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CLINICAL PROFILE OF OPPORTUNISTIC INFECTIONS IN HIV INFECTED CHILDREN AND ITS CORRELATION WITH CD4 COUNT: A MULTICENTRIC STUDY FROM EASTERN INDIA

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ABSTRACT

Background & objective: India harbors world's third highest number of HIV infected people. Children usually have higher viral load, weaker immune system, variable latency period, fewer opportunistic infections & fewer medicines approved for management. Knowledge of the clinical profile in HIV infected children will help in better understanding of the disease and management. Hence the present study was done with an objective to study the clinical presentation, opportunistic infections, WHO clinical stage, nutritional status and its correlation with CD4 count.

Method: 75 children below 14 years of age and seropositive for HIV were included in this Detailed clinical evaluation and relevant laboratory investigations were done as per the Performa. Based on clinical presentations, the children were categorized into WHO clinical stages. Weight for age was used to grade the PEM. They were further classified based on CD4 count values in accordance with WHO classification of immunodeficiency.

Results: In the study 30% of children were in the age group of 4 to 7 years. The mean age of presentation was 7.12 years. 56% of children presented with WHO clinical stage III & 30% with stage IV at first visit. Female children had higher mean CD4 count (488 cells/cmm) than male children (340 cells/cmm). Vertical transmission was the predominant mode of transmission (92%). Anemia (48%), fever (42%) and cough (34%) were common symptoms. Pulmonary tuberculosis (28%) was the most common opportunistic infection seen at mean CD4 count of 267 ± 5.37, Oral candidiasis at CD4 count of 364.8±6.5, Pneumocystis jirovecii pneumonia at CD4 count of 261.25±0.8. Children with opportunistic infection had lesser CD4 count. With the increasing grades of WHO clinical stage there was CD4 count decline, the severity of immune suppression increases with increasing WHO clinical stages. The severity of PEM increases when CD4 count decreases.

Interpretation & Conclusion: The manifestations of HIV infection in children are protean and mimic a number of other illnesses. Perinatal transmission is the common mode of acquiring HIV in pediatric age group. Anaemia, fever & cough were the common presenting clinical features. Tuberculosis is the most common opportunistic infection in HIV infected children. As WHO clinical stage and grade of PEM increases CD4 count decreases. CD4 count is a reliable marker of disease progression in HIV infected children.

KEYWORDS : HIV, CD4 count, PEM, Opportunistic infection

INTRODUCTION:

Paediatric HIV is a major world health problem, which is progressing at an alarming rate. HIV in India has now existed over three decades. India has the 3rd largest no. of people living with HIV/AIDS. Based on HIV sentinel surveillance 2008-09 it is estimated that 23.9 lakh people are infected with HIV in India out of which 4.4% are children. However half of these children are undiagnosed before their 2nd birthday.[1] 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.[2,3,4].

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 & 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 %.[5]The determination of CD4 count became the standard measure of immunodeficiency in HIV infected patients. The relative ease of CD4 cell monitoring also led to its advocacy in treatment guidelines for determining when 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. The objectives of this study were to assess the incidence opportunistic infections in HIV infected children less than 14 years of age, to study the clinical profile of opportunistic infections in HIV infected children under 14 years of age and to correlate opportunistic infections with CD4 count.

MATERIALS AND METHODS:

STUDY SETTING: Department of paediatrics, Kalinga institute of medical science, Bhubaneswar and MKCG Medical College, Berhampur

STUDY DESIGN: Prospective observational study.
STUDY PERIOD: October 2014 to September 2016.

Ethical committee clearance was taken before starting this observational study from the ethical committee of MKCG Medical college and hospital, berhampur. HIV seropositive cases admitted to the indoor, department of paediatrics in both the hospitals.

INCLUSION CRITERIA: All children seropositive for HIV/DBS positive/ whole blood PCR positive upto 14 years of age are included in the study.

EXCLUSION CRITERIA: Patients with negative laboratory test for HIV are excluded from the study.

SAMPLE SIZE: The number of cases included in this study based on the above criteria was 75.

INVESTIGATIONS DONE FOR DIAGNOSIS OF OPSI: Monoclonal Antibody Panels, Sample Analyse, Oral swabs ,Stool, Sputum, Urine , Cerebrospinal fluid (CSF), Blood, Serology.

STATISTICAL MEASURES: Statistical analysis were done by SPSS Software version 24. Rates and proportions were calculated with 95% confidence intervals. The proportions were compared using students *T*-test. Level of significance was set at $P < 0.05$.

RESULTS:

- The study was conducted from October 2014 to September 2016.

75 children, positive for HIV were studied. Among them 42 were males and 33 were females. Male to female ratio is 1:0.78. Mean age of presentation is 7.12 years. Mean age of presentation in male children is 7.91 ± 3.29. Mean age of presentation in female children is 5.18 ± 2.95. The Mean age of presentation in male children was higher than female children which is statistically also significant $p < 0.05$, ($t = 3.05$, DF=48). Out of 75 children 54% of children are from rural area, 30% are from urban area, 16% are from urban slum.

