

RESEARCH ARTICLE

A study of compliance to highly active antiretroviral therapy in a tertiary care hospital in South India

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ABSTRACT

Background: Compliance plays a major role in success of antiretroviral therapy (ART) since it requires lifelong treatment and is associated with side effects. Decrease in patient compliance attenuates the clinical effectiveness, so in this regard, both patient and the health-care providers face significant challenges with respect to adherence to highly active ART (HAART). Therefore, there is a need to identify the various factors which influence the patient compliance to ensure better outcome. **Aims and Objectives:** This study aims to assess the patient compliance of National AIDS Control Organization (NACO) recommended HAART regimen and to explore the impact of CD4 count with factors affecting compliance. **Materials and Methods:** The prospective study conducted to assess the patient adherence to NACO recommended HAART among newly enrolled patients in ART center at KIMS Hospital and Research Centre, Bangalore, during January 2010–June 2011 (18 months) after obtaining institutional ethics committee approval. HAART consisting of two NRTIs and one NNRTI was instituted in 158 properly selected subjects. The initial therapy in most of the subjects was AZT+3TC+NVP. AZT was substituted by d4T in patients with Hb% <8G. NVP was substituted by EFV in the event of non-availability, adverse effects, or possible interactions. All the subjects received cotrimoxazole prophylaxis. Patients were monitored for 24 weeks at regular intervals. Patients were monitored for any side effects and adverse drug reactions/events during the study period. Patient compliance for adherence to therapy was assessed by pill count method. **Results:** There was a good compliance with 85.26% of study subjects showed >95% compliance and only 2.07% were poorly compliant in adherence to medication. 10.12% of the subjects were lost to follow-up during ART and death occurred in 5.71% of subjects ($n = 9$). The good compliance was due to effective counseling and involvement of field workers for outreach follow-up. **Conclusion:** The NACO-sponsored HAART regimen was found to have good compliance with greater improvement in adherence during subsequent follow-up period due to providing the backup services for effective patient counseling, outreach field visits, and transport facilities that may uplift the quality of care.

KEY WORDS: Acquired Immunodeficiency Syndrome; Human Immunodeficiency Virus; Highly Active Antiretroviral Therapy; Compliance; Adherence

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INTRODUCTION

As quoted by Hippocrates, Decorum in context to patient adherence - Keep a watch... on the faults of the patients, which often make them lie about the taking of things prescribed. For through not taking disagreeable drinks, purgative, or others, they sometimes die.^[1]

National Journal of Physiology, Pharmacy and Pharmacology Online 2019. © 2019 Padmanabha T S *et al.* This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

Medication adherence is defined by the World Health Organization as “the extent to which a person’s behavior corresponds with agreed recommendations from a health-care provider in respect of taking medication, following a diet and/or implementing lifestyle changes” or “Patient compliance, i.e., the ability to adhere to the recommended regimen is very vital.”^[2] Adherence to human immunodeficiency virus (HIV), tuberculosis, and non-communicable diseases treatments is an increasing challenge and non-adherence to long-term therapies results in poor health outcomes and increases overall health-care costs.^[2]

Acquired immune deficiency syndrome (AIDS) caused by HIV is a major global health problem, affecting nearly 33.3 million people worldwide, with an adult incidence of about 30.8 million.^[3] Although India is one of the largest population on planet, only small proportion, i.e., 0.29% of the population is estimated to be living with AIDS. However, it amounts to approximately 2.3 million people in number.^[4] Antiretroviral therapy (ART) has a role in both the prevention and treatment benefits in overcoming the AIDS epidemic.^[5]

More than >95% adherence to ART has been suggested for the patient to have maximum effect, i.e., to achieve maximal viral suppression.^[6-10] Hence, adherence to ART has played a major role in association with the poor outcome.^[6-10]

In the Indian scenario, when the number of AIDS cases are taken into account, adherence to ART is considered to be very important due to the poor socioeconomic status and poor education status of the infected individuals.^[6-10] Non-adherence is related to the development of ART resistance, progression to AIDS, and death.^[11-13]

According to the World Health Organization (WHO), the degree of non-adherence to treatment is pervasive internationally, and the consequences are of such concern that more people worldwide would benefit from efforts to improve adherence than the development of new medical treatments.^[2]

Hence, the present study was conducted to explore the patient’s compliance to highly active ART (HAART) in a tertiary care hospital in South India.

