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Research Article

Clinical profile of human immunodeficiency virus infection in children: an interesting prospective study

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ABSTRACT

Background: HIV infection has become a pandemic affecting both industrialized & developing countries. The increase in pediatric HIV infection has had a substantial impact on childhood mortality both in industrialized countries and developing countries. It is believed that this study will motivate research worker to work for further improvement of the disease, clinical presentation, diagnostic measures and management in already existing health care delivery system in a tertiary care centre in the tribal area and which may lead to even better survival and quality of life for these children. With the above background, the study is taken up to find the clinical profile of HIV infection in pediatric population in the study area.

Methods: The current hospital based prospective study was carried out in the department of pediatrics, Shri V. N. Government Medical College, Yavatmal (Maharashtra), India from 1st January 2011 to 30th June 2012. 108 cases of HIV attending the pediatric OPD and IPD were included in the study. Importance of test was explained to the parents. HIV was diagnosed by using Standard Protocol. All those who were positive by ELISA, confirmed it by repeat test after 3 months. Western blot was not possible due to non availability of kits. Confirmations of all infections were done as per strategies suggested by WHO. Due to non-availability of specific but expensive test like PCR, p24 antigen assay or HIV Culture, children of PPTCT positive mother were tested on follow up after 18 month age to determine whether the transmission was vertical.

Results: Majority (60.18%) cases in this study are below 5 years of age. Maximum cases 33(30.55%) were between 5-10yrs of age and 5 cases (4.62%) were below 18 months. Males 69(63.88%) outnumbered females 39(36.11%) with M: F ratio of 1.76:1. In the present study predominant route of transmission of HIV to the child was by perinatal (vertical) transmission (98.15%). Maximum 64(59.25%) were home delivered cases followed by 29(26.85%) normal hospital delivered and 6(5.55%) LSCS/instrumental delivered cases. In present study 60(55.55%) severe malnutrition (Group III and IV) was the most common examination finding. Of the total 108 cases enrolled in the study, 75 cases had regular follow up for 250 times and 33 cases did not follow up. Majority of follow ups were for respiratory complaints (23.20%) and fever (17.60%). Only 7.20% patients came for follow up were asymptomatic. Most of the follow up were for OI's. In this study, 108 cases of the study group visited 250 times in our hospital. Out of these 90 cases had 212 episodes of OI's and 18 cases had no evidence of OI's.

Conclusions: HIV infection is an unpredictable disease in infants, children and adolescent 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. 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.

Keywords: Opportunistic infection, Pediatric HIV, Clinical profile

INTRODUCTION

HIV means Human Immunodeficiency Virus. HIV is virus that causes AIDS (Acquired Immunodeficiency Syndrome) also known as SLIM disease.

Children of today are the youth of tomorrow. HIV affects this very precious generation and bears grave consequences to our future, our nation, the continent and the world at large. It will adversely impact the health statistics, economic growth and above all the morale of nations.[1]

Since its first description in 1981, AIDS has spread like wild fire to engulf all the continents of the world to assume proportion of a pandemic. Initially children were not identified as the principle victims of the AIDS epidemic. However, with more data becoming available, the gravity of the problem is being better understood and HIV infection in children and adolescents is being recognized as a major issue.[2]

Thirty years have lapsed since its discovery and the disease has dramatically changed the global health scenario. HIV infection has become a pandemic affecting both industrialized & developing countries.[3] The increase in pediatric HIV infection has had a substantial impact on childhood mortality both in industrialized countries and developing countries.[4,5] Though India is a country with low HIV prevalence; it has the third largest number of people living with HIV/AIDS. In 2009, it was estimated that there were 2.39 million people living with HIV in India. Of these, women constitute 36 per cent while children comprised 4.4 per cent. The estimated numbers of children living with HIV was 1,05,000. Of these, 77,044 children were registered in 285 ART (antiretroviral therapy) centres, with 21,343 receiving free ART till August 2010.[6]

As per Shivananda et al, it is important to concentrate on pediatric HIV as it differs from adult HIV regarding epidemiology, mode of transmission, diagnosis, immunology, pathology, clinical spectrum, management and presentation. HIV infection 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.[7]

With the availability of antiretroviral therapy (ART), HIV infection, which was once considered a progressively fatal illness, has now become a chronic treatable condition in children, as in adults. However, the challenges these children are forced to face are far more daunting. The most significant shortcoming in response to pediatric HIV remains the woefully inadequate prevention of mother to child transmission (PMTCT), allowing a large number of children to be born with HIV in the first place, in spite of it being largely preventable.

