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Perinatal Depressive Symptoms in HIV-Infected Versus HIV-Uninfected Women: A Prospective Study from Preconception to Postpartum

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Abstract

Objective: Depression is common among HIV-infected women, predicts treatment nonadherence, and consequently may impact vertical transmission of HIV. We report findings from a study evaluating preconception, pregnancy, and postpartum depressive symptoms in HIV-infected vs. at-risk, HIV-uninfected women.
Methods: We examined the prevalence and predictors of elevated perinatal (i.e., pregnancy and/or postpartum) depressive symptoms using a Center for Epidemiological Studies-Depression (CES-D) scale score of ≥16 in 139 HIV-infected and 105 HIV-uninfected women (62% African American) from the Women's Interagency HIV Study (WIHS).
Results: The prevalence of elevated perinatal depressive symptoms did not differ by HIV serostatus (HIV-infected 44%, HIV-uninfected 50%, $p = 0.44$). Among HIV-infected women, the strongest predictor of elevated symptoms was preconception depression (odds ratio [OR] 5.71, 95% confidence interval [CI] 2.67-12.19, $p < 0.001$); crack, cocaine, and/or heroin use during preconception was marginally significant (OR 3.10, 95% CI 0.96-10.01, $p = 0.06$). In the overall sample, additional significant predictors of perinatal depression included having multiple sex partners preconception (OR 2.20, 95% CI 1.12-4.32, $p = 0.02$), use of preconception mental health services (OR 2.51, 95% CI 1.03-6.13, $p = 0.04$), and not graduating from high school (OR 1.92, 95% CI 1.06-3.46, $p = 0.03$).
Conclusions: Elevated perinatal depressive symptoms are common among HIV-infected and at-risk HIV-uninfected women. Depressive symptoms before pregnancy were the strongest predictor of perinatal symptoms. Findings underscore the importance of early and ongoing assessment and treatment to ensure low vertical transmission rates and improving postpregnancy outcomes for mothers and children.

Introduction

Psychiatric illnesses, in particular mood disorders, commonly co-occur with the human immunodeficiency virus (HIV).[1–4] Numerous studies report high rates of depression and depressive symptoms in HIV-infected individuals compared to uninfected individuals in the general population, and the rates have been reported to be significantly higher in women than in men.[5] The relationship between depression and HIV infection is clinically important

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because the co-occurrence of the two conditions provides an additional health burden and can contribute to poor treatment adherence in women[6,7] and thereby affect disease progression, viral suppression, and survival.[8–11] For example, the Women's Interagency HIV Study (WIHS), a large multicenter investigation of 3766 women, found that in analyses adjusting for possible confounding factors, HIV-infected women with high levels of depressive symptoms were significantly less likely to be on highly active antiretroviral therapy (HAART) regimens.[6] Depressive symptoms in HIV-infected women are associated with substance use, including the use of crack, cocaine, heroin, and amphetamines,[7] and injected drugs.[12] Depression in HIV-infected women has also been shown to be related to AIDS-related mortality,[13] social and economic adverse events, and risk-taking behaviors, such as an increased number of sexual partners.[12] Other predictors of depressive symptoms in HIV-infected women include low income, less than a high school education, and Hispanic ethnicity.[12] Taken together, these findings suggest that reducing depressive symptoms in HIV-infected women may contribute to increased medication adherence, improved health, and a reduction in drug use and other maladaptive behaviors.

Despite a wealth of knowledge about factors related to depression and depressive symptoms in HIV-infected women, little is known about the prevalence of and risk factors for perinatal depression symptoms in this high-risk population. Perinatal depression encompasses major and minor depressive episodes that occur during pregnancy or within 1 year after childbirth. Prevalence estimates of perinatal depression in the general population range from 8.5% to 11% during pregnancy and from 6.5% to 12.9% during the first year postpartum depending on the assessment method (i.e., self-report measures, clinical interview), timing of the assessment (i.e., first, second, or third trimester of pregnancy or number of weeks after delivery), and population characteristics.[14] Depressive symptoms that occur during this specific reproductive time are a serious mental health problem in the general population, and the consequences have critical implications for the mother; mother-infant relationship[15]; the emotional, behavioral, and cognitive development of the child[16,17]; and marital and family relationships.[18] Early diagnosis and treatment interventions are critical to ensure the welfare of the mother, child, and family.

