



Survival and Mortality Analysis for HIV Patients in Khartoum State, Sudan 2017

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Abstract: HIV epidemic in Sudan is low with prevalence of 0.3% among general population. The prevalence is higher among key population such as female sex workers and men having sex with men. Thirty percent of the estimated people living with HIV know their status, and 50% were on care by the end of 2016. Attrition rate in Sudan was highest in first 6 months, it was around 60% in 2014. This paper intends to conduct survival analysis for HIV/AIDS and investigate factors determining it, in Khartoum state, 2017. The study is retrospective cohort, facility based using data from the clinical records of adult HIV/AIDS patients who were enrolled in anti-retroviral therapy in Khartoum state between January and December 2015. Cox regression and Kaplan-Meier analyses were performed to examine factors that influence time to death and survival over time. Total of 547 people living with HIV on antiretroviral therapy- ART from all ART centres in Khartoum states during 2015 were included in the study, data collection and compilation was conducted in October 2017. The retention rate was (45.3%), AIDS related mortality rate was (9.9%), and lost to follow up rate was (37.1%). Cox regression model for mortality indicated significant association between survival and the following parameters: the functional status at start of ART (Hazard ratio - HR 4.765), alcohol use has (HR: 4.392), and world health organisation clinical stage at start of ART (HR: 1.859), all had negative impact on survival and increased risks for mortality. Literacy level status reduces mortality and increases survival time, as (HR: 0.338) and adherence to CTX (HR: 0.013). The study concluded that average survival time is significantly associated literacy level, duration between diagnosis and initiation of ART, functional status at start of ART, WHO stage at start of ART, and adherence to CTX. It is recommended that care providers showed modify existing follow up mechanisms to ensure provision of needed care to the patients with the identified determinants. In addition, the National HIV Guidelines should emphasize shortening the duration between diagnosis and linkage to care and early initiation of ART.

Keywords: Anti-retroviral Therapy, HIV Survival Analysis, Determinants of HIV Mortality, Literacy Level, Functional Status, Initiation of ART, World Health Organization Clinical Stage

1. Introduction

Background: The HIV and AIDS are considered among major issues in global agenda, as indicated in both the MDGs and SDGs. UNAIDS indicated that the epidemic trend is changing, as both new infection rates and AIDS related

deaths were declining [1]. In 2016, globally the total number of PLHIV was estimated at 36.7 million, and AIDS related deaths were estimated at one million on 2016 [1]. HIV in Sudan is classified as low epidemic, by 2016 the estimated number of PLHIV was 56000, new infections were 5000, and AIDS related deaths were 3000 [1]. HIV in Sudan

disproportionately affect key population at higher risk of infection [2]. The national responses is guided by the HIV strategic plan, the main donor is GFATM. There are total of 37 ART centres and 262 counselling and testing centres distributed across Sudan [3].

Sudan National ART Treatment Guidelines adopted the WHO 2015 updates that ART should be initiated in all adults living with HIV regardless of clinical stage and at any CD4 cell count, and all adults with severe or advanced HIV clinical disease (WHO clinical stage III or IV) and adults with CD4 count ≤ 350 cells/mm³ should be prioritised [3, 4]. Mortality analysis study conducted in Sudan for patient cohort enrolled in ART in 2014, indicated that AIDS related deaths and the lost to follow up-LTFU rates were higher in the first six months of initiation of ART. The study showed that female sex, literacy, good functional status at of start of ART all were associated with better treatment outcomes [5].

A retrospective cohort study conducted in Debre Markos Referral Hospital, Ethiopia, indicated that 32% of deaths occurred in the first 12 months. Male sex and adherence to Cotrimexazole showed better survival rate. Additionally it showed that ambulatory and bed ridden functional status, poor adherence to ART and advanced WHO clinical stage were significant predictors of mortality [6]. Similar study was conducted in a rural hospital in Tanzania resulted in higher mortalities rates during the first three months of treatment. The study also indicated that severe anaemia (adjusted Hazard ration 9.2), severe malnutrition (adjusted hazard ratio at 2.12) were strong independent predictors of mortality [7].

