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Original Article

Prevalence of prolonged QTc interval among HIV infected patients on highly active antiretroviral therapy (HAART) and its relationship with CD4 cells count and viral load at a tertiary hospital in North Eastern Nigeria.

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Abstract

Background: Patients living with HIV infection remain at increased risk of cardiovascular diseases and sudden cardiac death. Various prevalence of electrocardiographic (ECG) abnormalities among HIV-infected patients were reported: Attamah et al reported the prevalence of electrocardiographic abnormalities among HIV-infected patients as 34.5%, while Orunta et al reported a prevalence of 42.9%, and Njoku et al reported a prevalence of 93.0%. Human immunodeficiency virus-infected patients are at increased risk of developing prolonged QT interval. Sani et al reported the prevalence of prolonged corrected QT interval among HIV-infected patients as 45.0%. Innocent et al reported a prevalence of48.0%, while Ajala et al reported a prevalence of 18%. Prolonged QTc interval increases the risk of premature ventricular contraction which can degenerate into ventricular tachycardia and or ventricular that can result in sudden cardiac death.

Methodology: The study was a cross-sectional conducted among HIV-infected patients receiving HAART at the Federal Medical Centre Nguru, Yobe State, North Eastern Nigeria.

Results: One hundred and seven (107) subjects were recruited into the study comprising thirty-three (37.0%) males and 70(65.4%) females. The mean CD4 cell count, and viral load of the studied patients were 612.64±34.75 cells/µL and4646.30±58.68 copies/mL respectively. Twenty (18.7%) patients had prolonged QTc interval, this gave us the prevalence of prolonged QTc in this study as 18.7%. The commonest cardiac rhythm was sinus rhythm (69.2%), followed by sinus tachycardia (26.2%) and atrial fibrillation 5(4.7%). Other electrocardiographic findings include First-degree atrioventricular block was seen in seven (6.5%) patients, Premature ventricular contractions were found in16.8%, RBBB was observed in 2.8%, 3.7% of patients had LBBB and 4.7% had left posterior hemiblock. The distribution of QTc interval according to CD4 cells count and viral revealed a statistically significant difference across the groups. All the patients with prolonged QTc interval had lower CD4 cells count and higher viral load suggesting that HIV disease severity is associated with prolonged QTc interval.

Conclusion: In conclusion, the study revealed that the prevalence of prolonged QTc interval among HIV infected patients on highly active antiretroviral therapy was found to be 18.7%, and that HIV disease severity increases the risk of developing prolonged QTc interval.

Key words: QTc interval, HIV, Highly Active Antiretroviral Therapy, CD4 cells count and viral load.

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Introduction.

The roll out of highly active antiretroviral therapy (HAART) in sub-Saharan Africa about two decades ago has improved survival with a subsequent decrease in acquired immunodeficiency syndrome (AIDS) related morbidity and mortality among Human Immunodeficiency Virus (HIV) infected patients[1]. However, HIV infection continues to be a major public health problem globally despite improvements in patient survival. The overall prevalence of HIV infection in Nigeria among adults aged 15-49 years was 2.1% in a recent population-based survey, with Yobe state having the lowest prevalence of 0.4%[2]. Patients living with HIV infection remain at an increased risk of cardiovascular diseases and sudden cardiac death[3]. Numerous studies on electrocardiographic (ECG) abnormalities among HIV-infected patients have reported with different prevalence rates across diverse regions and populations for example Attamah et al reported the prevalence of electrocardiographic abnormalities among HIV-infected patients as 34.5%[4], while Orunta *et al* reported a prevalence of 42.9%[5], and Njoku et al reported a prevalence of 93.0%[6]. Human immunodeficiency virus-infected patients are at increased risk of developing prolonged QT interval. Sani et al reported the prevalence of prolonged corrected QT interval (QTc) among HIV/AIDS patients in Jos, North Central Nigeria as 45.0%[7]. Innocent et al in South-East Nigeria reported a prevalence of prolonged QT interval among HIV-infected patients as 48.0%[8], while Ajala et al, in Port Harcourt South-South Nigeria reported a prevalence of prolonged QTc among HIV-infected patients as 18%[9].

