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Cardiovascular Risk Profile of Transgender Women with HIV: A U.S. Healthcare Database Study

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Abstract

We sought to characterize the cardiovascular disease (CVD) risk factor profile of transgender women with HIV identified through a U.S. healthcare database. Compared with age- and race-matched cisgender men with HIV, transgender women with HIV had an increased prevalence of anemia and lower absolute hemoglobin levels. HIV control was sub-optimal and prevalence of HCV co-infection was high among transgender women. Further study of non-traditional CVD risk factors/immune activation among transgender women with HIV is warranted.

Keywords

HIV; transgender; women; cardiovascular disease risk

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RESEARCH LETTER

Nearly a third of transgender women in the U.S. test positive for HIV infection, according to a meta-analysis from the Centers of Disease Control.[1] U.S. epidemiologic studies suggest HIV infection confers a heightened risk of myocardial infarction (MI)[2] and heart failure (HF).[3] Parameters influencing increased cardiovascular disease (CVD) risk among people living with HIV (PLHIV) include traditional and non-traditional risk factors,[4] as well as preventive care delivery patterns.[5] In parallel, observational studies conducted among broad groups of transgender women (HIV serostatus not reported) signal increased CVD risk in this population.[6,7] CVD risk research among transgender women has primarily focused on metabolic effects of gender-affirming hormonal therapies. No prior studies have systematically examined CVD risk factors among transgender women with HIV in the U.S.

We sought to characterize the CVD risk factor profile of transgender women with HIV identified through the Partners HIV Cohort - an observational virtual cohort of PLHIV receiving care through the Partners Healthcare System (PHS) in Boston, Massachusetts and diagnosed with HIV through November 2013 (n=5502). Partners HIV Cohort data elements derive from the PHS Research Patient Data Registry, which features complete PHS clinical information.[8] As part of this study, transgender women in the Partners HIV Cohort were identified through electronic data mining employing the search terms “transgender,” “transsexual,” and “gender dysphoria”. Next, a control group from within the Partners HIV Cohort was developed matched to the group of transgender women on sex-at-birth, age/birth year, and race (4:1 ratio; transgender women n=23; cisgender men n=92). Cisgender men were selected as the comparator group to address the following question: For PLHIV with male sex at birth, how does gender identification influence parameters relevant to CVD risk? Electronic medical records were manually reviewed to confirm HIV status and gender identity, and to ascertain the most recent available data on traditional and non-traditional CVD risk factors. Normally distributed data are presented as mean ± standard deviation (SD) and non-normally distributed data are presented as median, interquartile range (IQR). Comparisons of CVD risk parameters between transgender women and cisgender men with HIV were made using the chi-square test, the Student’s two-tailed *t*-test, or the Wilcoxon test, as appropriate. JMP Pro software (version 12.0, SAS Institute, Cary, North Carolina, U.S.A) was used for analyses, with statistical significance set at $P \leq 0.05$.

The CVD risk factor profiles of transgender women with HIV and age- and race-matched cisgender men with HIV are presented in Table 1. Median age in both groups was 51 years. Within each group, approximately half identified as Black/African-American while nearly one fifth identified as Hispanic. Among transgender women with HIV, estrogen was prescribed to 83% while suppression of endogenous testosterone production (surgical or pharmacologic) was documented among 30%. Compared with cisgender men with HIV, transgender women with HIV had lower hemoglobin levels (13.0 (11.2, 14.3) vs. 13.8 (12.4, 15.0) g/dL, p=0.04), and thereby higher rates of anemia (65% vs. 38%, p=0.02). With respect to traditional CVD risk factors, there were no significant between-group differences in prevalence of hyperlipidemia or hypertension. Diabetes prevalence was 22% among transgender women with HIV and 14% among cisgender men with HIV. With respect to non-traditional CVD risk factors, depression prevalence tended to be higher among

transgender women with HIV, though this finding did not reach statistical significance. Notably, only 68% of transgender women with HIV were on ART as compared to 83% of cisgender men with HIV (p=0.14). There was a non-significant trend toward a lower CD4 count and nadir CD4 count among transgender women with HIV. Additionally, there tended to be higher rates of hepatitis C virus (HCV) co-infection among transgender women with HIV vs. cisgender men with HIV (43% vs. 26%, p=0.11).

