

## Article

# From Undetectable Equals Untransmittable (U=U) to breast-feeding: is the jump short?

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**Abstract:** Background: Vertical transmission of HIV infection can occur during pregnancy, during childbirth or through breastfeeding. The recommendations issued by the various international guidelines (WHO 2010, EACS 2017, DHHS 2017) on the safety of breastfeeding of HIV-infected women in effective antiretroviral treatment do not provide univocal indications referring to individual countries the choice to advise or advise against such procedure. Methods: A retrospective study was conducted in a small cohort of HIV-infected pregnant women who, despite the information received, decided to breastfeed their children. The observation was carried out in the period between March 2017 and June 2021. In all newborns, prophylaxis therapy was initiated at birth, according to the treatment guidelines, the scheme adopted involved the administration of zidovudine (AZT) orally for 4 weeks, started immediately after the childbirth. Breastfeeding time was, on average, 5 months. Results: No contagion was diagnosed. All infants were tested for HIV-RNA at birth, 1, 3, and 6 months after birth, and 1, 3 and 3 months after stopping breastfeeding. Conclusions: The data obtained represent, in our opinion, a solicitation to discuss and re-evaluate scientific evidence that starting from "Undetectable Equals Untransmittable" (U = U) can open a scientific and cultural review of breastfeeding.

Keywords: female, HIV infections, breastfeeding, vertical transmission, patient's autonomy.

## 1. Introduction

Vertical transmission of HIV infection is the most common mode of contagion in infants, which can occur through the placenta, during childbirth or through breastfeeding.

Multiple studies have demonstrated that ART to the mother throughout the entire period of vertical HIV transmission risk (pregnancy, delivery and the duration of breast feeding) are critical to prevent new infant infections [1-5]. The PROMISE trial [6] provided clear evidence on the beneficial effect on early vertical HIV transmission of maternal ART initiated during pregnancy compared to zidovudine (ZDV) prophylaxis in women with high CD4 counts. The French Perinatal Cohort (EPF) demonstrated that women on ART pre-conception have the lowest risk of perinatal HIV transmission, with increasing risk of transmission by each advancing trimester of ART initiation [8]. Additionally, independent of timing of ART initiation, HIV viral load (VL) at delivery of 50–400 copies/ml was associated with 4-fold greater odds (95% CI 1.9-8.2) of Vertical transmission compared with VL < 50 copies/ml [28].

A first sign of openness to breastfeeding was recorded in 2010, a time when the WHO and UNICEF issued new universal recommendations on breastfeeding women with HIV on effective antiretroviral treatment [7].

A few years later, in 2017, the European AIDS Clinical Society (EACS) considers the possibility of breastfeeding by recommending a precise counseling plan aimed at optimizing therapeutic adherence and a close follow-up for both clinical and virological monitoring of the mother and of the child [8]. Across the ocean, the guidelines of the Department of Health and Human Services (DHHS) [9] dissociate themselves from the EACS recommendations, clearly advising against breastfeeding in this population even in women with a strong desire to breastfeed, since the risk of vertical transmission was highlighted in a percentage between 0.3 and 1% [10].

Consolidated data from the scientific literature demonstrated the efficacy of antiretroviral therapy for the prevention of vertical HIV transmission, both during pregnancy and during childbirth. However, only 3/4 of pregnant women living with HIV receive ART. Despite the benefits of ART for maternal and child health, challenges remain related to joining ART, maintaining care, and equitable access to care. With expanded antiretroviral drug availability in resource-limited settings, the risk of breast milk-associated HIV transmission becomes low, making early breastfeeding cessation relatively more risky than longer periods of breastfeeding, in terms of nutrition and other benefits. Nevertheless, the safety of breastfeeding in women on effective antiretroviral treatment remains to be verified. This observational study aims to assess the risk of vertical HIV transmission in a small cohort of HIV-infected women who have decided to breastfeed.

## 2. Aim

Describe the absence of vertical contagion in a small cohort of 13 women who, correctly informed about the potential risks of contagion, still decided to breastfeed their children.

## 3. Materials and Methods

A retrospective study was conducted in a small cohort of HIV-infected pregnant women who, despite information relating to the risk of HIV infection through breastfeeding, still decided to breastfeed their children. The observation was conducted in the period between March 2017 and June 2021. All women gave their consent to gathering data anonymously. The women who made this choice were 13, aged between 18 and 34 years (average age 26 years). Two Italians and eleven Africans (Nigeria 4, Ivory Coast and Ghana 2, Mali, Cameroon, Senegal 1). The time spent in Italy was between 6 and 72 months (average time 17 months). Four of the 13 women were diagnosed with HIV during the first 10 weeks of pregnancy. All were promptly initiated on antiretroviral therapy in accordance with antiretroviral treatment guidelines. In the remaining 9 women the diagnosis was known, and all were effectively taking antiretroviral therapy (Table 1). At the time of pregnancy and during the pre-birth follow-up, all women, as usual and in accordance with the guidelines on the management of HIV infection in pregnancy and on the prophylaxis of vertical contagion, were informed on the rules and strategies of treatment and prevention of HIV infection to the unborn child, stigmatizing the need for replacement breastfeeding for the prevention of infection to the unborn child. In the various meetings, supported by the presence of a cultural mediator, each patient had the opportunity to interact with the team, so as to be able to freely discuss all the positive aspects, the risks of contagion and the importance of a precise counseling plan aimed at optimizing therapeutic adherence and close follow-up for clinical and virological monitoring of both mother and child.

