Original Research Article

Baseline characteristics and immunological response to antiretroviral therapy in HIV-2 patients

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Abstract

Background: HIV-2 differs from HIV-1 as it is associated with lower viral load levels and slower rates of CD4 decline and clinical progression compared with HIV-1. **Aim:** To study baseline characteristics and immunological response to antiretroviral therapy in HIV-2 patients. **Material and Methods:** This cross-sectional study included HIV-2 patients who visited ART centre in tertiary care hospital through SACEP and / or HIV-2 patients admitted in the medical wards and who were documented HIV-2 reactive with western blot confirmation. Every 6 monthly CD4 counts of all patients were noted. Immunological response to ART was evaluated during the course of study period. **Results:** Median baseline CD4 count of study population was 211 (123.7-303.2 cells /µl). The immunological response to ART after 6 months and after 12 months of starting ART was analysed in 164 patients. An increase in median CD4 count from baseline at 6 months (+102.5 cells /µl) and at 12 months (+135 cells /µl) was observed. **Conclusion:** An increase in median CD4 count at 6 months and 12 months from the baseline median CD4 count was observed. The response to ART and the pattern of resistance to ART is unique; and further studies should be carried out for the same.

Key Words: HIV-2, CD4 count, ART treatment, Immunological response

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Received Date: 22/11/2019 Revised Date: 19/12/2019 Accepted Date: 08/01/2020
DOI: https://doi.org/10.26611/10211314

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 09 January 2020

INTRODUCTION

HIV-1 and HIV-2 are closely related retroviruses of the same genus (Lentiviridae) and share the same modes of transmission. However, HIV-2 differs from HIV-1 as it is associated with lower viral load levels and slower rates of CD4 decline and clinical progression compared with HIV-1;[1,2] 86% to 95% of people infected with HIV-2 are long-term nonprogressors.[3,4] Recent data show that survival of persons with undetectable HIV-2 viral load is similar to that of the general population.[4] However, HIV-2 can cause immune-suppression, as well as AIDS characterized by the same signs, symptoms, and opportunistic infections that are seen in HIV-1. HIV-2-associated AIDS may often be associated with lower viral load levels than HIV-1 (>10,000 copies/mL in HIV-2 versus sometimes millions of copies/mL in HIV-1).[4]

The prolonged course of human immunodeficiency virus (HIV) infection is marked by a decrease in the number of circulating CD4+T helper cells and persistent viral replication, resulting in immunologic decline and death from opportunistic infections and neoplasm.[5,6] Our institution has an ART centre which is one of the largest in the country and has a centre of excellence which caters to special situations like HIV-2 patients, first line ART failure and patients with adverse reaction to ART. The present study was conducted to study baseline characteristics and immunological response to antiretroviral therapy in HIV-2 patients.

How to cite this article: Kashmira Rajendra Hajare, Rahul Kadu, Priya Patil. Baseline characteristics and immunological response to antiretroviral therapy in HIV-2 patients. *MedPulse International Journal of Medicine.* January 2020; 13(1): 13-16.
https://www.medpulse.in/Medicine/

MATERIAL AND METHODS

Study design

This cross-sectional study included HIV-2 patients who visited ART centre in tertiary care hospital through SACEP and / or HIV-2 patients admitted in the medical wards and who were documented HIV-2 reactive with western blot confirmation. Western blot confirmation was obtained by sending samples to NARI, Pune. The study protocol was reviewed and approved by the Institute Ethics Committee.

Patient definition

Any HIV-2 reactive with western blot confirmation patient registered at ART centre or admitted in medical wards and who fulfilled the inclusion criteria.

Patients selections

All the HIV-2 patients who visited ART centre in tertiary care hospital through and / or HIV-2 patients admitted in the medical wards were included in the study provided they fulfilled the following criteria.

Inclusion criteria

- All HIV-2 reactive patients with western blot confirmation enrolled at ART centre.
- HIV-1 and HIV-2 co-infected patients.
- All above patients who gave written informed consent were included in study.

Exclusion criteria

- All HIV-1 reactive patients who were non-reactive for HIV-2 infection.
- Patients who did not give written informed consent.

Data collection

Sociodemographic data, WHO clinical staging of study population at the time of initial visit, 6 monthly CD4 counts, ART data were obtained from patient admitted in medicine wards, from ART centre, from white cards available at ART centre, from green book (ART registration book), from SACEP records with NACO permission and from previous case paper records if any available.