Only a few studies have examined the prevalence and risk factors of perinatal depression in high-risk populations, such as HIV-infected women and at-risk HIV-uninfected women. To our knowledge, only one study has examined the rate of perinatal depression among HIV-infected women. That study was a retrospective cohort design and involved 273 predominantly minority HIV-infected women from Los Angeles between 1997 and 2006.[19] Perinatal depression was based on medical records or multidisciplinary chart notes indicating an onset of depression during pregnancy and/or within 4 weeks after delivery. The overall prevalence of perinatal depression was 30.8%, of depression during pregnancy was 22%, and of depression within 4 weeks postpartum was 18.3%. Estimates of the rate of perinatal depressive symptoms in HIV-infected women were not presented in the study.

There is also limited research on potential risk factors for perinatal depression in HIV-infected women. Only one study in HIV-infected women specifically examined correlates of depression in both the pregnancy and postpartum periods. Kapetanovic et al.[19] reported that past history of a psychiatric illness, substance use during pregnancy, social stress during pregnancy, and lower CD4+ pregnancy nadir were associated with an increased risk of perinatal depression as defined by medical records and multidisciplinary notes in their sample of HIV-infected women ($n = 273$). Other studies have attempted to elucidate the predictors of depressive symptoms in HIV-infected women during either pregnancy or postpartum but not both time periods. One study ($n = 307$) examined correlates of depression during pregnancy as defined by the Center of Epidemiological Studies—Depression scale (CES-D) (interval measure with somatic items removed) in a sample of young, pregnant (≥ 24 weeks), HIV-infected women who were predominantly low-income, low-education (< 12 years), and minority women (71% African American, 20% Hispanic).[20] Depression during pregnancy was significantly associated with ineffective coping styles, stress, social isolation, and drug and alcohol use. Another study ($n = 245$) examined postpartum depressive symptoms operationally defined by the CES-D (median split of ≥ 15 was used to define depression) in a sample of young, low-income, low-education (< 12 years), unmedicated, asymptomatic HIV-infected patients who had recently given birth (18–24 months postpartum) in Thailand.[21] Postpartum depression was related to broken relationships, ineffective coping strategies, having an HIV-infected infant, and nondisclosure of HIV status to others. Taken together, these studies help to elucidate some of the determinants of depression during pregnancy and the postpartum period in HIV-infected women.

The primary objective of the present investigation was to assess the prevalence of elevated perinatal depressive symptoms in a sample of HIV-infected vs. at-risk HIV-uninfected women. The study design involved prospective evaluations of depressive symptoms as measured by the CES-D scale during preconception, pregnancy, and postpartum. Based on previous findings, we hypothesized that perinatal depressive symptoms would be increased in HIV-infected compared to at-risk HIV-uninfected women. The secondary objective was to examine risk factors for elevated perinatal depressive symptoms in HIV-infected and at-risk HIV-uninfected women. Given demonstrations that risky health behaviors[7,12] (e.g., drug use, multiple sexual partners), sociodemographic factors[12] (e.g., ethnicity, education, income), and service features[6] (e.g., insurance status, use of mental health services) related to depressive symptoms in past studies of HIV-infected women, we examined these factors as risk factors of elevated perinatal depressive symptoms. We also examined unintended pregnancy as an additional risk factor, given that unintended pregnancy is associated with an increase in smoking, illicit drug use, and alcohol use compared with intended pregnancy.[22]

Materials and Methods

Study population

WIHS is a longitudinal, multicenter study of the natural and treated history of HIV in women and includes six clinical sites: Bronx/Manhattan and Brooklyn, NY; Chicago, IL; Washington, DC; and San Francisco and Los Angeles, CA.[23,24] Starting in 1994–1995 and again in 2001–2002 and with institutional review board approval, HIV-infected and at-risk uninfected women matched by age, race/ethnicity, level of education, recruitment site, and risk factors, including history

of injection drug use and number of sexual partners were enrolled into WIHS.[23,24] The HIV-uninfected women are considered at-risk because they are low income and they engage in high rates of risky behaviors (e.g., drug use, multiple sex partners), which are risk factors for HIV.

