HIV Infection and Zidovudine Use in Childbearing Women

Jasmine Sia, MPH*; Sindy Paul, MD, MPH‡; Rose Marie Martin, MPH‡; and Helene Cross, PhD‡

ABSTRACT. Objective. The risk of vertical HIV transmission from mother to child has been shown to be markedly decreased through HIV education, counseling, testing, and zidovudine (ZDV) use. The US Public Health Service published guidelines in 1994 for the use of ZDV on the basis of results of the AIDS Clinical Trials Group Protocol, a multicenter clinical trial of ZDV. The Public Health Service followed these guidelines with recommendations for routine HIV counseling and testing with informed consent for all pregnant women. New Jersey adopted these guidelines as the standard of care and created a program implementing the standard in all hospitals with maternity units. The purpose of this report was to study the trends in the rate of HIV infection in childbearing women over the past decade and to follow patterns of use of ZDV in the HIV-positive women, as a marker for the success of New Jersey’s policy and program to reduce mother-to-child transmission.

Methods. Since 1988 in New Jersey, blood from heel-stick filter papers has been tested for the presence of HIV antibody through anonymous, unlinked surveys. Excess blood from screening for inborn errors of metabolism for all infants who were born in the state from July through September of each year was tested using a Food and Drug Administration–approved HIV-1 and Western blot test. Age, race, and ethnicity were recorded, as well as the results from the HIV-1 and Western blot tests. Since 1994, specimens confirmed to be HIV-1 positive by Western blot test were tested for the presence of ZDV, and the results were recorded.

Results. The number of New Jersey women included in the study for the period 1990 through 2002 numbered 37,230. The percentage of childbearing women who tested positive for HIV declined by 55% during the period, although the declines were not uniform in all subgroups. In the early 1990s, women who were <30 years old had higher infection rates than older women, but this has not been a consistent pattern during the period. Younger women again had a higher rate in 2002. When HIV-positive rates are examined by 5-year age groups, the declines are dramatic for younger women. The rate per 100 women 20 through 24 years decreased from 0.46 per 100 tested women in 1990 to 0.29 in 2002 and for women 25 through 29 years from 0.51 per 100 in 1990 to 0.25 in 2002. The rate for women 30 through 34 years of age declined from 0.54 in 1990 to 0.13 in 2002. During the same time period, the rate per 100 tested women 35 though 39 years of age increased from 0.23 to 0.33. Black non-Hispanic women who give birth to live infants have the highest HIV-positive rates, followed by Hispanic women and white non-Hispanic women. In 2002, this rate was 0.74 per 100 in black non-Hispanic women, 0.22 per 100 in Hispanic women, and 0.08 in white non-Hispanic women. Although major disparities continue, the infection rate in black non-Hispanic women demonstrated the greatest decrease during the period, followed by the decline among Hispanic women. The use of ZDV in HIV-positive women increased dramatically during the period, from 13.3% in 1994, when it was first tested in New Jersey, to an all-time high of 88.5% in 2002.

Conclusions. Reducing perinatal HIV transmission is a priority for the New Jersey Department of Health and Senior Services. Reducing perinatal transmission can be accomplished by reducing the number of infants who are exposed perinatally or decreasing the percentage of exposed infants for whom transmission occurs or both. The decrease in prevalence of HIV-positive status in childbearing women is in opposition to an overall increasing trend in prevalence rates. This decrease is thought to be attributable in part to the positive impact of numerous education and prevention programs but may also be the result of a voluntary decision on the part of HIV-infected women not to become pregnant or not to carry to term. In addition, the cohort of women who became infected in the early years of the epidemic may be aging out of their childbearing years, may have more advanced disease with a concomitant difficulty with fertility and carrying to term, or may have died. In New Jersey, a greater proportion of women with newly diagnosed HIV disease are past their childbearing years as compared with earlier years. Increased use of ZDV is thought to be attributable to several factors: dissemination of information to health care providers via continuing medical education activities; dissemination of information to the public, in particular to women; outreach via community-based organizations; and New Jersey Department of Health and Senior Service regulations and policies for mandatory counseling and voluntary testing of all pregnant women. A recent addition to New Jersey’s comprehensive program to decrease perinatal transmission occurred in 2002 with dissemination to hospitals of the department’s standard of care for women who present in labor with unknown HIV status. Physicians, nurses, and hospitals play vital roles in preventing vertical transmission of HIV by providing preconception and postconception counseling, testing with consent of pregnant women, and treatment for HIV-positive mothers, including administration of ZDV. This study not only provides an estimate of the prevalence of HIV infection in the population of childbearing women but also provides a means of examining the vertical transmission of HIV infection from mother to child. Continued research on this subpopulation as well as on other groups will provide additional knowledge to help in the overall goal of reducing HIV prevalence.

