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Assessment of the Safety and Efficacy of Tenofovir-Lamivudine-Dolutegravir Combination Therapy a mong HIV-infected Patients in University of Uyo Teaching Hospital, Uyo, Nigeria

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ABSTRACT

Background: Clinical outcomes are measurable changes in health, function or quality of life that result from professional care. Examples of clinical outcomes are cure, clinical worsening and death. Due to life-threatening toxicity of Zidovudine, Lamivudine and Nevirapine combination and Tenofovir, Lamivudine and Efavirenz antiretroviral combination in Nigeria, a new therapy, Tenofovir, Lamivudine and Dolutegravir (TLD) combination had become first-line drug regimen. Study aimed at assessing the safety and efficacy of TLD combination therapy.

Method: This was a longitudinal, multi-phase non-interventional study involving 194 asymptomatic HIV-infected patients attending antiretroviral clinic in University of Uyo Teaching Hospital. Data were collected through a purposive convenience sampling technique after obtaining ethical approval and informed consent were filled. Questionnaires were administered to the study participants for demographic and medication information and clinical parameters such as viral load and CD4-count were collated from their case files. A 5mL venous blood sample was collected from participants for liver and kidney function tests at baseline (0 month), 3 months- and 6 months-post baseline respectively. Blood samples of study participants were stored in the freezer after separation and were analyzed at the end of every week in the hospital laboratory. Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) and Aspartate aminotransferase (AST) were biomarkers evaluated for liver functions while serum creatinine was evaluated for kidney function. The blood samples were properly disposed by the hospital laboratory scientist. Biochemical assays of liver enzymes ALT and AST and creatinine test were carried out by using Randox® reagents. The results obtained were analyzed using SPSS version 25. ANOVA was used to compare data of biochemical parameters across the three phases of study while $p \leq 0.05$ was considered significant.

Results: The results showed that 55 participants completed the three phases with CD4-counts 482.90±251.72, 486.67±172.28 and 617.0±180.60cells/mm^3 at 0-, 3- and 6-month respectively. The Liver enzyme ALT was normal in all Phases while AST mean-values were elevated in all Phases. ALT, AST and AST/ALT ratio were significantly varied from the baseline at 3-month (0.001, 0.000 and 0.000) and 6-month (0.093, 0.000 and 0.000) respectively. The creatinine clearance was below normal limit and continued to fall with time for both males (67.79±20.96-, 65.26±18.76- and 64.70±19.62mL/min) and females (75.8±20.66-, 70.07±20.66- and 69.60±21.90mL/min) respectively.

Conclusion: This study indicated that there was significantly decreased viral load of study participants while CD4 count was increased. The study also indicated that biochemical parameters of liver function, enzymes ALT and ALP were significantly increased in participants. The study also indicated that creatinine clearance of participants was significantly reduced in post-baseline follow-up. The most common complaint by participants on TLD was insomnia. Six study participants on TLD were confirmed dead.

INTRODUCTION

Clinical outcomes, such as cure, clinical worsening and death, are measurable changes in health, function or quality of life that result from healthcare. Human immunodeficiency virus (HIV) infection continues to be a major global public health issue which claimed about thirty three (33) million lives.[1] However, HIV infection has become a manageable chronic health condition due to increasing access to effective HIV prevention, diagnosis, treatment and care including better management for opportunistic infections resulting in HIV-infected people living longer and healthier lives.[1] Antiretroviral combination therapy for human immunodeficiency virus (HIV) infection is delivered universally through the use of the public health model recommended by the World Health Organization (WHO), consisting a small number of standardized regimens and simplified monitoring and care.[2] Dolutegravir, an integrase strand-transfer inhibitor, taken with tenofovir and lamivudine, both belong to the nucleoside reverse-transcriptase inhibitor, is the WHO-recommended first-line regimen. Also, it is recommended as second-line therapy in patients who are not responding to non–dolutegravir-containing first-line regimens. The efficacy of dolutegravir when given with nucleoside reverse-transcriptase inhibitors that are predicted to be compromised by cross-resistance is uncertain.[3,4] Darunavir and other drugs from the protease inhibitor class with two nucleoside reverse-transcriptase inhibitor is currently recommended as an alternative second-line regimen and is known to have good efficacy even with nucleoside reverse-transcriptase inhibitor that have extensive cross-resistance. WHO guidelines also recommend changing one of the nucleoside reverse-transcriptase inhibitors from tenofovir to zidovudine when switching to second-line therapy; both drugs are given with lamivudine.[3,4]

