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Electrocardiography And Echocardiography As Diagnostic Tools For HIV Heart Disease.

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ABSTRACT
Background: *Human Iimmunodeficiency Virus (HIV)is a multisystemic disease affecting a plethora of organs in the body of which the heart is one. Histologic, electrocardiographic and echocardiographic studies have all corroborated involvement of the heart in HIV infection. While Echocardiography is a very valuable tool in evaluating structural abnormalities. Electrocardiography remains the gold standard for rhythm abnormalities and has the added value of being able to assess some structural and ischemic changes in the heart of HIV positive patients. In addition, it is cheap and readily available in resource poor settings and can allow the attending physician make prompt and important decisions. This study assessed the electrocardiographic abnormalities in HIV positive, highly active antiretroviral therapy (HAART) naïve patients and compared the ability to use echocardiography and electrocardiography to detect heart abnormalities.*
Method*: A prospective cross-sectional study carried out in the University of Port Harcourt which deployed the use of Electrocardiography (ECG)and Echocardiography (ECHO) to evaluate cardiac abnormalities in HIV positive HAART naïve patients who consented to be part of the study. Electrocardiographic and Echocardiographic evidence of heart disease in the study population was evaluated and the prevalence of Heart abnormalities seen with Electrocardiography was compared to that seen on Echocardiography.*
Results*. One Hundred and fifty-six (78%) of the 200 HIV cases recruited for this study had electrocardiography done: 111(71.15%) females and 45 (28.85%) males. The commonest electrocardiographic cardiac abnormality noted was sinus tachycardia(20.5%). Other abnormalities seen were,LVH,RVH,ischeamic changes,sinus bradycardia, one patient had a supraventicular tachycardia and four had heart blocks (three had first degree heart block while one had a RBBB). In seven(7) of the patients the only abnormality was poor R wave progression. Comparing the prevalence of cardiac abnormality using electrocardiography and echocardiography, more cardiac abnormalities were detected with echocardiography when compared with electrocardiography; Sixty-eight-point five percent (68.5%) of patients showed cardiac abnormality using echocardiography against 64.5 % with electrocardiography.*
Conclusion: *Cardiac abnormalities picked by electrocardiography compared with that picked by the use of Echocardiography. Considering that ECG is cheap, readily available in resource poor settings and highly sensitive in detecting cardiac abnormalities. It should be considered a screening tool for all HIV positive patient and should be included as part of the free package of the HIV positive patients.*
Keywords: HIV, HEART, ECG, ELECTROCARDIOGRAPHY, ECHOCARDIOGRAPHY.

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I. INTRODUCTION

Globally there were 37.7 million people living with the Human Immunodeficiency virus (HIV) in 2020, with 1.5 million new infection[1]. In the same year, six hundred and eighty thousand deaths were attributed to HIV and AIDs related illnesses [1]. Also, twenty-eight million, two hundred people living with the virus have access to antiretroviral therapy [1]. The current figure shows a significant reduction of 52% in the prevalence of HIV, since the peak of the pandemic in 1997. Africa has the highest population of people living with HIV and there are about 4.7million in the sub-Saharan region [2]. The HIV prevalence in Nigeria is 1.4% and an estimated 1.9 million Nigerians are living with HIV [2].

HIV affects a plethora of organs of which the heart is one. The effect of HIV on the heart is dependent on the stage of the disease,the opportunistic co-infections and also on the drug therapy. HIV is well known to penetrate cells that bear CD4 cell receptors, notably the cardiac insterstitial cells. [3] The myocytes because they do not bear CD4 receptors were thought to evade invasion by the HIV [3]. However studies have isolated viral sequences in cardiac myocytes obtained from endocardial biopsies[4]. The effect on the heart is belived to be

both direct and indirect by stimulating the release of cytokines that are cardiotoxic and by opportunistic co-infections[5].

