. 5.51 $\times$ 10^4 copies/mL, p = 0.005). These disparities suggest that male patients often remain undiagnosed longer, permitting unchecked viral replication and more serious immune damage before linkage to care.

Following ART initiation, immune recovery was robust. CD4 counts rose rapidly within the first month and exceeded 350 cells/mm^3 by six months and 420 cells/mm^3 by year 1. Median levels continued to increase, reaching 470 cells/mm^3 at year 2, 560 at year 3, and peaking at 610 cells/mm^3 by year 5, before stabilizing between 560 and 570 cells/mm^3 through years 6 and 7. This early rapid gain, followed by a long-term plateau, reflects effective immune reconstitution under sustained viral suppression. However, patients initiating therapy at very low CD4 levels recovered more slowly and often incompletely, leaving them vulnerable to both opportunistic disease and non-AIDS comorbidities.

These findings strongly support the test-and-treat strategy recommended by the World Health Organization since 2015 and adopted in Morocco in 2016, which advocates immediate ART initiation for all individuals, regardless of CD4 count.[36] Our results show that delayed presentation continues to blunt the potential of this policy, particularly among men.

Analysis of CD4 immunological categories further illustrated this recovery pattern: the proportion of patients with CD4 ≥ 350 cells/mm^3 increased from less than one-third at baseline to nearly 60% by year 1 and to 70–80% between years 2 and 6. This steep early improvement, followed by a long-term plateau, reflects effective immune reconstitution under sustained viral suppression. However, the plateau observed beyond year five highlights the inherent limits of immune restoration once chronic immune injury is established. Even with durable viral suppression, persistent immune activation and immunosenescence, reflecting premature immune aging, may hinder full recovery of immune function. These processes are well documented in long-term treated populations and have been linked to elevated risks of cardiovascular disease, malignancies, and frailty among aging people living with HIV.[37] Taken together, these observations underline that viral suppression alone does not completely reverse immune dysfunction. Earlier diagnosis and timely ART initiation remain essential to minimize irreversible immune damage, improve long-term immune reconstitution, and reduce the burden of non-AIDS comorbidities in the growing population of aging individuals living with HIV.

Despite these baseline differences, ART regimens and treatment duration were comparable across sexes, indicating equitable clinical management once patients are linked to care. Nonetheless, the worse immuno-virologic status at entry for men could translate into slower recovery and higher long-term morbidity, reinforcing the need for targeted testing and engagement strategies tailored for both sexes.

Collectively, these results align with and strengthen current global recommendations promoting the early initiation of potent, well-tolerated ART regimens, preferably INSTI-based, as the foundation of effective HIV treatment programs. They also underscore the need for tailored long-term monitoring strategies that integrate virologic and immunologic markers, especially in resource-limited settings where delayed presentation and high baseline viremia remain prevalent. In addition, the limited availability of baseline resistance testing in our context must be acknowledged, as genotyping is not routinely performed outside of research protocols or documented treatment failure.

Morocco has made notable strides in HIV awareness and prevention, supported by national programs and international partnerships, yet critical gaps remain, especially in reaching women, young adults, and marginalized communities. A major advance has been the adoption of a new national diagnostic algorithm, which combines serology with confirmatory polymerase chain reaction, enabling earlier diagnosis and rapid

ART initiation. This innovation is particularly valuable in Morocco, where Western blot is not available in all laboratories, and supports the global test-and-treat strategy by reducing delays in linkage to care. Generalizing this approach across all healthcare settings would further accelerate early treatment uptake and improve long-term outcomes.

Beyond diagnosis, ensuring durable adherence remains a challenge. The COVID-19 pandemic tested Morocco's healthcare infrastructure but also catalyzed innovations in ART delivery, including multi-month dispensing and decentralized care models. Building on these successes, Morocco could further expand differentiated service delivery through peer-led support, mobile health tools, and telemedicine platforms, approaches that have proven effective in South Africa and Kenya.[38,39] Morocco is also advancing toward digital modernization of HIV care, with initiatives to transition from partially paper-based records to unified electronic medical systems. Although beyond the scope of the present analysis, these developments represent an important direction for strengthening HIV program performance nationally.

Another critical frontier is HIV drug resistance monitoring. While Morocco's ART regimens are fully aligned with the World Health Organization's guidelines, the limited availability of genotypic resistance testing and third-line therapies constrains options for patients experiencing virologic failure. By contrast, Western European countries have integrated routine genotyping into clinical practice, enabling targeted regimen selection and optimized salvage therapy. The generalization of genotyping in Morocco would represent a transformative step, allowing personalized treatment, better resistance surveillance, and future-proofing national strategies against emerging resistance patterns.

This study has certain limitations. First, it was conducted in a single national referral center, which may limit generalizability to all people living with HIV in Morocco, although the sociodemographic and clinical characteristics of our cohort closely mirror national surveillance data. Second, baseline genotypic resistance testing was not routinely available during the study period due to resource and access constraints. The few available genotypes were generated through separate research projects and were therefore not included here to avoid redundancy or analytical bias.

5. Conclusion

Human immunodeficiency virus infection management in Morocco must extend beyond prescribing ART to a patient-centered model that integrates immunological and virological monitoring, strengthens adherence, and reduces side effects. Scaling up HIV testing, accelerating diagnosis through simplified algorithms, and ensuring equitable access to care, including gender-sensitive and rural health strategies, are essential to closing current gaps. Building on the resilience demonstrated during COVID-19, Morocco is well-positioned to expand innovations such as telemedicine and resistance genotyping. With sustained commitment, these advances could help Morocco and the wider MENA region move decisively toward ending HIV as a public health threat by 2030.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Ethics approval and consent to participate

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Faculty of Medicine and Pharmacy at Mohammed V University in Rabat, Morocco (Approval ID: CERB 47/23). Given the retrospective nature of the study and the use of anonymized patient data extracted from clinical records, the Ethics Committee waived the requirement for individual informed consent in accordance with national regulations.

Consent for publication

Not applicable due to the retrospective nature of the study.

Availability of data

The data supporting the findings of this study are not publicly available due to patient confidentiality constraints and institutional regulations at the Mohamed V Military Training Hospital. Data may be made available from the corresponding author upon reasonable request and subject to approval by the relevant ethics committee.

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