Impact of Antiretroviral Drugs on Renal Doppler Indices of Adult Patients with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome in Sub-Saharan African Population

Mohammed Sidi[6*], Anthony C. Ugwu[1], Manafa Onochie Patrick[2], Joseph Dlama Zira[3], Abdu Hamisu Dambatta[4], Umar Jibo[5], Mohammed Kabir Saleh[4], Anas Ya'u[6], Umar Mansur[6] and Sha'awa Abdullahi Mahmud[6]

1. *Department of Radiography and Radiological Sciences, Faculty of Health Sciences and Technology, Nnamdi Azikiwe University Awka, Nigeria.*
2. *Department of Laboratory Medical Sciences, Faculty of Health Science and Technology, Nnamdi Azikiwe University Awka, Nigeria.*
3. *Department of Radiography, Federal University of Lafiya, Nigeria.*
4. *Department of Radiology Aminu Kano Teaching Hospital/Bayero University Kano Nigeria*
5. *Department of Radiology, Dutse General Hospital, Jigawa State, Nigeria*
6. *Department of Medical Radiography, Faculty of Allied Health Sciences, Bayero University, Kano, Nigeria.*

***Corresponding author:** Mohammed Sidi, Department of Medical Radiography, Faculty of Allied Health Sciences, Bayero University, Kano, Nigeria. Email: msidi.radg@buk.edu.ng.

Summary

BACKGROUND

The use of highly active antiretroviral therapy in the management of patients with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome has drastically reduced the morbidity and mortality as a result of HIV infections worldwide. However, there have been associated organ toxicities including nephro-toxicity. The main objective of the study was to determine the impact of antiretroviral drugs on renal Doppler indices of adult patients with HIV/AIDS in a Sub-Saharan Africa population.

MATERIALS AND METHODS

This study design was a prospective cohort conducted from July 2019 to April 2020 in Kano, Nigeria. A purposive sampling method was employed to obtain a sample size of 396 participants. The sampling for the renal RI and PI was performed at the level of the interlober arteries in between the medullary pyramids.

RESULTS

Subjects on Zidovudine/Lamivudine/Navirapine regimen had the highest values of resistive index (RI) and pulsatility index (PI) (0.66±0.05 and 1.44±0.09). Those on Tenofovir Disoproxil Furamate /Lamivudine /Lopinavir/ritonavir had the lowest values of resistive index (RI) and pulsatility index (PI) (0.61±0.01 and 1.38±0.06). There was a statistically significance difference in the mean of the RI and PI between the different groups of the drugs regimens (p=0.000).

CONCLUSION

In this study Zidovudine/Lamivudine/Navirapine regimen had the highest negative impact on RI and PI while Tenofovir Disoproxil Furamate /Lamivudine /Lopinavir/ritonavir had the lowest.

Keywords: *Resistive Index, Pulsatility Index, Antiretroviral Drugs, HIV/AIDS*

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Introduction

Human Immunodeficiency Virus (HIV) is a lentivirus, a subgroup of retroviruses that attack the immune system of the human body, mainly the T-Lymphocytes, thereby predisposing the infected individual to infectious diseases. These diseases then affect the various systems of the body and, if left untreated, progress to acquired immunodeficiency syndrome (AIDS).[1]Human Immunodeficiency Virus-Associated Nephropathy (HIVAN), a renal parenchymal disease, is associated with HIV/AIDS. The pathogenesis of HIVAN is not known, however, studies have suggested that it may be as a result of direct infection of the renal cells with the HIV 1 or as a result of the changes due to the release of cytokines as a result of the HIV infection.[2]

Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) remains a major global public health challenge as more than 32 million died out of the diseases.[3] As at the end of 2018, 37.9 million people were living with HIV/AIDS worldwide, 770 000 people died from HIV-related illnesses while 1.7 million new infections were reported.[3]

