

HIV and Pregnancy in Resource-Poor Settings

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There are 33.4 million people living with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome. Globally, HIV/AIDS is the leading cause of death among women of reproductive age. In the United States and other developed countries, aggressive efforts to treat HIV-positive pregnant women with highly active antiretroviral therapy have decreased the maternal-to-child transmission (MTCT) from over 20% to less than 2%. However, in resource-poor settings, access to antiretroviral therapy (ART) is not readily available, and perinatal transmission rates remain as high as 45%. Women are at greater risk of heterosexual transmission of HIV, which is compounded by lack of condom use, imbalance of social power, and the high fertility rate. Prevention programs are needed to empower and educate women and engender community awareness for condom use. Prenatal screening and treatment, intrapartum ART, and postpartum prophylaxis must be made available to all women and children to prevent MTCT.

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Human immunodeficiency virus (HIV) and AIDS are recognized as major contributors to maternal mortality worldwide. Of the 33.4 million people affected with HIV/AIDS, 22.4 million live in sub-Saharan Africa, 3.8 million live in Southeast Asia, and 2 million live in Latin America (Figure 1). Almost 16 million (47%) are women, and 2.7 million (6.2%) are children.¹ According to the World Health Organization (WHO), approximately 60,000 fewer maternal deaths would have occurred in 2008 in the absence of HIV, and the maternal mortality rate from 1980 to 2008 would have dropped much more significantly

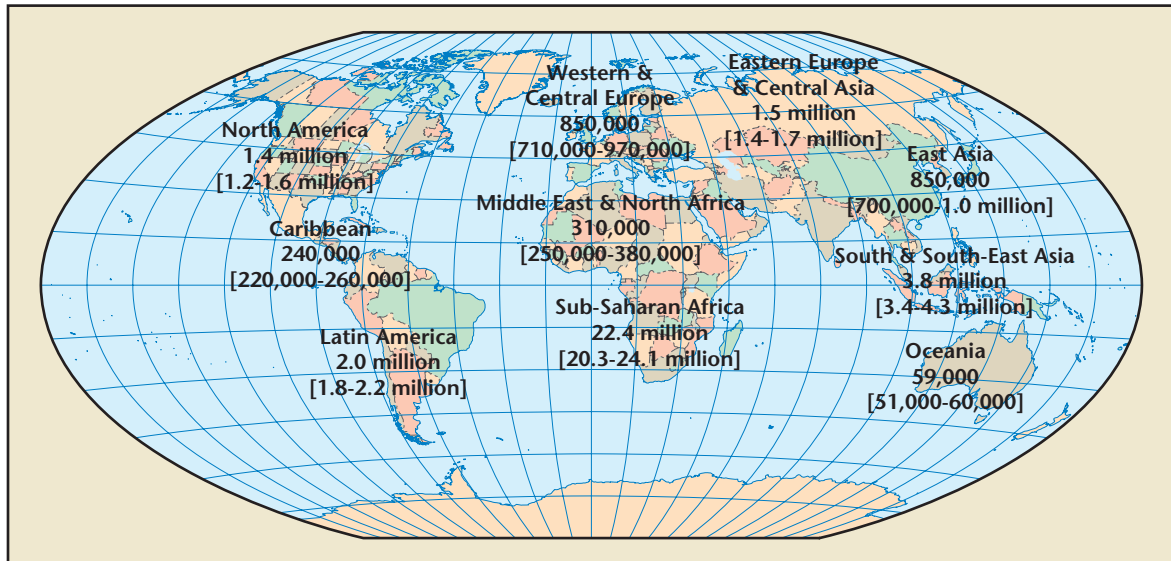


Figure 1. Adults and children estimated to be living with human immunodeficiency virus (2008). Reproduced with permission from UNAIDS/World Health Organization.¹ ©UNAIDS.

