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Clinical Spectrum of Presentation in HIV Infected Children with Correlation to CD4 Percentage

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ABSTRACT

India harbors world's second highest number of HIV infected people. HIV infected children differ from HIV infected adults. 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 its 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 to CD4%. 50 children seropositive for HIV were studied. 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% values in accordance with WHO classification of immunodeficiency. 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 IV at first visit. Female children had higher mean CD4 %(16.85%) than male children (15.14%). Vertical transmission was the predominant mode of transmission (92%). Pallor (48%), fever (42%), cough (34%) were common symptoms. Pulmonary Tuberculosis (28%) was the most common opportunistic infection seen at mean CD4% of 11.89 $\pm$ 5.37. Oral candidiasis at CD4% of 15.2 $\pm$ 6.5, Pneumcystitis carnii pneumonia at CD4% of 15.2 $\pm$ 10.8 were seen. Children with opportunistic infection had lesser CD4%. With the increasing grades of WHO clinical stage there was CD4% decline, the severity of immune suppression increases with increasing WHO clinical stages. The severity of PEM increases when CD4% decreases. 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. Anemia, 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% decreases. CD4% is a reliable marker of disease progression in HIV infected children.

Keywords: HIV, CD4%, WHO clinical stage, PEM, Opportunistic infection.

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INTRODUCTION

Pediatric HIV is a major world health problem, which is progressing at an alarming rate. HIV in India has now been there over three decades. By this time, India now has the dubious distinction of being the country with second highest number of people living with HIV/AIDS. As per UNAIDS around 5.7 million people in India are affected with AIDS. [1] The estimated number of children living with HIV/AIDS in India is 202,000 as per UNAIDS. However half of these children die undiagnosed before their 2nd birthday. [1] The predominant mode of transmission of HIV in children is vertical i.e., it is acquired through intrauterine, intrapartum or through breast feeding from an HIV infected mother. Other routes such as sexual transmission and blood transfusion are not as common.[2] Since children have a biologically weaker immune system they are more prone to faster disease progression and most of the children become symptomatic within 1-2 years of acquisition of HIV infection and majority if untreated die by 76-90 months of age.[3] 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 medicines approved for the management, different spectrum of clinical manifestations, diagnostic differences, and patterns of disease progression.[4]

Clinical spectrum of presentation of HIV in children: [6, 7]

The clinical presentation of HIV commonly seen in children is hepatosplenomegaly, generalized lymphadenopathy and failure to thrive. Common opportunistic infections are tuberculosis (TB), herpes zoster and simplex, recurrent pneumonias, chronic diarrhea and oral thrush. PCP pneumonia is common in infants. Organ dysfunctions due to HIV are seen in older children and include HIV encephalopathy, HIV cardiomyopathy, hematological problems and proteinuria. Thus, untreated HIV in children is associated with high morbidity and mortality. Currently, it is the latest world health organization (WHO) clinical staging of HIV/AIDS for children, which is preferred than the earlier centre for disease control (CDC) classification, especially in resource limited regions.[8] Soon after HIV was found to be 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. [5]

With the increased availability of equipment to perform CD4counts 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 (OIS). This despite the fact that CD4 count does not always correlate with functional immunity. Some patients with normal CD4 counts do not seem unduly susceptible to OIS. This study also attempts to correlate CD4 count with opportunistic infections. Despite the magnitude of the problem there is paucity of data on various issues in pediatric HIV infection from south India. The present study is done to know pediatric aspects of HIV infection and clinical spectrum and their immunological staging.