Clinical evaluation

Detailed history and clinical examination were done on every ART visit days starting from the day of inclusion into study. All the patients were evaluated at the time of each visit at ART centre for associated symptoms, opportunistic infections. Every 6 monthly CD4 counts of all patients were noted and occurrence of opportunistic infections with respect to CD4 count was evaluated. Immunological response to ART was evaluated during the course of study period. For the patients who were admitted in medical wards, detailed history and clinical examination were done and details of opportunistic infections, clinical profile and 6 monthly CD4 were taken.

Statistical analysis

Stata SE 13.1 was used to analyse data. Mean, Standard deviation, Standard error, 95% Confidence intervals were calculated. If the variable is not normally distributed, Median and Interquartile range were used. Normality was assessed by the Shapiro-Wilk procedure. Mann Whitney U test was used to test variables that were not normally distributed with 2 groups. Spearman`s correlation coefficient (rho) was used to correlate 2 quantitative variables. A p value (significance) of < 0.05 (Sig.) was deemed statistically significant, $p < 0.01$ as highly significant (HS) and $p < 0.0001$ as very highly significant (VHS).

RESULTS

In our study, total 289 patients of HIV-2 were enrolled. A majority of them 158 (54.7%) belonged to the age group of 41 to 50 years and the median (IQR 25%-75%) age was 46 (42-51) years. Of the 289 individuals analyzed, 203 (70.24%) were males and 86 (29.76%) were females. Male to female ratio was 2.4:1. Thus, in our study prevalence of HIV-2 was more in male as compared with female. This may be due to high risk behaviour in male individual. In our study, out of 289 HIV-2 patients 223 (77.16%) were married, 19 (6.57%) were unmarried and 47 (16.26%) were widow and widower.

Table 1: Distribution of study population according to baseline CD4 count

Baseline CD4 (cells /µl)	No. of cases		Percentage (%)	
≤50	11		3.81%	
51-200	122	238	42.21%	82.35%
201-350	116		40.14%	
>350	40		13.84%	
Total	**289**		**100%**	

In the present study, we evaluated the study population according to baseline CD4 categories and we observed that, maximum cases (238, 82.35%) had baseline CD4 count in between 51 to 350 cells /µl. 40 (13.84%) cases had CD4 count >350 cells /µl and 11 (3.81%) cases had CD4 count ≤50 cells /µl. Median baseline CD4 count of study population was 211 (123.7-303.2 cells /µl).

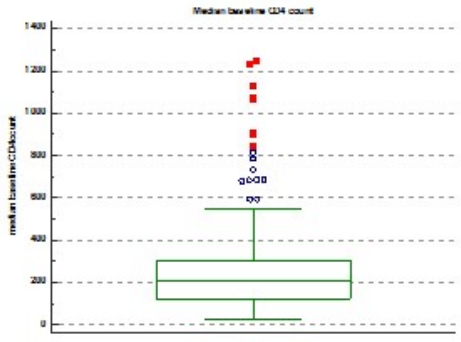

Fig. 1: Median baseline CD4 count of study population

In our study, 141 (48.79%) cases belonged to WHO stage I while 35 (12.11%) cases belonged to WHO stage II, 60 (20.76%) cases belonged to WHO stage III and 53 (18.34%) cases belonged to WHO stage IV indicating slower progression of HIV-2 infection as maximum cases were had WHO stage I category.

Table 2: Median baseline CD4 count according to WHO clinical staging

Categories	No. of cases	Median baseline CD4 (cells /µl)	IQR (25% - 75%)
WHO stage I	141	249	160.750 to 317.500
WHO stage II	35	248	113.250 to 284.750
WHO stage III	60	196.5	108.000 to 310.500
WHO stage IV	53	139	85.000 to 231.750
Total	**289**	**211**	**123.750 to 303.250**

Median baseline CD4 count in WHO stage I was 249 cells /µl (IQR 25%-75%=160.750 to 317.500) and in WHO stage IV was 139 cells /µl (IQR 25%-75%=85.000 to 231.750). This indicates fall in CD4 count from WHO stage I to WHO stage IV. WHO clinical staging of 289 HIV-2 patients was statistically analysed by using Spearman`s correlation coefficient (rho) with baseline CD4 counts. Results suggest negative linear relationship between WHO clinical staging and CD4 count; rho= -0.258, p <0.0001, 95% CI for rho = - 0.363 to -0.147) HIV-1 and HIV-2 dual infection was observed in 13 (4.50%) cases. Out of 289 HIV-2 infected individuals, 264 (91.43%) were started on ART either due to low CD4 count (<350) or due to OIs. 25 (8.65%) individuals were not started on ART. We observed that ART was started to majority of the study population.

