International Journal of Women's Health

Dovepress
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REVIEW

Mother-to-Child Transmission of HIV Through Breastfeeding Improving Awareness and Education: A Short Narrative Review

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Abstract: Despite critical progress registered in the reduction of mother to child transmission (MTCT) of HIV worldwide, transmission through breastfeeding still contributes to almost 50% of pediatric HIV infections recorded every year. In this short narrative review, after development of an extensive background on HIV and breastfeeding, some directions are suggested to address the key bottlenecks. Specifically, reinforcing the prevention of MTCT through breastfeeding (BF) in order to move towards elimination of MTCT prior to 2030 may require, among others strategies: tracking all women of child bearing age through HIV testing, improving testing and retesting of women during pregnancy and breastfeeding, strengthening adherence on antiretroviral therapy (ART) among pregnant and lactating women, ensuring continuum and retention in care of mother and baby-pairs up to 24 months, switching ART in non-viral suppressed mothers after improvement of adherence counseling. In addition, due to the burden of seroconversion during pregnancy or thereafter through BF, pre-exposure prophylaxis (PreP) for most at risk women should be implemented urgently. The opportunity to extend the infant prophylaxis to the whole lactating period should be assessed to address residual transmission amongst viral suppressed mothers.

Keywords: HIV, transmission, breastfeeding

Introduction and Epidemiology of Transmission Through BF

Preventing HIV transmission from mother-to-child is the most measurable intervention in the area of HIV, and has resulted in evidence and documented success stories during the past decades. [1–3] It can be estimated than 1.2 million deaths and 2.5 million HIV contaminations have been averted thanks to prevention of mother to child transmission (PMTCT) programmes, from the times where almost 800,000 new pediatric infections were recorded yearly to the latest data posting less than 160,000 new HIV infections in children per year.[1,4]

Guidelines on the prevention of HIV infections in infants have been evolving from option A, to option B and option B+ and then antiretroviral therapy (ART) for all (ART should be initiated for all people living with HIV regardless of WHO clinical stage and at any CD4 cell count).[4] Thus, this has resulted in an extended access to HIV testing amongst women of childbearing age and pregnant women followed by an increased access to lifelong antiretroviral regimens for those HIV positive.[5,6] The reduction of HIV transmission from mother to child, is now documented in many countries, and some, such as Sri Lanka, have achieved a total elimination of which Cuba was the first country receiving WHO's certification.[5–8]

Despite the many success stories in the area of PMTCT, it's unfortunate to state that rates of transmission are still very high in many parts of the world and have generated the total number of new infections of 160000 [100,000–240,000] in 2020. The majority of cases being recorded in sub-Saharan Africa (SSA), notably in western and central Africa, where the challenges of maintaining breastfeeding are critical in regard to HIV-free survival.[1,9]

The various roads and causes of MTCT are under 4 main categories. Nearly 65,000 (42%) children's infections are due to unknown HIV positive women (no diagnosis, no ART), 35,000 (23%) additional vertical transmissions occurred through acquired HIV infection during pregnancy and breastfeeding (BF). Among the remaining, 38,000 child infections

Received: 11 November 2021
Accepted: 12 April 2022
Published: 13 May 2022

occurred following interruption of ART during pregnancy and breastfeeding (25%), while 14,000 (9%) occurred among women under ART but virally unsuppressed.[1,10]

Factors explaining those pediatric infections include: shortage in HIV testing of women of childbearing age and pregnant women, lack of testing of partner which may increase the risk of contamination during pregnancy and breastfeeding; low rate of retention in care especially in breastfeeding populations which increases the postnatal rate of transmission through BF.[11,12] Lastly, the lack of viral load (VL) monitoring among both pregnant women and lactating woman increases the BF transmission risk, as viral load is a key factor that affects mother-to-child transmission of HIV.[13,14]

Therefore, with the increase of access to extended ART regimens in pregnancy and thereafter, the biggest challenge in the elimination of MTCT is in achieving it in lactating populations.[14–16] In fact, since the onset of the e-MTCT Plan launched in 2010, rates and threshold of achievement of the e-MTCT were settled differently for breastfeeding and non-breastfeeding populations, respectively, at 5% and 2%. Facing the challenge of this global elimination prior to 2030, it seems important to review the state of the ART of preventing MTCT in breastfeeding populations in line with the need to improve education and awareness in order to attain a HIV free generation. This mini narrative review will attempt an overview of four main issues: 1) the importance of BF, 2) the mechanisms and factors of transmission of HIV during BF, 3) the interventions to reduce MTCT in BF populations, and 4) the challenges and future of eliminating MTCT in the BF population.

