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A Study of Opportunistic Infections in Children Living With HIV/AIDS – A Hospital Based Study

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Abstract

Background: HIV in pediatric age group is a major world health problem. In India childhood HIV amounts to around 4.4% of all cases. It is a large contributor to childhood morbidity and mortality in India. Usually the commonest cause of death in these children is opportunistic infections which are more seen in CD4 cell count depleted children.

Aims And Objectives: The study was carried out with the objectives to find out the incidence of OI in HIV positive children and its relation to CD4 cell count.

Materials And Methods: Hospital based observational study conducted over on period of 2 years (Sept 2015 to Aug 2017) at pediatrics Dept. of SCB Medical College, Cuttack, India. HIV seropositive children less than 14 years of age were included in the study. Detailed clinical evaluation and lab investigations were done and they were put into WHO clinical stages. They were further classified based on CD4 count.

Results: Out of total 50 cases, 28 presented in stage-III and 15 in stage-IV at first visit. Girls had higher mean CD4 count (488) than boys (340). PTB was most common OI (28%) followed by oral candidiasis. Children with OI had less CD4 cell count.

Conclusion: The clinical manifestations of HIV infection in children may be similar to number of other diseases. As the WHO clinical stage and grade of malnutrition increases, CD4 count decreases thus can be a reliable marker of disease progression in HIV infected children.

Keywords: HIV, CD_4 cell count, OI, WHO Clinical Stage, PEM, Pulmonary TB.

Introduction

HIV infection is becoming a prominent cause of childhood morbidity and mortality in India. Although children represent only 6% of all people infected with HIV/AIDS, out of this about 50% die within 2 yrs. of onset, constituting about 18% out of the 3.2 million deaths due to HIV every year[1].

The predominant mode of transmission in children is vertical i.e., it is acquired through intrauterine, intrapartum or through breast feeding from a HIV infected mother. Other routes such as sexual transmission and blood transfusion are not as common[2]. Children with HIV infection differ from HIV infected adult patients. Children usually have higher viral load, weaker immune system, variable latency period, fewer opportunistic infections, fewer medicine approved for the management, different spectrum of clinical

manifestations, diagnostic differences, and patterns of disease progression.

Soon after HIV was found to the cause of AIDS, it was shown that the virus binds to receptors on CD4 cells, enters the cells and uses them to create new virus, destroying them in the process. This results in the depletion of CD4 cells and immunodeficiency.

Opportunistic infections (OIs) are the most common cause of death among children living with HIV/AIDS. These infections are called "opportunistic" because they take advantage of the weakened immune system and they can cause devastating illnesses. OIs are a sign of declining immune system. OIs in children are usually primary and have a more fulminant course in comparison to adults. OIs in HIV children are typically seen in children with severe depression of CD4 count or CD4%[3].With the increased availability of equipment to perform CD4 counts and the knowledge that CD4 cells were the primary target of HIV, the determination of CD4 count became the standard measure of immunodeficiency in HIV infected patients in resource rich countries. The relative ease of CD4 cell monitoring also led to its advocacy in treatment guidelines for determining when to start, stop or change ART and for deciding when to initiate prophylaxis for opportunistic infections. This is despite the fact that CD4 count does not always correlate with functional immunity; some patients with normal CD4 counts are susceptible to OIs and some patients with significantly depressed CD4 counts do not seem unduly susceptible to OIs. Hence this study attempts to correlate CD4 count with opportunistic infections.

Aims and Objectives

The present study was carried out with the objectives to find out the incidence and clinical profile of opportunities infections in HIV infected children less than 14 years of age and to correlate it with CD4 counts.

Materials and Methods

This was a hospital based observational study carried out over a period of 2 years (Sept 2015 to Aug 2017). All HIV positive children below 14 years of age presenting to Dept. of pediatrics, SCB medical college, Cuttack, India during the study period were enrolled, followed up and studied. Ethical clearance was taken from institutional ethical review board. Standard consent was taken from parents or caretaker. Demographic, clinical and laboratory details were recorded at presentation and updated in each visit. Details of opportunistic infections, treatment, compliance, complications and outcome were recorded during follow up visits. Nutritional status was classified according to World Health Organization (WHO) classification of protein energy malnutrition in under-five children and according to body mass index above the age of 5 years, using WHO growth charts. Weight for height or height for age or body mass index for age between -2 to -3 SD score was classified as moderate undernutrition and SD score below -3 was classified as severe undernutrition. Anemia was defined as Hb <11.0 g/dL in children 6 months to 59 months of age or <11.5 g/dL in children 5-12 years or <12.0 g/dL in children 12 to 14 years of age as per WHO guideline for diagnosis of anemia.