The UNAIDS reported that about thirty eight million people worldwide comprising of 36.2 million adults and 1.8 million children below 15 years old were living with HIV/AIDS.[5] An estimated 1.7 million people worldwide acquired HIV in 2019 making a twenty three percent (23%) decline in new HIV infections since 2010. The new infections involved 1.5 million adults and 200,000 children.[5] Africa has the highest HIV prevalence worldwide with 4.0% in Kenya, 1.3% in Nigeria, 18.3% in South Africa, 18% in Botswana, and 27.9% in Eswatini for individuals aged 15–49 years. The region accounts for 50% of global new HIV infections.[6]

Nigeria has the second largest HIV epidemic in the world, with 1.9 million HIV-infected persons in Nigeria mostly adult aged 15 to 49 years. There were 130,000 new HIV infections in 2018.[5] It was documented that about 45,000 people died from AIDS-related illness in Nigeria in 2019. There was about 35% reduction in AIDS-related deaths since 2010 to 2019 and 89% of those with a positive diagnosis in Nigeria are currently accessing antiretroviral treatment (ART).[6]

Irrespective of the efficacy, many ART agents are associated with well-established risks of long-term toxicities and co-morbidities including coronary disease, liver failures osteoporosis, renal failure, chronic kidney disease and diabetes.[7] The prevalence of co-morbidities associated with HIV leads to poly-pharmacy increasing the risk of frequent interactions and severe complications. Thus, this study aimed at evaluating the safety and efficacy of Tenofovir, Lamivudine and Dolutegravir (TLD) combination.

METHOD

STUDY DESIGN

This was a longitudinal, non-interventional multi-phase study.

STUDY SITE AND SETTING

The research was carried out at the Antiretroviral Clinic of University of Uyo Teaching Hospital (UUTH) has attended to more than 3,000 sero-positive patients. The hospital is a 500-bed tertiary hospital located in Uyo metropolis, Akwa Ibom State in the South-South region of Nigeria. The hospital serves a population of about 4 million people from within and outside the state.

STUDY POPULATION

Study recruited asymptomatic adult sero-positive individuals who were registered at the anti-retroviral clinic of the hospital but did not have HIV symptoms according to WHO HIV stage I. The target populations for the study were patients who had started the TLD combination therapy for at least 3 months.

Sample size calculation

The sample size of participants was calculated by using the equation below;[8]

$N = Z^{\wedge 2} X (P) \times 1\text{-}P/C^2$

Calculated sample size was 340 persons. An attrition of 15% was added to arrive at a sample size of 391 persons for the study

SAMPLING METHOD

Purposive convenience sampling was employed in the recruitment of study participants. Following an ethical approval from the UUTH Ethics and Research Committee with a reference number UUTH/AD/S/96/VOL.XXI/379, patients were informed of the study during clinic visitation which held every day of the week in a non-random manner. Volunteers were recruited to participate in the study. Written consent was obtained from participants.

Eligibility criteria

i. Those who were adherent to their prescribed medication during the study
ii. Patients that were at least 18 years old
iii. Patients who provided written consent to participate in the study
iv. Asymptomatic, non-pregnant patients

DATA COLLECTION

i. QUESTIONNAIRES

At the start of the study, structured questionnaires consisting of demographic and medication details of participants were administered to the participants.

ii BLOOD SAMPLE COLLECTION

A 5mL venous blood sample was collected from each study participant at baseline (0 month) for analyzing biochemical parameters for liver and renal function test. Blood samples of study participants were stored in the freezer after separation and were analyzed at the end of every week in the hospital laboratory. Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) and Aspartate aminotransferase (AST) were biomarkers evaluated for liver functions while serum creatinine was evaluated for kidney function. The venous blood samples were properly disposed by the hospital laboratory scientist. The collection and testing process were repeated after 3 months and after 6 months post-baseline consecutively. Biochemical assays of liver enzymes ALT and AST and creatinine test were carried out by using Randox® reagents. The laboratory procedures were previously described by Ajulo.[9] Patients' folders were also used as sources of data collection. The folders were retrieved and information like viral load and CD4 count were obtained. The blood samples collected from participants were not used for analyzing CD4 count and viral load because renal and hepatic functions biomarkers were not evaluated at same period as viral load and CD4 count due to inadequate reagent and instruments for assessing viral load and CD4 count. The health care facility sends out patients' blood samples to referenced laboratory for assessing viral load and CD4 count every six months when reagents are available. Creatinine clearance was calculated from the value of creatinine by using Cockcroft-Gault formula given below:[10]

