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ORIGINAL ARTICLE**Pediatric HIV/AIDS in Pakistan - Experience of a Tertiary Care Centre**

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ABSTRACT

Objectives: To determine the demographic, clinical, biochemical and immunologic profile and outcome of children admitted at the Pediatric HIV/AIDS treatment center of a tertiary care hospital in Pakistan.

Study Design: Descriptive study.

Place & duration of study: HIV/AIDS treatment Centre, Department of Pediatrics, Dow University of Health Sciences/Civil Hospital Karachi. December 2010 to April 2016.

Method: This study evaluated 82 children registered at the HIV treatment unit between the study time. Detail information were noted on a predesigned proforma and analyzed on SPSS version 17.

Results: There were 51 males and 31 females, between one month to 17 years of age (Mean age 5.54 ± 4.28 years). Eight asymptomatic neonates, acquired HIV infection through Parent to Child Transmission (PTCT). All were started on prophylaxis with Nevarapine. Among symptomatic children (N=65) unexplained fever (26.15%), Hepato splenomegaly (24.61%) <10%, weight loss (20.00%), oral thrush (18.46%) and cough (15.38%) were the main clinical presentations. PTCT followed by blood transfusion was the most common mode of transmission. Fifty children were started on Anti-Retroviral Therapy (ART), of these twelve expired and nine (10.97%) did not come for follow up.

Conclusion and Recommendations: Parent to Child Transmission followed by transfusion of unscreened blood was the most common mode of transmission of HIV. High dropout need to be explored to increase compliance. Regular screening of blood for HIV infection, mandatory counseling of parents and home visiting program need to be incorporated in the management to increase compliance and ensure good outcome.

Key Words: Pediatric HIV, Children AIDS, Prevalence HIV/AIDS Pakistan.

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INTRODUCTION

Acquired Immune deficiency syndrome (AIDS) is a chronic, potentially life-threatening condition caused by the human immune deficiency virus (HIV). By damaging the immune system, HIV interferes with the body's ability to fight the organism that causes the disease. Transmission

through sexual contact, transfusion of infected blood, from mother to child during pregnancy or childbirth and through breast feeding are other commonly described routes.

Globally the World Health Organization (WHO) has estimated that 36 million individuals were affected with HIV in 2014. Of these children below

five years of age comprised of 2.6 million. Of the 1.2 million people dying of Aids, 150,000 were children below 15 years of age. Majority of adults and childhood deaths were seen in Sub Saharan Africa, Asia and Pacific region¹

The general population prevalence of HIV infection in Pakistan is 0.1 to <0.5% However high risk group exists in Pakistan, that maintains several fold high prevalence rate^{2,3}.

According to WHO, 94,000 (58,000-180,000) persons are living with HIV in Pakistan. Women aged 15 and above and children aged zero to 14 living with HIV are 2,100 (1,300-3,700). Deaths due to AIDS are 2,800 (1,800-4,900)⁴. There has been an 11 percent increases in mortality from HIV/AIDS in Pakistan. The mortality rate was found to be much higher (1.5 deaths /100,000) in Pakistan than in Afghanistan and Iran (<1 per 100,000) according to a study that evaluated data from three countries⁵.

There are 18 HIV/AIDS treatment centers for adults and children in Pakistan⁶. At present in Sindh, the second largest province has only two treatment centers for children both located at Karachi. One in a private sector and another in a Government run tertiary care center. This descriptive study analyzed the demographic, clinical, biochemical and immunologic features and outcome in children admitted at the Pediatric HIV/AIDS treatment center, established in 2010 at Pediatric department Civil Hospital Karachi.

METHODOLOGY

Between Dec 2010 and April 2016, 82 Children were registered at Pediatric HIV treatment center. These children were examined by trained doctors, all received training on WHO guidelines on the management of HIV/AIDS by Sindh Aids Control Program (SACP).

A detail history and thorough physical examination was done in each child. The information's obtained were entered on a pre-structured proforma. Children were investigated, CBC and CD4 count done in each child and repeated every

four months .Viral load was repeated every six months. Other investigations done were LFTs, S. Creatinine, Chest X-ray, viral markers for Hepatitis B and Hepatitis C, CD4 count, ICT and ELISA. Children with suspected co- morbid conditions were further investigated for underlying problems. The criteria considered for Anti-Retro viral therapy was CD4 count of <500 and positive ICT and ELISA in children above 18 months of age. A combination of two nucleoside reverse transcriptase (NRTI's) namely Zidovudine (ZDV) and lamivudine (3TC) plus a non-nucleoside reverse transcriptase inhibitor (NNRTI), Nevirapine or the protease inhibitor (PI) Nelfinvir was started as per WHO guidelines. These children were followed closely in order to check their compliance. Follow-up CD4 count was done every four months.

