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Original Research Paper

Study of clinical profile of HIV infected children and the response to Anti-retroviral therapy at ART centre, Government general hospital,Kakinada

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ABSTRACT:

Background: Pediatric HIV is a significant cause of childhood morbidity and mortality. HIV is a growing concern in the pediatric population and a large number of children are registered and treated at ART centers across the country. Combination Antiretroviral therapy (ART), or Highly active antiretroviral therapy (HAART), is the current stone of H IV management to improve the quality of life clinically and prolong the lives of people living with H IV. **Objective:** To study the clinical profile of HIV infected children started on antiretroviral therapy at Government General Hospital, Kakinada , the immunological response of HIV-infected children started on antiretroviral therapy , the adverse reactions of antiretroviral therapy in HIV infected children. **Results:** In the present study, 188 HIV children were enrolled, and 84% of children are regularly followed for six months at the ART centre.The most commonly used ART regimens in children were Zidovudine based regimen(52%) followed by Tenofovir based regimen(31%). The mortality of HIV-infected children was 5%, and all were in the age group of below 5 years. **Conclusion:** The study reported ART benefits in clinical and immunological disease progression and nutritional status in HIV infected children after six months of treatment.

Keywords : HIV , Anti retroviral therapy .

INTRODUCTION:

Pediatric HIV is a significant cause of childhood morbidity and mortality. HIV is a growing concern in the pediatric population and, a large number of children are registered and treated at ART centers across the country. As per UNAIDS estimates, in 2019, around 38 million people and 1.8 million children under the age of 15 years of age globally were living with HIV, newly infected approximately 1.7 million people and 1,50,000 children under 15 years of age with HIV in 2019 . HIV infection is an unpredictable disease in infants, children, and adolescents. It involves multiple organ systems characterized by progressive clinical deterioration and the ultimate development of severe immune dysfunction with opportunistic infections and secondary cancers resulting in chronic and very complicated illness . About 95% of new HIV infections now occur in developing countries , which lack the resources required to tackle such a monumental task. Despite the magnitude of illness, there is a lack of a sufficient number of studies describing the correlation between clinical staging and immunological staging in HIV infected children .

MATERIALS AND METHODS:

The present study was a prospective observational study conducted in the ART center over 18 months from January 2019 to June 2020. The study included asymptomatic and symptomatic children who accompanied parents and siblings but became HIV positive on routine screening .

INCLUSION CRITERIA:

The children between 18 months to 18 years were included in this study.

EXCLUSION CRITERIA:

Children less than 18 months and > 18 years of age , Children died or lost to follow up during the study period were excluded in the present study.

STATISTICAL ANALYSIS:

The results were tabulated, and the SPSS(STATISTICAL PACKAGE FOR SOCIAL

SCIENCES) 17.0 version was used to analyze the result after collecting data. The standard error of proportion and CHI SQUARE TEST is used to compare categorical variables.

OBSERVATION AND STATISTICS:

A total of 188 HIV infected children on ART were enrolled in present study.

TABLE 1 : OUTCOME AMONG FOLLOWED UP CHILDREN

OUTCOME	NO OF CHILDREN	%
TOTAL ELIGIBLE PATIENTS DURING STUDY PERIOD	188	100
ON FOLLOW UP	158	84.0
DROPPED OUT DURING THE STUDY PERIOD.	20	10.6
TRANSFER OUT TO OTHER ARTs	10	5.3

Out of 188 enrolled HIV infected children, 158 were followed till 6 months(84%),20 children were lost to follow up (10%), and ten transferred out to other ART center's (5.3%).

TABLE 2 : RURAL, URBAN DISTRIBUTION OF HIV INFECTED CHILDREN ON ART

RESIDENCE	NO OF CHILDREN	PERCENTAGE
RURAL	77	48.7
URBAN	81	51.3
TOTAL	158	100

Out of 158 HIV-infected children on ART , 81 children (51.3 %) resided in urban, and 77 (48.7%) children resided i n rural areas .

