

Follow-Up Care Among HIV-Infected Pregnant Women in Mississippi

Aadia I. Rana, M.D.,¹ Fizza S. Gillani, Ph.D.,¹ Timothy P. Flanigan, M.D.,¹
Binford T. Nash, M.D.,² and Curt G. Beckwith, M.D.¹

Abstract

Background: Data from the Centers for Disease Control and Prevention (CDC) indicate that reproductive-age black women in the Southeast are disproportionately affected by the HIV epidemic. There are few data describing HIV infection, pregnancies, and follow-up care in this population.

Methods: A retrospective chart review was performed at the Perinatal HIV Service at the University of Mississippi Medical Center in Jackson, Mississippi, to identify HIV-infected women ≥ 18 years of age with deliveries from 1999 to 2006. Optimal follow-up was defined as at least two follow-up visits with an HIV provider within 1 year of delivery. Univariate and multivariate logistic regression analyses were used to identify factors associated with optimal adherence.

Results: We identified 274 women with 297 total deliveries. Median age was 25, and 89% were black. Only 37% of women had two or more visits with an HIV provider in the postpartum year. On univariate analysis, presentation before the third trimester was associated with optimal follow-up ($p = 0.04$). On multivariate analyses, presentation before the third trimester was the only variable associated with optimal follow-up (odds ratio [OR] 2.1, $p = 0.02$).

Conclusions: The poor follow-up rates in this growing population highlight the critical need for research and development of targeted interventions to improve rates of retention in care, particularly in women with late trimester presentation.

Introduction

THE IMPACT OF HIV/AIDS among women has increased both in the United States and globally. Early in the epidemic, women represented $<10\%$ of the AIDS diagnoses in the United States; by 2007, the proportion increased to almost 30%.^{1,2} Heterosexual contact is the primary risk factor for HIV transmission in women, accounting for $>70\%$ of new AIDS cases.^{3,4} Black women disproportionately represent the majority of new HIV/AIDS cases among women. In 2007, whereas black women made up only 14% of the U.S. female population, they accounted for 66% of estimated AIDS cases among women.^{1,3,5} This disparity is particularly accentuated in the Southern United States, where black women accounted for approximately 75% of the 5000 AIDS cases in women in 2007.¹ Seven of the ten states with the highest AIDS case rates among women are in the South.¹ Access to early diagnosis of HIV and long-term medical care are often challenging in poor communities in the South, likely attributable to limited access to medical services and to HIV testing services secondary to

poverty and other factors.^{6,7} Prior studies indicate that HIV-infected women were more likely than men to report postponing medical care because of lack of transportation, illness, or other competing needs.⁷⁻¹¹

The majority of the estimated 120,000–160,000 HIV-infected women in the United States are of childbearing age, with >6000 HIV-infected women giving birth each year, yet this population has not been a focus of evaluation regarding morbidity related to HIV infection and the quality of HIV care.^{1,12} To investigate these issues, we conducted a retrospective review of HIV-infected pregnant women in Mississippi in order to assess HIV status at the time of pregnancy and longitudinal HIV care during the postpartum period.

Materials and Methods

A retrospective chart review was performed at the Perinatal HIV Service at the University of Mississippi Medical Center (UMMC) in Jackson, Mississippi, to identify HIV-infected women ≥ 18 years of age with deliveries from 1999 to

¹Warren Alpert Medical School at Brown University, Providence, Rhode Island.

²University of Mississippi Medical Center, Jackson, Mississippi.

2006 with at least one consult visit with the Perinatal HIV service before delivery. Three hundred nineteen charts were reviewed, and 274 met the inclusion criteria. The excluded charts were of women <18 years or those charts where only a phone consultation was performed by the Perinatal HIV Service. Data on the excluded charts were not collected.

