

## Virological outcomes of second-line antiretroviral therapy for HIV-1 patients in center of excellence, Gandhi Hospital, Secundrabad, Telangana

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**Introduction:** In India, ART service was established in 2004 and viral load facility was started in 2009 through National Public Health Laboratory (NPHL). Phased scale-up has been planned to efficiently and successfully expand viral load testing services, taking into account the targets for enrollment of People Living with HIV in to Anti Retroviral Therapy program. **Methods:** This is an observational study conducted at the Centre of Excellence (COE), Gandhi Hospital Secundrabad. It is a referral centre for evaluation of patients suspected of treatment failure from ART centers. Data of all patients >18 years of age who were started on second line therapy due to failure of first line ART was taken in the study. The data of patients admitted between the time period of January 2009 to January 2010 was included. **Results:** A total of 147 HIV infected patients received second line ART of which 114 were men and 33 were women. Of these, 147 were treated with regimen TL, ATV/r. The most common cause to switch on second line ART was combined immunological and clinical failure (135) followed by all three failure (12). Mean baseline CD4 count was 220.06 (95% confidence interval [CI]: 243.73-196.38) and mean base line of PVL of patients was 291356.6 cells/mm<sup>3</sup> (95% CI: 364843.8-217869.29) copies/ml, respectively. **Conclusion:** Good long term outcome as well as virological suppression in patients starting second line therapy under programmatic conditions in India. This early mortality can be circumvented by introducing routine virological monitoring in the program which will help in early detection of patients with failure.

**Keywords:** Antiretroviral therapy, Second line, TL ATV/r, Viral load

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## Introduction

India has gained an incredible ground in controlling HIV since the start of the pandemic. The National AIDS Control Organization (NACO) realized early on that the western model of specialist physician management and advanced laboratory monitoring was not feasible in India. From 2004 onwards, the NACO set up antiretroviral treatment (ART) focuses, which gave one of the world's biggest free ART, and HIV testing and directing destinations all over the nation.

The present program, National AIDS Control Program IV (NACP-IV) (2012-2017) is gone for diagnosing and decreasing yearly new HIV cases by 50 percent through complete HIV treatment, instruction, care and backing for the overall public and to expand on focused mediations for the key influenced groups and those at a high danger of HIV transmission [1]. Efficacy of ART is monitored by both clinical and laboratory measures, including estimation of HIV-1 viral load and CD4 cell count, while on treatment.

WHO recommends viral load estimation as the preferred monitoring approach to diagnose and confirm treatment failure [2]. The 90-90-90 treatment targets call for 90% of those living with HIV to know their status, 90% of those who know their status to be on treatment, and 90% of those on treatment to be virally suppressed [3]. However, in low and middle-income countries, such monitoring has proved difficult given the inadequate laboratory facilities, shortage of trained staff and expensive reagents. The success of ART depends on the maintenance of long-term virological suppression, which is particularly challenging.

Plasma HIV-1 RNA (viral load) testing quantifies the HIV viral burden in the plasma. The viral load is a standard tool used to monitor treatment response in patients taking ART and, in conjunction with the CD4+ T cell count, to assess HIV progression. In some situations, viral load may factor into decisions to initiate or change ART [4]. A study have shown that patients who have high plasma viral loads have an increased risk of progression to symptomatic disease and AIDS compared with patients who have low or undetectable levels [5]. Based on the recommendations of Consolidated Treatment Guidelines of World Health Organization (WHO) and National Consolidated guideline on HIV prevention, treatment, and care.

This study was conducted to establish baseline information on virological status of the PLHIV receiving ART for more than six months from various regions of Telangana, and also to estimate virological suppression among HIV-infected people receiving second lineART.

## Methods

**Study site:** This observational study was conducted at the Centre of Excellence (COE), Gandhi Hospital Secundrabad. It is a referral centre for evaluation of patients suspected of treatment failure from ART centers.

**Sample Size:** A total of 147 patients aged >18 years are included in the study

**Study population:** The study was approved by the Ethics Committee of the Institute Gandhi hospital. Data of all patients >18 years of age who were started on second line therapy due to failure of first line ART was taken in the study. The data of patients collected between the time period of January 2009 to January 2010 was included. Informed consent was obtained from all patients.

