Critical Reflection

Reducing perinatal HIV transmission in developing countries through antenatal and delivery care, and breastfeeding: supporting infant survival by supporting women’s survival

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In 1998, a joint UNAIDS/UNICEF/WHO working group announced an initiative to pilot test an intervention to reduce perinatal transmission of human immunodeficiency virus (HIV), based on new guidelines on HIV and infant feeding. This intervention for developing countries includes short-course perinatal zidovudine (AZT) treatment and advice to HIV-positive women not to breastfeed their infants, where this can be done safely. The present paper raises questions about the extent of the public health benefit of this intervention, even though it may be cost-effective, due to the limited capacity of antenatal and delivery services to implement it fully. It argues that it is necessary to provide universal access to replacement feeding methods and support in their safe use, not only for women who have tested HIV-positive during pregnancy, but also for untested women who may also decide not to breastfeed, some of whom may be infected with HIV or may acquire HIV during the breastfeeding period. It further argues that additional funding, more staff, staff training, and improved capacity and resources are also needed to integrate this intervention successfully into antenatal and delivery care. The intervention will prevent some infants from getting HIV even in the absence of many of these changes. However, a comprehensive approach to HIV prevention and care in developing countries that includes both women and infants would promote better health and survival of women, which would in turn contribute to greater infant health and survival. If combination antiretroviral therapy in the latter part of pregnancy and/or during the breastfeeding period can be shown to be safe for infants, preliminary evidence suggests that it might reduce perinatal HIV transmission as effectively as the current intervention and, in addition, might allow the practice of breastfeeding to be preserved.

Keywords: HIV/AIDS; perinatal HIV transmission; HIV testing; antiretroviral HIV therapy; AZT (zidovudine); antenatal and delivery services; maternal health and survival; breastfeeding; breastfeeding replacements.

Introduction

In southern African countries, where the pandemic of human immunodeficiency virus (HIV) is moving faster than prevention efforts, paediatric wards of hospitals are becoming overcrowded with infants and children dying of acquired immunodeficiency syndrome (AIDS) (1), and the average rate of HIV infection in women attending antenatal clinics can be 30% or more (2). In 1997, UNAIDS/WHO estimated that 590,000 children worldwide were newly infected with HIV in utero or during birth or breastfeeding, and that over 2 million HIV-positive women would give birth during 1998 (3).

In 1998, a joint UNAIDS/UNICEF/WHO working group announced a series of pilot studies of an intervention to reduce perinatal transmission of HIV (4). These were to involve 30,000 HIV-positive pregnant women at 30 sites in 11 countries (eight in sub-Saharan Africa, two in Asia and one in Latin America), and were based on the new guidelines on HIV and infant feeding (5).

Available information, however, raises questions about the extent of the public health benefit that can be achieved through this intervention in the poorer developing countries, in view of the limited capacity of antenatal and delivery services and the practical and ethical dilemmas involved in women using breastfeeding replacements without adequate counselling and support (6, 7). This paper argues that these dilemmas would be better resolved through integrated pregnancy, delivery, and HIV/AIDS care that protects both women’s and infants’ health and lives, even though it would cost more.

The UNAIDS/UNICEF/WHO intervention and increased infant survival

The UNAIDS/UNICEF/WHO intervention is based on a package of six components (4).

- Early access to adequate antenatal care.
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- Voluntary and confidential counselling and HIV testing for women and their partners.
- A short course of perinatal antiretroviral treatment (AZT) given to HIV-positive women in the last weeks of pregnancy and during delivery (and possibly also to their newborn infants).
- Improved care during labour and delivery.
- Counselling for HIV-positive pregnant women on alternative methods of infant feeding.
- Support for HIV-positive mothers who choose not to breastfeed, to enable them to use breastfeeding replacements safely without violating the International Code of Marketing of Breast-milk Substitutes and related World Health Assembly resolutions.