Table 3: CD4 trend in HIV-2 patients on ART

CD4 trend on ART	No. of cases	Mean CD4 cells /µl	Median CD4 cells /µl	IQR (25%-75%)
Baseline CD4	164	205.7	200	110.5 – 278
CD4 after 6 months	164	338.9	302.5 (+102.5)	205.5 - 441.5
CD4 after 12 months	164	411.7	335 (+135)	228 – 553

We could analyse the immunological response to ART after 6 months and after 12 months of starting ART in 164 patients. We observed an increase in median CD4 count from baseline at 6 months (+102.5 cells /µl) and at 12 months (+135 cells /µl).

DISCUSSION

Median baseline CD4 count of study population was 211 (123 -303). This median baseline CD4 count was compared with following studies and similar results were obtained.

Table 4: Comparison of median baseline CD4 count

Author	Median baseline CD4 count (IQR 25%-75%)
Drylewicz J *et al*[7]	267 (163 -381)
Ruelle J *et al*[8]	226 (124 -359)
Harries K *et al*[9]	208 (103 -459)
Present study	211 (123.7-303.2)

In the present study, 11 (3.44%) cases had CD4 count <50 cells/µl, 122 (42.21%) cases had CD4 count in between 51-200 cells/µl, 116 (40.14%) cases had CD4 count in between 201-350 cells/µl and 40 (13.84%) cases had CD4 count >350 cells/µl. Maximum cases (238, 82.35%) had baseline CD4 count in between 51 to 350 cells/µl. Similar results were noted in the study of Chiara M *et al*.[10] In their study 7% had CD4 count <50 cells/µl, 75% had CD4 count of 51-200 cells/µl, 4% had CD4 count of 201-350 cells/µl and 14% had CD4 count >350 cells/µl. Maximum 82.35% cases had CD4 count between 51-350 cells/µl. Late diagnosis might be a reason for such a low CD4 count in maximum subjects due to late reporting to ART centre making them vulnerable to number of OIs. In the present study, median CD4 count decreased from WHO clinical stage I to IV. This demonstrates correlation of WHO clinical staging with CD4 T-cell counts. Spearman's correlation coefficient (rho) = -0.258; P<0.0001*(VHS). Thus, these findings support the use of WHO clinical staging as a surrogate marker for the level of immunosuppression in leau of CD4 T-cell counts and the same correlation is observed in the present study when compared with Ilovi CS.[11] (spearman`s correlation coefficient; rho= -0.583 p <0.0001). In our study, 264 (91.34%) individuals were started on ART (2NRTI + PIs). We could analyse the immunological response at 6 months and 12 months after starting of ART in 164 individuals. We observed an increasing trend of median CD4 count at 6 months (+102.5 cells/µl) and 12 months (+135 cells/µl) from the baseline median CD4 count. Similar results were obtained in the studies shown below.

Table 5: Comparative studies of immunological response after ART treatment

Author	Results		
	Baseline median CD4	Median CD4 after 6 months	Median CD4 after 12 months
Chiara M *et al*[10]	78	171	254
Van Der Ende *et al*[12]	90 (10–360)	230 (40–380)	270 (60–410)
Matheron S *et al*[13]	177 (98–328)	181(123–290)	221 (133–374)
Present study	200 (110.5-278)	302.5(205.5-441.5)	335 (228-553)

In our study, patients received ART regimen of 2 NRTIs (zidovudine / tenofovir + lamivudine) and Ritonavir boosted Lopinavir which is the regimen of choice for HIV-2 as these patients are inherently resistant to NNRTI (efavirenz / nevirapine); as a part of National Programme through our centre of excellence. In the study by Chiara M *et al*,[10] there was a comparison of immunological response between HIV-2 patients who received 3NRTIs and 2 NRTIs and PIs. It was observed that CD4 counts of HIV-2 patients improved satisfactorily on 2 NRTIs and PIs than with 3NRTIs. In the present study, we found same results in patients on 2 NRTIs and PIs.

CONCLUSION

There was statistically significant correlation between WHO clinical staging and immunological status (CD4 count) of HIV-2 individuals. An increase in median CD4 count at 6 months and 12 months from the baseline median CD4 count was observed. The response to ART and the pattern of resistance to ART is unique; and further studies should be carried out for the same.

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Source of Support: None Declared
Conflict of Interest: None Declared