



## Research Article

### **A COMPARATIVE STUDY OF ANTIRETROVIRAL THERAPY INDUCED CD4 T-CELL CHANGES AMONG HIV INFECTED PATIENTS**

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#### **ABSTRACT**

The main objective of the study was to assess the CD4 induced T-cell changes after initiation of first-line ART in patients attending ART centre, Palakkad, Kerala, India. This study was designed as a hospital based combined prospective and retrospective study. The data collection was carried out from January to July 2014. A total of 261 who were naive to ART were included in the study. The majority of the patients were between the age group of 28-47 years. The male (49.43 %) and female (50.57 %) populations were almost in similar proportion. 63.60 % were married. 47.12 % of the patients had completed the secondary education. Heterosexual was the major cause for transmission for about 81.23 %. After 24 months of treatment, CD4 T-cell increased to 471.52 cells/mm<sup>3</sup> in ZLN/E and increased up to 514.43 cells/mm<sup>3</sup> in TLN/E. The body mass index was increased to 1.76 kg/m<sup>2</sup> in TLN/E and 1.13 kg/m<sup>2</sup> in ZLN/E. ZLN/E and TLN/E had 82 and 68 HIV infected patients who had acute respiratory infection, followed by oral candidiasis accounting for 53 and 44. Zidovudine induced anaemia were more common adverse drug reaction followed by nevirapine rashes. The study documented the efficacy of ART regimens and provides information about the improvement of immunological status in HIV infected population, who were under the first-line regimen of antiretroviral therapy. The study shows TLN/E is safer than ZLN/E and the efficacy is relatively similar in both the regimens.

**Keywords:** HIV, ART, ZLN/E, TLN/E.

#### **INTRODUCTION**

India is burdened with a larger HIV/AIDS epidemic than any other country in the world. More than 4 million Indian adults are infected with human immunodeficiency virus (HIV). HIV slowly attacks the immune system, causing people infected with the virus to gradually succumb to a variety of illness they would normally be able to resist. Medical treatment for HIV infection consists partly of treatment of the opportunistic illness and partly of efforts to combat HIV directly so that the body's natural defence can resume their role in fending off such illness. Advanced pharmaceutical products that combat HIV are referred to as antiretroviral therapy (ART). ART does not cure HIV infection, but it can increase the life expectancy. Globally, an estimated 35.5 (32.2- 38.3) million people were living with HIV in 2012. There were 2.3 million new HIV infections globally, showing a 33 % decline in the number of new infections from 3.4 (3.1 -3.7) million in 2001. At the same time the number of AIDS deaths is also declining with 1.6 (1.4-1.9) million in 2012, down from 2.3 (2.1-2.6) million in 2005.<sup>1,2</sup> According to the HIV estimations 2012, the estimated number of people living with HIV/AIDS in India was 20.89 lakhs in 2011. The adult (15-49 age group) HIV prevalence at national level has continued its steady decline from estimated level of 0.41 % in 2001 to 0.27 % in 2011. But still, India is estimated to have people living with HIV/AIDS, after South Africa and Nigeria.<sup>3</sup> AIDS destroys the ability of the immune system to mount a defence against any infection. HIV, the virus that causes AIDS, induces a state of immune deficiency by attacking and destroying CD4 T cells. The main target of HIV appears to be the CD4 cell population. A progressive reduction in the number and function of the CD4 cell population is one of the most striking and consistent immunological feature of HIV related disorder.<sup>4</sup> Availability of free antiretroviral drugs to HIV infected individuals has provided a new lease of life to these patients. Treatment of HIV infected patients with

currently available highly active antiretroviral (HAART) drugs is successful in reducing the burden of the disease but it is associated with various side effects.<sup>5</sup> Hence it is imperative to better understand biological and clinical effects of these molecules. Therefore this study has been undertaken to assess the CD4 induced T-cell changes after initiation of first-line ART in patients attending ART centre, Palakkad, Kerala, India.

#### **MATERIALS AND METHODS**

##### **Study Site**

The study was conducted in Ushus Antiretroviral (ART) centre, District hospital, Palakkad, Kerala, India which started its functioning on 1<sup>st</sup> March 2009.