**Exclusion criteria:** Patient refusal or inability to provide informed consent

**Virological failure:** Under the national programme, it is defined as a Plasma Viral Load (PVL) value of 1,000 or more copies/ml at or after six months of ART, with patient being treatment adherent by > 95%. Viral rebound after being undetectable is also considered as virological failure. A low-level viral rebound (<1000copies/ml), termed blips, usually indicates a statistical variation in the determination of PVL and this does not require switch in therapy. Viral load remains the most sensitive indicator of ART failure. Recognizing early failure facilitates the decision to switch drugs before multiple resistance mutations develop to drugs of the first-line regimen.

In general, the clinical status and the serial CD4 cell counts should be used in an integrated fashion to suspect treatment failure, while the patient is on ART. However, the switch of a regimen from the first-line to second-line therapy should be made on basis of virological failure only.

It is important to note that the current clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure.

Compared to clinical or immunological monitoring, viral load provides an early and more accurate indication of treatment failure and the need to switch from first-line to second-line drugs, reducing the accumulation of drug resistance mutations and improving clinical outcomes. Measuring viral load can also help to distinguish between treatment failure and non-adherence. Studies suggest that around 70% of patients on first-line ART, who have a first high viral load, will be suppressed following an adherence intervention, indicating non-adherence as the reason for the initial high viral load in the majority of cases [6].

Each patient was followed-up every month for clinical assessment (body weight, WHO stage, opportunistic infections) and adverse drug reaction (ADR) till completion of 1 year of second line treatment. CD4 count was monitored at baseline, 6 and 12 months while plasma viral load (PVL) was tested at baseline and 6 months after switching to second line ART regimen. Patients were offered adherence counseling at each visit. Adherence to second line ARTs was assessed by pill count. The data was recorded in Microsoft Excel Worksheet and analyzed with Excel software programs.

## Results

### Study population and baseline characteristics:

A total of 147 patients aged >18 years initiated second-line therapy between January 2009 to January 2010.

**Baseline characteristics:** A total of 147 HIV infected patients received second line ART of which 114 were men and 33 were women. All the 147 patients were treated with regimen TL, ATV/r. The mean age of patients was 38.3±8.2 years. Of 147 patients, 142 had at least one HIV positive family member; of which 5 patients were serodiscordant. The most common cause to switch on second line ART was combined immunological and clinical failure (135) followed by all three failure (12). Duration of first line ART therapy below 5 years – 106, and above 5 years was 41.

Mean baseline CD4 count was 220.06 (95% confidence interval [CI]: 243.73-196.38) and mean baseline PVL of patients was 291356.6 cells/mm<sup>3</sup> (95% CI: 364843.8-217869.29) copies/ml, respectively. Baseline characteristics, mean CD4 count and mean PVL of patients receiving regimen TL, ATV/r were comparable.

At second line ART initiation, majority of the patients were categorized as WHO clinical stage I (70), followed by IV (10), III (26) and II (41) [Table 1]. The most common opportunistic infection (OI) was tuberculosis (9), followed by diarrhea (8) candidiasis (6), herpes (3), and *Mycobacterium avium complex* (MAC) (1).

**Table-1: Baseline characteristics of patients included in the study (n=147).**

Parameter	Regimen TDF+3TC,ATV/R
Mean age(years)	38.3 ± 8.2
Gender	
Man	114 (77.55%)
Women	33(22.44%)
Body weight (Kg)	54±6.5
CD4 Count (cells/mm <sup>3</sup> )	220.06(CI: 243.73 – 196.38)
PVL (Copies/ML)	291356.6(CI:364843.8-217869.2)
WHO clinical stage (no.of patients)	
Stage 1	70(47.6%)
Stage II	41(27.9%)
Stage III	26(17.7%)
Stage IV	10(6.80%)

**Table-2: Predictors of treatment outcome of second line antiretroviral drugs in human immunodeficiency virus positive patients (n=147)**

Parameters	Treatment Success (PVL<400 copies/ml) (n=122)	Treatment Failure (PVL> 400 copies/ml) (n=25)
Gender		
Male	94	20(80.0%)
Female	28	5(20.0%)
Mean age (years)	38±2.5	39±5.2
Personal habits (Tobacco, alcohol and smoking)	23(18.85%)	15(60.0%)
Mean duration of first line ART Below 5yrs	113(92.6%)	1(4.0%)
Above 5years	9(7.37%)	24(96.0%)
Baseline WHO stage		
Stage (III/IV) condition (%)	16(13.11%)	20(80.0%)
Mean baseline CD4 count (cells/mm <sup>3</sup> )	220.24	135.68
Mean baseline PVL (copies/ML)	20218.9	373504.04

**Variables and treatment outcome-** An attempt was made to predict the variables associated with viral suppression. Of 147 patients 116 showed TND (Target not detected) and 6 patients were showing

With viral suppression (<400 copies/ml) at 12 months. 25 patients were expired till now. It was found that poor personal habits (tobacco, smoking, and alcohol), WHO stage III/IV condition, low baseline CD4 count and high baseline PVL were associated with poor treatment outcome in terms of failure to achieve virological suppression [Table 2].

