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Evaluation of CD4 count and viral load as predictors of clinical progression and treatment failure in newly diagnosed Human Immunodeficiency Virus-positive patients - a cross sectional study

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Summary

Background and Aims: Human Immunodeficiency Virus (HIV) is a major global public health issue. India contributes third highest burden. CD4 T cells are prime target for HIV virus, so as the HIV infection progresses, the number of these cells declines. HIV-1 RNA Viral load used as a marker to progression of the disease. The aim of this study was to determine and correlate the role of CD4 count and Viral load as predictors of clinical progression and treatment failure in newly diagnosed HIV positive patients.
Materials and Methods: a cross-sectional study was conducted from July 2022 to February 2023. Sample collection (for both CD4 count and Viral load), packaging, storage, transportation and processing are done according to NACO guidelines.
Results: In the present study comparison of baseline, third and sixth month CD4 count, viral load and TND (Target Not Detected) were carried out after three months of HAART treatment where clinical progression and treatment failure were predicted earlier. Even after six months of HAART treatment 21 patients showed ≤350 cells/mm^3 CD4 count and 23 patients showed ≥1,000 copies/ml viral load may develop opportunistic infections due to treatment failure. Whereas, patients with viral load ≥150 copies/ml reduced to 39 (14.6%) after six months due to enhanced adherence to treatment and Opportunistic Infection (OI) management.
Conclusions: Estimation of CD4 count and viral load at third month from the time of ART initiation which is different from routine sixth month testing will increase the chance of predicting clinical progression and treatment failure earlier to control OIs and non-adherence to treatment.

Key words: CD4, viral load, HIV, antiretroviral therapy.

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Introduction

Human Immunodeficiency Virus (HIV) is a major global public health issue. It has created a storm across the world because of its spread, unlike that of any other disease. There were 38.4 million [33.9-43.8 million] people living with HIV at the end of 2021, according to the World Health Organization (WHO) [28].

The first ever known case of HIV infection was diagnosed in June 1981 in Los Angeles, USA. Initially, the HIV epidemic emerged from the developed and industrialized countries, but now focus is shifting fast to South East Asia [29].

CD4+T cells are prime target for HIV virus, so as the HIV infection progresses, the number of these cells declines [23]. The close relationship between clinical manifestations of HIV infection and CD4 count plays an important role in the routine evaluation of HIV-infected individuals [6].

Plasma HIV-1 RNA viral load refers to the number of viral particles found in each millilitre of blood. The higher the amount of HIV RNA in the blood, the faster the CD4 cell count will fall and the greater the risk of becoming ill [21,10].

HIV-1 RNA viral load provides an early and more accurate indication of treatment failure, the need to switch to second-line drugs and distinguish between treatment failure and non-adherence. Also, it is used as a marker for progression of the disease [19].

HIV was once thought to result in “medical apocalypse”. However, with the advent of prevention, diagnosis, care and treatment with Antiretroviral Therapy (ART), the disease transformed from a virtual death sentence in the early 1980s into a chronic manageable disease nowadays. Adherence to ART helps to keep the viral load under control and prolong the time of progression to Acquired Immunodeficiency Syndrome (AIDS), resulting in near normal life expectancy. ART has allowed improvements in HIV-1 viral loads and CD4 cell counts [2].

Even with the introduction of ART, a substantial number of patients have higher rates of poor treatment adherence due to lack of family and social support, adverse drug effects, complex drug regimens, literacy, social stigma, psychological distress and low patient self-efficacy [7].

Despite the move towards universal provision of ART

regardless of the clinical symptoms and conditions, CD4 testing and expansion of viral load monitoring should be continued to assess the effectiveness of ART in People Living with HIV (PLHIVs) and get a complete picture about how the immune system is fighting against HIV.

Hence, this study aims to determine and correlate HIV-1 viral load and CD4 count so that treatment response can be monitored and it will also help in transmission prevention.

Materials and Methods

A total of 267 newly diagnosed HIV-1 seropositive patients attended the ART clinic were included in this study. The study settings were an ART centre, a viral load and CD4 laboratory in a tertiary care hospital, and the Department of Microbiology, Government Medical College of Nagpur, India. The study period was from July 2022 to June 2024.

Inclusion criteria were: newly diagnosed HIV-1 seropositive cases, patients equal to or of more than 15 years, patients willing to participate after written informed consent.