##### **Study Design**

The study was designed as a hospital based combined prospective and retrospective study. A predesigned proforma was used to obtain the clinical and demographic data. Proforma was filled up on the basis of the data obtained from the White Cards (Patient treatment record) and information about the patient from the doctors and counsellors.

##### **Study Duration**

The data collection was carried out for a period of seven months (January to July 2014).

##### **Study Population**

All antiretroviral treatment naive adult patients registered between January 2012 and February 2014 were included in the study.

##### **Study Treatments**

First-line regimen of antiretroviral therapy as per National AIDS Control Organisation (NACO) guidelines which includes

- ZLN (Zidovudine [300 mg] + Lamivudine [150 mg] + Nevirapine [200 mg])
- ZLE (Zidovudine [300 mg] + Lamivudine [150 mg] + Efavirenz [600 mg])
- TLN (Tenofovir [300 mg] + Lamivudine [150 mg] + Nevirapine [200 mg])
- TLE (Tenofovir [300 mg] + Lamivudine [150 mg] + Efavirenz[600 mg])

changes in CD4 cells/mm<sup>3</sup>, body mass index (BMI), OI and adverse drug reactions.

#### Statistical Analysis

The data were entered in Microsoft office excel 2007 worksheet, mean, percentage and standard deviation (SD) were used. Data were analysed using Graph Pad.

#### Laboratory investigations

The CD4 counts were estimated using the standard flow cytometer (FACSort, Becton Dickinson).

#### Study Criteria

##### Inclusion Criteria

- HIV positive ART naïve patients of both sexes
- HIV infected patients who are on first-line antiretroviral therapy
- Patients with adherence more than 95 %

##### Exclusion Criteria

- Below 18 years of age
- Cases with missing values of CD4 count
- Terminally ill patients.

##### Parameters for Evaluation

- Sociodemographic characteristics- age, gender, risk factors, marital status etc.
- Comparison of first line antiretroviral regimen using CD4 and BMI and clinical condition as a tool of assessment.

#### Data Collection Method

For the study, a data collection form was used to extract data from patient profiles, treatments received and therapeutic outcomes. Data were generated for each patient at baseline and 6 months, 12 months, 18 months and 24 months. Indicators for antiretroviral effectiveness and safety included

#### RESULTS

Between January 2012 and February 2014, 437 patients were on-antiretroviral therapy. Of these, 261 were naïve to ART. The sociodemographic characteristics of these naïve patients are shown in Table 1. There was not much difference in the male (49.43 %) and female (50.57 %) populations. The majority of the patients were between the age group of 28-47 years (28-37 years-39.08 % and 38-47 years-38.31 %). 63.60 % were married. 47.12 % of the patients had completed the secondary education. 61.30 % were under ZLN/E and 38.69 % were under TLN/E. Figure 1 shows mode of transmission among the HIV positive patients. Heterosexual was the major cause for transmission for about 81.23 %. Table 2 shows comparison of CD4 count of the ZLN/E and TLN/E, after 24 months of treatment ZLN/E had an increase of 471.52 cells/mm<sup>3</sup> and TLN/E had increase up to 514.43 cells/mm<sup>3</sup>. Figure 2 shows immunological outcomes by time on treatment TLN/E showed more increase up to 319.64 after fourth follow-up, while ZLN/E had increase up to 288.35. Table 3 shows mean change in body mass index 1.76 kg/m<sup>2</sup> was increased in TLN/E and 1.13 kg/m<sup>2</sup> was increased in ZLN/E. Figure 3 shows distribution based on opportunistic infection, ZLN/E and TLN/E had 82 and 68 HIV infected patients who had acute respiratory infection, followed by OC accounting for 53 and 44. 23 and 10 had pulmonary TB for ZLN/E and TLN/E respectively. Table 4 shows adverse events shown by the patients. Zidovudine induced anaemia (30 events) were more common followed by nevirapine rashes (19 events).