Prolonged QTc interval increases the repolarization period of cardiac myocytes, the premature ventricular contractions (PVCs) that occur during the repolarization period are the RonT phenomenon which can degenerate to Torsade de Pointes (TdP) a form of ventricular tachycardia (VT)that can progress to ventricular fibrillation[10]. Patients with prolonged QT interval are at increased risk of sudden cardiac death (SCD)[11,12] and the risk of developing prolonged QT interval increases as the HIV disease advances[7,13,14].A corrected QT interval is considered prolonged if it is greater than 440ms in males or 460ms in females, while a QTc interval of greater than 500ms is associated with an increased risk of TdP[10]. The exact pathophysiologic mechanism linking HIV infection and QT interval prolongation remains unclear. However, several mechanisms were proposed these include Chronic inflammation triggered by non-specific immune response to the virus, persistent circulation of inflammatory cytokines, and activated immune system cells are among the possible reasons for autonomic neuropathy, subclinical cardiomyopathy, or subclinical myocarditis, eventually leading to cardiacarrhythmias[15]. Electrolyte abnormalities associated with advanced HIV infection and use of some antiretroviral drugs like protease inhibitors and efavirenz has as well been reported as a cause of QTc interval prolongation[16,17,18].There are however very few studies if any on QT interval prolongation among HIV-infected patients on HAART in the northeastern region of Nigeria. We therefore decided to conduct this study to determine the prevalence of QTc interval prolongation among HIV-infected patients on HAART and its relationship with CD4 cell count and HIV-1 viral load.

Method:

Study Design:

The study was a cross-sectional one conducted among HIV-infected patients receiving HAART at an HIV treatment and care unit at the Federal Medical Centre Nguru, Yobe State, North Eastern Nigeria.

Ethical consideration:

Ethical approval for the study was obtained from the Ethics and Research Committee of the Federal Medical Centre Nguru Yobe State, North Eastern Nigeria (study reference number: FMC/N//CLSERV/355/VOL III/155 dated 11 January 2022). All studied subjects signed an informed consent form after a full explanation of what the study is all about before enrolment.

Data Collection:

As part of our exclusion criteria, patients on commonly used drugs associated with QT interval prolongation such as macrolides, fluroquinolones, fluconazole, ketoconazole, chlorpromazine, loratidine, methadone, haloperidol, olanzapine, risperidone, amitriptyline, protease inhibitors class of antiretroviral drugs as well as patients that recently used Quinine or artemisinin combination therapy for the treatment of malaria were all excluded from the study. Patients with laboratory and/or clinical evidence of hypocalcaemia, hypercalcaemia, hyperkalaemia or hypokalaemia were also excluded from the study. Patients with a history of heart disease predating the diagnosis of HIV infection and those with a clinical diagnosis of hypothermia, hypothyroidism or hyperthyroidism, as well as patients with a significant history of cigarette smoking and alcohol consumption were also excluded. One hundred and seven (107) consenting adults (age ≥18 years) HIV-positive patients were enrolled into the study. Information on the socio-demographic and clinical characteristics of the patients was obtained from their respective clinical case notes. General physical examinations including anthropometric measurements were carried out for all study subjects, and their body mass indices (BMI) were calculated as well. All patients had a full cardiovascular examination. Venous blood samples of the patients were taken for fasting blood glucose, serum electrolytes, urea, creatinine, and packed cell volume (PCV) analysis and eGFR was calculated using the Cockcroft and Gaultequation[19] viz

$$\text{Creatinine clearance} = \frac{(140-\text{age in years}) \times (\text{weight in kg}) \times 1.23}{\text{serum creatinine in micromole/l}}$$

Serum CD4 cell count measurement was done (using Cyflow laser product Patec GmbH Am plus Platz 13 D028282010 machine, while viral load estimation was done using Cobas Ampliprep Cobas tagman (48 samples per batch) model 395808 Ampliprep/4312 machine with a viral detection limit above 50 copies/ml. Patients were grouped according to CD4 cell count as follows: < 200 cells/µl, 200-500 cells/µl, 501-1000 cells/µl and >1000 cells/µl while viral loads were grouped as undetectable (<50 copies/ml), 50-1500 copies/ml,1501-10,000 copies/ml and >10,000 copies/ml

Electrocardiography was done by a trained electrocardiography technician using an electrocardiogram machine model -12 Express (serial number SE122B0911291BF Shanghai International Holding Corp. GmbH (Europe). Edan Instrument, Inc. 3/F-B Nanshan medical equipment Park Nanhai). Electrocardiography (ECG) interpretation was done by the first author, The QT interval was measured from the beginning of the QRS complex to the end of the T wave using Lead II, V5, or V6which clearly demonstrates all portions to be measured. Corrected QT interval (QTc) was calculated using the Bazett formula[20](QTc = QT / √R-R), three readings were taken, and the average was considered as the patient`s QTc.

