

Original article

SURVIVAL PROBABILITIES OF PAEDIATRIC PATIENTS REGISTERED IN ART CENTRE AT NEW CIVIL HOSPITAL, SURAT

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ABSTRACT

Aims and Objectives: To study the profile of paediatric HIV patients registered in ART centre of New Civil Hospital, Surat, Gujarat (India) and provide an estimate of 3 years survival probabilities of paediatric HIV patients on ART.

Material and methods: Data of 175 paediatric patients (of age less than 15 years), registered from 2007 to 2010 was collected and analyzed. Kaplan Meir method for survival analysis and Log rank test to test statistical significance were used.

Observations: Survival analysis of 161 patients could be done (registered from Oct 2006 to Oct 2010). The survival probability after 8 years of diagnosis of HIV is 91.7 %. After 3 year of start of ART according to WHO criteria survival probability is 85.7 %. The 3-year survival rate of paediatric HIV patients with WHO Stage 1 is 100%, Stage 2 is 75%, Stage 3 is 61.9% and Stage 4 is 40.8% which was statistically significant ($p < 0.001$).

Conclusions: The survival probability was 91% after 3 years of diagnosis of HIV and remained same till 8 years and the probability was independent of age groups and sex. The survival probability was 85.7 % after 3 years of start of ART. There was no difference in survival probability with different baseline CD4 counts but was significantly low in patients who were in WHO stage 3 and 4 at the time of registration.

Recommendations: With ART definitely proving increase in survival probability, it is now time to study different drug regimens and their respective survival probabilities. There are many studies on adverse effects of the ART drugs but there is need for research on their effect on survival. There is a scope for continuing of this study further with at least median follow up of 5 years. Larger sample and regression model can be used to understand more precisely the predictors of survival.

Key words: Paediatric HIV, Survival probability, Kaplan-Meier, WHO staging, India,

INTRODUCTION

The number of annual AIDS-related deaths worldwide is steadily decreasing from the peak of 2.1 million in 2004 to an estimated 1.8 million in 2009. The decline reflects the increased availability of antiretroviral therapy, as well as care and support, to people living with HIV, particularly in middle- and low-income countries; it is also a result of decreasing incidence starting in the late 1990s. Globally, death among children younger than 15 years of age is also declining. The estimated 260000 children, who died from AIDS-related illnesses in 2009 were 19% fewer than the estimated 320 000, who died in 2004. This trend reflects the steady expansion of services to prevent transmission of HIV to infants and an increase (albeit slow) in access to treatment for children.¹

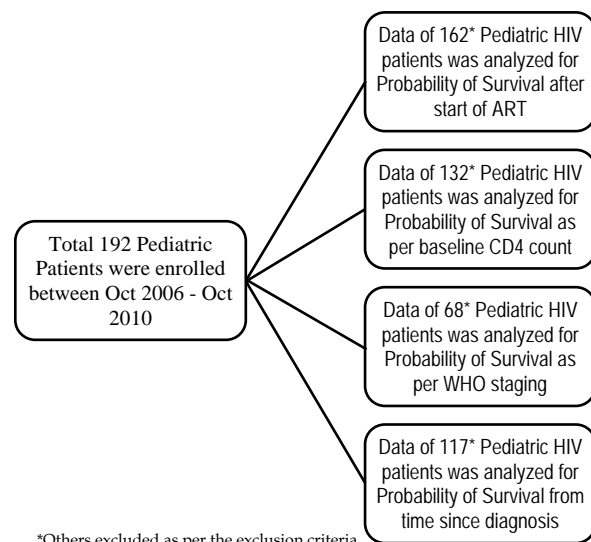
In India, Care Support Treatment programme as per the objectives under National AIDS Control Programme -3 provides prevention and treatment of opportunistic infections, Anti-Retroviral Therapy (ART), psychosocial support, home-based care, positive prevention and impact mitigation. Around 3.84 lakh PLHA including 22,837 children are receiving free ART through 292 ART centres and 550 Link ART Centres.² Early Infant Diagnosis programme to closely monitor HIV-exposed infants, identify their HIV status and provide them appropriate treatment to reduce HIV related mortality and morbidity, has been rolled out through 766 ICTCs and 181 ART centres; 9,016 infants and children under 18 months of age were tested under this programme till January 2011.²

Out of the total paediatric HIV positive patients in India, 4.3% have been reported from Gujarat. That amounts to 979 patients. In Gujarat there were 18 ART centres in 2010 catering a load of 18,754 HIV patients out of which 17,775 were Adult and 979 were Paediatric HIV patients. Gujarat had 4.9 percent of country's HIV patients and 4.3 percent of Paediatric HIV patients. Survival probabilities of these patients have not been studied yet in India. The following study was done with objective of estimating survival probabilities of Paediatric HIV patients on Anti Retroviral Therapy.

