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Dramatic decline in substance use by HIV-infected pregnant women in the United States from 1990–2012

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Abstract

Objective—We aimed to describe temporal changes in substance use among HIV-infected pregnant women in the US from 1990–2012.

Design—Data came from two prospective cohort studies (Women and Infants Transmission Study and Surveillance Monitoring for Antiretroviral Therapy Toxicities Study).

Methods—Women were classified as using a substance during pregnancy if they self-reported use or had a positive biological sample. To account for correlation between repeated pregnancies by the same woman, GEE models were used to test for temporal trends and evaluate predictors of substance use.

Results—Over the 23-year period, substance use among the 5,451 HIV-infected pregnant women sharply declined; 82% of women reported substance use during pregnancy in 1990, compared to 23% in 2012. Use of each substance decreased significantly ($p < 0.001$ for each substance) in an approximately linear fashion, until reaching a plateau in 2006. Multivariable models showed substance use was inversely associated with receiving antiretroviral therapy. Among the subset of 824 women with multiple pregnancies under observation, women who used a

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Contributions: K.R. and G.R.S. were the primary authors who conceived and designed the study. K.R. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. K.R. was responsible for conducting statistical analyses, and led the writing of the manuscript. G.R.S., K.C.R., R.Y., D.K., K.T., and R.G. provided leadership and oversight of the SMARTT study. All authors provided input on the study design, interpretation of analyses, and revisions to manuscript.

substance in their previous pregnancy were at elevated risk of substance use during their next pregnancy (RR, 5.71; 95% CI, 4.63–7.05).

Conclusions—A substantial decrease in substance use during pregnancy was observed between 1990 and 2012 in two large US cohorts of HIV-infected women. Substance use prevalence in these cohorts became similar to that of pregnant women in the general US population by the mid-2000s, suggesting that the observed decrease may be due to an epidemiological transition of the HIV epidemic among women in the US.

Keywords

HIV; Substance Abuse; Pregnancy; Epidemiology

INTRODUCTION

Approximately 8,700 HIV-infected women give birth in the US annually [1, 2]. Rates of substance use in this population have historically been high; in the late 1980s and early 1990s, half of HIV-infected pregnant women used illicit substances [3, 4]. Substance use during pregnancy in HIV-infected women has negative implications for transmission [5–8], infant outcomes [9–19], and the health of the mother [20].

Over time, the route of HIV acquisition among women has changed in the US. While approximately 50% of female AIDS cases were linked to injection drug use in 1990 [21], by 2011, it was the suspected source of infection in only 14% of HIV diagnoses among females [22]. However, to our knowledge, no studies have examined substance use patterns in HIV-infected pregnant women over the last two decades.

Using data from two large US-based cohorts, we describe the dramatic decrease in maternal substance use during pregnancy from 1990 to 2012 among HIV-infected women, and explore possible explanations for the decrease.

METHODS

Study participants and design

This study included women enrolled in the Women and Infants Transmission Study (WITS) or the Surveillance Monitoring for ART Toxicities (SMARTT) protocol of the Pediatric HIV/AIDS Cohort Study (PHACS). WITS enrolled women who gave birth from 1990 to 2005 [23], while SMARTT is ongoing, with the first delivery occurring in 1995 [24]. In WITS/SMARTT, written informed consent was obtained from each participating woman, and the institutional review board at each study center approved study protocols.

In WITS, women had multiple study visits during pregnancy. In SMARTT, two groups of women and children (dynamic and static) were enrolled. In the dynamic cohort, women were enrolled during pregnancy through 72 hours post-delivery. The static cohort enrolled women with children aged 0–12 years. For both WITS and SMARTT, trained study personnel conducted structured interviews at enrollment to assess demographic characteristics.

Women were eligible for this study if they were enrolled in WITS/SMARTT, gave birth from January 1, 1990 to December 31, 2012, and provided self-reported information on substance use during pregnancy.

Substance use

In WITS, a questionnaire was administered at each pre-delivery visit to ascertain use of alcohol, tobacco, marijuana, heroin, cocaine, and injected drugs during pregnancy. One urine sample for drug testing was collected at the intake visit and one was collected during labor or immediately postpartum. Urine was screened for cocaine, heroin/opiates, marijuana, alcohol or their metabolites using a radioimmunoassay followed by confirmatory gas chromatography and mass spectrometry [7].