Women eligible for WIHS were aged ≥13 years and were able to provide informed consent and complete an interview in either English or Spanish. Although enrollment has been closed since the end of 2002, participants continue to undergo a clinical examination and extensive interview and provide biologic specimens every 6 months. Study methodology, training, and quality assurance procedures and the cohort's baseline characteristics have been reported previously.[23,24] The study sample for this analysis was restricted to WIHS participants who experienced one or more pregnancies between October 1994 and May 2005 ($n = 531$), experienced a live birth ($n = 474$), had a known delivery date on file ($n = 447$), and had CES-D scores across three reproductive stages: preconception (>10 months before delivery), pregnancy (≤10 months before delivery), and postpartum (≤12 months after delivery)(N = 244). The primary reason why only 244 of the 447 with known delivery dates had CES-D scores available for each of the three stages was that WIHS administered the CES-D annually from 1994 until October 1998 and then began more frequent administrations, every 6 months, from October 1998 until the present. In the Results section we compare the characteristics of women who were included in this analysis and those who were excluded. CES-D scores at all three time points were necessary because (1) the primary outcome measure (i.e., perinatal depression) was operationally defined as elevated depressive symptoms during pregnancy and/or within 1 year postpartum and (2) the predictor variables, including elevated depressive symptoms before pregnancy, were from the preconception study visit.

Measures

Depressive symptoms. Elevated perinatal depressive symptoms were assessed with the CES-D,[25] a 20-item self-report measure. In accordance with standard definitions of perinatal depression,[14] elevated perinatal depressive symptoms were defined as a CES-D score ≥16 during pregnancy (≤10 months before delivery) and/or postpartum (≤12 months after delivery). In secondary analyses, we examined a more stringent cutoff of 23 and an interval-level version of the subscale that excluded somatic items (i.e., fatigue, poor appetite, lack of energy, restlessness, poor concentration) similar to HIV symptoms. The CES-D has excellent reliability, validity, and factor structure[25] and is commonly used in studies of HIV,[12] including women with HIV.[26] Its sensitivity for the DSM diagnosis of major depression is excellent, in the range of 80%–90%, with a somewhat lower specificity, in the range of 70%–80%.[27–29] The Black Women's Health Study has demonstrated that the CES-D is a valid measure in African American women.[30]

Independent measures/potential risk factors of perinatal depressive symptoms. Potential predictors of perinatal depression were obtained from the preconception visit, which was defined as the most recent visit at least 10 months before delivery. WIHS participants are asked about health-related variables in the 6 months since their last visit, so these preconception variables represent status/exposure in the 6 months preceding the preconception visit (e.g., drug use represents drug use within the 6 months preceding the preconception visit). In addition to HIV status, we examined risky health behaviors, including current smoking status, alcohol—abstainer, light (<3 drinks/week), moderate (3–13 drinks/week), heavy (≥14 drinks/week)—marijuana/hash use, crack, cocaine, and/or heroin use, and current number of sexual partners (male and/or female, <2, ≥2). The sociodemographic factors examined included age, race (Hispanic, African American, Caucasian), level of education (<high school education, ≥high school education), average household income (≤$12,000, >$12,000), employment status, marital status (married/partner, all others). We also examined intention of getting pregnant, depression during preconception (CES-D ≥16 greater than 10 months before delivery), and service features, including current insurance and use of mental health services. Interactions were also examined between HIV status and risky health behaviors, sociodemographic factors, service features, and intention of getting pregnant. In analyses restricted to HIV-infected women, additional variables included HAART use (yes, no), HAART adherence (≥95% of the time considered adherent, <95% of the time considered nonadherent), CD4+ cell count (an indicator of the progress of HIV infection where lower counts indicate more severe disease) (<200, 200–500, >500 cells/μL), and viral load (a measurement of the amount of HIV in the blood where higher counts indicate more severe disease) (HIV RNA using cutoffs of 500 and 10,000 copies/mL).

