Correlation between Clinical Features and Degree of Immunosuppression in HIV Infected Children

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ABSTRACT

We conducted this study to find out correlation of CD4% with clinical status in 102 HIV infected antiretroviral naïve children. Mean age of presentation was 4.8 years. Perinatal transmission was the commonest mode of transmission (94%). Fever (53%), chronic diarrhea (36%), and cough (29%) were the commonest presenting symptoms. Protein energy malnutrition was seen in 56.7% of children. 33.3% children were asymptomatic, whereas 45.1% were in WHO clinical stages III and IV at the time of presentation. The most common opportunistic infection was tuberculosis. CD4% correlated significantly with the deterioration of the WHO clinical stages (P<0.01) and increasing grades of protein energy malnutrition (P<0.05).

Key words: *CD4%, Children, HIV, Protein energy malnutrition, WHO clinical stage* .

INTRODUCTION

India harbors world's second highest number of HIV infected people(1). HIV infection is increasingly becoming a prominent cause of childhood morbidity and mortality in India. Presently, 2,02,000 children are living with HIV/ AIDS in India. 50% of these die within 2 years, constituting about 18% of 3.1 million AIDS deaths every year(2). Despite the magnitude of the problem, there is paucity of published data on various issues in pediatric HIV infection from Eastern India. We report correlation of CD4% with the clinical spectrum of HIV infected children from Eastern India.

METHODS

We included antiretroviral naïve children (0-18 years) who presented at antiretroviral therapy (ART) center of Sir Sundarlal Hospital, Banaras Hindu University between May 2005 to August 2006. Screening for HIV was done after a written informed consent from the parents/ caregivers after obtaining clearance from the Institutional ethical committee. Diagnosis of HIV was confirmed by ELISA using two different antigens and a rapid test for children over 18 months and DNA PCR (repeated twice) in less than 18 months.

Clinical details were recorded including demographic details, possible modes of transmission, presenting symptoms, nutritional status and opportunistic infections at the time of presentation. Opportunistic infections were diagnosed using the standard protocol. Baseline CD4 lymphocyte counts were determined by FACS count (Becton-Dickinson). Based on the clinical presentations, the children were categorized into various WHO clinical stages (I to IV)(3). Weight for age was used to grade them (IAP classification) for protein energy malnutrition(4). They were further classified based on CD4% values in accordance with WHO classification of immunodeficiency(3). CD4 cell count varies with age so CD4% was used to define immunologic category(5). Antiretroviral therapy was started according to National AIDS Control Organization (NACO) guidelines(3). Patients were followed up every month and CD4 counts were repeated at 6 monthly interval.

One way ANOVA (analysis of variance) test was used to compare the means and Fisher's exact/ Chi square test for categorical variables.

RESULTS

During the study period, 512 children were screened for HIV infection, of which 102 were positive. Their demographic profile is given in ***Table* I**. The mean age of first presentation was 4.8 years (0-18 years). Vertical transmission was the assumed mode of transmission in 94% children in view of maternal seropositivity. Blood transfusion was considered the cause of infection in 1 child (received transfusion from his HIV infected uncle). Multiple injections was presumed mode in 2 children (history of injection at village and camp respectively). In two male adolescents, heterosexual route was considered as the mode of transmission (history of contact was present) and in 1 child mode of transmission could not be determined. Fever was the most common presenting symptom (53%), followed by chronic diarrhea (36%), cough (29%), generalized lymphadenopathy (24%), hepato-splenomegaly (12%) and skin manifestations (14%). Among bacterial infections, pneumonia (8%), otitis media (12%) and other manifestations (10%) were present. Parotitis was seen in 2% children and 1 child had Kala-azar. One third of the children were asymptomatic. CD4% declined with deterioration of WHO clinical stages of the disease (***Table* II**) ($P<0.01$). Protein energy malnutrition was present in 56.7% children. Mean CD4 percentage was 21.6%±10.7 in children without malnutrition (43.3%). The various grades of protein energy malnutrition with their corresponding mean CD4 values are given in ***Table* II**. The correlation of severity of malnutrition with decline in CD4 percentage was significant ($P<0.05$). Twenty one children (20.6%) had opportunistic infections at the time of evaluation. Patients with opportunistic infections had lower CD4 values (15.9%±10.2) as compared to patient without any opportunistic infections (21.4%±9.6). Tuberculosis was the most common opportunistic infection. Disseminated tuberculosis and pneumocystis pneumonia had the least CD4 values.