MATERIALS AND METHODS

The prospective study conducted to assess the patient adherence to National AIDS Control Organization (NACO) recommended HAART among newly enrolled patients in ART center at KIMS Hospital and Research Centre, Bangalore, during January 2010–June 2011 (18 months) after obtaining institutional ethics committee approval. Written informed consent was obtained from all the study subjects after fully explaining the study procedure to their satisfaction, in both English and vernacular language. Anonymity, confidentiality, and professional secrecy were maintained for all the study subjects.

Inclusion Criteria

158 Subjects aged between 18 and 65 years with confirmed HIV infection were included. Criteria for inclusion was stage I and stage II of WHO clinical staging with CD4 Count <350 cells/mm³ and Stage III irrespective of CD4 count. Informed written consent was taken from the subject.

Exclusion Criteria

Patients already on HAART, asymptomatic patients with CD4 count >350 cells/mm³, pregnant and lactating women, and patients with preexisting severe opportunistic infections (OIs) (WHO Stage IV) were excluded from the study.

Method of data collection

The demographic data, history, relevant clinical data, and the results of laboratory investigations were recorded for all the study subjects. The study subjects received ART as per NACO guidelines consisting of AZT (300 mg BID)/d4T (30 mg BID) + 3TC (150 mg BID) + NVP (200 mg OD)/EFV (600 mg OD). All these drugs were used as fixed-dose combinations, but EFV was administered separately whenever used. The preferred initial therapy was based on the hemoglobin status and liver function tests. In patients with Hb% <8G, AZT was substituted by d4T, and in clinical hepatitis/raised alanine transaminase (ALT) (>5 times the upper normal limit), NVP was substituted by EFV, and any further change in the regimen or drug substitutions were also recorded. In patients receiving NVP, the dose was escalated from 200 mg OD to BID after 2 weeks in the absence of any occurrence of rashes. All the study subjects received cotrimoxazole prophylaxis (960 mg OD) from the baseline till the CD4 count increased to above 350 cells/mm³, and patients with mild OIs like diarrhea, RTI also received the therapeutic dose (960 mg OD) for 5–7 days.

The efficacy of ART was assessed by treatment response based on CD4 count, total lymphocyte count, and clinical improvement such as general health, weight gain, functional status, and improvement in the WHO clinical stage. OIs occurring during the course of therapy and the treatment instituted for the same were recorded.

Patients were monitored for any side effects and adverse drug reactions/events during the study period.

Patient compliance for adherence to therapy was assessed by pill count method.

As these medications were dispensed for self-administration without supervision, the compliance to medication was assessed by pill count method and graded depending on the number of doses missed over a period of 30 days, i.e., >95% = <3 doses missed in a period of 30 days; 80–95% = 3–12 doses

missed in a period of 30 days; $<80\% \Rightarrow$ 12 doses missed in a period of 30 days; and compliance of $>95\%$ is considered as good and $<80\%$ as poor.

For patients receiving AZT, Hb% was repeated after 2 weeks, 1 month, 2 months, and 3 months for early detection of anemia, and for those receiving NVP, ALT repeated after 2 weeks, 1 month, 2 months, and 3 months for any evidence of hepatitis.

The patients receiving ART were subjected to monitoring and counseling at regular visits, initially after 2 weeks (to consider escalation of nevirapine dose 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 past 3 months of the follow-up period. During each visit, patients were assessed for clinical improvement and also monitored for any adverse effects/events, OIs, and treatment compliance.