Children with co morbid conditions were additionally managed for the ailment as per WHO guidelines.

The data was entered on SPSS version 17 and analyzed. Descriptive statistical analysis was applied using central tendency and dispersion. The results were described as percentage, mean and Standard deviation (SD). Qualitative variables including gender, age, clinical features and outcome was described as frequencies and percentages while quantitative variable including hematological and cytological count etc. were described as mean and standard deviation. As the data is from highly selective population and does not represent the general population, inferential statistics were not applied.

RESULTS

Between Dec 2010 and April 2016, 82 children with HIV/AIDS were registered at Pediatric HIV centers, Civil Hospital Karachi. These children were between one month and 17 years of age. Among them there were eight neonates born to HIV positive mother. There was male sex predilection (male 51 and female 31). (Table 1).

TABLE 1: Age & Sex Distribution of Children Registered As HIV/AIDS at Pediatric HIV Treatment Centre, Pediatric Ward DMC/CHK*

Status	Male n (%)	Female n (%)	Total n (%)
0 to 1 month	04 (04.87)	04 (04.87)	08 (09.74)
>1 months - 12months	06 (07.31)	01 (01.21)	07 (08.52)
> 12 months to 5 years	21 (25.60)	09 (10.97)	30(36.57)
>5 years to 10 years	13 (15.85)	09 (10.97)	22 (26.82)
>10 years total	07 (08.53)	08 (09.75)	15 (18.28)
TOTAL	51(62.16)	31 (37.77)	82(100%)

*DMC/CHK: Dow Medical College/Civil Hospital Karachi

Mother to Child transmission was the predominant mode of transmission noticed in 63 (76.8%) children, followed by blood transfusion seen in 18 (21.9%) children.

Among the salient clinical manifestations, noted in 65 symptomatic children were unexplained fever (26.15%), hepato splenomegaly (24.61%), >10% weight loss (20%) and cough (15.38%) (Table 2)

TABLE 2: Clinical Presentations of Children with AIDS

Clinical Features	No	Percentage
Unexplained Fever	17	26.15
Hepato-splenomegaly	16	24.61
>10% weight loss	13	20.00
Oral Thrush	12	18.46
Cough /breathless	10	15.38
Asymptomatic	09	13.84
Diarrhea>1 month	08	12.30
Skin rash	06	09.23
Ear discharge	06	09.03
Fatigue>1month	01	01.53
Pallor	01	01.53

Eight asymptomatic neonates (4 males and 4 females) acquiring infection through Parent were started on six weeks Nevarapine therapy as Prophylaxis. All were negative for HIV in 3 months' time.

TABLE 3: Outcome of Children with HIV/AIDS, Mode of Transfusion & Response to Anti Retro Viral Therapy

Status	No of Children (Male/Female) (%)	Mode of Transmission	Outcome/Response to on anti retro viral therapy
Neonate for 6 weeks. (Prevention of parent to child transmission)	08 (04/04) (9.75)	Parent to child transmission (08)	All Negative on Anti Retro Viral Therapy prophylaxis in 3 months
Children on Anti Retro Viral Therapy (Mean duration of 5.6 months)	50(33/17) (60.97)	Blood Transfusion (14) Parent to child transmission (35) Information not available (01)	Good response on Anti Retro Viral Therapy
Children Expired on Anti Retro Viral Therapy	12(5/07) (14.63)	Blood Transfusion (03) Parent to child transmission (08) Information not available (01)	Expired due to co morbid conditions e.g. TB, thalassemia
Children waiting for CD4 result	03(02/01) (04.87)	Parent to child transmission (03) Blood Transfusion (01)	Under observation
Drop out	09 (07/02) (10.97)	Parent to child transmission (09)	Lost for follow up

Laboratory investigations in symptomatic children showed mean Hemoglobin of 9.41 gm/dl \pm 2.3 gm/dl, TLC 9402 cumm \pm 4429 cumm with the mean Neutrophil count of 4572 cumm \pm 1414 and Lymphocyte count of 2065 \pm 1280 cumm. The mean platelet count was 31, 0000 \pm 448419. Liver function test showed Serum Bilirubin within normal limit in all. The Serum ALT level was raised in 34% children with mean ALT level of 142 IU unit \pm 592 IU. Serum Alkaline Phosphatase was 4964 \pm 1548IU. Blood urea and Creatinine level was normal in all. Three children on ART was Hepatitis C antibody positive. All three succumbed during the treatment. None of the children were tested positive for Hepatitis B. Viral load was at undetectable level in 20 children. It was markedly raised in those who received anti-retroviral therapy (Mean 4.68E6 copies/ml \pm 1.619E7).

