



Prevalence and risk factors of pulmonary hypertension among adult patients with HIV infection in Ethiopia

Dawit Kebede Huluka¹ , Desalew Mekonnen², Sintayehu Abebe², Amha Meshesha², Dufera Mekonnen², Negussie Deyessa³ , James R. Klinger⁴, Corey E. Ventetuolo^{5,6}, Neil W. Schluger⁷, Charles B. Sherman⁴ and Wondwossen Amogne⁸

¹Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia; ²Division of Cardiology, Department of Internal Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia; ³School of Public Health, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia; ⁴Division of Pulmonary, Sleep and Critical Care Medicine, Rhode Island Hospital, Alpert Medical School of Brown University, Providence, RI, USA; ⁵Department of Medicine, Alpert Medical School of Brown University, Providence, RI, USA; ⁶Department of Health Services, Policy, and Practice, Brown School of Public Health, Providence, RI, USA; ⁷Division of Pulmonary, Critical Care, and Sleep Medicine, Columbia University, New York, NY, USA; ⁸Infectious Diseases Unit, Department of Internal Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia

Abstract

Globally, non-communicable diseases are increasing in people living with HIV. Pulmonary hypertension is a rare non-communicable disease in people living with HIV with a reported prevalence of <1%. However, data on pulmonary hypertension in people living with HIV from Africa are scarce and are non-existent from Ethiopia. This study aimed to examine the prevalence and severity of echocardiographic pulmonary hypertension and risk factors associated with pulmonary hypertension in people living with HIV in Ethiopia. A total of 315 consecutive adult people living with HIV followed at the Tikur Anbessa Specialized Hospital HIV Referral Clinic were enrolled from June 2018 to February 2019. Those with established pulmonary hypertension of known causes were excluded. A structured questionnaire was used to collect data on demographics, respiratory symptoms, physical findings, physician-diagnosed lung disease, and possible risk factors. Pulmonary hypertension was defined by a tricuspid regurgitant velocity of ≥ 2.9 m/sec on transthoracic echocardiography. A tricuspid regurgitant velocity ≥ 3.5 , which translates into a pulmonary arterial pressure/right ventricular systolic pressure of ≥ 50 mmHg, was considered moderate-to-severe pulmonary hypertension. The mean age of the participants was 44.5 ± 9.8 years and 229 (72.7%) were females. Pulmonary hypertension was diagnosed in 44 (14.0%) of participants, of whom 9 (20.5%) had moderate-to-severe disease. In those with pulmonary hypertension, 17 (38.6%) were symptomatic: exertional dyspnea, cough, and leg swelling were seen in 12 (27.3%), 9 (20.5%), and 4 (9.1%), respectively. There was no significant difference in those with pulmonary hypertension compared to those without the disease by gender, cigarette smoking, previous history of pulmonary tuberculosis treatment, physician-diagnosed chronic obstructive pulmonary disease or bronchial asthma, duration of anti-retroviral therapy or anti-retroviral regimen type. Pulmonary hypertension looks to be a frequent complication in people living with HIV in Ethiopia and is often associated with significant cardiopulmonary symptoms. Further studies using right heart catheterization are needed to better determine the etiology and prevalence of pulmonary hypertension in people living with HIV in Ethiopia compared to other countries.

Keywords

pulmonary hypertension (PH), people living with HIV (PLHIV), human immunodeficiency virus (HIV), Ethiopia, Africa

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Introduction

The development of highly active antiretroviral therapy (HAART) has led to increased survival and a change in the epidemiology of diseases in people living with HIV

Corresponding author:

Dawit Kebede Huluka, College of Health Sciences, Addis Ababa University, Gambia Street, P.O. Box 2384, Addis Ababa 2384, Ethiopia.
Email: dndrda97@gmail.com



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(PLHIV).^{1,2} Non communicable diseases such as cardiovascular disease, metabolic syndrome, and some malignancies are replacing Acquired Immunodeficiency Syndrome.³⁻⁵ as PLHIV are living longer. Pulmonary hypertension (PH) is one such disease that contributes to morbidity and mortality in these individuals. Although the reported incidence of PH in PLHIV is low, it occurs much more frequently in HIV patients than in the general population.^{6,7}