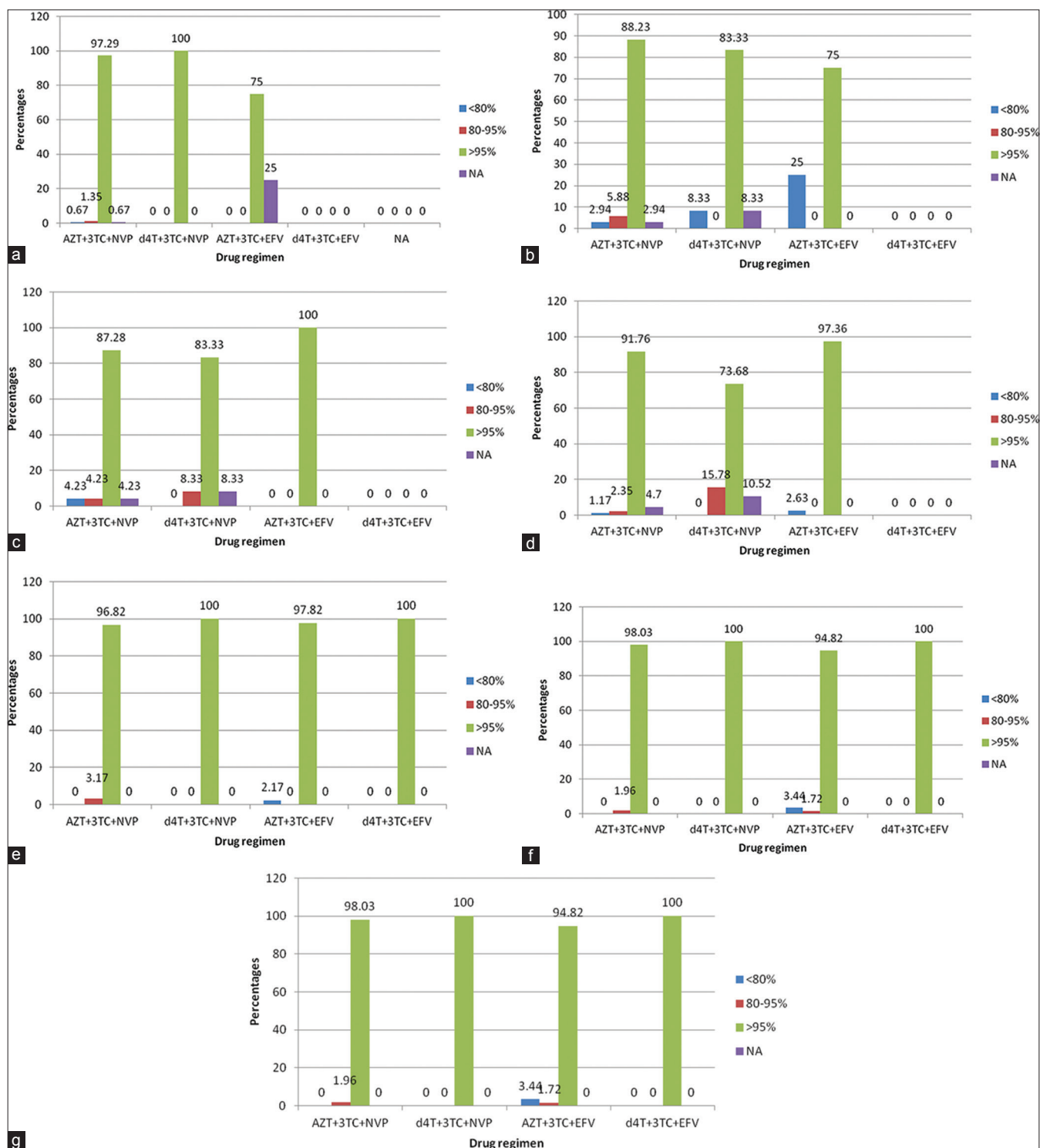


Figure 1: (a) Adherence at day 15, (b) Adherence at 1 month, (c) Adherence at 2 months, (d) Adherence at 3 months, (e) Adherence at 4 months, (f) Adherence at 5 months, (g) Adherence at 6 months