As at 14 March 2019 UNAIDS in collaboration with the National Agency for the Control of AIDS released new survey results that showed Nigeria had a prevalence of 1.4% and estimated that there were about 1.9 million people living with HIV/AIDS.[4] The North West zone where the Kano State belongs had a prevalence of 0.6%.[4]

The use of highly active antiretroviral therapy in the management of patients with HIV/AIDS has drastically reduced the morbidity and mortality resulting from HIV infections worldwide. However, there have been associated organ toxicities including nephro-toxicity and with the possible reason attributable to the key role the kidney plays in the excretion of the antiretroviral drugs.[5]

Antiretroviral drugs can contribute to renal dysfunction by inducing acute tubular necrosis, acute interstitial nephritis, crystal nephropathy and renal tubular disorders.[5]It is recommended that an antiretroviral (ARV) regimen for a treatment-naive patient generally consist of two nucleoside reverse transcriptase inhibitors(NRTIs) in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), anon-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (booster)(cobicistat or ritonavir).[6]The antiretroviral agents most strongly associated with direct nephrotoxicity include the NRTIs; tenofovir, and the PI (indinavir) although other agents have been implicated less frequently.[7]

Tenofovir and related nucleotide analogs have primarily been associated with proximal tubular dysfunction and acute kidney injury, whereas indinavir is known to cause nephrolithiasis, obstructive nephropathy, and interstitial nephritis.[7]

In the clinical practice the level of serum creatinine, urea, electrolytes and proteinuria are used to assess the renal function of HIV seropositive patients before the commencement of the antiretroviral therapy as well as during the follow up of the patients. However, about 50% of the renal function must be lost before a rise in serum creatinine can be detected. Serum urea may be raised with high protein diet or patients on corticosteroid therapy, and urine protein is not specific to renal pathology.[8]

Ultrasound has also been used in the diagnosis and follow up of renal diseases in patients with HIV/AIDS. However, most of the grayscale sonography morphological features are observed in the later course of the disease.[9]Renal Doppler sonography; resistive index (RI) and pulsatility index (PI) values can serve as early sonographic predictors of abnormal changes and a prognostic indicator in patients on antiretroviral therapy, which would have been very important in determining the necessity or otherwise of early intervention in preventing or halting the progress of the drugs-induced nephropathy.[10]

To the best knowledge of the researchers there are no published research works on impact of antiretroviral drugs on renal Doppler indices of adult patients with Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome. Therefore, this study is the first attempt at determining the effect of HAART on renal Doppler indices. The study was aimed at evaluating the impact of antiretroviral drugs on renal Doppler indices of adult patients with Human Immunodeficiency Virus / Acquired Immunodeficiency Syndrome in Kano, Nigeria.

Materials and Methods

The design was a prospective cohort conducted among HIV sero-positive adult individuals from July 2019 to April 2020 in the Radiology department of Aminu Kano Teaching Hospital, Kano, Nigeria. A purposive sampling method was employed in the study and a sample size of 352 derived from 8 different drug regimens and tagged regimen 1-8; 44 from each regimen; 22 males and 22 females respectively, were studied. The available drug regimens at the study area during the study period are shown in Table 1.

Table 1: Available Drugs Regimen at the Study Area during the Study Period

Drug Regimens	Names	Abbreviation
1	Abacabir/Lamivudine/Atazanavir/ritonavir	ABC/3TC/ATV/r
2	Tenofovir/Lamivudine/Dulotegravir	TLD
3	TenofovirDisoproxilFuramate/Lamivudine/ Atazanavir/ritonavir	TDF/3TC/ATVr
4	TenofovirDisoproxilFuramate/Lamivudine /Efaverenz	TDF/3TC/EFV
5	TenofovirDisoproxilFuramate/Lamivudine/ Lopinavir/ritonavir	TDF/3TC/LPV/r
6	TenofovirDisoproxilFuramate/Lamivudine/ Amprenavir/ritonavir	TDF/3TC/APV/r
7	Zidovudine/Lamivudine/Navirapine	ATZ/3TC/NVP
8	Zidovudine/Lamivudine/Lopinavir/ritonavir.	AZT/3TC/LPV/r

