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EFFICACY OF TENOFOVIR/LAMIVUDINE/ DOLUTEGRAVIR (TLD) IN THE TREATMENT OF HIV IN A TERTIARY CARE CENTRE IN SOUTH EAST NIGERIA

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***Abstract*: Highly Active Anti-Retroviral Therapy (HAART) is the mainstay in the management of Human Immunodeficiency Virus (HIV) infection. It is important to evaluate the efficacy of new drugs and HAART combinations. This study analysed clinical and virological data of patients on tenofovir/lamivudine/ dolutegravir (TLD) at baseline, 6 months and one year. Level of adherence was 90.0%. Proportion of patients on WHO clinical stage 1 at baseline, 6 months and 12 months was 89.1%, 91.8% and 99.1%, respectively. Proportion of patients who were viral suppression at 6 months and 12 months were 86.4% and 90.0%, respectively. Age ≥35 years was significantly associated with WHO clinical stage 1 at 6 months. Good adherence was significantly associated with viral suppression at 6 months.**

***Keywords*: Tenofovir, lamivudine, dolutegravir, HAART, HIV, WHO staging, viral suppression.**

I. INTRODUCTION

WHO has recommended dolutegravir as a part of first-line, second-line, and third-line ART combinations due to high prevalence of pre-treatment drug resistance to NNRTI. Dolutegravir is an integrase inhibitor that has a high barrier against resistance and is usually combined with lamivudine and tenofovir.(1) Also, following newer evidence weighing risks and benefits, WHO approves dolutegravir as the preferred first-line, second-line and third line treatment for all age groups, also women of childbearing age and pregnant ones. Initial studies had pointed to a possible association of dolutegravir with infants born with neural tube defects by mother who used it at the time of conception. This concern about its possible teratogenicity was documented in 2018 following a study done in Botswana where 4 out of 426 women delivered babies with this defect and were known to have become pregnant while on dolutegravir containing regimen. Based on these initial results, many countries adopted efavirenz combinations instead of dolutegravir for pregnant women and those of child bearing age or alternatively, to use an effective contraception while taking dolutegravir to prevent pregnancy.(2)

Fortunately, new data from other clinical trials in Africa which compared the safety and efficacy of dolutegravir and efavirenz have shown better safety profile. The risks of neural tube defects are found to be significantly lower than what the initial studies may have suggested. The WHO HIV treatment guidelines also considered mathematical simulations of the benefits and adverse effects that are linked with these two drugs; the preference of those on treatment, and also factors relating to the implementation of HIV programmes for various countries, and the cost of treatment. Dolutegravir has been found to be more effective, easier to adhere to having less side effects than other drugs that are presently in use. These qualities improve adherence to it. Dolutegravir has the ability to withstand resistance in the face of rising incidence of these with efavirenz and nevirapine-based combinations. It is based on these findings that the 2019 guidelines was updated.(2)

Dolutegravir can damage the liver including elevated liver enzymes, hepatitis and liver failure. Therefore, patients should be tested for elevated liver enzyme before commencement of dolutegravir therapy.(3) The efficacy and safety of ART have greatly improved with the introduction of newer classes of antiretrovirals that are now available for use.(4) Dolutegravir has been found to be equivalent or superior to existing treatment regimens, both in treatment-naïve and treatment-experienced patients. This efficacy combined with excellent tolerability makes it a good treatment option.(5)

A study done in Niger state, Nigeria on the impact of Tenofovir/Lamivudine/Dolutegravir (TLD) on the Health-Related Quality of Life (HRQoL) showed a statistically significant improvement in HRQoL scores across all domains after 3 months of transitioning to TLD. Predictors for overall HRQol scores included female gender, older age >65years, living with family, higher family income >N100,000 and duration on ART. Predictor of viral suppression was living with family.(6) Younger age was found to be a predictor of reduced adherence to dolutegravir based ART in a study done in South Africa. Also more than 95% adherence as compared with less than 90% adherence were strong predictors of viral suppression at 96 weeks.(7) A study done in Botswana found that 5·3% were viraemic at the commencement of TLD. At month 12, 97·9% had viral loads of less than 50 copies per mL, including 88·3% of those who were viraemic at baseline. There was an association between high baseline viral load and virological failure.(8)