The Importance of Breastfeeding

Breastfeeding for child survival is one of the cornerstone interventions to alleviate under five child mortality, especially in low resource settings. The benefit of breastfeeding on child survival has been documented worldwide as a key intervention to avoid mortality in children in low- and middle-income countries. Currently, reports show an annual 12% of deaths in children under 5, and 16% neonatal deaths. Overall, it is estimated that non breastfeeding costs 800,000 lives every year notably in jeopardized areas.[17] The benefits of breastfeeding especially exclusive breastfeeding during the first six months of life have been widely documented with an update of WHO 10 steps for implementation of exclusive breastfeeding. The global WHO target in improving exclusive breastfeeding during the first six months of life is fixed at 50% of all the children worldwide, prior to 2025. Apart from benefits for child survival due to immune, anti-infectious properties and nutrient components of breastmilk, lifelong benefits and specificity of the microbiome of breastfed children give an explanation in preventing metabolic syndrome, obesity, allergy and other non-transmittable diseases.[18–20]

In the context of HIV exposed infants, the balance between breastfeeding and bottle feeding was focused around one issue; ensuring HIV free survival.[21] Since 2010, WHO guidelines recommend breastfeeding plus antiretroviral therapy to mothers and infants, after evidence from many randomized controlled trials.[22–26] This recommendation has been changed over time, notably in regard to duration of breastfeeding. Therefore, to ensure the better survival of HIV-exposed infants, the current guidelines state that mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer while being fully supported for ART adherence.[27]

Generality on MTCT–Mechanisms of Transmission and Factors Associated to Transmission Through Breastmilk

Perinatal transmission of the HIV virus can occur during pregnancy, delivery or after birth during breastfeeding.[28] From the very beginning of the pandemic, discrepancies were noted between the rates of transmission among the lactating population compared to non-breastfeeding areas. It was then demonstrated that amongst the non-breastfed population the rate of transmission was around 15–20% without intervention, while the same rates would range from 20% to 45% according to the duration of breastfeeding.[11] Without any intervention the likelihood of transmission is rated at 1% per month.[28]

Many factors of transmission have been identified including those affected by the virus, to the host and to the practices of breastfeeding. Maternal factors of transmission may include the severity of the maternal disease: level of RNA viral load, low level of CD4 cell count, high level of CD8 lymphocytes cell count, and vitamin A deficiency.[29,30]

The quantity of virus in the maternal blood compartment is not linearly correlated with the quantity of the virus in the mammary gland. The virus HIV present in the breastmilk can be transmitted as cell free virus or cell associated virus.

Both cell free or cell associated virus can be responsible for an infection.[31] The quantity of virus and the viral load in the breastmilk are the main factors that would affect the rate of transmission. However, some transmissions have occurred from mothers holding undetectable viral load which raises the issue of viral reservoirs in the breastmilk.[32] So the equation, undetectable equals non transmittable can fail in some cases.[33] The risk of transmission is correlated to a cumulative level of viral load in the breastmilk, ingested by the child. Though the transmission can occur at any moment of breastfeeding, emphasis has been put on an increased risk during the early post-natal period. Among other factors that may limit the risk of transmission through breastfeeding, the importance of local immune response has been outlined and could include T cytotoxic lymphocytes, interferon gamma response to VIH antigen.[34]

Mucosal and mechanical factors

After uptake of breastmilk by the baby which contains both cell free virus and cell associated virus, transmission may be easier in cases of mucosal lesions such as oral thrush and other local conditions of the breast.[35] Those conditions, through inflammation and infections may stimulate the secretion of local cytokines resulting in an increased risk of HIV transmission,[36,37] However in some cases, despite unaltered membranes, transcytosis can explain the passage of the virus with the possible role of M cell and Peyer's glands and other immune agents of the intestine.[38]

Interventions to Reduce Transmission of Virus During Breastfeeding

After the first decade of focusing on counseling interventions amongst breastfed mothers to reduce HIV of MTCT, lifelong ART is currently the gold standard since the latest 2010s.

