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Study of Clinical Profile of HIV Infection in Paediatric Age Group at a Tertiary Care Hospital

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ABSTRACT

Spectrum of clinical manifestations of HIV infection varies in infants and children in different areas of the world. Present study was aimed to study clinical profile of HIV infection in paediatric age group at a tertiary care hospital. Present study was single-center, prospective, observational study, conducted in children between 18 months 14 years of age confirmed to have HIV infection by ELISA/DOT assay according to WHO strategy II and/or III OR children between 0 to 18 months born to seropositive mothers. Total 120 HIV seropositive pediatric patients attending ART OPD and IPD were studied. Maximum children were between 18 months 4 years (45%) were boys (58.3%) delivered vaginally (70.8%) had vertical Mode of Transmission (97.5%) and were completely immunized for age (64.2%). Mean age of presentation was 4.67±1.95 years. 118 (98.3%) mothers and 116 (96.7%) fathers were found to be reactive. According to WHO classification system for clinical staging of HIV disease, majority 45 children presented with clinical stage IV (37.5%) followed by stage III (25%) stage I (20.8%) and stage II (16.7%) at time of registration. Majority children had no evidence of immunosuppression (33.3%) followed by children with mild immunosuppression (22.5%) children's with advanced immunosuppression (23.4%) and children with severe immunosuppression (20.8%). Tuberculosis was the most common opportunistic infection followed by chronic diarrhea. Conclusion: Most common symptom was failure to thrive followed by prolonged fever. Majority of children were in WHO clinical Stage 3 and 4. Tuberculosis was most common opportunistic infection.

INTRODUCTION

HIV means Human Immunodeficiency Virus. HIV is virus that causes AIDS (Acquired Immunodeficiency Syndrome) also known as SLIM disease. It is now estimated that half of all new episodes of HIV transmission in children occur during the breastfeeding period, when the majority of HIV positive lactating women may not be receiving the prophylaxis necessary for prevention of mother to child transmission (PMTCT) of HIV^[1,2].

Although the prevalence of HIV infection is low in India but due to large population, India has the third largest number of PLHIV and their estimated number in 2011 was 2.09 million. Children less than 15 years of age accounted for 7% (0.145 million) of all HIV infections^[3]. The proportional contribution of the number of children living with HIV (CLHIV) out of the total PLHIV population was estimated to be 6.3% in 2007 and 7% in 2011^[4].

Understanding the epidemiology of pediatric HIV infection and progression of disease may reveal opportunities to reduce and perhaps eliminate perinatal transmission in resource poor settings; and when Prevention is not possible, identification of infected children will allow appropriate treatment to significantly improve their quality of life. Spectrum of clinical manifestations of HIV infection varies in infants and children in different areas of the world. Knowledge of clinical and epidemiological profile is crucial for clinicians to meet the diagnostic and management challenges presented by HIV infected children in resource poor setting^[5]. Present study was aimed to study clinical profile of HIV infection in paediatric age group at a tertiary care hospital

MATERIAL AND METHODS

Present study was single-center, prospective, observational study, conducted in department of pediatrics, at XXX medical college and hospital, XXX, India. Study duration was of 18 months (from Oct-May 2015-2017). Study approval was obtained from institutional ethical committee.

Inclusion criteria:

- Children between 18 months 14 years of age confirmed to have HIV infection by ELISA/DOT assay according to WHO strategy II and/or III attending ART center
OR
- Children between 0-18 months born to seropositive mothers
- Parents willing to participate in present study

Exclusion criteria:

- HIV positive children in whom consent is not obtained from parents or people who refused to participate
- Children with confirmed HIV above 14 years of age

120 newly diagnosed HIV seropositive consecutive children were enrolled from the ART OPD and admitted in pediatric ward. The study subjects along with their parents were given information about the study by using patient information sheet in a language understood by them. The consent was taken from parents or guardians of the subjects prior including them in to the study. A detailed history including HIV status of the parents and birth history, probable mode of transmission and immunization history were noted. A detailed physical examination was done. Anthropometric assessment with regards to weight, length, height, head circumference and chest circumference was done in all cases. Relevant Laboratory evaluation included complete hemogram, Liver Function Test, Renal Function Test and stool culture. Special investigation Imaging studies and Sputum examination/gastric aspirate for AFB. Absolute CD4 cell count analysis was carried out by flow cytometry Details were recorded regarding suspected mode of transmission, features of immune dysfunction, opportunistic infections, childhood bacterial infections, malnutrition cutaneous manifestations and antiretroviral Therapy. Cases were classified according to world health organization (WHO) clinical staging of HIV/AIDS for children,^[6] as

