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ESTIMATION OF MORTALITY RATE IN FIVE YEAR COHORT ANALYSIS AMONG HIV INFECTED PATIENTS

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ABSTRACT

HIV disease is a scourge which has led to marked increase of mortality. Globally 2.90 millions of HIV infected clients died every year. Since 2004, Government of India has revolutionized and integrated HAART treatment and have remarkably achieved decline of disease progression, mortality and morbidity. ART has improved survival of patients and increased the Quality of life domain, there are limited study pertaining to estimation of long survivability on HAART patients. The present study aims to estimate mortality rate, cause of death and its predictors among five years cohort of HIV infected patients. A retrospective five years cohort study was conducted among HIV patients on ART. A random sample of 597 patients who started treatment between April, 2004 and Jan 2006 were included in this study. Secondary data was extracted from ART records. The data was analysed by using SPSS -16.50 versions. KPM –Survival analysis was employed to draw the significant inference. Over five years of cohort, it was found that 108 patients died (18.16%) and it comprised of males 47(7.87%), Females 60(10.50%) and TG 01(0.16%). Overall mean duration of HAART over 5yrs of cohort was found to be 1934±121.97 (CI-95% 1695.038-2173.18). Survivability is statistically significant with mean HAART treatment duration. Low baseline CD4 count, advanced WHO staging and Age is considered as the important parameter of survivability. Heart attack, H. Lymphoma, cardiac and Renal failure is the common cause of death, So early initiation of HAART, if CD4 counts is more than 350µ/dl, then the patients mortality rate & susceptibility to OI 's can be reduced.

KEYWORDS: CD4, HAART, PLHIV, NACO, Parameters

INTRODUCTION

Development of highly active antiretroviral treatment (HAART) in the 2004 revolutionized the care of HIV-infected patients and led to marked reductions in HIV-associated morbidity and mortality in India. ART has clearly shown to be effective in reducing mortality among those, who remain in treatment and adhere to therapy2. In recent years in developing countries with a high burden of AIDS, ART has become more widely available.

According to estimation by the World Health Organization (WHO), about 6 650 000 PLHIV were receiving ART in low- and middle-income countries by the end of 2010 [5], this is a huge improvement from the levels in 2009 [6,7]. India have achieved universal access target (treatment coverage of 80% or more of patients in need) at the end of (NACO), as per the documented record country has achieved Mortality reduction and incidence rate.

There were more than 2.50 lakhs PLHIV on antiretroviral treatment at the end of 2010 (NACO).ART has improved survival of patients with HIV/AIDS and quality of life (QOL) of patients in the country [12]. Due to this morbidity and mortality among HIV-infected persons, the incidence rate have dramatically decreased [8,9]. The primary goals of antiretroviral therapy are preventing HIV-related morbidity and mortality, mean while improving the quality of

life by restoring immunological function through suppression of RNA-plasma viral load [10]. There are limited studies reporting the long term survival of patients on HAART treatment in India.

Such studies could provide valuable information to evaluate the NACP program in this country. The Main objective of this study is to estimate mortality rate, cause of death and its predictors among five years cohort of HIV infected patients on HAART treatment.

MATERIALS AND METHODS

A retrospective cohort study was conducted among HIV patients on ART. A random sample of 597 patients who started treatment between April, 2004 and Jan 2006 were included in this study. Socio-demographic profiles, baseline characteristics, CD4 follow up, clinical and laboratory parameters were extracted from ART records.

Death was ascertained by reviewing white cards, patients care takers, health care workers and NGO's. The data was analysis by using SPSS-16.50 version. Survival analysis, Kaplan-Meier test were used to interpret the results.