METHODOLOGY

Study setting: The ART centre at New Civil Hospital, Surat (NCHS) was established in the year 2006, under National Aids Control Program

III (NACP-III), funded by National Aids Control Organization (NACO). 5,422 HIV-infected individuals are registered with the ART Centre since September 2006 until December 2010, out of which, 192 were paediatric patients. The patient flow of paediatric patient is through Paediatrics Department of NCHS, PPTCT (Prevention of Parent to Child Transmission) program, other departments of NCHS, various other government health and private clinics. The patients are first counselled then consent is taken and tests for HIV are done. The positive patients are then examined; their CD4 cell counts are recorded and they are registered at ART centre. Baseline clinical and demographic data are recorded for all enrolled patients. Demographic data include gender, age, residence, status of parents. Clinical data include baseline CD4+ cell counts, WHO staging, weight at registration, initial ART regimen, change in ART regimen, recent WHO staging, HIV sero status of parent,



mode of transmission of HIV, CD4 count at regular visit, or period of illness, etc. All HIV-positive children who meet the standard WHO clinical and immunological criteria for starting ART in children are considered eligible to receive ART.

Selection Criteria: Retrospective and prospective data collected from October 2006 until October 2010 of children enrolled in ART centre was analysed. For general profile, all the individuals with age 1-15 years were included. Survival probabilities were analyzed with epidemiological factors including gender, age, immune status (CD4 count) at HIV diagnosis,

and baseline WHO staging of those individuals whose first centre of registration (or first centre of treatment) was ART centre, NCHS.

Exclusion Criteria: Those patients who were transferred to the ART centre in study period were not included. Data cleaning was done accordingly and those data that were available for all years uniformly were analysed.

Outcome Measure: Death of a HIV patient was taken as the primary end point.

Statistical Analysis: Descriptive statistics for general profile of the patients was carried out. While Kaplan-Meier analysis and log-rank tests were used to compare survival curves stratified by epidemiological group, SPSS version 16 was used to analyze the data.

OBSERVATIONS

During the time of retrieving the data 192 paediatric age group patients were enrolled at ART. There were 77 females and 115 males. Out of these 192 patients, 162 had directly enrolled

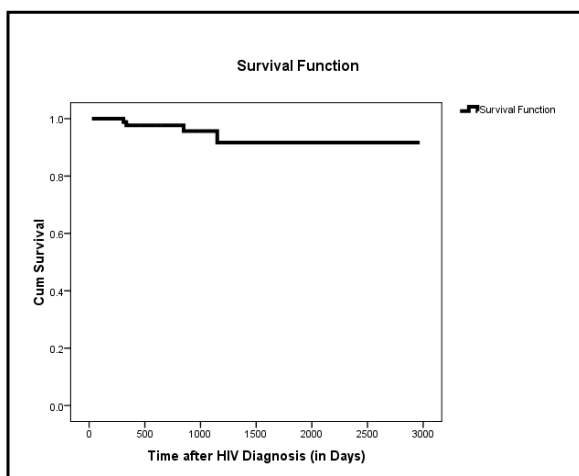
and 30 were referred to the ART centre. There was uncertainty of the data being reliable regarding the date of HIV diagnosis and start of ART of patients who were referred. Number of patients lost to follow up, transferred in and out of ART centre was 30, which were excluded from the further data analysis. The mean age of patients was 7.5 years with SD of 3.7 years. The proportion of patients in the age group 1-4 years, 5-8 years and 9-12 years was similar of about 27%. Only 5% and 12% of the patients were in age group <1year and 13-15 years respectively. Mean CD4 cell count at time of enrolment was 159 cells/ μ L, median 237 cells/ μ L, SD 291 cells/ μ L. The patients with CD 4 count less than 200 were 48%. Twelve percent patients had s CD 4 counts between 200-250 and fifteen percent had CD 4 counts between. Only 5% had CD 4 count between 350-500 while there were 20% patients having CD 4 count >500. According to WHO staging done at registration, approximately 50 % of patients were in Stage 3 and 4 and about 50% were in State 1 and 2. Most common route of transmission was perinatal. (Table 1)

