Original Article

Evaluation of Prognostic response in HIV positive patients after Antiretroviral Therapy

Nadya Usman[1], Muhammad Abdul Rehman[2], Muhammad Bilal Ghafoor[3], Muhammad Ali Malik[4], Muhammad Shoaib Khan[5], Ajmal Shah Bukhari[6]

[1] Biochemist, Department of Pathology, Shiekh Zayd Medical College, Rahim Yar Khan, Punjab.
[2] Professor and HOD, Department of Pathology, Shiekh Zayd Medical College, Rahim Yar Khan, Punjab.
[3] Associate Professor, Shiekh Zayd Medical College, Rahim Yar Khan, Punjab.
[4] Senior Medical Technician, Shiekh Zayd Medical College, Rahim Yar Khan, Punjab.
[5] Professor and HOD, Department of Biochemistry, Bannu Medical College, Bannu.
[6] Professor, Department of Surgery, Bannu Medical College, Bannu.

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Corresponding Author
Dr. Nadya Usman,
Biochemist,
Department of Pathology,
Shiekh Zayd Medical College,
Rahim Yar Khan, Punjab, Pakistan
Email: n.usman84@gmail.com

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Abstract

Objective: The present study was aimed to monitor the prognostic response of antiretroviral therapy in HIV positive patients.

Methodology: The study was conducted on confirmed HIV positive patients registered at HIV treatment and care centre, PIMS. Islamabad from January 2013 to December 2015. Among all HIV positive patients, 276 adult cases were selected. There were 263 patients on first-line antiretroviral (ARV) therapy and 13 patients were shifted to 2nd line ARV therapy. CD4 cell counts and viral load (Polymerase chain reaction) monitoring was done after one year of starting ARV therapy.

Results: Out of 276 adult patients, 75% (n=207) were male and 25% (n=69) were females. Among 276 adult cases, 95.3% (n=263) patients were on first line ARV therapy. Patients on first line ARV therapy showed good prognostic response. There were 15.5% (n=40) patients having CD4+cells less than 350 cells/µL. There were 84.5% (n=223) patients having CD4 +cells count greater than 350 cells/µL There were 69% (n=182) patients having viral load <50 copies/ml and 31% (n=81) patients who had viral load >50 copies/ml.

Conclusion: First line ARV therapy given to HIV positive patients proved itself best both in respect of increasing the immunity of HIV positive patients by increasing the number of CD4 cells and also results in effective viral load suppression.

Keywords: Antiretroviral therapy, CD4+ cells, HIV patients.

Introduction

Human immunodeficiency virus is responsible to cause HIV infection and Acquired Immunodeficiency Syndrome (AIDS), thus people with AIDS are at a very high risk of acquiring multiple infections, cancers, and other AIDS-related complications. HIV testing and counseling is the first crucial step for linkage to HIV treatment and prevention. When HIV infection proceeds, CD4 cell count starts to decline. At present, CD4 cell count is considering a strong predictor of monitoring the risk of AIDS. When HIV positive patients have CD4 cell count below 250cells/ml, antiretroviral therapy is going to be initiated.[1]

CD4 cell count has given central importance in deciding ARV initiation, ARV switching, and managing opportunistic infections timely. Immunity in HIV positive patients will decline continuously when their CD4 cell count falls below 200 cells/ml and ARVs have not been initiated yet.[2]

In a study conducted in South Africa, HIV positive patients had given ARVs at a CD4 cell count of 200 cells/ml and 92% of patients showed a good prognostic response. The same findings had been shown in the Uganda cohort study. These patients also showed viral load suppression with CD4cell count > 200 cells/mm.[3,4]

Polymerase Chain Reaction (PCR) test is used for early detection and quantitation of human immunodeficiency virus in plasma of HIV infected patients. This test is also helpful in deciding for switching to second-line ARV therapy and monitoring their prognostic response as well. In HIV infection, approximately 10 $\log^{10}$ virions of HIV are produced per day and a PCR test is used to detect this viral load in plasma of HIV-infected patients. AIDS will be developed in those HIV positive patients having very high plasma viral load and low CD4 lymphocytes.[5]