Fifty children in whom CD4 count was less than 500 were started on anti-retroviral therapy (Table 3). All received therapy for the mean duration of 5.6 months. Their mean CD4 count before treatment was 349.37 \pm 252.84. The CD4 count after the mean duration of six month therapy with ART was 927 \pm 974.

Nelfinvir was started in 50 children. Twelve patients on treatment expired within six months of therapy. They all had co morbid conditions like tuberculosis, hepatitis C or thalassemia. Nine patients started on anti-retroviral therapy did not return for follow up after initial 1-2 visit. They all came from interior Sindh. The dropout rate was 12.5%.

DISCUSSION

The impact of the HIV pandemic on children has been huge in recent years. Children accounts for around 10% of new global HIV infections. Since the first cases of children with AIDS were reported in 1982, the number of children infected with HIV has risen dramatically, mainly in the developing countries. Globally an estimated 3.4 million children aged less than 15 years were living with HIV in 2010, of these approximately 240,000 were new infections (58% lower-than in 2002) and an estimated 190,000 AIDS deaths occur in children in 2013⁷. In Pakistan there are 130000 persons are living with HIV and 5500 patients with AIDS died in 2016⁸.

In Pakistan too there is an unprecedented rise in the prevalence of HIV/AIDS in children. The first case was diagnosed in 1987. From 1986 to 1999 a total of 23, 40,000 blood samples were screened for the presence of antibodies against Human Immunodeficiency Virus (HIV) at various officially designated surveillance and diagnostic centers throughout the country. The data gave an overall prevalence rate of 0.07. The general population prevalence was estimated as 0.1% and high-risk population prevalence as 1-2% in another study⁹.

As of February 2013, a total of approximately 7,750 cases had been diagnosed, (Reports from National AIDS Control Program (NACP) treatment centers). Indeed National AIDS Control Program, UNAIDS, and the Ministry of National Health Services, Regulation and Coordination estimated 112,000 people currently living with HIV in Pakistan. The number of HIV infection in Pakistan grew at an average 17.6% per year from 2005 till 2015, the highest in the world¹⁰.

Of the 82 patients registered with HIV/AIDS in our study, 78% acquired the infection via vertical transmission. Parent to child transmission was found to be the significant mode of transmission in other studies where mother-to-child transmission

has been responsible for more than 90% of all HIV infections in children under the age of 15 years¹¹.

Most HIV-infected children acquire the infection from their mother, either during pregnancy (5-10%), labor and delivery (10-20%), or during breast-feeding (5-20%). In the absence of any intervention, the risk of mother-to-child transmission of HIV is 15-30% in non-breast-feeding populations, and 30-45% among populations with prolonged breast-feeding¹².

In 2003, the Global Surveillance of HIV/AIDS and sexually transmitted infections (STIs), a joint effort of WHO and UNAIDS, working closely with the Federal Government of Pakistan calculated the HIV/AIDS burden of the country. This group estimated HIV/AIDS positive adults aged 15-49 years in Pakistan to be 73,000, 8,900 being women. With the increasing number of women becoming HIV positive, the number of HIV positive neonate is likely to rise in the future. Risk of transmission from mother to child (40%) can be reduced to less than 2% with use of Prevention of parent to child transmission intervention¹³. Of the mother who is transmitting HIV infection through vertical route or horizontal route, majority 25% acquired the infection from their husband¹⁴. The HIV status of fathers cannot be tested in our study because of their non-availability at the time of admission or their refusal to give consent for the test. We presume that these mothers acquired the infection from their husband as all mothers were housewives and have not travelled abroad or received transfusion/s.

HIV screening of mother are not done in most of the centers in Pakistan even in places where consent can be obtained. However where HIV/AIDS center are established, screening of high risk mother have very high yield 0.2%¹⁵.

