Ann Natl Acad Med Sci (India), **43(1):** 79-86, 2007

Rising Trend of Pediatric HIV Infection In North India:

Experience of a Tertiary Care Center

*Shobha Sehgal, Usha Datta, Sunil Arora, Neelam Pasricha, N Sachdeva, Isaac James and Surjit Singh**
Department of Immunopathology &
Pediatrics*, PGIMER, Chandigarh

Abstract

Pediatric HIV infection continues to pose a serious threat in the developing world. While in the developed world, mother to child transmission has been reduced to less than 3%, in India large-scale AZT intervention programs have still to operate in full swing. Some 25 million babies are born each year and the number of infected babies cold be >50000 per year. The present study was designed to assess the change, if any, in the time trends of HIV infection in children over the last 18 years as observed at the surveillance center attached to Nehru Hospital Chandigarh.

All patients reporting to the surveillance center at the PGIMER Chandigarh were subjected to a detailed history and screened for HIV by the three tests protocol recommended by the WHO. DNA analysis was done to confirm infection in babies less than 18 months. Time trends were ascertained over an extended period of 18-years to assess the impact of IEC programme launched by NACO. Data indicates that the total number of HIV positive cases increased 10 fold over the last 10 years. During 1991, 41 cases were recorded; the number increased to 439 in year 2001, 574 in 2004 and 857 in 2005 (r=0.98)). A similar trend was observed in the pediatric age group. During the initial 5 years, i.e. 1987 to 1992 only 7 pediatric cases were documented positive while the number increased to 45 in the year 2001 and to 77 in the year 2005 with a cumulative figure of 400

Correspondence : Shobha Sehgal, Emeritus Professor, Department of Immunopathology, PGIMER, Chandigarh. E-mail : shobhasehgal@yahoo.com

children. Linear regression analysis showed a highly significant trend (r-0.94). Out of these, 49% were symptomatic. Maximum number of babies was observed in the age group of 3-5 years. A significant number of babies (12%) had acquired the infection through blood. It calls for urgent antiretroviral intervention in antenatal mothers to control the emerging pediatric HIV epidemic in high-risk areas.

Introduction

The HIV epidemic is now more than two decades old, yet the grim scenario continues. While in the developed world, a plateau has been achieved; the situation in Africas, South East Asia and South Asia is alarming (1,2). Globally, by the end of 2006, 39.5 million were living with HIV infection and out of these, 2.3 million were children, while in 2006,2.5 to 3.5million had died globally (3). Taking the UNAIDS statistics into consideration, cumulative figures for AIDS patients since the beginning would exceed 75 millions. The number of children orphaned due to AIDS stood at 15 millions and less than 10 % had access to antiretroviral therapy and other support (4).

In India the prevalence of HIV among pregnant women varies widely from state to state and figures range from 0.9% to as high as 4.7% as in Namakkal a small village in Tamil Nadu (5). Considering that some 25 million infants are born each year and taking positivity in mothers at 7 per thousand as the lowest average figure, one would end up with a staggering figure of 175000 infected mothers. Although stray small reports are available (6,7) yet only one major HIV study in the pediatric age group is available in India (8)

The present study describes the time trends of pediatric and neonatal infections as observed in Nehru Hospital attached to PGIMER since the beginning of the epidemic.

Material and methods

All patients reporting to the Surveillance Center since 1987 for HIV testing were meticulously questioned for high-risk behavior, history of blood transfusion, drug abuse, homosexuality etc. In case of patients in the reproductive age group showing positivity, small children and spouses were also tested. Pregnant women if positive, their family was also subjected to HIV test after an informed consent. Similarly any child reporting to the pediatric department detected as positive, the parents were also subjected to screening. The diagnosis of HIV infection was established from peripheral blood sample according to the WHO/NACO (National Aids Control Organization) criteria after pre and post test counseling (9). Till 1998 all samples were confirmed by a Western blot assay, however, subsequently, WHO modified guidelines for developing countries

adopted by NACO were used in which ERS (ELISA, Rapid and Simple test) algorithm was used for diagnosis. Western blot was no longer considered mandatory. In a selected number of cases enumeration of CD4 (T helper cells) and CD8 (T suppressor cell) were also undertaken using 2 ml EDTA blood in a Becton Dickinson FACS Scan using anti CD3, anti CD4 and anti CD8 antibodies using initially a simulset and later a cell quest soft ware (10) .The number of total CD4 and CD8 cells were calculated from the total lymphocyte count obtained in an automatic coulter counter. After 1998, if the baby was below 18 months, infection was confirmed by a nested cum amplification refractory mutation system (ARMS) PCR. The primer sequences were as follows:

