EDITORIAL

HIV-exposed Uninfected Children: A Vulnerable and Neglected Population

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In India, transition from single-dose nevirapine (NVP) to multi-drug anti-retroviral (ARV) drugs as a strategy for prevention of parent-to-child transmission (PPTCT) under National AIDS Control Program (NACP) has significantly reduced the rate of transmission from mother to child to 2-3% [1]. As a result, a majority of these HIV-infected mothers are delivering HIV-exposed but uninfected children (HEU). Several factors – impact of perinatal exposure of HIV on immature immune system, exposure to pathogenic organisms from immuno-suppressed family members, *in-utero* exposure to antiviral drugs, nutritional challenges, and socioeconomic impact of HIV infection on their family – increase the vulnerabilities of these children. Consequently, these children have substantially increased morbidity and mortality, predominantly from infectious and nutritional causes as well as adverse neuro-developmental outcome as compared to children born to uninfected mothers [2].

Several immunological abnormalities have been described in HEU infants that may lead to increased susceptibility to infection. Apart from the consequence of HIV exposure *in utero* and early life, immune abnormalities could also be due to exposure to anti-retroviral drugs, as well as early transmission of persistent opportunistic infections such as cytomegalovirus. These factors synergistically undermine the developing immune system of young infants, especially in resource-limited settings. Additionally, immune recovery from these insults may be impaired by other frequent horizontally-transmitted infections such as tuberculosis from immuno-suppressed family members, together with malnutrition and poor socioeconomic circumstances. Few studies have raised the concerns on the impaired T-cell responses to infant vaccines in these HEU infants questioning the longevity of vaccine responses and thus making them vulnerable to some life-threatening infections [3].

HIV infection and neuro-developmental outcomes in infancy are determined by maternal and infant host factors both of which also influence HIV disease onset and severity. Many factors like *in utero* exposure to HIV and anti-retroviral drugs, socio-cultural status and poverty influence the neurobehavioral and developmental outcomes in these children. In a systematic review, it was found that HIV exposure influenced growth of children, including those above 5 years. HEU children had lower weight and length Z-scores at birth compared to HIV unexposed uninfected children, and also seemed to have suboptimal postnatal growth even in breastfeeding populations from low-income settings. This review also found that HEU children had substantially increased morbidity and mortality compared with children born to uninfected mothers, predominantly from infectious causes [4].

However, data regarding early morbidity in relation to feeding options of HEU infants in India is not available in the literature. The study by Ray, *et al*. [5], published in this issue of *Indian Pediatrics*, is an important attempt of comparison of growth, anemia prevalence and sickness frequency in HIV-exposed uninfected infants on different feeding methods. This study documented no difference in growth parameters or prevalence of anemia in HIV-exposed infants on animal milk feeding (AMF) as compared to commercial infant formula (CIF) or exclusive breast feeding (EBF) during first 6 months of life. However, significantly higher incidence of sickness, especially diarrhea, was seen in infants on AMF and CIF as compared to those on EBF (OR 2.5 and 2.49, respectively; $P<0.01$). There was no difference between AMF and CIF with respect to frequency of sickness. This work provides data that AMF along with iron and multivitamin supplementation is a possible alternative to CIF in HIV-exposed infants where breastfeeding is not feasible /opted for. In an African study [6], the contextual factors like early nutritional intervention and prevention of infection-related morbidity are associated with better neuro-developmental outcomes in HEU. Hence, the various outcomes with respect to feeding methods explored in this study assume importance to provide nutritional counseling.

With declining risk of transmission of HIV from mother to child, the cohort of HEU children is expanding. This cohort with inherent vulnerability due to the impact of HIV infection in the family members, pose a great medico-socio-psychological challenge. There is a need for a public health approach to address these challenges as integration into mainstream public health program may be difficult due to the stigma and discrimination faced by these families. Hence research focusing on determining and establishing the burden of these challenges are required. An extended study period of more than six months would have provided a better insight into these challenges. This study provides a platform for future research on various aspects like neuro-developmental outcomes, impact on immune system and long-term nutritional and growth outcomes in these children.

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