Data Analysis:

Statistical analysis was done using a statistical package for social sciences (SPSS) version 27.0 (IBM SPSS Statistics), data were presented as mean ± standard deviation (SD) for continuous variables, while categorical variables were expressed as frequencies and proportions. A P value of < 0.05 was considered statistically significant.

Results:

Demographic and clinical characteristics of the studied population

One hundred and seven (107) subjects were recruited into the study comprising 37(34.6%) males and 70(65.4%) females. The mean age, BMI and duration of HIV treatment in years of the studied subjects were 37.32±9.52 years, 22.03±1.88 kg/m^2 and 5.44±2.17 years, respectively. The mean systolic and

diastolic blood pressure of the subjects were 128.13mmHg ±11.50mmHg and 82.42mmHg ±7.50mmHg respectively. Table 1 shows the demographic and clinical characteristics of the studied population.

Table 1: Demographic and clinical characteristics of the studied population

Age group years Numbers (%)	
Gender	
Male	37(34.6%)
Female	70(65.4%)
18-28 years	20(18.7%)
29-39 years	33(30.8%)
40-49 years	40(37.4%)
50-59 years	12(11.2%)
60-69 years	2(1.9%)
Body mass index (kg/m^2)	
Less than 18.0 kg/m^2	1(0.9%)
18.5 24.9 kg/m^2	105(98.1%)
25- 29.9 kg/m^2	1(0.9%)
≥ 30kg/m^2	0(0.0%)

BMI= Body Mass Index

Laboratory findings among the studied Population:

One patient (0.9%) had HIV/Hepatitis B virus (HBV) co-infection, and none had Hepatitis C virus (HCV) co-infection. The mean serum electrolytes, fasting blood glucose and packed cell volume were all within the normal limit. The mean packed cell volume (PCV) and estimated glomerular filtration rate (eGFR) of the studied patients were31.02±5.73% and 77.36±32.32ml/min respectively. Low eGFR was predominantly observed among patients with low CD4 cell count and high viral load. The mean CD4 cell count, and viral load of the studied patients were 612.64±34.75 cells/µl and 4646.30±58.68 copies/ml, respectively.

Table 2: Laboratory results of the studied patients

Parameters	Mean value (±) SD or %
CD4 cells count (cells/µl)	612.64±34.75.
Viral load (copies/ml)	4646.30±58.68
PCV (%)	31.02±5.73
Serum Creatinine(µmol/l)	121.86±38.86
Serum Urea(mmol/l)	6.44±2.93
eGFR(mls/min)	77.36±32.32
FBG (mmol/l)	4.55±0.60
Serum Sodium (mmol/l)	140.00±3.53
Serum Potassium (mmol/l)	3.60±0.34
Serum chloride (mmol/l)	105.45±3.74
Serum Bicarbonate (mmol/l)	22.14±20.52
Proteinuria	
Proteinuria positive	45(42.1%)
Proteinuria negative	62(57.9%)
Anaemia	
Anaemia present	35(32.7%)
No anaemia	72(67.3%)

CD4 = Cluster of differentiation, PCV Packed cell volume, eGFR= estimated Glomerular Filtration Rate, FBG = Fasting Blood Glucose.

Table 2 shows the laboratory results of the studied patients. Thirteen13(12.1%) patients had CD4 cells count of < 200 cells/µl while 14(13.1%) had CD4 cells count >1000 cells/µl. On the other hand, 14(13.1%) patients had undetectable viral load (i.e. <50copies/ml) while 15(14.0%) had a viral load >10,000 copies/ml.

Table 3 shows the distribution of CD4 cell count and viral load among the studied patients, while

Table 3: Distribution of CD4 cell count and viral load among the studied patients

CD4 cells count(cells/µl)	**Frequency (%)**
< 200 cells/µl	13(12.1%)
200-500cells/µl	32(29.9%)
501-1000cells/µl	48(44.9%)
>1000cells/µL	14(13.1%)
Viral load(copies/ml)	
Undetectable (<50 copies/ml)	14(13.1%)
50-1500 copies/ml	47(43.9%)
1501-10,000 copies/ml	31(29.0%)
>10,000 copies/ml	15(14.0%)

Table 4 shows the distribution of eGFR, proteinuria and anaemia according to CD4 cell count and viral load among the studied patients.