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 addition, these growing children are left with inescapable challenges of facing not only lifelong adherence with complex treatment regimens, but also enormous psychosocial, mental and neuro-cognitive issues. These unique challenges must be recognized and understood in order to provide appropriate holistic management enabling them to become productive citizens of tomorrow. To address these multi-factorial issues, there is an urgent need for a concerted, sustainable and multipronged national and global response.

It is believed that this study will motivate research worker to work for further improvement of the disease, clinical presentation, diagnostic measures and management in already existing health care delivery system in a tertiary care centre in the tribal area and which may lead to even better survival and quality of life for these children.

With the above background, the study is taken up to find the clinical profile of HIV infection in pediatric population in the study area.

METHODS

The current hospital based prospective study was carried out in the department of pediatrics, Shri V. N. Government Medical College, Yavatmal, Maharashtra, India from 1st January 2011 to 30th June 2012. 108 cases of HIV attending the pediatric OPD and IPD with following inclusion and exclusion criteria were included in the study. Ethical considerations were met through intuitional ethical committee.

Inclusion criteria

- Children up to 12 year of age with reactive ELISA test.
- Presence of at least 2 major and 2 minor signs in absence of known cause of immunodeficiency.
- Infants and children <18 months with clinical suspicion of HIV infection as per WHO criteria for presumptive diagnosis of severe HIV disease in infants and children <18 month of Age.[1-3]

A presumptive diagnosis of severe HIV disease was made if the infant is confirmed HIV antibody positive and diagnosis of any AIDS indicator condition(s) like Pneumocystitis Carinii pneumonia, oesophageal candidiasis, cryptococcal meningitis, cerebral toxoplasmosis, HIV wasting and Kaposi's sarcoma can be made or the infant is symptomatic with two or more of

the following; (1)Oral thrush;(2) Severe pneumonia;(3) Severe sepsis.

Other factors that support the diagnosis of severe HIV disease in an HIV seropositive infant include as following; (1) Recent HIV-related maternal death; or advanced HIV disease in the mother; (2) $CD4^+$ <20%; (3) Confirmation of the diagnosis of HIV infection should be sought as soon as possible.

Exclusion criteria

Children of PPTCT positive mother who after 18 months of age shows negative result after 2 ELISA tests, 3 months apart.

Methodology

Written and informed consent of all parents and care takers was taken before performing the tests and examination. Importance of test was explained to the parents. HIV was diagnosed by using following spots kits. (Standard Protocol); (1) HIV comb (P. mittrs and Co. Pvt. Ltd., New Delhi); (2) Tri-Dot (3) Callipus as rapid screening test and then ELISA was done.

All those who were positive by ELISA, confirmed it by repeat test after 3 months. Western blot was not possible due to non-availability of kits. Confirmations of all infections were done as per strategies suggested by WHO. Due to non-availability of specific but expensive test like PCR, p^{24} antigen assay or HIV Culture, children of PPTCT positive mother were tested on follow up after 18 month age to determine whether the transmission was vertical. Mother and father of HIV positive children were tested to determine whether the transmission was vertical.

All children who were thus confirmed HIV seropositive were included in this study. A detail history, physical examination and investigations were carried out as in all cases and entered in predesigned and pretested proforma. Anthropometric assessment with regards to weight, length, height, head circumference and chest circumference was done in all cases. Relevant Laboratory evaluation was done and diagnosis of different opportunistic infections was also made. The data thus obtained was studied and the observations and results were tabulated and analyzed.

Precautions taken during investigations

Full precautions were taken by using AIDS KIT containing disposable gown, face mask, cap, gloves, goggle, etc.

RESULTS

From Table 1 it is seen that majority (60.18%) cases in this study are below 5 years of age. Maximum cases 33(30.55%) were between 5-10 years of age and 5 cases (4.62%) were below 18 months. Males 69(63.88%) outnumbered females 39 (36.11%) with M: F ratio of 1.76:1.