RESULTS

A total of 597 PLHIV on HAART were included in this study. The sample comprised of 335 (56.11%) females, 261 (43.71%) males and TS/TG-01(0.16%) respectively. Occupational status; employed 294(49.24%), unemployed 392(65.66%) and not known 28(4.69%). Marital status; Married 492(82.41%), unmarried 112(18.76%) and not known 93(15.57%). Economic status; Low 492(82.41%), Medium 82(13.73%) and High income group 23(3.85%), literate; 23.42%. Risk factors; Heterosexual 491(%), Homosexual 12(%), IDU's 13(%) and not known 81(%).

The mean, median and inter-quartile range (IQR), age was 32.05±.98, 30.09±1.28 years and (IQR 28–40) respectively. WHO Clinical stage was assessed and it was recorded, stage I (%), stage II (%), stage III (%) and stage IV (%). As per the analysis, the mean duration of survivability of PLHIV on HAART treatment was found to be 2211±138.545, 361.924±48.48 in days (CI-95% 1939.26-2482.35) (CI-95% 266.88-456.96) respectively in Table (1).

Overall mean survival rate over 5yrs of cohort was found to be 1934±121.97 (CI-95% 1695.038-2173.18). Survivability is statistically significant with mean HAART treatment and duration (log rank, mantel Cox, chi square-595.85, $P \leq 0.05$).

The Mortality rate was determined by using Kaplan Meyer's curve as shown in the Figure (1), probability of cumulative survival rate was found to be 0.82 with mean duration 1400 days and is positively correlated with mortality rate and the probability attained was found to be 0.18 with mean duration 200 days.

The survival function 1-S (t) is presented in Figure (2). The Cox regression analysis was used to know the significance of hazard ratio in Table (2) & (3). The Patient age was not statistically significant with survivability [β(-0.02, SE(0.005), Wald(0.602), CI-95%(0.499-4.980) and regimen β(-0.276), SE(0.268), Wald(1.058), CI-95%(0.449-0.284)].

Table 1: Mean and Median Survival Rate over Five Years Cohort Analysis of PLHIV (N=597)

	Mean Survival Rate				Median Survival Rate			
	Estimates	SE	CI-95%		Estimates	SE	CI-95%	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Death (Code 0)	361.924	48.488	266.889	456.960	230.000	37.714	156.080	303.920
Survival(Code 1)	2.211E3	138.545	1939.263	2482.358	1.998E3	34.976	1929.446	2066.554
Overall	1.934E3	121.977	1695.038	2173.187	1.698E3	67.696	1565.317	1830.683

Estimation is limited to the largest survival time if it is censored. Log Rank (Mantel-Cox) Chi square-595.85*