- Stage I-asymptomatic,
- Stage II-mild symptoms,
- Stage III-moderate symptoms
- Stage IV-severe symptoms with AIDS

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS

Total 120 HIV seropositive pediatric patients attending ART OPD and IPD were studied. Maximum children were between 18 months 4 years (45%) were boys (58.3%) delivered vaginally (70.8%) had vertical Mode of Transmission (97.5%) and were completely immunized for age (64.2%). Mean age of presentation was 4.67 ± 1.95 years. 118 (98.3%) mothers and 116 (96.7%) fathers were found to be reactive. Both children's were orphan whose mother's and father's

Table 1: General characteristics

	No. of patients	Percentage
Age groups (in years)		
≤18 Months	9	7.5
18 Months 4 years	54	45.0
4-6 years	27	22.5
6-10 years	22	18.3
≥10 years	8	6.7
Mean age (Mean±SD)	4.67±1.95	
Gender		
Boys	70	58.3
Girls	50	41.7
Mode of delivery		
Vaginal	85	70.8
LSCS	35	29.2
Suspected mode of transmission		
Vertical	117	97.5
Blood	3	2.5
Immunization status		
Complete	77	64.2
Partial	35	29.2
Unimmunized	8	6.6

Table 2: HIV status of parents

	Mother		Father	
	Frequency	Percentage	Frequency	Percentage
HIV status				
Non-reactive	0	0	0	0
Reactive	118	98.3	118	98.3
Unknown	2	1.7	2	1.7

Table 3: Clinical features

Clinical features	Frequency	Percentage
Symptoms		
Failure to Thrive	99	82.5
Prolonged Fever	88	73.3
Cough	86	71.7
Skin Disease	56	46.7
Chronic Diarrhea	33	27.5
Altered Sensorium	25	20.8
Convulsion	24	20.0
Parotitis	12	10.0
Ear Discharge	10	8.3
Signs		
Pallor	100	83.3
Hepatomegaly	92	76.7
Lymphadenopathy	67	55.8
Splenomegaly	66	55.0
Signs of Dehydration	50	41.7
Oral Thrush/Candidiasis	40	33.3
Signs of Respiratory Distress	38	31.7
Signs of Vitamin Deficiency	26	21.7
Clubbing	13	10.8
Ascites	9	7.5
Oedema	9	7.5
Bleeding Tendency	4	3.3
Icterus	3	2.5

Table 4: Clinical staging (As per WHO)^[34]

Clinical staging	Frequency	Percentage
I	25	20.8
II	20	16.7
III	30	25.0
IV	45	37.5

Table 5: WHO immunological classification for HIV^[34]

HIV associated immunodeficiency	Frequency	Percentage
None or not significant	40	33.3
Mild	27	22.5
Advanced	28	23.4
Severe	25	20.8

Table 6: Nutritional status of children (according to IAP classification)

PEM**	Frequency	Percentage
Normal	5	4.2
Grade I	9	7.5
Grade II	22	18.3
Grade III	41	34.2
Grade IV	43	35.8

Grade I: 71-80% Grade II: 61-70% Grade III: 51-60% Grade IV: <50% of weight for age

Table 7: Opportunistic infections

Opportunistic infections	Frequency	Percentage
Tuberculosis	39	32.5
Diarrhea	33	27.5
Oral thrush	10	8.0
Herpes simplex	6	4.8
HIV Encephalopathy	4	3.2
Pneumocystis carinii	2	1.7
Molluscum contagiosum	1	0.8

Table 8: Laboratory investigations

Investigations	Frequency	Percentage
Hemoglobin		
≤6	8	6.7
6-9	87	72.5
≥9	25	20.5
Platelet count		
Adequate	111	92.5
Low	9	7.5
Total WBC count		
≤4000	2	1.7
4000-11000	118	98.3
≥110000	0	0.0
Sputum for AFB		
Positive	08	25
Negative	24	75
Stool culture		
Negative	12	17.1
Salmonella	20	28.6
Giardia	16	22.9
Crypto sporidium parvum	13	18.5
Campylobacter	9	12.9
CSF studies		
Normal	13	65.0
Tuberculous	3	15.0
Cryptococcal	2	10.0
Pyogenic	2	10.0