Maximum 61 (56.48%) patients were from rural area with male predominance and remaining was from urban area (Table 2).

Table 1: Age/sex distribution in HIV.

Age group in months	Male (%)	Female (%)	Total no of cases	Cumulative frequency (%)
<18	3(2.77)	2(1.85)	5(4.62)	4.62
>18-36	20(18.51)	11(10.18)	31(28.70)	33.32
>36-60	19(17.59)	10(9.25)	29(26.85)	60.18
>60-120	21(19.44)	12(11.11)	33(30.55)	90.72
>120	6(5.55)	4(3.70)	10(9.25)	100
Total	69(63.88)	39(36.11)	108(100)	

Table 2: Area distribution in HIV.

Age groups in months	Rural (n=61)			Urban (n=47)		
	Male	Female	Total n=61(%)	Male	Female	Total n=47(%)
<18	2	1	3	1	1	2
>18-36	12	5	17	8	6	14
>36-60	9	6	15	10	4	14
>60-120	13	7	20	8	5	13
>120	4	2	6	2	2	4
Total	40	21	61(56.48)	29	18	47(43.51)

In the present study predominant route of transmission of HIV to the child was by perinatal (vertical) transmission (98.15%) (Table 3).

Table 3: Source of infection.

Mode of transmission	No. of patient	Percentage
Perinatal (vertical)	106	98.15
Blood / blood Product	02	01.85
Others	00	00.00

Table 4 shows, maximum 64 (59.25%) were home delivered cases followed by 29 (26.85%) normal hospital delivered and 6 (5.55%) LSCS/instrumental delivered cases.

Table 4: Mode of delivery.

Mode of delivery		No. of patients
Home delivery		64 (59.25%)
Hospital delivery	Normal	29 (26.85%)
	LSCS/ instrumental	06 (5.55%)
Not known		09 (8.33%)
Total		108

Perinatal transmission was seen in 96 (88.88%) cases who presented below 5 years of age for the first time. Of them, 42 (38.89%) were symptomatic even before 18 months of age (Table 5). Mean age of presentation was 5.5 years. Median age of presentation was 4.8 years and Mode is 3 years.

Table 5: Age of presentation in perinatal transmission.

Age group in months	No. of patients (n=108)	Percentage (%)
<18	42	38.89
>18-36	30	27.77
>36-60	23	21.29
>60-120	09	8.33
>120	04	3.07
Total	108	100

Table 6 shows the symptomatology of paediatric HIV on first presentation. Majority (58.33%) had fever as main complaint followed by cough (45.37%), not gaining weight (41.66%), diarrhoea (39.81%), skin rash (23.15%), ear discharge (19.44%), oral ulcers (13.88%) and parotid swelling (8.33%).

In present study 60 (55.55%) severe malnutrition (Group III and IV) was the most common examination finding followed by pallor 58 (53.70%), respiratory signs 51(47.22%), lymphadenopathy 49 (45.37%), fever 37 (34.26%), skin manifestations 36 (33.33%), hepatosplenomegaly 33 (30.55%), signs of vitamin deficiency 32 (29.63%), hepatomegaly 26 (24.07%), CSOM 24 (22.22%), oral thrush 21 (19.44%), dental caries 19 (17.59%), splenomegaly 9 (8.33%), parotitis 9 (8.33%), clubbing 7 (6.48%), CNS manifestation 6 (5.55%), ascitis 2 (1.85%) and bleeding tendency 1 (0.92%) were the other observed signs (Table 7).

Table 6 : Complaints on first presentation.

Complaints	No of cases (n=108)	Percentage (%)
Fever	63	58.33
Cough	49	45.37
Not gaining weight	45	41.66
Diarrhoea	43	39.81
Skin rash	25	23.15
Ear discharge	21	19.44
Oral ulcers	15	13.88
Parotid swelling	09	08.33
Bleeding tendencies	01	0.92

Table 7: Physical examination (signs).