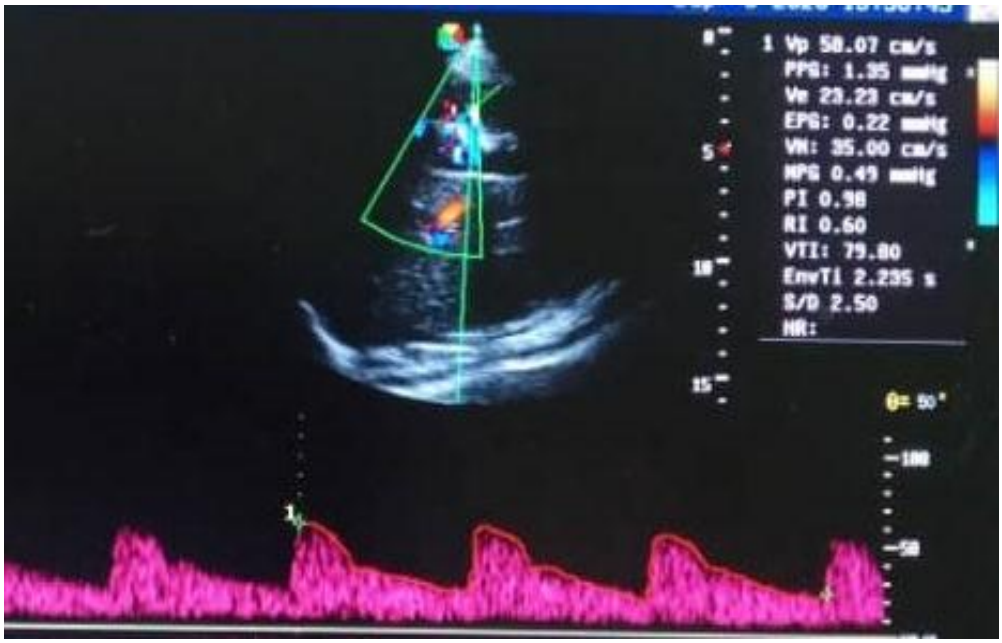

Figure 1: Shows the technique for the measurement of RI and PI of the interlober artery for 26 years HIV-sero positive individual. The sample volume was 3mm; the wave was acquired as shown above. The RI value was 0.60 and the PI was 0.98.

Regimens 1-6 were the first line while regimen 7 and 8 were the second line. Adult patients aged 18-65 years, living with HIV/AIDS and placed on antiretroviral therapy for a period of six months and above were included in the study. Excluded from the study were patients with a history of acute or chronic hepatitis B or C infection, diabetic and hypertensive patients[12], pregnant women, pediatric patients, geriatric patients[7], and patients unable to hold their breath during the scan were excluded from the study, as well as patients diagnosed with HIV/AIDS but not yet on antiretroviral therapy.

Ethical approval to conduct the study was obtained from the Human Research and Ethics Committee of the Aminu Kano Teaching Hospital, and informed consent obtained from participants after they agreed to the objectives and significance of the study.

A SONOSCAPE SSI–8000, 2014 digital color Doppler ultrasound system, Schenzhen China machine, equipped with a 3.5MHz curvilinear transducer and electronic calipers was used as an instrument for data collection. Acoustic gel was used as the coupling medium.

The patients were examined in the prone position, the radiologist positioned on the left side of the patient and ultrasound gel was applied at the para-vertebral area of the lumbar region. The resistance to blood flow increased from the renal hilar vessels towards the peripheral parenchymal vessels.[7] Therefore, sampling for the renal resistive index was performed at the level of the interlobar arteries in-between the medullary pyramids. The target vessel was then insonated using a 2–4 mm Doppler gate[7]. The waveforms were obtained from the upper pole, the middle part and the lower pole of the kidney. The wave form was traced and the machine displayed the resistive and pulsatility indices automatically in each case as shown in Figure 1. The average of the resistive and pulsatility indices of the three regions of the kidney was recorded as the resistive and pulsatility index of the kidney.