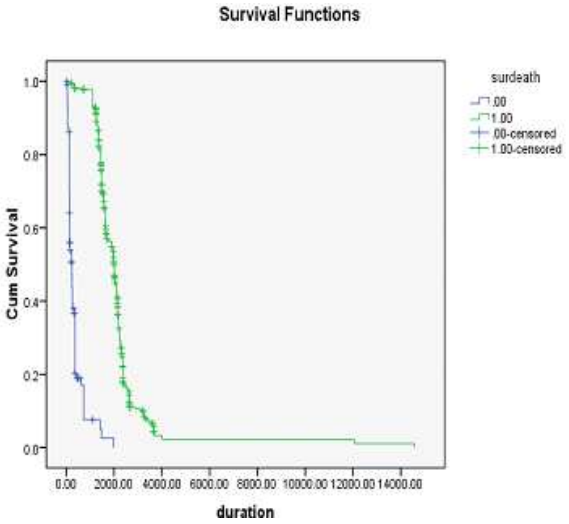

Figure 1: KPM –Survival Curve on Five Year Cohort of PLHIV

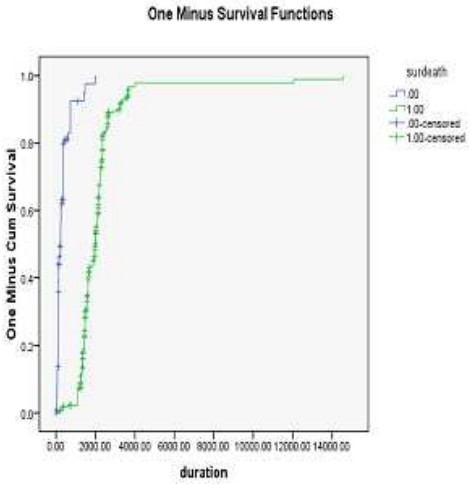

Figure 2: KPM –Survival Curve on Five Year Cohort of PLHIV

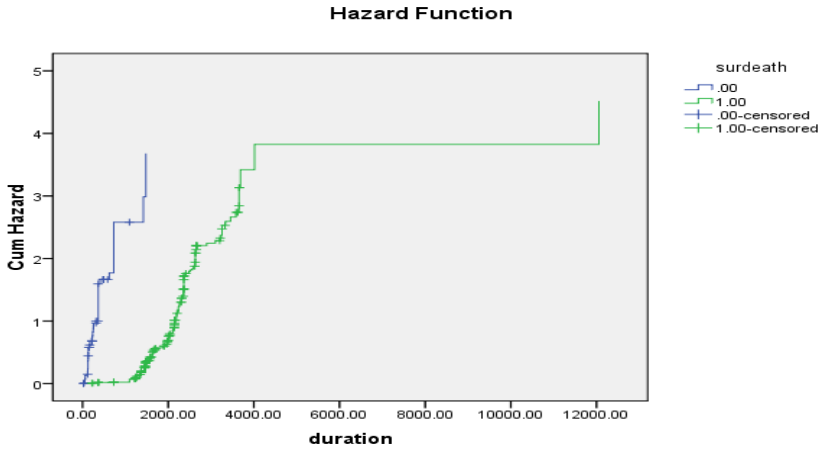

Figure 3: Hazard Function (Hz) on Five Year Cohort of PLHIV

Table 2: Cox Regression Analysis of Hazard Ratio Analysis of PLHIV over Five Year Cohort Analysis

Omnibus Tests of Model Coefficients[a,b]									
-2 Log Likelihood	Overall (Score)			Change From Previous Step			Change From Previous Block		
	Chi-Square	df	Sig.	Chi-Square	df	Sig.	Chi-Square	df	Sig.
4717.293	1.740	3	.628	1.737	3	.629	1.737	3	.629

a. Beginning Block Number 0, initial Log Likelihood function: -2 Log likelihood: 4719.030

b. Beginning Block Number 1. Method =Enter

Table 3: Significance of Associated Parameters of PLHIV over Five Year Cohort Analysis

Variables in the Equation								
	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
Age	-0.002	0.005	.257ns	1	0.612	0.998	0.989	1.007
OI's	0.455	0.587	.602*	1	0.438	1.576	0.499	4.98
Regimen	-0.276	0.268	1.058**	1	0.304	0.759	0.449	1.284

Significant at P<0.05

Table 4: Characteristics Variables and Defined Features of Death of PLHIV

SL	Age Groups	Gender	Mean Age Mean±SD	Mean Duration of Seropositive Mean±SD	Mean Base Line CD4 Mean±SD	Mean Duration of CD4 Follow up Mean±SD	MeanCD4 @the Time of Death(Days) Mean±SD	Mean Duration of HAART (Days) Mean±SD	Mean Adherence (%) Mean±SD
01	Reproducti-ve age group(18-35 yrs)	Male-21 Female-15	29.33±6.05 (36)	1.90± 2.55 (36)	155.28± 111.01 (36)	1.5± 2.96 (36)	208.5± 188.9 (36)	407.94± 624.40 (36)	88± 10.03 (36)
02	Middle age group (36-50 yrs)	Male-10 Female-43	41.20±3.66 (53)	1.69± 2.24 (53)	168.01± 151.51 (53)	1.63± 3.06 (53)	252.32± 254.41 (53)	471.81± 697.53 (53)	86.32± 11.26 (53)
03	Older age group >50 yrs	Male-16 Female-02 TS/TG-01	56.77±6.15 (19)	1.45± 3.04 (19)	207.73± 232.61 (19)	1.05± 3.15 (19)	235.36± 208.65 (19)	320.10± 636.55 (19)	88.42± 9.82 (19)
	POOL	Male-47 Female-60 TS/TG-01	39.98±5.28	1.71± 2.61	170.75± 165.04	1.48± 3.05	234.72± 217.32	423.83± 652.82	87.249± 10.37