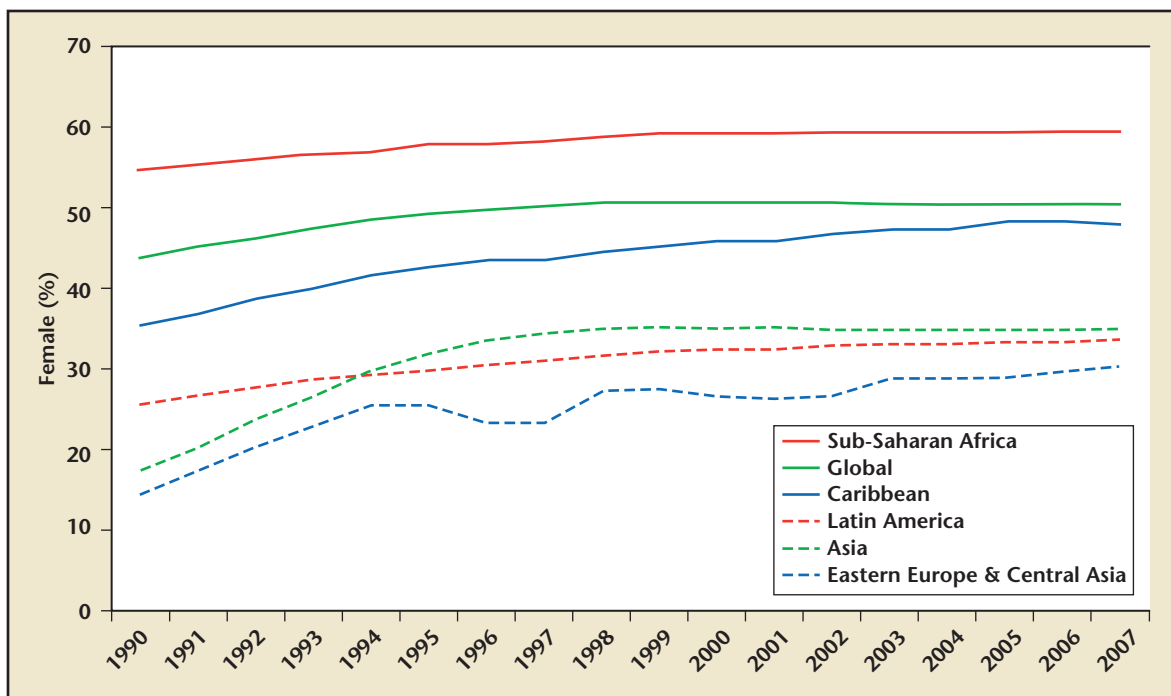


Figure 2. Percentage of female adults (age 15 years +) living with human immunodeficiency virus (1990-2007). Reproduced with permission from UNAIDS.

if it had not been for the introduction of the HIV epidemic.²

Impact on Women and Children

Women are twice as likely as men to contract HIV from unprotected intercourse.³ Over the past 2 decades, the

prevalence of HIV among women has increased dramatically. This increase has been felt most acutely in sub-Saharan Africa, where up to 60% of those living with HIV/AIDS are now women (Figure 2). Because 40% of those newly infected with HIV are be-

tween the ages of 15 and 24 years, the impact on reproductive-age women and their children has been particularly devastating.¹

Fear of testing positive for HIV prevents women from obtaining a definitive diagnosis. Women are particularly

afraid of the stigma associated with the disease and the possibility of abandonment and violence if they are found to be positive.⁴ One study in South Africa found that the HIV seroprevalence rate among women who refused routine antenatal HIV testing was 44%, compared with the general population of 29%.⁵ This finding is particularly significant because in 2008 an estimated 390,000 of the 430,000 new infections in children less than age 15 years occurred in sub-Saharan Africa.¹ Over 90% of these new infections occurred via maternal-to-child transmission (MTCT).⁶

Social and Economic Pressures on Women

Fertility

Women in developing nations face social and economic challenges. Married women are at increased pressure to immediately become pregnant and, therefore, have unprotected intercourse. In some regions, parents marry their daughters young to protect them from HIV/AIDS. However, African studies have demonstrated that married women are 50% to 59% more likely than unmarried women to

only places them at risk for HIV transmission, but it immediately decreases their opportunity to advance their education or find employment. As a result, they become even more economically dependent on men.⁴

Commercial Sex Workers

Commercial sex workers are particularly vulnerable to acquiring HIV. They are exposed to unstable work conditions and violence, which makes it difficult for them to negotiate safe sex practices. Some clients may offer to pay more for sex without a condom, threaten harm, or choose to hire others who do not require condom use. Sex workers are often stigmatized and marginalized, even by health workers, so that they face multiple barriers to accessing condoms, postexposure prophylaxis, and sexually transmitted infection (STI) and HIV testing and treatment.¹⁰ Their increased likelihood of having genital ulcers from both STIs and violence compounds their likelihood of acquiring HIV and, in turn, spreading it to others.¹¹ However, there have been a number of programs that have shown great success in reducing HIV transmission in this popu-

Antiretroviral Therapy for the Pregnant Patient

In 1994, the landmark Pediatric AIDS Clinical Trials Group (ACTG) 076 study demonstrated that a regimen of zidovudine (AZT) to the mother antepartum and intrapartum and to the neonate postpartum decreased the perinatal transmission rate from 25.5% to 8.3%, a 67.5% relative risk reduction.¹⁴ Since then, other studies have shown that more potent antiretroviral therapy (ART) is associated with perinatal transmission rates as low as 1%.¹⁵ In countries where ART is readily available, the recommendations are to treat all HIV-infected patients with ART (preferably highly active antiretroviral therapy [HAART]) after the first trimester, no later than 28 weeks, for the prevention of MTCT. If ART is needed for maternal health (eg, CD4 count < 350), it is initiated as soon as possible.^{16,17}