Means, standard deviations (SD) and range of the RI, PI, serum creatinine and urea were obtained using descriptive statistics. The difference in mean of the RI and PI between the different drug regimens was obtained using ANOVA. Post hoc test of multiple comparisons was used to find the difference between each group. The data was analyzed using Statistical Package for Social Sciences (IBM SPSS) Version 22.0. Preset ρ-value (0.05).

Results

Table 1 shows the available drug regimens at the study area during the study period. Eight different drugs regimens were used and tagged regimens 1-8. Regimens 1-6 were the first line regimens while 7 and 8 were the second line

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Table 2: Demographic Information of the Subjects

Drug Regimens	Demographic Data							
	Male(n=176)				Female(n=176)			
	Age(Yrs)	Du(Yrs)	Weight(Kg)	Height(Cm) Height(Cm	Age(Yrs)	DU(Yrs)	Weight(Kg)	
1	43.32±11.71 (22-62)	7.32±4.04 (2-16)	67.86±9.79 (49-81)	167.77±2.67 (162-172)	39.59±11.38 (20-60)	7.36±3.5 (2-14)	63.18±8.65 (50-80)	166.27±2.49 (158-172)
2	43.32±11.62 (21-63)	7.58±4.52 (1-19)	65.77±12.27 (42-87)	171.32±7.69 (160-190)	41.73±8.79 (25-59)	7.77±3.53 **(**1-13)	64.41±13.19 **(**45-86)	164.64±6.25 (152-183)
3	42.36±12.38 (19-62)	6.91±4.01 (1-14)	65.50±10.00 (50-82)	166.45±3.52 (160-172)	40.00±12.21 (21-61)	7.41±4.27 (2-16)	60.46±7.67 **(**48-74)	163.91±3.35 (159-172)
4	43.23±11.26 (20-60)	7.60±3.67 (2-13)	67.14±9.42 (50-83)	167.50±3.20 (162-172)	40.91±11.82 **(**20-61)	6.14±3.58 (1-13)	63.05±10.61 (43-80)	164.50±4.41 (160-180)
5	43.45±11.65 (22-62)	9.55±3.19 (3-15)	66.23±9.40 (54-83)	167.27±2.88 (162-172)	41.18±9.24 (23-60)	7.46±3.81 (2-14)	62.55±9.01 (50-86)	166.18±3.45 (158-170)
6	44.46±10.19 **(**26-60)	7.68±3.68 (1-14)	67.46±9.67 **(**50-83)	167.86±4.21 (162-180)	42.41±11.12 (24-62)	6.73±3.68 (1-13)	63.86±11.11 (43-82)	166.77±4.31 (155-174)
7	46.27±10.01 (23-60)	8.44±3.84 (2-16)	69.09±10.74 (50-95)	168.36±7.90 (162-200)	42.86±10.65 (23-61)	8.00±3.51 (2-15)	67.91±16.14 (48-116)	167.27±4.63 (160-182)
8	41.23±11.15 (20-62)	7.41±3.88 (2-14)	66.36±9.26 (50-85)	167.32±2.73 (162-172)	40.64±10.32 (19-60)	7.77±4.07 (1-15)	64.23±15.58 (42-88)	168.00±3.84 (162-175)

