

## Human milk and pediatric HIV infections: consensus and dilemma

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### Consensus

There is a consensus that human milk provides nutritional, immunologic, cognitive and emotional benefits to infants through breastfeeding. Human milk protects the infant against morbidity and mortality of infectious diseases. There is also a consensus on the presence of microorganisms, including pathogenic bacteria and viruses in the human milk. They are transmitted through breastfeeding, but rarely cause infections in infants. Human immunodeficiency virus type 1 (HIV1) is one such exception that is suspected to cause infection in infants through human milk. The suspicion that human milk could be a source of HIV1 infection came in the mid-1980s from a clinical case report of HIV1 infection in a healthy breastfed infant born to a healthy mother<sup>1</sup>. The consensus on the presence of HIV1 in human milk was, however, arrived at from experiential and experimental evidences of HIV1 infection in infants born to and breastfed by women already infected during the antenatal period (i.e. HIV1-positive mothers).

Experiential evidence from observational and interventional epidemiological reports, based their findings on issues related to breastfeeding in a cohort of breastfeeding and non-breastfeeding (i.e. formula feeding), HIV1-positive mother–infant pairs. Some studies quantified the rates and clarified the timing of HIV1 transmission in human milk. Others associated breastfeeding practices such as duration and mode of breastfeeding (i.e. exclusive or mixed) with infant infections.

Retrospective follow-up of HIV1-positive mothers, who received antiretroviral intervention during pregnancy, placed the risk estimates in the range 10–20% through breastfeeding<sup>2</sup>. A prospective follow-up of such HIV1-positive mothers, reports 150,000 infant infections per year in low-income settings, according to a UNAIDS report<sup>3</sup>.

A study of antiviral, naïve, HIV1-positive mother–infant pairs reported on an average 16% infection in babies, born uninfected, when breastfeeding continued for two years<sup>4</sup>. In a well-referred study of antiviral, naïve, HIV1-positive

mothers randomized during pregnancy for breastfeeding or formula feeding arm, 75% of pediatric HIV1 infection occurred within the first six months in both the arms, with 16% excess infections in the breastfeeding arm<sup>5</sup>.

Experimental evidence of milk-borne transmission of HIV1 came from laboratory analysis of characteristics and quantification of HIV1-specific indicators and anti-HIV1 factors in the milk of HIV1-positive mothers.

HIV1-specific nucleic acids – HIV1 RNA and DNA are detectable in 70% human milk samples<sup>6</sup> by a sensitive polymerase chain reaction assay, in various human milk compartments such as skim milk, lipid layer and cellular fraction. They vary in the milk of HIV-positive mothers during the breastfeeding period and also between the right and left breast. Both HIV1 DNA and RNA levels detectable in the milk of HIV1-positive mothers have been associated with infant infection, according to some investigators<sup>6</sup>. Others associate such risk solely to HIV1 DNA in infected milk cells, suggesting that the risk is independent of HIV1 RNA levels in human milk<sup>7</sup>.

Also, HIV1-specific antibodies, non-specific immune factors and antiviral substances such as lactoferrin, lysosomes and secretory leukocyte protease inhibitor have been quantified in the milk of HIV-positive mother. Their low concentration has been associated with higher HIV1 infection during the first several weeks of life, according to some but not all studies<sup>8,9</sup>.

### Dilemma

In the clinical case report<sup>1</sup> of 1980s, the suspicion that human milk could be a source of HIV1 infections in a healthy breastfed infant born to a healthy mother was inferred on circumstantial evidences, since no specific source of HIV1 exposure other than breastfeeds was identifiable. This inference, however, pertains to HIV1 transmission and infection in an infant born to a healthy woman, who herself acquired the primary HIV1 infection during breastfeeding. Any primary infection is associated with high levels of

virus and no infection-specific antibodies in blood circulation. Clearly, the situation in HIV1-positive mothers with stable infection and HIV1-specific antibodies in blood circulation and milk, is different from those mothers who are infected during their postnatal period.

Is this the reason that breastfed infants of HIV1-positive mothers consume more than half a million free virus and 25,000 infected cells per day through human milk<sup>10</sup>, and despite consuming such high levels, most babies (80–90%) remain uninfected? The dilemma is about its reported role in infection in about 10–20% breastfed infants.

The epidemiological evidence<sup>5</sup> of 16% excess infections in the breastfeeding arm than the formula feeding control arm was assumed to be due to transmission via human milk and not due to other differences between the groups. The differences between the trial arms in early HIV1 infection may be due to antenatal randomization bias. Again, infections in the formula feeding control arm, not exposed to human milk through breastfeeds, are not clear. Yet, the WHO 2004 report<sup>11</sup> estimated 5–20% post-birth infant infections to occur through breastfeeding and recommended exclusive breastfeeding. Exclusive breastfeeding is known to enhance the protection from the virus present in human milk. The moot question is how many of the mothers adhere to the advice? Yet 80% infants appear to remain uninfected, albeit prolonged and repeated exposure to HIV1 transmission through human milk. The questions that need to be addressed are what anti-HIV1 mechanisms in human milk protect 80% breastfed infants.