In resource-poor settings, obtaining a CD4 count is not always possible. As a result, WHO clinical staging is used to determine when a woman needs to start ART for maternal health reasons (Table 1).¹⁸ It is recommended that all pregnant women with WHO clinical stages 3 and 4 receive HAART, if available. Efforts to develop less expensive "short-courses" of AZT have been pursued. In 1998, a pilot program was initiated to prevent MTCT in 7 provinces in Thailand by offering AZT from 34 weeks gestation, during delivery, and postpartum to the infant for 1 to 6 weeks, with free powdered formula for 12 months. The HIV transmission rate decreased from 30% to 10%.¹⁹

In extremely resource-poor countries, the focus has been on the use of single-dose nevirapine for prophylaxis. The HIVNET 012 study in Uganda showed that a single dose of nevirapine given to pregnant women in labor and to the infant after birth could reduce MTCT by nearly 50% in

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become HIV infected. The women in these studies were virginal and at increased risk for hymenal, vaginal, and cervical lacerations. Their husbands were routinely older, with a history of multiple sexual partners, and potentially polygamous.⁷⁻⁹

Role as Caregivers

Women are the default caregivers of the family and are usually expected to care for family members who are ill or orphaned from HIV/AIDS. This not

only places them at risk for HIV transmission, but it immediately decreases their opportunity to advance their education or find employment. As a result, they become even more economically dependent on men.⁴

lation by increasing HIV awareness, counseling, testing, and treatment, even in resource-poor countries such as Haiti.¹² Success has been particularly notable in Thailand, where the government and nongovernment organizations (NGOs) worked together in the 1990s to implement a national HIV/AIDS program that targeted sex workers and the general population, which led to a decrease in the national transmission rate from 32% to 4% within a decade.¹³

Table 1
Interim WHO Clinical Staging of HIV/AIDS and HIV/AIDS
Case Definitions for Surveillance (2005)

Clinical stage 1: asymptomatic or generalized swelling of the lymph nodes

Clinical stage 2: includes minor weight loss (<10% body weight), minor mucocutaneous manifestations, and recurrent upper respiratory tract infections

Clinical stage 3: includes unexplained major weight loss (>10% body weight), chronic diarrhea >1 month, unexplained persistent fever, oral candidiasis or leukoplakia, severe bacterial infections, pulmonary tuberculosis, and acute necrotizing inflammation in the mouth; some persons with clinical stage 3 have AIDS

Clinical stage 4: includes wasting syndrome and 22 opportunistic infections or cancers related to HIV; all persons with clinical stage 4 have AIDS

HIV, human immunodeficiency virus; WHO, World Health Organization.

a breastfeeding population.²⁰ Single-dose nevirapine should be used with caution, though, as it has a long half-life and takes only a single-point mutation to become resistant and cause resistance to other non-nucleoside reverse transcriptase inhibitors. Adding nucleoside reverse transcriptase inhibitors (eg, AZT) to single-dose nevirapine for both the mother and infant has been shown to decrease viral replication and therefore, resistance. Studies are underway to determine the most optimal and cost-effective regimen.²¹

Optimal Mode of Delivery

By 2000, a multitude of studies had demonstrated that the HIV viral load was significantly associated with perinatal transmission.^{22,23} The risk of MTCT with a HIV viral load < 1000 was 1% to 2%, even with a vaginal delivery and without ART. At the same time, it was noted that, if a cesarean delivery was performed on a patient who was on AZT, the risk of perinatal transmission could be reduced from 5%-8% to 2%.²⁴ Given that cesarean delivery alone could potentially reduce the risk of perinatal

transmission to 2%, even for women with a viral load > 1000, the American College of Obstetricians and Gynecologists recommended that these patients should be counseled about the potential benefits of scheduled cesarean delivery at 38 weeks of gestation.²⁵

Since 2000, combination ART rather than single-dose AZT has become the standard of care for pregnant, HIV-infected patients, and it is likely that the risk of perinatal transmission has further decreased. In the developing world, scheduled cesarean deliveries are not always available for patients, and the potential risks of complications are higher, especially for women with low CD4 counts.^{26,27} Offering an elective cesarean delivery at 38 weeks is not the standard of care, and the focus instead has been on recognizing and preventing HIV infection with available ART.

Prenatal Care for the At-Risk or HIV-Infected Patient

HIV testing can be a challenge. Successful programs have ensured confidentiality and provided psychosocial support and social services. Counseling

emphasizes safe sex, partner disclosure, and preventive practices. At-risk patients are educated about the signs and symptoms of primary HIV infection during their first prenatal visit, including “acute retroviral syndrome” (which presents as fever, fatigue, rash, pharyngitis, myalgias, arthralgias, or lymphadenopathy), and AIDS-defining illnesses (Table 2).²⁸ Given the high coinfection rate with tuberculosis, malaria, and *Pneumocystis jiroveci* (formerly *Pneumocystis carinii*), prophylaxis for these diseases may be necessary.

