Disparities and Delay in the Use of Guideline-Based Antiretroviral Therapy for Treatment of Pregnant Women with HIV in the Southeast United States

Ellery R. Cohn, BA,[1] Jeffrey E. Korte, PhD,[2] and Gweneth B. Lazenby, MD MSCR[3]

DEPARTMENT OF HEALTH AND HUMAN SERVICES (DHHS) BEGAN ISSUING guidelines for the use of antiretrovirals (ARVs) among adults with HIV infection in 1998.[1] Since 2000, combination antiretroviral therapy (cART), defined as at least three ARVs in at least two antiviral classes, has been recommended for the prevention of perinatal HIV infection.[2] Single-drug or monotherapy (mARV) and two-drug or dual-therapy (dARV) are no longer recommended for use in pregnancy.

The use of cART has increased since the 1990s, resulting in improved quality of life and survival of persons with HIV.[3] Women and minorities may be less likely to receive ART recommended by the DHHS guidelines for the treatment of HIV.[4–6] Women who receive nonrecommended ART can have elevated HIV RNA viral loads and lower CD4 cell counts.[1] During pregnancy, inadequate HIV viral suppression may contribute to perinatal HIV infection.[7]

Our primary aim was to evaluate the use of DHHS-recommended ARVs by pregnant women with HIV. Our secondary aim was to determine trends in cART use among pregnant women with HIV.

We performed a retrospective cohort study approved by the South Carolina Department of Health and Environmental Control (SCDHEC) Institutional Review Board (IRB15-013). Data presented here are a secondary analysis of a study examining the relationship between rural residence in South Carolina and perinatal HIV infection.[8] Deidentified data were obtained from the SCDHEC Enhanced HIV/AIDS Reporting Surveillance System (eHARS) database for all women with HIV giving birth between 2004 and 2014 in South Carolina. The eHARS database is an application developed by the CDC with records for every mother/baby pair with known maternal HIV infection. Data are collected from prenatal records, hospitalizations, laboratory reports, birth/death certificates, and case interviews.[9]

The preferred ARV drugs for each year of the study were obtained from archived versions of the DHHS guidelines (https://aidsinfo.nih.gov/guidelines/archive/perinatal-guidelines/).[10] ARV drugs were categorized as a preferred drug if they were listed as "preferred or alternative" for treatment of pregnant women. ARVs were otherwise categorized as a nonpreferred.

All ARVs reportedly taken during pregnancy were recorded in eHARS. ARV regimens were reviewed and categorized by the number of drugs and number of ARV classes prescribed to each woman with HIV. We created three categories of ARV regimens: mARV, dARV, and cART. Women who did not report ARV use were classified as "no ARV."

Women were eligible for this study if they were diagnosed with HIV before delivery. Other maternal characteristics available for analysis were race, ethnicity, year of HIV diagnosis, number of prenatal visits, year of delivery, county of delivery, and HIV RNA viral load (copies/mL) before delivery. Maternal perinatal HIV infection was defined as a woman who contracted HIV infection from her birth mother.[11] A county was defined as rural if the total population was <30,000 persons according to the 2010 US Census.[8] Viral suppression was defined as an HIV RNA viral load of <40 copies/mL.

For the primary outcome, women reporting use of preferred ARVs were compared with those reporting nonpreferred ARV use. Bivariate outcomes were reported as percentages and compared using χ^2 or Fisher's exact test using SAS® 9.4 (SAS, Cary, NC). All continuous variables for this study were non-normal and reported as medians with corresponding interquartile ranges. Continuous variables were compared using Wilcoxon rank-sum tests or Kruskal–Wallis tests. When data are missing, the denominator reported reflects the number of results available for analysis. The Cochran–Armitage test was used to evaluate changes in ARV use over time. Univariate logistic regression analysis outcomes with a $p < 0.1$ were included in multivariate analysis. Results are reported as unadjusted and adjusted odds ratios with 95% confidence intervals (CIs). Interactions between variables were evaluated.

During the 10-year study period, 666 women delivered 680 infants, including 14 twin pairs. Women diagnosed with HIV in labor (7), postpartum (6), or with unknown timing (2) were excluded. Most women were taking ARVs (564, 88%):