Table 4: Estimated glomerular filtration rate, proteinuria, and anaemia according to CD4 cells count(cells/µl) and viral load(copies/ml)

CD4 cells count	**< 200**	**200-500**	**501-1000**	**>1000**	**P-value**
eGFR(mls/min)					
> 900(0.0%)	3(9.4%)	19(39.6%)	10(71.4%)		
60-901(7.7%)	7(21.9%)	25(52.1%)	4(28.6%)		
30-59	8(61.5%)	13(40.6%)	3(6.3%)	0(0.0%)	
15-294(30.8%)	9(28.1%)	1(2.1%)	0(0.0%)		
< 150(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)		< 0.001*
Proteinuria					
No proteinuria	0(0.0%)	0(0.0%)	48(100.0%)	0(0.0%)	
Proteinuria present	13(100.0%)	32(100.0%)	0(0.0%)	14(100.0%)	< 0.001*

Anaemia					
Anaemia present	13(100.0%)	21(65.6%)	1(2.1%)	0(0.0%)	
No Anaemia	0(0.0%)	11(34.4%)	47(97.9%)	14(100.0%)	< 0.001*

Viral load	**Undetectable**	**50-1500**	**1501-10,000**	**>10,000**	**P-value**
eGFR(mls/min)					
> 9010(71.4%)	19(40.4%)	3(9.7%)	0(0.0%)		
60-904(28.6%)	24(51.1%)	7(22.6%)	2(13.3%)		
30 – 590(0.0%)	3(6.4%)	12(38.7%)	9(60.0%)		
15 – 290(0.0%)	1(2.1%)	9(29.0%)	4(26.7%)		
< 150(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)		< 0.001*
Proteinuria					
No proteinuria	14(100.0%)	47(100.0%)	1(96.8%)	0(0.0%)	
Proteinuria present	0(0.0%)	0(0.0%)	30(3.2%)	15(100.0%)	< 0.001*
Anaemia					
Anaemia present	0(0.0%)	1(2.1%)	19(61.3%)	15(100.0%)	
No anaemia	14(100.0%)	46(97.9%)	12(39.7%)	0(0.0%)	< 0.001*

eGFR = estimated glomerular filtration rate, * = Significant at P = < 0.05

Electrocardiographic results of the studied patients.

Twenty (18.7%) patients had prolonged QTc interval while 87(81.3%) patients had normal QTc interval. The most common cardiac rhythm was sinus rhythm (69.2%) followed by sinus tachycardia (26.2%) and atrial fibrillation5(4.7%). Seven (6.5% patients had first-degree atrioventricular block while the remaining 100(93.5%) patients had no ECG features of AV block, Premature ventricular contraction was found among 18(16.8%) patients, 12(11.2%) had unifocal premature ventricular contraction while 6(5.6%) had multifocal premature ventricular contractions. Ninety-five (88.8%) patients had no evidence of bundle branch block (BBB), 3(2.8%) patients had right bundle branch block (RBBB), 4(3.7%) patients had left bundle branch block (LBBB) and 5(4.7%) had left posterior hemiblock.

Table 5: Electrocardiographic findings of the studied patients

Sinus rhythm	74(69.2%)
Sinus Tachycardia	28(26.2%)
Atrial Fibrillation	5(4.7%)
No AV blocks	100(93.5%%)
1st degree AV block	7(6.5%)
2nd degree AV block	0(0.0%)
3rd degree AV block	0(0.0%)
Prolonged QTc	20(18.7%)
Normal QTc	87(81.3%
No PVC	89(83.2%)
Unifocal PVC	12(11.2%)
Multifocal PVC	6(5.6%)
No NSIVCD	88(82.2%)
NSIVCD Present	19(17.8%)
LBBB	4(3.7%)
RBBB	3(2.8%)
No BBB	95(88.8%)
LPH	5(4.7%)
Normal ST-segment	107(100.0%)
Normal T-wave	97(90.7%)
Flattened T-wave	2(1.9%)
Inverted T-wave	8(7.5%)

AV = Atrioventricular, QTc = Corrected QT interval, PVC= Premature Ventricular Contraction, NSICD = Non -specific Intraventricular Conduction Defect, RBBB = Right Bundle Branch Block, LB BB = Left Bundle Branch Block, LPHB = Left Posterior Hemiblock

