



## Original Research

# A Prospective Study of Antiretroviral Therapy Naive Patients in Tertiary Care Hospital, Maharashtra

Authors

**Dr J.B Deshmukh, Dr Rajat Chhabra, Dr S.B Tamboli, Dr Laxmi Bhagunde**

Department of Pharmacology, Dr. Shankarrao Chavan Government Medical College, Nanded, Maharashtra

Corresponding Author

**Dr Rajat Chhabra**

Assistant Professor, Department of Pharmacology, Dr. Shankarrao Chavan Government Medical College, Nanded, Maharashtra

Phone no - +91 7972153228, Email: [dr.rajatchhabra@rediffmail.com](mailto:dr.rajatchhabra@rediffmail.com)

## ABSTRACT

**Background:** *AIDS can be called our modern pandemic, affecting both industrialized and developing countries. Globally education, counselling and behaviour modification are the cornerstones of an HIV prevention strategy. There has been dramatic decline in AIDS-related morbidity & mortality with introduction of Highly Active Anti-Retroviral Therapy (HAART). To address problems of high cost, need for lifelong therapy, poor compliance, lack of awareness, social stigma and occurrence of adverse effects proper monitoring and evaluation should be undertaken for successful implementation of ART programme.*

**Objectives:** *Present study was taken up to assess efficacy of NACO-recommended HAART regimen in antiretroviral therapy naïve subjects with HIV infection.*

**Material & Methods:** *120 properly selected subjects with confirmed HIV infection being newly started on ART were recruited as study subjects. HAART, consisting of two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor, was instituted. The initial therapy in majority of subjects was zidovudine (AZT)+lamivudine (3TC)+nevirapine (NVP). AZT was substituted by tenofovir disoproxil (TDF) in patients with Hb < 9 gm%, whereas NVP was substituted by efavirenz (EFV) in the event of non-availability, adverse effects, or possible interactions. Subjects were monitored at regular intervals for 24 weeks. Efficacy was assessed by response based on CD4 count, TLC count, weight gain, and improvement in functional status, WHO clinical stage and general health.*

**Results:** *Majority of subjects showed good clinical improvement with increase in CD4 count. ART showed good tolerability with mild and tolerable side effects. Death occurred only in 2.5% subjects.*

**Keywords:** *Acquired immunodeficiency syndrome (AIDS), human immunodeficiency virus (HIV), highly active antiretroviral therapy (HAART), naïve, efficacy.*

## INTRODUCTION

AIDS (acquired immunodeficiency syndrome) is caused by human immunodeficiency virus (HIV; previously known as HTLV-III or LAV), a

retrovirus.<sup>(1)</sup> In India, the current adult HIV prevalence is 0.27%. The total number of people living with HIV/AIDS in India was estimated at around 20.9 lakhs in 2011, 86% of whom were in

15-49 years age-group. Children less than 15 years of age accounted for 7% (1.45 lakhs) of all infections in 2011. Of all HIV infections, 39% (8.16 lakhs) were among women. <sup>(2)</sup>

Downward trends in prevalence are occurring in several countries partly as a result of effective prevention measures and partly due to scaling up of antiretroviral access. <sup>(3)</sup> In India, provision of free antiretroviral therapy (ART) for eligible persons living with HIV/AIDS was launched on 1<sup>st</sup> April 2004 has scaled up to 425 fully functional ART centres and 7,68,840 patients have been receiving free ART by March 2014. Highly Active Anti-Retroviral Therapy (HAART) has led to a dramatic decline in AIDS related morbidity and mortality. However, the major problems encountered are high cost, need for lifelong therapy, poor compliance, lack of awareness, social stigma and occurrence of adverse effects. To address these problems proper monitoring and evaluation should be undertaken for successful implementation of ART programme. Guidelines to this effect are provided by the NACO <sup>(4)</sup>

The aim of the study was to assess efficacy of NACO-recommended HAART regimen in antiretroviral therapy naïve subjects with HIV infection.