After 2 years of treatment, 74% of patients receiving dolutegravir achieved plasma HIV-1 RNA less than 50 copies per mL. Virological failure (>1000 copies per mL) was observed in 8/310 (0.03%) of patients. The incidence of new WHO HIV-related stage 3 and 4 events was 4%. These were found by a study done in Cameroon.(9) Another survey in Cameroon conducted among patients taking TLD showed viral suppression rate (<1000 copies/mL) of 96.45%. Age, gender, residence, duration on ART and WHO stages were not associated with viral response.(10) After 3 months of transition from tenofovir/lamivudine/efavirenz (TLE) to TLD, 88% of transitioned participants had achieved untransmissible viral load suppression level (< 200 copies/ml) compared to 76.3% while on TLE (P value < 0.005). Binomial logistic regression shows clients while on TLD had 3.064 times higher odds to achieve viral load less than 200 copies/ml than when on TLE. The model was statistically significant.(11)

The aim of this study was to determine the efficacy of TLD and factors associated with WHO clinical staging and viral suppression.

II. RESEARCH METHODS

This was a cross-sectional analytical study carried out among HIV patients on TLD in Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH), Awka, Sout East Nigeria. Baseline and follow-up clinical information and laboratory investigations were collected between August 2021 and April 2022 using a proforma.

Ethical Consideration

Permission for the study was obtained from the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Ethical Review Committee. All data collected were kept strictly confidential.

Data analysis

Data was analysed using SPSS version 26.0. Chi square test was used to test associations at 5% level of significance.

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III. RESULTS

Table 1: Sociodemographic characteristics

Socio-demographic characteristics	N=110 n (%)
Age group (yrs)	
≤ 24	3 (2.7)
25-34	12 (10.9)
35-44	25 (22.7)
45-54	39 (35.5)
≥ 55	31 (28.2)
Mean age (±SD)	47.6 (±11.0)
Sex	
Male	46 (41.8)
Female	64 (58.2)
Religion	
Christianity	109 (99.1)
Islam	1 (0.9)
Marital status	
Single	24 (21.8)
Married	76 (69.1)
Separated	0 (0.0)
Widowed	8 (7.3)
Divorced	2 (1.8)
Residence	
Anambra	105 (95.5)
Others	5 (4.5)

Adherence to HAART

The majority of participants (90.0%) adhered well to their medication, while 10% did not as shown in Figure 1.

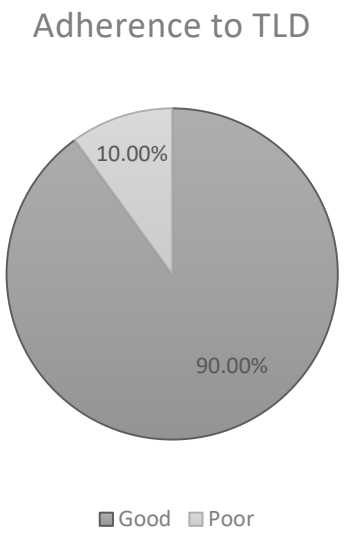

Figure 1: Adherence to HAART (TLD)

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WHO Clinical Staging

WHO clinical staging at baseline, at 6 months and at 1 year are shown in Table 2. No patient commenced treatment on stage 4. There was an improvement in staging over one-year treatment period with the proportion of patients in stage 1 after one year of treatment being 108 (99.1%). Despite the improvement, 1 (0.9%) patient deteriorated clinically.

Table 2: WHO clinical staging of study participants

WHO Clinical Staging	N=110 n (%)
Baseline	
Stage 1	98 (89.1)
2	11 (10.0)
3	1 (0.9)
4	0 (0.0)
6 months	
Stage 1	101 (91.8)
2	7 (6.4)
3	2 (1.8)
4	0 (0.0)
1 year	
Stage 1	108 (99.1)
2	1 (0.9)
3	0 (0.0)
4	0 (0.0)

Viral Load

The proportion of patients that were virally suppressed at 6 months was 86.4% after 6 months of therapy, and increased to 90% after 12 months (Table 3).