Table 5 shows the distribution of electrocardiographic findings among the studied population. The distribution of electrocardiographic findings according to CD4 cell count revealed a statistically significant difference in QTc interval across the Cd4 cell count groups, all the thirteen (100.0%) patients with CD4 cell count <200 cells/µl, had prolonged QTc. Among the 32(100.0%) patients with CD4 cell count range between 200-500 cells/µl,7(21.9%) patients had prolonged QTc interval, and 25(78.1%) had normal QTc interval. All 62 (100.0%) patients with CD4 cell count >501 cells/µ had normal QTc intervals. Analysis of the variance of mean QTc interval across CD4 cell count groups revealed a significant difference (F= 33.46, P = < 0.001). However, on post hoc analysis the results showed only a significant difference in mean QTc interval between patients with CD4 cells count < 200cells/µland those with 200-500cells/µl, between the group with CD4 cells count 501-1000cells/µland those with greater than 1000cells/µl. P-values< 0.001, < 0.001, < 0.001 respectively.

Table 6 shows the distribution of electrocardiographic findings according to grouped CD4 cell count.

Table 6: Distribution of electrocardiographic findings according to grouped CD4 cells count in cells/µl.

	< 200	200-500	501-1000	> 1000	P-value
Rhythm					
Sinus rhythm	2(15.4%)	10(31.3%)	48(100.0%)	14(100.0%)	
Sinus tachycardia	6(46.2%)	22(68.8%)	0(0.0%)	0(0.0%)	
Atrial fibrillation	5(38.5%)	0(0.0%)	0(0.0%)	0(0.0%)	< 0.001*
A-V block					
No A-V blocks	6(46.2%)	32(100.0%)	48(100.0%)	14(100.0%)	
1st degree	7(53.8%)	0(0.0%)	0(0.0%)	0(0.0%)	< 0.001*
QRS axis					
Normal axis	3(23.1%)	21(65.6%)	48(100.0%)	14(100.0%)	
Left axis deviation	4(30.8%)	5(15.6%)	0(0.0%)	0(0.0%)	
Right axis deviation	6(46.2%)	6(18.8%)	0(0.0%)	0(0.0%)	< 0.001*
QTc					
Normal	0(0.0%)	25(78.1%)	48(100.0%)	14(100.0%)	
Prolonged	13(100.0%)	7(21.9%)	0(0.0%)	0(0.0%)	< 0.001*
PVCs					
Unifocal PVCs	7(53.8%)	10(31.3%)	0(0.0%)	0(0.0%)	
Multifocal PVCs	6(46.2%)	8(25.0%)	0(0.0%)	0(0.0%)	
No PVCs	0(0.0%)	14(43.8%)	48(100.0%)	14(100.0%)	< 0.001*
BBB					
No BBB	1(7.7%)	11(34.4%)	48(100.0%)	14(100.0%)	
LBBB	4(30.8%)	4(12.5%)	0(0.0%)	0(0.0%)	
RBBB	2(15.4%)	6(18.8%)	0(0.0%)	0(0.0%)	
LAH	4(30.8%)	5(15.6%)	0(0.0%)	0(0.0%)	
LPH	6(46.2%)	6(18.8%)	0(0.0%)	0(0.0%)	< 0.001*

NSIVCD					
Present	13(100.0%)	15(46.9%)	0(0.0%)	0(0.0%)	
Absent	0(0.0%)	17(53.1%)	48(100.0%)	14(100.0%)	< 0.001*
ST-Segment					
Normal	9(69.2%)	27(84.4%)	48(100.0%)	14(100.0%)	
Depressed	4(30.8%)	5(15.6%)	0(0.0%)	0(0.0%)	
Elevated	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	< 0.001*
T-wave					
Normal	5(38.5%)	17(53.1%)	48(100.0%)	14(100.0%)	
Flattened	2(15.4%)	6(18.8%)	0(0.0%)	0(0.0%)	
Inverted	6(46.2%)	9(28.1%)	0(0.0%)	0(0.0%)	< 0.001*

AV = Atrioventricular, PVC= Premature Ventricular Contraction, NSICD = Non-specific Intraventricular Conduction Defect, RBBB = Right Bundle Branch Block, LBBB = Left Bundle Branch Block, LPHB = Left Posterior Hemiblock* = Significant at Fishers exact P = < 0.05