The best and standard way of treatment for HIV infection is ARV therapy in the form of a three to the four-drug combination. The following are the main classes of ARV therapy: nucleoside, nucleotide, and non-nucleoside reverse transcriptase inhibitors and integrase inhibitors. They block the HIV genome replication process. Fusion inhibitors and C-Chemokine Receptor (CCR5) antagonists work by blocking HIV viral entry into host cells. Protease inhibitors block the function of proteins that are vital for viral development. When these drugs are given in combination form, low viral levels can be maintained.[6]

To achieve better responses, these drugs are given to HIV positive patients in the form of a regimen. The first-line regimen includes mostly two Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) and one Nucleoside Reverse Transcriptase Inhibitor (NRTI) and 2nd line regimen include drugs that inhibit protease enzyme, which prevent cleavage of viral precursors. The most common 2nd line drug is Kaletra and the regimen include protease inhibitor+1 NRTI+1 NNRTI.[7]

The World Health Organization (WHO) recommends a first-line ARV therapy should consist of two nucleoside reverse transcriptase inhibitors and a non-nucleoside reverse transcriptase inhibitor.[8] The goal of treatment is to lower the plasma HIV RNA level and enhance CD4+ cell counts. Generally, 1-2 log decrease in viral load and an increase of CD4 immune cells per year is taken as an indication of positive drug effects.[9]

ARV therapy provides more beneficial results when it is being initiated at a CD4 cell count of 500cells/ml instead of 350 cells/ml.[10]

Keeping these in mind the present study was designed to see that after one year of starting ARV therapy, prognostic responses are checked by monitoring CD4 cells count and HIV PCR testing in HIV-infected patients. The rationale of the study was to emphasize the importance of CD4 testing for initiating antiretroviral therapy in newly diagnosed HIV positive patients and the importance of both CD4 testing and PCR testing in HIV positive patients who were on the first line and second line ARV therapy.

Materials and Methods

Prospective observational study design and Random sample technique were used in this study. For CD4 cell count, 3ml whole blood is taken in K3EDTA tubes (BD Diagnostics, USA). CD4 cell count was done by the FACSCALIBUR flow cytometer. A measured quantity of 20µL of Tritest CD4FITC/ CD8PE/ CD3PERCP reagent (BD Biosciences, USA) was added to the BD Trucount tm tube (BD Diagnostics, USA) containing beads and 50ul of whole blood added in it. The instrument was calibrated by running Calibritetm 3 reagent (BD Biosciences, USA) with sheath fluid using BD Facscomp tm version 2.0 to set photomultiplier tubes (PMT) voltages, fluorescence compensation, to check instrument sensitivity and to adjust the threshold to minimize debris. Sample acquisition and analysis were done using MULTISET software.

HIV RNA in plasma was quantified by polymerase chain reaction(PCR) Test. The Cobas Ampliprep and Cobas AMPLICOR HIV-1 MONITER test was used as automated PCR technology for the quantitative

detection of HIV-1 RNA in EDTA anticoagulated plasma. Its sensitivity is over range 50-1000000 copies/ml.

Automatic specimen preparation was done to extract HIV-1 RNA using the DNA probe capture technique. Reverse transcription of target RNA was done with the help of specific primers and rth polymerase. rth pol had both reverse transcriptase and DNA polymerase activity. Amplification of target complementary DNA was done using HIV-1 specific complementary primers.

Automated denaturation did use, HIV-1DN4 reagent(Roche Molecular Systems, USA), and detection is done using reagents HIV-1AD3, HIV-1CN4, and HIV-1 SB3 (Roche Molecular Systems, USA).Probes for detection of quantitation standard present in reagent HIV-1 SQ4(Roche Molecular Systems, USA).