Table 1: Profile of HIV positive paediatric patients at NCHS

Categories	Total (%)	Deaths (%)	Person years	Mortality density (per 100 person years)
Total Individuals	192(100)	19(10)	240	7.9
Referral				
Direct	162(84)	18(9.3)	185	9.7
Indirect	30(16)	1(0.7)	55	1.8
Sex(n=162)				
Male	96(59)	12(7.4)	111.2	10.8
Female	66(41)	6(3.7)	73.4	8.2
Age (yrs)(n=162)				
<1	8(5)	0	2.4	0
1-4	45(27.7)	9(5.5)	46.6	19.3
5-8	44(27.2)	2(1.3)	63.2	3.2
9-12	45(27.7)	3(1.8)	55.6	5.4
13-15	20(12.4)	4(2.5)	17.1	23.4
CD4+ T cell counts (n=132)				
<200	63(48)	8(6)	95.1	8.4
200-250	16(12)	1(0.8)	21	4.8
250-350	20(15)	2(1.5)	22.9	8.7
350-500	7(5)	2(1.5)	7.5	26.7
>500	26(20)	3(2.3)	31.2	9.6
WHO Staging(n=68)				
1	11(16)	1(1.5)	23.1	4.3
2	24(35)	2(2.9)	50.1	3.9
3	23(34)	4(5.9)	36.6	10.9
4	10(15)	5(7.4)	13.5	37

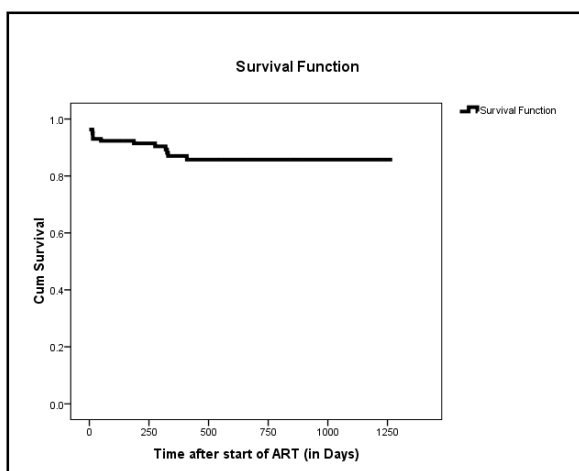
Males had higher mortality density (10.8 per 100 person years) than females (8.2 per 100 person years). Mortality density was highest in age group of 13-15 years (23.4 per 100 person years). Mortality density was highest in patients with CD 4 count 350-500 and those who were initially classified in WHO stage 4. (Table 1)

Among the data of 162 patients only 117 had reliable date of diagnosed to be having HIV. The survival probability once the patient is diagnosed as HIV of 162 patients was calculated. Survival probability of patients after 8 years of diagnosis of HIV was found to be 91.7 %. It was similar in all age groups and, males and females. (Figure 1)



* Median days of follow up 21.3 months (25th percentile: 9.7 months; 75th percentile: 37.3 months)

Figure 1: Survival probability after HIV diagnosis (n=117*)



*Median days of follow up 10.6 months (25th percentile: 3.7 months; 75th percentile: 22 months)

Figure 2: Survival probability after start of ART (n=162*)

After 3 years of start of ART, survival probability is 85.7 %. (Figure 2) When survival probability was seen among patients with different baseline CD4 counts, no significant difference was seen. But survival probability was significantly low in patients who were in WHO stage 3 and 4 at the time of registration. So, the role of gender, age and CD4 count as predictor of survival of children on ART could not established. (Figure 3)