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MATERIAL AND METHODS

This study was a prospective hospital based study conducted over a period of 1yr at Vijayanagar Institute of Medical Sciences; Bellary. All children Seropositive for HIV more than 18 months of age up to 13 years were included in the study. Neonates and Infants <18 months and children >13yrs were excluded from the study. 50 cases of HIV positive patients were recruited from all treating units in the hospital and a detailed clinical evaluation (history and examination) and relevant laboratory investigations was done for all subjects as per the proforma. Complete Hemogram, ELISA (Tridot,Coombs and Capillus) test for HIV and CD4% using age specified charts were done for all patients. Optional investigations like Sputum for AFB/Gastric lavage for AFB, Chest X ray, Mantoux test, Blood Culture and sensitivity ,CSF analysis and Culture sensitivity, Stool routine and Culture sensitivity ,Ultrasonography (USG) abdomen/chest/cranium, Fine needle aspiration cytology of lymph node , CT scan and others were done depending on the clinical presentation.

Based on clinical presentations, the children were categorized into various WHO clinical stages. Weight for age was used to grade them (IAP classification) for protein energy malnutrition. They were further classified based on CD4% values in accordance with WHO classification of immunodeficiency. CD4 cell count varies with age so CD4% was used to define immunologic category.

RESULTS

The study was conducted for 1year; Fifty children, positive for HIV were studied. The results are as follows.

Table 1: Age and Gender wise classification of Children

Age group	Male (%)	Female (%)	Total (%)
18 m - 4 y	4(14)	7(31)	11(22)
4y - 7y	6(21)	9(41)	15(30)
7y - 10y	8(29)	3(14)	11(22)
10y - 13y	10(36)	3(14)	13(26)
Total	28(56)	22(44)	50

Total no of children included in the study were 50. Among them 28 were males and 22 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 $\pm$ 3.29. Mean age of presentation in female children is 5.18 $\pm$ 2.95. The Mean age of presentation in male children is higher than female children which is statistically also significant $p < 0.05$, ($t = 3.05$, DF=48).

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Table 2: **Age and WHO classification of immunodeficiency.**

Age group	No evidence of suppression	Evidence of moderate suppression	Severe suppression	Total
18m - 4y	02(18%)	05(46%)	04(36%)	11
4y - 7y	04(27%)	04(27%)	07(47%)	15
7y - 10y	03(27%)	03(27%)	05(46%)	11
10y - 13y	00	06(46%)	07(54%)	13
Total	09(18%)	18(36%)	23(46%)	50

The study shows as the age advances the severity of immune suppression increases, highest immune suppression is seen in the age group of 10 to 13 yrs.

Table 3: Frequency of various symptoms and sign in HIV infected children

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

The common presentation in the study was, Anemia (48%), fever (42%) followed by Cough (34%).

Table 4: Opportunistic infections in HIV infected children

Opportunistic infections	Percentage
Pulmonary Tuberculosis	28%
Abdominal Tuberculosis	2%
Tubercular meningitis	8%
Oral candidiasis	12%
Pneumocystis carinii pneumonia	8%
Molluscum contagiosum	4%
Herpes Zoster	6%

The most common opportunistic infection in the present study is pulmonary tuberculosis (28%) & oral candidiasis (12%)

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Table 5: **Correlation of CD4% with opportunistic infections**

Opportunistic infections	Number (%)	MeanCD4% ± SD
Abdominal TB	01(2%)	16
Pulmonary TB	07(14%)	11.89 ± 5.37
Oral candidiasis	06(12%)	15.2 ± 6.5
Tubercular meningitis	03(6%)	9.03 ± 3.36
Pneumocystis carnii pneumonia	03(6%)	15.2 ± 10.8
Herpes zoster	01(2%)	26.4
Total	21(42%)	

Study showed opportunistic infections in 42% of children. Pulmonary TB is the most common opportunistic infection (14%) followed by oral candidiasis(12%), Pneumocystis carnii pneumonia is seen in 6% of children. Pulmonary TB is seen at mean CD4% of 11.89 +_ 5.37, Oral candidiasis is seen at mean CD4% of 15.2 ± 6.5, Pneumcystis carnii pneumonia is seen at mean CD4% of 15.2 ± 10.8, Tubercular meningitis is seen at mean CD4% of 9.03 +- 3.36.