TABLE 3 : ART REGIMENS USED IN HIV INFECTED CHILDREN

REGIMENS	NO OF CHILDREN	PERCENTAGE
1.ZLE(ZIDOVUDINE+LAMIVUDINE+EFAVIRENZ)	72	45.6
2.TLE(TENOFOVIR+LAMIVUDINE+EFAVIRENZ)	50	31.6
3.ZLN(ZIDOVUDINE+LAMIVUDINE+NEVIRAPINE)	11	7.0
4.ALE(ABACAVIR+LAMIVUDINE+EFAVIRENZ)	10	6.3
5.ALN(ABACAVIR+LAMIVUDINE+NEVIRAPINE)	9	5.7
6.AL/LPV/r(ABACAVIR+LAMIVUDINE+LOPINAVIR)	6	3.8
TOTAL	158	100

All newly diagnosed HIV infected children were started on ART as per new NACO guidelines irrespective of WHO /Immunological staging. Among 158 HIV infected children,72 children (45.6%) were started with ZLE regimen,50 children (31.6%) were started with TLE regimen,11 children (7%) were started with ZLN regimen, ten children (6.3%) were started on ALE, nine children (5.7%) were started on ALN regimen and six children were started on protease inhibitor-based regimens.

TABLE 4 : NUTRITIONAL STATUS BEFORE AND DURING FOLLOW UP OF HIV INFECTED CHILDREN

MALNUTRITION GRADES	BEGINNING OF ART (N=158)	DURING FOLLOW UP(150)	P VALUE	TEST OF SIGNIFICANCE
NORMAL	15(9.5%)	67(44.6%)	<0.00001	SIGNIFICANT
GRADE 1(MILD)	22(14%)	44(29%)	<0.00001	SIGNIFICANT
GRADE2(MODERATE)	57(36%)	25(16%)	<0.00001	SIGNIFICANT
GRADE 3(SEVERE)	40(25%)	9(6%)	<0.00001	SIGNIFICANT
GRADE 4(VERY SEVERE)	24(15%)	5(3.3%)	<0.00001	SIGNIFICANT

At the beginning of ART, most HIV-infected children belonged to moderate malnutrition (36%),severe malnutrition 25%,very severe malnutrition 15%, and 24% children belonged mild to normal nutritional status. After six months of ART, no of children with very severe acute malnutrition reduced from 15% to 3.3%,no of children with severe acute malnutrition reduced from 25% to 6%, no of children with moderate malnutrition reduced from 36% to 16% and no of children with mild to normal nutritional status increased from 24%to 73% which was statistically significant(<0.00001)

TABLE 5 : ADVERSE EFFECTS OF ART DRUGS SEEN IN HIV INFECTED CHILDREN

ADVERSE EFFECTS	ZIDOVUDINE(83)	ABACAVIR (25)	TENOFOVIR(50)	LAMIVUDINE(158)	EFAVIRENZ(132)	NEVIRAPINE(20)	LOPINAVIR(6)
GIT DISTURBANCES	71(72.9)	12(60)	29(58)	111(79)	124(71)	16(60)	2(33)
PERIPHERAL NEUROPATHY	20(24)	6(24)	0	57(36)	28(21)	7(35)	0
HEADACHE	3(3.6)	6(24)	0	52(33)	20(33)	3(15)	0
ANEMIA	16 (19)	2(8)	0	5(3.2)	3(2.3)	2(10)	1(17)
RASH	0	8(32)	0	0	0	5(25)	0
HEPATOMEGALY	0	0	2(3.5)	0	0	1(5)	1(16.6)
VITAMIN DEFICIENCY	0	0	7(14)	0	0	0	0

Gastrointestinal disturbances like nausea,vomitings were the most common adverse effects of ART drugs.It was mostly seen with Efavirenz,Lamivudine, and Zidovudine.Other adverse effects like peripheral neuropathy were seen with Lamivudine and Efavirenz, and Zidovudine.Anemia was seen with regimens containing Zidovudine.