The inclusion criteria for the present study included those HIV-positive patients who had been confirmed HIV positive status by all three tests i.e Rapid test, ELISA test, and Western blot test. Only adults HIV positive patients, registered at HIV treatment and care centre in PIMS, Islamabad were selected. Patients of both gender age 30-40 years were selected.and Exclusion Criteria included HIV positive patients with age less than 30 years, HIV positive pregnant females, and HIV positive transgenders.

Results

The data was entered on SPSS version 23. The quantitative data were presented as mean. The qualitative data were presented as a percentage**.** In this given statistics, no test of significance was applied.

Among 276 HIV positive adult cases, 75% (n=207) were males and 25% (n=65) were females. 263 HIV patients were taking first-line ARV therapy.

The number and percentages of adult HIV patients taking first-line Antiretroviral therapy had been shown in Table 1. Maximum HIV positive patients were on regimen efavirenz, lamivudine, and zidovudine. (EFV+3TC+ZDV)

Table 1: Number of HIV Patients on first line Antiretroviral Therapy

Sr. Number	*Regimen*	*No. of Patients*
1	3TC+D4T	0.38% (n=01)
2	3TC+ZDV	1.90% (n=05)
3	EFV+3TC+D4T	11.40% (n=30)
4	EFV+3TC+TNF	0.38% (n=01)
5	EFV+3TC+ZDV	24.71% (n=65)
6	EFV+ZLM	37.64% (n=99)
7	NEVILAST40mg	0.76% (n=02)
8	NFV+3TC+ZDV	0.38% (n=01)
9	NVP+3TC+D4T	1.90% (n=05)
10	NVP+3TC+ZDV	17.49% (n=46)
11	NVP+ZLM	1.52% (n=4)
12	Zidolam	1.52% (n=4)

Baseline CD4 Cell count monitoring was done before the initiation of antiretroviral therapy. One year after the initiation of first-line ARV therapy, CD4 cell count was monitored. There were 84.5% (n=223) patients having CD4+ cell count greater than 350 cells/uL and 15.5% (n=40) patients having CD4+ cell count less than 350 cells/uL as shown in Figure 1. THE mean CD4 cell count of patients on first-line ARV therapy was 361 cells/UL and SD was ± 181 of the mean value.

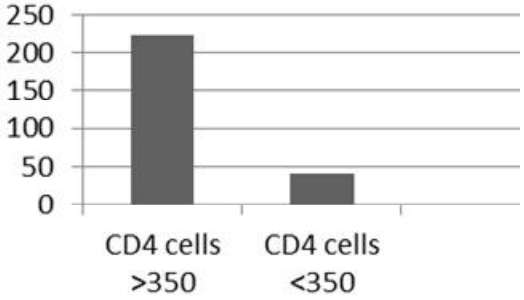

Figure 1: CD4+ cell count of HIV positive patients on first-line ART

The baseline viral load of HIV positive patients were not monitored. The viral load outcome of HIV positive patients was measured after one year of initiating first-line antiretroviral therapy. The mean outcome was 88023. There were 182 patients having viral load <50copies/mL (69%). 81 patients had a viral load >50copies/mL (31%) shown in Figure 2.

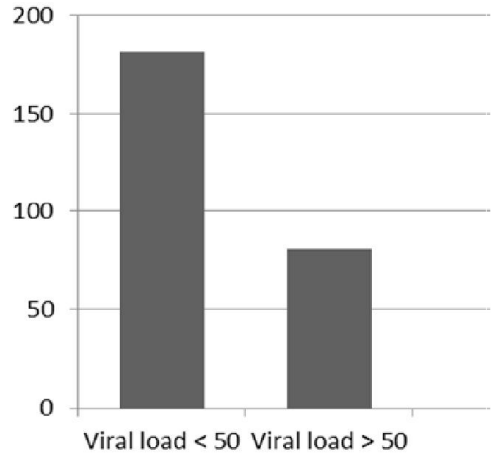

Figure 2: Viral load of HIV positive patients on first-line ART

The number and percentages of adult HIV patients taking second-line Antiretroviral therapy had been shown in Table 2.