Table 6: Correlation of opportunistic infections with immunological category

Opportunistic infections	No evidence of suppression	Evidence of moderate suppression	Severe suppression	Total
Abdominal TB	00	02(100%)	00	02
Pulmonary TB	00	01(20%)	04(80%)	05
Oral candidiasis	00	03(50%)	03(50%)	06
Tubercular meningitis	00	03(50%)	03(50%)	06
Pneumocystis carnii pneumonia	00	00	01(100%)	01
Herpes zoster	01(33%)	02(67%)	00	03

The study showed 100% of children with pneumocystis carnii pneumonia, 80% of children with pulmonary tuberculosis had evidence of severe immune suppression. Oral candidiasis and tubercular meningitides occurred with equal incidence (50%) with evidence of moderate suppression & severe suppression. hence it is concluded that increasing immunological category.

Table 7: Comparison of mean CD4% between children with and without opportunistic infection.

Category	Number	Mean CD4% ± SD
Children with opportunistic infection	21	13.78 ± 6.77
Children without opportunistic infection	29	17.41 ± 9.95

Children with opportunistic infection has mean CD4% 13.78 and children without opportunistic infection has mean CD4% 17.41. Comparison shows the children with opportunistic infection have lesser CD4%. But the difference is not statistically significant = 1.45, $p > 0.05$.

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Table 8: Correlation of CD4% with WHO clinical stages

WHO clinical stage	Number	Mean CD4% ± Standard deviation
I	04	34.43 ± 10.73
II	03	27.47 ± 1.85
III	28	14.15 ± 5.70
IV	15	11.89 ± 6.09

The study showed with the increasing grades of WHO clinical stage there was CD4% decline. The mean CD4% in WHO clinical stage I is 34.43 ± 10.73. The mean CD4% in WHO clinical stage II is 27.47 ± 1.85. The mean CD4% in WHO clinical stage III is 14.15 ± 5.70. The mean CD4% in WHO clinical stage IV is11.89 ± 6.09. This is statistically also significant. $F = 18.44$, degrees of freedom = (3, 46) and $p < 0.01$.

Table 9: Correlation of WHO clinical stages with immunological Category

WHO clinical stages	No evidence of Suppression (stage 1)	Evidence of moderate suppression (stage 2)	Severe suppression (Stage 3)
I	05(100%)	00	00
II	03(100%)	00	00
III	01(4%)	13(46%)	14(50%)
IV	00	04(29%)	10(71%)

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.

Table 10: Correlation of nutritional status with immunological category

Nutritional status	No evidence of suppression (stage 1)	Evidence of moderate suppression (stage 2)	Severe suppression (stage 3)	Total
Normal	05(56%)	02(22%)	02(22%)	09(100%)
Grade I PEM	01(16%)	02(34%)	03(50%)	06(100%)
Grade II PEM	02(22%)	02(22%)	05(56%)	09(100%)
Grade III PEM	00	04(44%)	05(56%)	09(100%)
Grade IV PEM	00	08(47%)	09(53%)	17(100%)

The study showed 50% of children with Grade I PEM, 56% of children with Grade II PEM, 56% of children with Grade III of PEM, 53% of children with Grade of IV PEM,had evidence of severe immune suppression. Nutritional status in children in HIV infected children depends not only on immunosuppression but also on various factors like recurrent infections, health status of parents,child rearing pactices, social factors and emotional factors. Hence severe suppression is seen in all grades

DISCUSSION

The present study was conducted in the department of Pediatrics, VIMS, Bellary. 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% values in accordance with WHO classification of immunodeficiency. CD4 cell count varies with age, so CD4% was used to define immunologic category.

Out of 50 cases in the study, 15(30%) of children are in the age group of 4 to 7 years. The mean age of presentation is 7.12y**.** Shah et al [10] 2 reported mean age of presentation of 4.7 years & Study conducted by Ramesh.R Pol [11] reported mean age of 5.75 years.

