Results:

Clinical and demographic characteristics of the studied population

One hundred and seven (107) subjects were recruited into the study comprising thirty-seven (34.6%) males and seventy (65.4%) females. The mean age, body mass index (BMI) and duration of HIV infection in years of the studied subjects were 37.32±9.52, 23.52±6.16 and 5.50±2.34 respectively. Eight subjects (7.5%) with HIV were hypertensive while the remaining 99(92.5%) were normotensive, the mean systolic and diastolic blood pressure of the subjects were 137.66±96.56 and 82.52±7.53 respectively, none of the subjects were diabetic.

Laboratory findings among the studied population

One patient (0.93%) had HIV/Hepatitis B virus (HBV) co-infection and none had Hepatitis C virus (HCV) co-infection. While the mean packed cell volume (PCV) and estimated glomerular filtration rate (eGFR) were 31.02±5.78 and 77.36±32.32 respectively. The mean CD4 cell count and viral load were 612.65±347.62 cells/µL and 315.44±271.11copies/mL respectively. There was a significant positive correlation between eGFR and PCV with CD4 cell count (r = 0.601 p-value = < 0.001), (r = - 0.529, P-value = < 0.001), respectively. While the relationship between eGFR and PCV with viral load were negative and significant (r = -0.603, p = < 0.001), (r = -0.681, p = < 0.001) respectively. Similarly on regression analysis, the relationship between eGFR and PCV with CD4 cells count remained positive and significant (beta = 0.459, p = < 0.001), beta = 0.309, p = < 0.001) respectively. While that between eGFR and PCV with viral load remained negative and significant (beta = - 0.368, p = <0.001), (beta = - 0.505, p = <0.001) respectively. Among the 107 subjects, 15 (14.1%) had CD4 cell count of less than 250 cells/µL, 31(28.97%) had CD4 cell count of 250 – 500 cells/µL, 47(43.92%) had CD4 cell count of 501 – 1000 cells/µL, while 14 (13.08%) had CD4 cell count greater than 1000 cells/µL.

Echocardiographic variables for the assessment of the probability of pulmonary artery hypertension among the studied population.

The mean tricuspid regurgitant velocity, pulmonary artery regurgitant velocity and pulmonary artery trunk diameter were 2.53±0.66m/s, 1.75±0.91m/s and 2.25±0.29cm respectively. The mean left ventricular eccentricity index, right ventricular acceleration time, right atrial area and right ventricular to left ventricular internal diameter ratio were 0.98±1.83, 104.61±3.65ms, 17.54±1.85cm^2 and 0.97±0.16 respectively. Table 1 showed the echocardiographic variables used in assessing the probability of pulmonary hypertension. Sixty-one (57.0%) had a low probability of pulmonary hypertension, 9(8.4%) had an intermediate probability of pulmonary hypertension and 38(35.51%) had a high probability of pulmonary hypertension.

There was a significant negative correlation between CD4 cell count with tricuspid regurgitant flow velocity (TRv), pulmonary regurgitant flow velocity (PRv), pulmonary artery trunk diameter (PATd), right ventricular to left ventricular internal diameter (RV/LV) ratio, left ventricular eccentricity index (LVEI), and right atrial area (RAA), while the relationship between CD4 cell count and right ventricular acceleration time (RVAT) was positive and significant. However, the relationship between CD4 cell count and the duration of HIV treatment was positive and significant.

On the other hand, the relationship between viral load and TRv, PRv, PATd, RV/LV ratio and RAA were positive and significant while that between viral load with RVAT and duration of HIV treatment in years were negative and significant. The study also revealed a significant negative relationship between the duration of HIV treatment and variables associated with the probability of pulmonary artery hypertension (TRv, PRv, PATd, RV/LV ratio, LVEI, RAA), and a positive relationship with RVAT. Table 2 showed the correlation between CD4 cells count, Viral load (VL) and Duration of HIV treatment (DHT) with echocardiographic variables associated with the probability of pulmonary artery hypertension. On regression analysis, only TRv and PRv maintained a significant negative relationship with CD4 cells count and a significant positive relationship with viral load. **Table 3:** showed the regression analysis between CD4 cells count and Viral load (VL) with Echocardiographic variables associated with the probability of pulmonary artery hypertension.