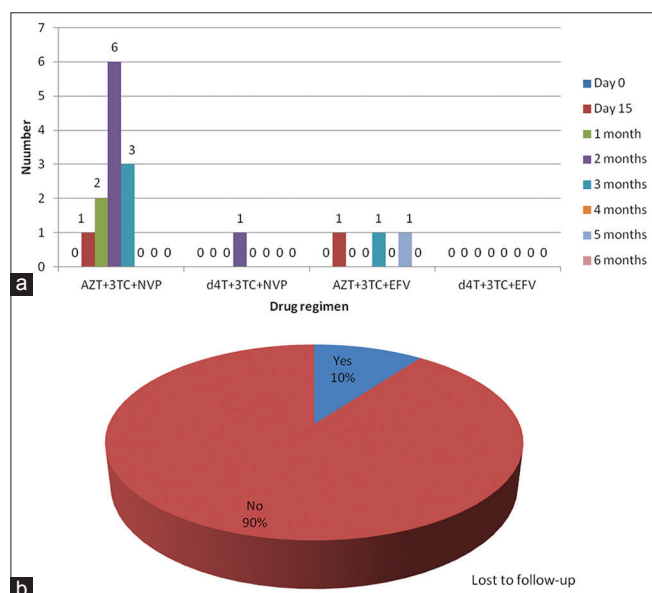


Figure 2: (a) Patients lost to follow-up during antiretroviral therapy (ART), (b) Patients lost to follow-up during ART

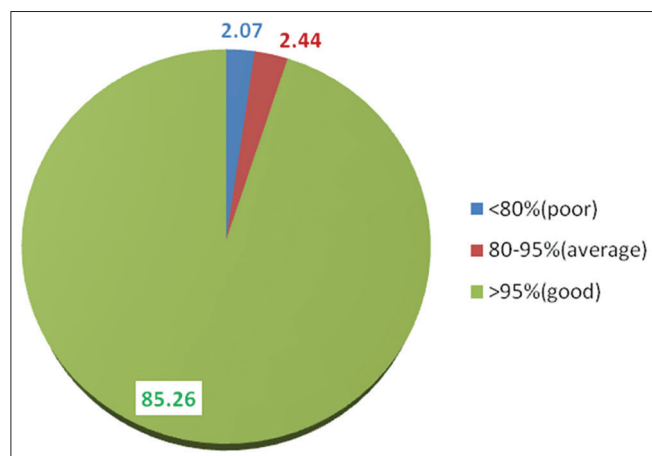


Figure 3: Overall adherence of patients during antiretroviral therapy

The data collected were analyzed using descriptive statistics, namely mean, standard deviation, standard error of mean, *t*-test, and confidence intervals for quantitative variables. The results were also depicted in the form of tables and graphs. Statistical software, namely SAS 9.2 and SPSS 15.0, were used for the analysis of the data and Microsoft Word and Excel to generate graphs and tables.

RESULTS

As these medications were dispensed for self-administration without supervision, the compliance to medication was assessed by pill count method and graded depending on the number of doses missed over a period of 30 days:

- >95% = <3 doses missed in a period of 30 days; 80–95% = 3–12 doses missed in a period of 30 days;
- <80% = >12 doses missed in a period of 30 days.

Table 1: Patients reasons for non-compliance

Forgetting to take the pills.
Frequent traveling.
Going out of station
Transport difficulty in reaching the antiretroviral therapy center to collect the medication on the scheduled visit.
Due to the side effects.
Frustration due to the need for lifelong medication.

Table 2: Factors determining adherence [2]

I. Five interacting dimensions affect adherence	II. Intervening in the five dimensions
1. Social and economic factors	1. Social and economic intervention
2. HCT and system-related factors	2. HCT and health system interventions
3. Condition-related factors	3. Therapy-related interventions
4. Therapy-related factors	4. Condition-related interventions
5. Patient-related factors	5. Patient-related interventions

HCT: Health-care team

- Compliance of >95% is considered as good and <80% as poor.

DISCUSSION

In the present study, the ART was instituted according to NACO guidelines in 158 patients with HIV infection fulfilling the inclusion and exclusion criteria. The therapy was initiated with the combination of three drugs including two NRTIs and one NNRTI. PIs were not included in the present study due to complex dosing schedule, more frequent adverse effects, and drug interactions. The medications were dispensed directly to the patients with proper instructions and counseling. Outreach field workers were also employed to assist the patients from remote or rural areas.