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 (56%) & 4 (30%) .In the present study, 28(56%) were males and 22(44%) were females. Male to female ratio is 1:0.75. In the present study commonest mode of transmission is vertical transmission (92%) , which is comparable to Agarwal et al [9] (94 %), Ramesh.R Pol [11] (94.37%) study.Gender wise CD4% of HIV infected children were compared and found that female mean CD4% was 16.85 and for male it was 15.14 which is slightly less but the difference is statistically not significant. $t = 0.67$, $p>0.05$.Study showed that children with WHO clinical stage I, had mean CD4% of 34.43 ± 10.73(8%), children with WHO clinical stage II, had mean CD4% of 27.47 ± 1.85 (6%), children with WHO clinical stage III, had mean CD4% of 14.15 ± 5.70 (56%), children with WHO clinical stage IV, had mean CD4% 11.89 ± 6.09 (30%) which is in accordance with study conducted by Agarwal et al [9].WHO clinical stages correlated with CD4%. As WHO clinical stage increases CD4% decreases. This is statistically also highly significant. $F = 18.44$, degrees of freedom = (3, 46) and $p < 0.01$. Nutritional status and CD4% also correlated. As nutritional status indicated by grades increases the CD4% decreases. However this is not statistically significant. $F = 1.61$, D.F = (4, 45), $P > 0.189$ .Clinical profile of HIV infected children The most common presentation in the present study is Anaemia (48%), fever (42%) 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.

The study showed Tuberculosis(pulmonary and extrapulmonary) in 38% which is in accordance with study conducted by Ramesh.R Pol.(38.3%), 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 Tuberculosis in HIV infected children The study showed Pulmonary Tuberculosis in 28% which is in accordance with study conducted by Aggarwal et al (13.8%), Extrapulmonary Tuberculosis is seen in 10% which is in accordance with study conducted by Shah et al (10%).

CONCLUSION

The manifestations of HIV infection in children are protean and mimic a number of other illnesses. A proper history, detailed clinical examination, high index of suspicion would therefore help in making early diagnosis and a management plan. Perinatal transmission is the most common mode of acquiring HIV in Pediatric age group. Anaemia , fever & Cough were

the common presenting clinical features. Tuberculosis & oral candidiasis are the most common opportunistic infections in HIV infected children. As WHO clinical stage increases, CD4% decreases. CD4% decreases as the grade of PEM increases.CD4% is a reliable marker of disease progression in HIV infected children.

REFERENCES

[1] Joint United Nations program on HIV/AIDS (UNAIDS)/WHO.AIDS epidemic update 2006. Available from URL: http://www.unaids.org/en/Publications/default.asp. Accessed October 1, 2008.

[2] Joint United Nations Program on HIV/AIDS (UNAIDS) /WHO.AIDS epidemic update. 2004.Available from URL: http://www.unaids.org/en/Publications/default.asp. Accessed October 11,2008.

[3] Shah I. JK Science 2006; 8 (4): 183-4.

[4] Beauchamp B. Overview of pediatric HIV infection- Florida/Caribbean AIDS education and Training center. HIV care link 2008 ; 9(11)

[5] Dowbenko D, Nakamura G, Fennie C. J Viral 1988; 62(12): 4703-11.

[6] Shah I. J Trop Pediatr 2005; 51(5): 300-3.

[7] Shah I, Prabhu SS, Sumitra V, Shashikiran HS. Indian Pediatr 2005; 42: 146-49.

[8] WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. WHO: Geneva, Switzerland; 2006.

[9] http:/www.who.int/hiv.Accessed October 28, 2008.

[10] Shilpa R, Shah, Milind S, Tullu, Jaishree R. Kamat. Arch Med Res 2005; 36: 24–31.

[11] Pol RR, Shepur TA, Ratageri VH. Indian J Pediatr 2007; 74(12):1071-1078.

[12] Sehgal R, Baveja UK, Chattopadhya D, Chandra J, Lal S. Indian J Pediatr 2005; 72(11):925-30.