DISCUSSION:

HIV infection is a growing concern in the pediatric population, and a large number of children are registered and treated at Antiretroviral treatment (ART) centers across the country. Dysfunction of the immune system and resultant illness is more rapid in HIV infected children than adults.HIV affects virtually all the systems of the body and presents with varied clinical manifestations [1] The present study findings may help policymakers plan better health care of CLHIV in resource constrained countries like India.[2] In the present study, out of 188 HIV-positive children, 158(84%) were followed up, and 20 (10%) children were lost to follow up during the study period . The present study was in contrast to another study done by Patel et al . from Surat, in which, out of 75 H IV-infected children, only 54(72%) children were followed up, and the remaining children, 21(28%), were lost to follow up . Regular follow up is essential to decrease the morbidity and mortality of HIV infected children . Higher percentages of children (84%) with good follow-up in the present study indirectly indicate that antiretroviral treatment compliance is good. In the present study, out of 158 HIV infected children on ART, females accounted for 52.5%, and males accounted for 47.5%. In the studies done by Seth A et al. from New Delhi, Brown et al. from Nigeria, Patel et al. from Surat Rajasekaran et al. from Chennai, Pedrini et al. from Spain, Natu et al. from Pune, and Gomber et al. from New Delhi, the proportion of male children with HIV infection was more ranging from 54% to 75% .In the study, the mean age of presentation with HIV infection was 6.32 years± 2.98S D. T he mean age of presentation in this study was almost similar to many other studies. The mean age of presentation was reported as 5.4± 2.9 years in the study by Seth A et al. from New Delhi,4.2±3.5 years in the study by Brown et al. from Nigeria,7.6years±3.2 in a study by Rajasekaran et al. from Chennai,6.58 years in the study by Natu et al. from Pune and 6.24±2.93 years in the study by Gomber et al. from New Delhi.

In the present study, the proportion of children diagnosed and presented to ART center before five years of age was small (10%), and the majority of children (90%) presented after five years of age. This may be due to a lack of

facilities for early infant diagnosis. It may also be due to late reporting to ART centers after becoming symptomatic even though HIV was diagnosed earlier. As per the new guidelines, ART is recommended to all children as soon as a diagnosis of HIV is made without waiting for them to become symptomatic. This early diagnosis and treatment are essential to ensure better outcomes in HIV infected children. In the present study,51.3% of the children resided in urban areas, and 48.7% of the children were living in rural areas.

In contrast, this is to a study by Rajasekaran et al. from Chennai, in which 61.4% of children were from rural areas and 38.6% from urban areas . Family dimensions play a crucial role in the proper treatment and follow up of HIV- infected children. The increasing number of orphan children due to HIV is an emerging problem in many developing countries.[3,4,5,6.] Knowledge of the mode of acquisition of HIV infection is essential for planning, prevention and control strategies. According to National AIDS Control Organization (NACO), mother to child transmission (MTCT) is the most common mode of transmission of HIV infection among children. It is estimated that without taking proper precautions and interventions, the risk of transmission of HIV from an infected mother to her child is between 20 to 45%. In the present study, MTCT was the most common route of transmission of HIV infection. The mode of transmission of HIV infection from mother to children was 139/ 158(89%) in the present study, and the remaining children were infected through blood transfusion (4%), injections(4%), and 3.8% mode of transmission was unknown. In the present study, Blood transfusion was responsible for HIV infection in 4%of children, whereas 2%, 12%,2%and 4% respectively was reported by Brown et al.,Seth A et al.,Patel et al.Gomber et al. In the present study, five children (3.2%) were orphans and brought to the ART center by the local Nongovernmental organization (NGO), and their birth details and family details were not available. Linking these children to NGOs near their residence is essential to ensure regular follow-up and long-term antiretroviral therapy and other aspects of child care like providing good nutrition, clothing, placement in good schools, and medical care during illness. The most common clinical manifestations of HIV-infected children in most studies were fever,diarrhea,pulmonary Tuberculosis,cough,skin lesions, pneumonia, and failure to gain weight. The predominant clinical features at presentation in the present study were prolonged fever, persistent diarrhea, chronic cough, and failure to gain weight. These findings were similar to the study done by other workers. Diagnosis of HIV infection when they are asymptomatic is important to decrease the morbidity and mortality of HIV infected children.In the present study, 3.1% of HIV infected children were asymptomatic at the time of diagnosis. These asymptomatic children were diagnosed during the siblings screening procedure in the present study. Pulmonary Tuberculosis was the most common opportunistic infection among HIV-infected children in the study. HIV infection is a significant factor driving the resurgence of TB; incidence rates of TB