The risk of vertical HIV transmission from mother to child has been shown to be dramatically decreased through HIV education, counseling, testing, and zidovudine (ZDV) use. In 1994, the US Public Health Service published guidelines for the use of ZDV on the basis of results from the AIDS Clinical Trials Group Protocol 076 (ACTG 076), a multicenter clinical trial of this antiviral medication. It was found that giving ZDV to HIV-positive women during pregnancy and labor and to their infants after birth reduced the rate of HIV transmission from 25.5% to 8.3%.\(^1\)\(^2\) In the following year, the US Public Health Service recommended routine HIV counseling and testing with informed consent for all pregnant women.\(^3\) Limiting HIV testing to women with identified risk factors would miss a significant number of HIV-positive women.\(^4\)\(^5\) Since the adoption of these 2 sets of guidelines, the national rate of reported cases of pediatric AIDS has decreased remarkably by 75% from the rate in 1992.\(^6\)

There have been advances in medical management since the ACTG 076 clinical trial. These advances include combination therapy, an elective cesarean section for women with a viral load >1000, resistance testing for HIV, and rapid HIV testing and short-course therapy for women who present in labor with unknown HIV status. Taking advantage of these advances can result in a decline in vertical HIV transmission rates to a level of 1.0% to 2.0%.\(^7\)

Although vertical HIV transmission has declined, there are still 300 to 400 cases of perinatal transmission of HIV infection each year in the United States.\(^8\) Lack of or inadequate prenatal care, lack of counseling and testing, and lack of awareness of available treatments contribute to this outcome. Since 1993, New Jersey has maintained an active follow-up system, Enhanced Surveillance for Perinatal Prevention, which is designed to determine infection status for all perinatally exposed children. This system provides information on the outcomes of births to HIV-positive women. Follow-up is designed also to collect information on prenatal, intrapartum, and pediatric care, including antiretroviral use and prophylaxis for opportunistic infections.

As of 2002 data, New Jersey ranks fifth in the nation in cumulative reported AIDS cases, has the highest percentage of women reported with AIDS (28%), and has the third most reported pediatric AIDS cases. The overwhelming majority (96%) of pediatric HIV and AIDS cases are attributable to vertical transmission of the disease, further emphasizing the importance of prevention efforts.\(^9\)

Since 1988, the New Jersey Department of Health and Senior Services’ (NJDHSS) Division of HIV/AIDS Services has conducted yearly anonymous HIV serosurveys of the state’s childbearing women.\(^10\) As a result of the findings from the ACTG 076, since 1994, NJDHSS has also been monitoring the use of ZDV in HIV-positive childbearing women. This article studies trends in the rate of HIV infection in childbearing women over the past decade and follows patterns of use of ZDV among the HIV-positive women, as a marker for the success of New Jersey’s policy to reduce mother-to-child transmission.

METHODS

Data Collection

The survey has been exempted from the need for institutional review board approval, as the process is an anonymous, unlinked study that uses no identifiers. Blood specimens from all newborns were tested for the presence of HIV antibody. In New Jersey, all infants are routinely screened at birth for inborn errors of metabolism by analyzing blood samples collected on heel-stick filter papers. Excess blood spots that remained on the heel-stick filter papers were obtained for the purpose of this study for all infants who were born from July through September of each year. Each specimen was assigned a study number linking it to specific information about the mother and the newborn (eg, age, race, ethnicity). The study numbers were not linked in any way to the identity of the mother and the newborn. The specimens were then analyzed using a Food and Drug Administration–approved HIV-1 test and a Food and Drug Administration–approved Western blot test. Specimens that were confirmed to be HIV-1 positive by Western blot test were then tested for the presence of ZDV. The Centers for Disease Control and Prevention (CDC) performed the ZDV tests from the mid- to late-1990s as part of the process of analyzing data in the national HIV Seroprevalence Survey Among Childbearing Women. For this test, the CDC modified and evaluated a radioimmunoasay for serum and used the modified radioimmunoasay to measure ZDV in dried blood-spot specimens collected for the newborn screening tests that were positive for HIV.\(^11\)\(^12\) Since the 2001 survey, the University of California (San Diego) has performed the ZDV tests on New Jersey’s positive specimens and controls. The procedure used is a modification of a plasma ZDV enzyme immunoasay assay validated by the University of California (San Diego) for dried blood spots. This procedure consists of eluting the dried blood spots in assay buffer and adding the eluted sample to the enzyme immunoasay microtiter plate wells in duplicate along with standards and controls prepared in the same way. The assay is based on the competition between the ZDV in the sample and the ZDV enzyme conjugate for binding to ZDV antibodies coated onto the microtiter plate wells. The sensitivity of the assay is 12.5 ng/mL, and overall recovery is 92%. Interassay precision is <14.5% coefficient of variation, and accuracy is within 5% deviation (n = 35; Diane Holland, University of California–San Diego, La Jolla, CA, personal communication, December 2003).