DISCUSSION

CD4 T-lymphocyte is the immune system cell that HIV infects and destroys, and the CD4 count roughly reflects the state of the immune system. An important observation of this study is that CD4 percentage declined with progression in the WHO clinical stages of HIV infection as has been observed

TABLE I DEMOGRAPHIC PROFILE OF HIV INFECTED CHILDREN

Variables	Number	Mean CD4% ±SD	WHO classification of immunodeficiency			
			Not significant	Mild	Advanced	Severe
Gender						
Male	76 (74.5%)	19.8	21 (27.6%)	12 (15.8%)	19 (25%)	24 (31.6%)
Female	26 (25.5%)	23.5	10 (38.4%)	5 (19.3%)	5 (19.3%)	6 (23.0%)
Age*						
0–<18 mo	3 (2.9%)	21.0±15.6	2 (75.0%)	0	0	1 (25.0%)
18 mo–<4 yr	27 (26.4%)	23.4±10.9	10 (37.1%)	4 (14.8%)	4 (14.8%)	9 (33.3%)
4 yr –<7 yr	29 (28.5%)	20.9± 9.5	11 (37.9%)	5 (17.2%)	6 (20.7%)	7 (24.2%)
7 yr–<10 yr	21 (20.6%)	18.2± 8.1	4 (19.1%)	4 (19.1%)	7 (33.3%)	6 (28.5%)
10 yr–<13 yr	13 (12.8%)	16.7± 8.1	2 (15.7%)	3 (23.1%)	4 (30.6%)	4 (30.6%)
13 yr–<16 yr	7 (6.9%)	13.3± 6.6	0	1 (14.4%)	3 (42.8%)	3 (42.8%)
16 yr–<18 yr	2 (1.9%)	35.5±28.9	2 (100%)	0	0	0

**Age vs. CD4%: F=0.129, P>0.05* [*ANOVA* (*Analysis of variance*) - *one way test*]

TABLE II CD4 CORRELATION WITH CLINICAL PROFILE OF HIV INFECTED CHILDREN

Variables	Number	Mean CD4% ± SD	WHO classification of immunodeficiency			
			Not significant	Mild	Advanced	Severe
WHO Clinical Stage*						
I	34 (33.3%)	24.9±11.1	14 (42.9%)	5 (14.3%)	6 (17.1%)	9 (25.7%)
II	22 (21.6%)	20.7± 7.4	7 (30.9%)	7 (30.9%)	4 (19.1%)	4 (19.1%)
III	41 (40.2%)	18.0± 9.3	9 (21.9%)	5 (12.2%)	13 (31.7%)	14 (34.2%)
IV	5 (4.9%)	15.6±13.0	1 (20.0%)	0	1 (20%)	3 (60.0%)
PEM**						
Grade I	22 (21.5%)	21.7± 9.1	9 (40.9%)	3 (13.6%)	7 (31.9%)	3 (13.6%)
Grade II	12 (11.7%)	21.7±9.1	5 (41.7%)	1 (8.3%)	3 (25.0%)	3 (25.0%)
Grade III	15 (14.7%)	18.8± 9.1	3 (20.0%)	3 (20.0%)	2 (13.3%)	7 (46.7%)
Grade IV	9 (8.8%)	10.0± 8.7	0	1 (11.1%)	2 (22.2%)	6 (66.7%)
Opportunistic infections***						
Tuberculosis	19 (18.6%)	16.3	3 (15.8%)	3 (15.8%)	4 (21.0%)	9 (47.4%)
Pulmonary	14 (13.8%)	15.5	2 (12.5%)	3 (25.0%)	3 (25.0%)	6 (37.5%)
Extra pulmonary	3 (2.9%)	15.2	1 (33.3%)	0	1 (33.3%)	1 (33.3%)
Disseminated	2 (1.9%)	7.0	0	0	0	2 (100%)
Oral candidiasis	3 (2.9%)	16.3	1 (33.3%)	0	1 (33.3%)	1 (33.3%)
Pneumocystis pneumonia	2 (1.9%)	3.5	0	0	0	2 (100%)
Herpes zoster	1 (0.9%)	24.0	0	1 (100%)	0	0
Molluscum contagiosum	1 (0.9%)	11.0	0 `	0	0	1 (100%)

** Clinical stage vs.CD4%: F=3.749, P < 0.01* [*ANOVA* (*Analysis of variance*)-*one way test*].
*** PEM vs. CD4%: F=2.969, P< 0.05 [ANOVA* (*Analysis of variance*) - *one way test*].
**** Opportunistic infection vs. CD4%: P<0.05* (*t pair test*).
Some children had more than one opportunistic infection.

in another study from this center(6). The progression of disease is related to gradual disruption of lymph node architecture leading to high levels of viremia and disappearance of CD4 cells during later stages of disease(5). This suggests CD4% as reliable marker of clinical status. HIV weakens the immune system so that opportunistic infections develop. Children with opportunistic infection have lower CD4 values as compared to children without opportunistic infection as has been reported in other studies(6,7). HIV is associated with malnutrition as was evident from our study, similar observation has been reported in other studies as well(8). Protein energy malnutrition leads to depletion of CD4 counts, and this is perhaps exacerbated by the presence of HIV infection(9,10), as has been observed in this study.

CD4 estimation is the backbone of AIDS control program in developing nations. It has been studied as a marker of progression of HIV infection and as a measure of relative risk of developing opportunistic infections. Protein energy malnutrition impacts the course of HIV by contributing to immuno-suppression. However, further studies of CD4 counts in relation to antiretroviral therapy in children needs to be done.

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WHAT THIS STUDY ADDS?

- CD4% has significant correlation with increasing severity of protein energy malnutrition and WHO clinical stages in HIV infected children.

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