Cardiovascular disease in HIV Patients may be seen as part of the lipodystrophy syndrome [6]; as a consequence of antiretroviral therapy. Soon after the introduction of protease inhibitors and nonnucleoside reverse-transcriptase inhibitors for the management of human immunodeficiency virus (HIV) infection, clinicians observed unexpected cardiovascular events among patients receiving these new, combination, "highly active" antiretroviral regimens. Angina, myocardial infarction, and stroke were seen in patients who were relatively young. This led to the search for the etiopathogenesis and it later became clear that Protease inhibitors were asociated with lipodystrophy which resulted in atherosclerosis **[6]** The effect of Protease inhibitor has also been corroborated by other authors[7].

Therefore, with increasing access to HAART comes the challenge of antiretroviral complications which would mean an increase in the prevalence of cardiovascular complications. HIV disease has been associated with increased risk for cardiovascular events like stroke and myocardial events [8-11].

Cardiac abnormalities have been evaluated with various screening tools. electrocardiography, echocardiography and cardiac MRI have been deployed to evaluate cardiac abnormalities in HIV positive individuals. [12-20]. The prevalence of cardiac diseases has been dependent on the screening modality and the geographical area. Electrocardiography has reported a prevalence of 73% in HIV-positive HAART -naïve patients and as high as 93% in patients on HAART in Eastern Nigeria [21]. Whilst another African study from south Africa that deployed both electrocardiography and echocardiography [13], did not note any significant difference in cardiac findings between controls and HIV positive individuals.

Electrocardiography has been used locally to evaluate the relationship of clinical parameters in HIV heart disease. Okeahialam and Sani evaluated Electrocardiography in HIV/AIDS from the middle belt of Nigeria [22]. The study described the role of Cachexia in heart disease and noted low voltages and sinus tachycardia were common findings. Electrocardiography has also been used to study heart problems in children. A 15years study [23] utilizing electrocardiography during the asymptomatic phase or latency period, noted a progressive the corrected QT, [19] Another study [24] that employed echocardiography, chest x-ray and electrocardiography as screening tools. With the aim of assessing the most useful tool to detect precocious cardiac abnormalities in HIV patients. Results from the study showed cardiac abnormalities in 53.3 % using electrocardiography, 24.4% using echocardiography and only 3 patients had cardiomegaly on chest xray.

II. METHOD

Study Design:

This was a prospective, descriptive, cross-sectional study.

Study Site:

This study was conducted at the University of Port Harcourt Teaching Hospital. This hospital serves as a major referral centre for Rivers state, Bayelsa state and its subregions. It is situated in in Choba. Port Harcourt is a cosmopolitan city with residents from all over the country.

Ethical Consideration:

Clearance for this study was obtained from the Ethical Committee of the University of Port Harcourt Teaching Hospital. At all stages the researcher adhered to the guidelines of the ethical committee and standard research protocol. All case and control subjects gave informed consent.

Study Population:

Patients: The total study sample was made up of 200 HIV positive patients, who were antiretroviral naive. They were randomly selected without fore knowledge of their CD4+ count. The random numbers were generated using the table of random numbers**.** Two hundred were recruited (200) all had echocardiogram, while one hundred and fifty-six (156) had ECG and chest x-ray

Inclusion Criteria For Patients

Newly diagnosed HIV positive, antiretroviral naïve individuals, irrespective of
CD4 count and who have consented to be a part of the study.

Exclusion Criteria For Patients

1. Hypertensives.
2. Diabetics.
3. Patients with no significant history of alcohol ingestion. (Patients that consume less than 30g/day)
4. History of cigarette smoking.
5. Poor Echocardiography window.

Clinical Evaluation:

Baseline demographics,clinical history and detailed physical examination of all subjects were carried out including their age, ,gender, height, weight and baseline blood pressure.Packed cell volume and fasting blood sugar was assessed.