Data from the newborns of women who were not residents of New Jersey were excluded from the final analysis, as the responsibility of the state is its residents. Out-of-state residents who deliver in New Jersey form a very small proportion of the total population of the state is its residents. Out-of-state residents who deliver in New Jersey form a very small proportion of the total population. The survey was conducted with data from the CDC’s enhanced surveillance program for perinatal HIV infection. The women who were not residents of New Jersey, so their exclusion has minimal effect. Newborns of mothers who were reported as living in New Jersey but did not have specific addresses were included. In instances of multiple births, only the data of 1 infant were included in the study to prevent counting the mother more than once.

Statistics

Various software packages have been used to manage and analyze the data resulting from the survey. Among the packages used were Prodis, Access, and Excel. For the 2002 data, Epi-Info Version 2002 statistical software from the CDC was used to calculate frequencies and percentage distributions for the number of women who were HIV positive; the number of women who received ZDV before giving birth; and the rates of HIV infection in women on the basis of their age, race, and ethnicity.

The ages of the women were grouped into 6 categories spanning 5 years each and 2 open-ended categories covering the

ABBREVIATIONS. ZDV, zidovudine; ACTG 076, AIDS Clinical Trials Group Protocol 076; NJDHSS, New Jersey Department of Health and Senior Services; CDC, Centers for Disease Control and Prevention.
youngest and oldest women in the survey, respectively. The race/ethnicity categories for analysis were derived from combining responses to items on Mother’s Race and Mother’s Spanish/Hisp
panic Origin. If a woman reported that she was Hispanic (Mex
ican/ American, Puerto Rican, Cuban, or other), then she was considered to be Hispanic. If the mother stated that she was not Hispanic, then the reported race was used in conjunction with the non-Hispanic status, i.e., “white non-Hispanic,” “black non-Hispanic,” “Asian/Pacific Islander non-Hispanic,” “American Indian/Alaskan Native non-Hispanic,” or “other race non-Hispanic.” If a respondent did not report being Hispanic and the race category was reported as “undetermined,” then she was considered to be of unknown race/ethnicity. Only data from the 3 largest race/ethnicity groups in New Jersey are presented in this report (white non-Hispanic, black non-Hispanic, and Hispanic) because of small numbers in the other groups.

RESULTS

From 1990 through 2002, a total of 372305 women were included in this study. In 1990, 0.49% of childbearing women in New Jersey tested positive for HIV. The next year, this rate increased to 0.56% but since decreased steadily to 0.19% in 2001, the lowest it has ever been. The latest data from 2002 show that a shift has occurred in this trend. For the first time since 1991, the percentage of childbearing women who test positive for HIV increased, from 0.19% in 2001 to 0.22% in 2002 (Table 1).

From 1990 until 1995, more childbearing women who were <30 years old (0.62% in 1990 to 0.38% in 1995) were HIV positive than their older counterparts (0.43% to 0.21%). Since then, the rates of HIV prevalence have at times been greater in older than in younger women. In 2002, younger childbearing women again had a greater rate of HIV infection than older women did (0.25% and 0.19%, respectively). However, when the HIV-positive rates are examined by 5-year age groups (data not shown), the declines are dramatic for younger women. The rate per 100 women 20 through 24 years decreased from 0.46 per 100 women tested in 1990 to 0.29 in 2002 and for women 25 through 29 years from 0.51 per 100 in 1990 to 0.25 in 2002. In addition, the rate declined from 0.54 in 1990 to 0.13 in 2002 for women 30 through 34 years of age. During the same time period, the rate per 100 tested women aged 35 through 39 years increased from 0.23 to 0.33.