Table 1: Socio demographic profile

Sociodemographic characteristics of patients	No. of patients (n = 261)	Percentage (%)
<b>Gender</b>		
Male	129	49.43
Female	130	50.57
<b>Age group (years)</b>		
18-27	26	9.96
28-37	102	39.08
38-47	100	38.31
48-57	29	11.11
58-67	4	1.53
<b>Marital status</b>		
Single	32	12.26
Married	166	63.60
Divorced	05	1.91
Widow	68	26.05
<b>Educational status</b>		
Illiterate	19	7.27
Primary schooling	91	34.86
Secondary schooling	123	47.12
College and above	28	10.73
<b>Therapy wise distribution</b>		
ZLN/E	160	61.30
TLN/E	101	38.69

**Table 2: Comparison of CD4 T-cell count after antiretroviral therapy**

Duration	ART	ZLN/E	TLN/E
Baseline (B) (cells/mm <sup>3</sup> )	n	160	101
	Mean (SD)	220.52 ± 132.69	177.93 ± 132.86
After 6 months of ART (T1) (cells/mm <sup>3</sup> )	n	160	101
	Mean (SD)	352.54 ± 156.26	363.05 ± 180.74
After 12 months of ART (T2) (cells/mm <sup>3</sup> )	n	112	65
	Mean (SD)	395.69 ± 187.32	434.86 ± 172.97
After 18 months of ART (T3) (cells/mm <sup>3</sup> )	n	75	46
	Mean (SD)	440.04 ± 188.91	429.30 ± 211.64
After 24 months of ART (T4) (cells/mm <sup>3</sup> )	n	31	15
	Mean (SD)	471.52 ± 210.19	514.43 ± 197.52

CD4 T cell count expressed in (cells/mm<sup>3</sup>), n is number of patients, SD is Standard deviation

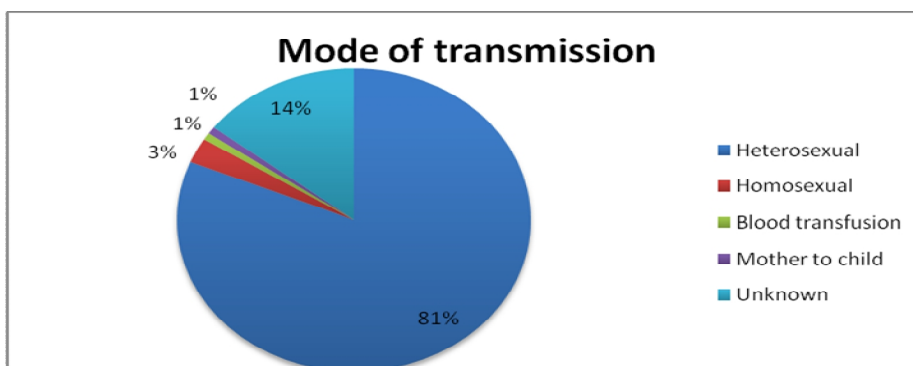
**Table 3: Mean change in BMI**

	ZLN/E	TLN/E
Mean change in BMI (SD) (kg/m <sup>2</sup> )	1.13 (± 2.40)	1.76 (± 2.11)

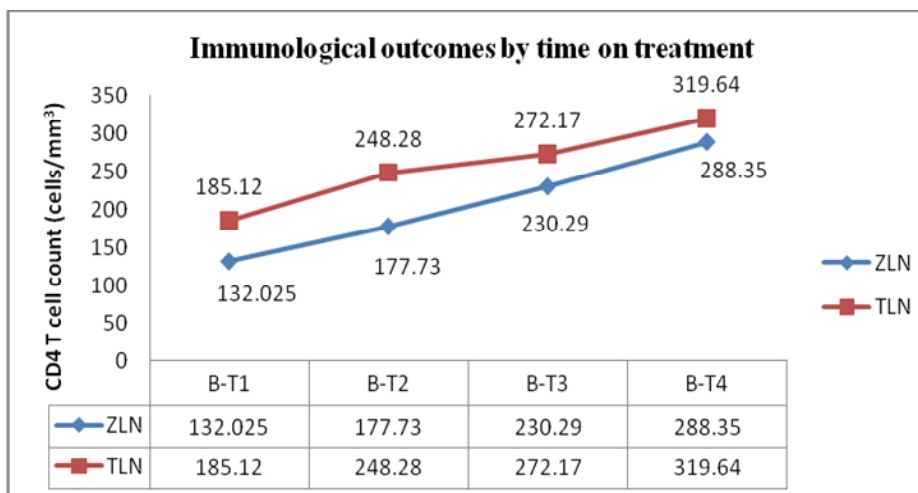
Body mass index (BMI) is expressed in kg/m<sup>2</sup>