Creatinine clearance (ml/min) (females) =

$$\frac{140-age(years)*weight(kg)}{Serum\ creatinine(\mu mol/l)}$$

Creatinine clearance (ml/min) (males) =

$$\frac{140-age(years)*weight(kg)*1.2}{Serum\ creatinine(\mu mol/l)}$$

DATA ANALYSIS

Data collated from the questionnaires were coded to keep participants' information secret. Descriptive analysis such as mean and standard deviation were used. Inferential analysis such as ANOVA was used also. $P \leq 0.05$ was considered statistically significant. SPSS version 25 software package was used for the analysis.

RESULTS

All participants

All participants include all participants in the study and those who did not complete the three phases. The result at base line showed that females (138, [71.13%]) were more than males (56, [28.87%]) participants. About a quarter of the participants indicated that they were married (51, [26.29%]). Most common adverse event experienced by study participants was insomnia (45, [23.20%]). Six (3.09%) casualties were reported (Table 1). The result showed a higher number of the participants (77, 39.69%) did not have formal education. The result also showed a higher number of unemployment rate among participants (130, [67.01%]) (Table 2).

The results of renal and hepatic function biomarkers of 55 participants were invalidated at baseline of study because they were excessively high and were regarded as confounders. The remaining validated results were that of 139 participants. Demographic characteristics of participants at baseline showed that 139 study participants were observed in the study which comprised of 44 males and 95 females, the average age of the participants were 39.22 ± 9.45years. The 44 males had average weight of 65.07 ± 9.15 kg with BMI of 25.26 ± 4.5 kg/m^2 while the average weight for females was 63.34 ± 11.01 kg with BMI of 25.61 ± 6.05 kg/m^2 (Table 3). The results of biochemical

parameters for liver function showed that mean ALT was within normal range at baseline (6.32 ± 6.46 IU/L), mean AST/ALT ratio was higher than the normal limit (6.8 ± 10.25), mean AST at baseline was also higher than the normal limit (21.29 ± 18.81 IU/L) (Table 4). The mean viral load of 95 study participants at baseline (44.33 ± 56.19 copies/mL) and 67 study participants at follow up after 6 months were within the normal range (Table 5).

Table 1: All participants characteristics at baseline

Characteristics	Frequency	Percentage %
Gender		
Male	56	28.87
Female	138	71.13
Total	194	
Marital Status		
Single	47	24.23
Married	51	26.29
Widow	16	8.25
Widower	5	2.58
Divorced	2	1.03
Living as married	4	2.06
Not filled	69	35.6
Total	194	
Patients' complaints of effect of antiretroviral drugs		
Insomnia	45	23.20
Diarrhoea	15	7.73
Rashes	5	2.58
HTN	38	19.59
Weakness	4	2.06
Heat	9	4.64
Dermatitis	4	2.06
Arthritis	10	5.15
Cough	8	4.12
Hyperglycemia	9	4.64
*Death	6	3.09
Not filled	41	21.13
Total	194	
Educational attainment		
Primary education	19	9.79
Secondary education	56	28.87
Tertiary education	42	21.65
No formal education	77	39.69
Total	194	
Employment Status		
Employed	29	14.95
Unemployed	130	67.01
Self employed	26	13.40
Student	9	4.64
	194	

***Data obtained from the hospital by investigator**

Table 2: Health Status

Variable	Frequency	Percentage %
Very good	25	12.89
Good	82	42.27
Poor	7	3.61
Not filled	80	41.23
TOTAL	194	

Table 3: Demographic characteristics of participants who attended any of the 3 phases of the study

Variable	Study period		
	Baseline	**3 months post baseline**	**6 months post baseline**
Number of participants	N = 139 (M = 44, F = 95)	N = 90 (M = 29, F = 61)	N = 76 (M = 28, F = 48)
Age (years)			
Male	41.61 ± 10.01	42.86 ± 9.76	43.00 ± 9.57
Female	38.04 ± 9.03	37.43 ± 8.99	36.60 ± 7.69
BMI (kg/m^2)			
Male	25.26 ± 4.5	24.81 ± 2.82	24.90 ± 2.64
Female	25.61 ± 6.05	25.67 ± 4.42	25.99 ± 4.51
Weight (kg)			
Male	65.07 ± 9.15	64.97 ± 7.98	67.62 ± 8.52
Female	63.34±11.01	65.28 ± 11.46	65.44 ± 10.54