DISCUSSION

The number of people dying of AIDS-related causes fell to 1.8 million [1.6 million–1.9 million] in 2010, down from a peak of 2.2 million [2.1 million–2.5 million] in the mid-2000s. A total of 2.5 million deaths have been averted in low- and middle-income countries since 1995 due to antiretroviral therapy being introduced, according to new calculations by UNAIDS. Much of that success has come in the past two years when rapid scale-up of access to treatment occurred; in 2010 alone, 700 000 AIDS related deaths were averted.³ Without ARV treatment, half of all children infected with HIV at birth die from AIDS before their second birthday.⁴ Early HIV diagnosis and early ARV treatment lower infant mortality by 76 percent and the rate of progression to AIDS by 75 percent.⁵ Survival probability was 0.93 (95% CI: 0.91-0.95) and 0.91 (95% CI: 0.88-0.93) at 24 and 36 months after ART initiation, respectively reported by Issakidis P et al in their study.⁶ In our study survival probability, was 0.91 and 0.86 at 12 and 24 months after ART initiation, respectively. In a study by Alibhai A, Kipp W et al, mortality in female patients (9.0%) was lower than mortality in males (13.5%), with the difference being almost statistically significant (adjusted hazard ratio for females 0.55; 95% confidence interval [CI]: 0.28–1.07; P = 0.08). In our study, the mortality in males is 12.5 % and in females it is 9.1 % which is not found to be statistically significant after applying log rank test. In their study, at baseline, female patients had a significantly higher CD4+ cell count than male patients (median 147 cells/ μ L vs 120 cells/ μ L; P-0.01).⁷ Whereas in our study, females and males had similar median of baseline CD4 count. Antiretroviral treatment reduces illness and mortality among children living with HIV in much the same way that it does among adults. In one study in Brazil by Matida, L.H. et al (2004), three-quarters of HIV-positive children receiving ART were alive after a four-year follow-up

period.⁸ A study released by O'Brien D.P. et al in 2007, which monitored 586 HIV-positive children receiving antiretroviral treatment in 14 countries