**Table 4: Distribution based on adverse drug reaction**

Adverse drug reactions	No. of events
Zidovudine induced anaemia	30
Zidovudine induced nausea and gastritis	08
Efavirenz toxicity	01
Nevirapine rashes	19
Tenofovir toxicity	03
Leucopenia	01
Thrombocytopenia rash	01



**Figure 1: Mode of transmission**



**Figure 2: Immunological outcomes by time on treatment**

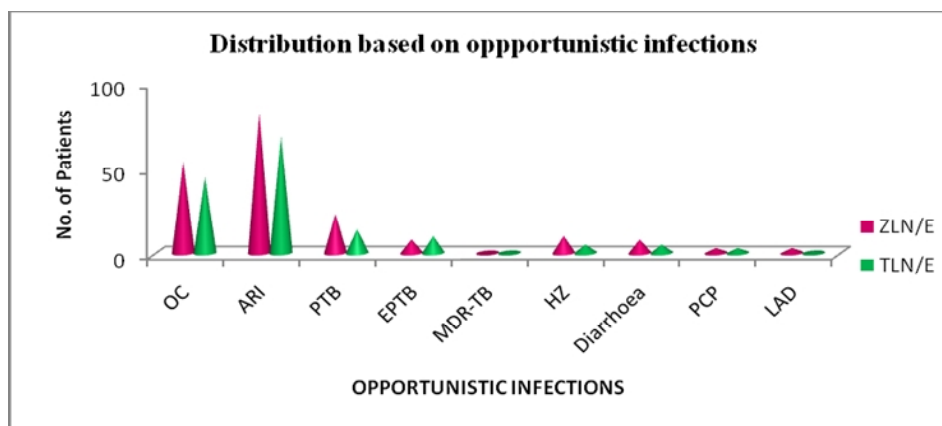


Figure 3: Distribution based on opportunistic infection

## DISCUSSION

The study documented the efficacy of ART regimens and provides information about the improvement of immunological status in HIV infected population, who were under the first-line regimen of antiretroviral therapy. The commonest mode of acquiring infection was heterosexual contact; Manisha Ghate *et al* reported similar findings, emphasizing the need to strengthen the information, education and communication strategies to HIV/AIDS. The study assessed the changes in the CD4 count, BMI after initiation of antiretroviral therapy. Janneke H van Dijk in their study found out the mean CD4 increased from 16.3 % at treatment initiation to 29.3 %, 33.9 %, 33.0 % and 35.0 % at 6, 12, 18 and 24 months on ART and Tovi Wahon Marie Odile *et al* in their study also had a gradual increase in the CD4 count, after 36 month of therapy the CD<sub>4</sub> count was around 400 cells/mm. The two ART regimens showed sustained improvement in the CD4 count and BMI, but TLN/E showed a slighter more increase in CD4 changes than ZLN/E. The most common opportunistic infection was found to be acute respiratory infection, followed by oral candidiasis. M. V Ghate *et al* in their study reported that major clinical conditions in HIV infected persons were oral candidiasis, herpes zoster, pulmonary tuberculosis, lymphadenopathy, weight loss, rash, diarrhoea and fever. The incidence of adverse effects was more in ZLN/E (anaemia, rashes, gastritis and nausea) regimen compared to the TLN/E (renal toxicity, rashes). In a study conducted at Nigeria the most common ADR was skin rashes (24 events) followed by nausea and vomiting. This shows TLN/E is safer than ZLN/E and the efficacy is relatively similar in both the regimens.

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