Exclusion criteria were: HIV-1 positive patients who are not on naive ART treatment, HIV non-reactive patients, pregnant women, paediatric population less than 15 years, non-willing patients.

Collection and processing of specimens

After taking written informed consent, clinical history of each patient is noted. All newly diagnosed HIV positive patients blood samples received in ART clinic, were separated simultaneously into two tubes for both CD4 count and viral load testing.

CD4 count testing was performed by Sysmex Partec CyFlow(R) Counter flow cytometer and Abbott Real Time RT-PCR detected the amplified DNA. Sample collection, package, transportation & storage and processing were done according to NACO guidelines [17-19].

Results

Among 267 newly diagnosed HIV-1 seropositive patients,167 were males (62.5%) and 100 were females (37.5%) with male to female ratio 1.67:1. The age of the patients ranged from 15 to 65 years. Maximum number of patients 82 (30.7%) were in the young sexually active age group of 25-34 years.

The majority of the patients were from urban areas and heterosexual route was the most common mode of transmission followed by homosexual. Labourers were the most common occupation. Bacterial opportunistic infections were found to be the most common in the study group. Maximum number of patients were on TDF+3TC+DTG (TLD) combination.

Table 1 shows the number of patients with CD4 count ≤350 cells/mm³ were decreased from at the start of treatment (baseline) 197 (73.8%) to both third month 80 (30.0%) and sixth month 21 (7.9%) whereas, patients with CD4 count ≥350 cells/mm³ were increased from at the start of treatment (baseline) 70 (26.2%) to both third month 187 (70.0%) and sixth month 246 (92.1%) due to adherence and Opportunistic Infections (OI) management.

Comparison of baseline, third month and sixth month CD4 count which shows 80 (30.0%) patients with ≤350 cells/mm³ CD4 count after three months of Highly-Active Antiretroviral Therapy (HAART) treatment where clinical progression and treatment failure of these patients were predicted earlier. Out of these 80 patients, even after six months of HAART treatment 21 patients who shows ≤350 cells/mm³ CD4 count may develop opportunistic infections due to treatment failure as depicted in Table 1 and Figure 1.

Table 2 shows the number of patients with viral load ≥1,000 copies/ml were decreased from at the start of treatment(baseline) 210 (78.7%) to both third month 115 (43.1%) and sixth month 23 (8.6%) whereas, patients with viral load ≤1,000 copies/ml were increased from at the start of treatment(baseline) 57 (21.3%) to both third month 152 (56.9%) and sixth month 244 (91.4%) due to adherence and OI management.

Comparison of baseline, third month and sixth month viral load

Table 1. Correlation of CD4 count at the start of treatment (baseline), third and sixth month in HIV-1 seropositive patients (n=267).

CD4 count	At the start of treatment (baseline)	Third month	Sixth month
≤350 cells/mm³	197 (73,8%)	80 (30,0%)	21 (7,9%)
≥350 cells/mm³	70 (26,2%)	187 (70,0%)	246 (92,1%)
Total	267 (100%)	267 (100%)	267 (100%)

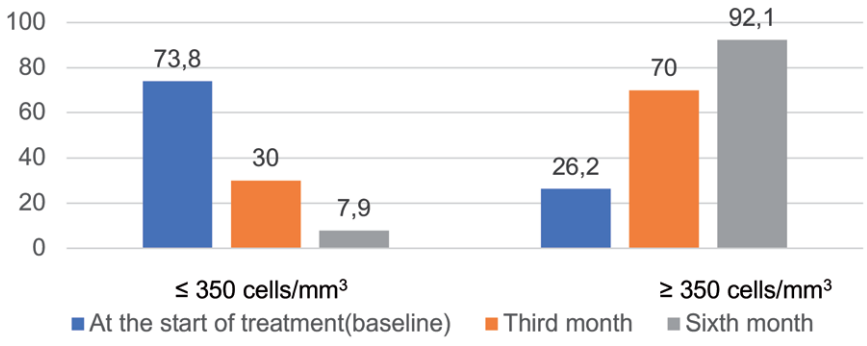

Figure 1. Correlation of CD4 count at the start of treatment (baseline), third and sixth month in HIV-1 seropositive patients.

testing which shows 115 (43.1%) patients with ≥1,000 copies/ml viral load after three months of HAART treatment where clinical progression and treatment failure of these patients were predicted earlier. Out of these 115 patients, even after six months of HAART treatment 23 patients who shows ≥1,000 copies/ml viral load may develop opportunistic infections due to treatment failure as depicted in Table 2 and Figure 2.

