SHORT COMMUNICATION

Rapid Progression of HIV Infection in Infancy

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Manuscript received: January 10, 2007; Initial review completed: February 8, 2008; Revision accepted: March 24, 2008.

Transmission of HIV from mother to child can occur in utero, during labor or after delivery via breast feeding. Data on the fate of babies born with HIV in India are scarce. We present details of 25 infants with perinatally acquired HIV infection (virologically confirmed) to highlight the observed high rate of morbidity and mortality within the first 18 months of life. Our findings of rapid disease progression among perinatally infected HIV positive children underline the importance of early diagnosis and treatment.

Keywords: *HIV, India, Infant, Progression, Transmission.*

The natural history of pediatric HIV infection in infants is well documented in many countries showing a characteristic bimodal pattern of disease progression(1,2). Studies from Africa have shown 26-45% mortality by 1 year of age and up to 89% by 3 years of age(3-5). There is little data from India regarding the clinical course of exposed babies followed from birth(6,7). We describe the clinical features and outcome of 25 infants, confirmed to be HIV-1 positive by DNA-PCR.

Methods

This was a prospective, observational study conducted in Tuberculosis Research Centre (TRC) Clinics of Madurai and Chennai between March 2004 and June 2007. Infants born to HIV-1 positive women at Chennai and Madurai were referred to TRC for confirmation of diagnosis by DNA-PCR. 19 infants were referred to TRC Madurai unit while 6 were referrals from hospitals in Chennai. The study had Institutional Ethics approval and informed consent was obtained from a parent/guardian. Clinical examination including anthropometry was done and blood drawn for DNA-PCR and CD4/CD8 counts. CD4 and CD8 counts were measured on a Coulter Epics flow cytometer (Beckman Coulter, USA) using a standard 4-colour protocol. DNA-PCR was done using the Roche AMPLICOR HIV-1 DNA Test Version 1.5.

Detailed counseling was provided including the feeding options; however the choice was left to the mother. Babies were followed every 3 months, till 18 months of age. All babies were given cotrimoxazole 5mg/kg orally daily and opportunistic infections were managed appropriately. Diagnoses of opportunistic infections were based on clinical and disease specific criteria. Patients were referred to government ART centres in Madurai and Chennai but pediatric formulations became available only in November 2006 and most of these infants could not access ART, at the time of this study.

Results

The baseline immunological profile and age at the time of presentation, sex, type of feeding, CD4

TABLE I CLINICAL AND IMMUNOLOGICAL FEATURES OF 25 HIV INFECTED INFANTS

S. No	Age (days)	Sex	CD4%	CD4 count (cells/ mm^3)	CD4/ CD8 ratio	Feeding choice	Clinical features	Anti-retroviral treatment	Outcome
1	36	M	71*	5807	4.73	Mixed	Hepatosplenomegaly, TB, oral thrush	No	Died
			28**	1065	0.67				
2	12	F	63*	3847	4.2	Breast	Bronchopneumonia	No	Died
			24**	2019	0.5				
3	50	F	67*	4159	2.79	Breast	LRI	No	Alive
			26**	1265	0.68				
4	18	F	56*	4436	2.07	Bottle	Skin lesion,diarrhoea	yes	Alive
			10**	1224	0.48				
5	45	M	NA	NA	NA	Breast	Bronchopneumonia	No	Died
6	75	M	26	890	0.65	Mixed	Seizures	No	Died
7	50	M	18	626	0.37	Breast	Bronchopneumonia	yes	Died[$]
8	80	M	39	3747	0.975	Mixed	Hepatosplenomegaly, LRI	yes	Alive
9	120	M	12	525	0.21	Breast	Diarrhea	No	Died
10	180	M	NA	NA	NA	Bottle	Diarrhea	No	Died
11	45#	F	38	6207	2.24	Mixed	Bronchopneumonia, CMV retinitis	yes	Died[$]
12	150	F	19	3158	0.4	Mixed	Diarrhea, oral thrush	No	Alive
13	150	M	NA	NA	NA	Breast	LRI	No	Alive
14	300	F	39	3902	1.18	Breast	LRI	No	Alive
15	210	F	53	4025	1.51	Breast	LRI, oral thrush	No	Alive
16	365	M	28	918	0.5	Mixed	Diarrhea,vomiting,seizures, fever	No	Alive
17	42	F	9	894	0.14	Mixed	Diarrhea	No	died
18	270	M	19	1456	0.37	Mixed	Vomiting and diarrhea	No	died
19	365	F	8	301	0.12	Breast	LRI	No	died
20	150	M	28	2551	0.74	Bottle	Bronchopneumonia, FTT, diarrhea	No	Alive
21	180	F	14	1037	0.2	NA	Delayed milestones, FTT, diarrhea	Yes	Alive
22	300	F	17	1989	0.71	Breast	LRI	No	Alive
23	300	M	19	1202	0.44	Breast	Delayed milestones, FTT	No	Alive
24	48	F	8	212	0.16	NA	LRI, diarrhea	No	Died
25	300	F	39	1597	0.975	Breast	LRI, FTT, oral thrush, delayed milestones	No	Alive