Table 1: Echocardiographic variables used to assess the probability of pulmonary artery hypertension in the studied population

Parameters	Mean Values ± SD
TRv (m/s)	2.53±0.66
PRv (m/s)	1.75±0.91
PATd (cm)	2.25±0.29
RV/LV ratio	0.98±0.17
LVEI	0.98±1.83
RVAT (ms)	104.61±3.65
RAA (cm^2)	17.54±1.85

TRv = Tricuspid Regurgitant flow Velocity, PRv = Pulmonary Regurgitant flow Velocity, PATd = Pulmonary Artery Trunk diameter, RV/LV = Right Ventricular to Left Ventricular internal diameter ratio, RVAT = Right Ventricular Acceleration Time, LVEI = Left = Ventricular Eccentricity Index, RAA = Right Atrial Area, *** = Significant at P = <0.05

Table 2: Correlation between CD4 cells count, Viral load (VL) and Duration of HIV treatment (DHT) with echocardiographic variables associated with the probability of pulmonary artery hypertension

Parameters	CD4 Correlation coefficient ®	P-Value
Trv (m/s)	- 0.831	<0.001***
PRv (m/s)	- 0.871	<0.001***
PATd (cm)	- 0.600	<0.001***
RV/LV	- 0.725	<0.001***
RVAT (ms)	0.488	<0.001***
LVEI	- 0.730	<0.001***
RAA (cm^2)	- 0.444	<0.001***
Parameters	**VL Correlation coefficient (r)**	**P-Value**
TRv (m/s)	0.835	<0.001***
PRv (m/s)	0.792	<0.001***
PATd (cm)	0.691	<0.001***
RV/LV	0.830	<0.001***
RVAT (ms)	- 0.567	<0.001***
LVEI	0.841	<0.001***
RAA (cm^2)	0.567	<0.001***
Parameters	**DHT Correlation coefficient (r)**	**P-Value**
TRv (m/s)-0.287	0.007***	
PRv (m/s)-0.375	<0.005***	
PATd (cm)-0.234	0.028***	
RV/LV-0.313	0.003***	
LVEI-0.329	0.002***	
RVAT (ms)0.242	0.023***	
RAA (cm^2)-0.291	0.006***	

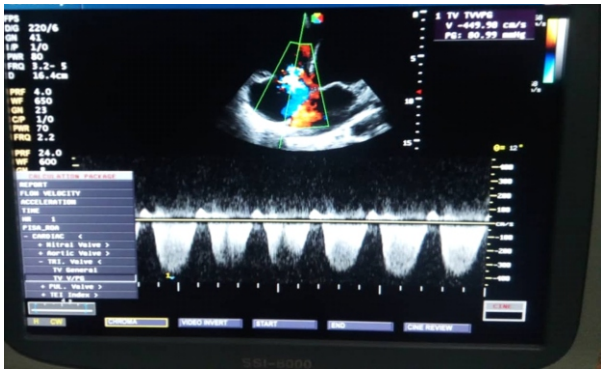
TRv = Tricuspid Regurgitant flow Velocity, PRv = Pulmonary Regurgitant flow Velocity, PATd = Pulmonary Artery Trunk diameter, RV/LV = Right Ventricular to Left Ventricular internal diameter ratio, RVAT = Right Ventricular Acceleration Time, LVEI = Left = Ventricular Eccentricity Index, RAA = Right Atrial Area, DHT= Duration of HIV Treatment *** = Significant at P = <0.0

Table 3: Regression analysis between CD4 cells count, Viral load (VL) with Echocardiographic parameters of pulmonary hypertension

Parameters	CD4 Beta value	P-Value
TRv (m/s)	- 0.386	<0.001***
PRv (m/s)	- 0.559	<0.001***
PATd (cm)	0.048	0.433
RV/LV	- 0.006	0.959
RVAT (ms)	- 0.015	0.805
LVEI	- 0.091	0.509
RAA (cm^2)	0.021	0.709
Parameters	**VL Beta Value**	**P-Value**
TRv (m/s)	0.333	<0.001***
PRv (m/s)	0.184	0.010***
PATd (cm)	0.093	0.131
RV/LV	0.170	0.152
RVAT (ms)	0.040	0.514
LVEI	0.244	0.074
RAA (cm^2)	0.043	0.437

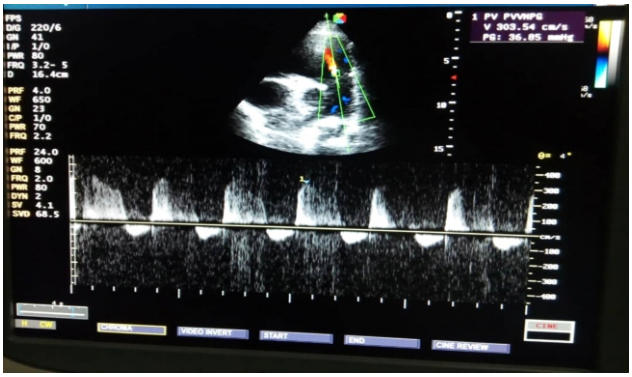
TRv = Tricuspid Regurgitant flow Velocity, PRv = Pulmonary Regurgitant flow Velocity, PATd = Pulmonary Artery Trunk diameter, RV/LV = Right Ventricular to Left Ventricular internal diameter ratio, RVAT = Right Ventricular Acceleration Time, LVEI = Left = Ventricular Eccentricity Index, RAA = Right Atrial Area, *** = Significant at P = <0.05

