

Zidovudine and Perinatal Human Immunodeficiency Virus Type 1 Transmission: A Population-Based Approach

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ABSTRACT. *Objective.* This study examined the impact of the full 3-arm zidovudine regimen on the perinatal transmission of human immunodeficiency virus type 1 (HIV-1) using population-based data.

Methods. We retrospectively ascertained information on zidovudine prescription and other characteristics of HIV-infected pregnant women and children for birth cohort years 1993, 1995, 1996, and 1997 using HIV/acquired immunodeficiency syndrome registry data from a state health department supplemented by medical record reviews.

Results. The transmission rate decreased from 12.5% in 1993 to 4.6% in 1997. The proportions of HIV-1-infected mothers and children who were prescribed all 3 arms of zidovudine increased from 68% in 1995 to 93% in 1997. Unadjusted and adjusted odds ratios for the relationship between the prescription of 3 arms of zidovudine and the infants' HIV status were 0.19 (95% confidence interval: 0.05–0.84) and 0.15 (95% confidence interval: 0.02–0.96), respectively.

Conclusion. Perinatal HIV-1 transmission rates have decreased over time. This study demonstrates the effectiveness of the rapid implementation of the United States Public Health Service recommendations for the comprehensive use of zidovudine among HIV-1-infected pregnant women in a predominantly rural state. *Pediatrics* 2002;109(4). URL: <http://www.pediatrics.org/cgi/content/full/109/4/e60>; HIV infection, disease transmission, prevention and control, zidovudine, female, infant, newborn, population surveillance.

ABBREVIATIONS. HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; ACTG 076, AIDS Clinical Trial Group 076; USPHS, United States Public Health Service; STD, sexually transmitted disease; OR, odds ratio; CI, confidence interval.

The connection between human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) in children and mothers with AIDS or at risk for HIV was recognized in the early 1980s.¹ Since then, the number of AIDS cases among children has increased dramatically,

and >90% of these cases among children have been acquired perinatally.² The transmission of HIV from mother to child has been estimated to occur in approximately 15% to 30% of children born to HIV-infected women in the United States.¹

Zidovudine is the first antiretroviral medication approved worldwide for the treatment of HIV/AIDS. It is also the first drug to be used in a clinical trial of HIV-infected pregnant women to determine its efficacy in reducing perinatal HIV transmission.³ This randomized trial—AIDS Clinical Trial Group 076 (ACTG 076)—demonstrated a reduction of perinatal HIV transmission with zidovudine by almost 70%.³

Since the successful use of zidovudine in HIV-infected pregnant women in the ACTG 076, recommendations have been published for the use of zidovudine to reduce perinatal HIV infection.⁴ In addition, other studies have demonstrated the success of zidovudine in reducing perinatal HIV transmission.^{5–10} The US and European epidemiologic studies demonstrating striking decreases in the perinatal transmission of HIV from prophylactic (zidovudine) administration have used data from hospitals, public health clinics, and private physicians' offices. This study uses data from a population-based HIV/AIDS surveillance database from a state that has HIV infection reporting by name. The objective of this study was to explore the relationship between zidovudine prescription and perinatal HIV-1 transmission among mother-child pairs in which the mother is known before delivery to be infected with HIV.

METHODS

Data were provided by the state health department for all mother-child pairs who had been reported to the HIV/AIDS surveillance registry, a population-based registry that contains all of the reported HIV-positive or AIDS cases in the state, for calendar years 1993, 1995, 1996, and 1997. Eligible cases included mother-child pairs in which the mother's first confirmed HIV-positive test preceded the birth of the child, prenatal care and delivery occurred in the state, and birth outcome resulted in a live birth. Medical and demographic data were obtained from the maternal labor and delivery record, the neonatal birth record, the maternal HIV clinic record, the pediatric HIV medical record, sexually transmitted disease surveillance record, prenatal care clinic record, the birth certificate, and the HIV/AIDS surveillance record.

The transmission rate for each birth cohort year was defined as the number of HIV-1-infected infants in a birth cohort year divided by the total number of infants in the sample born during the birth cohort year. The transmission rate for each arm of zidovudine use was defined as the number of HIV-1-infected infants

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whose mothers were prescribed a certain level of zidovudine divided by the total number of infants whose mothers were prescribed that level of zidovudine.