ART During Breastfeeding

Current recommendations on the use of antiretroviral drugs during pregnancy are relevant too for the lactating woman. Efficacy and safety of most drugs have been defended and the main classes of first line of ART can be used for pregnant women. The current recommendations according to the WHO is the association of TDF/3TC/EFV 400 mg or Dolutegravir (DTG) were phasing of EFV has started. Main worries about the side effects of Tenofovir on kidney and bone, including the outcome of use of Dolutegravir (neural tube defects) may need more attentions and closely follow-up of perinatal antiretroviral registries. In the latest WHO guidelines, benefits of ART during pregnancy and breastfeeding outweigh risks.[4,39] The classes of antiretroviral not specifically recommended during breastfeeding are inhibitors of CCR5 and fusion inhibitors. The advantage of DTG, recently proposed as a component of first line ART, is based on its very high genetic barrier, which anticipates not only on its efficacy to suppress viral replication but also to reduce risk of emergence of viral resistant strains.[39,40]

ART for Lactating Women

Many protocols targeting both mother and child have been demonstrated to be effective to reduce MTCT through BF. Results from these studies have supported the revised WHO guidelines on infant feeding and HIV. Lately, the generalization of lifelong ART for all has encompassed the uptake of ART restricted to the breastfeeding period for mothers.[41]

The first objective of this access to ART for lactating mothers is to achieve a completely suppressed viral load in the blood in order to expect a similar reduction in the breastmilk. The greater need is to ensure a permanently suppressed viral load, as mothers with unsuppressed viral loads are more likely to transmit the virus than those permanently suppressed.[39,42] This therefore stresses the need for close viral monitoring among HIV-BF mothers, to immediately detect any unsuppressed viral load within weeks and adjust ART treatment, whenever necessary.[39,43] It is admitted that in cases of elevated viral load, apart from switching to another ART regimen, emphasis should be put on counseling for appropriate BF practices. These issues are relevant as any unsuppressed permanent ART exposed to viral resistance and transmission of a resistant strain in cases of child being infected.[39,43] The issue of reducing transmission during breastfeeding starts from pregnancy. HIV infected mothers under ART prior to pregnancy may have a different profile of viral load at birth/delivery.

Infant Prophylaxis

Infant prophylaxis is acting as pre-exposure prophylaxis for infants exposed for months to breastfeeding. To reduce MTCT of HIV, the regimens of infant prophylaxis have changed over time; notably around the antiretroviral protocol (monotherapy or dual therapy) and its duration.[44–46] The current recommendation stresses the following:

- Infants born to mothers with HIV who are at high risk of acquiring HIV should receive dual prophylaxis with daily AZT and NVP for the first six weeks of life, whether they are breastfed or formula fed.
- Breastfed infants who are at high risk of acquiring HIV, including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional six weeks (total of 12 weeks of infant prophylaxis) using either AZT and NVP or NVP alone (conditional recommendation, low-certainty evidence).
- Infants of mothers who are receiving ART and are breastfeeding should receive six weeks of infant prophylaxis with daily NVP.

The considerations of women at high risk are the key bottleneck of these recommendations in regard to eliminating HIV transmission among lactating women. The requirement is to detect: women at high risk who are eligible for PreP, women unsuppressed at the time of delivery, those with a high level of viral load following a seroconversion in late pregnancy, and those lately diagnosed or having less than 4 weeks of ART prior to delivery.[39,47]

The most embarrassing point is around the length and duration of infant prophylaxis. As mentioned earlier, the risk of transmission exists at each exposure to breastmilk, even if a decrease of this risk is expected overtime. The need to cover all the breastfeeding period is then necessary and has been tested in some settings.[48,49] The theoretical risk of surdosing of ART taken by both mother and child for a long period should be balanced with the usefulness of giving drugs to infants of mothers who are virally suppressed.