Table 2: Number of HIV patients on second-line Antiretroviral Therapy

Sr. Number	*Regimen*	*No. of Patients*
1	KLT+3TC+D4T	7.69% (n=01)
2	KLT+3TC+ZDV+DDI	7.69% (n=01)
3	KLT+DDI+TNF	46.15% (06)
4	KLT+DDI+ZLM	7.69% (n=01)
5	KLT+TNF+D4T+3TC	7.69% (n=01)
6	KLT+TNF+ZLM	15.38% (n=02)
7	KLT+ZLM	7.69% (n=01)

There were 95.3% (n=263) HIV positive patients on first-line ARV therapy and 4.7% (n=13) patients were on second-line ARV therapy. Second-line ARV therapy was initiated only in those HIV positive patients who had failed to respond to first-line ARV therapy. Only 13 out of 276 patients did not give a good response with first-line ARV therapy. Their mean CD4 Cell count was 205 and SD ± 122 of the mean value.

Discussion

HIV and AIDS have become the most prevailing disease in Pakistan. ART is recommended for HIV infected patients. ART is the use of medicine to treat HIV infection. When taken in combination, HIV medicines can prevent the replication and transmission of the HIV virus.

Awareness regarding HIV transmission, diagnosis, treatment, and ARV therapy prognosis comes with the establishment of different HIV and AIDS treatment centers in different regions of Pakistan. Patients registered in the PIMS centre until 2009 were observed to monitor CD4+ and viral load outcomes.

All registered patients in centre were confirmed HIV positive cases. Most HIV patients were male. Age ranges from 30 to 40 years. CD4+ cell count and HIV PCR test was monitored in patients on first-line ARV and second-line antiretroviral therapy. Maximum numbers of HIV patients were on the first-line combination of ARVs than second-line ARVs therapy. Their CD4+ cell count was monitored after one year, showing good CD4+ cells response to first-line ARVs. CD4 cell count increase in our study was 361 cells/ul. While in a study at ShriBhausaheb, Maharashtra, CD4 cell count was monitored before and after initiation of ARV therapy. The mean CD4 count in 57 patients before initiation of ARV therapy was 222, and SD ± 149 of the mean value. After 6 months of ARV therapy, the mean CD4 count increased to 306 and SD ± 178 of the mean value.[1]

Adherence towards ART had been studied in 546 HIV positive Kenyan patients receiving HAART for up to 228 months and found good adherence to ART. 65.8% of Patients showed HIV viral suppression with enhanced CD4 immune cells.[11]

In the present study viral load of HIV patients taking first-line ARV therapy was monitored one year after initiation of therapy. 67% of patients were having a viral quantity of fewer than 50 copies/mL showing good suppression of HIV in plasma against first-line ARV therapy.

The virological outcome had been studied among sub-Saharan African patients, virological success monitored at 12 months and 24 months since ART initiation was 87.7% and 83.7% respectively.[12]

In an estimate from the study in Europe and the United States, the proportion of individuals with suppressed virological replication was greater for immediate universal cART initiation earlier in the follow-up. By 7 years, all strategies resulted in estimated proportions of virological suppression between 83% and 87%.[13]

A study had been conducted in Thailand on people living with HIV aged 10-24 years who initiated ART from 2008 to 2013 through the Thai National AIDS Programme and who were followed up until 2014. At one year after initiating ART, 84% of patients showed good suppression and only 16% experienced

virological failure. Their mean CD4 cell count was also raised from 190 cells to 310 cells/mm^3.[14]

Good response of CD4 cell count and RNA viremia towards HIV medicines depends upon the type of regimen taken by HIV patients. Some patients did not enhance their CD4+ cell count and showed no better viral response. They did not show response because of greater HIV replication and greater chances of viral mutation. That was the reason specific drugs against specific enzymes did not properly work, leading to poor prognosis of patients towards treatment.

Maximum HIV positive patients had shown good adherence to first-line ARV treatment.

Conclusion

First-line ARV therapy given to HIV positive patients proved itself best both in respect of increasing the immunity of HIV positive patients by increasing the number of CD4 cells and also results in effective viral load suppression.

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