Key: Regimens 1= ABC/3TC/ATV/r (Abacabir/Lamivudine/Atazanavir/ritonavir), 2= TLD (Tenofovir/Lamivudine/Dulotegravir), 3= TDF/3TC/ATVr (Tenofovir Disoproxil Furamate /Lamivudine/Atazanavir/ritonavir), 4= TDF/3TC/EFV (Tenofovir Disoproxil Furamate/ Lamivudine/Efaverenz), 5= TDF/3TC/LPV/r (Tenofovir Disoproxil Furamate /Lamivudine /Lopinavir/ritonavir), 6= TDF/3TC/APV/r (Tenofovir Disoproxil Furamate/Lamivudine/ Amprenavir/ritonavir), 7= ATZ/3TC/NVP (Zidovudine/Lamivudine/Navirapine), 8= AZT/3TC/LPV/r (Zidovudine/Lamivudine/Lopinavir/ritonavir), DU(yrs)=Duration of antiretroviral therapy.

Table 2 shows the mean±SD and range of the age, duration of the antiretroviral therapy, weight and height of the selected subjects of drug regimens 1-8 were 43.32±11.71, 43.32±11.62, 42.36±12.38, 43.23±11.26, 43.45±11.65, 44.46±10.19, 46.27±10.01, and 41.23±11.15 respectively. For female subjects were 39.5±11.38, 41.73±8.79, 40.00±12.21, 40.91±11.82, 41.18±9.24, 42.41±11.12, 42.86±10.65, and 40.64±10.32, respectively.

Table 3 shows that male subjects on regimen 7 had the highest resistive and pulsatility index of 0.66±0.06 and 1.44±0.09, respectively. Female subjects on regimen 7 also had the highest resistive and right pulsatility index of 0.65±0.05 and 1.40± 0.10, respectively.

Table 4 shows a statistically significant difference in RI and PI between different drug regimens (P =0.00).

Table 3: Resistive and Pulsatility Indices of the Subjects Based on Drugs Regimens

Drugs regimen	Male				Female			
	RRI	**RPI**	**LRI**	**LPI**	**RRI**	**RPI**	**LRI**	**LPI**
1	0.62±0.03 (0.58-0.72)	1.39±0.06 (1.26-1.48)	0.62±0.03 (0.59-0.70)	1.38±0.07 (1.25-1.46)	0.61±0.03 (0.59-0.73)	1.37±0.06 (1.0-1.42)	0.61±0.03 (0.58-0.73)	1.36±0.07 (1.01-1.40)
2	0.65±0.05 (0.59-0.74)	1.40±0.16 (0.93-1.55)	0.65±0.05 (0.58-0.73)	1.39±0.16 (0.92-1.52)	0.63±0.05 (0.55-0.73)	1.38±0.15 (0.98-1.52)	0.62±0.05 (0.53-0.73)	1.36±0.15 (0.96-1.50)
3	0.65±0.05 (0.58-0.73)	1.39±0.09 (1.3-1.57)	0.65±0.04 (0.58-0.72)	1.38±0.09 (1.28-1.56)	0.63±0.04 (0.59-0.72)	1.38±0.12 (0.99-1.54)	0.62±0.03 (0.58-0.71)	1.36±0.12 (0.99-1.53)
4	0.64±0.04 (0.60-0.70)	1.38±0.07 (1.28-1.57)	0.63±0.04 (0.58-0.69)	1.37±0.06 (1.32-1.56)	0.62±0.02 (0.60-0.67)	1.36±0.06 (1.34-1.54)	0.62±0.02 (0.60-0.66)	1.34±0.05 (1.33-1.52)
5	0.61±0.01 (0.60-0.63)	1.38±0.06 (1.28-1.54)	0.61±0.02 (0.59-0.66)	1.36±0.06 (1.22-1.52)	0.60±0.02 (0.60-0.67)	1.36±0.06 (1.26-1.51)	0.60±0.02 (0.60-0.66)	1.35±0.06 (1.33-1.50)
6	0.65±0.04 (0.60-0.73)	1.42±0.11 (1.24-1.54)	0.64±0.04 (0.58-0.72)	1.40±0.06 (1.22-1.52)	0.64±0.04 (0.56-0.72)	1.41±0.09 (1.24-1.52)	0.63±0.04 (0.55-0.70)	1.39±0.09 (1.21-1.50)
7	0.66±0.05 (0.60-0.76)	1.44±0.09 (1.07-1.58)	0.65±0.05 (0.59-0.76)	1.42±0.09 (1.06-1.57)	0.65±0.05 (0.59-0.78)	1.40±0.09 (1.07-1.54)	0.64±0.05 (0.59-0.78)	1.38±0.09 (1.06-1.52)
8	0.65±0.04 (0.60-0.73)	1.41±0.09 (1.29-1.58)	0.64±0.04 (0.60-0.72)	1.40±0.09 (1.28-1.57)	0.64±0.04 (0.59-0.73)	1.39±0.10 (1.28-1.56)	0.63±0.04 (0.60-0.72)	1.38±0.09 (1.28-1.54)