in countries with high HIV prevalence have increased appreciably . Prevention, early diagnosis, and treatment of TB are essential components of care of HIVinfected children since the development of TB has been shown to accelerate HIV infection through induction of HIV - 1 replication. Among 158 HIV infected children, 72 children (45%) on ZLE regimen, 50 children (31%) on TLE regimen, 11 children(7%) on ZLN regimen, ten children (6.3%) started on ALE,9children (5.7%) on ALN regimen and six children were started on protease inhibitor-based regimens. The most commonly used regimens in the study were Zidovudine based regimens, followed by Tenofovir based regimens. Early identification of HIV infected children in the asymptomatic stage can decrease morbidity and mortality. With deteriorating immunity, there is worsening of clinical staging and an increase in opportunistic infections. Clinical and immunological improvement is expected only when individuals strictly adhere to ART. After six months of ART in the present study, the percentage of children in clinical staging (stage 1) increased from 7% to 55.7%, which is statistically significant ($p < 0.00001$). The percentage of children in Stage 2 decreased from 48.7% to 29.7%, and stage 3 decreased from 38.6 % to 8.9%, and stage 4 decreased from 5.7% to 0.6%, which is statistically significant ($p<0.00001$). After six months of ART, 125(83%) of HIV infected children's immune function became normal compared to 7(4.4%) of HIV infected children with normal immune function before ART. Children with mild category of immune function improved from 3.2% to 13.3%,advanced category decreased from 117(74%) to 3(2%) ,severe category decreased from 29(18%)to 2(1.3%) . In children with HIV infection, associated opportunistic infections increase the need for energy, proteins, and micronutrients like iron, zinc, vitamin C, etc. Opportunistic infections like TB, Pneumonia, diarrhea, etc., further increase the body's nutritional demands and accelerate the decline in the nutritional status. Proper Nutrition intake can positively influence the adherence to antiretroviral drugs(ARVs) and ensure a good response of HIV infection to the ART drugs . In the present study,76 % of the children were malnourished, which was in contrast to 59% of the children in the study by Gomber et al. . After six months of ART, malnutrition decreased from 76% to 25.3%, statistically significant($p<0.00001$).In CLHIV, poor nutrition worsens the effects of HIV by weakening the immune system further. Side effects of ART drugs in children reported in various studies were very few. The most common side effects reported were anemia, rash, gastrointestinal problems,peripheral neuropathy, hepatitis, myopathy, nephrotoxicity, pancreatitis, lactic acidosis, and failure to thrive. Anemia was common with Zidovudine, which required a change of ART regimen in the present study. Anemia due to Zidovudine was reported to be 19% in the present study, whereas it was reported as 12% in a study by Kumaraswamy et al. Another important side effect noticed in the present study was rash. This was seen with Abacavir in 32% of children in the present study. It was reported to be 9% in the study by Kumaraswamy et al . In the present study, out of 158 children, only 8 (5%) children died during the follow-up and belonged to the age group of below five years. In contrast, in the study done by Patel et al. from Surat, out of 54 children, 15% of the children died during the follow-up and belonged to the age group 6- 10 years.

CONCLUSION:

The study reported ART benefits in clinical and immunological disease progression in HIV infected children after six months of treatment. The nutritional status of children on ART also showed significant improvement after six months of ART.Early diagnosis and initiation of ART in all HIV infected children and providing ART to all HIV pregnant women without interruption are essential to prevent HIV infection in children and achieve better outcomes in HIV infected children.

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