Breastfeeding

In the developed world, where formula is readily available, breastfeeding is not recommended for the HIV-infected patient because there is up to a 5% to 20% risk of transmission. However, in the developing world this recommendation is not culturally or financially feasible, and mixed feeding and formula feeding have both been associated with an increase in infant mortality from diarrhea and respiratory infections. In these settings, the standard of care is for exclusive breastfeeding for the first 6 months of life. Solid food and formula can then be introduced at that time, but breastfeeding should be continued until age 1 to 2 years if feasible. Recent studies have shown that continuing either maternal or infant ART during breastfeeding reduces postnatal transmission. The WHO recently revised its guidelines to suggest that either treatment should be offered when available and continued until 1 week after exposure to breast milk has ended.²⁹

Conclusions

The deadline for the United Nations Millennium Development Goal 5—a three-quarters reduction in the maternal mortality ratio between 1990 and

Table 2
AIDS-Defining Illnesses

Candidiasis of bronchi, trachea, lungs, or esophagus
Cervical cancer, invasive
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal (>1 month duration)
Cytomegalovirus disease (other than liver, spleen, or nodes) or retinitis (with loss of vision)
Encephalopathy, HIV-related
Herpes simplex: chronic ulcer(s) (>1 month duration); or bronchitis, pneumonitis, or esophagitis
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis: chronic intestinal (>1 month duration)
Kaposi's sarcoma
Lymphoma, primary (of brain), Burkitt's or immunoblastic (or equivalent term)
<i>Mycobacterium avium</i> complex or <i>Mycobacterium kansasii</i> , disseminated or extrapulmonary
<i>Mycobacterium</i> , other species, disseminated or extrapulmonary
<i>Pneumocystis jiroveci</i> pneumonia (formerly <i>Pneumocystis carinii</i>)
Pneumonia, recurrent
Progressive multifocal leukoencephalopathy
<i>Salmonella</i> septicemia, recurrent
Toxoplasmosis of the brain
Tuberculosis, any site (pulmonary or extrapulmonary)
Wasting syndrome due to HIV
HIV, human immunodeficiency virus.

2015—is fast approaching. It has become increasingly apparent that this goal cannot be achieved without targeted efforts to recognize and treat reproductive-age women with HIV, particularly when they are pregnant. Protecting women and children from HIV has become the responsibility of the community. Involving fathers, religious leaders, NGOs, and ministries of health is critical. Education and strategies to prevent both HIV transmission and unintended pregnancies are of utmost importance to stemming the tide of new infection. Appropriate care and support should be offered to women and children living with HIV, so that they are willing and able to universally access prevention and treatment options available to them. The data are clear that a comprehensive approach to HIV prevention can reduce the perinatal transmission rate to < 2%. If ART becomes more affordable and comprehensive health care is delivered to women with HIV, thousands of maternal lives can be saved, and HIV/AIDS can be virtually eliminated in children worldwide. ■

Main Points

- The prevalence of human immunodeficiency virus (HIV) among women has increased dramatically in the last 20 years, particularly in sub-Saharan Africa, where up to 60% of those living with HIV/AIDS are now women. Because 40% of those newly infected with HIV are between the ages of 15 and 24 years, the impact on reproductive-age women and their children has been particularly devastating.
- Programs have shown great success in reducing HIV transmission among commercial sex workers by increasing HIV awareness, counseling, testing, and treatment. Success has been particularly notable in Thailand, where organizations worked together to implement a national HIV/AIDS program that targeted sex workers and the general population, which led to a decrease from 32% to 4% in the national transmission rate within a decade.
- The landmark Pediatric AIDS Clinical Trials Group 076 study demonstrated that a regimen of zidovudine to the mother antepartum and intrapartum and to the neonate postpartum decreased the perinatal transmission rate from 25.5% to 8.3%, a 67.5% relative risk reduction. Other studies have since shown that more potent antiretroviral therapy is associated with perinatal transmission rates as low as 1%.
- In extremely resource-poor countries, the focus has been on the use of single-dose nevirapine for prophylaxis. The HIVNET 012 study in Uganda showed that a single dose of nevirapine given to pregnant women in labor and to the infant after birth could reduce maternal-to-child transmission by nearly 50% in a breastfeeding population.
- A comprehensive approach to HIV prevention can reduce the perinatal transmission rate to < 2%. If antiretroviral therapy becomes more affordable and comprehensive health care is delivered to women with HIV, thousands of maternal lives can be saved, and HIV/AIDS can be virtually eliminated in children worldwide.

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