Key: Regimen 1= ABC/3TC/ATV/r (Abacabir/Lamivudine/Atazanavir/ritonavir), 2= TLD (Tenofovir/Lamivudine/Dulotegravir), 3= TDF/3TC/ATVr (Tenofovir Disoproxil Furamate /Lamivudine/Atazanavir/ritonavir), 4= TDF/3TC/EFV (Tenofovir Disoproxil Furamate/ Lamivudine/Efaverenz), 5= TDF/3TC/LPV/r (Tenofovir Disoproxil Furamate /Lamivudine /Lopinavir/ritonavir), 6= TDF/3TC/APV/r (Tenofovir Disoproxil Furamate/Lamivudine/ Amprenavir/ritonavir), 7= ATZ/3TC/NVP (Zidovudine/Lamivudine/Navirapine), 8= AZT/3TC/LPV/r (Zidovudine/Lamivudine/Lopinavir/ritonavir). RRI=right resistive index, RPI= right pulsatility index, LRI=left resistive index, LPI= left pulsatility index.

Table 4: One Way ANOVA Test of the Resistive Index and Pulsatility Index Based on Drug Regimens

Renal Indices	Statistical Output F	P-value
RRI	7.48	0.000
RPI	17.36	0.000
LRI	7.99	0.000
LPI	22.78	0.000

Key: RRI=right resistive index, RPI= right pulsatility index, LRI=left resistive index, LPI= left pulsatility index.

Table 5 shows a comparison of each group with the other groups. There was a statistically significant difference in RI values between group 1 and groups 7 and 8 in both males and females. However, a statistical significant difference was observed in PI values between group 1 and groups 3, 4, 5, 6, 7 and 8. A statistically significant difference was also observed in RI and PI values between group 3 and group 5 in both males and females. In both males and females a statistically significant difference was observed in PI values between group 4 and group 1 and in RI values between group 4 and 8.

Table 5: Turkey Post Hoc Test of Multiple Comparisons

Gender		Males		Females	
Drug regimens		RI	PI	RI	PI
		P-values			
1	**2**	0.272	0.857	0.323	0.102
	3	0.185	0.005	0.248	0.006
	4	0.985	0.003	0.997	0.004
	5	0.983	0.009	0.791	0.029
	6	0.980	0.001	0.873	0.000
	7	0.000	0.002	0.000	0.000
	8	0.026	0.000	0.007	0.000
2	**1**	0.272	0.087	0.323	0.102
	3	1.000	0.986	1.000	0.984
	4	0.838	0.969	0.775	0.972
	5	0.250	0.996	0.547	1.000
	6	1.000	0.908	0.987	0.644
	7	0.120	0.078	0.235	0.000
	8	0.968	0.986	0.848	0.585
3	**1**	0.850	0.085	0.248	0.006
	2	1.000	0.986	1.000	0.984
	4	0.734	1.000	0.689	1.000
	5	0.014	0.012	0.003	0.000
	6	1.000	1.000	0.970	0.990
	7	0.185	0.068	0.307	0.890
	8	0.990	0.963	0.906	0.983