## MATERIALS AND METHODS

### Setting of the study

The present study was conducted from January 2014 to June 2015 with purposive sampling involving one hundred twenty (120) newly enrolled patients of HIV in our institutional ART centre at tertiary care hospital, Nanded, Maharashtra. Subjects were informed about the study in their local/didactic language which they understood. Before initiation of study, approval from Institutional Human Research Ethics committee was obtained and informed written consent of study subjects was taken before conducting the study.

### Study design

It was a prospective, observational study. One hundred twenty (120) antiretroviral therapy naïve

subjects of either sex with confirmed HIV infection (as screened by rapid immunoassay test [TRI-DOT] and confirmed by ELISA using two types of antigens recommended by NACO) being newly started on ART, willing to participate in the study, aged between 18-65 years, were recruited as study subjects. Subjects with WHO clinical staging of stage I & II (CD4 Count < 350 cells/mm<sup>3</sup>) and stage III (irrespective of CD4 count) were included in the study. Subjects already on HAART, asymptomatic with CD4 count >350 cells/mm<sup>3</sup>, pregnant and lactating women and subjects with pre-existing severe opportunistic infection (WHO stage IV) were excluded. Subjects were followed up for 6 months. Anonymity, confidentiality and professional secrecy was maintained for all the study subjects.

### Study procedure

The demographic data, history, clinical data and laboratory investigations were recorded for every study subject included in the study.

The subjects received ART as per NACO guidelines. ART consisted of zidovudine (AZT) (300mg BD)/tenofovir disoproxil (TDF) (300mg OD) + lamivudine (3TC) (150mg BD) + nevirapine (NVP) (200mg OD)/efavirenz (EFV) (600mg OD). The preferred initial therapy was based on the status of haemoglobin and on the status of liver function tests. In study subjects with Hb < 9gm% AZT was substituted by TDF. In study subjects with raised ALT (> 5 times upper normal limit), skin rash, newly developed tuberculosis and due to non-availability from NACO supply NVP was substituted by EFV. The dose of NVP was escalated from 200mg once daily to twice daily after two weeks in subjects without any evidence of intolerance. All the study subjects received co-trimoxazole prophylaxis (960mg OD) from baseline.

The efficacy of ART was assessed by response based on CD4 count, TLC count, weight gain, improvement in functional status and improvement in WHO clinical stage and improvement in general health.

The patients receiving ART were subjected to monitoring and counselling at regular visits, initially after 2 weeks (to consider nevirapine dose escalation in the absence of any intolerance) followed by monthly visits up to 6 months. Follow-up was extended beyond 6 months for those patients who were lost to follow up in the last 3 months of the follow up period. During each visit, patients were assessed for clinical improvement and also monitored for any adverse effects/events and opportunistic infections.

### Statistical Analysis

The data were presented in form of tables and graphs. Microsoft word and excel were used to generate tables and graphs. Data was tabulated and analysed by using SPSS version 20 for paired t-test.

### RESULTS

Of the 120 patients that were included in this study, 65% (78/120) were males and 35% (42/120) were females. Mean age of the study subjects was  $37.51 \pm 8.49$ . Majority of study subjects i.e. 99 out of 120 (82.5%) were in the age group between 26-45 years. The youngest subject was 18 years old and the oldest was 64 years old. Study subjects received HAART as per the NACO guidelines. Antiretroviral drugs were used in combination, consisting of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor

(NNRTI). The NRTIs included AZT, 3TC and TDF and NNRTIs included NVP and EFV. The preferred initial regimen or first-line option recommended by NACO was AZT+3TC+NVP and was used in 112 (93.33%) of the study subjects during baseline visit. In 6 (5%) subjects at baseline visit AZT was substituted by TDF because of anaemia; NVP was substituted by EFV in 2 (1.67%) subjects because of its non-availability from NACO supply. Any further change in the regimen or drug substitutions were also recorded. At the end of six months only 73 subjects were under AZT+3TC+NVP regimen, a total of 21 subjects under TDF based regimen and a total of 19 subjects were under EFV based regimen. 11 (9.17%) subjects were not available for follow up (Table 1).