* *CD4 at the time of registration (DNA-PCR found to be negative); ** CD4 at the time of HIV suspicion (Repeat DNA-PCR found to be positive);* NA*–Not available;* [#] *LSCS; $ soon after ART initiation; FTT: Failure to thrive.*

counts and CD4/CD8 ratio, status at the time of writing the report (October 2007) and cause of death are shown in ***Table* I**. The mean age at presentation was 154 days (SD 68). DNA-PCR was found positive in 21 infants at presentation. Four infants whose test was negative and CD4% was high at baseline, had a fall in CD4% along with a positive PCR at 6 months of age. All infants were delivered vaginally except one. Fourteen mother-infant pairs received nevirapine prophylaxis as per the

WHAT THIS STUDY ADDS?

- A large proportion of children born with HIV-1 infection in India are rapid progressors.

prevention of mother to child transmission guidelines of National AIDS Control Organization. Eleven infants were breast-fed, 3 were artificially fed while nine were given mixed feeds. Feeding details for 2 infants were not known. All four infants who showed a later conversion of DNA-PCR to positive result were given mixed feeds.

The mean (SD) birth weight was 2.6(0.5) kg. The mean (SD) CD4 count was 1855 (1503) cells/mm^3. Mean (SD) CD4% was 23.6 (12), CD8 3081 (1633) cells/mm^3, and CD8 % 44 (14) at the time of HIV-1 positivity. The CD4/CD8 ratio (mean 0.64±0.50) was less than 1 and the hemoglobin was less than 10 g/dL (mean 9.47±1.65) in all infants.

Twelve children died before 18 months of age. Five children received antiretroviral treatment, of whom 2 died and 3 are surviving. Of 20 children who did not receive ART, 10 died and 10 are under follow up. The most common diagnoses during the course of the disease are shown in ***Table* I**.

DISCUSSION

Of the 25 HIV-1 infected infants enrolled in this study, 10 died before antiretroviral treatment could be initiated and 2 died shortly after initiation of ART. This suggests that a substantial proportion of HIV-1 positive children infected perinatally in India are rapid progressors and will die in infancy unless diagnosed and treated early.

We observed that four children who initially had a CD4/CD8 ratio >1.0 and were later found to have a ratio <1.0 had become HIV positive. These infections are likely to have occurred due to breastfeeding. The practice of breastfeeding has been shown to diminish the long-term efficacy of perinatal prophylactic antiretroviral therapy(8). Two African studies have found that infants assigned to be formula fed or breastfed had similar mortality rates and incidence of diarrhea and pneumonia during the first 2 years of life. However, HIV-1-free survival at 2 years was significantly higher in the formula arm(9,10). Replacement feeding with animal milk or formula should be encouraged whenever it is acceptable, feasible, affordable, sustainable and safe. Our preliminary observation that the CD4/CD8 ratio can be used as a supporting diagnostic test for HIV-1 needs confirmation in controlled trials.

The WHO guidelines 2006 recommend ART be initiated for infants <12 months who have CD4 <25% or CD4 count <1500 cells/mm^3(11). In our study, some of the infants who subsequently died had CD4 counts above this cut-off, suggesting that these may not always be predictive of outcome. Children <1 yr of age are at high risk for disease progression, and immunologic and virologic tests to identify those likely to develop rapidly progressive disease are less predictive than in older children. Therefore infants should be treated with antiretroviral agents as soon as the diagnosis of HIV infection is confirmed, regardless of clinical or immunologic status, or viral load(12). Recent clinical trials suggest that initiation of ART before 12 weeks of age reduces early mortality by 75%(13). Though long-term HAART allows for restoration of CD4+ cell counts and control of viral loads in HIV-1-infected children, initiating HAART after severe immunosuppression had occurred is detrimental for the restoration of cell mediated immunity(14). In summary, our experience with HIV infection in Indian infants suggests that without early diagnosis and treatment, the outcome is likely to be poor in a substantial proportion.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the assistance provided by Ms Gomathy, Nutritionist, in nutritional assessment of the children and Mr Thiruvalluvan, Medical Social Worker in sociological assessment and follow-up of mothers. We are grateful to the staff members of the clinical and HIV laboratory divisions for their cooperation and Ms D Kalaivani for secretarial assistance. We thank Dr V Kumaraswami,

Deputy Director (Sr Grade) for his critical comments on the manuscript and the Director, Dr P R Narayanan for his encouragement and support.

Contributors: NPGD and SS conceived and coordinated the study and drafted the manuscript. RS and SNR were involved in patient recruitment and follow-up and KR performed the laboratory investigations.

Funding: Indian Council of Medical Research.

Competing interests: None Stated.

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