Efforts to protect infants at risk of perinatally transmitted HIV have been universally welcomed, and many infants will be protected from HIV infection if this package is implemented fully. However, unless additional resources and skilled health personnel are found, most developing countries are likely to focus on only two of the six components, restricted to women with a positive HIV test, i.e. short-course perinatal AZT treatment and provision of baby milk powder to replace breastfeeding. Implementing these two components, all other things being equal, is far better than doing nothing. The two together would also be more effective than short-course perinatal AZT treatment on its own (8), since the benefit gained during delivery would be reduced by the risk of infection through breastfeeding. The guidelines acknowledge that it may be necessary to limit the intervention to AZT treatment alone when the use of a breastfeeding replacement is not feasible, but this reduces the potential public health benefit even further. Since a variety of factors must be taken into account, trial-based evidence will be needed to show the extent to which actual implementation of this intervention results in an overall reduction in infant mortality and morbidity (6).

Ensuring that breastfeeding replacements can and will be used safely

Deaths from AIDS have increased infant mortality in all the developing countries where HIV in women of childbearing age is found. Prior to the advent of AIDS, infant mortality levels had been falling, mostly due to campaigns in support of breastfeeding; breastfeeding protects infants from respiratory infection and diarrhoeal disease, the main causes of infant mortality where conditions for replacement feeding are unsafe (9, 10).

In acknowledgement of the risk of HIV transmission, messages promoting universal, exclusive breastfeeding for the first 4–6 months of life were revised in 1992 (9) and became more complex. HIV-positive women in developing countries who can safely use breastfeeding replacements are now advised not to breastfeed. Those HIV-positive women for whom breastfeeding replacements are unaffordable or risky are advised that they should still breastfeed.

Only anecdotal evidence exists as to what has been happening as a result of this new policy. Newspaper headlines have labelled breast milk unsafe, but have not always given sufficient information on the risks of not breastfeeding (11). There is anecdotal evidence in some countries that women who fear, but do not know, that they are infected with HIV are also not breastfeeding, or are combining some breastfeeding with formula feeding in the hopes that risk is reduced.

The impact of these policy changes and their effects on practice in developing countries need to be documented. To prevent an increase in the deaths of infants of HIV-positive women from causes other than AIDS, controlled studies should be carried out in different developing country settings to determine the safety of introducing breast-milk replacements (6). Comparative research would also be useful, and in a few cases has already begun, on the risks of breastfeeding for shorter versus longer periods, partial versus exclusive breastfeeding, and of using goat’s milk and other locally available and affordable sources of milk for infants (12).

Research is also needed on women’s knowledge of pregnancy- and breastfeeding-related HIV transmission to infants, and about replacement feeding methods, to determine what information is required by newly pregnant women. This could help maternal and child health care workers to provide counselling and support in effective and appropriate ways.

In Zimbabwe, for example, as a result of successful breastfeeding promotion campaigns, all women who give birth in hospital receive support to start breastfeeding before they are discharged, and no alternatives are offered. A qualitative study (13), which asked HIV-positive women how they felt about transmitting HIV to their infants, found that they considered both breastfeeding and the prevention of transmission of HIV to their babies important. However, they rejected the assumption that women in developing countries had no choice but to breastfeed, and felt that individual needs and circumstances should be taken into account. On the other hand, the women were reluctant to resist pressure to breastfeed because it might lead to disclosure of actual or feared HIV status. Mothers of children who were HIV-positive expressed great regret that they had not bottle-fed their infants.

To support HIV-positive women in the safe use of breastfeeding replacements, dedicated programmes would need to be set up, some aimed at very poor women. WAMATA, a Tanzanian non-governmental organization for people affected by HIV/AIDS, has explored alternative feeding practices with women. They found that if a woman started her baby on an alternative feeding method, the baby tended to adjust better after the woman died and its chances of

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survival increased. However, some WAMATA members lacked the knowledge and resources to sustain these practices, which led to infant deaths (14). These anecdotal reports point to the need for more in-depth attention to developing safe practices and programmes.

