REVIEW ARTICLE

Acquired Immune Deficiency Syndrome : An Upcoming Menace in Women & Children

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Introduction

Women and children constitute a vulnerable group as far as acquired immune deficiency syndrome (AIDS) is concerned. (1). The epidemiology, natural history and preventive measures suggest that AIDS may be a different epidemic in these groups. AIDS is caused by a lentivirus, human immune deficiency virus (HIV). Two major types are HIV-1 and HIV-2. HIV-1 is more prevalent of the two with HIV-2 being found mainly in Central Africa and South-East Asia. 'O' and 'M' are two major groups of HIV-1 with 'M' being further divided into eight sub-groups from 'A' to 'H'. These sub-groups are also called clades. Clade 'B' is the predominent form in Europe and North America whereas clades 'B' and 'E' predominate in South-East Asia. It is estimated that 34 million people are infected with HIV worldwide (2). About 12 million people died of AIDS in 1997, one-fourth of which were children (3,4). An estimated 16,000 infections occur each day worldwide (5). Mere presence of HIV virus in body is not AIDS. Counts of $CD4^+$ lymphocytes less than 200/µl or AIDS indicator infections should be present in addition (6). Assays for the detection of HIV load or estimation of $CD4^+$ counts are not readily available in developing countries. The need for these is obviated in the WHO case definition for AIDS surveillance (7).

Epidemiology

HIV risk for women is on the rise throughout the world (2). In US, while till 1987, only 8% of AIDS cases were women, they represented 22% of total cases reported in 1997 (8). In France, their share rose from 12 % in 1985 to 20% in 1995 (2). In India, women represent 21.06% of total AIDS cases (9). One-third of all prostitutes are infected in India (2). HIV infection rate among commercial sex workers in Mumbai was 52% in 1997 (10). Of 34 million people living with HIV infection worldwide in 1998 more than 40% were women (2). In sub-saharan Africa, 6 out of 11 HIV positive cases are women (2). Now, about 50% of new HIV cases are women (2). HIV infection rates among pregnant women are still low in Asia but are rising alarmingly. About 2% of pregnant women are HIV positive in Thialand (2). In some areas in Mumbai, HIV prevalence among pregnant females is 6% (9), though overall HIV prevalence in pregnant females in India is 1% (9).

Children constitute 5.4% of total AIDS cases in South-East Asia (11) and 4% in India and the infection rates are estimated to rise more in future. AIDS incidence among children is on the decline in US due to success of antiretroviral agents (12).

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Routes of transmission

HIV infection is a sexually transmitted disease. Three-fourth of all infections are transmitted through heterosexual or homosexual contact (13). Heterosexual transmission causes more than 80% of HIV infections in females (2). A woman has a disproportionately large chance of getting infected : male to female transmission is 20 times more than female to male transmission (13).

Cervical inflammation, genital ulcerations and other STDs increase the chance of transmission (13-18). In this context, it is to be noted that presence of HIV in the seminal fluid is independent of the viral load in the blood (19). A receptive anal. intercourse predisposes to a greater risk owing to fragility of rectal mucosa. Other important routes of transmission are blood and blood products and intravenous drug abuse (IVD). IVD is a major cause of HIV infections in US women. Women are also disproportionately larger recepients of blood products that may be infected. In rare instances, infection may spread from child to mother who is the sole care-giver to the former (13).

Eighty percent of the children are infected due to mother-to-child transmission (MTCT) (11). MTCT rates vary and appear to be higher in African countries (39%) than in Europe (14.4%) (20,21). Cell -to-cell placental transmission is more common than free virus-to-cell infection of the fetus (22). Infection can also be acquired during labor and delivery (23,24). Presence of genital ulcerations, chorioamnitis and funisitis increases the risk of transmission (25). Birth of second twin is associated with lower MTCT and this indicates that flushing out of virus from birth canal occurs during first birth (26). Virus also spreads through human colostrum and breast feeding (27). Women with vitamin A deficiency are more prone to transmit virus in their milk (13). Street children are also vulnerable to intravenous drugs and sexual abuse.

Pathogenesis

The primary cellular receptor for HIV is the CD^{4+} molecule. For efficient fusion and entry of HIV-1 into the cells, a CD receptor (CXCR4 on T cells and CCR5 on macrophages) must be present. The CD^{4+} molecue is expressed on the surface of a subset of T-cells, monocytes/macrophages and dendritic/langerhans cells. Following binding of HIV with the CD^{4+} molecule, fusion with the host cell membrane occurs and HIV genome is internalized into the target cell. The reverse transcriptase enzyme, by transcripting the HIV RNA yields double-stranded DNA. Infection in CD^{4+} cells is followed by wide dissemination of the virus to lymphoid organs. This stage is clinically manifested by acute HIV syndrome. It is followed by establishment of chronic and persistent infection. In this stage CD^{4+} T-lymphocyte count goes on decreasing gradually. The state may persist upto 10 years. When CD^{4+} T cell count falls below 200 cells per microlitre, the patient becomes susceptible to opportunistic infections to which he ultimately succumbs (13).