The substitutions were made for some of the drugs used in the initial regimen at different periods of follow up. A total of 29 substitutions were made during the study. Out of this, substitution of AZT with TDF took place in 16 patients because of anaemia. Substitution of NVP with EFV was done in 17 subjects because of NVP induced skin rash in 5 subjects, deranged LFT (ALT > 5 times upper normal limit) in 1 subject and 7 subjects with newly diagnosed tuberculosis were also changed from NVP to EFV based regimen to avoid interaction with rifampicin. NVP was also substituted with EFV in 4 subjects when the former drug was out of NACO supply (Figure 1).

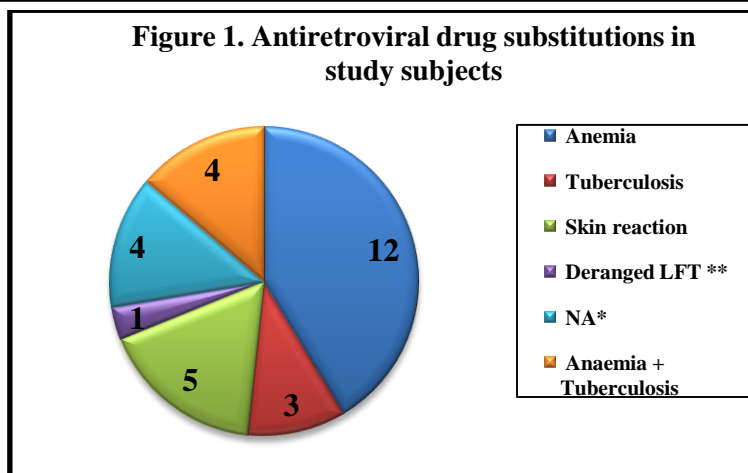
**Table 1.** ART regimens used in study subjects as per NACO guidelines (n = 120)

|          | AZT+3TC+NVP | TDF+3TC+NVP | AZT+3TC+EFV | TDF+3TC+EFV | NA <sup>#</sup> |
|----------|-------------|-------------|-------------|-------------|-----------------|
| Day 0*   | 112 (93.33) | 6 (5)       | 2 (1.67)    | –           | –               |
| Day 15   | 104 (86.67) | 10 (8.33)   | 6 (5)       | –           | –               |
| 1 month  | 96 (80)     | 12 (10)     | 11 (9.17)   | –           | 1 (0.83)        |
| 2 months | 91 (75.83)  | 11 (9.17)   | 12 (10)     | 2 (1.67)    | 4 (3.33)        |
| 3 months | 83 (69.17)  | 14 (11.67)  | 12 (10)     | 3 (2.5)     | 8 (6.66)        |
| 4 months | 78 (65)     | 16 (13.33)  | 13 (10.84)  | 4 (3.33)    | 9 (7.5)         |
| 5 months | 74 (61.66)  | 17 (14.17)  | 14 (11.67)  | 4 (3.33)    | 11(9.17)        |
| 6 months | 73 (60.83)  | 17 (14.17)  | 15 (12.5)   | 4 (3.33)    | 11(9.17)        |

(Figures in parenthesis denote percentages)

\*Initial therapy

<sup>#</sup> Not available for follow-up at the scheduled visits or lost for follow-up or dead.



\*Not available      \*\* Liver function test

Table 2 shows the treatment outcome based on WHO clinical stage, weight (kg) and functional status.