Children on ART visited the clinic every month and children not on ART visited every 2-3 months, apart from emergency visits and admissions when required. Diagnosis of HIV was made by rapid diagnostic tests above 18 months of age and by two DNA PCR tests between 6 weeks to 18 months of age following WHO

guideline for diagnosis of paediatric HIV as adopted by government of India. Clinical staging of HIV, use of ART and change of ART were based on the same guideline. Diagnoses of opportunistic infections were largely based on history, symptoms, signs, clinical examination findings and supported by available laboratory test results. When tuberculosis bacilli could not be demonstrated despite strong clinical suspicion of disease, clinical judgment was used for diagnosis of tuberculosis. Such clinical diagnosis of tuberculosis was made depending upon history of contact, suggestive clinical features and indirect markers like Mantoux test or positive radiological findings. Mantoux test positivity was defined as induration size>5 mm as per WHO and national guidelines for HIV infected children.. Absolute CD4 count was obtained using BD FACS Count 1.5, Becton, Dickinson and Company, BD Biosciences, USA. Though CD4 percent count is better for children, the machine used in our hospital provides only absolute count. CD4 count was obtained at presentation and every 6 months. Change in CD4 count for each case was calculated by subtracting CD4 count at presentation from CD4 count at latest follow up. Mann Whitney U test was applied to test the change in median CD4 count between children receiving ART and children not receiving ART. The significance level was set at 5.0%. Data were recorded in predesigned record sheet, entered and screened for error in MS Excel and analyzed using Graph Pad Prism version 8.0 statistical software.

Results

Table – 1: Age and Gender wise classification of Children

Age group	Male (%)	Female (%)	Total (%)
0 – 5Yr	4 (14)	7 (31)	11 (22)
5 – 7Yr	6 (21)	9 (41)	15 (30)
7 – 10Yr	8(29)	3 (14)	11 (22)
10 – 13Yr	10(36)	3 (14)	13 (26)
Total	28 (56)	22 (44)	50 (100)

Table – 2: Age group and mean CD4 count

Age group	Number (%)	Mean CD4 count ± SD
0 – 5Yr	11 (22)	635 ± 11.49
5 – 7Yr	15 (30)	428 ± 9.61
7 – 10Yr	11 (22)	213 ± 8.13
10 – 13 Yr	13 (26)	209 ± 5.94
Total	50 (100)	--

Table – 3: Gender wise CD4 count of HIV infected children

Gender	Number	Mean CD4 count ± SD
Male	28 (56%)	340 ± 8.31
Female	22 (44%)	488 ± 9.63

Table – 4: Frequency of various symptoms and sign in HIV infected children

Symptoms and sign	Percentage
Fever	52
Recurrent / Chronic diarrhea	7
Cough	40
Weight loss	32
Skin lesions	15
Lymphadenopathy	17
Hepatomegaly	7
Hepatosplenomegaly	3
Anemia	45
Recurrent/persistentbacterialpeneumonia	10
CNS involvement	8

Table – 5: Opportunistic infections in HIV infected children

Opportunistic infections	Percentage
Pulmonary tuberculosis	26%
Abdominal Tuberculosis	2%
Tubercular meningitis	8%
Oral candidiasis	10%
Pneumocystis carinii pneumonia	8%
Herpes Zoster	2%

Table – 6: Correlation of CD4 count with opportunistic infection

Opportunistic infections	Number (%)	Mean CD4 count ± SD
Abdominal TB	1 (2%)	348
Pulmonary TB	13 (26%)	267 ± 5.37
Oral candidiasis	5 (10%)	364.8 ± 6.5
Tubercular meningitis	4 (8%)	319 ± 3.36
Pneumocystis Jirovecii pneumonia	4 (8%)	261.25 ± 10.8
Herpes zoster	1 (2%)	613

Table – 7: Correlation of opportunistic infections with immunological category

Opportunistic infections	No evidence of suppression	Evidence of moderate suppression	Severe suppression	Total
Abdominal TB	0	1 (100%)	0	1
Pulmonary TB	0	3 (20%)	10 (80%)	13
Oral candidiasis	0	2 (40%)	3 (60%)	5
Tubercular meningitis	0	2 (50%)	2 (50%)	4
PCP	0	0	4 (100%)	4
Herpes Zoster	0	1 (100%)	0	1

Table – 8: Correlation of CD4 count with WHO clinical stages

WHO clinical stage	Number	Mean CD4 count ± SD
I	4	1093 ± 10.73
II	3	611±8.85
III	27	338.5 ± 5.70
IV	16	307 ± 6.09

Table – 9: Correlation of WHO clinical stages with immunological category

WHO clinical stage	No evidence of suppression (stage1)	Evidence of moderate suppression (stage 2)	Severe suppression (stage 3)
I	5 (100%)	00	00
II	3 (100%)	00	00
III	1 (4%)	13 (46%)	14 (50%)
IV	00	4 (29%)	10 (71%)

Discussion

Table-1 shows, out of 50 cases in the study majority of children were in the age group of 4 to 7 years. The mean age of presentation was 7.12yrs. Shah et al reported mean age of presentation of 4.7 years and study conducted by Ramesh R Pol reported mean age of 5.75 years and most of the children presented late with WHO clinical stage 3 (56%) and 4 (30%). In the present study, 28 (56%) were males and 22 (44%) were females. Male to female ratio was 1:0.78. Similar male predominance was noted in other studies like Agarwal et al[4], Shah et al[5] and Sehgal et al[6].