Table 5: Cause of Death, WHO Clinical Staging and TB Status of PLHIV Deaths

Age Groups	Gender	WHO-Clinical Stage	TB HIV Co Infection	Cause of Death	Exact Cause of Death	Regimen
Reproductive age group(18-35 yrs)	Male-21 Female-15	Stage I-07(6.48%) Stage II-10(9.25%) Stage III-05(4.62%) Stage IV-14 (12.96%)	Yes-22(20.37%) No-14(12.96%)	Sucide-01(0.92%), Stroke-01(0.92%), PCP-02(1.85%), Anemia-01(0.92%) Viral fever-02(1.85%), Accident-01(0.92%), Chronic diar-02(1.85%), H.Lymphoma-01(0.92%), CMV Retinitis-01(0.92%), Immunological failure-01(0.92%), RF-01(0.92%), Not known-23(21.29%)	TBM-05(4.62%), PTB-04(3.70%), EPTB-03(2.77%)	AZT+3TC+EFV-10(9.25%) AZT+3TC+NVP-12(11.11%) D4T+3TC+NVP-11(10.18%) TDF+3TC+NVP-03(2.77%)
Middle age group (36-50 yrs)	Male-10 Female-43	Stage I-07(6.48%) Stage II-15(13.88%) Stage III-10(9.25%) Stage IV-21(19.44%)	Yes-25(23.14%) No-27(25%)	Heart attack – 05(4.62%), Accident-02(1.85%), Septecemia-01(0.92%), IHD-01(0.92%), Cardiac failure-04(3.70%), Sucide-01(0.92%), Dengue fever-03(2.77%), Respiratory failure-02(1.85%), H.Lymphoma-03(2.77%), Dermentia-01(0.92%), Viral fever-02(1.85%), Taxoplasmosis-01(0.92%), Not known-28(25.92%)	TBM-08(7.40%), PTB-02(1.85%), EPTB-07(6.48%)	AZT+3TC+EFV-12(11.11%) AZT+3TC+NVP-14(12.96%) D4T+3TC+NVP-25(23.14%) TDF+3TC+EFV-01(0.92%) TDF+3TC+NVP-01(0.92%)
Older age group >50 yrs	Male-16 Female-02 TS/TG-01	Stage I-01(0.92%) Stage II-03(2.70%) Stage III-06(5.55%) Stage IV-09(8.33%)	Yes-10(9.25%) No-09(8.33%)	Jaundice-01(0.92%), Cardiac Failure-01(0.92%), Oesophageal Candidiasis-02(1.85%), Lymphoma-01(0.92%), Pneumonia-01(0.92%), AZT induced Anemia-01(0.92%), Fever+Cough-01(0.92%), Natural death-01(0.92%), Thrombocytopenia-02(1.85%), Not known-01(0.92%)	TBM-02(1.85%), PTB-06(5.55%), EPTB-02(1.85%)	AZT+3TC+EFV-02(1.85%) AZT+3TC+NVP-11(10.18%) D4T+3TC+NVP-04(3.70%) TDF+3TC+NVP-02(1.85%)
POOL	Male-47 Female-60 TS/TG-01	Stage I-15(13.88%) Stage II-28(25.92%) Stage III-21(19.44%) Stage IV-44(40.74%)	Yes-57(52.77%) No-50(46.29%)	Heart attack – 05(4.62%), Accident-03(2.77%), Septecemia-01(0.92%), IHD-01(0.92%), Cardiac failure-05(4.62%), Sucide-02(1.85%), Dengue fever-03(2.77%), Respiratory failure-02(1.85%), H.Lymphoma-05(4.62%), Dermentia-01(0.92%),Viralfever-04(3.70%), Taxoplasmosis-01(0.92%), Stroke-01(0.92%), PCP-02(1.85%), Anemia-02(1.85%), Chronic diar-02(1.85%), CMV Retinitis-01(0.92%),Immunological failure-01(0.92%), RF-01(0.92%), Jaundice-01(0.92%), Oesophageal Candidiasis-02(1.85%), Pneumonia-01(0.92%), Fever+Cough-01(0.92%), Natural death-01(0.92%),Thrombocytopenia-02(1.85%), Not known-57(52.77%)	TBM-15(13.88%), PTB-12(11.11%), EPTB-12(11.11%) Non TB-69(63.88%)	AZT+3TC+EFV-24(22.22%) AZT+3TC+NVP-37(34.25%) D4T+3TC+NVP-40(37.03%) TDF+3TC+NVP-06(5.55%) TDF+3TC+EFV-01(0.92%)