Zidovudine prescription, the dependent variable, was categorized into 4 levels and used for descriptive purposes: all 3 arms (during pregnancy, delivery, and neonatally), 2 arms (only 2 of the 3 arms), 1 arm (only 1 of the 3 arms), and 0 arms (no zidovudine prescription). The zidovudine prescription variable used for modeling was dichotomized as "all 3 arms versus not all 3 arms," meaning that it was prescribed during pregnancy, during labor, and for the neonate versus not being prescribed for all 3 arms. Because mother-child pairs would not have been prescribed all 3 arms of zidovudine in 1993 (the year before the United States Public Health Service [USPHS] recommendations), the sample was restricted to birth cohort years 1995 to 1997 for the analysis of transmission rate by Zidovudine ($N = 217$). The sample was further restricted to women who had CD4 counts during pregnancy and who did not have missing illicit drug use information. The final sample size was 149 mother-child pairs. HIV infection was defined as infants who were classified as having HIV or AIDS by the current Centers for Disease Control and Prevention pediatric HIV/AIDS case definition.¹¹ Uninfected infants were defined as those who had seroreverted or who were born exposed to HIV-1 but whose infection status had not been determined as of May 1, 1999.

Maternal age was defined as mother's age at the time of delivery and was calculated by taking the difference between the mother's date of birth and the delivery date (infant's date of birth). The initial time criteria for CD4 count/mm³ during pregnancy was those measured 6 months before pregnancy, during pregnancy, and 6 months after pregnancy ($N = 143$). Six additional mother-child pairs were identified when the CD4 count/mm³ time criteria was extended to those measured 12 months before pregnancy, during pregnancy, and 12 months after pregnancy. Alcohol use, cigarette use, and illicit drug use were defined as occurring during pregnancy and were recorded from medical records. Prenatal care was determined using the Kotelchuck Adequacy of Prenatal Care Index.¹² This index uses 2 subscales: the Adequacy of Initiation of Prenatal Care, which takes into account the month in which prenatal care was initiated, and the Adequacy of Received Services, which describes the proportion of recommended prenatal care visits made, adjusted for gestational age at birth. These 2 subscales were combined to produce a summary index with 5 levels that describe prenatal care: Adequate Plus, Adequate, Intermediate, Inadequate, and No prenatal care. The maternal county of residence at the time of HIV-1 diagnosis was dichotomized into urban counties and rural counties. Rural counties were those in which >50% of the population in the county live in the rural areas of the county, whereas urban counties were defined as those in which >50% of people in the county live in the urban areas of the county.¹³ Sexually transmitted disease (STD) was defined as 1 of the following STDs having been diagnosed during pregnancy: syphilis, gonorrhea, chlamydia, or herpes. Chorioamnionitis was defined as an infection of the chorionic/amniotic sac as recorded on the medical record. Premature rupture of membranes was dichotomized into having ruptured membranes >4 hours versus ≤4 hours before delivery and was calculated by taking the difference between the membrane rupture time and date and the delivery time and date (infant's date and time of birth). Type of delivery was dichotomized into vaginal or caesarean section and was abstracted from the medical record. Missing and unknown observations for chorioamnionitis and all zidovudine prescription variables were assumed not to have occurred. Missing and unknown for type of delivery was assumed as vaginal delivery.

Stratified analysis was used to examine the relationship of the covariates with HIV infection status of the infant. The Mantel-Haenszel procedure, adjusting for 1 variable at a time in a model of zidovudine and HIV transmission, was used to select potential confounding factors for initial inclusion in the logistic model. The covariates included maternal age at delivery, race/ethnicity, CD4 counts during pregnancy, alcohol use, smoking, illicit drug use, STDs, maternal county of HIV diagnosis, type of health insurance, prescription of zidovudine before this pregnancy, and prenatal care. To reduce possible multicollinearity by having associated variables in the same model, we used χ^2 tests and Fisher's exact tests to test the association of each covariate with the others. A χ^2 test for trend was used to test for trends in zidovudine prescrip-