Signs	No. of cases (n=108)	Percentage (%)
Severe malnutrition (Group III and IV)	60	55.55
Pallor	58	53.70
Respiratory signs	51	46.78
Lymphadenopathy	49	45.37
Fever	37	34.26
Skin manifestations	36	31.48
Hepatosplenomegaly	33	30.55
Signs of vitamin deficiency	32	29.63
Hepatomegaly	26	24.07
CSOM	24	22.22
Oral Thrush	21	19.44
Dental Caries	19	17.59
Splenomegaly	9	8.33
Parotitis	9	8.33
Clubbing	7	6.48
CNS manifestations	6	5.55
Ascitis	2	1.85
Bleeding tendency	1	0.92

According to Table 8, of the total 108 cases enrolled in the study, 75 cases had regular follow up for 250 times and 33 cases did not follow up. Majority of follow ups were for respiratory complaints (23.20%) and fever (17.60%). Only 7.20% patients came for follow up were asymptomatic. Most of the follow up were for OI's.

In this study, 108 cases of the study group visited 250 times in our hospital. Out of these 90 cases had 212 episodes of OI's and 18 cases had no evidence of OI's.

Thus prevalence of OI's in HIV was 83.33%. Among the opportunistic infections majority of cases had tuberculosis 46 (42.39%). This was followed by recurrent diarrhoea 38 (35.18%), recurrent pneumonia 31(28.70%), oral candidiasis 26 (24.07%) (Table 9).

Table 8: Clinical symptoms on follow up.

Complaints on follow up	No. of follow up (n=250)	Percentage (%)
Recurrent URI/LRTI	58	23.20
Fever	44	17.60
Not gaining weight	34	13.60
Recurrent gastroenteritis	33	13.20
Skin rash	22	08.80
Ear discharge	19	07.60
Asymptomatic	18	07.20
Oral thrush	15	06.00
Parotid swelling	07	02.80

Table 9: Opportunistic infections (OI's).

Opportunistic infections	No. of cases (n=108)	Percentage (%) Prevalence (n=108)
Tuberculosis	46	42.39
Recurrent diarrhoea	38	35.18
Recurrent pneumonia	31	28.70
Oral candidiasis	26	24.07
Disseminated scabies	16	14.81
Recurrent otitis media	14	12.96
Sepsis	08	07.40
Herpes zoster	06	05.55
Fungal infection of skin	06	05.55
Warts	04	03.70
Lymphoid interstitial pneumonitis (LIP)	04	03.70
Pneumocystis carinii (jiroveci) pneumonia	04	03.70
HIV encephalopathy	03	02.77
Recurrent pyoderma	02	01.85
Molluscum contagiosum	02	01.85
CMV Chorio-retinitis	2	01.85

DISCUSSION

Majority of children 65 (60.17%) included in this study were below 5 years (60 months) of age (Table 1) and 33 (30.55%) children were between 5-10 years (60-120 months). This study correlates with Lahiri S et al , who found majority of children 71(58.9%) presenting below 5 years of age.[8]

In the study by Asnake S, Soloman A, in northwest Ethopia, median age reported was 2.8 yrs.[9] But in the study by Sirisanthana V et al, in Thailand, the median age seen was 3 months which is very low as compared to present study.[10] Other Indian studies conducted by Lodha R et al, found median age to be 4.5 years and the same author Lodha R et al , found median age as 4 years.[11,12] This was probably because in his study all the patients were less than 12 months old and only one patient was 48 months old.

In present study, children who got infection by blood transfusion presented nearly after 9 years for the first time which is similar to study conducted by Sehgal R et al.[13]

This study reveals a progressive increase in number of children diagnosed to have HIV infection and opportunistic infections. The increase in number of cases diagnosed could be due to increasing prevalence of infection or increasing awareness of disease. Also there are increased referrals of children for screening after the parents are diagnosed to have HIV infection.

Children might present at any age but incubation period with perinatally acquired infection is much shorter than incubation period in other modes of transmission (Pol R. et al).[14] HIV infected children progress more rapidly than adults in the development of immune dysfunction and resultant illness by Kathleen A , et al.[15] The highest incidence of AIDS occurs in the first year of life and almost all cases are due to perinatal infection.