Data on sociodemographics and HIV-related parameters were extracted from the medical charts into standardized data abstraction forms. Information on follow-up visits in the postpartum period was accessed through the database administered by the HIV/AIDS program at the UMMC Department of Medicine, which is used by 90% of the Ryan White C.A.R.E Act providers who administer HIV care in the state of Mississippi (Cheryl Hamill, personal communication). Sociodemographic and medical data, as well as outpatient and emergency room visits, are recorded in this database for any HIV-infected patient who has entered into care at the UMMC. Because the HIV-1 plasma viral load assay used in clinical care until mid-2005 had a limit of detection of <400 copies/mL, this was the cutoff value collected in the study for consistency in comparison. Substance abuse history, both current and prior, was per self-report data collected from the initial Perinatal HIV consultation visit form.

For the purposes of this analysis, optimal follow-up was defined as at least two follow-up visits with an HIV provider in the postpartum year. The demographic and clinical characteristics of the women with optimal follow-up were compared with those of women with inadequate follow-up (less than two visits during the 365 days after delivery) using the chi-square test. Univariate and multivariate logistic regression analyses were used to identify factors associated with optimal adherence. Covariates with $p < 0.10$ in the univariate analysis and other parameters of interest were included in the multivariate model. All covariates in the multivariate model with $p < 0.05$ were considered significant. Missing data were noted and accounted for in the analyses.

Results

There were 274 women with a total of 297 deliveries reviewed in this cohort (Table 1). The median age was 25 (range 18–42), and the population was overrepresented by racial minorities: 89% black, 11% white, and 2% Hispanic. Almost 40% did not complete high school ($n = 97$), and >60% were not employed upon entering care ($n = 129$). Rural residence, designated by living outside of a Metropolitan Statistical Area (MSA) at the time of delivery, was a characteristic of 48% of the women.¹³ Although specific data on income before the pregnancy were not available, the majority of these women (92%) were enrolled in Medicaid during their pregnancy, suggestive of lower socioeconomic status (SES).

The median time since HIV diagnosis at time of presentation was 2 years (range <1–17 years). Heterosexual transmission was the primary risk factor in 99% of the women in this cohort. In this cohort, 102 women (37%) were newly diagnosed with HIV during prenatal testing for a pregnancy included in this study. Of the women with previously diagnosed HIV, 51% tested positive during a prior prenatal screen. The state of Mississippi initiated opt-out prenatal HIV testing in late 1994 (Dr. Hannah Gay, personal communication); a study of one of the largest public obstetric clinics in the state reported a testing rate >99% using the opt-out method.¹⁴

TABLE 1. DESCRIPTIVE CHARACTERISTICS OF POSTPARTUM HIV-INFECTED WOMEN IN MISSISSIPPI, 1999–2006

Variable	Patients (n = 274 except where otherwise noted)
Total number of deliveries	297
Age, median years (range)	25 (18–42)
Race/ethnicity	
Black	244 (89%)
White	29 (11%)
Hispanic	5 (2%)
Native American	2 (1%)
High school/GED level of education, $n = 97$	58 (60%)
Not employed, $n = 120$	77 (64%)
Residing in rural area	131 (48%)
New HIV diagnosis during prenatal period	102 (37%)
Time since HIV diagnosis in years, median (range)	2 (<1–17)
Baseline CD4+ cell count, $n = 266$	
<200/mm ³	63 (24%)
200–350/mm ³	69 (26%)
≥ 350/mm ³	134 (50%)
Proportion undetectable HIV PVL at delivery, $n = 245$	66%
Presentation trimester, $n = 297$	
1	94 (32%)
2	132 (44%)
3	64 (22%)
Immediately before delivery	7 (2%)
Substance abuse	
During prenatal period	17%
Any history of substance abuse	23%
Depression	16%
Sexually transmitted illness (STI)	
During prenatal period, $n = 120$	26, 22%
Any history of STI	26%

PVL, plasma viral load.