tion from 1995 through 1997. Unconditional logistic regression was used for estimating the relative risk (odds ratio [OR]) and 95% confidence interval (CI) for the zidovudine prescription and HIV infection status of the infant while simultaneously adjusting for potential confounding variables. Effect modification for the association of zidovudine prescription and HIV infection status of the infant by chorioamnionitis, premature rupture of membranes, and type of delivery was assessed using the likelihood ratio test. Interaction terms were retained in the model when they were statistically significant at $\alpha = 0.05$ level. Confounders were defined as variables that changed the odds ratios of the exposure-outcome relationship by approximately 5% to 10% or more. Variables that contributed to the model using the likelihood ratio test at $\alpha = 0.05$ were considered strong risk factors. The final model included the major independent variable, all variables identified as confounders, and strong risk factors for the association between zidovudine prescription and HIV infection status of the infant.

RESULTS

Table 1 presents the transmission rates by birth cohort year. The transmission rate for the baseline year, 1993, was 12.5% and by birth cohort year declined from 8.4% in 1995 to 4.6% in 1997 ($P = .27$ for trend). The 3-year average (1995-1997) transmission rate was 5.5% compared with 12.5% in 1993 ($P = .04$). The transmission rates for mother-child pairs that were prescribed all 3 arms of zidovudine and not all 3 arms of zidovudine were 4.4% and 8.8%, respectively. Those mother-child pairs that were prescribed only 1 arm of the drug experienced the highest transmission rate, 16.7% (95% CI: 0.42%-64.0%).

CD4 counts were missing for a large proportion of the data (24%); therefore, we excluded those with missing CD4 counts ($N = 51$). Illicit drug use during pregnancy was identified as a confounder, and those with missing values ($N = 30$) were excluded to accommodate the logistic regression analyses. Among those excluded were 13 with both missing CD4 count and illicit drug use data. The transmission rates for the remaining sample of 149 mother-child pairs are also presented in Table 1.

Table 2 presents the distribution of selected characteristics of HIV-infected mothers by zidovudine prescription status. In each birth cohort year, the percentage of mother-child pairs that were prescribed all 3 arms of zidovudine increased. Eighty percent of the black mothers compared with 94% of the white mothers were prescribed all 3 arms of zidovudine. One hundred percent (100%) of the mothers with 0 to 199 CD4 counts/mm³, which constitutes AIDS,¹⁴ 81% with 200 to 499 CD4 counts/mm³, and 78% with ≥500 CD4 counts/mm³ were prescribed all 3 arms of zidovudine. The majority of mothers who drank alcohol, smoked cigarettes, used illegal drugs during pregnancy, and had received a diagnosis of an STD during pregnancy had been prescribed all 3 arms of zidovudine. A slightly higher proportion of the women who lived in rural areas than those who lived in urban areas had been prescribed all 3 arms of zidovudine.

Variables that were positively associated with zidovudine prescription but not statistically significant were 0 to 199 and 200 to 499 CD4 count/mm³, maternal county of residence at time of HIV diagnosis, type of health insurance, premature rupture of membranes, and type of delivery. Women with CD4 counts 0 to 199/mm³ were 10 times more likely and

TABLE 1. Perinatal HIV-1 Transmission Rates* for Eligible Mother–Child Pairs for Total and Reduced Samples, 1995–1997

	Total Sample (N = 217)				Reduced Sample (N = 149)			
	Number Infected	Total Number of Infants	Transmission Rate	P Value	Number Infected	Total Number of Infants	Transmission Rate	P Value
Baseline birth year (1993)	11	88	12.5%					
Transmission by birth year	12	217	5.5%	.04‡				
3-year average (1995–1997)								
1995	7	83	8.4%	.27§	5	60	8.3%	.39§
1996	2	68	2.9%		1	46	2.2%	
1997	3	66	4.6%		2	43	4.7%	
Transmission by zidovudine prescription								
All 3 arms†	7	160	4.4%	.3	4	122	3.3%	.04
Not 3 arms	5	57	8.8%		4	27	14.8%	
Transmission by zidovudine prescription								
All 3 arms†	7	160	4.4%	.76§	4	122	3.3%	.02§
2 arms	4	36	11.1%		3	23	13.0%	
PRE and IP	0	2	0%		0	1	0%	
IP and NEO	2	13	15.4%		1	8	12.5%	
PRE and NEO	2	21	9.5%		2	14	14.3%	
1 arm	1	6	16.7%		1	4	25.0%	
PRE only	1	2	50.0%		1	2	50.0%	
IP only	0	0	0%		0	0	0%	
NEO only	0	4	0%		0	2	0%	
0 arms	0	15	0%		0	0	0%	

PRE indicates zidovudine prescribed prenatally; IP, zidovudine prescribed intrapartum; NEO, zidovudine prescribed neonatally.