**Safety assessment and adherence-** A total of 25 adverse drug reactions (ADRs) were observed in during the study period. The most common ADR was diarrhoea, anemia, dyslipidemia, nephro toxicity.

The pill count showed that the majority of patients (94%, 95% CI: 89-97) on second line ART were adherent to the treatment with more than 95% compliance. The number of tablets to be consumed by each patient per day in regimen TL, ATV/ris 2per day respectively.

## Discussion

This study reports the outcome of patients receiving secondline antiretroviral therapy under the National AIDS control program of India. To our knowledge, this is the first study to systematically evaluate the Virological outcomes of second-line ART in patients who fail first-line therapy in Telangana and Andhra Pradesh.

As the extent of ART in developing countries continues, and the number of patients switching to second line therapy will inevitably increase. Our study shows an analysis describing the outcomes of 147 patients on second line TL, ATV/r based ART regimens for 12 months treated at Centre of Excellence (COE), Gandhi Hospital Secundrabad, Telangana, India. After 12 months of follow-up on second line regimens, Of 147 patients 116 showed TND (Target not detected) and 6 patients were showing with viral suppression (<400 copies/ml) at 12 months. 25 patients were expired till now.

The pill count showed that the majority of patients (94%, 95% CI: 89-97) on second line ART were adherent to the treatment with more than 95% compliance. In another study [7] interestingly, 17/50 (34.0 %) of patients who had ongoing viremia or virological failure at 6 months adequately suppressed their viral load at 12 months. Another Similar findings were observed in a study where 62 % patients suspected of second-line ART failure, responded to enhanced adherence support and had a two-log decrease in their level of HIV on subsequent VL testing [8].

These findings further endorses the WHO guidelines which recommends that patients failing virologically be subject to an adherence support intervention, after which a second viral load test should be performed prior to deciding on a regimen change. A strong immune reconstitution with clinical improvement (body weight, WHO stage and OI) was observed at 12 months of follow-up on second line ART regimens. The immunologic and virological data supports our observation that the patients were indeed adhering well (>95%), even though high pill count and difficulties to store TL, ATV/r.

In our study the most common age group was 30-49 years followed by 15-29 years. Thus, nearly 82.5% of our patients belonged to the reproductive age group (15-49 years). Secondly, the mean age of patients in our study was higher (38.3 ± 8.2 years) as compared to studies documented at Thailand, Médecins Sans Frontières (MSF) countries and South Africa (35 years) [9-11].

There were more men 114 and 33 women in our study indicating high HIV prevalence among males. However, national data shows that 61% of the total HIV infected patients are men and 31% were female, which is nearly similar to our finding [12].

Probably, TL, ATV/r based regimen being more potent cause rapid suppression of viraemia resulting into greater increase in CD4 in the initial 6 months of second line ART. Median increase in CD4 count at 12 months treatment was higher as compared to similar studies done at Cambodia and MSF countries (252 vs. 135 cells/mm) [13]. In another study by Dishank Patel et al [14] a significant immune reconstitution with increase in mean CD4 count and viral suppression (PVL < 400 copies/ml) in 103 (82%) patients ( $P < 0.0001$ ) was also observed. A total of 83 ADRs were observed in 69 (55%) patients, the most common being dyslipidemia (57) followed by anemia (9).

From the studies, it can be concluded that the second line ART regimen has satisfactory early treatment outcome with respect to viral suppression. However, further research is needed to determine if these early outcome can be sustained over the following years of treatment.

## Conclusion

In this observational study there was high early mortality but good long term outcome as well as virological suppression in patients starting second line therapy under programmatic conditions in India.

This early mortality can be circumvented by introducing routine virological monitoring in the program which will help in early detection of patients with failure.

## Author's contribution

**Dr. Raja Rao** and **Dr. P. Deepak** Supervised the research work and guided, **Dr. Krishna** analyzed data and wrote the paper. **P. Malikarjun** performed bioinformatics analyses.

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**Competing Interests:** The authors declare that they have no competing interests.

### Abbreviations

ART: antiretroviral therapy

TL: Tenofovir + lamivudine

LPV/r: lopinavir/ritonavir

NACO: National AIDS control organization;

PLHIV: people living with HIV

VL-viral load

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