TTC-CCA TTA GTC CTA TTG AAA CTGT (outer primer 1)

TCA TTG ACA GTC CAG CTA TCC TTT T (outer primer 2)

GGA TGG AAA GGA TCA CCA GCA (inner primer 1)

TGA TGT TTC TTG TCT GGT GTG GT (inner primer 2)

The conditions for PCR have been published earlier (11).

Results

There has been an exponential rise in overall HIV positive cases as detected at the surveillance center over the past 18 years. During 1987to 1992, 140 seropositives were documented with 55 having full blown AIDS. There after, there was a steady increase in the number of cases reporting every year and during 1998 to 2000 the total number of cases reporting to the center increased to 292, 330 and 348 cases respectively (Fig 1). Between 1998 and 2004 the number of patients reporting to the surveillance center also doubled. Linear regression analysis showed a highly significant up ward trend (r-0.98). The trend continued in 2005 when 757 positive cases were recorded.

Pediatric Cases

Out of the total of approximately 2800 patients documented by the end of 2002, 223 pediatric cases were documented (10%of the total). Initially cases of blood borne infection were noticed in thalassemic children in the older age group. However, after policies of the National AIDS Control Organization (NACO) were implemented, a dramatic decrease in blood borne infections was recorded and the major group of materno foetal infections emerged.

During 1987 to 1992, only seven children were detected positive i.e. one child per year, while the number increased to 64 out of 574 cases in 2004.Secondly, the ratio of symptomatic to asymptomatic also increased significantly over the years (r-0.7). In 2005, 77 children reported positive, again showing a significant increase over the last year (fig.2, 3).

Out of a total of 400 children with HIV/AIDS, 252 were males and 148 females; and nearly 49% children were