Pakistan is facing an early concentrated epidemic among intravenous drug users (IDUs) in at least eight major cities. The high prevalence among intravenous drug users in Pakistan is as high as 5% in major cities. The numbers are continually rising. These intravenous drug users are potential threat to the community. The Asian Epidemic Modeling (AEM), conducted study in 2015, reconfirmed that the use of contaminated injection equipment among people who inject drugs (PWID) remains the main mode of HIV transmission in the country. The estimated

number of people who inject drugs (PWID) ranges from 104,804 to 420,000. HIV prevalence in this population is above 40 % in several cities, including Faisalabad (52.5%), D.G. Khan (49.6%), Gujrat (46.2%), Karachi (42.2%) and Sargodha (40.6%), respectively¹⁶.

The prevalence of HIV among intravenous drug users is an alarming situation. Family Health International (FHI) sponsored a cross sectional study in 2002-2003 which indicated 23% sero prevalence in Karachi¹⁷. These intravenous drug users are not only at high risk of acquiring HIV infection but many are potential blood donors. Thus they are potential threat to children requiring regular blood transfusions like thalassemia.

Transmission via blood transfusion was the second most common mode of transmission in our children. Of the 17 children who acquired this infection through the blood transfusion 16 were thalassemics. 5% of Pakistani population carries B thalassemia gene (26) nearly 5000 cases of transfusion dependent beta thalassemic children are born every year. Routine blood screening for HIV infections are not done in most of the blood transfusion centers. These multiply transfused children are at increasing risk of acquiring parenteral HIV infection. In our study 3 children were tested positive for hepatitis C infection and none for Hepatitis B infection.

A cross-sectional study revealed high Sero prevalence of hepatitis B, hepatitis C and HIV in multi-transfused thalassemia major patients. Thirty-four out of 79 (43%) patients enrolled in the study were serologically tested positive for hepatitis C (mean age \pm standard deviation 12 \pm 4.1 years), four (5.1%) for hepatitis B and none for HIV (28) In another study sero prevalence of HBs Ag was found to be 1.25% and HCV 13.1% respectively¹⁹. A similar study done in India showed the prevalence of the three major transfusion transmitted infection as HIV 0.35%, Hepatitis B 1.66%, Hepatitis C 0.65%²⁰.

The clinical manifestation of children with AIDS in our study is not much different than other reported studies. Fever and weight loss of \geq 10% was common among children in our study. Another study²¹ showed more or less similar results, where common features were fever (44.6%), malnutrition (37.6%), lymphadenopathy (34.4%), respiratory tract infections (34.4%) and diarrhea (24.5%)²¹

A study of 43 patients from 2005 to 2011 at Shifa International Hospital shows 63% of children are symptomatic anti retro viral therapy was started in 65%. CD4 count improved in 65% of patients within 12 months of starting anti retro viral therapy²². In our study CD4 count showed an improvement in an average of 5.6 months.

HIV infection and malnutrition often coexist, and the two conditions overlap and interact. Prevalence of concurrent HIV infection in children presenting with severe acute malnutrition (SAM) is variable, with figures of up to 71.8% reported. 28 Meta-analysis of 17 large studies in sub-Saharan Africa suggested that 29.2% of children presenting with severe acute malnutrition were HIV-positive²³. In one study done at Civil Hospital Karachi the prevalence of HIV in malnourished children was as high as 13.7% (unpublished data). HIV infection should be considered in all children who presented with illness not responding to routine care and treatment.

Sixty one percent (n=50) children in our study has low CD4 count. All these children were started on Anti- Retro Viral Therapy. Twenty eight (46%) showed clinical improvement with significant increase in CD4 count. Our results are comparable with similar reported studies from resource – constrained countries²⁴. Twelve children expired during Anti- Retro Viral Therapy. Mortality is higher than what is reported from other countries²⁴. This may be due the advance stage of disease in which these children were brought or due to the presence of co morbid conditions like TB, HCV and malnutrition.

High dropout rate (15%) is one of the major challenges faced during this study period. Lack of parental education, poor socio economic status of the affected families and poor health infrastructure, non-availability of Anti Retro Viral drugs at the door step and stigma attached to the disease itself are some of the few reasons that needed further exploration²⁵.

CONCLUSION

There is unprecedented rise in HIV infection in children in Pakistan.

Regular screening of blood for HIV infection, mandatory counseling of parents/care takers and initiating home visiting program will improve the

compliance and will optimize management of HIV/AIDS in children.

CONFLICT OF INTEREST

No conflict of interest is declared.

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