HIV RNA and DNA are detectable in about 70% human milk samples<sup>6</sup>, but no lower threshold of HIV1 nucleic acids responsible for 5–20% reported infant infections is known. There is no consensus on whether HIV1 RNA or DNA in human milk or both are causal for infant infection<sup>6,7</sup>. Whether they are responsible for infectivity of mother's milk is also not certain. Detection of HIV1 nucleic acid in human milk does not necessarily mean presence of 'infectious virus'. Evidence of infectious virus is suggested by the detection of HIV1 quasiespecies in

milk and blood compartment of HIV-positive mothers by some, but there is no agreement on such HIV1 diversity in either compartment.

Limitations in epidemiological studies and lacunae in the laboratory evidence of the presence of infectious HIV1 or anti-HIV1 responses in human milk, call for studies to pinpoint marker/s of HIV infectivity in human milk, if any. Besides resolving the dilemma of human milk as a reservoir of HIV1 transmissions, such studies may identify transmitting HIV1-positive mothers.

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## Conflicts and dilemma of human right to water\*

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According to the World Health Organization (WHO), fifth of the world population, i.e. 1.1 billion lack access to safe drinking water.

In July 2010, the United Nations General Assembly adopted a resolution calling on States and International Organizations to grant financial resources, transfer of technology to developing countries and enhance efforts to provide ‘safe, clean, accessible and affordable drinking water, and sanitation for all’. The Bolivian-introduced text was adopted by 122 in favour and 41 abstentions with none against the resolution, thus recognizing the human right to safe, clean, accessible and affordable water and sanitation for all. The recognition of right to safe, clean, accessible and affordable water as a human right by the United Nations, if adopted by governments world over, would empower every human being with legal entitlement for safe, clean, accessible and affordable water despite several limitations and shortcoming to do so. But, it would bind governments with legal obligation to ‘respect, protect and fulfill this human right to water’<sup>1</sup>.

The United Nations has adopted and recognized human right to water. Now, it

is left to the States and International Organizations to adopt the same. But, a closer scrutiny of the resolution, particularly ‘safe, clean, accessible and affordable water for all’, would provide a different picture than the impetuosity with which the resolution has been adopted by the United Nations General Assembly. The success of human right to water depends on the availability of freshwater – a finite resource shared by multiple users like agriculture, industry and environment. According to a study by Molden<sup>2</sup>, ‘many river basins do not have sufficient water to meet demands; further appropriation of water for human use is not possible as the limits have been reached and in many cases it has already breached’. Thus, it is apparent that conflicts are inevitable when human right to water is adopted by States and International Organizations without a plan-of-action, investigation and feasibility, as the right confers legal entitlement of water for all.

‘Freshwater is a finite and vulnerable resource, essential to sustain life, development and the environment’<sup>3</sup>, and it has wide variations across regions both in space and time – probably the greatest limitation for ensuring human right to water. In many regions water use has exceeded water availability<sup>4</sup>. The International Water Management Institute (IWMI) in its Comprehensive Assess-

ment of Water Management, 2007, for the near future indicates physical water scarcity in Peninsular India, northern China and large parts of the Middle East, and economic scarcity of water in northern India, large parts of Sub-Saharan Africa, Peru and Bolivia (Figure 1). Several countries in the Middle East comprising the Asian part of Turkey, Syria, Jordan, Israel and Iraq, and those of North Africa face acute scarcity of freshwater (Figure 2) in addition to countries like Mexico, Pakistan, South Africa, and large parts of both India and China<sup>5</sup>. Water scarcity according to Falkenmark *et al.*<sup>6</sup> is water availability below 1000 m<sup>3</sup>/capita/yr of water availability while below 1700 m<sup>3</sup>/capita/yr is regarded as water-stressed. Thus, Middle East, North African countries, Mexico, Pakistan, South Africa, India and China adopting human right to water would have to face serious repercussions due to legal entitlement granted to citizens by the right. In the case of India, water availability per capita per year which was 5176 m<sup>3</sup> in 1951 (ref. 7) has dropped to 2309 m<sup>3</sup> in 1991 to about 1902 m<sup>3</sup> in 2001 (ref. 8). Further as of 2010, considering a projected population of 1.1 billion based on Census of India<sup>9</sup>, water availability per capita per year has dropped below 1700 m<sup>3</sup>, pushing India under water-stress category considering total water flow of

\*The views of the author are purely personal and shall in no way be construed as views of his employer.