Fig. 1 : Time Trends of AIDS in North India

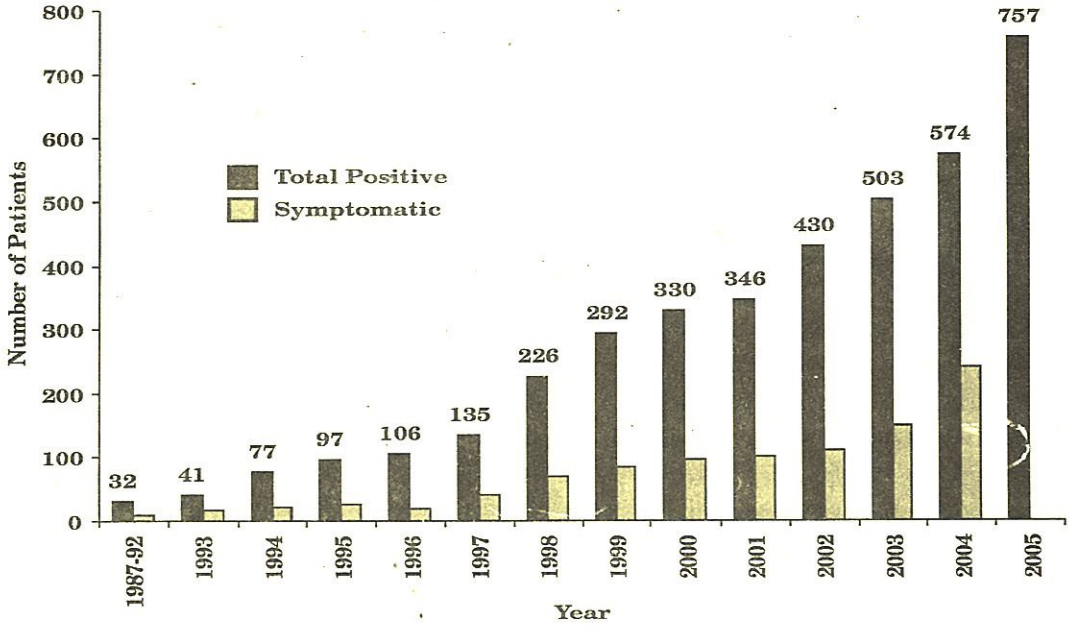
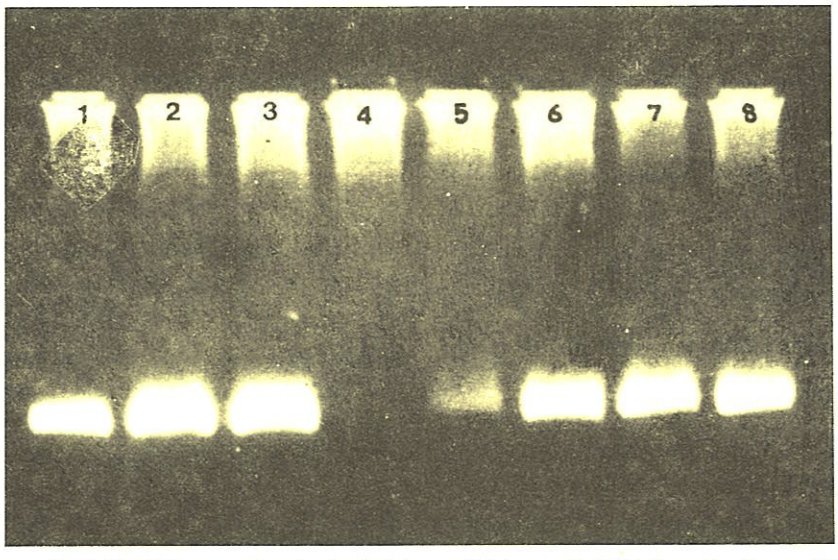
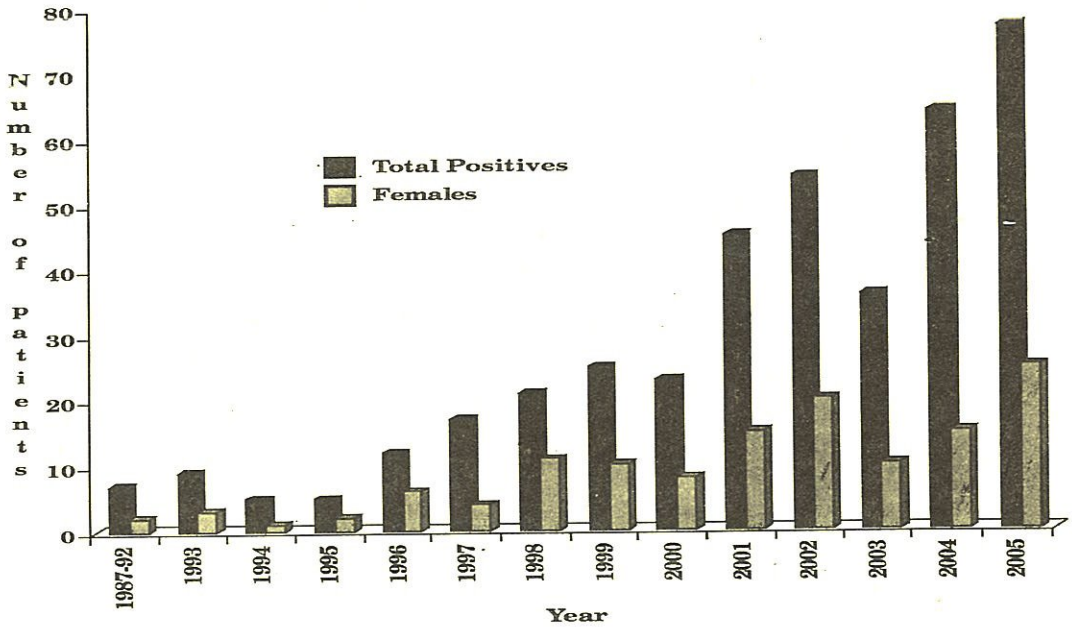


Fig. 2 : DNA test for HIV / AIDS in Children



Nested cum ARMS PCR results in 8 children. Note a 210 kb band of amplified codon 215 of pol gene. All children show a positive test except the sample in lane 4, which contains DNA sample from a negative control.