**Table 2.** Outcome of treatment in study subjects (Based on WHO clinical stage, weight (kg) and functional status) (n = 120)\*

| Treatment outcome measure          | Baseline      | At 6 months   | % improvement <sup>#</sup> |
|------------------------------------|---------------|---------------|----------------------------|
| WHO clinical stage                 |               |               |                            |
| I                                  | 47 (39.17)    | 90 (75)       | + 35.83%                   |
| II                                 | 53 (44.16)    | 7 (5.83)      | - 38.33%                   |
| III                                | 20 (16.67)    | 11 (9.17)     | - 7.5%                     |
| IV <sup>s</sup>                    | 0 (0)         | 1 (0.83)      | + 0.83%                    |
| NA <sup>@</sup>                    | 0 (0)         | 11 (9.17)     | + 9.17%                    |
| Weight in kg (Mean ± SD)           | 54.69 ± 13.01 | 55.63 ± 12.75 |                            |
| Functional status <sup>&amp;</sup> |               |               |                            |
| Working (W)                        | 111 (92.5)    | 106 (88.33)   | - 4.17%                    |
| Ambulatory (A)                     | 7 (5.83)      | 2 (1.67)      | - 4.16%                    |
| Bedridden (B)                      | 2 (1.67)      | 1 (0.83)      | - 0.84%                    |
| NA <sup>@</sup>                    | 0 (0)         | 11 (9.17)     | + 9.17%                    |

(Figures in parenthesis denote percentages)

\* On the basis of intent-to-treat criteria all the participants were included in the calculation

# Percentage of shift of study subject i.e., entry or exit from respective group

<sup>s</sup> Patients in WHO clinical stage 4 at initiation were not included in the study

<sup>@</sup> Not available for follow-up at visit or lost for follow-up or dead

<sup>&</sup> Assessed by WAB: W = Able to perform usual work in or out of the house like harvest, normal activities.

A = Able to perform activities of daily living but not able to work.

B = Not able to perform activities of daily living.

Table 3 summarizes the improvement in CD4 counts and TLC.

**Table 3.** Outcome of treatment in study subjects (Based on CD4 cell count and TLC) (n = 120) \*

| Treatment outcome measure       | Baseline        | At 6 months     | % improvement <sup>#</sup> |
|---------------------------------|-----------------|-----------------|----------------------------|
| CD4 count                       |                 |                 |                            |
| < 50 cells/mm <sup>3</sup>      | 10 (8.33)       | 2 (1.67)        | - 6.66%                    |
| 50 – 200 cells/mm <sup>3</sup>  | 74 (61.67)      | 27 (22.5)       | - 39.17%                   |
| 200 – 350 cells/mm <sup>3</sup> | 36 (30)         | 47 (39.16)      | + 9.16%                    |
| > 350 cells/mm <sup>3</sup>     | 0 (0)           | 33 (27.5)       | + 27.5%                    |
| NA <sup>@</sup>                 | 0 (0)           | 11 (9.17)       | + 9.17%                    |
| Mean CD4 count ± SD             | 154.68 ± 68.9   | 286.27 ± 142.7  |                            |
| TLC                             |                 |                 |                            |
| Normal                          | 98 (81.67)      | 93 (77.5)       | - 4.17%                    |
| Lymphopenia                     | 15 (12.5)       | 7 (5.83)        | - 6.67%                    |
| Lymphocytosis                   | 7 (5.83)        | 9 (7.5)         | + 1.67%                    |
| NA <sup>@</sup>                 | 0 (0)           | 11 (9.17)       | + 9.17%                    |
| Mean TLC count ± SD             | 5678.3 ± 2188.2 | 5563.3 ± 2279.1 |                            |

(Figures in parenthesis denote percentages)

\*On the basis of intent-to-treat criteria all the participants were included in the calculation

# Percentage of shift of study subject i.e., entry or exit from respective group

<sup>@</sup> Not available for follow-up at visit or lost for follow-up or dead

Table 4 shows the statistical significance of mean CD4 count, mean TLC and mean Hb%. A total of 73 (60.83%) subjects had received the AZT+3TC+NVP regimen throughout the study

period without any interruption. There was significant improvement of CD4 count under this regimen ( $p < 0.0001$ ) with little change in TLC ( $p = 0.3203$ ) and Hb% ( $p = 0.963$ ).