Statistical analysis

Differences between HIV-infected and uninfected women in characteristics measured at preconception were examined using independent t tests for continuous variables and chi-square tests for categorical variables. To compare the prevalence of perinatal depression (i.e., ≥16 on the CES-D during pregnancy and/or postpartum) in HIV-infected vs. uninfected women, chi-square analyses were conducted. To compare the prevalence on the interval-level version of the subscale that excluded somatic items, an independent t test was conducted. Next, logistic regression models were used to identify significant predictors (i.e., serostatus, risky health behaviors, sociodemographic factors, service features, intention to get pregnant as well as interactions with serostatus) of elevated perinatal depressive symptoms first in the entire sample and then separately for HIV-infected and at-risk uninfected women. Forward and backward selection procedures were used to determine the best predictors of elevated perinatal depressive symptoms. Likelihood ratio tests were used to compare models, and the most parsimonious model was selected. All p values were two-sided. The statistical significance level was set at $p = 0.10$ in order to examine marginally significant results/trends (standard criteria in the literature). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each of the significant predictor variables using maximum likelihood estimates from logistic regression models. All analyses were conducted using SAS (version 9.2 for Windows, Cary, NC).

Results

Sample characteristics at preconception

Of the 244 participants, 139 were HIV-infected women and 105 were at-risk HIV-uninfected women. Each woman was

included in the analysis only once and was included for the first birth in WIHS only. Overall, the 244 women included in the analysis were similar across most sociodemographic and clinical variables to the 230 women who experienced a live birth but did not have a known delivery date on file or CES-D scores for each of the three reproductive stages. The exception was that women included in the analysis more frequently reported crack, cocaine, and/or heroin use during preconception (15%) compared to women not included in the analysis (5%); chi-square (1, $n=474$) = 11.31, $p<0.001$.

Table 1 provides demographic information at preconception for both HIV-infected ($n=139$) and uninfected ($n=105$) women and for the two groups combined ($n=244$). The sample ranged in age from 17 to 44 years (mean = 29.38, standard deviation [SD] = 5.70). Notably, our sample was largely representative of HIV-infected women in the United States in terms of ethnicity (62% African American), education (55% high school graduates or equivalent), employment status (39% employed), and household income (54% with <$12,000/year).[31] Among HIV-infected women, the median CD4+ lymphocyte count was 423 cells/μL (range 0–1608, median 423), and 8% had CD4+ cell counts <200 cells/μL. Fifty percent had been prescribed antiretroviral (ARV) therapy, and 77% were treatment adherent.[32] Plasma viral load was undetectable for 31%, above the lower limit of quantitation (LLQ) but <10,000 copies/mL for 42% and >10,000 copies/mL for 27% of HIV-infected women.

Overall, HIV-infected and uninfected women were similar across many sociodemographic, clinical, and behavioral variables, although there were significant differences between HIV-infected and uninfected women in mean age (30.37 vs. 28.08 years, $p=0.002$), health insurance status (80% vs. 64% insured, $p=0.01$), and current number of sex partners (17% vs. 38% with ≥2 partners, $p=0.001$). There were also trends for HIV-infected and uninfected women to differ on marijuana/hash use (20% vs. 31%, $p=0.07$) and use of mental health services (17% vs. 10%, $p=0.095$) during preconception.

Prevalence of perinatal depressive symptoms

Table 2 provides the frequency of clinically significant depressive symptoms during preconception, pregnancy, postpartum, and perinatal for HIV-infected women, HIV-uninfected at-risk women, and for the two groups combined. The overall prevalence of elevated perinatal depressive symptoms across the two groups combined was 46%. There were no significant differences in overall prevalence as a function of HIV serostatus ($p=0.44$). There were no significant differences between HIV-infected and HIV-uninfected women in the prevalence of depressive symptoms during preconception ($p=0.44$), pregnancy ($p=0.50$; first trimester, $p=0.51$; second trimester, $p=0.40$; third trimester, $p=0.98$), or postpartum ($p=0.49$).

In some studies of HIV-infected women, probable depression is defined with a more stringent cutoff of 23 or with an interval-level version of the subscale that excludes somatic items that overlap with symptoms of HIV.[6,20] Notably, the prevalence of elevated perinatal depressive symptoms did not differ by HIV serostatus using the more stringent cutoff of 23 (HIV-infected 26%, HIV-uninfected 31%, $p=0.47$). There were also no differences between HIV-infected and HIV-uninfected women on the interval level version of the scale excluding somatic items during preconception ($p=0.91$), pregnancy ($p=0.26$; first trimester, $p=0.25$; second trimester, $p=0.82$; third trimester, $p=0.92$), or postpartum ($p=0.43$).