Of the 195 women with known HIV before their pregnancy, only 80 had at least one documented visit with their established HIV provider in the year before pregnancy. Less than one quarter of these women (22%) were on antiretroviral therapy (ART) at their first prenatal consultation visit. The median CD4+ T cell count at the prenatal visit was 353 cells/ μ L (range 0–1396, $n = 266$), the median CD4+ cell count at delivery was 486 cells/ μ L (range 44–1254, $n = 153$), and the median HIV RNA plasma viral load (PVL) at delivery was 400 copies/mL (range 50–56,784, $n = 245$). Sixty-six percent of women had PVL below the limit of detection (<400 copies/mL) at the time of delivery. No significant differences were observed in immunologic and virologic parameters between women who were newly diagnosed with HIV and those who were previously diagnosed and became pregnant. There were no reported opportunistic infections during the course of the pregnancy in these women, and a previous history of an opportunistic infection was rare (5%).

Medical comorbidities were common in this population at the time of prenatal evaluation, including sexually transmitted infection (STI) in the prenatal period (22%), depression (16%), and substance abuse (23%). Forty-six women (17%)

TABLE 2. VARIABLES OF INTEREST FOR UNIVARIATE AND MULTIVARIATE ANALYSIS IN PREDICTORS OF OPTIMAL FOLLOW-UP CARE

Sociodemographic	Age: 18–24 (young age), 25–32 (median), >33 (older age) Race: White, black, Native American Metropolitan Statistical Area (MSA) residence vs. non-MSA Employment (employed vs. nonemployed) Education (grade school vs. GED equivalent or higher)
HIV related	New vs. prior HIV diagnosis CD4+ T cell/ μ L: <200, 200–350, >350 History of opportunistic infection Use of HAART before pregnancy Indication for HAART in postpartum period Having a primary care provider before pregnancy (HIV or otherwise)
Pregnancy related	Presentation trimester: Early (1st or 2nd) vs. late (3rd) Number of pregnancies (≤ 2 , ≥ 3) Number of alive children (≤ 2 , ≥ 3) ¹⁰
Other medical history	Smoking history Substance abuse history (alcohol or any illicit drug use) Other medical history (diabetes, asthma) Psychiatric diagnoses ² Sexually transmitted illness history

HAART, highly active antiretroviral therapy.

reported substance abuse, with the most common being crack/cocaine, marijuana, and alcohol. Of the 135 women with Papanicolaou smear results during their pregnancy, 11 (8%) had atypical cells of undetermined significance (ASCUS), 26 (19%) had low-grade squamous intraepithelial lesions, and 8 (6%) had high-grade squamous intraepithelial lesions. There were no reports of cervical carcinoma in these women.

The majority of the women (76%) received their first consult with the Perinatal HIV Service during either the first or second trimester of pregnancy; 24% appear in the third trimester, with 7 women coming at the time of delivery. For the 160 women for whom planned postpartum contraception information was available, 72% planned for bilateral tubal ligation, 20% preferred hormonal contraception, and 9% indicated reliance on barrier methods.

Only 109 (37%) of the women had optimal HIV follow-up, defined as at least two visits with an HIV provider in the year after delivery, 52 women (18%) had only one visit, 85 women (29%) had no documented visits, and for 51 women (17%), follow-up visit information was unknown. Factors evaluated on univariate analysis included race, ethnicity, transmission risk, rural residence, education, new HIV diagnoses, CD4+ T cell count, history of opportunistic infection, use of highly active antiretroviral therapy (HAART) before pregnancy, indication for HAART in the postpartum period, number of pregnancies, number of living children, smoking history, substance abuse history, psychiatric diagnoses, or history of an STI (Table 2). Only early presentation trimester, defined as first or second trimester presentation ($p = 0.04$) was significant on univariate analysis. On multivariate analysis, age, employment, and presentation trimester were included in the model (Table 3). Early presentation trimester was again the only variable significantly associated with optimal follow-up (odds ratio [OR] 2.1, $p = 0.02$) (Table 3).

Further analysis to better define women with early presentation trimester found that these women were more likely to be nonblack ($p = 0.02$), aged 25–32 ($p = 0.04$), have an established HIV primary care provider ($p = 0.003$), and carry

another non-HIV-related diagnosis, medical ($p = 0.002$) or psychiatric ($p = 0.03$) (Table 4).

There were two cases of mother-to-child transmission of HIV in this cohort.