**Table 4.** Change in Mean CD4, mean TLC and mean Hb% in subjects in AZT+3TC+NVP group (n = 73)\* Paired samples t-test (Two-tailed)

| Parameter     | Baseline          | At 6 months       | p value <sup>#</sup> |
|---------------|-------------------|-------------------|----------------------|
| Mean CD4 ± SD | 176.89 ± 63.77    | 333.73 ± 119.72   | <0.0001              |
| Mean TLC ± SD | 5936.99 ± 2189.84 | 5587.67 ± 2139.18 | 0.3203               |
| Mean Hb% ± SD | 11.895 ± 1.124    | 11.864            | 0.963                |

ABBREVIATIONS: AZT, Zidovudine; 3TC, Lamivudine; NVP, Nevirapine

\* Seventy-three (73) subjects received AZT+3TC+NVP therapy throughout the study period.

<sup>#</sup> Statistical significance was considered at  $p < 0.05$ .

Total 408 side effects/adverse events were observed during the study period. The side effects were nausea (59.17%), fatigue (42.5%), weakness (35.83%), vomiting (31.67%), headache (27.5%), gastritis (25%), anorexia (23.33%), pain abdomen (18.33%), skin rashes (14.17%), anaemia (11.67%), giddiness (11.67%), pigmentation of nail/skin (7.5%) and insomnia (6.67%). Others include myalgia (5%), fever (4.17%), palpitations (3.33%), bad dreams, depression, itching (2.5% each) and mouth ulcer, drowsiness, deranged LFT's (0.83% each). Serious side effect/adverse event were severe anaemia in two subjects (1.67%) and severe skin rash in one subject (0.83%).

Opportunistic infections (OIs) occurred in 34 subjects. Commonest OI was oral candidiasis occurring in 14 subjects (11.67%). Recurrent respiratory tract infection (RRTI) occurred in 9 subjects (7.5%) followed by tuberculosis in 7 subjects (pulmonary in 6, extra-pulmonary in 1). Other OIs were diarrhoea in 2 subjects (1.67%), herpes zoster in 1 subject (0.83%) and fungal vaginitis in 1 subject (0.83%).

Most commonly used medication was antifungal agent clotrimazole used as mouth paint for the treatment of oral candidiasis. The other drugs were azithromycin and doxycycline for RRTI, anti-tubercular drugs category I for TB, fluconazole for vaginitis and oral candidiasis, ciprofloxacin for diarrhoea and acyclovir for herpes zoster.

## DISCUSSION

Antiretroviral drugs were used in combination as per the NACO guidelines.<sup>(5)</sup> The preferred initial regimen or first-line option recommended by NACO was AZT+3TC+NVP. In study subjects with Hb < 9gm% AZT was substituted by TDF. In study subjects with raised ALT (> 5 times upper normal limit), skin rash, newly developed tuberculosis and due to non-availability from NACO supply NVP was substituted by EFV. The dose of NVP was escalated from 200mg once daily to twice daily after two weeks in subjects without any evidence of intolerance.

Figure 1 shows ART substitutions during the study period. A total of 29 substitutions were made during the study. These substitutions were mainly because of side effects/adverse events, the possible drug interaction with the drugs used for OIs or because of non-availability due to out of supply. Similar pattern of ART substitutions has been reported in other studies.<sup>(6,7)</sup>

Table 2 summarizes the outcome of antiretroviral therapy on the basis WHO clinical stage, weight (kg) and functional status at the end of six months. Out of 120 subjects included for the study, only 109 subjects were available for the follow up monitoring at the end of six months. However, all the patients were considered for the calculation based on the intention-to-treat criteria. The improvement in various parameters is shown as the percentage shift from the group. The number of subjects with stage III was reduced from 20 at

baseline to 11 at the end of six months and the number of subjects with stage II reduced from 53 at baseline to 7 at the end of six months. The number of subjects with stage I at baseline increased from 47 at baseline to 90 at the end of six months. However, 1 subject progressed to stage IV, had developed abdominal tuberculosis in the 2<sup>nd</sup> month after initiation of HAART.