[1]College of Medicine, Medical University of South Carolina, Charleston, South Carolina.
[2]Department of Public Health Sciences, Medical University of South Carolina, Charleston, South Carolina.
[3]Division of Infectious Diseases, Departments of Obstetrics and Gynecology and Medicine, Medical University of South Carolina, Charleston, South Carolina.
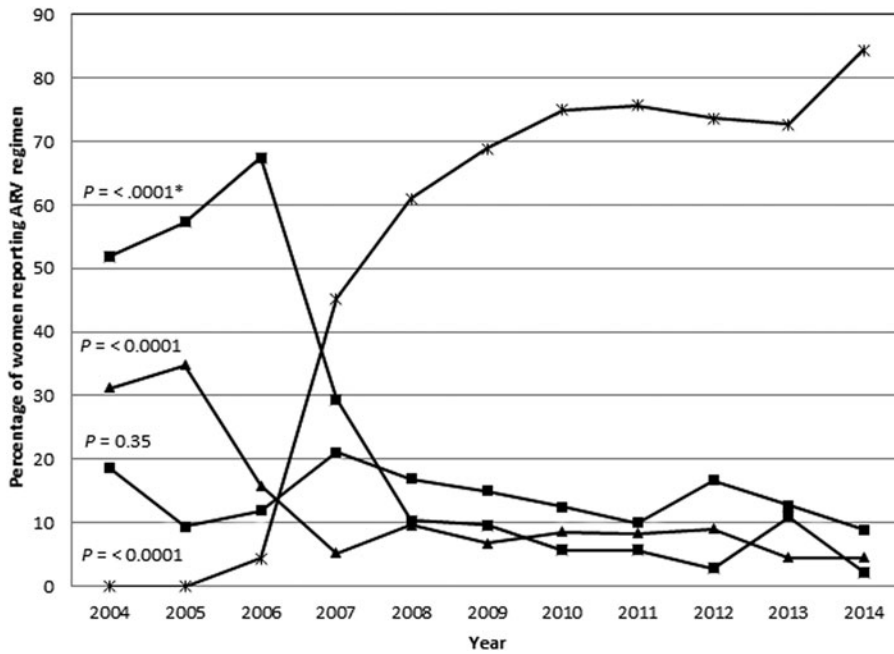
FIG. 1. Results of the Cochrane–Armitage trend test are depicted as p values inserted above the corresponding line within the graph. The X-axis describes the sequential years of the study. The Y-axis represents the percentage of women using each ARV regimen per year. Women reporting no ARV use are represented as the line with a square. Women reporting cART use are represented by the line with an asterisk. Women reporting mARV use are represented by the line with a triangle. Women reporting dARV use are represented by the line with a diamond. ARV, antiretroviral; cART, combination antiretroviral therapy.

mARV (98, 15%), dARV (135, 21%), and cART (331, 52%). Remaining women reported no ARV use (12%).

Half of the women were taking only preferred ARVs (286, 51%), one-third were taking some preferred ARVs (210, 37%), and the remainder were taking nonpreferred ARVs (68, 12%). Bivariate analysis comparing women on all or any preferred ARVs with those taking nonpreferred ARVs was performed. Characteristics of women were similar between those taking preferred and nonpreferred ARVs, except that women taking preferred ARVs were more likely to deliver in a rural county ($p = 0.03$). Women with perinatal HIV infection were less likely to take DHHS-preferred ARVs during pregnancy [unadjusted odds ratio (uaOR) 0.4 (95% CI 0.1–1.0)]. When controlling for perinatal HIV infection and year of delivery, women delivering in rural counties were more likely to report taking DHHS-preferred ARVs [aOR 3.0 (95% CI 1.1–8.4)].

cART increased significantly over time ($p < 0.0001$) (Fig. 1). In an unadjusted analysis, non-Hispanic black

women were less likely to report cART use [uaOR 0.7 (95% CI 0.4–1.1)]. When controlling for perinatal HIV infection, maternal race, and prenatal visits, the year of delivery was significantly associated with cART use [aOR 1.6 (95% CI 1.5–1.8)]. Interactions between variables were not significant.

Only half of the pregnant women reported using DHHS-recommended ARVs. Consistent with previous studies of guideline-based HIV therapy in nonpregnant persons, we observed that minority women were less likely to take cART.[4–6] Women who delivered in rural counties were more likely to take preferred ARVs; the reason for this is unclear. HIV RNA viral loads before delivery were no different between women taking preferred or nonpreferred ARVs, suggesting that nonpreferred ARVs, such as integrase inhibitors, are reasonable (Table 1).

Combination ART was recommended by DHHS to prevent perinatal HIV infection 4 years before the study period. The

TABLE 1. COMPARISON OF MATERNAL CHARACTERISTICS ACCORDING TO ANTIRETROVIRAL THERAPY REGIMEN

	cART (331)	Dual therapy (135)	Monotherapy (98)	No ARV (79)	p^a
Source of maternal HIV infection					
Heterosexual contact	217 (66)	122 (83)	74 (76)	49 (62)	0.0005
Parenteral drug use	17 (5)	3 (2)	7 (7)	8 (10)	0.08
Perinatal HIV infection	18 (5)	0	2 (2)	1 (1.3)	0.01
Year of maternal HIV diagnosis	2005 (2001–2008)	2003 (1998–2005)	2002 (1998–2004)	2004 (2000–2007)	<0.0001
Non-Hispanic black race	243 (73)	107 (79)	83 (85)	67 (85)	0.03
Delivery in rural county	48 (15)	24 (18)	14 (14)	17 (22)	0.42
Any prenatal care	286 (99)	127 (99)	88 (99)	36 (66)	<0.0001
HIV RNA viral load copies/mL before delivery	67 (20–150)	47 (0–641)	55 (0–683)	82 (20–10874)	0.005
Viral suppression	100/270 (37)	47/89 (53)	35/77 (46)	15/51 (29)	0.02

$N = 643$, first pregnancy, excluding women diagnosed during labor and postpartum and two women for whom data are missing. $N = 509$ for analysis of viral suppression. All continuous variables are reported as medians with corresponding interquartile ranges.

