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Trends in Prevalence of Opportunistic Infections in HIV Infected Children and Their Correlation with CD4 Count

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Abstract:

HIV infection has both medical and socio-economical implications such as social stigma and demise of parents. The children constitute 6% of global HIV disease burden. Major proportion of morbidity and mortality is due to Opportunistic infection (OI). The major determinant of OI is the CD4 cell count and its suppression by the virus. Studies are available to estimate the OI prevalence in HIV, however, after the institution of Anti-retroviral therapy, scenario has changed, and so has the spectrum of disease. It was our endeavor to find out the impact of adequate therapy on OI and CD4 count. Hence this study was taken up in an urban ART center.

Type of study: A Cross-sectional observational study

Objectives: (i) To study the clinical and immunological profile of HIV infected children attending the ART centre;

(ii) To correlate CD4 count with clinical staging

Keywords: HIV, Opportunistic infection, CD4 count.

1. Introduction

HIV stands for Human Immunodeficiency virus, causative agent of Acquired Immunodeficiency syndrome. The children constitute 6% of global HIV disease burden. In paediatric age group the disease mortality and morbidity is high when compared to adults. Due to availability of antiretroviral therapy and improved drugs to treat opportunistic infections it has become a chronic disorder. (i) The global paediatric HIV epidemic is shifting into a new phase as children on antiretroviral therapy (ART) age into adolescence and adulthood. The evolution of HIV into a chronic disease has no greater impact than on the life of a child. Children that families, clinicians and policymakers at one time expected to die are living into their 20s and having children of their own. Unanticipated issues such as reproductive health, higher education and career training are now urgent needs. (ii) All over the world the prevalence of Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS) has become a stumbling stone in progress of human civilization and is a huge concern for people worldwide. In 2011, the total number of people living with HIV was 34.2 million, newly infected with HIV was 2.5 million, and AIDS deaths was 1.7 million. The majority new infections are transmitted heterosexually, while the risk factors vary. In some countries, men who have sex with men (MSM), injecting drug users (IDUs), and sex workers (SW) are at significant risk. Most people living with HIV or at risk for HIV do not have access to prevention, care, and treatment, and there is still no cure. (iii) Globally the number of children living with HIV increased from 1.5 million in 2001 to 2.5 million in 2007. However, estimated new infections among children declined from 460000 in 2001 to 420000 in 2007. deaths due to aids among children have increased. (iv) Infection with HIV is acquired by children most often from the mother through the placenta or at birth, but may come through breast milk, blood transfusion, unsterile injections, traditional incisions, sexual abuse, or, in older children, early sexual activity. Infection is followed, after about 6-12 weeks in most adults and older children, by the presence of antibodies to the virus, but children under 18 months old may have acquired antibodies through the placenta from the mother before birth.

The diagnosis of HIV infection may lead to ART, but only when there is a diagnosis of AIDS (or in children under 18 months of presumptive AIDS, as finding HIV antibodies is not conclusive for HIV infection at that age). In most of Malawi clinical features will be used to stage immune deficiency, but laboratory counts of the CD4 lymphocytes, those primarily damaged by HIV and involved in immunity, can help. Where CD4 counts cannot be done, a total and differential white count to give a total lymphocyte count can help indicate immunodeficiency. (v) 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.

The natural history of opportunistic infections among children might differ from that observed among HIV-infected adults. Many opportunistic infections in adults are secondary to reactivation of previously acquired opportunistic pathogens, which were often

acquired before HIV infection at a time when host immunity was intact. However, opportunistic infections among HIV-infected children more often reflect primary infection with the pathogen. In addition, among children with perinatal HIV infection, the primary infection with the opportunistic pathogen is occurring after HIV infection is established when the child's immune system might already be compromised. This can lead to different manifestations of disease associated with the pathogen among children than among adults. (vi) Considering all the above factors present study was planned to study prevalence of opportunistic infections in HIV infected children and correlate the prevalence of opportunistic infections with their CD4+ T helper lymphocyte count.

2. Material and Methods

This study was a cross-sectional observational study conducted in a well equipped ART (Anti-retero viral therapy) center in Urban Pune. All children attending the HIV clinic, who were seropositive were enrolled. The diagnosis of HIV was confirmed by ELISA in children more than 18 months. Children up to and including age of 15years were included after taking Informed consent and Assent. 33 seropositive cases were taken up for study. Demographic profile, clinical presentation and mode of transmission of enrolled children were recorded in a predesigned proforma. Anthropometric assessment was done and WHO classification for malnutrition was adopted to classify children. Detailed history and examination was done. CD4 count was estimated by FACS (fluorescent activated cell sorter) method (Becton-Dickinson). Immunological assessment was done in terms of CD4 counts as per WHO classification [4] Relevant hematological, radiological, microbiological and biochemical investigations were done. Based on clinical presentations children were categorized into WHO clinical stages, WHO immune staging.

3. Results

Age Group	Male (%)	Female (%)	Total (%)
3-7 years	1(3)	0(0)	1(3)
8-12years	6(18)	6(18)	12(37)
13-15years	13(39)	7(21)	20(60)
Total	20	13	33

Table 1: Age and Gender wise classification of Infected children

Total no. of children included in study were 33, 20 male patients and 13 female patients.