Hiv Confirmation: Double Elisa using a rapid screening kit was used to confirm a diagnosis of HIV infection. This was the method used in University of Port Harcourt Teaching Hospital[25]. The World Health Organization (WHO) endorses alternative algorithm for use in recourses-limited setting where a double Elisa confirms HIV positivity.[26]

Cd4 count:CD4 count was assayed using the Apogee A50 micro flow cytometer.
Electrocardiography: 12 lead ECG was performed on patients using the GE medical systems MAC 1200 ST.

Data Analysis : Data for the 150 subjects that had ECG was analysed for cardiac abnormalities and findings compared with findings at Chest x-ray and Echo findings. Analysis was performed using the Statistical Package for Social Sciences version 23(SPSS 23). Continuous variables were expressed as means± (standard deviation) while categorical variables were expressed as percentages. Differences of the means between two groups were compared with students ' t' test. Proportions or the categorical parameters was be analysed with the chi-square. A p -value of < 0.05 was considered statistically significant. Correlation was carried out between the CD4 count and echocardiography parameters, using Pearson correlation coefficient.

III. Results

A total of 200 HIV positive, antiretroviral naive patients and 100 HIV negative controls who met the inclusion criteria for this study were recruited**.**

Base Line Demographic Parameters

The study subjects were made of 76(38%) males and 124(62%) femaleswith a male to female ratio of 1:1.6. The age range was 18 - 56 years, with a mean of 33.13 ± 8.4years. The controls were made up of 64 females (64%) and 36(36%) males with age range between 19 to 54 years and a mean of 31.82 ±8.72years.There was no statistically significant difference between the ages of the cases as compared to the controls

The mean ages for the female cases and controls; 30.95 ± 8.04 ,31.25 .± 10.26 years respestively were similar; as were the mean ages of the male cases and the male controls; 32.13.± 9.9 and 32 .± 9.1 years repectively.The second and third decades made up the largest no of subjects in both control and HIV cases.

Electrocardiography Findings.

One hundred and fifty-six (78%) of the 200 HIV cases recruited for this study had electrocardiography done,111 females and 49 males. Abnormalities noted were mostly arrythmias which is a valuable information obtained by Electrocardiography in contrast with echocardiography. Forty-two (42) 26.92%; sinus tachycardia, sinus bradycardia and heart blocks. followed closely by LVH, other abnormalities seen were ischaemic changes, and in seven (7) the abnormalities noted were poor R wave Progression (see Table 3)

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TABLE 1:COMPARISON OF SOME CLINICAL AND LABORATORY PARAMETERS OF CASES AND CONTROLS

PARAMETERS	CASES N = 200	CONTROLS N = 100	*t*-test	P-value
BMI{kg/m^2)	21.09 ± 4.0	25.06 ± 6.2	-6.40	<0.001*
Systolic BP(mmHg)	113.09 ± 16.1	114.9 ± 22.3	0.52	0.60
Diastolic BP(mmHg)	71.87 ± 11.3	72.72 ±15.11	-1.64	0.094
Pulse Rate (beats/min)	90.24 ± 18.3	67.82 ± 15.71	7.04	<0.001*
CD4 Count(cells/l)	246 ± 176			

***P values ‹ 0.05 are significant**

TABLE 2: COMPARISON BETWEEN SEXES;HIV POSITIVE CASES

PARAMETERS	MALES N=76 Mean± SD	FEMALES N=124 Mean± SD	t-test	P-Value
PCV(%)	33.14 ± 8.66	28.67 ± 7.40	-3.86	0.000*
DIASTOLIC BP(mmHg)	71.6 ± 14.0	71.31± 12.04	0.791	0.430
SYSTOLIC BP (mmHg)	114.45±20.58	111.13 ± 17.27	1.886	0.064
PULSE RATE (Beats/min)	85.31 ± 18.8	92.17 ± 19.9	. 2.21	0 .029*
CD4 COUNT (Cells/l)	251.34 ± 88.6	237.91 ± 171.0	-.050	0.618
BMI Kg/m^2	**20.71 ± 4.2**	**21.05 ± 4.41**	**0.313**	**0.744**