[a]From χ^2 or Kruskal–Wallis tests.

ART, antiretroviral therapy; ARV, antiretroviral; cART, combination antiretroviral therapy.

use of cART increased significantly over time, illustrating a delay in the use of guideline-based therapies in clinical practice. A relatively lower percentage of pregnant women taking cART achieved virologic suppression before delivery. Noncompliance with therapy is a possible explanation. The higher rates of viral suppression in the dARV group are consistent with other studies that have reported noninferiority when compared with cART.[12]

Limitations in this study are related to missing data. Factors that may influence ARV regimen choice, such as maternal medical comorbidities and antiviral resistance, could not be assessed. The timing of initiation and duration of ARV use were not available. Medication compliance could not be assessed. Despite these limitations, our study strength is in the number of observations in a detailed database. We anticipate that our findings are generalizable to most women with HIV in the Southeast. In our review of the literature, we did not find other studies describing guideline-based HIV therapy during pregnancy for comparison.

In conclusion, we noted a significant delay in the use of cART in clinical practice after publication of guidelines that recommended its use for the prevention of perinatal HIV infection. Specifically, non-Hispanic, black women were less likely to report cART use during pregnancy. Future studies should evaluate the role of unconscious bias and institutional racism in HIV care of women during pregnancy. In addition, we suggest improved strategies for relaying changes in clinical guidance to providers.

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References

1. Cocohoba J, Wang QJ, Cox C, et al. Consistency of initial antiretroviral therapy with HIV treatment guidelines in a US cohort of HIV-infected women. J Acquir Immune Defic Syndr 2008;47:377–383.
2. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. U.S. Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the United States. United States Department of Health and Human Services. 2000.
3. Gebo KA, Fleishman JA, Conviser R, et al. Racial and gender disparities in receipt of highly active antiretroviral therapy persist in a multistate sample of HIV patients in 2001. J Acquir Immune Defic Syndr 2005;38:96–103.
4. Cocohoba JM, Althoff KN, Godfrey R, Palella FJ, Greenblatt RM. Influence of gender on receipt of guideline-based antiretroviral therapy in the era of HAART. AIDS Care 2012;24:20–29.
5. Wandeler G, Keiser O, Hirschel B, et al. A comparison of initial antiretroviral therapy in the Swiss HIV Cohort Study and the recommendations of the International AIDS Society-USA. PLoS One 2011;6:e27903.
6. Beer L, Mattson CL, Bradley H, Skarbinski J; Medical Monitoring Project. Understanding cross-sectional racial, ethnic, and gender disparities in antiretroviral use and viral suppression among HIV patients in the United States. Medicine (Baltimore) 2016;95:e3171.
7. Tubiana R, Le Chenadec J, Rouzioux C, et al. Factors associated with mother-to-child transmission of HIV-1 despite a maternal viral load <500 copies/ml at delivery: A case-control study nested in the French perinatal cohort (EPF-ANRS CO1). Clin Infect Dis 2010;50:585–596.
8. Lazenby GB, Powell AM, Sullivan SA, Soper DE. The impact of delivery in a rural county on a cohort of women living with HIV infection and their infants. J Rural Health 2019;35:319–329.
9. Centers for Disease Control and Prevention. eHARS v4.7 Technical Reference Guide. In: National Center for HIV/AIDS VH, STD and TB Prevention Division of HIV/AIDS Prevention. Quantitative Sciences and Data Management Branch, ed. 2015.
10. Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission. Recommendations for use of antiretroviral drugs in pregnant HIV-1 infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States: United States Department of Health and Human Services. 2014.
11. Centers for Disease Control and Prevention. Revised surveillance case definition for HIV infection—United States, 2014. MMWR Recomm Rep 2014;63:1–10.
12. Llibre JM, Hung CC, Brinson C, et al. Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: Phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies. Lancet 2018;391:839–849.

Address correspondence to:
Gweneth B. Lazenby, MD MSCR
Division of Infectious Diseases
Departments of Obstetrics and Gynecology and Medicine
Medical University of South Carolina
96 Jonathon Lucas St CSB 628a
Charleston, SC 29425

E-mail: lazenbgb@musc.edu