The association of HIV with PAH is well established⁸ and the prevalence of pulmonary arterial hypertension (PAH) PAH in HIV-positive persons is about 0.5% which is nearly 2500 times greater than in HIV-negative people.⁹ The cause of PAH in HIV is not well understood but is believed to be due to HIV-related proteins such as transcriptional trans-activator (Tat), Negative factor (nef), and Gp120 that target the pulmonary endothelium and promote inflammation, endothelin secretion, and down regulation of BMPR2.¹⁰ However, various other factors contribute to an increasing prevalence of PH in PLHIV. These include extended survival after HIV diagnosis, female gender¹¹, and in some populations increased prevalence of smoking and associated diseases such as chronic obstructive pulmonary disease (COPD), pulmonary tuberculosis treatment, uncontrolled viral infection (high viral load and low CD4),¹¹ and current use of protease inhibitors.¹² Current use of the antiretroviral drug tenofovir was reported to be less associated with PAH.¹³

Although definitive diagnosis of PAH requires right heart catheterization, transthoracic echocardiography has become the standard screening tool for assessing the presence of PH in cohort studies of patients at increased risk of having the disease.¹⁴ Numerous studies have used echocardiography to indirectly estimate systolic pulmonary arterial pressure by measuring the tricuspid regurgitant velocity (TRV) and the modified Bernoulli formula to calculate right ventricular peak pressure.^{9,11,15-22}

The prevalence of PH associated with HIV in the developed world varies from 0.5% in studies using right heart catheterization²³ to 6% in echocardiography-based studies.¹⁵ Data on HIV-associated PH are scarce in Africa and only three large studies in adults have been published thus far.¹⁹⁻²¹ The three studies included symptomatic patients and only one screened for the presence or absence of associated risk factors. In a systematic review that included those three studies, the pooled prevalence of PH in HIV was 14%, more than double that of any study outside of Africa.²⁴ While this could be due to methodology, contributing risk factors of schistosomiasis and high altitude may have synergistic effect.

Data on PH in PLHIV in Ethiopia are non-existent. This study aimed to examine the prevalence and associated factors for echocardiographic PH in adult PLHIV cared for at the largest HIV referral center in Ethiopia.

Methods

We conducted a cross-sectional study in the HIV clinic of Tikur Anbessa Specialized Hospital (TASH) which is located in the capital of Ethiopia, Addis Ababa. TASH is the largest tertiary teaching hospital in the country with a total bed capacity of nearly 700 and provides specialized referral services throughout Ethiopia. It has an established HIV referral clinic run by HIV/anti-retroviral therapy (ART)-trained nurses, residents, and infectious diseases specialists. All consenting HIV participants ≥ 18 years old who were seen at the HIV referral clinic from June 2018 to February 2019 were included. Patients with evidence of Group 2 PH on echocardiography and those with already known Group 3 PH from interstitial lung disease (ILD), COPD, or post-tuberculosis structural parenchymal pathologies were excluded. The study was approved by the institutional review board of our University.

Sample size was calculated using Statcalc in EPI info version 7.1 software. Based on the assumption of 14% expected proportion of PH in the HIV patients,¹² with a confidence level of 95%, and margin of error 3.8, a total of 320 patients were needed.

A structured questionnaire was employed to collect data on the clinical manifestations, demographics, risk factors, and echocardiography findings of all the participants irrespective of the presence or absence of symptoms. All echocardiography examinations were performed by cardiologists on the same echocardiography machine (GE-Vivid E 9) with an S3MHz transducer. It included M-mode, bi-dimensional imaging, pulsed and continuous Doppler. Color Doppler was used to help identify the presence of tricuspid regurgitation and to achieve a parallel position to the ultrasound beam. The noninvasive assessment of the pulmonary artery pressure was estimated by the addition of the trans-tricuspid gradient (obtained by the peak systolic velocity of the tricuspid regurgitation and applying the Bernoulli formula) to the right atrium pressure according to the American Society of Echocardiography recommendations.¹⁸ PH was defined as a tricuspid regurgitant (TR) velocity ≥ 2.9 m/sec which translated to a right ventricular pressure above 35 mmHg. Bubble study was not done during the examination.

Statistical analysis was conducted using SPSS version 20. Descriptive analysis was performed for socio-demographic variables, respiratory symptoms, PH risk factors, and echocardiography values. Chi-square tests were performed to look for association between HIV status, ART duration, age of the patient, recent viral load/CD4 level, and PH status. Bivariate analysis was conducted to see associations between associated factors and PH. Values are reported as mean \pm standard deviation.