Data from 1990 to 2002 on race and ethnicity clearly show that a disproportionate number of black non-Hispanic women are HIV positive compared with white non-Hispanic women (Fig 1). In 2002, of the 62 HIV-positive mothers, 21.88% were non-Hispanic whites and 51.61% were non-Hispanic blacks. In terms of the rate of HIV infection within the 3 largest racial and ethnic groups, black non-Hispanic women have the highest rates, Hispanic women have the second highest rates, and white non-Hispanic women have the lowest rates. These 3 groups all have experienced declines in rates of HIV infection since 1991. Black non-Hispanic women have had the most dramatic decrease in HIV infection rate, from 1.88% in 1991 to 0.74% in 2002. Of note, the rate of HIV infection in black women had been stable between 0.87% and 0.89% since 1998, until the rate dropped substantially again in 2002 to 0.74%. Among Hispanic women, HIV infection rates have also decreased steadily from 0.84% in 1991 to 0.22% in 2002, which represented an increase from the rate in the previous year. The rate increase in Hispanic women in the most recent year must be viewed cautiously, as efforts were made in that year to improve reporting of Hispanic ethnicity. Rates of HIV infection in white non-Hispanic women with HIV have not declined as steadily as those in the other 2 groups. In 1990, 0.15% of white non-Hispanic women were HIV positive. This rate decreased to 0.05% in 1996 but rose again in 2000 and 2002 to 0.08%.

Use of ZDV in HIV-positive pregnant women has increased dramatically from 13.27% in 1994, when it was first measured in New Jersey, to an all-time high of 88.52% in 2002 (Fig 2, Table 1). Between 1994 and 1997, the use of ZDV increased 5 times to 69.86%. In 1998 and 1999, there were lower rates of use (64.94% and 60.00%, respectively). The presence of ZDV in HIV-positive specimens was not tested in 2000 because of a change in testing technology that did not allow for ZDV testing, but in 2001, the rate had once again jumped, to 73.58%. Data from 2002 indicate that the use of ZDV continues to increase.

DISCUSSION

Reducing perinatal HIV transmission is a priority for NJDHSS. This can be accomplished by reducing the number of infants who are exposed perinatally or decreasing the percentage of exposed infants for whom transmission occurs or both. Health objectives issued by NJDHSS call for a decrease in the rate of HIV infection in pregnant women to 0.10% by 2010.12 Although in opposition to an overall increasing trend in prevalence rates, the HIV infection rate in childbearing women declined dramatically during the study period. The steady decrease in HIV-positive rates in childbearing women are thought to be a result of the positive impact of the numerous prevention messages that have been disseminated through governmental and other sources. The prevalence rate decreases may also reflect a voluntary decision on the part of HIV-infected women not to

<table>
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<th>No. of HIV+ Tested</th>
<th>No. of ZDV+ Tested</th>
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<td>70</td>
<td>0.24</td>
</tr>
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</table>

— indicates that testing for ZDV in New Jersey was not done until 1994.
* Testing for ZDV was not done in 2000, because a change in the test kit used for HIV resulted in specimens that were unsuitable for additional testing.

become pregnant or not to carry to term. In addition, the cohort of women who became infected in the early stages of the epidemic may be aging out of their childbearing years, may have more advanced disease and therefore be experiencing difficulty with fertility and carrying to term, or may have died.\(^{13}\) In addition, in New Jersey, a greater proportion of women with newly diagnosed HIV disease are past their childbearing years as compared with earlier years.\(^{14}\) Similar to the findings of a recent study in New York, the rates of HIV infection in minority women showed disproportionate declines.\(^{15}\) The relative declines in prevalence among childbearing women of the various race/ethnic groups may reflect the effect of targeted prevention efforts for minority women and the low HIV prevalence among white non-Hispanic childbearing women throughout the study period. Although the HIV infection rate has decreased during the study period, since 1995, the rate in white non-Hispanic women of childbearing age has ranged from 0.05% to 0.08% and is once again at 0.08%. Caution must be exercised in interpreting changes in this rate, as it is based on a small number of cases.