Risk factors of perinatal depressive symptoms

Table 3 provides the significant predictors from the final logistic regression models examining predictors of perinatal depressive symptoms (CES-D ≥16) in the entire sample ($n=244$) and in HIV-infected ($n=139$) and HIV-uninfected ($n=105$) women separately. In the overall sample, preconception depression ($p<0.001$), education (less than high school, $p=0.03$), current number of sexual partners preconception (≥2 partners, $p=0.02$), and mental health service use preconception ($p=0.04$) were significant predictors of perinatal depressive symptoms (i.e., during pregnancy and/or postpartum); crack, cocaine, and/or heroin use preconception was a marginally significant predictor ($p=0.08$). Serostatus was not a significant predictor of perinatal depressive symptoms in the overall sample and, thus, was not included in the final model. Among HIV-infected women, preconception elevated perinatal depressive symptoms ($p<0.001$) was a significant predictor of perinatal depression, and crack, cocaine, and/or heroin use almost reached statistical significance ($p=0.058$). Among at-risk HIV-uninfected women, preconception depression ($p<0.001$) and current number of sexual partners preconception (≥2 partners, $p=0.01$) were significant predictors of perinatal depressive symptoms, and having less than a high school education almost reached statistical significance ($p=0.08$).

In models using a more stringent CES-D cutoff of 23, many of the same variables were significant. In the overall sample, serostatus was not a significant predictor and, thus, was not included in the final models. Significant predictors in the overall sample included preconception depression (OR 4.78, 95% CI 2.51-9.08, $p<0.001$), current number of sexual partners preconception (≥2 partners, OR 2.05, 95% CI 1.06-3.96, $p=0.03$), and average household income (≤$12,000, OR 2.19, 95% CI 1.16-4.14, $p=0.02$). Among HIV-infected women, the only significant predictors of elevated perinatal depressive symptoms were preconception depressive symptoms (OR 7.50, 95% CI 3.05-18.41, $p<0.001$) and average household income (≤$12,000, OR 2.79, 95% CI 1.13-6.89, $p=0.03$). Among at-risk HIV-uninfected women, preconception depression (OR 3.38, 95% CI 1.33-8.56, $p<0.001$), and current number of sexual partners preconception (≥2 partners, OR 3.18, 95% CI 1.29-7.83, $p=0.01$) were significant predictors.

In models using the interval-level version of the subscale, serostatus was not a significant predictor of elevated depressive symptoms during the perinatal period (pregnancy or postpartum) (Table 4). Significant predictors in the overall sample included preconception depression ($p<0.001$), current number of sexual partners preconception ($p<0.01$), having less than a high school education ($p=0.02$), and crack, cocaine, and/or heroin use ($p=0.01$). Among HIV-infected women, the only significant predictors of perinatal depressive symptoms were preconception depression ($p<0.001$) and being of Hispanic origin ($p=0.02$); mental health service use preconception ($p=0.05$) and average household income (≤$12,000, $p=0.05$) were marginally significant predictors. Among at-risk HIV-uninfected women, preconception depression ($p<0.001$) and current number of sexual partners

Table 1. Demographics at Preconception (>10 Months Before Delivery) for HIV-Infected Women, HIV-Uninfected Women, and the Two Groups Combined ($n=244$)