* Calculated on the basis of follow-up of infants' HIV infection status through May 1, 1999.

† All 3 arms = zidovudine prescribed prenatally, during intrapartum, and neonatally.

‡ P value comparing transmission rate average (1995–1997) to baseline year, 1993.

§ Mantel-Hansel χ^2 test for trend.

|| Fisher exact test.

women with CD4 counts 200 to 499/mm³ were only 1.23 times more likely to have been prescribed all 3 arms of zidovudine compared with women with CD4 counts \geq 500/mm³. It is interesting that women who resided in rural counties at the time of HIV diagnosis were 1.73 times more likely to have been prescribed all 3 arms of zidovudine compared with women who resided in urban counties. In addition, women who experienced premature rupture of membranes >4 hours before delivery were 3 times more likely to have received all 3 arms of zidovudine. As expected, women with inadequate prenatal care were somewhat less likely to have been prescribed all 3 arms of zidovudine as compared with women who had adequate care (OR: 0.75; 95% CI: 0.32–1.73).

Table 3 presents the distribution of selected characteristics of HIV-infected mothers by infants' HIV infection status. Mother–child pairs that were prescribed all 3 arms of zidovudine were less likely to have an infected infant (crude OR: 0.19; 95% CI: 0.05–0.84), translating to an 81% reduction in the risk of perinatal transmission of HIV-1. As expected, women with 0 to 199 CD4 counts/mm³ were almost 2 times more likely to have an infected infant (OR: 1.97; 95% CI: 0.33–11.77) compared with women with \geq 500 CD4 counts/mm³. Women who participated in risky behaviors, such as drinking alcohol, smoking cigarettes, and using illegal drugs, or received a diagnosis of an STD were more likely to have an infected infant compared with women who did not participate in those risky behaviors. Living in rural counties as compared with living in urban counties at the time of HIV diagnosis essentially did not in-

crease the risk of having a HIV-infected infant. In addition, women who had inadequate prenatal care and women who were prescribed zidovudine before pregnancy were more likely to have an infected infant than women without these characteristics.

For the logistic modeling, variables that constituted the full model were zidovudine prescription (all 3 arms), CD4 count (3 levels), maternal age, illicit drug use, and urban/rural county of residence at maternal HIV diagnosis. The likelihood ratio test was used to determine variables that were needed in the model. No significant interactions were identified. In the final multivariate model, the odds of the infant's developing HIV infection among pregnant HIV-positive women who received all 3 arms of the zidovudine regimen was 85% lower than the odds of the infant's developing HIV infection among pregnant HIV-positive women who did not receive all 3 arms of the zidovudine regimen, controlling for CD4 count/mm³, illicit drug use, and maternal age (adjusted OR: 0.15; 95% CI: 0.02–0.96; data not shown).

DISCUSSION

In this study, we found a transmission rate in 1993 of 12.5%, which is similar to several other studies^{5,15} but not as high as 18% to 19%^{16,17} or approximately 25%^{5,9,18–20} observed by others. The overall transmission rate for 1995 through 1997 was 5.5% compared with 12.5% in 1993 ($P = .04$). The transmission rates decreased from 12.5% in 1993 to 2.9% in 1996 and then increased slightly to 4.6% in 1997; the trend was not significant. This decline was similar to that seen in a North Carolina study (21% in 1993 to 9% in 1994)⁵ and a study of 4 US cities (22% before 1992 to

TABLE 2. Distribution of Selected Characteristics of Mother–Child Pairs With Maternal CD4 Counts by Zidovudine Prescription (*N* = 149)*