Male to female ratio in the present study was 1.76: 1 where males outnumbered females. This ratio is comparable to study by Madhivanan P et al, who found it to be 2.05:1, Shahab T et al, who found it to be 2.3:1 and Pol R et al, in Karnataka found the ratio as 1.73:1.[14,16,17]

This male preponderance might be due to the social structure of our society especially in rural areas where males are given better care than females, from where this study is done.

Maximum 61 (56.48%) cases were from rural areas. Out of which 40 (37.03%) were males and nearly twice that of females 21 (19.44%).

In contrast to present study, study conducted by Asnake S, Soloman A found that the urban prevalence was more than rural prevalence as more than 90% cases were from urban areas.[9]

In our study 106 (98.15%) patients out of 108 were infected by vertical transmission and only 2 (1.85%) by blood transfusion. (Table 3) This study is comparable with Diack et al , who found vertical transmission in 99% cases, Pol R et al, reported it in 94.37% cases.[14,18] But in our study vertical transmission was seen in 98.15% cases which is slightly higher than that reported by Merchant RH et al, as 86.6%.[19] Verghese VP et al, found vertical transmission in 87% cases.[20] Dhurat R et al, reported vertical transmission in 74.5%, Lodha R et al, reported in

70.4% and same author Lodha R et al , reported vertical transmission in 74.6% cases in 2006.[11,12,21]

Transmission by blood or blood products in present study was seen in 1.85% cases which is very much low as compared to Lodha R et al, who reported it in 29.6% cases, same author Lodha R et al, reported it in 19.3% cases and Dhurat R et al, reported blood transmission in 21.8% of cases.[11,12,21]

This gross difference in present study is probably because of good blood products screening which has been made mandatory by FDA since 1985 and the studies with high incidences of blood transmission might have had cases who received blood transfusion during the window period.

Infants who acquired HIV perinatally usually have growth retardation in future infancy. Various factors have been implicated like chronic diarrhoea, recurrent OI's, HIV enteropathy etc. (Merchant RH et al).[19] Growth failure is a poor prognostic factor in HIV infected children.

Severe malnutrition in present study was observed in 60 (55.55%) cases. Similar finding was also reported by Pol R et al, where he found severe malnutrition in 54.9% cases and Verghese VP et al, reported severe malnutrition in 58% cases.[14,20] Merchant RH et al, reported malnutrition only in 27% cases in his study.[19] Diack et al, found severe malnutrition 89% cases in HIV infected children, which is very high figure as compared to present study and necessitating early nutritional intervention in HIV infected children.[18]

OI's are the hallmark of immunodeficiency which are associated with HIV (NACO-2007).[22] OI's are seen in children with severe depression of the CD4 counts. In contrast to adults, young children generally have primary infection and often have more fulminant course of disease reflecting the lack of prior immunity.[23] However with use of pediatric ART and prophylaxis with Cotrimoxazole the incidence and prevalence of OI's might be decreasing thereby improving quality of life and survival in pediatric HIV patients.[24]

Of the 108 cases during study period, 90 had some or the other evidence of OI's. Hence the prevalence of OI was 83.33 % in HIV infected children in the present study. Gupta R et al, reported the prevalence of OI's as 65% in HIV patients which is slightly lower than the present study, which may be due to small sample size.[24]

CONCLUSION

HIV infection is an unpredictable disease in infants, children and adolescent 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.

The clinical features of HIV in pediatric population is like other common illnesses in pediatric age group, hence a high degree of suspicion is required to ascertain the diagnosis. The HIV prevalence in present study was 0.38%, thus indicating thus that amongst every 250 patient seen in either OPD or IPD, one is likely to be HIV positive. The prevalence of OI's in HIV was 83.33%. Hence it becomes paramount importance to look for evidence of opportunistic infections in pediatric HIV patient, as OI's are the leading cause of death as seen in present study. The common OI's in decreasing order of frequency were tuberculosis, recurrent diarrhoea, recurrent pneumonia, oral candidiasis, scabies, otitis media, sepsis, herpes, LIP, PCP, and meningoencephalitis. 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. HIV is a preventable disease in children. Children are nothing but the innocent bystander of the disease, proper awareness should be spread among younger generation regarding the route of transmission and safety measures. When infected, effective treatment should be given to all children.

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