Figure 2: Echocardiography showing Tricuspid regurgitation



Tricuspid regurgitant flow with velocity of 4.49m/s

Figure 3: Echocardiography showing pulmonary regurgitation



The pulmonary regurgitant flow velocity of 3.03m/s

Discussion

Human immunodeficiency virus (HIV)-related pulmonary hypertension is a progressive disease leading to right ventricular disease, right ventricular failure and death with a worldwide prevalence of 0.06-2.0%.[13] Reports from other parts of Africa however suggest a much higher prevalence of about 5% (3). Our study was aimed at assessing the probability of pulmonary hypertension among HIV patients and not to establish the diagnosis. In this study, we found that eGFR was significantly lower in patients with low CD4 cell count and high viral load indicating that the relationship between eGFR and CD4 cell count was positive and significant while that between viral load was negative and significant in keeping with the study by Brito et al.[14] The pathogenesis linking HIV infection and chronic kidney disease is the disruption of multiple cellular pathways in all renal compartments, including podocytes and tubular epithelial cells by the HIV resulting in the classical pathological changes of HIV associated nephropathy: collapsing glomerulopathy and tubular microcystic disease.[15] Chronic kidney disease in HIV is the result of complex interactions between viral genes, host proteins, and host genetic factors.[16] Similarly we also found a positive and significant relationship between packed cell volume and CD4 cell count and a negative relationship between packed cell volume with viral load. Several causes of anaemia have been reported in HIV patients, among which were iron, vitamin B12, folate and minerals deficiencies. Other causes include drugs and cytokines induced marrow

toxicity.[17] Majority of the patients in this study were on first-line HAART in which Zidovudine is one of the components which might have contributed to the development of anaemia seen in these patients.

In this study, we found that 38(35.5) of patients had a high probability of PAH and is predominantly among patients with low CD4 cell count and high viral load. Nine (8.4%) had an intermediate probability of having pulmonary artery hypertension, while the majority of patients (57.0%) with low viral load and high CD4 cell count had a low probability of having pulmonary artery hypertension. We also observed a negative but significant relationship between variables associated with the probability of pulmonary artery hypertension (TRv, PRv, PAT diameter, RAA, RV/LV internal diameter ratio, and LVEI) with CD4 cell count and a significant positive relationship with viral load. Furthermore, we also observed a significant negative correlation between the duration of HIV treatment and variables associated with the probability of PAH except that with right ventricular acceleration time (RVAT) which was positive and significant. The exact pathogenesis of HIV-associated PAH (HIV-PAH) is not clearly understood, however certain factors were said to play important roles. The pulmonary endothelium is constantly exposed to blood cellular components and interacts with the extracellular matrix, while vasculitides are known outcomes from infectious pathogens. However, it is not certain if the vasculitides are due to persistent viral infection, exposure to toxic viral proteins, or virus-induced immune activation. Viral proteins such as Nef and Tat have been shown to induce endothelial dysfunction and increase inflammation through activation of adhesion molecules and the production of inflammatory chemokines independent of the virus.[18,19] HIV-infected individuals are frequently co-infected with other viruses and bacteria that may contribute to the development of PAH. In this study, however, only one patient had HIV-HBV co-infection suggesting that findings in this study were mainly due to HIV infection. Our findings also suggest that patients with HIV when adequately treated (with suppressed viral loads and high CD4 cell counts), the probability of developing PAH decreases. Similarly, it also suggests that there is a need to look out for PAH in patients with HIV who have virologic and immunologic failure on HAART.

Conclusion

This study revealed that HIV patients with low CD4 cells count and high viral load had a high probability of developing PAH as there was a significant negative relationship between variables associated with the probability of PAH with CD4 cell count and a significant positive relationship with viral load., Adequately treated HIV patient (with suppressed viral loads and high CD4 cell counts), decrease the probability of developing PAH. We, therefore, recommend a routine assessment of the probability of PAH in patients with HIV infection particularly those with low CD4 cell count and high viral load and encourage early commencement of HAART to prevent the development of pulmonary artery hypertension.

Declaration: There is no conflict of interest

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