- As the age advances severity of immune suppression increases and hence the CD4 count decreases, however the statistical significance was not found using analysis of variance, $F = 1.01$, $p > 0.05$. The study revealed as the age advances the severity of immune suppression increases, highest immune suppression was seen in the age group of 10 to 13 yrs.(table:3) In the study female children had mean CD4 count 488± 9.63, and male children had mean CD4 count 340± 8.31, but the difference is statistically not significant. $t = 0.67$, $p>0.05$.
- Vertical transmission was found to be the predominant mode of transmission in the study, which is 92%, based on maternal seropositivity. 2 cases were transfusion associated and mode of transmission unknown in 8% cases.(Table: 1)
- In the study 38% of the children were breast fed up to 1year 5 months, 30% of the children were breast fed for 2years and above.(table:2)
- The common presentations in the study were anemia (48%) followed by fever (42%) and Cough (34%).(table:4)
- Study showed opportunistic infections in 56% of children. Pulmonary TB is the most common opportunistic infection (26%) followed by oral candidiasis (10%), Pneumocystis Jirovecii pneumonia is seen in 8% of children. Pulmonary TB is seen at mean CD4 count of 267±5.37, Oral candidiasis is seen at mean CD4 count of 364.8±6.5, Pneumocystis Jirovecii pneumonia is seen at mean CD4 count of 261.25±10.8, tubercular meningitis is seen at mean CD4 count of 319±3.36. (table:5,6)
- The study showed 100% of 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:7)
- Study showed children with WHO clinical stage 1& II had no evidence of immune suppression in 100% of cases, 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.

DISCUSSION:

- All children seropositive for HIV at first visit were included in the study. Based on clinical presentations, the children were categorized into various WHO clinical stages. Weight for age was used to grade protein energy malnutrition using IAP classification. They were further classified based on CD4 count values in accordance with WHO classification of immunodeficiency.
- Out of 75 cases in the study majority of children were in the age group of 4 to 7 years. The mean age of presentation was 7.12y. It was similar to previous studies [6]. In the present study, 42(56%) were males and 33(44%) were females. Similar male predominance was noted in other studies[6,7].
- It was observed 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, [$F = 1.01$, $p > 0.05$].
- Female mean CD4 count was 488 and for male it was 340, which was lower but the difference was statistically not significant. [$t = 0.67$, $p > 0.05$]. Similar result had been observed[7].
- Out of 75 children majority of children were from rural area, followed by urban area and least from urban slum. Similar incidence had been found with study[8,9].
- In the present study commonest mode of transmission was vertical transmission (92%). Many other studies also reported that vertical transmission was predominant route of transmission during first 14 years of life[6,7,8]
- Study showed 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[7] .WHO clinical stages correlated with CD4 count. As WHO clinical stage increases CD4 count decreases. This was statistically also highly significant.
- The most common presentation in the present study is Anemia (48%), followed by fever (42%), cough (34%), weight loss (25%), skin lesions (23%) in descending order least being hepatosplenomegaly (3%). Higher incidence of anaemia, fever, cough and weight loss had also been observed in studies before[6,7].
- The study showed Tuberculosis (pulmonary and extrapulmonary) in 26%, Oral candidiasis in 12%, Pneumocystis carinii pneumonia in 8% , Molluscum Contagiosum in 6% & Herpes zoster in 7.14% which is in accordance with study conducted by Shah et al[6,10].
- Study showed opportunistic infections in 56% of children. Pulmonary TB was the most common opportunistic infection (26%) followed by oral candidiasis (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[8,11,12].
- The study showed all of 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[8,12,13].
- Study showed children with WHO clinical stage 1& II had no evidence of immune suppression cases, 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[14,15].

CONCLUSION: There was high incidence of HIV cases in our study area because of the large number of migratory labour population residing in the area whose livelihood was maintained by daily earning duty.

- Tuberculosis & oral candidiasis were the most common opportunistic infections in HIV infected children.
- With lower mean CD4 counts more likely to suffer from PCP and Pulmonary tuberculosis than other types of opportunistic infections.
- Perinatal transmission was the most common mode of acquiring HIV in Pediatric age group.
- As WHO clinical stage of HIV increases CD4 count decreases.
- CD4 count decreases as the grade of PEM increases.
- Besides ART, early diagnosis and prompt management of opportunistic infections is the cornerstone of HIV management.

TABLES:

Table : 1- Mode of transmission

Mode of transmission	Number of children	%
Mother to child transmission	69	92
Blood transfusion	02	03
Unknown	04	05
Total	75	100

Table : 2- Breastfeeding status of children

Number of months	No of children	Percentage
0-6m	05	06
6m – 1y	15	20
1y – 1.5y	28	37
1.5 – 2y	05	07
2yr and above	22	30
Total	75	100

Table : 3- Age and WHO classification of immunodeficiency

Age group	No evidence of suppression	Evidence of moderate suppression	Severe suppression	Total
0 - 5y	03	08	06	17
5y - 7y	06	06	11	23
7y - 10y	04	05	07	16
10y - 13y	00	09	10	19
Total	13	28	34	75

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

Symptoms and sign	Percentage
Fever	42
Recurrent /Chronic diarrheoa	7
Cough	34
Weight loss	25
Skin lesions	23
Lymphadenopathy	17
Hepatomegaly	7
Hepatosplenomegaly	3
Anemia	48
Recurrent /persistent bacterial pneumonia	10
CNS involvement	9

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 infections

Opportunistic infections	Number (%)	MeanCD4 count± SD
Abdominal TB	02(2%)	348
Pulmonary TB	18(26%)	267±5.37
Oral candidiasis	08(10%)	364.8±6.5
Tubercular meningitis	06(8%)	319±3.36
Pneumocystis Jirovecii pneumonia	06(8%)	261.25±10.8
Herpes zoster	02(2%)	613
Total	42(56%)	

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	2(100%)	0	2
Pulmonary TB	0	4(20%)	15(80%)	19
Oral candidiasis	0	3(40%)	5(60%)	8
Tubercular meningitis	0	3(50%)	3(50%)	6
PCP	0	0	6(100%)	6
Herpes Zoster	0	2(100%)	0	2

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