M= Male, F= Female, BMI = Body Mass Index, Yrs= years, T= Total, Kg= Kilogram

Table 4: Biochemical profile of Liver and Kidney functions of participants who attended any of the 3 phases of study

PERIOD	No of participants	Liver function test (mean ± SD)				Kidney Function Test (mean ± SD)	
		ALT 0-12 IU/L	AST 0-12 IU/L	AST/ALT RATIO ≤ 1	ALP 9-35 IU/L	Creatinine µmol/L M = 74-135 F = 59-104 mg/dl	Creatinine Clearance M = 110- 150 F = 100 – 130 mL/min
Baseline	139	6.32 ± 6.46	21.29 ± 18.81	6.8 ± 10.25	-	M = 111.38 ± 32	M = 76.58 ± 26.29
						F = 343.88 ± 15.41	F = 81.63 ± 32.43
3 months	90	6.84 ± 4.61	15.94 ± 7.81	3.25 ± 2.22	52.3 ± 17.99	M = 119.6 ± 34.63	M = 68.87 ± 20.08
						F= 106.73 ± 31.39	F = 69.84 ± 19.68
Baseline vs. 3 months (P value)		0.179	0.111	0.000		0.674	0.556
6 months	76	8.89 ± 6.41	17.48 ± 14.80	2.53 ± 1.71	60.61 ± 15.83	M = 119.39 ± 22.7	M = 67.19 ± 1708
						F = 104.43 ± 20.15	F = 69.81 ± 18.11
Baseline vs 6 months (P- value)		0.179	0.011	0.180		0.523	
3 months vs 6 months		0.263	0.588	0.000	0.000		0.231

ALT=Alanine Aminotransferase, AST=Aspartate Transferase, ALP=Alkaline Phosphatase

Table 5: Viral load and CD4 of Participants

PERIOD	No of participants	VIRAL LOAD (40-75 copies/mL)	No of participants	CD4 COUNT (500-1200 cells/mm^3)
Baseline	95	44.33 ± 56.19	71	483.97 ± 282.24
3 months		-	3	486.67 ± 172.28
Baseline vs 3months P- value		-		-
6 months	67	35.84 ± 12.61	3	617.0 ± 180.60
Baseline vs 6 months P - value		0.000		0.02

STUDY PARTICIPANTS THAT COMPLETED THE THREE PHASES

The result showed that 55 participants completed the three phases of study comprising of 19 males and 36 females. The average age of the participants was 40.61 ± 10.10 years. The 19 males had BMI of 24.68 ± 4.55 kg/m^2 at baseline and 36 females with BMI of 24.71 ± 2.8 kg/m^2 (Table 6).

Result of the viral load of the 55 study participants that completed the 3 phases of the study showed that the viral load was within normal range (32.82 ± 15.59 copies/mL) at baseline and follow up (36.17 ± 10.81 copies/mL) (Table 7).

The result of biochemical profile of liver function showed that ALT was within normal range at baseline (5.40 ± 5.58 IU/L). The AST at baseline (21.29 ± 18.81 IU/L) and follow-up at 3months (15.73 ± 10.09 IU/L) were slightly above the normal range and AST/ALT ratio was also higher than the normal limit at baseline (6.51 ± 12.35) and follow-up at 3 months (3.57 ± 2.15) respectively. ALT and AST at 3-month follow-up varied significantly ($p < 0.05$) from ALT and AST at baseline respectively (Table 8).

Table 6: Profile of participants who completed three phases of study

		MEAN±SD			
PERIOD	No of participants	SEX	AGE (yrs)	BMI (kg/m^2)	WEIGHT (kg)
Baseline	55	T = 55 M = 19 F = 36	T = 40.61 ± 10.10 M = 47.0 ± 9.4 F = 40.61 ± 10.1	T = 24.41 ± 4.08 M = 23.85 ± 2.96 F = 24.68 ± 4.55	T = 62.91 ± 10.93 M = 63.89 ± 8.87 F = 64.39 ± 10.67
3 months	55	T = 55 M = 19 F = 36	T = 40.61 ± 10.10 M = 47.0 ± 9.4 F = 40.61 ± 10.1	T = 25.22 ± 4.11 M = 24.71 ± 2.8 F = 25.47 ± 4.63	T = 64.39 ± 10.63 M = 65.67 ± 8.73 F = 62.91 ± 10.83
6 months	55	T = 55 M = 19 F = 36	T = 40.61 ± 10.10 M = 47.0 ± 9.4 F = 40.61 ± 10.1	T = 25.63 ± 4.00 M = 24.90 ± 2.64 F = 25.99 ± 4.51	T = 65.87 ± 10.40 M = 66.78 ± 8.54 F = 65.87 ± 10.40