Characteristic	All 3 Arms	Not 3 Arms	OR	95% CI
Birth cohort year				
1995	41 (68%)	19 (32%)	0.16	0.04–0.59†
1996	41 (89%)	5 (11%)	0.62	0.41–0.52†
1997	40 (93%)	3 (7%)	1.00	Referent
Age (y)				
≤26	72 (81%)	17 (19%)	0.85	0.36–2.00
>26	50 (83%)	10 (17%)	1.00	Referent
Race/ethnicity				
Black/other	107 (80%)	26 (20%)	0.27	0.04–2.17
White	15 (94%)	1 (6%)	1.00	Referent
CD4 count during pregnancy‡				
0–199/mm ³	17 (100%)	0 (0%)	10.25	0.58–181.08
200–499/mm ³	56 (81%)	13 (19%)	1.23	0.53–2.87
≥500/mm ³	49 (78%)	14 (22%)	1.00	Referent
Alcohol use during pregnancy				
Yes	14 (74%)	5 (26%)	0.60	0.20–1.83
No	103 (82%)	22 (18%)	1.00	Referent
Missing	5 (100%)	0 (0%)	—	—
Cigarette smoking during pregnancy				
Yes	31 (76%)	10 (24%)	0.47	0.19–1.18
No	86 (87%)	13 (13%)	1.00	Referent
Missing	5 (56%)	4 (44%)	—	—
Illicit drug use during pregnancy				
Yes	18 (67%)	9 (33%)	0.35	0.14–0.89†
No	104 (85%)	18 (15%)	1.00	Referent
STD diagnosed during pregnancy				
Yes	29 (60%)	19 (40%)	0.13	0.05–0.34†
No	92 (92%)	8 (8%)	1.00	Referent
Missing	1 (100%)	0 (0%)	—	—
Maternal county of residence at HIV-1 diagnosis				
Rural	46 (87%)	7 (13%)	1.73	0.68–4.41
Urban	76 (79%)	20 (21%)	1.00	Referent
Type of health insurance				
Medicaid/other/none	109 (82%)	24 (18%)	1.30	0.25–6.64
Private	7 (78%)	2 (22%)	1.00	Referent
Missing	6 (86%)	1 (14%)	—	—
Zidovudine before pregnancy				
Yes	101 (80%)	26 (20%)	0.19	0.02–1.44
No	21 (95%)	1 (5%)	1.00	Referent
Prenatal care				
Inadequate	50 (79%)	13 (21%)	0.75	0.32–1.73
Adequate	72 (84%)	14 (16%)	1.00	Referent
Presence of chorioamnionitis				
Yes	12 (80%)	3 (20%)	0.87	0.23–3.33
No	110 (82%)	24 (18%)	1.00	Referent
Ruptured membranes				
>4 h	25 (93%)	2 (7%)	3.05	0.67–13.95
≤4 h	82 (80%)	20 (20%)	1.00	Referent
Missing	15 (75%)	5 (25%)	—	—
Type of delivery				
Cesarean	17 (85%)	3 (15%)	1.30	0.35–4.78
Vaginal	105 (81%)	24 (19%)	1.00	Referent

* Excludes missing or unknown drug use during pregnancy.

† Significant at *P* < .05.

‡ Row percentage.

11% in 1995).¹⁶ As expected, the transmission rates for those mother–child pairs that were prescribed all 3 arms of zidovudine was the lowest (4.4%; 95% CI: 1.21%–7.54%). The rates increased as the number of arms decreased.

This study also demonstrates how quickly a small, southern, rural state responded to the recommendations for the use of zidovudine in HIV-1-infected pregnant women and their children⁴; the proportions of HIV-1-infected mothers and their children being offered all 3 arms of zidovudine increased from 68% in 1995 to 93% in 1997 (*P* = .003). In another population-based study of 4 states that assessed the im-

plementation of the USPHS guidelines in 1993, 1995, and 1996, the proportions of women and children who were offered prenatal, intrapartum, and neonatal zidovudine increased from 27% to 85%, 5% to 75%, and 5% to 76%, respectively.²¹ Nationally, the percentage of women and children who received any zidovudine increased from 7% to 91%, and the percentage of those who received all 3 arms of zidovudine increased to 61%.²² The percentage of women and children who received all 3 arms of zidovudine in our study from 1995 to 1997 is 73.7%, which is higher than the national figure.