TABLE 3: ELECTROCARDIOGRAPHIC CARDIAC ABNORMALITIES IN CASES

ECG ABNORMALITIES	TOTAL	PERCENTAGES (%)
SINUS TACHYCARDIA	24	15.39
SINUS BRADYCARDIA	4	2.56
ST SEGMENT CHANGES	9	5.77
SUPRAVENTRICULAR TACHYCARDIA	1	0.64
HEART BLOCKS	4	2.56
LOW VOLTAGES	10	6.41
ISOLATED LVH	22	1410
ISOLATED RVH	11	7.05
LAE	3	1.9
RAE	1	0.64
POOR R WAVE PROGRESSION	7	4.49
MULTIPLE ABNORMALITIES	**5**	**3.31**
NORMAL	**55**	**35.25**
TOTAL	**156**	**100**

LVH: left ventricular hypertrophy, RVH: right ventricular hypertrophy,
LAE :left atrial enlargement, RAE: right atrial enlargement.

TABLE 4 : THE SPECTRUM OF ECHOCARDIOGRAPHIC CARDIAC ABNORMALITIES IN HIV POSITIVE PATIENTS .

CARDIAC ABNOMALITIES	HIV POSITIVE N(%)	CONTROLS (N%)	p-value
DCM	7(3.5)	0(0)	0.058
PERICARDIAL EFFUSION	89(44.5)	5(5)	< 0.001*
RWMA	10(5)	0(0)	0.023*
DEPRESSED LV EF	25(12.5)	3(3)	0.007
DEPRESSED RV EF	20(10)	6(6)	0.246
DEPRESSED LV EF/ DEPRESSED RV EF	11(9)	3(3)	0.055
PULMONARY HYPERTENSION	15(7.5)	0(0)	0.005*
ISOLATED LV DIASTOLIC DYSFUNCTION	55(27.5)	21(21)	0.222
ISOLATED RV DIASTOLIC DYSFUNCTION	12(6)	3(3)	0.017*
RV AND LV DIASTOLIC DYSFUNCTION	36(18)	6(6)	0.261
TUMOUR	1(0.5)	0(0)	0.478
AORTIC ROOT DILATATION	2(1)	0(0)	
DESCENDING AORTA DILATATION	1(.5)	0(0)	0.316
MR	7 (3.5)	1(1)	0.103
TR	55(27.5)	5(5)	0.001*
PR	70(35)	18(18)	0.002*
AR	15(7.5)	1(1)	0.018*
ENDOCARDITIS	1(.5)	0(0)	0.478
MVP	1(0.5)	0	0.478

DCM: dilated cardiomyopathy; RWMA: regional wall motion abnormality;EF: ejection fraction; MR: mitral regurgitation; TR:tricuspid regurgitation; PR:pulmonary regurgitation, AR: aortic regurgitation. MVP: mitral valve prolapse. Significant = p<0.05.

TABELE 5: COMPARISON OF HEART ABNORMALITY ECG :ECHO

Test Modality	Total	Normal	Abnormal	% Patient with Cardiac Abnormalities
Echocardiograpy	200	63	137	68.5%
Electrocardiography	156	55	101	64.74%

CHEST X-RAY FINDINGS

Chest x-rays were carried, and findings largely consisted of cardiomegaly with cardiothoracic ratio> 0.5 in 9 (4.56%), most showed a cardiothoracic ratio < 0.5 in 140(69.8%) but for the rest 51(25.64%) the cardiac sihouette was obscured by patchy opacities of chest infection and by pleural effusion

IV. DISCUSSION:

Two hundred HIV positive patients, irrespective of CD4 T lymphocyte count and 100 controls were recruited in this study matched at a ratio of 2:1.