M= Male, F= Female, BMI = Body Mass Index, Yrs= years, T= Total, Kg= Kilogram

Table 7: Viral load results for those that completed all 3 phases

PERIOD	No of participants	VIRAL LOAD (≤40-75 copies/mL)	No of participants	CD4 COUNT (500-1200 cells/mm^3)
Baseline	49	32.82 ± 15.59	30	482.90 ± 251.72
3 months		-	3	486.67 ± 172.28
P- value		-		0.98
6 months	52	36.17 ± 10.81	3	617.0 ± 180.60
0month vs. 6 months P - value		0.29		0.001

Table 8: Biochemical profile of liver function and kidney function tests of participants who completed the 3 phases

PERIOD	No of participants	Liver function test (mean ± SD)				Kidney Function Test (mean ± SD)	
		ALT 0-12 IU/L	AST 0-12 IU/L	AST/ALT Ratio ≤ 1	ALP (9-35 IU/L)	Creatinine M = 74-135 F = 59-104 µmol/L	Creatinine clearance M = 110- 150 F = 100-130 mL/min
Baseline	55	5.40 ± 5.58	21.29 ± 18.81	6.51 ± 12.35		M =109.62 ± 42.1	M = 67.79 ± 20.96
						F = 343.88 ± 15.41	F = 75.8 ± 20.66
3 months	55	5.84 ± 5.52	15.73 ± 10.09	3.57 ± 2.15	55.48 ± 15.01	M = 119.6 ± 34.63	M = 65.26 ± 18.76
						F = 93.7 ± 26.41	F = 70.07 ± 20.66
Baseline vs. 3months (P-value)		0.001	0.000	0.000		M = 0.364	M = 0.133
						F = 0.131	F = 0.264
6 months	55	11.52 ± 5.39	18.99 ± 7.66	2.01 ± 1.26	63.69 ± 14.81	M = 122.88 ± 22.7	M = 64.70 ± 19.62
						F = 100.78 ± 19.9	F = 69.60 ± 21.90
Baseline vs. 6 months (P- value)		0.093	0.000	0.000		M = 0.677	T = 0.000 M = 0.192
						F = 0.40	F = -
3months vs. 6 months		0.015	0.000	0.114		M = 0.193	M = -
						F = 0.02	F = 0.67

ALT= Alanine Aminotransferase, AST=Aspartate Transferase, ALP= Alanine Phosphatase, M= Male, F= Female, T= Total

DISCUSSION

ALL PARTICIPANTS

The people that participated but did not complete the three phases of study were observed to experience increase in liver enzymes, ALT. This increase of ALT probably suggested that the drug combination had impacted injury on the liver. This observation corroborates previous work which showed that DTG when administered concomitantly with ABC and lamivudine would increase liver biomarkers.[11] Liver enzyme, AST was significantly elevated during the study, suggesting a sign of damage not only to the liver but probably to other parts of the body like the muscles of the heart. These two biomarkers suggested hepato-cellular injury. AST is available in cytosolic and mitochondrial iso-enzymes in the liver, cardiac muscle skeletal muscle, kidneys, brain, pancreas, lungs, leucocytes, and red cells. AST is not specific for the liver, and elevation in AST may be due to non-hepatic cause. Hill had reported cardiovascular adverse effect caused by dolutegravir in HIV-infected patients receiving antiretroviral therapy.[12] ALT is a cytosolic enzyme that is available in high proportion in the liver. Hepato-cellular injury and not cell death is the cause for the release of these enzymes into the circulation.[13,14] The ratio of liver enzymes was observed to be significantly higher than the expected ratio suggesting possibility of damage in the muscles. When an AST/ALT ratio is higher than one, it is suggestive of liver cirrhosis.[13]