In our study, we observed a little improvement in mean body weight (in kg) from 54.69 to 55.63 at baseline and at 6 months respectively. There was little overall improvement in the functional status. The number of bedridden subjects which was 2 (1.67%) at baseline had dropped to 1 (0.83%) at the end of 6 months. There was significant clinical improvement as indicated by WHO clinical staging, but there was little improvement in the functional status.<sup>(8)</sup> Other studies have reported significant improvement in the body weight but deterioration in WHO staging and functional status in spite of longer duration of therapy<sup>(9, 10)</sup> which may be probably because of including the patients with late/advanced stages (WHO stage IV) with very low CD4 count (< 200 cells/mm<sup>3</sup>).

Table 3 summarizes the outcome of antiretroviral therapy on the basis of CD4 count and TLC at the end of six months. The mean CD4 count improved from  $154.68 \pm 68.9$  at baseline to  $286.27 \pm 142.7$  after 6 months. The number of subjects with CD4 counts <200 cells/mm<sup>3</sup> decreased from 84 (70%) at baseline to 29 (24.2%) at the end of six months. The number of subjects with CD4 counts 200 – 350 cells/mm<sup>3</sup> increased from 36 (30%) at baseline to 47 (39.2%) at the end of six months. In 33 (27.5%) subjects the CD4 counts increased to >350 cells/mm<sup>3</sup>.

There was little alteration in mean TLC after 6 months. The number of patients showing lymphocytosis increased from 7 (5.83%) at baseline to 9 (7.5%) after 6 months. In the present study, there was improvement in the CD4 count in those subjects with baseline CD4 count < 200 cells/mm<sup>3</sup>, and 27.5% of the subjects showing increase in CD4 count >350 cells/mm<sup>3</sup>. Other studies have reported significant improvement in

those subjects with baseline CD4 count 200-350 cells/mm<sup>3</sup>, however with less significant improvement in those with baseline CD4 count < 200 cells/mm<sup>3</sup>, in spite of continued therapy up to two years, and even with shifting to boosted or unboosted PI based therapy.<sup>(11, 12)</sup> This may be probably because of infection with resistant / mutant HIV strains and also because of severe OIs.

Table 4 shows the statistical significance of mean CD4 count, mean TLC and mean Hb%. A total of 73 (60.83%) subjects had actually received the AZT+3TC+NVP regimen throughout the study period without any interruption. There was significant improvement of CD4 count under this regimen ( $p < 0.0001$ ) with little change in TLC ( $p = 0.3203$ ) and Hb% ( $p = 0.963$ ).

Total 408 side effects/adverse events were observed during the study period. Most were generally mild and self-limiting not requiring discontinuation of therapy, and were managed by reassurance and symptomatic therapy. Most of the side effects gradually disappeared with continued ART. Other studies have also reported similar range of side effects with varying incidences.<sup>(13, 14)</sup>

Two subjects had developed severe anaemia (Hb% < 6.5 gm%) in the 3<sup>rd</sup> month. These patients were hospitalized and received blood transfusion, and were also further changed to TDF based regimen. One subject developed severe skin rash at day 12, required hospitalization and treated with glucocorticoids and was further changed into EFV based regimen. The overall incidence of NVP induced rash was 14.17%. A similar pattern of NVP associated rash rates of 3% to 26% incidence have been reported in other studies.<sup>(15, 16, 17)</sup>