In practice, the drugs chosen for infant's prophylaxis must have adequate concentrations in breastmilk after maternal uptake. Both Lamivudine and Nevirapine have demonstrated such profiles.[49,50]

Due to the uncertainty of maternal adherence to ART, improving infant prophylaxis can address this weakness. In South Africa, infant NVP adherence among breastfeeding infants rated at 75%, was higher than maternal adherence to ART thus suggesting to continue infant prophylaxis, especially in cases of mothers being virally unsuppressed.[48] Those who argue on the prolonged infant prophylaxis support their arguments with the potential risk of residual transmission of HIV even in the case of viral suppression due to HIV reservoirs in the breastmilk.[51] On the other hand, maternal non adherence to ART can anticipate non adherence to infant prophylaxis and should be addressed with priority.[39,48]

Pre Exposure Prophylaxis (PREP) and MTCT Through Breastfeeding

It can be assumed, that among breastfeeding women, PreP can be useful among those who are at high risk of acquiring HIV infection during the breastfeeding period. Mothers to target could be those in serodiscordant couples and sex workers who are a key road of MTCT of HIV. In fact, some high burden MTCT countries have opted to integrate PreP in their national strategy.[47]

Safe Breastfeeding Practices

The recurrent query on breastfeeding as an option for women living with HIV outlines the new feature created by breastmilk secured by antiretroviral drugs, thus giving to every single HIV woman the possibility of a choice. This may not lead to minimize other strategies notably supportive of counseling for infant feeding.[52,53] Objectives of infant feeding counseling sessions, should focus on helping mothers to reduce HIV transmission through breastmilk in special situations such as: clinical/subclinical mastitis, and oral thrush. Expressed breastmilk and practicing of breast pumping when needed, would be emphasized. In addition, reducing the prevalence of mixed feeding during the first 6 months of life remains important.[22,27] So far, supportive counseling interventions during breastfeeding could be maintained with an emphasis on adherence counseling to ART at each contact. Every mother should be informed about alternative strategies to properly feed their babies in crisis situations. The duration of such support should cover the whole duration of the lactating period. Proper counseling will help to determine the timely period of weaning assuming appropriate complementary foods are available to prevent malnutrition.[27] The risk of HIV transmission may be different in those starting ART during pregnancy. There is a critical need of adherence

counseling among lactating women as the rate of viral rebound has been found to be high among them. Even in those suppressed at delivery, a special tracking for retention in care is required up to the complete cessation of breastfeeding.

Key Challenges

Though much progress have been recorded in the reduction a MTCT of HIV through breastfeeding, many challenges remain as BF continues to account for almost 50% of new pediatric infections. This therefore compromised the issue to eliminate the MTCT of HIV prior to 2030.

The interventions based on ART have documented effective evidence in reduction of transmission of HIV amongst breastfed infants; rates of transmission moving from almost 1% per month without intervention to 0.2% per month of breastfeeding in cases of suppressive ART and even lower to 0.06–0.13% in case of infant PreP.[46–49]

To ensure the effectiveness of those strategies, there is a critical need to extend and capture women through both testing and access to ART prior and during pregnancy. Furthermore, tracking any contamination during pregnancy and or lactating period should remain a constant concern. For those women on ART, consistent and continuous breastfeeding counselling will help to maintain both safe breastfeeding practices and adherence to ART. Retention in care, which is a key problem in long term follow-up should be strengthened using communities and mothers' counselors, with appropriate linkages between community and ART and maternity centers. The need of viral monitoring to ensure permanent viral suppression cannot be overemphasized; it is a must. Lastly, improving the duration of infant prophylaxis is a road not only to tackle low maternal adherence to ART but also to thwart viral reservoirs; the issue of PreP for lactating women is critical for most at risk women.

Conclusion

In conclusion, with a past story of many evolving recommendations, MTCT transmission through breastfeeding remains a key issue to achieve the e-MTCT in high priority countries prior to 2030. This should compel countries to ensure that 95% of pregnant and lactating women have access to HIV prevention services including perinatal testing and re-testing antenatal testing; that 95% of those infected are put on ART and virally suppressed prior to delivery and during the whole breastfeeding period. Therefore, it is urgently needed to enable the environment through policies, programmes and services delivery taking into account restrictive resource allocation due to the Covid-19 pandemic.

Abbreviations

ART, antiretroviral therapy; AZT, zidovudine); BF breastfeeding; CCR5, C-C chemokine receptor type 5; CD4, cluster of differentiation 4 coreceptor for T cell receptor; DTG, dolutegravir; HIV, human immunodeficiency virus; MTCT, mother-to-child transmission; NVP, nevirapine; TDF, tenofovir; WHO, World Health Organisation.

Disclosure

The author reports no conflicts of interest in this work.

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