Women in dynamic SMARTT completed a substance use interview within seven days of delivery, and women in static SMARTT completed this interview at time of enrollment (Median=3.7 years after pregnancy, IQR=1.8–6.2 years). In a subsample of the dynamic cohort, meconium – an infant's first stool – was collected and screened for cocaine, heroin/opiates, marijuana, alcohol, tobacco, or their metabolites using an immunoassay technique followed by confirmatory gas chromatography and mass spectrometry [25].

Women were classified as using a substance if they self-reported or had a positive biological sample for alcohol, tobacco, marijuana, cocaine, or heroin during pregnancy. Poly-substance use was defined as using two or more substances during pregnancy.

Statistical methods

The proportion of women in each substance use category was calculated, stratified by year of delivery. To test whether the proportion of women using substances during pregnancy changed over time while accounting for correlation between repeated pregnancies, we used log binomial generalized estimating equation (GEE) models. Because meconium samples were not available for all SMARTT participants, we conducted two sensitivity analyses; the first included only WITS pregnancies, while the second also included the SMARTT pregnancies with meconium data.

Multivariable logistic GEE models were constructed to evaluate predictors of substance use in the pre-highly active ART (HAART) (1990–1995) and HAART (1996–2012) eras. These models included: race/ethnicity, age, education, household income, marital status, HIV diagnosis prior to pregnancy, and antiretroviral therapy regimen.

To evaluate trends within individuals, log binomial GEE models were used in the subset of women with multiple pregnancies under observation in WITS/SMARTT.

We compared substance use prevalence in WITS/SMARTT to use among pregnant women in a nationally representative household survey, the National Survey on Drug Use and Health (NSDUH). In NSDUH, substance use during pregnancy is defined as self-report of past 30-day substance use and being pregnant. We compared WITS/SMARTT and NSDUH beginning in 1994 [26–44], the first year NSDUH collected data on pregnancy.

All analyses were performed in SAS version 9.2 (SAS Institute Inc, Cary, NC).

RESULTS

Of the 5,724 pregnancies in WITS/SMARTT, we excluded 233 because self-reported substance use information was unavailable and 40 because delivery year was unknown. Therefore, a total of 5,451 pregnancies from 4,408 individual women were included in this analysis. Maternal characteristics for each pregnancy are described in Table 1.

Nearly 82% of respondents used at least one substance in 1990; this proportion decreased linearly over time until 2006, when it plateaued at approximately 23% (Figure 1). A similar pattern was observed for each individual substance over the 23-year period. The prevalence of tobacco use decreased from 64.9% to 18.2%; alcohol from 57.4% to 9.3%; marijuana from 25.5% to 6.7%; cocaine from 36.2% to 1.3%; and heroin from 27.7% to 0.0%. The prevalence of injection drug use declined from a peak of 17.1% in 1991 to 0.0%, and poly-substance use fell from 64.9% in 1990 to approximately 10% from 2007 onwards (data not shown).

All decreases were statistically significant. Each year, risk of substance use among HIV-infected pregnant women decreased by 6%, on average (RR, 0.94; 95% CI, 0.94–0.95). The largest reductions in risk over the 23-year period were for injection drugs (RR, 0.80; 95% CI, 0.77–0.83), heroin (RR, 0.87; 95% CI, 0.85–0.88), and cocaine (RR, 0.87; 95% CI, 0.86–0.88). The smallest reductions in risk were for marijuana (RR, 0.94; 95% CI, 0.93–0.96) and tobacco (RR, 0.94; 95% CI, 0.94–0.95). Both sensitivity analyses produced estimates comparable to those presented above.

In the pre-HAART and HAART eras, multivariable models showed non-Hispanic white race, older age, less education, and being unmarried were associated with substance use during pregnancy (Table 1). In the pre-HAART era, not receiving any antiretroviral therapy was associated with substance use (OR, 1.50; 95% CI, 1.15–1.95). Similarly, in the HAART era, women receiving no antiretroviral therapy (OR, 2.12; 95% CI, 1.54–2.92), AZT monotherapy (OR, 2.37; 95% CI, 1.88–2.98), or another non-HAART antiretroviral therapy (OR, 1.34; 95% CI, 1.11–1.61) had greater odds of substance use, compared to women receiving HAART.

Of the 4,408 women included in the previous analysis, 824 had multiple pregnancies under study observation. For most substances, the risk of a woman using the substance did not change with successive pregnancies; the association between pregnancy order and use of tobacco, marijuana, cocaine, heroin, any substance, multiple substances, or injected drugs was not statistically significant. Risk of alcohol use was slightly reduced in later pregnancies (RR, 0.91; 95% CI, 0.82–1.00). Of note, women who used a substance in their previous pregnancy had an elevated risk of substance use during their next pregnancy (RR, 5.71; 95% CI, 4.63–7.05).