Fig. 3 : Time Trends of Pediatric AIDS in North India



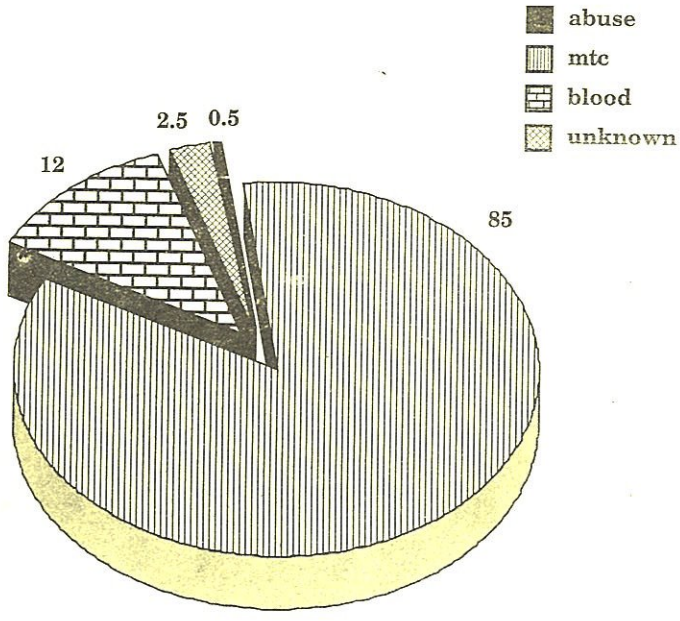
symptomatic. Maximum number of patients was observed in the age group of 3-5 years. Children who either had received multiple transfusions for thalassemia or factor VIII infusion for hemophilia in previous years generally reported in the older age group i.e. beyond 7 years. However, in the year 2005, 20/77 children who had acquired infection through the materno fetal route reported at 10 years or beyond. One older child had a definite history of sexual abuse.

In 16/ 400 children reporting before 1998, a definite diagnosis of HIV was not possible because children were asymptomatic and no follow up or PCR test was available. It is possible that in a few of these some patients were not true HIV cases and were just seropositives But this would not vitiate the trend data, rather it would support it. The infection was transmitted from the mother to the child in 85 % of the cases; blood borne infection was documented in 12% of the babies and in 2.5% of the babies, the risk factor could not be clearly ascertained while sexual abuse was documented in a single case (Fig 4).

Discussion

The present data indicates that the upward trend is unabated in this region and AIDS in children is emerging as a serious threat. Perinatal transmission accounts for nearly 90% of infections in the neonates. It was estimated that globally 5-6 million HIV infected women delivered babies each year resulting in 600000 new infections and 1600 HIV

Fig. 4 : Risk factors in paediatric HIV at PGIMER, Chandigarh



infected infants were born each day (12). The explosive global epidemic has disproportionately affected the developing world notably Africa and South East Asia including India. There are however no properly designed studies in India to indicate the precise mother to child transmission rates in the country as denying treatment to HIV positive mothers would be unethical. With a two-drug regimen in the pregnant mothers, the transmission rate could be reduced to less than 3% in the United States (13). A preliminary AZT trial was conducted by NACO/UNICEF at 11 centers in 6 states with HIV prevalence rates of more than 1%. Out of the 751 women studied, only 658 were monitored. The results indicated that AZT intervention is a cost effective strategy but doubts were raised about the safety issues (14).

Poor access to health care system, ignorance of the masses, financial constraints and NACO policy, of not screening all antenatal mothers unless the prevalence rate exceeds 1% in the area would mean that we would continue to witness increasing pediatric HIV infections in the coming years.

The situation in Punjab, however, is much more alarming as evident from the HIV positivity rates in adults and particularly in truck drivers (15-17). The two main reasons for this being growing awareness on part of experts in suspecting and diagnosing HIV/AIDS in children but the major factor being an over all increase

in the total number of positive cases reporting per year due to high risk behavior, notably of truckers. These in turn act as a reservoir for fresh infections in the spouses. In a recent study, the positivity rate in pregnant women in one district of Punjab was as high as 2%(16).

