ISSN 1993-4327
45 P.- Annals of Mechnikov Institute. 2026. N 2
www.imiamn.org.ua /journal.htm

DETERMINATION OF CD4+ CELL COUNT AND VIRAL LOAD IN HIV-POSITIVE PATIENTS AS POSSIBLE INDICATORS OF ART EFFECTIVENESS

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Background

Human immunodeficiency virus (HIV) epidemic has emerged as amongst the greatest threats to human health. Fighting the epidemic involves policies that reduce the new infections and increase the survival rates of those already infected. In recent time, highly active antiretroviral therapy (HAART) has become accessible to the patients [1]. The benefits of combined antiretroviral therapy are well acknowledged in literature [2,3]. The initiation of antiretroviral therapy (ART) among patients suppresses HIV replication and recovers CD4+ cell count [4, 5].

The global response to end Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS) by 2030 is crucially reliant on effective viral load (VL) monitoring and management [6, 7]. A strong predictor of the development to AIDS is the CD4+ T-cell (CD4+) count reported as an absolute level or count of cells (expressed as cells per cubic millimetre of blood) [8]. Soon after starting ART, there is a rapid increase in the peripheral CD4+ cell count [9–11]. Thus, CD4+ cell count recovery after initiation of ART is a potential marker of HIV patient's clinical outcome and an increase in CD4+ cell count indicates a favourable outcome related with both AIDS and non–AIDS-related conditions and the improvement in life expectancy [10–13]. Changes in CD4+ count constitute an important component in patient monitoring and assessment of response to treatment particularly for patients who do not have access to routine viral load testing. As per WHO recommendations CD4+ count monitoring is required every 6 months and viral load testing only when the capacity exists [14]. However, the measurements of CD4+ in most developing countries is not done on a customary basis.

Revision of WHO guidelines in 2010 incorporated some modifications in the management of HIV infected patients. Among them was use of less toxic antiretroviral drugs in first line [1]. In addition, the treatment was to be given to all patients unlike the earlier guidelines wherein the treatment was given only to patients with a CD4+ count <350cell/mm3. The victory of HAART however significantly depends on standard patient follow-up to the treatment during their lifetime. Previous studies have documented rise of CD4+ cell count of at least 25–50 cells/mm3 during the first 12 months on ART, to be correlated with improved clinical outcomes, even in the presence of detectable viremia and recommended that monitoring CD4+ cell count recovery presents an early chance to recognize patients at risk of poorer prognosis [11,15, 16].

Although most patients attain CD4+ cell count recovery after effective ART, a considerable proportion of up to 45% do not experience an appropriate increase in their CD4+ cell counts [4,17, 18]. Patients on ART with poor CD4+ cell count recovery, as defined by either an insufficient increase in CD4+ cell counts from baseline (e.g., < 50 or < 100 cells/mm3) or a failure to achieve a CD4+ cell count over specific thresholds (e.g., 200, 350 or 500 cells/mm3), are at bigger risk of AIDS and serious non-AIDS morbidity and mortality [15, 12–16]. The risk of these combined outcomes in association with a poor CD4+ recovery are greater when ART was initiated at lower CD4+ cell counts [14, 17]. Numerous contributing factors are responsible for poor CD4+ cell count recovery after ART initiation, which include age at the start of therapy, gender, WHO clinical disease stage, duration of untreated HIV infection, viral hepatitis co-infection, baseline CD4+ cell counts, and specific ART regimens [12, 19–23]. Genetic and environmental factors have also been correlated to poor CD4+ cell count recovery during ART, even after adjustment for factors known to influence CD4+ cell count rise [19, 24–26]. Even with existing facts that HIV-infected patients in Africa show least CD4+ cell count recovery as compared with other regions–large enough to potentially influence clinical outcomes [26, 27]; data on CD4+ cell count recovery following initiation of ART are still limited in Sub-Saharan Africa where most patients initiate ART at advanced stages of disease [28, 29].

One major question is whether treatment can be delayed without irreversible immune system damage [30–33], as might be suggested if CD4+ counts normalize irrespective of the pre-treatment CD4+ count. Another significant topic of concern is whether the beneficial effects of ART in raising CD4+ counts are maintained long-term, or are for a limited duration of time and CD4+ counts eventually stabilize or decline in patients on ART.

There are contradictory reports about the pattern of CD4+ counts after multiple years of ART.