We compared annual prevalence of alcohol, tobacco, marijuana, cocaine, and heroin use during pregnancy among HIV-infected women in WITS/SMARTT to estimates from NSDUH (see Figures, Supplemental Digital Content 1). From 1994 through the early 2000s,

use of these substances was substantially higher among women in WITS/SMARTT, compared to pregnant women in the general population. However, from the mid-2000s through 2012, prevalence of substance use appears comparable between the two groups.

DISCUSSION

We describe the substantial decline in licit and illicit substance use during pregnancy that occurred between 1990 and 2012 in a population of two US-based cohorts of HIV-infected women. While the prevalence of substance use was initially considerably higher in WITS/SMARTT, it has become similar to that of pregnant women in the general US population.

Women who used substances in previous pregnancies had over a 5-fold increased risk of using a substance in future pregnancies. Therefore, we posit that the observed decrease in substance use is not due to the cessation of substance use in women who previously used substances, but rather, HIV is affecting a different population of women. It is possible that an epidemiological transition has occurred, in which the types of women becoming infected with HIV in the US has changed. This is supported by data from the Centers for Disease Control and Prevention, which show that the primary route of infection among women has gradually transitioned from injection drug use to heterosexual contact [21, 22].

We observed that substance use is inversely associated with receiving antiretroviral therapy in pregnant woman, consistent with a past study of HIV-infected adults [45]. Others have reported current injection drug users were less likely than past users to receive antiretroviral therapy [46], and substance users not enrolled in treatment programs were less likely to receive antiretroviral therapy than those receiving treatment [47]. Because substance use is inversely associated with antiretroviral therapy and a number of potential outcomes, it may be an important confounder in antiretroviral safety studies, especially those using historical comparison data.

Our study has several limitations. First, our sample may not represent the larger population of HIV-infected women who gave birth from 1990–2012. Second, different biological specimens were used to confirm substance use in each cohort. Urine- and meconium-based tests have varying sensitivity, specificity, and windows of detection [48–50]. Third, only 22% of women in SMARTT had meconium samples analyzed for substances, and some women in the static SMARTT cohort had long recall periods. However, restricting our analysis to women with available biological assays suggest that our findings are not explained by recall or social desirability bias. Furthermore, past analyses of the dynamic SMARTT cohort have shown reliable sensitivity and specificity of self-reported substance use compared to biological measures [25]. Fourth, NSDUH's classification of substance use during pregnancy (being pregnant and using a substance in the past month) differs from that of WITS and SMARTT, and was not confirmed by biological assays, meaning data from NSDUH in the Supplemental Digital Content may be underestimated. Finally, this analysis could not investigate temporal trends in prescription opioids, as WITS did not collect necessary information. However, few women in SMARTT (4.4%) reported medical or non-medical use of prescription opioids during pregnancy.

This study provides important information about temporal trends in substance use among HIV-infected pregnant women in the US. We documented a dramatic decrease in prevalence of substance use during pregnancy since 1990, which may be due to a shift in the HIV epidemic among women in the US. The finding that substance use during pregnancy has historically been associated with lack of antiretroviral use is concerning and may warrant further investigation. Our observation that HIV-infected women who used substances in past pregnancies are at increased risk of use during future pregnancies suggests they may be important to target in efforts to further reduce substance use in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

The following institutions, clinical site investigators and staff participated in conducting PHACS SMARTT in 2012, in alphabetical order: **Baylor College of Medicine:** William Shearer, Mary Paul, Norma Cooper, Lynette Harris; **Bronx Lebanon Hospital Center:** Murli Purswani, Emma Stuard, Anna Cintron; **Children's Diagnostic & Treatment Center:** Ana Puga, Dia Cooley, Doyle Patton, Deyana Leon; **Ann & Robert H. Lurie Children's Hospital of Chicago:** Ram Yogev, Margaret Ann Sanders, Kathleen Malee, Scott Hunter; **New York University School of Medicine:** William Borkowsky, Sandra Deygoo, Helen Rozelman; **St. Jude Children's Research Hospital:** Katherine Knapp, Kim Allison, Megan Wilkins; **San Juan Hospital/Department of Pediatrics:** Midnela Acevedo-Flores, Lourdes Angeli-Nieves, Vivian Olivera; **SUNY Downstate Medical Center:** Hermann Mendez, Ava Dennie, Susan Bewley; **Tulane University Health Sciences Center:** Russell Van Dyke, Karen Craig, Patricia Sirois; **University of Alabama, Birmingham:** Marilyn Crain, Newana Beatty, Dan Marullo; **University of California, San Diego:** Stephen Spector, Jean Manning, Sharon Nichols; **University of Colorado Denver Health Sciences Center:** Elizabeth McFarland, Emily Barr, Robin McEvoy; **University of Florida/Jacksonville:** Mobeen Rathore, Kristi Stowers, Ann Usitalo; **University of Illinois, Chicago:** Kenneth Rich, Lourdes Richardson, Delmyra Turpin, Renee Smith; **University of Medicine and Dentistry of New Jersey:** Arry Dieudonne, Linda Bettica, Susan Adubato; **University of Miami:** Gwendolyn Scott, Claudia Florez, Elizabeth Willen; **University of**