The women gave birth, in accordance with the most recent national and international guidelines, vaginally since this procedure did not represent an additional risk of infection for the unborn child. Both women with a previous diagnosis and those in whom the diagnosis was made during pregnancy were treated with antiretroviral therapy which, in 100% of cases, resulted in an undetectable viral load (HIV-RNA) and a CD4 + T-Helper

lymphocytes > 400 cells / mmc (values between 402 and 1560 / mmc). Adherence was 100% in all patients.

Breastfeeding time was, on average, 5 months with a range of 6 weeks (interruption for maternal COVID-19 disease) to 11 months.

CDC	YEAR of birth	Age at Delivery	Stay in Italy (months)	Nationality	HIV + pregnancy yes (1) none (2)
A-1	1999	18	6	Nigerian	1
A-2	1997	20	6	Malian	2
A-1	1987	30	48	Ivorian	1
A-1	1991	26	11	Nigerian	1
A-1	1993	24	6	Cameroonian	1
A-2	1989	28	24	Ghanaian	2
A-2	1996	22	6	Ivorian	1
A-1	1985	33		Italian	1
A-1	1998	21	6	Nigerian	1
A-1	1994	34	36	Senegalese	2
A-1	1985	33	24	Ghanaian	1
A-1	1994	28		Italian	1
A-2	1994	24	72	Nigerian	2

**Table 1.**

<sup>1</sup>Clinical asocial and demographic findings of 13 cohort female patients.

#### 4. Results

All infants were tested for HIV-RNA at birth and subsequently 1, 3 and 6 months after breastfeeding. No contagion was diagnosed.

#### 5. Discussion

The observed data and recent observations on the problem of breastfeeding safety [11] represent, in our opinion, a solicitation to discuss and re-evaluate scientific evidence that starting from "Undetectable Equals Untransmittable" (U = U) can open a review of this problem with the aim of breaking the wall that has always divided the population with HIV from others [12-14]. In balancing risks and benefits, worthy of consideration, in developing countries, replacement feeding is associated with other significant risks, such as increased infant morbidity and mortality from diarrheal disease, pneumonia, and other infectious diseases, thus limiting the utility of this option [15-20]. Decreased rates of overall morbidity and mortality in infants who breastfeed have been attributed to protective antibodies passed from mother to infant in breast milk and decreased exposure to infectious pathogens via unsafe water [21].

Trial on antiretroviral prophylaxis studies demonstrated marked efficacy of decreasing transmission of HIV in both replacement feeding and breastfeeding women [22-24].

Thus, in the context of antiretroviral medications, the benefits of replacement feeding (eg, improving HIV-free survival) are no longer retained [25]

Considering the general scientific panorama described so far and the data of some studies that highlight results like those highlighted in our small and limited cohort of women [26-28], we believe that the scientific community must become aware of the fact that some mothers with HIV infection may experience social and / or cultural pressure to breastfeed their children or, more simply, want to fulfill this desire. These mothers, despite correct, adequate, and shared information on the risk of contagion (which means to clearly illustrate the efficacy of alternative feeding strategies), should receive support and guidance that can respond to their needs through specific paths of socio-health and psychological assistance. From a more strictly ethical point of view, the autonomy of the person, here of the woman, a fundamental and undisputed value, must be compared with the principle of precaution and prudence towards the health of the child, balancing all the possible positive effects (in terms of health and well-being) of the choice of breastfeeding, compared to the "predictability" of the negative effects of viral transmission.

## 5. Conclusions

Antiretroviral medications significantly decrease the risk of mother-to-child transmission of HIV during the antepartum, intrapartum, and early postpartum periods. However, risk of HIV transmission recurs if they are discontinued during the breastfeeding period. Although maternal and infant antiretroviral prophylaxis strategies during the breastfeeding period are comparably effective in reducing the rate of transmission, maternal ART is the preferred strategy, as it is recommended for all individuals with HIV and is essential for maternal health. As our results indicated, we consider it useful to emphasize the importance of the Italian Law on matter of Informed consent and advance treatment provisions [29], which highlights the autonomy of the patient who is confronted with the autonomy, competence, and responsibility of the physician [30]. The role of the healthcare professional, about the choices under discussion, is to accompany and support the woman's conscious decision, respecting her autonomy. In any case, we believe that the WHO guidelines [31] should be considered as a milestone to ensure the full safety of breastfeeding:

- mothers with HIV infection should exclusively breastfeed their infants introducing appropriate complementary foods thereafter and continue breast feeding.
- in settings where health services provide and support lifelong ART, including adherence counselling, and promote and support breastfeeding among women living with HIV, the duration of breastfeeding should not be restricted.
- breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.
- national and local health authorities should actively coordinate and implement services in health facilities and activities in workplaces, communities, and homes to protect, promote and support breastfeeding among women living with HIV.

It is reasonable that further evidence in this area will be useful for women in different settings to make informed decisions regarding breast or replacement feeding.

**Supplementary Materials:** The following are available online at [www.mdpi.com/xxx/s1](http://www.mdpi.com/xxx/s1), Figure S1: title, Table S1: title, Video S1: title.

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**Informed Consent Statement:** “Informed consent was obtained from all subjects involved in the study.”

**Data Availability Statement:** Data supporting reported results can be found at the Infectious diseases Unit, 2 Migrants reception service, Civic Hospital, Palermo, Italy.

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