Our unadjusted OR for the relationship of being

TABLE 3. Distribution of Selected Characteristics of Mother–Child Pairs by HIV-1 Infection Status of Infant (N = 149)*

Characteristic	Infected	Not Infected	OR	95% CI
Zidovudine prescription				
All 3 arms	4 (3%)	118 (97%)	0.19	0.05, 0.84†
Not all 3 arms	4 (15%)	23 (85%)	1.00	Referent
Birth cohort year				
1995	5 (8%)	55 (92%)	1.86	0.34–10.08
1996	1 (2%)	45 (98%)	0.46	0.04–5.21
1997	2 (5%)	41 (95%)	1.00	Referent
Age (y)				
≤26	6 (7%)	83 (93%)	2.01	0.41–10.75
>26	2 (3%)	58 (97%)	1.00	Referent
Race/ethnicity				
Black/other	7 (5%)	126 (95%)	0.83	0.10–7.25
White	1 (6%)	15 (94%)	1.00	Referent
CD4 count during pregnancy§				
0–199/mm ³	2 (12%)	15 (88%)	1.97	0.33–11.77
200–499/mm ³	2 (3%)	67 (97%)	0.44	0.08–2.49
≥500/mm ³	4 (6%)	59 (94%)	1.00	Referent
Alcohol use during pregnancy				
Yes	1 (5%)	18 (95%)	1.10	0.13–9.69
No	6 (5%)	119 (95%)	1.00	Referent
Missing	1 (20%)	4 (80%)	—	—
Cigarette smoking during pregnancy				
Yes	4 (10%)	37 (90%)	5.24	0.92–29.85
No	2 (2%)	97 (98%)	1.00	Referent
Missing	2 (22%)	7 (78%)	—	—
Illicit drug use during pregnancy				
Yes	3 (11%)	24 (89%)	2.93	0.65–13.07
No	5 (4%)	117 (96%)	1.00	Referent
STD diagnosed during pregnancy				
Yes	4 (8%)	44 (92%)	2.18	0.52–9.13
No	4 (4%)	96 (96%)	1.00	Referent
Missing	0 (0%)	1 (100%)	—	—
Maternal county of residence at HIV-1 diagnosis				
Rural	3 (6%)	50 (94%)	1.09	0.25–4.76
Urban	5 (5%)	91 (95%)	1.00	Referent
Type of health insurance				
Medicaid/other/none	8 (6%)	125 (94%)	1.29	0.07–24.04
Private	0 (0%)	9 (100%)	1.00	Referent
Missing	0 (0%)	7 (100%)	—	—
Zidovudine before pregnancy				
Yes	7 (6%)	120 (94%)	1.23	0.14–10.47
No	1 (5%)	21 (95%)	1.00	Referent
Prenatal care				
Inadequate	5 (8%)	58 (92%)	2.39	0.55–10.38
Adequate	3 (4%)	83 (96%)	1.00	Referent
Presence of chorioamnionitis				
Yes	0 (0%)	15 (100%)	0.48	0.03–8.73
No	8 (6%)	126 (94%)	1.00	Referent
Ruptured membranes				
≥4 h	1 (4%)	26 (96%)	0.62	0.07–5.34
<4 h	6 (6%)	96 (94%)	1.00	Referent
Missing	1 (5%)	19 (95%)	—	—
Type of delivery				
Cesarean	0 (0%)	20 (100%)	0.35	0.02–6.28
Vaginal	8 (6%)	121 (94%)	1.00	Referent

* Excludes missing or unknown drug use during pregnancy.