Table 9: Radiological investigations

Investigations	Findings	Frequency	Percentage
Chest X Ray	Normal	33	27.5
	Pneumonia	53	44.2
	Pleural effusion	10	8.3
	Miliary tuberculosis	9	7.5
	Consolidation	13	10.8
	Pneumocystis carinii	2	1.7
Abdominal USG	Normal	89	74.2
	Ascites	1	0.8
	Hepatosplenomegaly	30	25.0
	Normal	114	95.0
CT Scan	Cerebral and cerebellar atrophy with mild communicating hydrocephalus	3	2.5
	Basal exudate with meningeal		
enhancement	2	1.7	
oedema (Tuberculoma)	Ring enhancing lesion with cerebral		
	1	0.8	

serostatus was unknown. Majority (82.5%) had failure to thrive as main complaint followed by prolonged fever (73.3%) cough (71.7%) skin disease (46.7%) chronic diarrhea (27.5%) altered sensorium (20.8%) and convulsion (20%). Pallor (83.3%) was the most common examination finding followed by hepatomegaly (76.7%) lymphadenopathy (55.8%) splenomegaly (55%) signs of dehydration (41.7%) oral thrush/candidiasis (33.3%) signs of respiratory distress (31.7%) and signs of vitamin deficiency (21.7%). According to WHO classification system for clinical staging of HIV disease, majority 45 children presented with clinical stage IV (37.5%) followed by stage III (25%) stage I (20.8%) and stage II (16.7%) at time of registration. Majority children had no evidence of immunosuppression (33.3%) followed by children with

mild immunosuppression (22.5%) children's with advanced immunosuppression (23.4%) and children with severe immunosuppression (20.8%). As per IAP Classification, out of the 120 cases studied, 115 cases were found to have PEM. Maximum were 35.8% in Grade IV, followed by 34.2% in Grade III, 18.3 % in Grade II and 7.5% in Grade I.

Tuberculosis was the most common opportunistic infection followed by chronic diarrhea. Other opportunistic infections were oral thrush, Herpes simplex, pneumocystis carinii, diarrhea tuberculosis. Majority children were had anemia (76.7%) had adequate platelet count (92.5%) had normal WBC count (98.3%) were sputum negative (75%). Out of 70 children, stool culture was found positive for salmonella (28.6%) giardia (22.9%) cryptosporidium

parvum (18.5%) and campylobacter (12.9%). CSF Studies was done amongst 20 children, 15% were found positive for tuberculous organism, 10% for cryptococcus and 10% for pyogenic organism.

Chest X Ray picture suggests pneumonia (44.2%) consolidation (10.8%) pleural effusion (8.3%) miliary picture (7.5%) and pneumocystis carinii (1.7%). Abdominal USG reveals hepatosplenomegaly (25%) and ascites (0.8%). CT scan findings suggests 2.5% had cerebral and cerebellar atrophy with mild communicating hydrocephalus, (1.7%) basal exudate with meningeal enhancement and (0.8%) ring enhancing lesion with cerebral oedema (Tuberculoma).

DISCUSSION

The increase in pediatric HIV infection has had a substantial impact on childhood mortality both in industrialized countries and developing countries^[7,8]. There are several barriers to efficient management delayed infant diagnosis, lack of appropriate pediatric formulations, lack of skilled health personnel, etc. Poorly developed immunity allows greater dissemination throughout various organs. There is an increased frequency of malnutrition and infections that may be more persistent, severe and less responsive to treatment.

In the present study mean age of presentation was 4.67 years similar to a study Madhivanam *et al.*^[9] and Shah *et al.*^[10] with mean age of presentation was 48 month. Most commonly children affected in age group were between 18 months–4 years. Male children's were more infected than female children's Male: Female ratio was 1.4:1. Male predominance was seen in studies by Purnima Madhivanam *et al.*^[9] Shah *et al.*^[10] and Singh *et al.*^[11]. The age distribution of our cohort reflects both the natural progression of HIV in children and the difficulties inherent in early diagnosis of children in resource limited settings. The recent implementation of virological diagnostic testing in postnatal and pediatric clinics should improve the ability to identify HIV-infected infant's earlier in life and screen them for initiation of ART. It is likely that a majority of younger infected children die prior to diagnosis from illnesses not recognized as HIV-related e.g. gastroenteritis, pneumonia and that this leads to under representation of this age group.