Table 5: Turkey Post Hoc Test of Multiple Comparisons Continued

Gender		Males		Females	
Drug Regimens		RI	PI	RI	PI
		P-values			
4	1	0.984	0.003	0.997	0.004
	2	0.838	0.969	0.775	0.972
	3	0.734	1.000	0.689	1.000
	5	0.593	1.000	0.339	0.999
	6	0.557	1.000	0.998	0.995
	7	0.001	0.000	0.002	0.000
	8	0.208	0.983	0.061	0.991
5	1	0.983	0.000	0.791	0.029
	2	0.025	0.996	0.004	1.000
	3	0.015	1.000	0.003	1.000
	4	0.593	1.000	0.339	0.999
	6	0.005	0.030	0.037	0.049
	7	0.000	0.000	0.000	0.000
	8	0.001	0.033	0.000	0.028
6	1	0.980	0.771	0.873	0.698
	2	1.000	0.908	0.987	0.644
	3	1.000	1.000	0.970	0.990
	4	0.557	1.000	0.998	0.995
	5	0.005	0.009	0.047	0.017
	7	0.026	0.000	0.023	0.000
	8	0.999	0.997	0.291	1.000
7	1	0.000	0.002	0.000	0.000
	2	0.120	0.000	0.235	0.000
	3	0.185	0.000	0.307	0.000
	4	0.001	0.000	0.002	0.000
	5	0.000	0.000	0.000	0.000
	6	0.315	0.000	0.023	0.000
	8	0.700	0.000	0.974	0.000
8	1	0.018	0.000	0.007	0.000
	2	0.968	0.510	0.848	0.585
	3	0.990	0.963	0.906	0.983
	4	0.208	0.983	0.061	0.991
	5	0.001	0.034	0.000	0.028
	6	0.999	0.997	0.291	1.000
	7	0.700	0.000	0.974	0.000

Key: Regimen 1= ABC/3TC/ATV/r (Abacabir/Lamivudine/Atazanavir/ritonavir), 2= TLD (Tenofovir/Lamivudine/Dulotegravir), 3= TDF/3TC/ATVr (Tenofovir Disoproxil Furamate /Lamivudine/Atazanavir/ritonavir), 4= TDF/3TC/EFV (Tenofovir Disoproxil Furamate/ Lamivudine/Efaverenz), 5= TDF/3TC/LPV/r (Tenofovir Disoproxil Furamate /Lamivudine /Lopinavir/ritonavir), 6= TDF/3TC/APV/r (Tenofovir Disoproxil Furamate/Lamivudine/ Amprenavir/ritonavir), 7= ATZ/3TC/NVP (Zidovudine/Lamivudine/Navirapine), 8= AZT/3TC/LPV/r (Zidovudine/Lamivudine/Lopinavir/ritonavir). RI=right resistive index, PI= right pulsatility index.

Furthermore, there was a statistically significant difference in RI values between group 5 and groups 2, 3, 5, 6, 7 and 8 in PI values between group 5 and 1, 6, 7 and 8. There was also a statistically significant difference in RI and PI values between group 6 and groups 5 and 7 in both males and females. A statistically significant difference was also in RI values between group 7 and groups 1, 4 and 5 in males while in females between group 7 and group 4, 5 and 6.

Table 6: Correlation of Resistive Index and Pulsatility Index with Gender, Age and Duration of the Drug Therapy

	Renal Doppler Indices							
Demographic Variables	**RRI**		**RPI**		**LRI**		**LPI**	
	r	***p***	***r***	***p***	***r***	***p***	***r***	***p***
Duration of drugs therapy	0.016	0.903	0.10	0.926	0.020	0.774	0.019	0.702

There was also a statistically significant difference in PI values between group 7 and groups 1, 2, 3, 4, 5, 6 and 8 in both males and females. In both males and females there was a statistically significant difference in RI and PI values between group 8 and groups 1 and 5 ($p<0.05$) in all instances.