The problems faced by women living in poverty who have attempted, without support, to use breastfeeding replacements have not been extensively investigated in recent years. One study, published in 1998, found a significant level of bacterial contamination in infant feeding bottles in metropolitan São Paulo, a sign that this problem remains current (15). Even the most basic public health problem of all, lack of access to clean water, remains unresolved.

**Universal access to baby milk powder in high HIV prevalence areas?**

Supplying baby milk powder to HIV-positive mothers without violating the International Code of Marketing of Breast-milk Substitutes is problematic. Despite many years of international campaigning to ensure adherence to the Code, violations continue to occur in many countries. The cooperation of maternal and child health care staff is necessary, since in many cases violations of the Code arose because of a lack of information on their part.

There was talk at the Twelfth World AIDS Conference of the centralized distribution of six months’ supply of milk powder, using generic packaging with no commercial labels, and making it available only on prescription for women who have had a positive HIV test. The problems of distribution and of counselling women not to stretch out their supply to make it last longer, or of sharing it with women not eligible to receive it themselves, also need to be addressed. These issues have long been problematic because of the prohibitive cost of milk powder; restrictions on eligibility may create new problems even if milk powder is subsidized.

However, it is not only women who have been identified as HIV-positive during pregnancy, but also those who may become HIV-positive upon resumption of sexual relations postpartum and during the breastfeeding period who need counselling on infant feeding. Further, the “spillover” effect among those who do not know their HIV status but who fear or believe they may have the virus is serious. If they too decide not to breastfeed, the public health benefit of the proposed intervention may be reduced or reversed among their infants. Hence, wherever HIV is prevalent, all pregnant women need counselling on the alternatives available to them, so that they can assess the risks of the various options. Those women who are not willing to be tested and who decide not to breastfeed will also need access to free or subsidized baby milk powder (16). These issues need urgent public airing and debate because of their impact on child health.

A study carried out in Cape Town, South Africa, found that 83% of 88 HIV-positive women with children expressed a preference to formula-feed their next child to avoid the risk of HIV infection, after the risks were explained to them. Yet less than half of them had running water inside their homes and almost half said they could not afford to buy milk formula. Most of the women had not told anyone in their households of their HIV status. Those who had not been aware of their HIV status at the time of their last delivery had not always breastfed exclusively and breastfeeding was often short-lived, most commonly because they became ill or were hospitalized. The women also received less information from health workers about the risks of not breastfeeding than about the risks of HIV infection through breastfeeding (17).

**The stigma of HIV makes antenatal testing less acceptable**

A positive HIV test is the passport to the perinatal AZT intervention, and the success of the intervention depends on the widespread acceptance of antenatal HIV testing by pregnant women. A study in 1995–96 in Abidjan and Bobo-Dioulasso (18) found that the overall acceptability of voluntary HIV counselling and testing was relatively high. Of more than 5700 pregnant women in Abidjan and just under 4000 in Bobo-Dioulasso, 78% and 92%, respectively, accepted an HIV test and 58% and 82%, respectively, of those tested returned for the results. Overall acceptability was therefore just under 46% in Abidjan and 76% in Bobo-Dioulasso. However, a 1997 multicentre study of antenatal clinics in 12 African cities and Bangkok found wide variations in acceptability, ranging from 33% to 95% (median, 65%) (19).

Where AZT intervention is offered, there will be increased pressure on women to be tested, to ensure that uptake is high. Some clinicians may well decide to make HIV testing a routine part of antenatal screening, without discussing this with individual women or offering them a choice (20).

Antenatal HIV testing is not always either voluntary or confidential. Lack of privacy in many developing country antenatal settings may make it difficult to maintain confidentiality with HIV test results. This is also true for women taking AZT perinatally, e.g. where several family members attend labour and delivery. Any woman who does not breastfeed may be marked as HIV-positive, and if she does not wish to reveal her HIV status to her husband, family, and community she will need to use excuses such as breast pain or insufficient milk (21).