Variables	HIV status		
	HIV-infected n=*139* n *(%)*	*HIV-uninfected* n=*105* n *(%)*	*Overall sample* n=*244* n *(%)*
Age (mean, SD)**	30.37 (5.37)	28.08 (5.90)	29.38 (5.71)
Race			
African American	90 (65)	60 (57)	150 (62)
Hispanic	37 (27)	38 (36)	75 (31)
White	27 (19)	16 (15)	43 (18)
At least high school graduate or equivalent	75 (54)	58 (55)	133 (55)
Currently employed	52 (37)	43 (41)	95 (39)
Currently married	57 (41)	39 (37)	96 (39)
Average household Income (≤$12,000/year)	77 (55)	54 (51)	131 (54)
Carrying insurance**	111 (80)	67 (64)	178 (73)
Current number of sex partners (≥2)***	24 (17)	40 (38)	64 (26)
Trying to get pregnant	88 (63)	76 (72)	164 (67)
Mental health services†	24 (17)	10 (10)	34 (14)
Recent use[a]			
Smoking	66 (48)	46 (44)	112 (46)
Alcohol			
Abstainer	70 (50)	41 (39)	111 (46)
Light (<3 drinks/week)	46 (33)	41 (39)	87 (36)
Moderate (3–13 drinks/week)	18 (13)	13 (12)	31 (12)
Heavy (≥14 drinks/week)	5 (4)	10 (10)	15 (6)
Marijuana/hash†	28 (20)	32 (31)	60 (25)
Crack/freebase cocaine	15 (11)	11 (11)	26 (11)
Cocaine	7 (5)	8 (8)	15 (6)
Heroin	3 (2)	7 (7)	10 (4)
Composite crack, cocaine, and/or heroin	19 (14)	18 (17)	37 (15)
Disease			
CD4 number			
>500	59 (42)	-	-
≥200 and ≤500	69 (50)	-	-
<200	11 (8)	-	-
Viral load (HIV RNA, copies/mL)			
Undetectable	43 (31)	-	-
<10,000	58 (42)	-	-
≥10,000	38 (27)	-	-
Medication use			
HAART	47 (34)	-	-
Non-HAART	22 (16)	-	-
ARV naive	70 (50)	-	-
Medication compliance (≥95%)[b]	36 (77)	-	-
Intervals (days: Mean, SD)			
Preconception (>300 days before delivery)	440.30 (88.49)	453.81 (123.66)	446.11 (105.05)
Pregnancy (≤300 days before delivery)	116.76 (74.32)	111.66 (76.58)	114.57 (75.19)
Postpartum (≤365 days after delivery)	146.92 (82.10)	143.29 (83.83)	145.36 (82.70)

[a]Recent use refers to within 6 months of the preconception Women's Interagency HIV Study (WIHS) visit.
[b]Data were only available on 47 of the 69 women taking medication because this information was not collected until October 1998 in the WIHS. Therefore, the percentage of women who were medication compliant is based on 36 of 47 women.
***$p<0.001$; **$p<0.01$.
†$p>0.05$ and $p<0.10$.
ARV, antiretroviral; HAART, highly active antiretroviral therapy; SD, standard deviation.

preconception ($p<0.03$) were significant predictors. Crack, cocaine, and/or heroin use was a marginally significant predictor ($p=0.09$) during pregnancy and significant during postpartum ($p=0.03$).

Discussion

The aim of this article was twofold: first, to assess the prevalence of clinically significant perinatal depressive symptoms in a sample of HIV-infected vs. uninfected women and, second, to examine risk factors for elevated perinatal depressive symptoms in both HIV-infected and uninfected women. Consistent with previous findings,[19] the proportion of women with elevated perinatal depressive symptoms was high in our sample before conception (39%) and in the perinatal period (46%). There were no differences between HIV-infected and uninfected women in likelihood of clinically significant depressive symptoms. HIV-infected women were

Table 2. Frequency of Depressive Symptoms (≥16) as Measured by Center for Epidemiologic Studies-Depression Scale as Function of Stage of Pregnancy for HIV-Infected Women, At-Risk HIV-Uninfected Women, and the Two Groups Combined ($n=244$)

	HIV Status		
Stage of pregnancy	*Infected* (n=*139*) n *(%)*	*Uninfected* (n=*105*) n *(%)*	*Overall sample* n=*244* n *(%)*
Preconception	58 (42)	38 (36)	96 (39)
Pregnancy[a]	47 (34)	40 (38)	87 (36)
First trimester	7 (35)	7 (47)	14 (40)
Second trimester	24 (44)	21 (54)	45 (48)
Third trimester	30 (47)	24 (47)	54 (47)
Postpartum	43 (31)	37 (35)	80 (33)
Perinatal[b]	61 (44)	52 (50)	113 (46)

[a]There were no significant differences in elevated depressive symptoms across trimesters in the overall sample ($p=0.72$), HIV-infected women ($p=0.65$), or HIV-uninfected women ($p=0.79$).
[b]Perinatal depression was defined as ≥16 on the CES-D during pregnancy (≤10 months before delivery) and/or postpartum (≤12 months following delivery). Perinatal depression was the primary outcome variable in the regression analyses.

at increased risk for perinatal depression if they had a history of elevated depressive symptoms preconception or used crack, cocaine, and/or heroin preconception, although the substance use effect just missed statistical significance (p=0.06). Additional risk factors for perinatal depressive symptoms across the combined sample of HIV-infected and uninfected women included lower education, current number of sexual partners before pregnancy, and mental health service use before pregnancy.