On the other hand, QTc interval distribution according to viral load revealed a statistically significant difference across the viral load categories. All 14(100.0%) patients with undetectable (<50 copies/ml) viral load and all 47(100.0%) patients with viral load range between 50-1500 copies/ml had normal QTc interval. Five (15.6%) out of 31 patients with viral load range between 1501-10,000 copies/ml and all the 15(100.0%) patients with viral load >10,000 copies/ml had prolonged QTc interval. Analysis of variance revealed a significant difference in mean QTc interval across viral load groups (F = 54.56, P = <0.001). However, on post hoc analysis, the significant difference was only observed between the groups with undetectable viral load and those with viral load>10,000copies/ml, between 50-1500copies/ml and those with > 10,000 copies/ml, between 1501-10,000copies/ml and those with > 10,000copies/ml. P = < 0.001, P = <0.001and P= <0.001 respectively.

Table 7 shows the distribution of electrocardiographic findings according to grouped viral load.

Table 7: Distribution of electrocardiographic findings according to grouped viral load in copies/ml

	Undetectable	50-1500	1501-10,000	>10,000	P-value
Rhythm					
Sinus rhythm	14(100.0%)	47(100.0%)	11(13.5%)	2(13.3%)	
Sinus tachycardia	0(0.0%)	0(0.0%)	20(64.5%)	8(53.3%)	
Atrial fibrillation	0(0.0%)	0(0.0%)	0(0.0%)	5(33.3%)	< 0.001*
A-V block					
No A-V blocks	14(100.0%)	47(100.0%)	31(100.0%)	8(53.3%)	
1st degree	0(0.0%)	0(0.0%)	0(0.0%)	7(46.7%)	< 0.001*
QRS axis					
Normal axis	14(100.0%)	47(100.0%)	20(64.5%)	5(33.3)	
Left axis deviation	0(0.0%)	0(0.0%)	5(16.1)	4(26.7%)	
Right axis deviation	0(0.0%)	0(0.0%)	6(19.4%)	6(40.0%)	< 0.001*
QTc					
Normal	14(100.0%)	47(100.0%)	26(83.9%)	0(0.0%)	
Prolonged	0(0.0%)	0(0.0%)	5(16.1%)	15(100.0%)	< 0.001*
PVCs					
Unifocal PVCs	0(0.0%)	0(0.0%)	8(25.8%)	9(60.0%)	
Multifocal PVCs	0(0.0%)	0(0.0%)	8(25.8%)	6(40.0%)	
No PVCs	14(100.0%)	47(100.0%	15(48.4%)	0(0.0%)	< 0.001*
BBB					
No BBB	14(100.0%)	47(100.0%)	10(32.3%)	3(20.0%)	
LBBB	0(0.0%)	0(0.0%)	4(12.9%)	0(0.0%)	
RBBB	0(0.0%)	0(0.0%)	6(19.4%)	2(13.3%)	
LAH	0(0.0%)	0(0.0%)	5(16.1%)	4(26.7%)	
LPH	0(0.0%)	0(0.0%)	6(19.4%)	6(40.0%)	< 0.001*
NSIVCD					
Present	0(0.0%)	0(0.0%)	13(41.9%)	15(100.0%)	
Absent	14(100.0%)	47(100.0%)	18(58.1%)	0(0.0%)	< 0.001*
ST-Segment					
Normal	14(100.0%)	47(100.0%)	26(83.9%)	11(73.3%)	
Depressed	0(0.0%)	0(0.0%)	5(16.1%)	4(26.7%)	
Elevated	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	< 0.001*
T-wave					
Normal	14(100.0%)	47(100.0%)	16(51.6%)	7(46.7%)	
Flattened	0(0.0%)	0(0.0%)	6(19.4%)	2(13.3%)	
Inverted	0(0.0%)	0(0.0%)	9(29.0%)	6(40.0%)	< 0.001*

AV = Atrioventricular, PVC= Premature Ventricular Contraction, NSICD = Non-specific Intraventricular Conduction Defect, RBBB = Right Bundle Branch Block, LBBB = Left Bundle Branch Block, LPHB = Left Posterior Hemiblock

* = Significant at Fishers exact P = < 0.05

Distribution of Highly Active Antiretroviral Therapy (HAART) among the studied patients

The antiretroviral medications used among the studied patients revealed that 102 (95.3%) patients were on Zidovudine/Lamivudine/Nevirapine (AZT/3TC/NVP) combination therapy, 2(1.9%) were on Tenofovir/Lamivudine/Efavirenz(TDF/3TC/EFV) combination therapy, 3(2.8%) were on Zidovudine/Lamivudine/Efavirenz(AZT/3TC/EFV) combination therapy and none of the patients was on protease inhibitor (PI).