Studies of North American and European adults have concluded that CD4+ count continue to rise after 4 to 7 or more years of treatment [34–38] or that the CD4+ count stabilizes, overall [28,29] or in a subset of patients [38,39,40]. Most analyses have constrained CD4+ count assessment to times when plasma HIV-1 RNA (vRNA) was suppressed, e.g. to <50 copies/ml. The characteristics of patients who remain virologically suppressed are likely different from those who are not, resulting in potential selection biases. Therefore it is necessary to estimate CD4+ trajectories in entire populations initiating ART. Additional biases may happen if drop-out, often common, is ignored. For example, if more immunocompromised patients with lower CD4+ counts drop out more often, an analysis that simply includes the patients in follow-up will overestimate the CD4+ count trajectory in the entire population. Such issues may explain why different studies reach diverse conclusions regarding long-term CD4+ count trajectories.

DOI: 10.37321/AMI.2026.2-45-51

Early initiation of antiretroviral therapy (ART) is vital for suppressing viral replication, enhancing immune function, and reducing morbidity and mortality rates [41]. Viral suppression is defined as having a VL of fewer than 1000 copies/mL after a minimum of six months on ART [42]. The Joint United Nations Programme on HIV/AIDS (UNAIDS) 95:95:95 target aims to identify 95% of persons living with HIV (PLHIV), initiate 95% of those identified on ART, and ensure that 95% of those initiated on ART are virally suppressed by 2030 [43, 44]. This approach not only benefits individual patients but also reduces HIV transmission at the population level [42].

Sub-Saharan Africa (SSA) has made noteworthy progress by shifting from CD4+ cell count monitoring to VL monitoring, reflecting a more effective approach for managing HIV [45]. The availability of potent ART has revolutionised HIV care, leading to improved patient outcomes and sustained viral suppression [46]. However, challenges such as viral rebound and suboptimal suppression rates among specific demographic groups, particularly adolescents, continue to hinder effective HIV management [47, 48].

Aim: To compare CD4+ cell count and viral load before and after initiation of antiretroviral therapy in HIV-positive patients.

Methods

A retrospective, observational cohort study by reviewing the documents was conducted among HIV-infected patients initiating first-line ART at the HIV care and treatment clinic between January 2015 and February 2025. Document review was done for comparison of baseline CD4 and CD4 after initiation of ART. Viral load before and after initiation of ART was also compared. Patients were included in this study if they received their initial first-line combination ART regimen for at least 12 months, had complete information about baseline covariates, and had CD4+ cell count and viral load results available at baseline before and 12 months after the initiation of ART. Patients with missing data for essential variables were excluded from the study analysis. Median values of baseline and latest CD4 were calculated and compared. Data analysis was done using SPSS version 23 (SPSS, Inc., Chicago, IL, USA) software.

Written informed consent from patients was not required since this retrospective study only used routinely collected data, but patient records/information were anonymized and only code numbers were used throughout the study.

CD4+ cell counts are performed at baseline and every six months during follow up. CD4+ cell count results recorded at the baseline prior to and 12 months after the initiation of ART were taken for analysis in this study. CD4+ cell count was categorized into three categories, that is, less than 200, 200–500, 500-1500 and more than 1500 cells/mm3. Viral Load was distributed in the range <20 (TND), 20-50, 50-1000, 1000-10000, >10000, >100000 copies/ml.

Among 1008 HIV positive patients majority (80.4%) belonged to age group 21-50 years followed by 51-70 years (10.4%). Male comprised 62.9% of the patients coming to the ARTc for treatment followed by females (36.8%). Three (0.3%) patients were transgender.

Results

Following tables (Tables 1-3) show status of patients and comparison of CD4+ count and viral load before and after the initiation of ART.

Table 1: Status of patients

Status	**No. of patients in % (n=1008)**
Living on ART	60.2%
Died	18.8%
Loss of follow-up	7.7%
Opted-out	3.4%
Transfer-out	6.6%
Unknown status	3.1%

Table 2: Comparison of percentage of patients with CD4+ count in the specified range before and after initiation of ART.

CD4+ count range (cells/mm3)	% of patients with baseline CD4+ count(n=1008)	% of patients with latest CD4 count (after initiation of ART) (n=1008)
>1500	0.7%	0.79%
500-1500	19.1%	38.6%
200-500	39.2%	35.01%
<200	34.3%	19.1%
Unknown	6.54%	0.59%

Median of base line CD4 count was calculated to be 289 cells/mm3 which increased to 458 cells/mm3 after initiation of ART.

