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HIV infection is not associated with echocardiographic signs of cardiomyopathy or pulmonary hypertension among pregnant Ugandan women

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Keywords

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Human Immunodeficiency Virus (HIV) infection is a well-recognized cause of cardiomyopathy and pulmonary hypertension. HIV causes both systolic and diastolic dysfunction(1,2); more commonly in late stage AIDS, but also in patients with higher CD4 counts(3). However, little is known about the cardiac function of HIV-infected pregnant women. Peripartum cardiomyopathy (PPCM) is defined as the new onset of heart failure from left-ventricular systolic dysfunction during the last month of pregnancy or within five months after delivery in the absence of any identifiable cause or pre-existing cardiac disease(4). PPCM is more common in sub-Saharan Africa compared to the United States(5). Whether HIV-infection is a risk factor for PPCM which may partly explain this higher prevalence is not known.

The primary objective of our study was to examine whether HIV infection is associated with seven pre-specified echocardiographic signs of cardiomyopathy or pulmonary hypertension among pregnant Ugandan women. A secondary objective was to compare maternal and infant outcomes at the time of delivery among HIV-infected and control participants.

41 HIV-infected and 41 HIV-negative pregnant women in their third trimester of pregnancy and without symptoms of heart failure were recruited from the antenatal clinics of Mulago Hospital in Kampala, Uganda in February 2009. Informed consent was obtained. The protocol was approved by institutional review boards at the University of California San Francisco (UCSF), Mulago Hospital, and Makerere University.

A standardized transthoracic echocardiogram was performed on each participant in accordance with American Society of Echocardiography guidelines(6–8) using a Sonosite MicroMaxx version 3.4 portable ultrasound machine and P10 cardiac transducer (5-1 MHz, 17mm broadband phased array). Images were stored on CompactFlash cards and then

downloaded to a Siemens SyngoDynamics Image Management system at UCSF for analysis. All measurements were performed by study physicians at UCSF and were over-read by a senior cardiologist (EF). Records were reviewed in May 2009 to obtain follow-up outcomes for each participant who delivered at Mulago Hospital.

Baseline characteristics of the HIV-infected and control participants were similar (Table 1). Hospital records of the 24 HIV-infected participants reviewed after delivery indicated that 100% were on combination anti-retroviral therapy (cART) during pregnancy.

HIV-infection was not associated with any of the seven echocardiographic signs of cardiomyopathy shown in Table 2. Adjustment for age, country of birth, gestational age, prior miscarriages, prior pregnancies, body mass index, blood pressure, and heart rate did not affect these results. Unexpectedly, HIV-infection was associated with a slightly lower RVSP. However, the number of observations was small due to the lack of a complete tricuspid regurgitation jet among most participants. Notably, the mean pressure was low in each group, and only one participant in the control group had borderline elevated RV pressure suggestive of pulmonary hypertension (RVSP = 31mmHg). Doppler estimated cardiac output (CO) was lower than expected in both groups. CO ranged from 2.57 to 7.93 L/min among HIV participants and 2.69 to 6.66 L/min among control participants. No participants had valvular stenosis or greater than mild regurgitation. Follow-up maternal and fetal outcomes were similar (Table 3).

This study contributes evidence that HIV is an unlikely risk factor for peri-partum cardiomyopathy in the era of widespread cART use. Recently, Sliwa et al. showed that HIV-infected women, despite mild to moderate immunosuppression, have a similar 2-year prognosis compared to HIV uninfected women with PPCM in South Africa(9). However, mortality due to PPCM at two years was higher in both groups than the reported mortality in a recent retrospective multicenter cohort of HIV uninfected women in the United States(10). The reasons for disparities in prevalence and outcome warrant further study.

Our findings contrast with studies conducted during the pre-cART era that suggested a high prevalence of both systolic and diastolic dysfunction among asymptomatic HIV-infected adults(1,11,12). Twagirumukiza et al(12) described a 17.7% prevalence of dilated cardiomyopathy in 416 HIV-infected Rwandans who had no prior history of cardiovascular disease and who were not on anti-retroviral therapy. The significant predictors of cardiomyopathy were duration of HIV infection, CD4 count, HIV viral load, and late CDC stage. It is likely that with suppresion of viral load on cART, the women in our study were at lower risk of cardiac dysfunction from HIV.