Southern California: Toinette Frederick, Mariam Davtyan, Maribel Mejia; **University of Puerto Rico Medical Center:** Zoe Rodriguez, Ibet Heyer, Nydia Scalley Trifilio.

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Figure 1.
Proportion of HIV-Infected Women Using Substances during Pregnancy, by Delivery Year
(N = 5,451)

Table 1

Maternal Characteristics of Eligible WITS/SMARTT Pregnancies* and Odds Ratios of Substance Use during Pregnancy (Multivariable Model)

	WITS/SMARTT Demographics N = 5,451		Multivariable Predictive Model*			
	n	%	Pre-HAART era [†] n = 1,191		HAART era [‡] n = 3,913	
			Odds Ratio	95% CI	Odds Ratio	95% CI
Race/ethnicity						
Black/African American	2,974	54.6%	0.42	(0.28, 0.64)	0.36	(0.28, 0.46)
Hispanic	1,734	31.8%	0.38	(0.24, 0.59)	0.33	(0.25, 0.42)
White	657	12.1%			Ref	
Not available	86	1.6%				
Age						
15–21	820	15.0%	Ref		Ref	
22–34	3,681	67.5%	3.84	(2.60, 5.66)	1.50	(1.24, 1.82)
35–47	786	14.4%	4.89	(2.78, 8.61)	1.86	(1.45, 2.38)
Not available	164	3.0%				
Education						
Less than High School	2,107	38.7%	2.45	(1.82, 3.31)	1.39	(1.20, 1.62)
High School grad or above	3,292	60.4%	Ref		Ref	
Not available	52	1.0%				
Yearly household income						
Less than \$20,000	3,929	72.1%	Ref		Ref	
\$20,000–\$40,000	738	13.5%	0.84	(0.53, 1.34)	0.74	(0.61, 0.90)
\$40,000 or more	248	4.5%	0.77	(0.29, 2.04)	0.78	(0.56, 1.10)
Not available	536	9.8%	1.87	(0.67, 1.69)	0.85	(0.68, 1.07)
Marital status						
Married	1,409	25.8%	Ref		Ref	
Unmarried	4,007	73.5%	1.58	(1.16, 2.15)	1.96	(1.66, 2.33)
Not available	35	0.6%				
HIV diagnosis during pregnancy						
Diagnosed before pregnancy	3,265	59.9%	Ref		Ref	
Diagnosed during pregnancy	1,329	24.4%	0.63	(0.48, 0.82)	0.88	(0.74, 1.05)
Not available	857	15.7%	n/a	--	0.55	(0.47, 0.65)
ART use during pregnancy [§]						
No ART	805	14.8%	1.50	(1.15, 1.95)	2.12	(1.54, 2.92)
Any ART	--	--	Ref		n/a	--
AZT monotherapy	1,020	18.7%		--	2.37	(1.88, 2.98)
Other ART regimen	599	11.0%		--	1.34	(1.11, 1.61)
HAART	2,977	54.6%		--	Ref	
Not available	50	0.9%				

Abbreviations: HIV, human immunodeficiency virus; WITS, Women and Infants Transmission Study; SMARTT, Surveillance Monitoring for Antiretroviral Therapy Toxicities Study; ART, antiretroviral therapy; AZT, zidovudine; HAART, highly active antiretroviral therapy

Note: Pregnancies with missing covariate information were excluded from the multivariable model

* Maternal characteristics are listed separately for each pregnancy; 824 women had multiple pregnancies under study observation

[†] Deliveries in the “pre-HAART era” occurred between 1990 and 1995

[‡] Deliveries in the “HAART era” occurred between 1996 and 2012

[§] Most potent antiretroviral therapy regimen used during pregnancy for more than 2 weeks