Table 3: Proportion of patients that are virally suppressed

Viral Load (VL)	N=110 n (%)
6 months VL (copies/ml)	
Virally suppressed (<1,000)	95 (86.4)
Not-virally suppressed (≥1,000)	15 (13.6)
1 year VL (copies/ml)	
Virally suppressed (<1,000)	99 (90.0)
Not-virally suppressed (≥1,000)	11 (10.0)

Factors associated with clinical and virological outcomes

Age ≥35 years was significantly associated with WHO clinical stage 1 at 6 months, as shown in Table 4. The factor that was significantly associated with viral suppression at 6 months was good adherence (Table 5).

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Table 4: Characteristics of patients associated with WHO clinical stage 1 at 6 months

Factors	WHO clinical stage N=110 Stage 1 n (%)	Stages 2,3,4 n (%)	χ^2	p-value
Age				
≤ 34	11 (73.3)	4 (26.7)		
≥35	90 (94.7)	5 (5.3)	Fisher's exact	0.019*
Sex				
Male	42 (91.3)	4 (8.7)		
Female	59 (92.2)	5 (7.8)	Fisher's exact	1.000
Marital status				
Currently married	69 (90.8)	7 (9.2)		
Not currently married	32 (94.1)	2 (5.9)	Fisher's exact	0.718
Residence				
Anambra	96 (91.4)	9 (8.6)		
Others	5 (100.0)	0 (0.0)	Fisher's exact	1.000
Adherence				
Good	90 (90.9)	9 (9.1)		
Poor	11 (100.0)	0 (0.0)	Fisher's exact	0.594

*Statistically significant

Table 5: Characteristics of patients associated with viral suppression at 6 months

Factors	Virally suppressed (VL <1,000 copies/ml) N=110 VL <1,000 n (%)	VL ≥ 1,000 n (%)	χ^2	p-value
Age				
≤ 34	14 (93.3)	1 (6.7)		
≥35	81 (85.3)	14 (14.7)	Fisher's exact	0.688
Sex				
Male	37 (80.4)	9 (19.6)		
Female	58 (90.6)	6 (9.4)	2.360	0.124
Marital status				
Currently married	68 (89.5)	8 (10.5)		
Not currently married	27 (79.4)	7 (20.6)	Fisher's exact	0.227
Residence				
Anambra	90 (85.7)	15 (14.3)		
Others	5 (100.0)	0 (0.0)	Fisher's exact	1.000
Adherence				
Good	88 (88.9)	11 (11.1)		
Poor	7 (63.6)	4 (36.4)	Fisher's exact	0.042*

*Statistically significant

IV. DISCUSSION

Our study showed an improvement in clinical state as evidenced by the proportion of patients on WHO clinical stage 1 at baseline (89.1%), 6 months (91.8%) and 12 months (99.1%). This was similarly reported in Niger state, Nigeria as the Health-Related Quality of Life (HRQoL) and clinical outcomes showed a statistically significant improvement across all domains after 3 months of transitioning to TLD.(6) A study done in Botswana found that at 12 months of treatment with TLD, 97·9% had viral loads of less than 50 copies per mL.(8) Our study showed that the proportion that were virally suppressed at 12 months was 90.0%. These results are comparable and both studies were conducted in similar settings with the patients having similar demographic and clinical characteristics.

After 2 years of treatment, virological failure (>1000 copies per mL) was observed in 8/310 (0.03%) of patients, as found by a study done in Cameroon.(9) Our study showed virological failure at one year in 10.0% of patients. This is commendable considering that our study only followed up for one year. The incidence of new WHO HIV-related stage 3 and 4 events was 4%.(9) In contrast, our participants fared better as none of our participants was on stage 3 or 4 at one year of treatment. Another survey in Cameroon showed viral suppression rate (<1000 copies/mL) of 96.45%. Age, gender, residence, duration on ART and WHO stages were not associated with viral response.(10) Similarly, our study found good adherence to be the only factor that was associated with viral suppression.

Predictors for overall HRQol scores in a similar study in Nigeria included female gender, older age >65years, living with family, higher family income >N100,000 and duration on ART.(7) According to our study result, older age ≥35 years was significantly associated with WHO clinical stage 1 at 6 months. Also more than 95% adherence as compared with less than 90% adherence were strong predictors of viral suppression at 96 weeks.(7) Our study also found adherence to be significantly associated with viral suppression.

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