Table-2 shows that as age advances CD4 count decreases. As the age advances severity of immune suppression increases and hence the CD4 count decreases, however the statistical significance is not found using analysis of variance, [F = 1.01, p>0.05].

Table-3 shows female mean CD4 count was 488 and for male it is 340, which is lower but the difference was statistically not significant. [t = 0.67, p > 0.05]. Similar result had been observed by Agarwal et al[4].

Table-4 shows the most common presentation in the present study is fever (52%), Anemia (45%), followed by, cough (40%), weight loss (32%), skin lesions (15%) in descending order, least being hepatosplenomegaly (3%). Higher incidence of anaemia, fever, cough and weight loss had also been observed in studies by Shah et al[5] and Agarwal et al[4].

Table-5 shows, Tuberculosis (pulmonary and extrapulmonary) in 26% which is in accordance with

study conducted by Ramesh. R Pol. (38.3%), Oral candidiasis in 12%, Pneumocystis carinii pneumoria in 8%, Molluscum Contagiosum in 6% & Herpes Zoster in 7.14% which is in accordance with study conducted by Shah et al[5].

Table-6 shows, opportunistic infections in 56% of children. Pulmonary TB was the most common opportunistic infection (26%) followed by oral candidasis (10%), Pneumocystis Jirovecii pneumonia was seen in 8% of children. Pulmonary TB was seen at mean CD4 count of 267±5.37, Oral candidiasis was seen at mean CD4 count of 364.8±6.5, Pneumocystis Jirovecii pneumonia was seen at mean CD4 count of 261.25±10.8, tubercular meningitis was seen at mean CD4 count of 319±3.36. Similar findings were observed in studies by Ramesh R Pol[7].

Table-7 shows, all children with Pneumocystis jirovecii pneumonia, 80% of children with pulmonary TB and 60% of children with oral candidiasis had evidence of severe immune suppression. Tubercular meningitis occurred with equal incidence (50%) with evidence of moderate suppression & severe suppression. Hence it is concluded that opportunistic infections increases with increasing immunological category.

Table-8 shows that children with WHO clinical stage I had mean CD4 count of 1093 ± 10.73 (8%), children with WHO clinical stage II had mean CD4 count of 611 ± 8.85 (6%), children with WHO clinical stage III had mean CD4 Count of 338.5 ± 5.70 (56%), children with WHO clinical stage IV had mean CD4 count of 307 ± 6.09 (30%), which is in accordance with study conducted by Agarwal et al[4]. WHO clinical stages correlated with CD4 count showed, as WHO clinical stage increases CD4 count decreases. This was statistically also highly significant. $F = 18.44$, degrees of freedom = (3,46) and $p < 0.01$.

Table-9 shows, children with WHO clinical stage I and II had no evidence of immune suppression, children with stage III had evidence of moderate immune suppression in 46%, severe immune suppression in 50% of cases. Children with stage IV had evidence of moderate immune suppression in 29%, severe immune suppression in 71% of cases. The severity of immune suppression increases with increasing WHO clinical stages.

Conclusion

Tuberculosis and oral candidiasis are the most common opportunistic infections in HIV infected children. Children with lower mean CD4 counts more likely to suffer from PCP and Pulmonary tuberculosis than other types of opportunistic infections. Perinatal transmission is the most common mode of acquiring HIV in Pediatric age group. The knowledge that mixed feeding is associated with greater risk of vertical transmission compared to exclusive breast-feeding needs consistent emphasis in daily practice[8]. Moreover, new strategies where ARV drugs were given to the mother and breast-feeding the infant have shown encouraging results in reducing breast feeding related HIV transmission[9]. As WHO clinical stage of HIV increases CD4 count decreases. CD4 count decreases as the grade of PEM increases. Vaccination of a baby born to a HIV positive mother but with an indeterminate status of own should be as per the normal schedule[10]. Besides ART, early diagnosis and prompt management of opportunistic infections still remains the cornerstone of HIV management and will definitely decreases the morbidity and mortality and increase the quality of life of those affected children.

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