Results

A total of 315 patients were enrolled. The mean age of the participants was 44.5 ± 9.8 years and 229 (72.7%) were females (Table 1). Echocardiographic evidence of PH was seen in 44 patients (14.0%). Of these 44 patients, one-fifth (20.5%) had moderate-to-severe disease defined as pulmonary arterial systolic pressure (PASP) ≥ 50 mmHg or TRV of ≥ 3.5 m/sec and over one-third (38.6%) were symptomatic. The prevalence of PH was no greater in women (12.2%) than it was in men (18.6%).

Among patients with PH, the most common symptoms were exertional dyspnea (27%) cough (21%), and chest pain (18%; Table 2). Chest pain and shortness of breath were more common in patients with PH than in those without.

Although patients with PH associated with previously diagnosed chronic heart or lung disease were not included in this study, a small number of the patients we enrolled were found to have these conditions. Approximately 3%

Table 1. Sociodemographic characteristics and other health-related behaviors of adult patients visiting HIV-clinic at Tikur Anbessa Hospital, 2019.

Characteristics	TR velocity <2.8mt/ sec (n = 271)	TR velocity >2.8mt/ sec (n = 44)	Total (n = 315)	P value
Age				
18–29	7 (2.6)	1 (2.3)	8	0.080
30–39	90 (33.2)	6 (13.6)	96	
40–49	93 (34.3)	22 (50.0)	115	
50–59	56 (20.7)	12 (27.3)	68	
>60	25 (9.2)	3 (6.8)	28	
Sex				
Male	70 (25.8)	16 (36.4)	86	0.146
Female	201 (74.2)	28 (63.6)	229	
History of tobacco use				
Yes	24 (8.9)	4 (9.1)	28	1.000
No	247 (91.1)	40 (90.9)	287	
Bronchial asthma				
Yes	11 (4.1)	5 (11.4)	16	0.041
No	260 (95.9)	39 (88.6)	299	
COPD				
Yes	11 (4.1)	2 (4.5)	13	0.700
No	260 (95.9)	42 (95.5)	302	
Pulmonary tuberculosis				
Yes	111 (41.0)	15 (34.1)	126	0.388
No	160 (59.0)	29 (65.9)	189	
Connective tissue disease				
Yes	39 (14.4)	2 (4.5)	41	0.090
No	232 (85.6)	42 (95.5)	274	
Chest deformities				
Yes	1 (0.4)	0 (0.0)	1	1.000
No	270 (99.6)	44 (100)	314	

TR: tricuspid regurgitation; COPD: chronic obstructive pulmonary disease.

were found to have COPD, but all of these patients were felt to have PH out of proportion to the underlying lung disease. There were also a small number of patients who self-reported an asthma diagnosis but never had pulmonary function tests (PFTs) testing to confirm the diagnosis. This was found to be significantly associated with PH in our study population ($p = 0.041$). However, no significant association was seen between the presence of PH and sex, smoking history, COPD, connective tissue diseases, chronic heart diseases, or chest deformities. The prevalence of PH did not appear to be related to the severity of HIV infection or treatment history. We saw no association between the presence of PH and current CD4 levels, HIV viral load, duration of HIV infection, or ART regimen used (see Tables 1–3).

Discussion

In the present study, we used transthoracic echocardiography to screen for the presence of PH in consecutive HIV patients presenting for evaluation or follow-up at the HIV Clinic in TASH. Echocardiographic evidence of PH was seen in nearly 1 out of 7 patients. The great majority of patients (>86%) were between 40 and 59 years of age and men were affected at least as often as women. HIV patients with PH were more likely to have symptoms of shortness of breath and chest pain than those without PH.

Previous studies evaluating the prevalence of PH in PLHIV produced varied results depending on the

Table 2. Clinical manifestations of patients with pulmonary hypertension among adult patients visiting HIV-clinic at Tikur Anbessa Hospital, 2019.

Characteristics	TR Velocity <2.8mt/ sec (n = 271)	TR Velocity >2.8mt/ sec (n = 44)	Total (n = 315)	P value
Shortness of breath				
Yes	41 (15.1)	12 (27.3)	53	0.046
No	230 (84.9)	32 (72.7)	262	
Cough				
Yes	32 (11.8)	9 (20.5)	41	0.114
No	239 (88.2)	35 (79.5)	274	
Chest pain				
Yes	18 (6.6)	8 (18.2)	26	0.010
No	253 (93.4)	36 (81.8)	289	
Leg swelling				
Yes	26 (9.6)	4 (9.1)	30	1.000
No	245 (90.4)	40 (90.9)	285	
Overall symptoms				
Yes	76 (28.0)	17 (38.6)	93	0.153
No	195 (72.0)	27 (61.4)	222	

TR: tricuspid regurgitation.