Analysis pertaining to the PLHIV mortality was shown in Table (4), the median (IQR) baseline CD4 count was 135 (76.0–198.3) per millilitre. The mortality rate were classified based on age group of the patients, Reproductive age

(18-35yrs) comprises of Male(21) and Female(15).The mean age of the patient was 29.33±6.05(IQR 24-31yrs), Mean duration of HAART treatment was 407.94± 624.4 days and adherence was 88±10.03. Baseline CD4 count was 155.28±111.01µ/dl. Profounded five years cohort analysis the mean age of the patient was 31.01±5.30yrs. The middle age (36-50yrs) comprises of Male(10) and Female(43), mean age was 41.20±3.66(IQR 36-42yrs), Mean duration of HAART was 471.81± 697.53 days and adherence was 86.32±11.26.The Older age (>50yrs) comprises of Male(16), Female(02) and TS/TG(01), mean age of the patient was 56.77±6.1(IQR 36-42yrs), Mean duration of HAART treatment was 320.10±636.55 days and adherence was 88.42±9.82. Over five years of cohort, it was found that 108 patients were died (18.16%) and comprised of males 47(7.87%), Female 60(10.50%) and TG 01(0.16%) with good sensitivity (86.12%), specificity (90.15%), 2x2 contingency and also Cox Snell R -Square 80.26% . The predicted actual mortality was 23.43%. In reproductive age group the cause of death was documented and it was found that Sucide-01(0.92%), Stroke-01(0.92%), PCP-02(1.85%), Anemia-01(0.92%), Viral fevour-02(1.85%), Accident-01(0.92%), Chronic diar-02(1.85%), H.Lymphoma-01(0.92%), CMV Retinatis-01(0.92%), Immunological failure-01(0.92%), RF-01(0.92%), Not known-23(21.29%); WHO- clinical stage I-07(6.48%), Stage II-10(9.25%), Stage III-05(4.62%) and Stage IV-14(12.96%) are compared with different ART regimen AZT+3TC+EFV-10(9.25%), AZT+3TC+NVP-12(11.11%), D4T+3TC+NVP-11(10.18%), TDF+3TC+NVP-03(2.77%). Middle age group ; Heart attack – 05(4.62%), Accident-02(1.85%), Septecemia-01(0.92%), IHD-01(0.92%), Cardiac failure-04(3.70%), Sucide-01(0.92%), Dengue fever-03(2.77%), Respiratory failure-02(1.85%), H.Lymphoma-03(2.77%), Dermentia-01(0.92%), Viral fever-02(1.85%), Taxoplasmosis-01(0.92%), Not known-28(25.92%) with WHO clinical stage I-07(6.48%), Stage II-15(13.88%), Stage III-10(9.25%) and Stage IV-21(19.44%), with different ART regimen AZT+3TC+EFV-12(11.11%),AZT+3TC+NVP-14(12.96%),D4T+3TC+NVP 24(22.22%),TDF+3TC+EFV-01(0.92%), TDF+3TC+NVP-01(0.92%). Older age group ; Jaundice-01(0.92%), Cardiac Failure-01(0.92%), Esophageal Candidiasis-02(1.85%), Lymphoma-01(0.92%), Pneumonia-01(0.92%), AZT induced Anemia-01(0.92%), Fever+Cough-01(0.92%), Natural death-01(0.92%), Thrombocytopenia-02(1.85%), Not known-01(0.92%) with WHO clinical stage I-01(0.92%), Stage II-03(2.77%), Stage III-06(5.55%) and Stage IV-09(8.33%). In reproductive age group the exact cause of death was documented and it was found that TBM-05(4.62%), PTB-04(3.70%), EPTB-03(2.77%).Middle age group the cause of death was documented and it was found that TBM-08(7.40%), PTB-02(1.85%), EPTB-07(6.48%). Older age group the cause of death was documented and it was found that TBM-02(1.85%), PTB-06(5.55%), EPTB-02(1.85%). Regimen; AZT+3TC+EFV-02(1.85%), AZT+3TC+NVP-11(10.18%), D4T+3TC+NVP-04(3.70%), TDF+3TC+NVP-02(1.85%).