† Significant at $\alpha = 0.05$.

offered all 3 arms of zidovudine and the HIV infection status of the infant was 0.19 (95% CI: 0.05–0.84), but after adjustment for CD4 count, illicit drug use, and maternal age, the OR was reduced to 0.15 (95% CI: 0.02–0.96). The adjusted OR for the transmission of HIV-1 comparing those who were offered prenatal zidovudine with those who were not offered zidovudine controlling for CD4 count was 0.36 (95% CI: 0.14–0.92) in 1 study.²⁰ Simonds et al¹⁶ reported an unadjusted OR of 0.60 (95% CI: 0.4–0.9; $P = .01$) for the use of both prenatal and neonatal zidovudine on HIV transmission. In our study, the sample was too

small to compare women who were offered prenatal zidovudine with those who were not offered zidovudine. However, when we compared women who were offered or prescribed any zidovudine with women who were offered or prescribed no zidovudine controlling for CD4 count, the adjusted OR for the transmission of HIV-1 was 0.85 (95% CI: 0.32–2.29). In another southern predominantly rural state, the transmission rate for mothers and children who received any zidovudine was 5.7% (5/87) compared with that of mothers and children who did not receive any zidovudine 18.9% (20 of 106; $P = .007$).

In the present study, there was no difference in the transmission rates between mothers who took any zidovudine (7.6% [17 of 223]) compared with mothers and infants who had no zidovudine (7.3% [6 of 82]; $P = .93$). The lack of difference in the transmission rates could have occurred because we underestimated the transmission rates. Among those who had no zidovudine ($N = 82$) were 25 children with an unknown HIV status at the time of analysis. When a 25% transmission rate was applied as was observed in the ACTG 076 clinical trial,³ we estimated the transmission rate in our population to be 14.6%. Among those who had any zidovudine ($N = 223$) were 48 children with unknown HIV status at the time of analysis. Of those, 84% (38 of 48) received all 3 arms of zidovudine. When a 6.4% transmission rate was applied as was observed by a multistate enhanced perinatal surveillance evaluation funded by the Centers for Disease Control and Prevention,²³ we estimated the transmission rate to be 8.5%.

The strength of this study is that it is population based. The sample came from the HIV/AIDS surveillance registry of a state health department, and this study sample of women is representative of the HIV-1-infected pregnant women in this geographically defined population. The other studies that examined the relationship between zidovudine use and HIV-1 transmission have been clinic based^{8,9,15,17-20} and may not be generalizable to all populations of HIV-1-infected women and their children. However, there are limitations to our study. The small sample size accounts for large variances and wide CIs of the estimate of risk. Another limitation of this study is its inability to measure compliance with the zidovudine regimen as described.

These analyses included only the women with recorded CD4 counts and drug use. Both factors were identified as confounders, and the missing data were excluded to accommodate the logistic modeling. In the collection of these data, the prenatal care record (located in the obstetrical and gynecological offices) and the HIV medical care records (eg, the Ryan White Care Consortia) were not routinely abstracted because of lack of personnel, and we believe that the missing CD4 counts would be contained in those records.

Bias could have been in operation in the selection of the total sample ($N = 305$), but it is unlikely. The women and children who were included were those who had been reported to the HIV/AIDS surveillance registry as HIV or AIDS cases. Women who were not reported to the surveillance registry for one reason or another may have different characteristics and ultimately different risks for having an HIV-1-infected infant, which could result in an underestimation of the HIV-1 perinatal transmission rate. To explore this possibility, HIV/AIDS Surveillance staff conducted a match of the HIV/AIDS registry with the Vital Records Live Birth registry to identify HIV-1-infected women who had given birth in the state in calendar years 1993, 1995, and 1996. The sensitivity of the surveillance system was found to be $>80\%$ for all 3 years. The sensitivity was calculated as the number of mother-child pairs that were identified

via the vital records live birth and HIV/AIDS surveillance data match divided by the number of children born exposed to HIV-1 in the state as determined by the Survey of Childbearing Women.²⁴

CONCLUSION

This study reports the decreases in the perinatal HIV-1 transmission rates for a southern, rural state and also demonstrates the quick response to USPHS recommendations for the use of zidovudine among HIV-1-infected pregnant women. Nationally, the effectiveness of the USPHS guidelines have been reflected in the decreases in perinatally acquired AIDS cases. The epidemiologic literature has identified inadequate prenatal care and/or illicit drug use as obstacles to reducing further perinatal HIV infection. Strategies to address these obstacles are needed and will be critical in achieving maximum reduction of perinatal HIV infection in this population of rural, southern women.

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