Our data suggest that the occurrence of clinically significant depressive symptoms before pregnancy is a strong predictor of perinatal depression in both HIV-infected and

Table 3. Significant Predictors from the Final Logistic Regression Models Examining Predictors of Perinatal Depressive Symptoms (≥16 on Center for Epidemiologic Studies-Depression Scale During Pregnancy and/or Postpartum) in the Overall Sample ($n=244$) and in HIV-Infected ($n=139$) and HIV-Uninfected ($n=105$) Women Separately

Sample	*Significant predictors*	*OR*	*95% CI*	p *value*
Overall sample ($n=244$)	Preconception depression			<0.001
	No, CES-D<16 ($n=148$)	1.00	Reference	
	Yes, CES-D≥16 ($n=96$)	5.62	3.08-10.27	
	Education			0.03
	At least high school or equivalent ($n=133$)	1.00	Reference	
	Less than high school ($n=111$)	1.92	1.06-3.46	
	Crack, cocaine, and/or heroin use preconception			0.08
	No use ($n=207$)	1.00	Reference	
	Any use ($n=37$)	2.24	0.92-5.46	
	Current number of sexual partners			0.02
	<2 ($n=180$)	1.00	Reference	
	≥2 ($n=64$)	2.20	1.12-4.32	
	Mental health services used preconception			0.04
	No use of services ($n=210$)	1.00	Reference	
	Use of services ($n=34$)	2.51	1.03-6.13	
HIV-infected ($n=139$)	Preconception depression			<0.001
	No, CES-D<16 ($n=78$)	1.00	Reference	
	Yes, CES-D≥16 ($n=61$)	5.71	2.67-12.19	
	Crack, cocaine, and/or heroin use preconception			0.06
	No use ($n=120$)	1.00	Reference	
	Any use ($n=19$)	3.10	0.96-10.01	
HIV-uninfected ($n=105$)	Preconception depression			<0.001
	No, CES-D<16 ($n=67$)	1.00	Reference	
	Yes, CES-D≥16 ($n=38$)	8.96	3.26-24.65	
	Education			0.08
	At least high school or equivalent ($n=58$)	1.00	Reference	
	Less than high school ($n=47$)	2.31	0.91-5.84	
	Current number of sexual partners			<0.01
	<2 ($n=65$)	1.00	Reference	
	≥2 ($n=40$)	3.54	1.38-9.10	

CI, confidence interval; OR, odds ratio.

Table 4. Significant Predictors from the Final Regression Models Examining Predictors of Perinatal Depressive Symptoms (Interval-Level Subscale on Center for Epidemiologic Studies-Depression Scale During Pregnancy and Postpartum) in the Overall Sample ($n=244$) and in HIV-Infected ($n=139$) and HIV-Uninfected ($n=105$) Women Separately

	Stage			
	Pregnancy		*Postpartum*	
Sample	β	p	β	p
Overall sample ($n=244$)				
Preconception depression	0.60	<0.001	0.47	<0.001
Current number of sexual partners ≥2	0.14	0.01	-	-
Having less than a high school education	0.12	0.02	-	-
Crack, cocaine, and/or heroin use preconception	-	-	0.14	0.01
HIV-infected ($n=139$)				
Preconception depression	0.65	<0.001	0.55	<0.001
Hispanic origin	0.16	0.02	-	-
Mental health service use preconception	-	-	0.14	0.05
Average household income ≤$12,000	-	-	0.14	0.05
HIV-uninfected ($n=105$)				
Preconception depression	0.53	<0.001	0.36	<0.001
Current number of sexual partners ≥2	0.19	0.02	-	-
Crack, cocaine, and/or heroin use preconception	0.14	0.09	0.20	0.03

uninfected women. This logical finding stresses the importance of screening and treatment of depression in the preconception period that may lead to depression in the perinatal period. Additionally, our findings stress the need for continued monitoring and management of depression in HIV-infected women and in at-risk HIV-uninfected women during pregnancy and the postpartum period. Substance use (crack, cocaine, and/or heroin) was a marginally significant predictor of perinatal depressive symptoms, particularly among HIV-infected women ($p=0.06$). Substance abuse, like HIV disease, has been associated with depression[12] and has been shown to affect treatment adherence.[6,7] Thus, consideration of substance use among HIV-infected women remains of particular importance when studying depression in general. Having multiple sex partners was a significant predictor of perinatal depressive symptoms, particularly among at-risk HIV-uninfected women. Risky sexual behaviors, specifically having multiple sex partners, has also been associated with depression in a number of samples including both African American and white women,[33] impoverished women,[34] and inner-city drug users.[35] Continued reinforcement needs to be placed on the negative consequences of risky sexual behaviors in at-risk HIV-uninfected women, which may help to reduce depression as well as HIV transmission.