DISCUSSIONS

The study indicate that in five year survival cohort, there were 108 deaths in 1825 days of retrospective follow up, providing an incidence density of 0.18 mortality for 100 person per year (95% CI 0.9–2.01). About 43 (7.20%) patients were lost to follow up. Factors that were associated with mortality were weight loss, bedridden, functional status, baseline CD4 cells/ml, ART regimen and advanced clinical stages of the patients. Long-term retention of patients in antiretroviral treatment is a prerequisite for achieving any adherence at all.

Various studies have shown that mortality during the first 6 months after initiating ART is much higher than in developed countries and retention of patients in programs is poor [4,13]. However Our study signifies that ,the overall mortality rate of 0.18 deaths per 100 person/year is lower or comparable to that National ART guidelines elsewhere; The primary causes of death in AIDS patients could be the causes such immune reconstitution syndrome and opportunistic infections as a result of very weak immunity levels. In this study one of the factors associated with early mortality is late inception for ART. This may also account for the high rate of death in the first year.

According to reports, patients that start ART at WHO Stage III and IV are at an increased risk of dying [17,18]. Furthermore, early mortality risk is higher among those with low CD4 cell count [4,19]. The CD4 count is a proxy indicator of severity of disease which corresponds to the functional status, WHO stage and reflects the immune state of patients [20]. In the Present study, the functional status of patients at the entry level had a positive correlation with their disease stage and negative correlation with CD4 count. The majority of morbidity and mortality seen among individuals starting ART with low baseline CD4 cell count occurs during the first 3–6 months on treatment [2,3,15,16,22].

According to reports, illiteracy among patients is a contributing factor to late presentation for ART [25]. The more educated patient is better in understanding the disease state and comprehension of instructions given on drug usage. These could enhance treatment outcomes [26]. Most of the reports suggest that low educational level has consistently been associated with higher mortality, both overall and cause-specific [29,30]. Present study explains low education and low economic status, associated with a higher risk of mortality.

CONCLUSIONS

We detected a relatively lower level of mortality among the cohort of patients on HAART in Bowring and Lady Curzon hospital. HIV TB co infection (OI's) , low baseline CD4 count , advanced WHO staging , Middle & older age group is considered as the most important parameters or predictors of survivability. Heart attack, H Lymphoma, cardiac and Renal failure is the most common cause of death, So early initiation of HAART, ifCD4 counts is more than 350 μ/dl, then the mortality rate can be reduced and the patients susceptibility to OI 's will be declined.

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