Table 3 shows the number of patients with viral load ≥150 copies/ml were decreased from at the start of treatment(baseline) 250 (93.6%) to both third month 161 (60.3%) and sixth month 39 (14.6%) whereas, patients with viral load ≤150 copies/ml (TND, Target Not Detected) were increased from at the start of treatment(baseline) 17 (6.4%) to both third month 106 (39.7%) and sixth month 228 (85.4%) due to enhanced adherence to treatment and OI management.

Comparison of baseline, third month and sixth month TND which shows 161 (60.3%) patients with ≥150 copies/ml viral load after three months of HAART treatment whereas, patients with viral load ≥150 copies/ml reduced to 39 (14.6%) after six months due to enhanced adherence to treatment and OI management as depicted in Table 3 and Figure 3.

Table 2. Correlation of viral load during at the start of treatment (baseline), third and sixth month in HIV-1 seropositive patients (n=267).

Viral load	At the start of treatment (baseline)	Third month	Sixth month
≥1,000 copies/ml	210 (78,7%)	115 (43,1%)	23 (8,6%)
≤1,000 copies/ml	57 (21,3%)	152 (56,9%)	244 (91,4%)
Total	267 (100%)	267 (100%)	267 (100%)

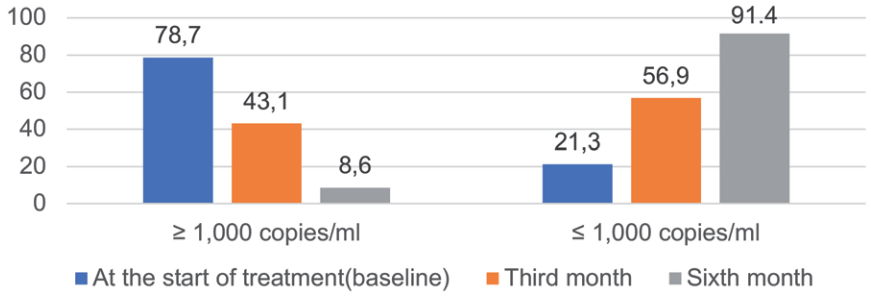

Figure 2. Correlation of viral load at the start of treatment (baseline), third and sixth month in HIV-1 seropositive patients (%).

Table 3. Correlation of TND (Target Not Detected) at the start of treatment (baseline), third and sixth month in HIV-1 seropositive patients (n=267).

Viral load	At the start of treatment (baseline)	Third month	Sixth month
≥150 copies/ml	250 (93,6%)	161 (60,3%)	39 (14,6%)
≤150 copies/ml(TND)	17 (6,4%)	106 (39,7%)	228 (85,4%)
Total	267 (100%)	267 (100%)	267 (100%)

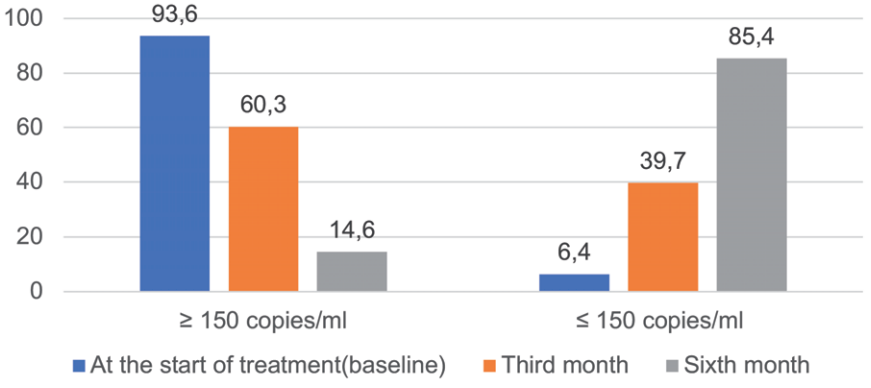

Figure 3. Correlation of TND (Target Not Detected) at the start of treatment (baseline), third and sixth month in HIV-1 seropositive patients (%).