DOI: 10.37321/AMI.2026.2-45-51

Table 3. Comparison of % of patients with viral load in specified range before and after initiation of ART.

Viral Load (copies/ml)	% of patients with baseline viral load (n=1008)	% of patients with latest viral load (after initiation of ART) (n=1008)
TND (<20)	20.5%	53.4%
20-50	8.1%	1.1%
Low (50-1000)	6.8%	4.5%
Moderate (1000-10000)	3.2%	0.7%
High (>10000)	3.3%	1.2
Very high (>100000)	2.3%	1.9%
Unknown	55.7%	37%

Maximum percentage of patients showed viral load suppression in patients with moderate viral load range (between 1000-10000) decreasing from 3.2% to 0.7%.
Percentage of patients showing undetectable target raised from 20.5% to 53.4%.

Discussion

Analysis of CD4+ count is an important component in monitoring and evaluating progression of HIV in resource limited settings. The median baseline CD4+ cell count of this study (289 cells/mm3) was similar to some of the studies, which reported median CD4+ cell counts of 240 cells/mm3 [49] and 257 cells/mm3 [50] at ART initiation. This was, however, higher than the median baseline CD4+ cell counts reported in some African studies, including 152 and 201 cells/mm3 in Northern Ethiopia [51, 52], 144 cells/mm3 in Northwest Ethiopia [53], 142 cells/mm3 in Nigeria [54] and 147 cells/mm3 in six sub-Saharan African countries [55]. At 12 months after starting ART, the median CD4+ cell count increased to 458 cells/ mm3 (an increase of +169 cells/mm3 from baseline) and the proportion of patients with CD4+ cell counts < 200 cells/mm3 decreased from 34.3% to 19.1%. This supports data from other studies that ART can lead to an increase in CD4+ cell counts and a decrease in the proportion of patients with severe immunosuppression [39, 52, 53, 54]. In a study from the Ethiopian HIV cohort [52], the median CD4+ count after ART increased from 201 to 423 cells/ mm3, and the proportion of patients with CD4+ count < 200 cells/mm3 decreased from 49.6 to 15.6%. In another Ethiopian HIV cohort study [53], the median CD4+ cell count increased from 144 cells/mm3 at baseline to 266 cells/mm3 at 12 months, and the proportion of patients with CD4+ count < 100 cells/mm3 decreased from 31 to 6%. In the South African HIV cohort study [56], the median CD4+ cell count increased from 97 to 261 cells/mm3 at 48 weeks and the proportion of patients with CD4+ count < 100 cells/mm3 decrease from 51 to 4%. In this study, the increase in CD4+ cell count varied according to baseline CD4+ counts and was larger in patients with low counts compared to those with high counts. Our results are similar to reports from other studies, indicating that a low baseline CD4+ count does not preclude an excellent CD4+ cell count response to ART [56]. This finding is clinically important, because a higher CD4+ cell count is associated with the greatest benefit for patients on ART with a low CD4+ count [9]. About 39.4% of our patients reached a CD4+ cell count >500 cells/mm3 at 12 months of ART. Of note, patients who regain their CD4+ cell count to this immunological point have a better clinical outcome with both HIV- and non-HIV-related morbidity and mortality [20, 22]. Studies from other parts of the country have estimated that 37.6% [57] and 38.8% [52] of patients had reached CD4+ cell counts >500 cells/mm3 after ART start. Recently, one Ethiopian HIV cohort study reported 39% of patients reached a CD4+ cell count >500 cells/mm3 at 12 months [50]. The South African HIV cohort study reported 6.8% of patients achieved a CD4+ cell count >500 cells/mm3 at 48 weeks [56]. Nearly 59% of our patients initiated ART with CD4+ counts >200 cells/mm3 and 39.4% achieved a CD4+ cell count >500 cells/mm3. Studies have reported that individuals initiating ART at higher counts have their CD4+ cell count return to nearly normal or normal (>500 cells/mm3) than those who initiated at lower counts (< 200 cells/mm3) [39, 51]. These findings supplement the evidence suggesting that, to facilitate immune recovery, ART should be started before CD4+ count has fallen below 200 cells/mm3. Studies propose that CD4+ cell count recovery after ART depends predominantly on the baseline levels with patients starting with low CD4+ counts failing to recover CD4+ cell count to >500 cells/mm3 [58]. In the Italian HIV cohort study, having baseline CD4+ count < 350 cells/mm3 was associated with poor CD4+ cell count recovery to >500/mm3 [59]. The Johns Hopkins HIV cohort study reported that delaying to initiate ART at low CD4+ count (< 350 cells/mm3) was associated with failure to recover CD4+ cell count to >500/mm3 [60]. The FHDH HIV cohort study reported that a higher CD4+ count at ART initiation was strongly associated with a higher probability of CD4+ cell count recovery to >500 cells/mm3 [61]. Other studies even reported that recovery to CD4+ cell count >500 cells/mm3 may be achievable only in patients starting with counts >350 cells/mm3 [62]. These results support current guidelines to start ART in all patients before they reach a critical CD4+ cell count and suggest that there may be immunological benefits associated with initiating therapy at even higher CD4+ counts. Patients who started ART at lower CD4 counts continued to have lower CD4 counts than those who began ART at higher CD4 counts.