Discussion

The women of this cohort were young and black and exhibited similar sociodemographic characteristics to HIV-infected women in the South, as previously reported.^{6,7} Over three quarters of the women in this cohort were diagnosed

TABLE 3. FACTORS ASSOCIATED WITH OPTIMAL FOLLOW-UP CARE ON UNIVARIATE AND MULTIVARIATE ANALYSES

Variable	OR (95% CI)	p value
Univariate analyses		
Age		
18–24	1.7 (0.8-3.3)	0.07
25–32	1.1 (0.5-2.2)	0.49
>33		
Presentation trimester		
1 or 2	2.1 (1.1-3.9)	0.04
3		
Prior HIV care provider	1.6 (0.9-2.8)	0.09
Employment (negative predictor)	0.4 (0.1-1.1)	0.07
Multivariate analyses		
Presentation trimester		
1st/2nd	2.09 (1.1-3.9)	0.02
3rd/delivery		

A p value <0.10 was considered significant for the univariate analyses.

Factors not significantly associated with follow-up care on univariate analyses or multivariate analyses included race, ethnicity, transmission risk, rural residence, education, new HIV diagnoses, CD4+ T cell count, history of opportunistic infection, use of HAART before pregnancy, indication for HAART in the postpartum period, number of pregnancies, number of living children, smoking history, substance abuse history, psychiatric diagnoses, or history of a sexually transmitted illness.

TABLE 4. FACTORS ASSOCIATED WITH EARLY PRESENTATION TRIMESTER

Factor	Early presentation		p value
	Yes (n = 226)	No (n = 71)	
Age			
18–24	69%	30%	0.04
25–32	83%	16%	
>33	73%	26%	
Race			0.04
Black	74%	25%	0.003
Nonblack	90%	10%	
Prior HIV provider			0.002
Yes	89%	11%	0.03
No	71%	28%	
Other medical diagnosis			0.002
Yes	90%	10%	0.03
No	71%	29%	
Psychiatric diagnosis			0.03
Yes	87%	13%	0.03
No	73%	27%	

Early presentation trimester is defined as presentation for HIV care before the third trimester of pregnancy.

with HIV during the prenatal period. These findings strongly support routine opt-out testing strategies for women seeking prenatal care.^{15,16} These findings also suggest a need to broaden community-based HIV testing programs, with the goal of identifying HIV infection before a woman becomes pregnant. The relative immune preservation (median CD4+ T cell count at presentation = 357) of this cohort of pregnant women is likely due to early identification of HIV infection through prenatal screening. Supporting this, there was a low rate of opportunistic infections among this cohort. Similar findings have been reported elsewhere.¹⁷

The most significant finding from this study was the low rate of HIV follow-up care after delivery. Only 37% of these women had two or more documented visits with an HIV provider in 1 year, which is less frequent than what is recommended as the standard of longitudinal care.¹⁸ Many of these women have low incomes, with likely limited health literacy, and may have competing responsibilities, such as employment, complicating the management of their illness and contributing to the low rates of follow-up. Previous research, including the HIV Cost and Services Utilization Study (HSCUS) and Women's Interagency HIV Study, has found that women with HIV were more likely to have a low income, less likely to receive combination antiretroviral therapy, and more likely to postpone care because of transportation issues or illness. They may also have more competing factors, such as child care, which may complicate their ability to manage their own illness.^{9–11,19–21} Our study found an association of employment with suboptimal follow-up rates.

The women seeking care in the third trimester were more likely to have suboptimal follow-up postpartum. They were more likely to be black and younger, not have a primary care provider, and carry a non-HIV-related diagnosis. These data are likely reflective of lack of access to healthcare before presentation. This cohort of women would most

benefit from targeted interventions to improve their longitudinal HIV care.