To avoid the stigma of being known as HIV-positive, women may refuse an HIV test or fail to return for the results, or refuse AZT treatment or not complete the course of treatment, or they may decide to breastfeed at least some of the time, even if replacement feeding is feasible. Thus, there is a need for wider social acceptance of this intervention,
which goes beyond the issue of its acceptability to individual women (12).

On the other hand, the availability of this intervention may well result in an increased demand by pregnant women for an HIV test, for the sake of protecting their infants. In either case, the availability of antenatal HIV counselling and testing is currently limited, and developing this capacity will involve additional training and staff increases, especially in places with a high prevalence of antenatal HIV.

**Improving antenatal care and integrating HIV counselling and support into training programmes**

In 1998, the Brazilian AIDS Programme and Ministry of Health reported that after 18 months of a national programme to provide perinatal AZT, the number of women participating remained low. This was attributed to deficiencies in maternal and infant care due to overloaded health services, a pattern of interventionist assistance during delivery, and lack of training and knowledge of HIV/AIDS among maternal and child health care providers (22).

In Thailand, although AZT has been available free of charge for perinatal programmes, a survey of 480 obstetricians and generalists found that nearly 80% did not routinely provide short-course perinatal AZT treatment, mainly because they believed it was not cost-effective, and because they were unfamiliar with the protocol. This was more likely to be the case outside Bangkok and among clinicians in smaller, provincial, district and non-teaching hospitals (23).

In major hospital centres in several developing countries, facilities for studying the efficacy of the perinatal AZT interventions have already been strengthened in order for clinical trials to be carried out. Elsewhere, however, many antenatal and delivery services, whether at primary or secondary level, particularly in sub-Saharan Africa, are not equipped to take on the additional burden of HIV testing and counselling and perinatal administration of AZT; many can barely cope as it is (24). Dedicated training and additional staff are going to be necessary to ensure the success and sustainability of this intervention (25, 26). Furthermore, HIV/AIDS clinics providing care to women of reproductive age will need to know where to refer women who are pregnant and how to advise them (27). One district AIDS team in South Africa estimated that providing group pre-test HIV counselling, repeated individual post-test counselling, and a 24-hour maternity service to the approximately 150 women attending each week for antenatal care across the district would require eight additional nurse-counsellors, four additional midwives and one additional laboratory technician, together with substantial logistic and managerial support (28).

Hope was expressed at the Twelfth World AIDS Conference, and following reports of studies in 1998 and 1999 (28, 29), that this intervention would provide an opportunity to improve antenatal and perinatal services. Yet more than a decade of insufficient investment in Safe Motherhood initiatives leaves little cause for complacency (30). Similar interventions to ensure sufficient nutrition for women of childbearing age, or to treat pregnant women with sexually transmitted diseases such as chlamydial infection, have all been considered too expensive to maintain (31). Interventions to test for and treat syphilis antenatally have not always succeeded, e.g. in Kenya where the existing infrastructure, even when strengthened, remained inadequate (32). Yet a syphilis intervention is considerably less complicated than perinatal AZT intervention and breastfeeding counselling.

Most pregnant women in developing countries where HIV is prevalent still do not attend for antenatal care more than once during a pregnancy, and this one visit often takes place at the end of the second trimester or later. Most women still give birth outside clinical settings, particularly in rural areas, many without skilled attendance (33). Hence, it cannot be assumed that they will be attended by health care workers with the skills and training to support the use of this intervention. Many others seek obstetric help only if complications occur, and an obstetric emergency may make it impossible for this intervention even to be considered.

Will pregnant women who are HIV-negative, or who refuse an HIV test, continue to receive minimal or no antenatal and delivery care for themselves and their infants, while women who test HIV-positive get more? Will there really be sufficient new resources available for this intervention to succeed beyond the pilot stage? Or in practice will money be diverted away from other, equally pressed and important services? The controversial decision by the South African Health Minister, to use the money intended for the pilot testing of the perinatal AZT intervention for broader HIV prevention and care instead, has highlighted these dilemmas (34).