Through this study, we discovered an increased prevalence of anemia and lower hemoglobin levels among transgender women with HIV vs. cisgender men with HIV. In the general population, anemia has been characterized as a risk factor for MI and HF.[910] Among PLHIV, anemia also has been shown to relate to accelerated HIV disease progression and increased systemic immune activation/inflammation,[111213] of relevance to HIV-associated CVD. Suppression of endogenous testosterone production may contribute to anemia among transgender women with HIV. Indeed, studies of individuals with testosterone-dependent malignancies have shown that androgen depletion induces anemia, and leads to loss of lean muscle mass and insulin resistance.[14]

Our study also reveals suboptimal HIV control and a high prevalence of HCV co-infection among transgender women with HIV. Baguso et al. previously demonstrated that transgender women with HIV had lower rates of viral suppression (by self-report through an AIDS Clinical Trials Group Adherence Questionnaire) as compared to a mixed control group of cisgender men and women.[15] Suboptimal HIV control (low CD4/high viral load) and HCV co-infection have been associated with CVD events among PLHIV.[16317] Propagation of heightened systemic immune activation may represent a common mechanism through which suboptimal HIV control and HCV-co-infection predispose to MI and HF.

Our characterization of the CVD risk factor profile among transgender women with HIV (vs. cisgender men with HIV) in a U.S. healthcare system reveals several key findings: increased prevalence of anemia, as well as suboptimal HIV control and a high prevalence of HCV co-infection. Anemia, poor HIV control, and HCV co-infection may all represent modifiable non-traditional CVD risk factors among transgender women with HIV. Limitations of our study include the relatively small sample size of transgender women with HIV and incomplete data capture on gender affirming hormonal therapy (including hormone therapy pursued outside PHS). To maximize our sample size, we systematically identified all transgender women with HIV receiving care at PHS across a wide date range. However, duration of HIV was similar between our group of transgender women and cisgender men, suggesting both groups may have had parallel exposure to older HIV treatment and CVD prevention strategies. Additional research is warranted on CVD risk (MI, HF, thromboembolism) and traditional / non-traditional risk-mechanisms among transgender women with HIV.[18]

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Table 1

Baseline Characteristics Among Transgender Women and Cisgender Men with HIV

Parameter	Transgender Women with HIV (N=23)	Cisgender Men with HIV (N=92)	P value
Non-HIV-specific Parameters			
Age (years)	51 (40, 63)	51 (41, 62)	0.93
Race/ethnicity			
White	9% (2/23)	11% (10/89)	
Black/African American	52% (12/23)	51% (45/89)	
Hispanic	17% (4/23)	19% (17/89)	0.49
Other	13% (3/23)	18% (16/89)	
Unknown	9% (2/23)	1% (1/89)	
Hyperlipidemia	26% (6/23)	29% (26/91)	0.81
Current statin use	13% (3/23)	20% (18/91)	0.44
Total cholesterol (mg/dL)	170 (145, 224)	171 (145, 211)	0.80
LDL-c (mg/dL)	97 ± 36	98 ± 36	0.89
HDL-c (mg/dL)	54 (32, 62)	44 (35, 55)	0.52
Triglycerides (mg/dL)	138 (88, 242)	123 (88, 213)	0.52
HTN	27% (6/22)	33% (30/90)	0.58
Systolic blood pressure (mmHg)	112 (110, 140)	128 (117, 137)	0.11
Diastolic blood pressure (mmHg)	73 ± 14	78 ± 12	0.12
DM	22% (5/23)	14% (13/91)	0.40
Current cigarette smoking	29% (6/21)	35% (29/84)	0.60
Current cocaine use	10% (2/21)	6% (5/86)	0.56
Current alcohol use	5% (1/21)	3% (3/86)	0.79
Depression	48% (11/23)	32% (29/90)	0.17
Anxiety	17% (4/23)	25% (22/89)	0.45
Creatinine (mg/dL)	1.0 (0.9, 1.2)	1.0 (0.9, 1.2)	0.88
Anemia *	65% (15/23)	38% (35/91)	**0.02**
Hemoglobin (g/dL)	13.0 (11.2, 14.3)	13.8 (12.4, 15.0)	**0.04**
HIV-specific Parameters			
Duration since HIV diagnosis (years)	17 ± 7	15 ± 8	0.38
Currently on ART	68% (15/22)	83% (73/88)	0.14
CD4 count (cells/mm^3)	374 (111, 610)	502 (276, 683)	0.19
Nadir CD4 (cells/mm^3)	102 (26, 356)	223 (72, 370)	0.19
CD4 to CD8 ratio	0.5 (0.3, 0.9)	0.6 (0.3, 1.1)	0.42
Undetectable viral load	63% (10/16)	61% (43/71)	0.89
HCV co-infection	43% (10/23)	26% (23/88)	0.11

Abbreviations: ART, antiretroviral therapy; CVD, cardiovascular disease; DM, diabetes mellitus; HCV, hepatitis C virus; HDL-c, high density lipoprotein cholesterol; HIV, human immunodeficiency virus; HTN, hypertension; and LDL-c, low density lipoprotein cholesterol. All available data points were incorporated into the summative presentation above, although a significant number of missing data points were noted for lipid

parameters. Normally distributed variables are presented as mean ± standard deviation; non-normally distributed data are presented as median (interquartile range).

*Anemia was defined using a hemoglobin threshold of < 13.5 g/dL.