BANGLADESH J CHILD HEALTH 2010; VOL 34 (1): 21-24

Review Article

Perinatal HIV Infection - An Update

SHAKEELA ISHRAT[1], MOHD. ZAHID HUSSAIN[2], ABM SHAHIDUL ALAM[3]

Introduction

The first cases of AIDS were reported in United states of America in 1981. AIDS appeared in Bangladesh in 1989. According to Maternal STD, AIDS program, MOHFW, estimated number of HIV positive in Bangladesh is 7500. In 2005, 658 people has been reported as HIV cases, 135 as AIDS cases and 74 as AIDS death[1].

Bangladesh is vulnerable to an exported HIV epidemic due to the prevalence of the behaviour pattern and risk factors that facilitate rapid spread of HIV. Risk factors are large commercial sex industry, low level of condom use, high rates of sexually transmitted infection, needle sharing among injectable drug users, lack of knowledge and high dependence on professional blood donars. Prevalence of HIV infection among intravenous drug users in Bangladesh has been steadily rising. A significance portion female IDUs (intravenous drug users) are also sex workers and professional blood donars. As greater number of women is infected, more infants will be at risk of acquiring HIV infection.

Risk Factors for Vertical Transmission

Nearly all the new cases of perinatal HIV are acquired during gestation, at birth or via breast milk. Vertical transmission or mother to child transmission of HIV is influenced by various factors

(1) Administration of antiretroviral drugs beginning in second trimester of pregnancy and continuing to sixth week postpartum reduces the risk of vertical transmission by about two-thirds. Antiretroviral therapy reduce mother to child transmission of HIV by lowering plasma viral load in pregnant women or through post exposure prophylaxis in the new born. In rich countries highly active antiretroviral therapy (HAART) has reduced the vertical transmission rate to 1-2%. But HAART is not yet widely available in low and middle income countries. In these countries various simpler and less costly antiretroviral regimen aimed at decreasing the risk of mother to child transmission by HIV has been offered to pregnant women, to their new born babies or both[2].

(2) Mother child human leukocyte antigen (HLA) concordance and maternal HLA homozygosity may increase the risk of vertical transmission of HIV-1 by reducing infant immune response. The increased risk may be due to reduced autoimmunity or less diverse protective immunoresponse[3].

(3) Selected antepartum conditions, e.g., long duration of membrane rupture prior to delivery in particular are independent risk factors for mother-infant transmission and suggest that preterm infants are especially vulnerable to intrapartum HIV exposure. Preterm infants may be more vulnerable to HIV transmission through risk factors as immature immune function, incomplete mucosal barrier or lower level of acquired maternal antibody[4]. Studies have revealed that a CD4 cell count below 500 cell/ micron,intrapartum use of invasive procedures, rupture of membrane more than 6 hours, labour length more than 5 hours and low birth weight are significant risk factors for vertical transmission. Elective caesarean section may reduce the chance of infecting the infants[5].

(4) Mother to child transmission of HIV is relatively high in breastfeeding population, perhaps more than 40%. Although avoidance of breastfeeding can eleminate HIV transmission through breastmilk, cost and stigma limits the use of formula feeding in many parts of the world. In high HIV prevalence resource constrained settings (e.g., Africa). HIV infected pregnant women face a dilemma regarding feeding practice where breastfeeding is widely practiced and usually prolonged 1 year after birth, the general risk of HIV transmission through milk was estimated to

1. Assistant Professor, Department of Gynae and Obstetrics, Dhaka Medical College, Dhaka
2. Professor of Paediatric Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka
3. Chief Consultant, Department of Paediatrics, Central Police Hospital, Dhaka

Correspondence: Dr. Shakeela Ishrat

be 8.6 new cases per 100 child-years of breast feeding. Breast feeding has a higher risk of early mortality, but infant formula has been associated with excess infant mortality and morbidity particularly when access to clean water is limited. HIV infected women should turn to cessation of breastfeeding only when they are consulted properly to provide adequate complementary feeding to take over breast milk[6].

Diagnosis of Perinatal HIV

Diagnosis of perinatal HIV infection is hampered by interference of passing acquired maternal antibodies. Natural HIV antibody transferred passively during pregnancy can persist for as long as 18 months in children born to HIV infected mothers. The interpretation of positive HIV antibody test results is more difficult in children below this age. To diagnose HIV infection definitely in children less than 18 months age, assays to detect virus and its components (e.g., virological tests) are required. A range of laboratory based techniques are available. Virological tests includes detection of HIV DNA or HIV RNA (viral load) or ultrasensitive p24 antigen (Up24 Ag). Virological tests can be used to confirm diagnosis of HIV infection at any age. Ideally a second virological test on a separate specimen should be done to confirm an initial positive test result. However, diagnosis of HIV infection in children less than 18 months in resource limited settings is at present not possible due to the lack of availability and accessibility to HIV DNA, HIV RNA, PCR and Up24 Ag test[7].

Significance of Perinatal HIV

Early culture positivity (i.e., intrauterine perinatal HIV infection) have been associated with immunologic and virologic changes including low mean CD4 and CD8 cell counts, thrombocytopenia, high IgM concentration and an increased viral burden early in life. Early culture positivity have been associated with lymphoadenopathy, splenomegaly, hepatomegaly and encephalopathy or a notable decrement in neurodevelopmental functioning in the first 30 months of life[8].