**Reduced infant survival when mothers do not survive**

It has been said that use of the perinatal AZT intervention is an attempt to rescue infants when it is not possible to rescue adults through treatment too. All women will want to prevent HIV infection in their children, whether or not anything is being done for their own health. But what is happening to infants in the longer term if their mothers are ill or do not survive to look after them?

Few studies have followed both mothers and their infants, and the separate assessment of the benefit of interventions to one or the other is disturbing, in view of the dependence of infants on their mothers. Interventions intended to prevent vertical HIV transmission often focus on mothers only to determine whether or not they are willing to
accept antenatal HIV testing, perinatal AZT, caesarean section or any other intervention for the sake of their infants. The literature is mostly silent about the health of the women themselves during and after pregnancy, or their perceptions of these interventions and their consequences for themselves and their infants and families, let alone their deaths and what happens to their babies after they die. However, the literature does record the rapidly growing number of AIDS orphans and the problems they encounter.

The few studies that have looked at the links between the survival of HIV-positive women and that of their infants when treatment is not available provide compelling data. A study comparing HIV-positive and HIV-negative pregnant women in Kampala and Harare (1990–94) from the second trimester of pregnancy to two years after delivery found that mortality and morbidity requiring hospitalization during pregnancy were not significantly different. However, HIV-positive women in Kampala were 31 times more at risk of dying between 42 days and 2 years after delivery than were HIV-negative women, while in Harare the relative risk was 18 (35).

A recent review of studies since the late 1980s on the association between maternal HIV infection and perinatal outcomes (36) found a real and large increase in the risk of infant death in developing countries, but the contribution of HIV compared to other factors was apparently not studied. In the Gambia, a controlled study (37) that included 121 women infected with HIV-1 and 488 matched HIV-negative controls followed infants from 2 to 18 months of age. It found that the number of deaths was significantly higher among children of HIV-1 positive mothers (16%) than among HIV-negative mothers (6%). Deaths were due to high infant mortality from HIV-1 infection, but were also related to maternal death. The increase in child mortality was significantly independent of HIV infection in the infants.

Surely the best way to support the lives of children is to ensure that mothers stay alive and well too. Yet in most of the developing countries where the perinatal AZT intervention is available or is due to be provided, HIV-positive women have little or no access to treatment for opportunistic infections or to antiretroviral therapy for themselves. Their survival times are much shorter than those of women in developed countries who have the full range of treatments available.

**Ensure infant survival by ensuring women’s survival**

Short-course perinatal AZT treatment is an intervention that uses women’s bodies to deliver preventive treatment to infants. Although the antiretroviral benefit to infants is clear, there is no benefit at all to their mothers. Whether or not this is ethical is questionable, given the existence of treatment that could benefit the women themselves. Indeed, some women who have accepted this intervention continue to express the hope that it will “cure” them as well as protect their infants, despite explanations to the contrary (21).

In the five years since 1994, when the ACTG 076 protocol was shown to be effective, combination antiretroviral therapy has succeeded in greatly reducing the numbers of AIDS deaths among adults and children who have access to it. Death rates from AIDS have been falling in Europe since 1995, for example, and by the beginning of 1998 were less than a fifth of their previous level (38).

In January 1998, the US Centers for Disease Control and Prevention approved the use of combination antiretroviral therapy during pregnancy (39), which many women had already begun to use. Several papers presented at the Twelfth World AIDS Conference (40, 41) suggest that full-time use of combination therapy by pregnant women may prevent perinatal HIV transmission at least as effectively as the ACTG 076 protocol. In San Francisco, a study of 60 infants whose mothers were on combination therapy throughout pregnancy (40) found that the maternal viral burden was lowered, usually to undetectable levels, and maternal–infant transmission was lowered to near zero without complications in mothers or infants. In a similar study (42), seven out of eight infants were HIV-negative and the status of the eighth was pending. A third small study is ongoing (41).