It is possible that HIV-infected postpartum women are more likely to successfully engage in longitudinal care compared with HIV-infected women who are not pregnant because of their ongoing engagement with obstetric healthcare providers, familiarity with antiretroviral medications, and an overall higher level of health literacy with respect to HIV infection because of education received during the pregnancy. Recent studies from South Africa, however, indicate that pregnant women are more likely to be lost to follow-up (LTFU) compared with their nonpregnant counterparts.^{22,23} One study comparing LTFU rates over 3 years between pregnant and nonpregnant women who were referred to an antiretroviral treatment center found that pregnant women had higher LTFU, and this continued throughout the follow-up period. This suggests that influences affecting follow-up extend beyond the immediate postpartum period. Clinical trials in the United States of pregnant HIV-infected women on antiretroviral therapy who were followed short term postpartum also found decreases in adherence to therapy.^{24,25} Further research is needed to elucidate these factors that decrease adherence with care and antiretroviral therapy in this population.

There were some limitations to this study. This was a homogeneous population of black women in a lower SES who primarily acquired HIV through heterosexual transmission. Although the findings of this study may not be generalizable to a larger HIV-infected population, the characteristics of these women are likely to be similar to those of other women in the Southern United States.^{1,7}

Given that this study was a retrospective clinical chart review, there were missing data on certain variables. Clinical staging of HIV was not recorded in the clinical charts, therefore could not be included in analysis. Although all women had a CD4+ T cell count checked at least once during the pregnancy, only 153 women had a CD4+ T cell count within 3 months of delivery for inclusion in the analysis. More detailed collection of infant follow-up and outcome data would have been helpful to assist in determining a correlation between infant care and mother's postpartum care. However, the IRB-approved protocol did not include collection of infant data. We did not include comparison follow-up data for women who were <age 18 at the time of delivery or women who did not have a consult visit with the Perinatal HIV Service before delivery. This would have provided important descriptive information on a subgroup that is even less likely to engage in longitudinal HIV care.

According to the Mississippi Department of Health, there were 14 mother-to-child transmissions during the time period of this study (1999–2006). However, of these 14, only 2 were from women who were seen in consultation at least once by the Perinatal HIV Service before delivery and, therefore, fulfilled the inclusion criteria for this retrospective review. The remaining women did not have any prenatal HIV care through the Perinatal HIV Service.

In addition, some of the records with missing follow-up data may represent women who sought care outside of the UMMC, which may underestimate the true rate of follow-up with HIV care. However, the database is a statewide database that collects information on outpatient visits to the majority of the state's HIV providers. Moreover, even if an assumption was made placing all women in unknown status into the

optimal category, there would still be a disappointing follow-up rate of 46% during the postpartum year.

Our study demonstrated low rates of longitudinal follow-up in this population of HIV-infected postpartum women in the South. Poverty, lack of access to medical care, and competing responsibilities may contribute to these rates, but there is a dire need for further research to ascertain barriers to care in this population. This study supports the development and implementation of novel interventions during the prenatal period to retain these marginalized patients in longitudinal HIV care. Our findings suggest that such interventions would be of most benefit to those women who seek HIV care after 24 weeks gestation, as they are at particularly high risk for inadequate follow-up.

Acknowledgments

We thank the staff of the University of Mississippi Medical Center Perinatal HIV Service for their assistance. This study was supported by the Lifespan/Tufts/Brown Center for AIDS Research (P30AI042853), the National Institute for Drug Abuse (P30DA013868 to T.P.F.), and a Bristol Myers Squibb Virology Fellows Research Program grant (A.I.R.). C.G.B is supported by the National Institute on Drug Abuse (K23DA021095) and has received recent research funding from Gilead Sciences, Inc.

Disclosure Statement

The authors have no conflicts of interest to report.