Serum creatinine of both male and female participants was elevated suggesting renal injury but higher elevation occurred in female participants. This observation was supported by research in Brazil that indicated elevation of serum creatinine with higher prevalence in female participants.[15] This study indicated that both male and female study participants had creatinine clearance below the normal limit suggesting impaired renal function. This observation was in consonant with a previous study by Lucas.[16] All INSTIs have been associated with an increase in serum creatinine levels. In vitro data indicated DTG to inhibit organic cat-ion transporter 2 (OCT2) on the baso-lateral side of proximal tubular cells. Therefore, DTG can block tubular uptake of creatinine from the blood, leading to increased serum creatinine and decreased eGFR or CrCl, without changing effective GFR.[17]

TLD-related weight gain and increased BMI were observed in this study. In previous studies, weight gain of greater than 10% of body mass was significantly more likely to occur in women taking dolutegravir. The emergence of obesity occurred in treatment with dolutegravir in this study. This observation was similar with the finding of the ADVANCE study in South Africa in which most of the participants were women with higher BMI than men.[18] A similar study reported increased BMI for both male and female.[19] The weight gain and increased BMI experienced in this study suggested higher tendency for obesity among participants. In previous studies, clinical obesity emerged more frequently in women during the follow-up period, especially in women that received tenofovir alafenamide.[20] A study by Mugglin *et. al*., suggested that people who switched to a combination that included an integrase inhibitor reported that women and black people gain more weight after switching to dolutegravir containing antiretroviral therapy.[21] Most frequent side effect experienced by participants was insomnia which might affect medication compliance. Quercia *et. al*., reported that neuropsychiatric side-effects leading to discontinuation of dolutegravir were observed to be more frequent among women.[22] There were evidences that suggested dolutegravir is associated with a higher incidence of neuropsychiatric side-effects such as insomnia, anxiety, depression and psychosis.[23,24]

In the course of the study, six (6) study participants were confirmed dead. Two of the study participants had started dialysis and a number of them were changed to an alternative first line therapy after second follow-up. A study had earlier reported deterioration of renal function in seropositive individuals receiving antiretroviral agents.[25] Another study confirmed high intolerance rate for patients that received antiretroviral combination therapy that contained dolutegravir which required switching from dolutegravir-containing antiretroviral combination.[26]

PARTICIPANTS THAT COMPLETED THREE PHASES OF STUDY

The increased BMI observed among the participants suggested obesity-related effects of the therapy. Earlier study had indicated that antiretroviral therapy caused elevated BMI.[19] Weight of study participants was also increased at follow up. Weight gain was reported in previous studies involving participants on antiretroviral therapy.[27,28] The viral load of study participants was suppressed during the study suggesting that many of the participants were medication adherent and the new antiretroviral therapy, TLD was efficacious. The specific biochemical parameters of liver function such as ALT and ALP were significantly and progressively increased at

follow-up suggesting the presence of liver injury due to intake of TLD. This observation supported the claim of previous study which indicated that antiretroviral therapy raised liver enzyme concentration in the blood.[29] It was observed that both creatinine clearance of male participants and female participants of the study were consistently decreased below normal limit during the study. Creatinine clearance of total population of the study was also significantly decreased during the study suggesting renal injury and impairment of renal function. Lucas *et. al.,* had earlier reported decreased creatinine clearance in patients receiving antiretroviral therapy.[16] Death of participants in the study might be associated with lack of continuous monitoring of vital organ functions at the healthcare facility. A previous study had associated the use of antiretroviral therapy with participants' death due to liver or renal failure caused by antiretroviral therapy.[9,30]

The study limitations were the inability to recruit TLD naïve healthy participants as control and loss of study participants to follow-ups. Shortly after commencement of the study in February 2020, there was a lockdown in the country due to the COVID-19 pandemic, which restricted movement of persons except on essential services or health purpose. The pandemic lockdown effect hampered the size of study participants and the follow-ups.

CONCLUSION

This study indicated that there was significantly decreased viral load of study participants while CD4 count was increased. The study also indicated that biochemical parameters of liver function, enzymes ALT and ALP were significantly increased in participants. The study also indicated that creatinine clearance of participants was significantly reduced in post-baseline follow-up. The most common complaint by participants on TLD was insomnia. Six study participants on TLD were confirmed dead. Monitoring of liver and renal functions on a routine basis for HIV-infected patients receiving TLD is hereby recommended.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interest exists. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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