If these results are confirmed, the lives of women as well as those of their infants might be prolonged. Additionally, the need to implement invasive perinatal HIV risk-reduction strategies such as Caesarean section would be reduced. Taking an even longer-term view, antiretroviral therapy during the breastfeeding period might enable HIV-positive women to breastfeed safely, which would help to preserve the practice of breastfeeding.

However, recent disquieting data suggest that 8 of 200 infants in a cohort of French women who were treated with one form of combination antiretroviral therapy (AZT + lamivudine (3TC)) died of respiratory chain dysfunction 6–12 months after birth (43). Although a direct causal relation has not been shown, further study and follow-up will be essential (44). Again, a longer period of follow-up of infants, as well as women, is required.

On the other hand, given the serious practical difficulties of promoting the use of breast-milk replacements without increasing infant deaths from causes other than AIDS, it is important to determine whether antiretroviral therapy taken by pregnant and/or breastfeeding women (or by infants alone) can prevent HIV transmission through breast milk safely and effectively. Research into simpler delivery methods for the long-term use of these drugs is also necessary.

It is time to challenge the assumption that antiretroviral drugs must be expensive. The question of distributive justice has been raised time and again.
by HIV/AIDS activists in forums on the global politics of health; and it clearly applies in this instance. UNAIDS, WHO and UNICEF should seek a greatly reduced public sector price for these drugs, as has happened with AZT and male and female condoms, as one step towards making these drugs more widely available.

Finally, antenatal, delivery and postpartum health care services need to be improved to make them able to support interventions related to HIV prevention. However, these services need strengthening for other, equally compelling reasons as well, i.e. the reduction of maternal and infant mortality and morbidity generally. It is important that this broader aim should be kept in sight whenever resources are made available (45).

Conclusions

Perinatal AZT treatment and breastfeeding replacement prevent many infants from getting HIV infection, even where little or no other action is being taken, though the extent of the long-term public health effect in developing countries remains to be seen. In settings where resources are already restricted and overstretched, additional funds as well as additional staff, staff training, and improved capacity and resources are needed to integrate this intervention successfully into antenatal and delivery care. Furthermore, access to replacement feeding methods, and support in using them safely, are needed, not only for women who have tested HIV-positive but also for untested women who fear they may be infected with HIV and as a result do not breastfeed, and for those at risk of infection in the breastfeeding period.

A more comprehensive, broad-based approach to HIV prevention and care in relation to pregnancy would include treatment for both women and infants in developing countries. The aim would be to promote prolonged health and survival in women, which would contribute to improved infant and child health and survival. If antiretroviral therapy during pregnancy and/or during the breastfeeding period can be shown to be safe for infants, preliminary evidence suggests that it might reduce perinatal HIV transmission as effectively as the current, more limited perinatal AZT intervention and might also allow the practice of breastfeeding to be preserved in the longer term.

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18. One such study in Côte d’Ivoire and Burkina Faso was reported by Cartoux M et al: HIV testing of pregnant women and prevention of vertical transmission in Africa. Late breaker oral session, Twelfth World AIDS Conference, Geneva, 3 July 1998.


25. For calculations of costs of implementing ACTG 076 in South Africa and the proportion of costs required by AZT, infant formula, testing and counselling, see: Kinghorn A. Interventions to reduce mother-to-child transmission in South Africa. AIDS analysis Africa, 5 October 1998, 8: 10–11.


41. Morris AB, Hanwell JI, Watson-Bitar MA. Triple combination therapy including nevirapine in pregnancy. Paper presented at: Twelfth World AIDS Conference, Geneva, 28 June–3 July 1998 (Abstract No. 32 419). Only five women had been enrolled in this study when the abstract was published; results were pending.


44. Case reports of this form of encephalopathy in two infants were presented at the conference (unpublished data). A further six cases have been identified in an on-going retrospective analysis of the French cohort (Blanche S, personal communication, 6 July 1999).

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