Male to female ratio is 1:0.53. Mean age of presentation was 12 years.

Age Group	Normal	Moderate Reduction in CD4	Severe Reduction in CD4
3-7 years		1	
8-12years	7	3	2
13-15years	1	11	8
Total	8	15	10
%	24%	45%	31%

Table 2: Age of the patient and CD4 count

IAP Classification	Number of Patients	CD4 Suppression
I	18 (54%)	Moderate
II	6 (18%)	Moderate
III	6 (18%)	Severe
IV	3 (10%)	Severe

Table 3: Nutritional status and HIV infection

Staging	Number of Patients	Percentage
I----Asymptomatic	8	
---Generalized Lymphadenopathy	18	78
II---Herpes Zoster infection	9	
-----CSOM	1	30
III-----Severe malnutrition	9	
-----Pulmonary Tuberculosis	2	33
IV-----Herpes Simplex infection	2	
-----CMV infection	1	
Extra pulmonary TB Including	5	
Meningitis	1	
Cryptococcal meningitis	1	24

Table 4: WHO Clinical staging for HIV and Percentage affected

There is an overlap due to some patients have more than one condition.
CSOM--Chronic suppurative otitis media

Sign/Symptom	%
Fever	12
Otitis Media	3
Pneumonia	24
Skin lesions	30
Generalized lymphadenopathy	54
Hepatomegaly	6
Anemia	87
CNS Involvement	12

Table 5: Signs and symptoms found in Patients of HIV

Opportunistic Infection	Percent of OI (%)	CD4 Suppression
Pulmonary Tuberculosis	9	Severe
Abdominal Tuberculosis	22	Severe
Tubercular meningitis	13	Severe
Oral Candidiasis	13	Moderate
Herpes zoster infection	40	Moderate

Table 6: Opportunistic Infections percentages and correlation with CD4 suppression

Children with OI	Children without OI
22(66%)	11(34%)

Table 7: Proportion of children with OI

4. Discussion

CD4 count and percentage are useful markers for assessing the severity of infection. In our study, we found the CD4 count profoundly suppressed for OI of Tubercular meningitis, cryptococcal meningitis, Disseminated kochs, while they were moderately suppressed for Herpeszoster and Oral candidiasis.

The mean age at diagnosis was found to be 12 years. The male to female ratio was 1:0.5

The higher mean age of presentation in the present study compared to other studies is probably because children less than 18 months are excluded in the study & most of the children presented late with WHO clinical stage 3 & 4. In the study by Prabhavathi R et al. study, 28(56%) were males and 22(44%) were females. Male to female ratio was 1:0.75.(vii)

In our study commonest mode of transmission is vertical transmission, which is similar to Agarwal et al [viii] (94 %), Ramesh.R Pol. [ix]

Normal CD4 count was seen in 24% of children, while moderate reduction was found in 45% and severe reduction of CD4 count was seen in 31% of patients.

18% of children were having grade I malnutrition, 6% grade II, 6% grade III, and 3% grade IV. The CD4 count was moderately suppressed in first two while it was severely suppressed in grade III and IV. In contrast in the study of Gomber et al. 41% of children were asymptomatic with normal nutritional status.(x)

We found that 8 patients were asymptomatic, 18 patients had lymphadenopathy thus categorizing them into clinical stage I.

9 patients showed skin lesions of herpes zoster while one had Chronic Otitis media--Stage II. 9 patients had severe malnutrition and two had pulmonary tuberculosis thus classifying them into clinical stage III.

Stage IV had 5 patients of Tubercular Meningitis, 2 of Herpes simplex lesions, one had Cryptococcal meningitis and one had CMV chorioretinitis with CNS involvement.

The overall incidence of CMV retinitis in the pediatric HIV-infected population (1.6%) appears to be much lower than in adults (20%) (xi). In Sirisanthana study there was only one case.(xii)

12% patients were febrile, 3% had otitis media, 24% had pneumonia while 30% had skin lesions. Hepatomegaly was seen in 6% and CNS involvement in 12%. Remarkably 87% had Anemia on Laboratory as well as clinical examination.

The most common presentation in the present study is Anaemia (87%) which is in accordance with study conducted by Shah et al and cough in 34% which is in accordance with study conducted by Sehgal et al. Opportunistic infections in HIV infected children.

Of the Opportunistic infections 9% were pulmonary TB, 22% were abdominal kochs, 13% were meningitis, 40% Herpes zoster infection. oral candidiasis was seen in 13% cases. Overall, 66% had OI, while 34% had none.

The limitations of our study include small sample size and the short study period. Provision of free-of cost medicines, efforts of a large number of social organization, and achievement of universal treatment access has indeed resulted in excellent compliance and scheduled regular follow up visit.(xiii) Availability of CD4 count assay is limited to tertiary care hospitals and cheaper and newer methods for estimation of CD4 count are being developed.(xiv)

5. Conclusion

In conclusion, it can be said that there is a trend favorably inclined towards decreasing severity of OI in HIV patients. This can be attributed to their being well controlled on ART. Also, it can be proposed that baseline CD4 count can be used better for monitoring of ART. However It is necessary that more studies with a larger sample size be done to substantiate this.

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