Patient compliance referring to adherence to ART medications was assessed during the different follow-up observations [Figure 1a-g; Figure 2a and 2b; and Figure 3]. Compliance of >95% is considered as good and <80% as poor. Among the study subjects, 85.26% showed >95% compliance, 2.44% (80–95%), and 2.07% (<80%) [Figure 3]. Compliance could not be assessed in those subjects who were lost to follow-up (10.12%) [Figure 2b]. The reason for non-compliance mainly included forgetting to take the pills, frequent traveling or going out of station, and also transport difficulty in reaching the ART center to collect the medication on the scheduled visit [Table 1]. In some patients, it was said to be due to the side effects or frustration due to the need for lifelong medication.^[14] Other studies have reported non-compliance of about 33%–88% probably due to poor optimizing of adherence measures, long duration of assessment, multiple daily dosing, or occurrence of side effects.^[15-18] In another study done by Bhuvana *et al.* showed that 93.59% showed >95% compliance, which was slightly more than the present study.^[19] Overall in the present study, the good compliance

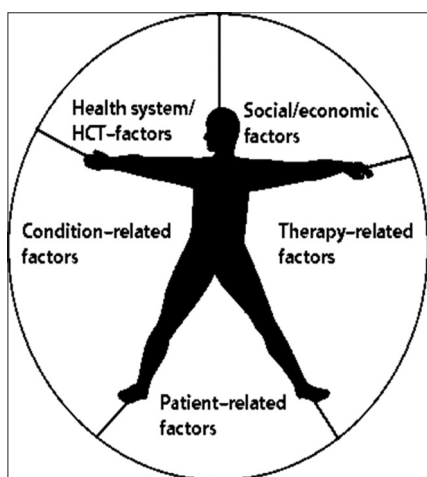


Figure 4: The five dimensions of adherence^[2]

was due to effective counseling and involvement of field workers for outreach follow-up.

Figures 2a and 2b show the number of subjects who are lost to follow-up during ART. Those subjects who had discontinued ART for >3 months are considered as lost to follow-up (drug defaulters). Measures were taken to trace these patients by contacting them through phone calls or home visits by outreach field workers. A total of 16 subjects (10.12%) were lost for follow-up, but four subjects returned for ART after 3 months and three subjects were reported to be deceased. The other nine subjects could not be traced due to wrong address or moved to some other place, or opted for alternative systems of medication. This was incongruence with the many studies from resource-poor countries that have shown, 5–25% of patients are reported as “lost to follow-up,” and about 20%–60% of such subjects had died, the cause of death could not be ascertained in most of them. Most of such patients were from lower socioeconomic status with very low baseline CD4 count; LFU and death occurring in the first 6 months.^[20-23] Therefore, the present study emphasizes the need for strict patient compliance to their HAART so that disease spreading as well as adverse drug reaction and development of drug resistance can be prevented, which was similar to the study done by Modi *et al.*^[24]

Routine effective implementation of commonly used interventions - cognitive behavioral therapy, education, treatment supporters, directly observed therapy, and active reminder devices; short waiting time; and good relationships - can improve ART adherence.^[25]

Hence, the proper strategic systematic monitoring, adherence monitoring, ART strategies^[2] [Table 2 and Figure 4] - once daily and fixed-dose combination to decrease the pill burden, counseling and support - one-on-one adherence support to patients, and offering peer/treatment support and interactive reminder devices - pill bottles and using communication technologies for weekly messaging, interactive component

for patients with poor adherence are required for long-term adherence as the treatment is lifelong.

Limitations of the Study

Limited period of observation and follow-up, small sample size, single-centered study, and only those without OIs were included in the study.

CONCLUSION

The present study showed that >85% of the subjects had a good compliance. Better accessibility to ART centers, effective counseling and outreach field visits, optimal doctor-patient ratio, and regular follow-up would bring awareness and contribute to very significant improvement in the patient compliance for treatment adherence.

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