Interventions for Prevention of Perinatal HIV-1 Transmission

(i) Antiretroviral prophylaxis initiated during pregnancy vertical transmission risk has decreased significantly from 18.2% without treatment to 8.6% with mono/dual therapy and 0.6% with HAART. HAART is the name given to the aggressive treatment regimen used to suppress HIV viral replication and progression of disease. The usual HAART regimen combines three or more different drugs, such as two NRTI (nucleoside reverse transcriptase inhibitor) and a PI (protease inhibitor), two NRT and NNRTI (non neucleoside reverse transcriptase inhibitor) or other such combination. HAART decrease maternal viral load and offer perinatal, preexposure prophylaxis of the fetus. Most HIV-1 infected pregnant women receive HAART in North America, UK and other developed countries[9,10].

Studies are underway in developing countries to evaluate shorter and simpler antiretroviral regimen along with other interventions to reduce the risk of mother to child transmission. A single dose nevirapine adminstered to the mother and neonate is the cornerstone of the regimen recommended by the World Health Organisation (WHO) to prevent mother to child transmission. A single dose nevirapine during labour reduces perinatal transmission of HIV-1, but often leads to viral mutation in mother and infants for nevirapine resistance. Another regimen is zidovudine administered to mother from 34 weeks gestation and to neonates for 7 days, and single dose nevirapine administered to both[11].

A single dose nevirapine to the mother with or without a dose of nevirapine to the infant added to oral zidovudine (ZDV) prophylaxis starting at 28 Wks gestation is highly effective in reducing mother to child transmission of HIV[12]. Currently addition of NVP as a single maternal intrapartum dose with a single neonatal dose is not recommended for women who have received highly antiretroviral therapy during pregnancy[10].

(ii) Antiretroviral prophylaxis initiated during labour: If the woman's HIV-1 infection status is determined only at the time of labour and delivery, several effective regimens for prevention of perinatal transmission are available. Single dose NVP intrapartum followed by single dose NVP for the infant 48-72 hrs after birth, intrapartum oral ZDV and 3TC (Lamivudine) followed by 1 week of oral ZDV and 3TC for the infant, intrapartum intravenous ZDV followed by 6 weeks of ZDV for the infants or single dose NVP intrapartum and single dose NVP for infants combined with intrapartum intravenous ZDV and 6 weeks ZDV for infants[10].

(iii) Postnatal antiretroviral prophhylaxis: When the mother's or the infant's HIV-1 infection status is known only after the infant's birth and thus maternal prenatal and intrapartum antiretroviral therapy is not received, observational data suggest that 6 weeks of antiretroviral prophylaxis with ZDV given to the infant may provide some protection against transmission if infected within 24 hrs of birth. HIV infection is established in most perinatally infected children by 1 to 2 weeks of age. Initiation of post exposure prophylaxis after 2 days of age is not likely be efficacious in preventing transmission and by 14 days of age infection would be established in most infants[10].

(iv) Avoidance of HIV-1 infection from human milk: Postnatal HIV-1 transmission can occur from ingestion of human milk from HIV-1 infected women. In the United States and Canada and other developed countries, where infant formulas are safe and readily available, HIV-1 infected mother should be advised not to breastfeed even when she is receiving antiretroviral therapy. Complete avoidance of breastfeeding (and milk donation) by HIV-1 infected women remains the only mechanism by which prevention of human milk transmission of HIV can be ensured.

(v) Access to obstetric interventions such as scheduled caesarean section at 38 wks gestation reduces perinatal trasnmission of HIV[9,10]. Sperm washing can remove HIV from semen allowing conception among HIV discordant couples without risk of infection for the seronegative female and eventually the child[13].

Care of the HIV-1 Exposed Infants

HIV exposed neonates should be assessed for growth and nutritional status, signs and symptoms suggestive of HIV infection or disease and signs and symtoms of opportunistic infections in the following months. Clotrimazole (CTX) prophylaxis is universally indicated starting at 4-6 wks after birth and maintained until cessation of risk of HIV transmission and exclusion of HIV infection. The aim is to reduce the morbidity and mortality associated with malaria, bacterial and diarrhoeal disease and pneumonia in addition to prevention of PCP (pneumocystis pneumonia) and toxoplasmosis. Infants with early HIV-1 culture positivity should be treated with multiple drugs with established. CNS penetration to reduce the likelihood that resistance will develop[9].

Monitoring of Toxicity from Exposure to Antiretroviral Drugs in Perinatal Period

The most common short term adverse consequence with ZDV prophylaxis is anaemia. Mitochondrial dysfunction causing severe neurological disease, transient cardiomyopathy and hepatitis have been reported. However if causal, significant disease or death seems to be extremely rare and the potential morbidity and mortality needs to be compared with the potential benefit of ZDV in decreasing mother to child transmission of fatal infection by nearly 70%. The data emphasize the importance of long term follow up of any child with exposure to antiretroviral drugs regardless of infection status. Until there are more data or safety of in utero antiretroviral exposure, the infant should be monitored by examination at birth for congenital anomalies and assessed at 6 months and at annual visits for long term adverse effects of drug exposure[10].

Conclusion

HIV pandemic is one of the most serious health crisis the world face today . Approximately 5-10% of all cases of HIV are children. Nearly all those children acquired infection through mother to child transmission either during pregnancy, delivery or by breastfeeding. So to protect the children from HIV perinatal transmission should be prevented. Whenever possible maternal HIV infection should be identified before or during pregnancy. This allows for earlier initiation of care for the mother and for more effective intervention to prevent perinatal transmission. A equitable and accessible maternal health system incorporating an effective AIDS screening program with adequate information provision, counseling and confidentiality is a prerequisite to this.

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