Table 3. Immunologic, virologic, and treatment status of adult patients visiting HIV-clinic at Tikur Anbessa, Hospital 2019.

Characteristics	TR Velocity <2.8 (n = 271)	TR Velocity >2.8 (n = 44)	P value
Current CD4 (mean ± SD)	488.07 (228.00)	430.5 (160.35)	0.108
HIV duration (mean ± SD)	10.40 (4.04)	9.89 (3.87)	0.434
ART duration (mean ± SD)	9.57 (3.94)	9.75 (3.88)	0.789
BMI (mean ± SD)	24.06 (4.35)	22.98 (3.97)	0.122
Second line ART, frequency (%)	43 (15.9)	6 (13.6)	0.705
Tenofovir-based ART, frequency (%)	210 (77.5)	29 (65.9)	0.096
Abacavir-based ART, frequency (%)	9 (3.3)	2 (4.54)	0.656
Viral load detectable, frequency (%)	20 (7.4)	0 (0.00)	0.089

HIV: human immunodeficiency virus; ART: anti-retroviral therapy; BMI: body mass index.

availability of HAART and the method of screening for PH. Prior to the availability of HAART, prevalence of PH in PLHIV was found to be about 0.5% using transthoracic echocardiography⁹ and a similar prevalence was reported during the HAART era in a large prospective study in France that use right heart catheterization.²³ However, subsequent studies using transthoracic echocardiography have found a higher prevalence of PH in PLHIV.^{11,15–18,22} Studies done in Africa have also reported higher prevalence rates,^{19–21,24} although some of these studies used a cut-off level of systolic pulmonary arterial pressure >30 mmHg or TR velocity greater than 2.5 m/sec to define PH and likely overestimated the true prevalence of elevated PA pressure. In studies like ours, that use the more acceptable echocardiographic estimate of PH as right ventricular systolic pressure >36 or TR velocity >2.8, the prevalence of PH has been <10%. In the present study, using the more stringent PH screening criteria, we found a prevalence higher than that reported in studies from the western,^{11,15,17,18} African,^{19–21} and Asian²² countries (see Table 4), but similar to the pooled prevalence reported from Africa.²⁴ However, unlike the other African studies which focused on symptomatic patients, our study included patients visiting the HIV referral clinic irrespective of the presence or absence of symptoms. The reason for what may be a higher prevalence of PH in HIV patients living in Sub-Saharan Africa is unclear, but could be due to the presence of delayed diagnosis of HIV resulting in a greater period of time in which HIV was present and untreated. Finally, it should be noted that Addis Ababa is at an altitude of 7800 feet where reduced oxygen tension could contribute to elevation of PA pressure. However, population-based studies of Ethiopians living in the Simien plateau in Northern Ethiopia suggest that native Ethiopians living at high altitude have evolved to maintain near normal oxygen saturation.²⁵ The impact of Schistosomiasis might not be undermined here.

None of the previously known factors such as age, gender, CD4 level, and viral load that are associated with

increased risk of PH were associated with the presence of PH in this study. Therefore, PH in this patient population may be related to HIV infection itself. Alternatively, the prevalence of PH in Ethiopia may be higher than other parts of the world. A history of asthma was found to be associated with PH in this study. However, asthma was self-reported and not confirmed by outside records or pulmonary function testing. Thus, it is possible that some of these patients had been misdiagnosed with “bronchial asthma” while they were symptomatic from PH. Asthma is a common diagnosis given to patients with unexplained dyspnea and PH can rarely masquerade as asthma.²⁶

The strength of the present study includes the large number of patients enrolled compared to previous studies conducted in Sub-Saharan Africa^{19,21} and that it screened for PH irrespective of the presence or absence of symptoms. Its limitations include the cross-sectional design of the study, the methodology of transthoracic echocardiography (TTE) compared to right heart catheterization (RHC) that may account for the higher estimated prevalence, the lack of additional diagnostic tests such as chest imaging, pulmonary function tests, or spirometry to exclude PH associated with lung disease, and the lack of right heart catheterization to confirm the diagnosis. However, right heart catheterization is not generally available in Ethiopia. In addition, details of the recruitment procedure were not documented (e.g., the number of patients who were excluded because of refusal to participate or inconvenience or those with established Group 2 or 3 PH).