Discussion

In the present study, the percentage of patients with CD4 count ≤350 cells/mm³ at the start of treatment (baseline) were 73.8% which is in accordance with the study by Gezie *et al.* (76.8%) [9]. Both clinical progression and treatment failure was predicted by CD4 count at third month which is in accordance with the study by Monforte *et al.* which concluded that the 3-month immunological response is a reliable predictor of long-term clinical outcome [16]. According to Chaisson *et al.* patients with opportunistic infections experienced monthly reductions in CD4 counts that were considerably greater than those without OIs [4].

A study by Testori *et al.* related both immunological and virological markers to the clinical outcome of HAART which concluded that within three months after starting HAART, half of the new AIDS-defining events happened. This could be attributed to a delayed immune restoration, as having CD4 cell counts ≥200×10⁶ cells/l did not prevent AIDS from occurring in the first few months but did lower the risk in the upcoming months. CD4 cell counts ≤200×10⁶ cells/l and baseline HIV-RNA levels ≥100,000 copies/ml after three months of HAART were independently predictive of treatment failure [26]. The CD4 count is a powerful predictor of HIV patient response to ART and should be used for appropriate management of the disease's progression. Disturbance in the ART treatment, patient's socioeconomic status, demographic & behavioural factors, accessibility and length of treatment can all affect the CD4 cell count.

According to Wilson *et al.* viral suppression occurred more slowly in patients whose baseline viral loads were >100,000 copies/mL which is in accordance with the current study and Broyles *et al.* (2023) stated that patients with viral loads <1000 copies/mL had zero risk of sexual transmission of HIV[27,3].

The proportion of patients receiving ART with sustained viral suppression increased over the past decade. New drugs and combination fixed-dose tablets have enhanced the efficacy, safety and tolerability of regimens. Better access to care and adherence to treatment may also have contributed to improved virologic suppression [30]. Unsuppressed HIV VL was independently associated with lower CD4 cell count, social isolation, high stigma, not receiving a single-tablet daily regimen, multiple late appointments in past year and immunological failure [22]. When initiating ART, sustained virological suppression is the goal because it leads to increase in CD4 cell count and hence markedly reduced risk of clinical events and reduces the risk of developing resistance [5,12,14,15,25].

A study by Shoko *et al.* concluded that although patients take more time to achieve a normal CD4 cell count and less time to achieve an undetectable viral load, once the CD4 cell count is normal, mortality risks are reduced. Therefore, both viral load and CD4 count monitoring can be used to provide useful information which improve life expectance of patients. However, viral load monitoring is a better predictor of HIV/AIDS progression than CD4 cell count and hence viral load is deemed superior [24]. Patients' health is closely correlated with the quality of patient-physician relationship and counselling [1,8]. Enhancing clinical practices is advised by Ickovics *et al.* (2002) in order to improve treatment outcomes for HIV patients. Even with the significant attention that adherence has received recently still there are more works has to be done to comprehend and encourage adherence to HAART [11].

A prospective cohort study conducted by Mellors *et al.* (1997) concluded that incorporating both HIV-1 RNA measurements and CD4+ lymphocyte counts provided better discrimination of outcome than either marker alone [13]. Although the pace of decline in CD4+ lymphocyte count, the development of AIDS and death are highly predicted by plasma viral load, the prognosis of HIV-infected individuals is more precisely determined by measuring both plasma HIV-1 RNA and CD4+ lymphocytes together [20].

Conclusions

HIV infection was found to be more common among sexually active young males and heterosexual was found to be the most common mode of transmission followed by homosexual, which can be reduced by educating about safe-sex practices. The present study indicates that early diagnosis, effective and aggressive treatment of HIV and co-infections according to available guidelines, strong commitment, a focused approach as well as strong coordination between all national control programmes is the need of the hour especially in countries like India.

The problem of nonadherence is global which can be overcome by counselling, identification of barriers with practical strategies to overcome them, usage of potent antiretroviral regimens, treating depression and other mental illnesses. The present study indicates estimation of CD4 count and viral load at third month from the time of ART initiation which is different from routine sixth month testing. It will increase the chance of predicting clinical progression and treatment failure earlier to control OIs and non-adherence to treatment. During third month, OIs and non-adherence can be ruled out & overcome early by treatment of OIs, enhanced adherence counselling and appropriate testing which will further help in increasing the life expectancy of patients.

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Informed consent: the patient gave her written consent to use her personal data for the publication of this case report and any accompanying images.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.

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