in Africa and Asia, found that 82 percent were still alive after two years.⁹

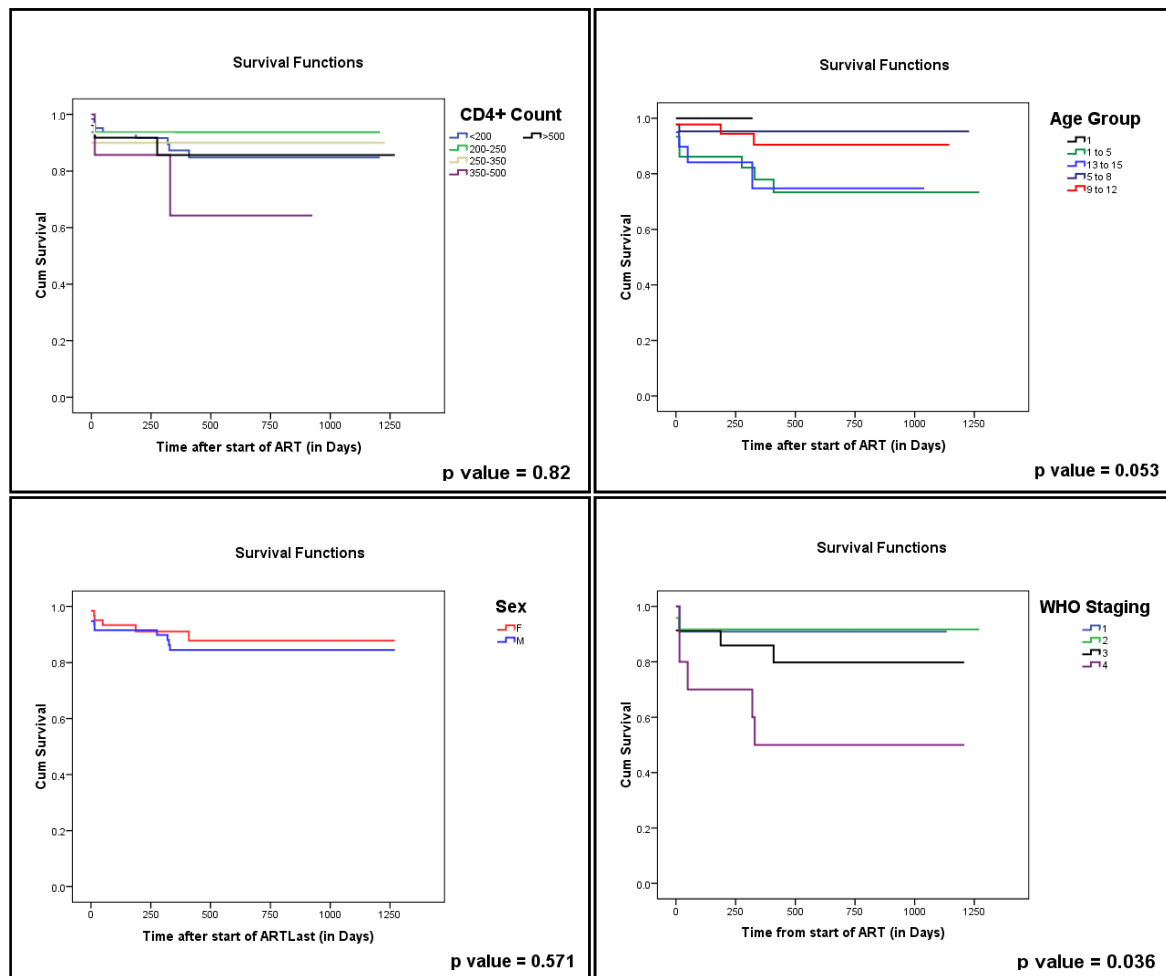


Fig. 3: Survival after start of ART stratified by various characteristics A. Age; B. Sex; C. CD4+ count; D. WHO staging

CONCLUSIONS

The mortality density was higher among males, age group of 13-15 years, patients with baseline CD 4 count 350-500 and who were initially classified in WHO stage 4. The survival probability was 91% after 3 years of diagnosis of HIV and remained same till 8 years and the probability was independent of age groups and sex. The survival probability was 85.7 % after 3 years of start of ART. There was no difference in survival probability with different baseline CD4 counts but was significantly low in patients who were in WHO stage 3 and 4 at the time of registration. So, the role of gender, age and CD4 count as predictor of survival of children on ART could not established but WHO staging had significant role.

Limitations: There can be many factors that affect survival status of a child like nutrition status, socio-economic status of parents, type of ART regimen started, etc which have not been explored in this study.

Recommendations: With ART definitely proving increase in survival probability, it is now time to study different drug regimens and their respective survival probabilities. There are many studies on adverse effects of the ART drugs but there is need for research on their effect on survival. There is a scope for continuing of this study further with at least median follow up of 5 years. Larger sample and regression model can

be used to understand more precisely the predictors of survival.

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REFERENCES

1. UNAIDS. Report On The Global AIDS Epidemic. Geneva, Switzerland 2010, p8
2. NACO, Department of AIDS Control, Ministry of Health & Family Welfare Annual Report 2009-2010, Janpath, New Delhi: NACO 2009-10, p1.
3. UNAIDS. UNAIDS World AIDS Day Report 2011 - How to get zero: Faster. Smarter. Better. 2011. Geneva, Switzerland: UNAIDS 2011, p6.
4. UNICEF Eastern and Southern Africa - HIV and AIDS - Preventing mother-to-child transmission (PMTCT) of HIV - Providing Paediatric Treatment cited on 12, Dec 2012.
5. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi S a, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *The New England journal of medicine* [Internet]. 2008 Nov 20;359 (21):2233-44.
6. Isaakidis P, Raguenaud M-E, Te V, Tray CS, Akao K, Kumar V, et al. High survival and treatment success sustained after two and three years of first-line ART for children in Cambodia. *Journal of the International AIDS Society* [Internet]. 2010 Jan;13:11.
7. Alibhai A, Kipp W, Saunders LD, Senthilselvan A, Kaler A, Houston S, et al. Gender-related mortality for HIV-infected patients on highly active antiretroviral therapy (HAART) in rural Uganda. *International journal of women's health* [Internet]. 2010 Jan;2:45-52.
8. Novaes A, Jr R. Improving survival in children with AIDS in Brazil : results of the second national Ampliação da sobrevida em crianças com AIDS no Brasil : resultados do segundo estudo nacional de 1999 a 2002. *Social Sciences*. 2011;1999-2002.
9. O'Brien DP, Sauvageot D, Olson D, Schaeffer M, Humblet P, Pudjades M, et al. Treatment outcomes stratified by baseline immunological status among young children receiving non-nucleoside reverse-transcriptase inhibitor-based antiretroviral therapy in resource-limited settings. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* [Internet]. 2007 May 1 [cited 2012 Apr 21]; 44(9):1245-8.