A single dose of nevirapine to the newborn can drastically reduce incidence as evidenced from the HIV NET 012 study but a 2-drug regimen is superior (18). Nevirapine obviously, cannot be administered to all the pregnant women in India. Therefore the first step is to screen all pregnant women at this stage and provide suitable prophylaxis, which will ultimately prove cost effective and reduce the burden of new infections in the babies.

Thus it is time to design a broad based national policy to combat the epidemic of pediatric HIV infection in India. It means that testing of mothers be made mandatory irrespective of the prevalence rates which are bound to increase. The non-government organizations can contribute significantly in this endeavor. Ministry of Health has started providing free antiretroviral drugs to a limited number of HIV patients in high prevalence states. Considering the extreme relevance of the problem recently, Government of India in collaboration with NACO, WHO, Clinton foundation and Indian Academy of Pediatrics launched a Pediatrics AIDS Programme in November 2006(19).It aims to provide antiretroviral drugs to 10000 children but implementation of the programme is going to be the greatest challenge

Acknowledgment

The Department of Biotechnology Government of India and National AIDS Control Organization funded the study.

References :

1. Schwartlander B, Garnett G, Walker N *et al*, (2000) AIDS in a new millennium. *Science,* **289:**64-67.
2. De Cock K M, Fowler, M G, Mercier *et al.* (2000) Prevention of mother to child HIV transmission in resource poor countries: translating research into policy and practice, *JAMA.* **283:** 1175-82.
3. www.unaids.org/epidemic_update/report 2006_jan.
4. www.unicef.org/uniteforchildren 2005.
5. Solomon S, Madhivanan P and Ganesh A K, (2000) Mother to child transmission of HIV: Situation in India and programme implications in round table conference series. *Ranbaxy Science foundation,* April **6:** 99-105.
6. Singh S, Gulati S, Marwaha R K, *et al* (1993) HIV sero surveillance in multi-transfused thalassemic children. *Indian Pediatrics,* **30:** 108-109.
7. Lodha R, Singhal T, Jain Y, K *et al.* (2000) Pediatric HIV infection in a tertiary care center in North India: early impressions. *Indian Pediatrics,* Sep; **37(9):** 982-986.

8. Merchant RH, Oswal JS, Bhagat RV *et al*, (2001) Clinical profile of HIV infection. *Ind Pediatrics* **38:** 239-246.

9. Operational characteristics of commercially available assays to determine antibodies to HIV-I and/or HIV-2 in human sera.(1998) WHO/ UNAIDS Report no. 9/10. WHO, Geneva, Switzerland.

10. Sehgal S, Dutta U, Mujtaba S. *et al.* (2003) Cellular and serological markers of disease activity in Indian patients with HIV and AIDS. *Methods in Cell Sc.,* **24:** 107-114.

11. Sachdeva N, Sehgal S and Arora S. Drug resistant variants of HIV coexist with wild type in treatment naïve patients in India *e Jour. Int. AIDS. Soc.* 2005, 7.27.7(3).

12. Mother to child transmission of HIV. UNAIDS, October 1998, Technical Update. Best practice collection technical update Geneva: UNAIDS, revision WC 503.71.

13. Proceedings of working group on perinatal, Pediatric and Adolescent HIV Research Priorities.(1999). Falls Church, Virginia June 10-11; PACTG mission statement p5

14. Rajalakshmi, TK. Programme and pitfalls: The national AIDS control organization programme to prevent mother to child transmission of HIV fails to take into account the serious side effects of drugs that are under consideration. WWW. unaids/ AZT intervention.

15. Sehgal S, HIV Epidemic in Punjab, India (1998). Time Trends Over a Decade. Bulletin of the world health organization. **76(5):** 509-513.

16. Sehgal S and Puri Vanita, High incidence of HIV infection in pregnant women in Punjab. (Unpublished data).

17. Singh B., Bedi Y.P., Singh S. and Sehgal S. (1994). AIDS awareness among truck drivers in Punjab. *Ann Nat Acad Med Sci (India),* **30(2):** 129-132.

18. Lallement M, Jourdain G, Le Coeur S, Mary JY, Ngo-Giang –Huong N, Koetsawang S, Kanshana S, Mackintosh K,Thaineua V. Single-dose perinatal nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *N Engl J Med.* 2004 Jul 15; **351(3):** 217 -228

19. WWW.UNICEF.org: UNICEF, India media center Nov.2006.