PH as suspected by transthoracic echocardiography appears to be common in PLHIV in Ethiopia. Over a quarter of PLHIV patients with PH have symptomatic dyspnea and/or chest pain. While further studies will be needed to confirm the prevalence of HIV-associated PH in Ethiopia, the present study adds considerably to the limited data available regarding this condition in Sub-Saharan Africa and suggests that PH may be an important comorbid condition of PLHIV. The high prevalence of possible PH in this population suggests that routine screening by

Table 4. Comparison of studies that used echocardiography to define Pulmonary Hypertension, 2019.

First author, publication year	Setting	Number	Age	Women (%)	Symptomatic (%)	Prevalence, %	Diagnostic	Associated factor
Speich et al. ¹⁰	Switzerland	748 symptomatic (of 1200 HIV cohort)	Mean ± SD 30 ± 5 (Range: 24–37)	Not mentioned	100	0.8% in the symptomatic & 0.5% in the cohort	RVSP > 30 mmHg	Not mentioned
Hsue et al. ¹⁷	USA	196	Median = 47 (IQR 42–52)	15	Not mentioned	35.2	sPAP > 30 mmHg	HIV itself
Reinsch et al. ¹⁸	Germany	802	Mean ± SD 44.3 ± 10.3	16.6	14	4.7	sPAP > 35 mmHg	HAART, female sex
Mondy et al. ¹⁹	USA	322	Not mentioned	Not mentioned	Not mentioned	57	RVSP > 31 mmHg	Current use of ritonavir
Chillo et al. ²⁰	Tanzania	102	Mean ± SD 42.4 ± 11.3	69	100	13	sPAP > 35 mmHg	None
Sliwa et al. ²¹	South Africa	518	Mean ± SD 40 ± 14	62	100	8	sAP > 25 mmHg	Not researched
Menanga ²²	Cameroon	44	Mean ± SD 48 ± 13	52.3	100	11.4	sPAP > 35 mmHg	CD4 > 200/mm ³
Schwarze-Zander et al. ¹⁶	Germany	374	Median = 46 (Range 21–73)	20	13	6.1	sPAP > 30 mmHg	IDU, shorter duration since HIV diagnosis
Quezada et al. ¹²	Spain	392	Median = 47	16.6	23	9.9	RVSP > 35 mmHg	Female sex, detectable viral load, HCV
Rasoulinejad et al. ²³	Iran	170	Mean = 41	42.5	0	3	sPAP > 35	None

RVSP: right ventricular systolic pressure; sPAP: systolic pulmonary arterial pressure; IDU: intravenous drug use; HAART: highly active antiretroviral therapy; HCV: hepatitis C Virus.

echocardiography may be warranted. In patients with HIV-associated PH, further testing to exclude hypoxemia, chronic heart and lung disease, and sleep-disordered breathing should be considered.

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Author contributions

Dawit Kebede Huluka contributed to inception of the research question, protocol preparation, organization of the work, data analysis and write of the manuscript. Desalew Mekonnen contributed to data collection and manuscript reviewing. Sintayehu Abebe contributed to data collection, organization of data collection, and write up of the manuscript. Amha Meshesha and Dufera Mekonnen contributed to data collection and manuscript reviewing. Negussie Deyessa contributed to protocol draft, data analysis, and write up. James R. Klinger and Corey E. Ventetuolo contributed to write up of the manuscript. Neil W. Schluger and Charles B. Sherman contributed to protocol draft and write up. Wondwossen Amogne contributed to protocol draft and write up.

Conflict of interest

The authors whose names are listed above certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. This case was presented at the American Thoracic Society International Conference in Dallas, Texas, May 2019.

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ORCID iDs

Dawit Kebede Huluka  <https://orcid.org/0000-0001-8287-6062>
Negussie Deyessa  <https://orcid.org/0000-0002-8843-7287>

Supplemental material

Supplemental material for this article is available online.