HIV infection is known to cause pulmonary arterial hypertension (PAH) with a prevalence of about 0.5% among Europeans(13,14). However, these and other studies in the western world are confounded by the high prevalence of IV drug abuse. Notably, all affected women in the Swiss cohort were IV drug users(13). In the French cohort, the significant predictors of PAH were male gender, IV drug use, and CD4<200(14). The statistically significant difference in RVSP in our study was small and not likely to be clinically relavant; however, it merits further study in larger populations of HIV-infected African women with higher CD4 counts and without a history of IV drug use.

A major strength of our study was the focus on HIV-infected women in the developing world, a population that is not frequently studied outside of mother-to-child transmission. In addition, the HIV-infected and control groups were closely matched in all demographic characteristics; therefore, the possibility of residual confounding that masks a true difference between groups is less likely. Cardiac output was lower in our study than in previous longitudinal studies of pregnant women(15,16), which may have limited our ability to

observe the effect of increased hemodynamic stress on heart function. Finally, because we do not have viral load and CD4 counts, we cannot objectively confirm the immune status of the HIV-infected women.

It is reassuring that HIV-infected pregnant women in the era of widespread use of combination anti-retroviral therapy do not appear to have sub-clinical echocardiographic signs of cardiomyopathy. Further studies are needed to examine the risk of dilated cardiomyopathy, pulmonary hypertension, and peripartum cardiomyopathy among HIV-infected African women.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology(17).

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Table 1

Baseline characteristics of HIV-infected and control participants

	HIV-infected n=41	Controls n=41	p-value*
Age (years)	28 (5.2)	28 (5.8)	1.00
Country of birth			
Ugandan	40	39	1.00
Kenyan	0	1	n/a
Rwandan	1	0	n/a
Congolese	0	1	n/a
Gestational age (weeks)	36 (3.8)	35 (3.6)	0.47
Prior pregnancies			
0	2	5	0.24
1 or more	39	36	n/a
Prior miscarriage or abortion			
0	29	36	0.06
1 or more	12	5	
Body mass index (kg/m^2)	27.5 (5.0)	27.6 (4.4)	0.85
Systolic blood pressure (mmHg)	106 (9.1)	108 (9.9)	0.62
Diastolic blood pressure (mmHg)	67 (8.2)	68 (8.7)	0.47
Heart rate (beats/min)	90 (11)	89 (10)	0.82

Continuous variables shown as Mean (Standard Deviation)

*Mann-Whitney U test for continuous variables and Fischer's Exact test for categorical variables

Table 2

Echocardiographic outcomes by HIV status

Outcome	HIV-infected (n=41)		Controls (n=41)		p-value
	n†	Mean (95% CI)	n†	Mean (95% CI)	
LV ejection fraction (%)	38	60.4 (58.5–62.4)	40	60.2 (58.3–62.1)	0.87
LV end-diastolic volume index (ml/m^2)	38	58.3 (55.0–61.7)	40	59.0 (54.9–63.0)	0.81
LV mass index (gm/m^2)	37	66.8 (62.5–71.1)	39	65.5 (61.7–69.4)	0.65
LA volume index (ml/m^2)	38	22.4 (20.7–24.1)	39	22.2 (20.8–23.7)	0.88
Mitral E/E' ratio	38	5.5 (5.0–5.9)	37	5.8 (5.4–6.3)	0.26
RV systolic pressure (mmHg)	12	18.0 (15.9–20.1)	16	22.6 (20.1–25.0)	**0.01**
Cardiac output (L/min)	41	4.2 (3.8–4.7)	41	4.3 (3.8–4.9)	0.84

† number of participants in whom the echocardiographic outcome was obtained

CI = confidence interval; LV = left ventricle; LA = left atrium; RV = right ventricle

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Table 3

Maternal and fetal outcomes by HIV status

Outcome	HIV-infected (n=41)		Controls (n=41)		p-value
	n†	Mean (95% CI)	n†	Mean (95% CI)	
Gestational age at delivery (weeks)	24	40.4 (39.0–41.8)	28	38.7 (37.3–40.0)	0.07
Infant birth weight (kg)	24	3.34 (3.14–3.54)	28	3.23 (3.11–3.36)	0.34
APGAR 1 (0–10)	23	8.87 (8.27–9.47)	25	8.4 (7.9–8.9)	0.23
APGAR 5 (0–10)	23	9.5 (9.2–9.9)	26	9.7 (9.5–10.0)	0.30
Fetal death	24	0	28	1 (3.6%)	n/a
Maternal death	24	0	28	0	n/a

† number of participants for whom the follow-up outcome was obtained

CI = confidence interval