HIV infections in pregnancy - A Review

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Summary:

Human Immunodeficiency virus (HIV) infections have become a global pandemic. In Asia alone about 3 millions are affected (mostly in Thailand and India) half of them being women and children. Seropositivity for HIV in pregnancy varies from 0.5% to 2.0% in Asia and the perinatal transmission rate from 15% to 30% depending on several factors. In India, with an estimated 25 millions births annually and seropositivity of 0.25% and perinatal transmission rate of 20%, about 10,000 infants with HIV infections are likely to be born each year. HIV infections do not influence the course of pregnancy; nor does pregnancy aggravate the disease process. The care during pregnancy, labour and puerperium of HIV infected mothers and the place of anti-retroviral drug therapy in these cases are briefly discussed. As there is currently no therapeutic cure or preventive vaccine against HIV, the prophylaxis is most important.

Introduction

Human Immunodeficiency Virus (HIV) discovered 15 years ago has led to a global pandemic and is responsible for millions of deaths due to the AIDS. Though it ranks 30th as a cause of mortality in the world (Murray and Lopez, 1997), its rapid spread recently to Asia calls for urgent action to control the disease.

Epidemiology:

In 1995 it was estimated that there were 250 million curable STDs in the world compared to 24 millions HIV infections with over 4 millions of them in Asia (Quinn, 1996). Next to the sub-Saharan Africa, Thailand and India have the largest number of HIV infected persons and what is worse, the number is increasing at an alarming rate. By the year 2000, 40 millions are likely to be affected globally, most of them in developing countries. Currently, the HIV prevalent rates in south Asia are as high as 13.4 per 1000 in Thailand compared to 7.4 in Myanmar and 2.67 per 1000 in India. Though the first case of HIV in India was reported in 1986, in just a decade over 2.5 millions have been affected, half of them being women and children. The seropositivity is seen in 26-50% of commercial sex workers, 5-36% of STD clinic attendees and 15-70% of the intravenous drug users (IVDUs) especially in the north-easthern region of the country. (AIDS Update 1995; Lalvani and Shastri 1996; Weigner and Brown 1996).

Modes of spread:

Sexual spread is the most common. The HIV can be quantified in the semen and infected genital secretions in the female. There seems to be a close 'epidemiologic synergy' with other STDs as HIV-1 infectivity is greater in them. (Cohen, 1998). The other important methods are parenteral through blood, blood products and infected needles. The virus also crosses the placenta from the mother to her infant. Rarely, it may be accidental as in needle-stick injuries in health workers.

Natural history of the disease:

Unlike other STDs, HIV does not give rise to any local genital lesion. Initially, this retro-virus enters a CD-4 cell and utilises the DNA and protein of the host cell destroying it as the virus replicates. The new virions

enter circulation infecting other CD-4 cells. With each and every cycle of generation, HIV destroys CD-4 cells in the host at a faster rate than the immune system could replenish them, leading to a steep decline in CD-4 counts ultimately resulting in AIDS and exposing the victim to infections like tuberculosis, pneumonia or to cancer and death in 8-10 years after the initial infection. IN India HIV-1 (subtypes A, B, C & E) is more common and HIV-2 is rare. (Esemberg, 1996, Gurtler, 1996).

Diagnosis

In the early asymptomatic stages, diagnosis is made by serological testing with ELISA. When screened positive, the Western blot (immunoblot) helps to confirm the infection and identify the type of virus. The viral load is estimated by plasma RNA assays (Gurtler, 1996).

Screening of HIV in pregnancy

Selective screening of high risk women is not useful. Anonymous unlinked testing gives only the prevalence rate. Serological screening should be offered along with other tests to all women attending a prenatal clinic. HIV positivity varies from 5-35% amongst the pregnant in African countries (Verkuyl, 1995). In Thailand, Myanmar and Bombay it was over 2% (Quinn, 1996). In some of our teaching hospitals the rates were 0.5 - 0.8% (Lakshmi and Kumar, 1991 Singh et al 1992). A recent sentinel survey in Tamilnadu showed a rise in HIV in antenatal-clinic attendees from 0.63 to 0.95% in 4 years and was as high as 2.25% in one urban area. It has now spread from urban to rural areas due to the density of population, poverty, ignorance and sexual behaviour.

Course of pregnancy :

Pregnancy does not have any impact on the course of HIV infections. Nor does the viral infection adversely affect maternal health or the course of pregnancy, labour, puerperium or lactation. (Johnstone, 1996). The rise in the abortion rates reported from few African countries may be due to some confounding factors. In the European Collaborative Study (1994), birth weight was the same both in the infected and control groups.

The virus readily crosses the placenta to affect the fetus and has been isolated in the aborted fetuses. The HIV-1 DNA has been also detected in the cervical discharge of pregnant women. The consequences of intrauterine infection on the fetus may vary depending on the period of gestation when infection occurs, duration and severity of viraemia, antiviral therapy in pregnancy and whether membranes are intact or ruptured prematurely. Breastfeeding increases the chances of infection by 20% as the virus is excreted in the breast milk. The perinatal transmission rate varies from 13% (Europ. Collab. Study, 1994) to as high as 42% in Zimbabwe (Verkuyl, 1995). In India, with an estimated 25 million births annually, a seropositivity of 0.25% and perinatal transmission rate of 20% we expect at least 10,000 HIV infected infants born yearly. In some endemic areas, the situation may be worse. A meta-analysis of 12 studies show the odds rates of 0.8 for such transmission in cases of abdominal delivery. Thus there is no evidence that caesarean section reduces the chances of perinatal HIV infections. Follow up of infected children shows higher infant and under-5 mortality rates.