In the present study, percentage of patients showing undetectable target raised from 20.5% to 53.4%. According to the WHO [21], PLHIV with an undetectable VL cannot transmit HIV to their partners during sexual intercourse. Additionally, pregnant women with undetectable VL are at low risk of transmitting HIV to their children during childbirth or breastfeeding. While early ART may be one of the most promising strategies to reduce HIV incidence, the extent to which rapid suppression of virus influence subsequent HIV transmission in the early phases after HIV diagnosis

remains unknown, as diagnosis of HIV infection is often associated with at least transiently reduced risk behaviours and a decreased risk of HIV transmission even in the absence of ART.

This study has some limitations. First, recommended ART regimens have changed during recent years, so CD4+ outcomes might be different for patients who are starting ART now. As current regimens tend to be better tolerated and possibly more efficacious, in part because of simpler dosing (e.g. once daily) leading to improved adherence, patients starting ART now might have better CD4+ count outcomes than in our study.

Third, it is possible that the better outcomes among patients starting ART at higher CD4+ counts are attributable to differences in other patient characteristics. For example, it is possible that starting ART at higher CD4+ counts is associated with health-seeking behaviour, so patients starting ART at higher CD4+ counts might be expected to fare better for this reason. The major limitation of the study is that the study methodology involved a review of records; therefore, the analysis and interpretation of the data are limited to only those variables that are routinely collected from patients and captured in patient records. Some variables, such as patients' clinical condition, which could have played a major role in initial VL testing and VL suppression, were not available. A baseline VL count was not available for some of the clients; hence, analysis of the baseline VL could not be performed for those patients. Since the study did not measure these other variables, the study was unable to account for the influence of these factors in the analysis.

Conclusion

In conclusion, CD4+ cell count failed to recover in a substantial proportion of patients initiating ART in this resource-limited setting. Therefore, novel therapeutic approaches, with good access to CD4+ cell count monitoring and a focus on those at greatest risk, are needed to maximize CD4+ cell count recovery and improve outcomes during therapy. VL suppression was low among the patients. Health promotion activities are needed for people who have been suppressed to maintain and achieve a lifetime undetectable VL, targeting the younger age group.

Determination of CD4+ cell count and Viral Load in HIV-positive patients as possible indicators of ART effectiveness

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The introduction of antiretroviral therapy (ART) among patients formerly naïve to treatment leads to suppression of HIV replication and CD4+ cell count recovery. The global response to end Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS) by 2030 is critically dependent on effective viral load (VL) monitoring and management cluster of differentiation 4 (CD4+) cell count recovery after initiation of ART is a potential indicator of HIV patient's clinical outcome and an increase in CD4+ cell count indicates a favourable outcome related with both AIDS and non–AIDS-related conditions and the improvement in life expectancy. Early initiation of antiretroviral therapy (ART) is essential for suppressing viral replication, enhancing immune function, and reducing morbidity and mortality rates. In conclusion, CD4+ cell count failed to recover in a substantial proportion of patients initiating ART in this resource-limited setting. Therefore, novel therapeutic approaches, with good access to CD4+ cell count monitoring and a focus on those at greatest risk, are needed to maximize CD4+ cell count recovery and improve outcomes during therapy. VL suppression was low among the patients. Health promotion activities are needed for people who have been suppressed to maintain and achieve a lifetime undetectable VL, targeting the younger age group.

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Received: 13.03.2026
Reviewed: 19.04.2026
Accepted for publication: 10.05.2026