References

- Farahani M, Vable A, Lebelonyane R, et al. Outcomes of the Botswana national HIV/AIDS treatment programme from 2002 to 2010: a longitudinal analysis. *Lancet Glob Health* 2014; 2: e44-50-e50.
- Samji H, Cescon A, Hogg RS, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. *PLoS One* 2013; 8: e81355.
- Barbaro G. Cardiovascular manifestations of HIV infection. *Circulation* 2002; 106: 1420-1425.
- Mesa RA, Edell ES, Dunn WF, et al. Human immunodeficiency virus infection and pulmonary hypertension: two new cases and a review of 86 reported cases. *Mayo Clinic Proc* 1998; 73: 37-45.
- Nunes H, Humbert M, Sitbon O, et al. Prognostic factors for survival in human immunodeficiency virus-associated pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2003; 167: 1433-1439.
- Humbert M, Sitbon O, Chaouat A, et al. Pulmonary arterial hypertension in France. *Am J Respir Crit Care Med* 2006; 173: 1023-1030.
- Basyal B, Jarrett H and Barnett CF. Pulmonary hypertension in HIV. *Can J Cardiol* 2019; 35: 288-298.
- Galiè N, Hoepfer MM, Humbert M, et al. Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J* 2009; 34: 1219-1263.
- Speich R, Jenni R, Opravil M, et al. Primary pulmonary hypertension in HIV infection. *Chest* 1991; 100: 1268-1271.
- Jarrett H and Barnett C. HIV-associated pulmonary hypertension. *Curr Opin HIV AIDS* 2017; 12: 566-571.
- Quezada M, Martin-Carbonero L, Soriano V, et al. Prevalence and risk factors associated with pulmonary hypertension in HIV-infected patients on regular follow-up. *AIDS* 2012; 26: 1387-1392.
- Mondy KE, Gottdiener J, Overton ET, et al. High prevalence of echocardiographic abnormalities among HIV-infected persons in the era of highly active antiretroviral therapy. *Clin Infect Dis* 2011; 52: 378-386.
- Olalla J, Urdiales D, Pombo M, et al. Pulmonary hypertension in human immunodeficiency virus-infected patients: the role of antiretroviral therapy. *Med Clin (Barc)* 2014; 142: 248-252.
- Frost A, Badesch D, Gibbs JSR, et al. Diagnosis of pulmonary hypertension. *Eur Respir J* 2019; 53: 1801904.
- Schwarze-Zander C, Pabst S, Hammerstingl C, et al. Pulmonary hypertension in HIV infection: a prospective echocardiographic study. *HIV Med* 2015; 16: 578-582.
- Hsue PY, Deeks Husam SG, Farah H, et al. Role of HIV and HHV-8 infection in pulmonary arterial hypertension. *AIDS* 2008; 22: 825-833.
- Reinsch N, Buhr C, Krings P, et al. Effect of gender and highly active antiretroviral therapy on HIV-related pulmonary arterial hypertension: results of the HIV-HEART study. *HIV Med* 2008; 9: 550-556.
- Mondy KE, Gottdiener J, Overton ET, et al. High prevalence of echocardiographic abnormalities among HIV-infected persons in the era of highly active antiretroviral therapy. *HIV/AIDS* 2011; 52: 378-386.
- Chillo P, Bakari M and Lwakatara J. Echocardiographic diagnoses in HIV-infected patients presenting with cardiac symptoms at Muhim-bili National Hospital in Dar Es Salaam, Tanzania. *Cardiovas J Africa* 2012; 23: 550-556.
- Sliwa K, Carrington MJ, Becker A, et al. Contribution of the human immunodeficiency virus/acquired immuno-deficiency syndrome epidemic to de novo presentations of heart disease in the heart of soweto study cohort. *Eur Heart J* 2012; 33: 866-874.
- Menanga AP, Ngomseu CK, Jingi AM, et al. Patterns of cardiovascular disease in a group of HIV-infected adults in Yaoundé, Cameroon. *Cardiovasc Diagn Ther.* 2015; 5: 420-427.
- Rasoulinejad M, M, Badie S, Salehi MR, et al. Echocardiographic assessment of systolic pulmonary arterial pressure in HIV-positive patients. *Acta Med Iran* 2014; 52: 827-830.
- Sitbon O, Lascoux-Combe C, Delfraissy JF, et al. Prevalence of HIV-related pulmonary arterial hypertension in the current antiretroviral therapy era. *Am J Respir Crit Care Med* 2008; 177: 108-113. [PMID: 17932378 DOI: 10.1164/rccm.200704-541OC].
- Bigna JJ, Nansseu JR, Um LN, et al. Prevalence and incidence of pulmonary hypertension among HIV-infected people in Africa: a systematic review and Meta-analysis. *BMJ Open* 2016; 6: e011921.
- Beall CM, Decker MJ, Brittenham GM, et al. An Ethiopian pattern of human adaptation to high-altitude hypoxia. *Proc Natl Acad Sci USA* 2002; 99: 17215-17218.
- Achouh L, Montani D, Garcia G, et al. Pulmonary arterial hypertension masquerading as severe refractory asthma. *Eur Respir J* 2008; 32: 513-516.