The study subjects that had Echocardiography were made of 76 males(38%)and 124 females(62%) with a male to female ratio of 1:1.6. They were aged between 18 yrs and 56 years, with a mean age of 33.13 ± 8.4years. The controls were made up of 64 females ((64%) and 36(36%) males with age range between 19 and 54yrs with a mean age of 31.82 .±8.72years, the HIV study population showed more women affected than male this corroborates the UNAIDS[94] finding that of the 33.3 million adults living with HIV more than half are women. assessed the Doppler echocardiographic pattern in patients at different stages of the disease, the mean age of subjects recruited was 34 ± 9 years. The studies mentioned above however recruited 44 patients and 84 respectively.

The subjects and Controls were adequately matched for sex and age. Their systolic and diastolic blood pressures showed no significant difference. However, there were significant differences in their BMI and pulse rates. This can be explained by the disease process, HIV /AIDS is associated with cachexia and anaemia. The impact of the anaemia can explain the sinus tachycardia that was present in a 15.4% of the patients that had ECG done. Opportunistic co-infection is associated with febrile illness that may further buttress the tachycardia, however a study carried out by Lubega et al[27]on 230 children who had electrocardiogram in addition to echocardiography; noted sinus tachycardia even after normalizing the PCV and temperature in the HIV cases with heart disease when compared to those without heart disease.

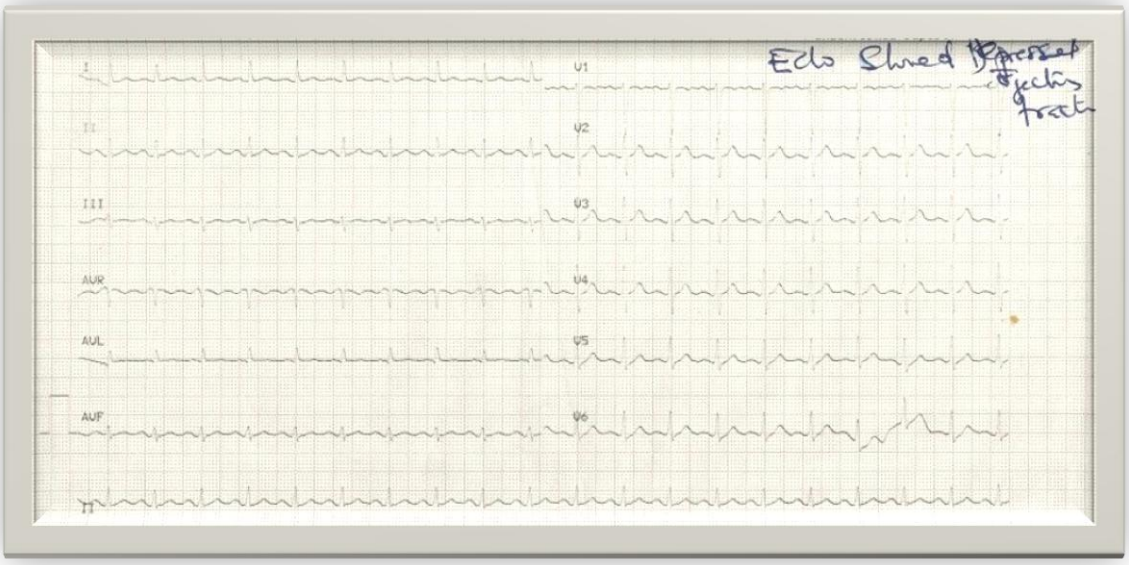
There was no significant variation in the sex distribution in BMI, but the heart rate was significantly higher in the HIV females when compared to the males. Anaemia was more marked in the female HIV patients this may explain the difference in heart rate. Nevertheless, males are known to have a higher normal PCV when compared to the females while the females on the other hand are more susceptible to anaemia because of the periodic loss of blood from menstruation despite the disease state.