Table 6 shows no correlation was observed between the right and the left RI and PI with duration of antiretroviral therapy ($p<0.1$).

Discussion

The findings of this study, as shown in Table 2, show that, the mean age and standard deviation of the participants are similar to the findings of the studies conducted by Sidi *et al*.[11], Eze *et al*.[12] and Astukwe *et al*.[13] that reported 42.87±10.1years,42.7 ± 9.4 years and 45.72 ± 8.89 years as the mean age and standard deviation of the HIV sero-positive participants. This similarity is possibly because the current study and the previous studies were conducted in the same country. Furthermore, in this study, the mean and standard deviation are almost similar in the eight different groups of the drugs regimens as also shown in Table 1.

The duration of the antiretroviral therapy of the selected subjects in the eight different groups of the drug regimens are almost the same. Therefore, the differences observed in the renal Doppler indices of the different drugs regimens might not be as a result of age or duration of the antiretroviral therapy.

A RI value of 0.60 ± 0.01 (mean ± SD) is usually taken as normal in adults with a value of 0.70 being considered the upper normal threshold[14]and the normal value of pulsatility index is 1.36–1.56.[15] The findings of this study as shown in Table 2 demonstrate that, only the selected subjects on TDF/3TC/LPV/r had a normal mean RI value, however, RI values of all the drug regimens were within the upper acceptable limit. The subjects on ATZ/3TC/NVP had the highest RI values followed by those on TLD, TDF/3TC/ATVr, TDF/3TC/APV/r and AZT/3TC/LPV/r who had the same values as also shown in Table 2.

The findings of this study as shown in Table two also show that, the male participants on ATZ/3TC/NVP and AZT/3TC/LPV/r regimens had abnormal PI values; however, the

female participants had normal PI values. Furthermore, both males and females that are on the other six regimens all presented with normal PI values, as also shown in Table 2. The participants on a drug regimen with high RI and PI or PI stood a higher risk of developing HIV associated nephropathy than those with lower RI and PI or PI. Therefore, those on drug regimens with high RI and PI or PI need to be monitored closely compared to those on drug regimen with lower RI and PI or PI. Furthermore, as shown in Table 2, male participants had higher RI and PI than the females, hence the males are more at risk of developing HIV associated nephropathy than their female counterparts.

The findings of this study show that, there was a statistically significant difference in the mean of the RI and PI between the groups of the drugs regimens as demonstrated by one-way ANOVA test (p=0.000) as shown in Table 3. Furthermore, Turkey post hoc test of multiple comparisons shows the difference between each drug regimen with the other seven drugs regimen as shown in Table 4. It showed that ATZ/3TC/NVP and AZT/3TC/LPV/r had statistically significant negative impact on resistive index and pulsatility index than ABC/3TC/ATV/r and TDF/3TC/LPV/r. Moreover, TDF/3TC/ATVr and TDF/3TC/APV/r had statistically significant negative impact on resistive index and pulsatility index than TDF/3TC/LPV/r.

This study shows that no correlation was observed between the right and the left RI and PI with duration of drugs therapy ($p<0.1$).

Conclusions

Antiretroviral drugs had a negative impact on RI and PI. In this study Zidovudine/Lamivudine/Navirapine regimen had the highest negative impact on RI and PI while Tenofovir Disoproxil Furamate /Lamivudine /Lopinavir/ritonavir had the lowest. Turkey post hoc test of multiple comparisons showed that ATZ/3TC/NVP and AZT/3TC/LPV/r had statistically significant negative impact on resistive index and pulsatility index than ABC/3TC/ATV/r and TDF/3TC/LPV/r

Recommendation

Renal Doppler indices are recommended in the monitoring of renal function in patients with HIV/AIDS on antiretroviral therapy.

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