The overall incidence of OIs occurring during the study period was 28.33%. A similar pattern of OIs have been reported by a study conducted in Bangalore, India by Kumaraswamy et al.<sup>(6)</sup> Other studies have also reported an almost similar pattern of OIs like tuberculosis, candidiasis, diarrhoea, herpes zoster, PCP, cryptococcal

meningitis, cerebral toxoplasmosis, cytomegalovirus retinitis. <sup>(18, 19)</sup> However, the incidence of tuberculosis and herpes zoster in the present study is very low and none of the patient had PCP, cryptococcal meningitis, cerebral toxoplasmosis or cytomegalovirus retinitis. This was probably because of excluding the patients with stage IV illness and also because of the limited duration of observation. The non-occurrence of PCP was also because of cotrimoxazole prophylaxis for all the subjects from baseline.

The anti-tubercular treatment was advised for duration of 6 months and all other drugs were used for a short course of 7 days. All the subjects received cotrimoxazole prophylaxis from baseline till the raise of CD4 count to >350 cells/mm<sup>3</sup>. Other studies conducted by Kumaraswamy et al. <sup>(6)</sup> and Seddon et al. <sup>(20)</sup> have reported similar pattern of drug therapy for OIs which mainly included ATT, antifungal drugs (clotrimazole, fluconazole), antiviral drugs (acyclovir, ganciclovir), cotrimoxazole (therapeutic dose for PCP) and pentamidine inhalation (for PCP) and other antibiotics depending upon the type of infections.

Thus, the present study indicates that the NACO recommended HAART involving 2NRTIs and 1NNRTI has shown good efficacy in overall clinical improvement, increasing the CD4 count and preventing OIs, even with the limited observation period and follow up of six months, and also good tolerability with mild tolerable, self-limiting and controllable adverse effects. However serious adverse events requiring hospitalization and specific therapy occurred in about 2.5% subjects. Cotrimoxazole prophylaxis has also contributed in preventing the opportunistic infection like PCP.

The major limitations of the present study include, a limited period of observation and follow up, using only a limited number of drugs, excluding the subjects in advanced stage of the disease with severe opportunistic infections and also special risk groups like pregnancy, children and elderly patients (above 65 years).

## CONCLUSION

The ART regimen in the present study involved a combination of 2NRTIs and 1 NNRTI as per NACO guidelines. ART showed good clinical improvement and increase in CD4 count with 27.5% of subjects showing elevation > 350 cells/mm<sup>3</sup>, also preventing opportunistic infections. ART showed good tolerability with mild and tolerable adverse effects and only 2.5% of subjects developed SAEs requiring hospitalization.

**Financial support and sponsorship:** None

**Conflicts of interest** There are no conflicts of interest

## REFERENCES

1. Sweetman SC, editor. Martindale: The Complete Drug Reference. 37<sup>th</sup> ed. London: Pharmaceutical Press;2011.938-1053.
2. National AIDS Control Organization, Ministry of Health & Family Welfare. Annual report 2014-15. March 2015 (cited 18 Dec 2015). Available from: [http://www.naco.gov.in/sites/default/files/annual\\_report%20\\_NACO\\_2014-15\\_0.pdf](http://www.naco.gov.in/sites/default/files/annual_report%20_NACO_2014-15_0.pdf)
3. Wilkins EGL. HIV infection and AIDS. In: Colledge NR, Walker BR, Ralston SH, editors. Davidson's principles and practice of medicine. 21st ed. USA: Churchill Livingstone: Elsevier Publishers; 2011.386-407.
4. National AIDS Control Organization, Ministry of Health & Family Welfare. Journey of ART programme in India, Story of a decade. March 2014 (cited 18 Dec 2015). Available from: <http://www.naco.gov.in/sites/default/files/Journey%20of%20ART%20Programme%20in%20India%20-%20Final.pdf>
5. National AIDS Control Organization, Ministry of Health & Family Welfare. Antiretroviral therapy guidelines for HIV-infected adults and adolescents. May 2013. (cited on 18 Dec 2015). Available from: <http://www.naco.gov.in/sites/default/files/>