HIV-infected women in our study did not show elevated perinatal depressive symptoms when compared to at-risk HIV-uninfected women. Factors, such as having multiple sexual partners, low education, mental health service use, and drug use (crack, cocaine, and/or heroin), were more important than serostatus in predicting perinatal depression in WIHS women overall. Although HIV-infected women may have a presumed vulnerability to perinatal depression because of their medical status, there are four possible reasons why the prevalence rates did not differ. First, HIV-infected women in our study and in the community frequently have greater access to medical care and social services compared with at-risk HIV-uninfected women,[36] and this may mitigate against elevated depressive symptoms. Second, women are living longer with HIV; thus, there are fewer concerns about low life expectancy in the context of raising a child. Third, the risk of mother-to-child transmission of HIV has been significantly reduced from rates of 25%–30%[37] to <1%[38] given routine HIV screening of pregnant women, use of ARV drugs and zidovudine therapy, avoidance of breastfeeding, and use of cesarean deliveries. Fourth, this sample, like the larger WIHS sample from which it was drawn, has a high background rate of depression[6,7,28,39] in part because of prevalence of other factors, including high rates of substance abuse. Those factors appear to have a stronger link to depression than pregnancy. However, this finding may be unique to the WIHS cohort and, thus, our findings need to be replicated in other prospective cohorts of pregnant women with HIV.

The present study is limited by several factors. First, we focused on elevated depressive symptoms as a marker of clinically relevant perinatal depression because we did not have clinical diagnoses. A better approach would have been to use a diagnostic interview, such as the Structured Clinical Interview for the DSM (SCID), to measure clinical depression.[6] Second, we did not have data on obstetric factors that may be associated with depression (e.g., preeclampsia, gestational diabetes, prematurity, HIV transmission to the infant, neonatal intensive care unit admissions, or other maternal or infant complications). We also lacked data on potential psychosocial predictors, including coping style, social stress, and broken relationships, as well as antidepressant use. Although these variables were not available for all the women in this study, these variables are currently being collected in WIHS and can be examined in future studies. Third, we did not have complete data for all women with live births in the WIHS, and this may have introduced biases. The primary reason CES-D scores were missing was because the CES-D was only administered annually at the onset of WIHS compared to once every 6 months later on. There was an overrepresentation of crack, cocaine, and/or heroin use among HIV-infected women

who become pregnant in WIHS but an underrepresentation of use among HIV-infected women regardless of pregnancy status.[7,40] Thus, the present results may still not be generalizable to the broader population of HIV-infected women who become pregnant. Our findings with respect to illicit substances as a predictor of perinatal depression particularly among HIV-infected women are important, however, as this factor seems to have a stronger link to perinatal depression than serostatus.

Future studies need to examine these variables as potential risk factors of perinatal depression in large samples of HIV-infected women with demographically matched comparison groups. Finally, as previously mentioned, women with HIV in WIHS receive social, medical, and other benefits by participating in WIHS, and these factors might mitigate against depressive symptoms. Therefore, studies are needed to see if HIV influences perinatal symptoms in women who do not benefit from participation in prospective clinical studies.

Conclusions

This is the first study to prospectively compare the prevalence of perinatal depressive symptoms in HIV-infected and at-risk HIV-uninfected women and to identify predictors of elevated perinatal depressive symptoms in these two groups. The present findings suggest that the risk of elevated perinatal depressive symptoms (1) does not differ between HIV-infected and at-risk HIV-uninfected women, (2) is associated with a history of depression before conception in both HIV-infected and HIV-uninfected women, and (3) is associated with illicit substances (i.e., crack, cocaine, and/or heroin), particularly among HIV-infected women. Identification and treatment of depression when a woman is trying to conceive may lead to decreased perinatal depression. HIV-infected women who use illicit substances should be monitored for the presence of elevated perinatal depressive symptoms.

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No competing financial interests exist.

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