Discussion:

Most of the study subjects in this cohort of HIV-infected patients were in their sexually active age group with female subjects constituting a higher proportion of patients. This finding may suggest a heterosexual mode of transmission of HIV infection among the study population. This finding is like that reported by Amobi et al in a study on the estimation of HIV prevalence and burden in Nigeria using a Bayesian predictive modelling method[2]. The laboratory results of the studied patients showed that the mean serum electrolytes and fasting blood glucose were all within the normal limit. This could be explained by the selection criteria adopted and perhaps because none of the patients was diabetic. Anaemia was predominantly observed among patients with low CD4 cell count and high viral load suggesting that advanced HIV disease is associated with anaemia. Studies have shown that HIV infection causes anaemia via the direct effect of the virus itself, which may inhibit haematopoiesis through infection of progenitor cells or upregulation of cytokines[21].Similarly, low eGFR and proteinuria seen among patients with advanced HIV disease explained the relationship between HIV infection and kidney disease as previously described[22]. In this study, we found the prevalence of prolonged QTc interval among the cohort of HIV-infected patients on highly active antiretroviral therapy as 18.7%. This prevalence is similar to that reported by Ajala *et`al*[9]in a study with a similar sample size (100), but lower compared to those reported by Sani *et`al*[7] and Innocent *et`al*[8]in two studies with relatively larger sample sizes of 178 and 250 respectively. The distribution of QTc interval according to CD4 cell count and viral groups revealed a statistically significant difference across the groups. The study revealed that all the patients with prolonged QTc interval had low CD4 cell count and high viral load suggesting that patients with advanced HIV disease are associated with prolonged QTc interval. This finding is similar to that reported by Sani etal[7]as well as other researchers [14,23&24]. The exact pathophysiologic mechanism linking HIV infection and QT interval prolongation remains unclear. However, several mechanisms have been postulated: Chronic inflammation, persistent circulation of inflammatory cytokines, and activated immune system cells may be plausible explanations for autonomic neuropathy, subclinical cardiomyopathy, or subclinical myocarditis, eventually leading to cardiac arrhythmias as is seen in advanced HIV infection[14,15]. Electrolyte abnormalities associated with advanced HIV infection and the use of some antiretroviral drugs such as protease inhibitors and efavirenz are also been reported to be associated with QTc interval prolongation[17,18]. However, in this study patients on PIs and other medications associated with QTc interval prolongation were excluded from the study and none of the patients with prolonged QTc were on Efavirenz containing combination therapy.These further buttresses the relationship between HIV disease severity and QTc interval prolongation rather than the effect of electrolyte abnormalities or antiretroviral drugs.Other electrocardiographic abnormalities found in this study were: Sinus tachycardia, atrial fibrillation, first-degree atrioventricular block, premature ventricular contractions, nonspecific intraventricular conduction defects, bundle branch block (LBBB & RBBB), left

posterior hemiblock, left anterior hemiblock and T-wave inversion. These ECG abnormalities were observed mainly among patients with lower CD4 cell count and higher viral loads these perhaps could be due to myocarditis associated with opportunistic infections in advance HIV disease or the direct effect of HIV on the myocardium[14,15].

Conclusion:

This study revealed the prevalence of prolonged QTc interval among HIV-infected patients on highly active antiretroviral therapy to be 18.7%, and that HIV disease severity is associated with prolonged QTc interval.

Recommendation: From this finding, we therefore suggest that patients with advanced HIV disease should have a routine ECG evaluation to detect patients with prolonged QTc interval and or other life-threatening arrhythmias to prevent fatal complications.

Study limitations: The study was cross-sectional and thus no follow-up of patients to determine if immune restoration and virologic suppression following adequate treatment can reverse QTc interval prolongation. Secondly, the study had no control subjects to compare the QTc interval between the cases and controls, thirdly serum magnesium was not analysed in this study as it can affect the QT interval. Lastly, our subjects were only one hundred and seven (107) therefore, there is a need to have a large multi-centred prospective studyto elucidate further the relationship between QTc interval prolongation with viral load and CD4 cell count.

Declaration: The authors declare no conflict of interest

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