References

1. CDC. HIV/AIDS surveillance report, 2006. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2008.
2. UNAIDS. 2008 report on the global AIDS epidemic, 2008. Available at www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/
3. CDC slide set: AIDS surveillance—Trends (1985–2006), 2008. Available at www.cdc.gov/hiv/topics/surveillance/resources/slides/trends/index.htm
4. CDC slide set: HIV/AIDS surveillance in women (through 2006), 2008. Available at www.cdc.gov/hiv/topics/surveillance/resources/slides/women/index.htm
5. U.S. Census population estimates program, 2006 population estimates, 2007. Available at www.census.gov/popest/archives/2000s/vintage_2006/
6. Gay CL, Napravnik S, Eron JJ Jr. Advanced immunosuppression at entry to HIV care in the southeastern United States and associated risk factors. *AIDS* 2006;20:775–778.
7. Holmes R, Fawal H, Moon TD, et al. Acquired immunodeficiency syndrome in Alabama: Special concerns for black women. *South Med J* 1997;90:697–701.
8. McNaghten A, Hanson D, Aponte Z, Sullivan P, Wolfe M. Gender disparity in HIV treatment and AIDS opportunistic illnesses (OI). In: XV International Conference on AIDS, Bangkok, Thailand, 2004.
9. Cunningham WE, Andersen RM, Katz MH, et al. The impact of competing subsistence needs and barriers on access to medical care for persons with human immunodeficiency virus receiving care in the United States. *Med Care* 1999;37:1270–1281.
10. Merenstein DJ, Schneider MF, Cox C, et al. Association between living with children and adherence to highly active antiretroviral therapy in the Women's Interagency HIV Study. *Pediatrics* 2008;121:e787–793.
11. Schuster MA, Kanouse DE, Morton SC, et al. HIV-infected parents and their children in the United States. *Am J Public Health* 2000;90:1074–1081.
12. CDC quick facts: Perinatal, April 2003–March 2005, 2005. Available at www.cdc.gov/hiv/topics/prev_prog/AHP/resources/factsheets/QF_Perinatal.htm
13. U.S. Census Bureau. Metropolitan and Micropolitan Statistical Areas, 2008. Available at <http://www.census.gov/population/www/metroareas/metrodef.html>
14. Ross EL, Morrison JC. Screening for human immunodeficiency virus infection during pregnancy. *Pediatr AIDS HIV Infect* 1997;8:12–14.
15. Mississippi: HIV AIDS. Available at www.statehealthfacts.org Accessed March 1, 2009.
16. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006;55:1–17.
17. Martin F, Navaratne L, Khan W, et al. Pregnant women with HIV infection can expect healthy survival: Three-year follow-up. *J Acquir Immune Defic Syndr* 2006;43:186–192.
18. Aberg JA, Gallant JE, Anderson J, et al. Primary care guidelines for the management of persons infected with human immunodeficiency virus: Recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis* 2004;39:609–629.
19. Bozzette SA, Berry SH, Duan N, et al. The care of HIV-infected adults in the United States. HIV Cost and Services Utilization Study Consortium. *N Engl J Med* 1998;339:1897–1904.
20. Shapiro MF, Morton SC, McCaffrey DF, et al. Variations in the care of HIV-infected adults in the United States: Results from the HIV Cost and Services Utilization Study. *JAMA* 1999;281:2305–2315.
21. Fleishman JA, Gebo KA, Reilly ED, et al. Hospital and outpatient health services utilization among HIV-infected adults in care 2000–2002. *Med Care* 2005;43:III40–52.
22. Kaplan R, Orrell C, Zwane E, Bekker LG, Wood R. Loss to follow-up and mortality among pregnant women referred to a community clinic for antiretroviral treatment. *AIDS* 2008;22:1679–1681.
23. Wang B, Losina E, Stark R, Munro A, Wilk M, Martin D. Loss to follow-up in community clinics in South Africa: Role of CD4 count, gender, and pregnancy. In: Fifteenth Conference on Retroviruses and Opportunistic Infections, Boston, 2008.
24. Mellins CA, Chu C, Malee K, et al. Adherence to antiretroviral treatment among pregnant and postpartum HIV-infected women. *AIDS Care* 2008;20:958–968.
25. Bardeguet AD, Lindsey JC, Shannon M, et al. Adherence to antiretrovirals among U.S. women during and after pregnancy. *J Acquir Immune Defic Syndr* 2008;48:408–417.

Address correspondence to:
Aadia I. Rana, M.D.
The Miriam Hospital
164 Summit Avenue
Building 1125
Providence, RI 02906

E-mail: aadiarana@gmail.com
arana@lifespan.org