Management in Pregnancy:

The fate of the unborn child is of concern in seropositive mothers. In parous women, medical termination of pregnancy is advised. In others opting to continue the pregnancy, counselling and regular prenatal care is offered including oral iron and tetanus immunisation. Efforts are made to prevent infections and to treat them promptly when detected.

Zidovudine (ZDV) has been found useful in slowing the disease and also in reducing the vertical transmission of infection. In a double blind placebo-controlled multicentric trial, ZDV in pregnancy has been found useful for reducing maternal-infant transmission of HIV-1 (Connor et al, 1994). The women 14-26 weeks or >26 weeks of gestation were randomly assigned to ZDV or placebo. The ZDV regimen consisted of 100 mg orally 5 times daily antepartum, followed by intrapartum ZDV 2mg/kg intravenously over 1 hour followed by 1.0 mg/kg/h IV till the delivery; and 2mg/kg orally of ZDV syrup every 6 hours for 6 weeks for the infant. In this trial, the treatment was given for a median of 11 weeks before

delivery. In the ZDV group 8.3% were infected compared to 25.5% in the placebo group. Thus a 67.5% relative reduction in the risk of transmission was observed in this trial. No teratogenicity was found in these infants. Though ZDV is available in India, the cost of prolonged therapy is heavy and beyond the reach of most of these patients.

However, the recent trials in Bangkok with a shorter course of therapy consisting of ZDV 300 mg given orally twice daily from 36th week of gestation followed by 300 mg every 3 hours during labor (with no antiretroviral drug or breastfeeding to the infant) resulted in relative efficacy of 50% compared to 68% with the earlier trial. With the shorter course, the cost was markedly reduced to US$ 50 compared to $800 with the longer one. A similar short term trial in the Ivory Coast where the breastfeeding was permitted, the efficacy was reduced to 38% (Mofenson, 1999).

Management of Labour:

The health worker should wear a mask, gloves and apron to minimise direct contact with liquor or blood. The vagina is disinfected with 0.25% chlorhexidine solution. ARM is avoided in these women. During labour, invasive procedures like scalp blood sampling etc are avoided to reduce risk of infection from the infected maternal fluids like liquor or blood. Normal vaginal delivery is encouraged and caesarean is done only when indicated. Once the baby is born, the cord is clamped early. The health worker should take care in the disposal of liquor, blood, placenta and the needles etc. The solid waste is incinerated and instruments disinfected and sterilised.

Breast feeding is encouraged in developing countries especially in low income groups for the nutrition and immunity it confers on the infants from other infections. (Ramachandran, 1994). However in all others, artificial feeding is advised to reduce chances of HIV infection.

Drug therapy in HIV infections:

Numerous anti-retroviral drugs are currently available for use in pregnancy. These may be divided into 3 groups.:

a. Nucleosides like Zidovudine, Didanosine (ddi) and Lamivudine
b. Non-nucleosides e.g., Nevirapine. Both these groups act by inhibiting reverse transcriptase necessary for viral multiplication.
c. The protease inhibitors like Ritonovir, Indinavir and Invirase. Lipsky (1996) favoured combination therapy to produce virostatic effect. Minkoff and Augenbraun (1997) advocate monotherapy with ZDV perinatally when CD-4 counts are high to reduce perinatal transmission. In those with CD count of <500/ml combination of ZDV and ddi give better results. Multidrug therapy is also advocated when the viral load remains high despite initial monotherapy. Triple drug therapy (ZDV+ Lamivudine and a protease inhibitor) yield best results with few side effects. The exact duration of therapy is not well defined but patients need monitoring with CD-4 counts and RNA antibody assays. Thus retro-viral therapy has definitely improved the chances of survival and markedly delayed the appearance of AIDS.

HIV vaccines:

In an attempt to control HIV infections, several types of vaccines have been tried. The vaccines from viral envelope or its core proteins, from attenuated or killed viruses and HLA based vaccines depending on the subtypes have all been used in different trials (Haynes, 1996). So far none has been found effective. Bangham and Philips (1997) feel that the obstacles for successful vaccine therapy may be the extremely rapid rate of multiplication of the virus, its frequent mutation, prolonged periods of survival in a latent state in cells and capacity of the attenuated virus to recombine with a wild type and turn virulent. The search is still on for more effective vaccines against this virus.

Prevention of HIV infections:

With no definite therapeutic cure or preventive vaccine in sight, the prophylaxis should be mainly based on proper health/sex education besides awareness of the problem.

1. As the commonest mode of spread is sexual,

development of messages to modify sexual behaviour, benefits of monogamous partnership, practice of safe sex and use of barrier contraception (Condom promotion) have to be emphasised.

2. Detection and early treatment of classic STD cases (and their partners) reduces viral infectiousness of these persons. Needle exchange program for the IVDUs and universal use of sterile disposable syringes and needles prevents the spread of the disease.
3. Similarly, monitoring of blood and blood products prior to their use in obstetric cases including emergencies is a useful prophylaxis.
4. Care by health workers is necessary of avoid needle-stick injuries or contact with liquor or blood in the labor ward/theatres besides disinfection and proper disposal of infected material.

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