Encouraging is that rates of infection in the 2 other major race and ethnic groups, black non-Hispanic and Hispanic women, have fallen. Although minority women had the largest decline in prevalence rate, the black non-Hispanic rate remained \(>9\) times and the Hispanic rate was almost 3 times the white non-Hispanic rate in 2002. This emphasizes the need for continued targeting of prevention efforts toward minority communities.

Despite the overall downward trend, HIV infection rates in New Jersey’s women of childbearing age have recently risen from 0.19% in 2001 to 0.22% in 2002. Because this increase is seen in only 1 year of data, additional years of data will be needed to determine whether this trend continues. The group that experienced the greatest increase in HIV infection in the last year of the study is younger women <30 years old, but the overall trend in the rates for younger mothers is a declining one. As with the overall HIV infection rate, additional years of data are needed to determine whether the increase in rate in 2002 is a lasting change in the existing trend. The recent increase in HIV infection in younger women
may be a result of perinatally infected adolescents’ now giving birth.16 In 2001, 1 of 53 childbearing women with HIV infection was <20 years old. In 2002, this ratio increased to 3 of 62. The cohort of perinatally infected children who are now reaching their childbearing years is one that needs additional monitoring and study. In addition, there has been an increasing proportion of HIV infections in New Jersey as a result of heterosexual transmission (Abdel Ibrahim, New Jersey Department of Health and Senior Services, Trenton, NJ, personal communication, August 2003). The only major age group without a decline in HIV infection among childbearing women was the 35 through 39 age group. This may reflect the cumulative risk of this age group. Increased age has also been associated with increasing risk of infection in other anonymous, unlinked surveys.17

Since 1994, ZDV has been recommended for all HIV-infected pregnant women and perinatally exposed newborns to prevent perinatal HIV transmission.18 Even starting ZDV in labor and delivery and continuing in the neonatal period as short-course therapy can reduce the risk of vertical transmission. In January 2004, the CDC recommended rapid HIV testing for women who are in labor with unknown HIV status or women who are at high risk for HIV and short-course antiretroviral therapy for those with a preliminary positive result.19 Because some HIV-positive women may have used ZDV at some earlier point in their pregnancies but not at the time of delivery, the reported rate of ZDV-positive women infected with HIV must be considered a minimum figure. In addition, laboratory assays are not available for all antiretroviral agents; therefore, the use of alternative agents other than ZDV cannot be evaluated. Some number of HIV-positive pregnant women may have used antiretroviral regimens that did not contain ZDV. Because the use of these agents cannot be evaluated, there may be an underestimation of the rate of antiretroviral use in this population.

The increase in ZDV use in New Jersey has led to a remarkable decrease in perinatal transmission rates from 75 (21%) perinatally infected children in 1993 to 4 (<2%) pediatric cases in 2002 (NJDHSS; data not shown). Increased use of ZDV can be attributed to several factors: 1) dissemination of information to health care providers via continuing medical education activities (eg, lectures, conferences, articles, a web site), 2) dissemination of information to the public/women, 3) outreach via community-based organizations, and 4) NJDHSS regulations and policies for mandatory counseling and voluntary testing of all pregnant women. In addition, dissemination to hospitals of the NJDHSS standard of care in 2002 for women who present in labor with unknown HIV status has helped to address the major missed opportunity for decreasing perinatal transmission in New Jersey: women who present in labor with unknown HIV status.

Physicians, nurses, and hospitals play vital roles in preventing vertical transmission of HIV by providing preconception and postconception counseling, testing with consent of pregnant women, and treatment for HIV-positive mothers. Continued education of health care providers about public health policy and recommendations for preventing vertical HIV transmission can further improve their performance.20 Delineating and disseminating uniform guidelines for prevention of vertical HIV transmission can promote a concerted and appropriate effort by health care providers. Continued education of the public and women about HIV infection and the availability of voluntary testing and treatment can also reduce perinatal transmission.

The CDC has highlighted the benefit of performing anonymous, unlinked serosurveys of all subpopulations to monitor the prevalence of HIV infection. Its studies have shown that in surveys that involve obtaining consent, participation bias has led to significantly decreased estimates of prevalence. For determining accurately the scope of the HIV epidemic and monitor the change in HIV prevalence, anonymous, unlinked serosurveys should be performed.21 In this study, examining the prevalence of HIV infection in childbearing women provides not only an estimate of the prevalence of HIV infection in this population but also a means of examining the vertical transmission of HIV infection from mother to child. Continued research on this subpopulation as well as others will provide additional knowledge to help in reducing HIV prevalence.

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