- Antiretroviral%20Therapy%20Guidelines  
%20for%20HIV-  
Infected%20Adults%20and%20Adolescen  
ts%20May%202013%281%29\_0.pdf
6. Kumaraswamy G, Thimmegowda N, Purushottam PH, Ramaiah V, Ramesh J, Lingegowda RK. A prospective study of highly active antiretroviral therapy in a tertiary-care hospital in south India Int J Med Sci Public Health 2015;4:35-41.
  7. Agarwal D, Chakravarty J, Chaube L, Rai M, Agarwal NR, Sundar S. High incidence of zidovudine induced anaemia in HIV infected patients in eastern India. Indian J Med Res 2010;132:386-9.
  8. Rosen S, Larson B, Brennan A, Long L, Fox M, Mongwenyana C, et al. Economic Outcomes of Patients Receiving Antiretroviral Therapy for HIV/AIDS in South Africa Are Sustained through Three Years on treatment. PLoS ONE 2010; 5(9): e12731.
  9. Thejus TJ, Jeeja MC, Jayakrishnan T. The Functional Status of Patients with AIDS Attending Antiretroviral Treatment Center. Indian Journal of Palliative Care 2009 Jan-June;15(1):57-60.
  10. Olawumi HO, Olatunji PO, Salami AK, Odeigah L, Iseniyi JO. Effect of Highly Active Antiretroviral therapy on CD4 count and weight in AIDS patient seen at the UITH, Ilorin. Niger J Clin Pract 2008 December;11(4):312-5.
  11. Waters L, Fisher M, Anderson J, Wood C, Delpech V, Hill T, et al. Responses to Highly Active Antiretroviral therapy and clinical events in patients with a low CD4 cell count. HIV Medicine 2011;12(5):289-98.
  12. Siegfried N, Uthman OA, Rutherford GW. Optimal time for initiation of antiretroviral therapy in asymptomatic, HIV-infected, treatment-naïve adults. Cochrane Database Syst Rev 2010;(3):CD008272.
  13. Getahun A, Tansuphasawadikul S, Desakorn V, Dhitavat J, Pitisuttithum P. Efficacy and Safety of Generic Fixed-Dose Combination of Stavudine, Lamivudine and Nevirapine (GPO-vir) in Advanced HIV Infection. J Med Assoc Thai 2006;89(9):1472-78.
  14. Nadkar MY, Bajpai S. Antiretroviral Therapy: Toxicity and Adherence. JAPI 2009; 57: 375-6.
  15. Severe P, Leger P, Charles M. Antiretroviral therapy in a thousandpatients with AIDS AIDS in Haiti. N Engl J Med 2005;353:2325-34.
  16. Singh H, Kachhap VK, Kumar BN, Nayak K. Nevirapine inducedStevens- Johnson syndrome in an HIV infected patient. IJP 2011;43(1):84-6.
  17. Rather ZA, Chowta MN, Prakash Raju GJ, Mubeen F. Evaluation of theadverse reactions of antiretroviral drug regimens in a tertiary carehospital. Indian J Pharmacol 2013;45:145-8.
  18. Mir MA, Ahmad PM, Siddeque MA, Sofi FA, Ahmad SN, Dar MR. Clinical and demographic profile of HIV/AIDS patients diagnosed at a tertiary care centre in Kashmir. J Pak Med Assoc 2010; 60(No.6):428-31.
  19. Ghate M, Deshpande S, Tripathy S, Nene M, Gedam P, Godbole S, et al. Incidence of common opportunistic infections in HIV-infected individuals in Pune, India: analysis by stages of immunosuppression represented by CD4 counts. International Journal of Infectious Diseases 2009;13:e1-e8.
  20. Seddon J, Bhagani S. Antimicrobial therapy for the treatment of opportunistic infections in HIV/AIDS patients: a critical appraisal. HIV/AIDS - Research and Palliative Care 2011;3:19–33.