In present study, 98.3% mothers and 98.3% fathers were found to be reactive contrary to findings of a study by Chauhan *et al.*^[12] where 66% of children's both parents were HIV infected and in 17.3% cases either parent was infected. The primary route of infection in the pediatric population is vertical transmission, accounting for almost all new cases. The highest percentage of HIV-infected children acquire the virus intrapartum. The mechanism of transmission

appears to be exposure to infected blood and cervicovaginal secretions in the birth canal, where HIV is found in high titers during late gestation and delivery. In present study, most common mode of transmission to children was vertical transmission (97.5%) similar to other studies by Rashid *et al.*^[13] Purnima Madhivanam *et al.*^[9] and Shah *et al.*^[10].

In present study, most common symptom was failure to thrive (82.5%) followed by prolonged fever (73.3%) similar to other studies by Rakesh *et al.*^[14] and Sharma *et al.*^[15] In present study, pallor (83.3%) was the most common physical finding followed by hepatomegaly similar to study by Subbaraman *et al.*^[16] In present study, majority of children's were in WHO clinical Stage III and IV in present study. Similar observations were found in other studies by Lingayat *et al.*^[17] and Verma^[18] In the present study, 33.3% children were found with no evidence of immunosuppression, similar to a study by Kumar *et al.*^[19] which showed 51% had no evidence of immunosuppression. In present study, as per IAP Classification, 95.8% cases were found to have PEM similar to various studies by Shah *et al.*^[10] and Gummadivan *et al.*^[20] Majority, 35.8% were in Grade IV followed by 34.2% in Grade III, 18.3 % in Grade II and 7.5% in Grade I similar to a study by Ramaswamy *et al.*^[21].

Tuberculosis was most common infection, similar to various other studies by Shah *et al.*^[22] Kumarasamy *et al.*^[23] Pol *et al.*^[24] and Abebe *et al.*^[25] Tuberculosis was most common opportunistic infection in India and it can develop at any stage of disease^[26]. Clinical course and pattern of opportunistic infections varies from patient to patient and from country to country. The progression and outcome of HIV/AIDS is influenced by factors such as baseline health and nutritional status, environment, endemic diseases and access to therapy. It is important to understand the presentation of HIV disease in the local context^[27]. Also, the occurrence of various clinical manifestations and opportunistic infections may be skewed as they studied only the patients who were admitted to the hospital and not those followed on an outpatient basis during the study period^[23].

HIV infection is an unpredictable disease in infants and children which involves multiple organ system and is characterized by progressive clinical deterioration and ultimate development of severe immune dysfunction with opportunistic infections and secondary cancers resulting in a chronic and very complex illness. With the advent of effective ARV drugs the disease has changes from a disease of high mortality to a disease of high morbidity. HIV infected infant and children now survive to adolescent and adulthood and the challenges of providing HIV care are evolving into the challenges of providing both acute

and chronic, lifelong care. As MCTC is a major route of acquiring HIV infection in children, emphasis must therefore be laid on PMTCT guidelines, investigations and treatment in pregnant mothers to prevent or reduce risk of HIV transmission to their children. Clinical manifestations and opportunistic infections of HIV infection are variable and mimic a number of other ailments. A high index of suspicion and appropriate investigation may help in early diagnosis. Training of pediatricians should also be organized on this subject for early diagnosis and management of HIV, related illnesses and opportunistic infections. Those children on treatment should be regularly followed up for drug adherence and treatment outcomes

CONCLUSION

Common findings in present study were male gender, children of age group between 18 months 4 years, had vertical transmission, parents were found to be HIV reactive. Most common symptom was failure to thrive followed by prolonged fever. Majority of children were in WHO clinical Stage 3 and 4. Tuberculosis was most common opportunistic infection. Majority of the cases were found to have grade IV PEM. Prevalence of mild to moderate anemia was most common, followed by severe anemia. Therefore it can be concluded that with the rapid and continue spread of HIV pandemic and the increased survival of these victims the opportunistic infections are on a rise. Most of them are life threatening adding to the morbidity in these cases.

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