Clinical features

Clinical features of AIDS are mainly due to immunodeficiency state created by the virus. The virus attacks itself to the cells possessing $CD4^+$ receptors i. e. helper T-cells and macrophages. Virus is cytopathic and destroys these cells leading to gradual decline in $CD4^+$ counts. Neurological manifestations and Kaposi's sarcoma can occur independent of fall in $CD4^+$ counts. The disease encompasses a spectrum ranging from asymptomatic infection to full blown AIDS culminating in death. Twenty-four conditions including carcinoma of cervix are listed in AIDS surveillance case definition

(1993 Revised Classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults).

Important gender differences exist. Esophageal candidiasis is more common in women (28). Vaginal candidiasis in HIV infected women is more severe and occurs earlier than oral candidiasis (29). Woman with more advanced disease is more likely to transmit infection to the child (30). On an average, it takes ten years to develop AIDS once HIV is introduced in body and death occurs within two years of onset of AIDS.

In infants with MTCT, incubation period varies. Some develop AIDS within the first two years of life whereas others have a more prolonged incubation period (31). In children, failure to thrive, lymphadenopathy, oral candidiasis and developmental delay commonly occur. Cardiomyopathy is a known complication of HIV in children.

Laboratory Diagnosis

Presence of HIV in body can be ascertained by detecting either antibodies against the virus or antigens and other viral products. ELISA and Western blot tests detect antibodies against the viral products. Direct estimation of viral products is done by viral protein capture assays and polymerase chain reaction (PCR) for HIV RNA and HIV DNA. Culture of the virus is used only for research purposes. $CD4^+$ counts and levels of β_2-microglobin and neopterin in blood predict the prognosis (13).

Treatment

AIDS has no cure. Primary goal of antiretroviral therapy is to achieve prolonged suppression of HIV replication. Reverse transcriptase inhibitors and protease inhibitors are the agents used to treat AIDS. Reverse transcriptase inhibitors are nucleoside analogues and non-nucleoside analogues. The reduction in AIDS cases and AIDS death in USA is attributed to highly active antiretroviral therapies-HAART (32,33). Combination chemotherapy is the cornerstone of HAART. Two reverse transcriptase inhibitors along with one or two protease inhibitors are used. Once initiated, therapy has to be life long. During therapy, $CD4^+$ counts and/or HIV RNA estimation is done. A fall in former or rise in the latter is generally an indication for reviewing therapy (13). Secondary infections are treated accordingly.

Zidovudine (AZT) is an important drug in preventing MTCT. In one study, a reduction in the risk of MTCT from 25.5% in the placebo group to 8.3% in the AZT group was found (34). Role of drugs with immuno-modulating activity and vaccines for use in conjunction with antiretroviral therapies is also under active investigation (35,36).

Prevention

Lack of care of AIDS has put emphasis on preventive measures. Prevention of AIDS at its simplest revolves around adopting 'safer' sexual practices and proper screening of blood and blood products. Use of disposable syringes in intravenous drug abusers (IDUs) may decrease the transmission of HIV infection. Antiretroviral therapy with AZT should be used during pregnancy to prevent MTCT (34). Similar measures are available for post-exposure prophylaxis (13).

Cornerstone of AIDS prevention is education. AIDS prevention is not just the responsibility of governments alone. Individuals, families, communities, legislators, professionals, youth and health personnel, all are to be involved. Most crucial role in this regard can be played by non-governmental organisations (10).

Vulnerability of women to HIV infection can be minimized by improving access of girls to formal schooling and sex education. Society should provide them with women-friendly services e. g. STD clinics exclusively for women. Female controlled prevention methods e. g. female condoms and vaginal microbicides are to be made easily available. Women organisations are to be involved in framing proper legislation for preventing child abuse, rape and sexual coercion. Men should be educated to respect rights of women. Economic emancipation of women will prevent their sex slavery. All of us have to realize that though women are more vulnerable, menace of AIDS respects none, thus necessitating a comprehensive strategy to tackle it.

Conclusion

AIDS is essentially a social disease. It has assumed pandemic proportions in a short period of time mainly due to lack of proper information regarding its natural history. Information dissemination has been the main reason of decrease of the epidemics in the developed world. AIDS will be the major cause of morbidity and mortality in the developing countries in the coming years. Gross under reporting in developing countries can result in wrong prioritization of the limited resources. Women and children are most susceptible to HIV infection. Decreasing the susceptibility of this sub-group through proper education and politico-economic empowerment, besides adopting safe sexual practices, proper screening of blood products and antiretroviral treatment is the need of the time.

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