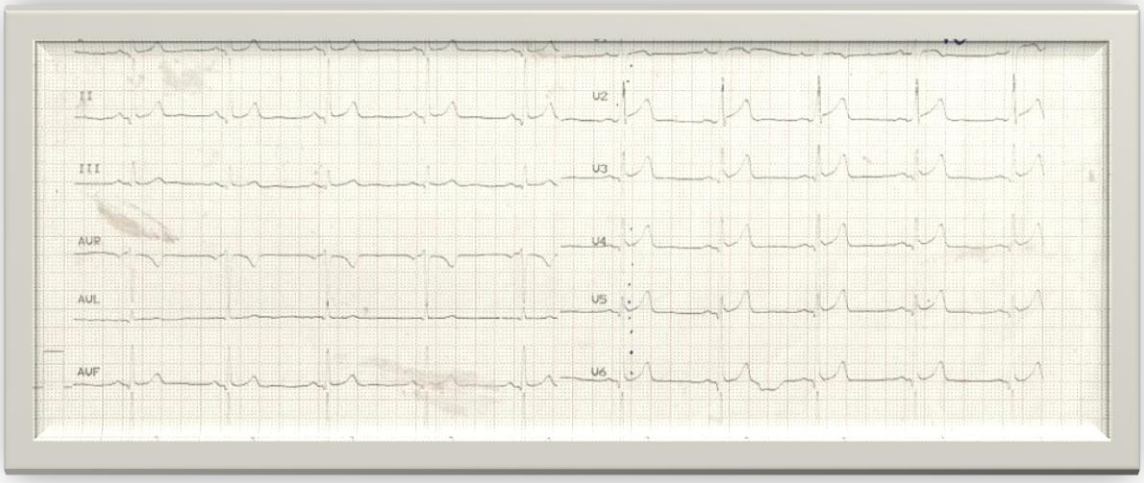
One hundred and fifty-six (156) of the 200 patients had electrocardiography. Electrocardiography evaluation showed: low voltages accounting for 23% of the cardiac abnormalities. This was followed by LVH(20.51%) which was also a common finding. Sinus Tachycardia accounted for (15.4%) and was commoner in the female group who showed more marked anaemia. Opportunistic infection with febrile illness is also a cause of tachycardia but the temperature was not assessed in this study and studies have not assessed sex as a predictor of HIV heart disease. Heart blocks were seen in 4(2.6%) and one patient had supraventricular tachycardia. This is comparable to the finding by Morozov et al[19] in which they studied electrocardiographic abnormalities in evolutive phase of AIDS. The study noted low voltages as a frequent finding. Also in the study by Okeahialam et al[22], sinus tachycardia and low voltages were very frequent findings.

Comparing prevalence of cardiac abnormality detected by electrocardiography and echocardiography while more cardiac abnormalities were detected with echocardiography when compared with electrocardiography; Sixty eight point five percent (68.5%) of patients showed cardiac abnormality using echocardiography as the screening modality when compared with 64.5 % with electrocardiography, However the values compared favourably.

HIV disease has been associated with poor socioeconomic burden and the cost of treatment was a huge burden at the initial emergence of the virus, but currently in some African [28] countries drug treatment is free and most initial baseline investigations; Complete blood count, renal function indices, and CD4count are offered free at most hospital sequalae to the 14th International Conference of Sexually Transmitted and AIDS of the World Health Organization held in Abuja December 2005[29]. This is quite an enormous support when compared to other developed countries where care is either out of pocket or from Health Insurance. Nonetheless, many HIV complications can be very expensive and are not covered by free access. HIV heart diseases is a late complication and some patients would need more expensive care. Considering the high prevalence of HIV heart disease amongst HIV positive patients an advocacy is being made by this paper to consider the place of free ECG as part of the free access plan in the care for patients with HIV.

Conclusion: Electrocardiography should be included in the preliminary investigations in patients with HIV to screen for cardiac diseases and echocardiography recommended for those in advanced disease. (CD4 count < 200cells/L)





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