A prospective mortality analysis study conducted in South east Uganda showed that Low baseline CD4 count, low body weight, advanced clinical condition (WHO stages III and IV), not being on cotrimoxazole prophylaxis and male gender were associated independently with increased mortality [8]. The evaluation of Sudan HIV national strategic plan indicated that treatment outcome for the cohort analysis for 2016, PLHIV alive at end of 12 month of treatment were 66%, those alive at 24 month of treatment were 63%, and at 60 months only 52%. The 2016 cohort analysis showed increased proportion of survival compared to the situation in 2011, where at 60 month of treatment the survival rate was 0% [3]. Sudan National AIDS control program HIV test-treat-retain cascade analysis conducted in 2013 showed that 41% of the estimated number of PLHIV were in need of care, and only 9% of diagnosed of PLHIV whom are in need of treatment were enrolled in treatment [9].

In order to improve treatment outcomes and reduce deaths associated with AIDS, the existing services should be responsive to the major determinants of survival. This paper intends to study the survival in 2017 for HIV/AIDS and its determinants among PLHIV enrolled in ART during 2015, in Khartoum state, 2017. As Khartoum represent s around 17% of the total PLHIV in Sudan, the outcome of this study would contribute in shaping the response to the major determinants of HIV survival in Khartoum state as well as which if managed to be addressed well; will have great implication

over the whole of Sudan.

2. Methods

2.1. Study Design

Observational, analytical, retrospective non-concurrent cohort study, both facility based and community based study.

2.2. Study Area

Khartoum state which is the capital of Sudan, it's the most populous city in Sudan with census of 5,274,321 [10]. It is one of the 18 states of Sudan. There are 7 ART centres in Khartoum (Omdurman teaching hospital, Khartoum dermatology and venereal disease hospital, Bahri teaching hospital, Police hospital, Military hospital, Elban Jadid hospital, and Bashir hospital.). The ART centers are distributed within Khartoum state in different cities and are located with the secondary level hospitals. Khartoum acts as referral center for the whole of Sudan, majority of initial diagnosis occurs in Khartoum health facilities.

2.3. Study Population

The included PLHIV who were enrolled in ART in the period between January and December 2015 in Khartoum seven ART centres.

2.4. Inclusion and Exclusion Criteria

Eligibility to be included in the study were all PLHIV, who enrolled in ART in the period between January and December 2015, in the public facilities in Khartoum state including those who were missed or lost to follow up were traced to be interviewed. The exclusion criteria was those deceased PLHIV who died for reason not related to HIV/AIDS.

2.5. Sample Size

The total number of patients who were enrolled in ART during 2015 was 547 as confirmed by the by state ministry of health and the seven ART centres in Khartoum state, were included in the study.

2.6. Study Variables

Biographic & socioeconomic variables, WHO stage at start of ART, TB status, duration between diagnosis and enrolment in ART, treatment outcome, cause of death, time until outcome of treatment.

2.7. Data Sources and Collection

The data was collected from the seven ART centres in Khartoum state, all eligible patients' records were retrieved, arranged by month of initiation of ART, and the study variables were collected from the patients' records in to the compilation sheet. Based on the distribution of the treatment outcomes, study participants were stratified. Those who were

lost to follow up were interviewed through phone, using a pretested structured questionnaire. Those deceased, their family member were contact through phone to conduct verbal autopsy. Total of seven data collectors were trained on the methodology and data collection tools, the training was in conducted in faculty of medicine university of Khartoum, in August 2017. Data collection was completed in two months.

2.8. Data Quality Assurance

Regular supervision and spot check during data collection was made by the principal investigator, the compilation sheet was shared on daily bases with the principal investigator for cleaning and quality assurance.

2.9. Data Analysis

Initial analysis was done using Microsoft excel 2013, descriptive and inferential statistic, including survival analysis was done using SPSS version 20. Association between the outcomes and the baseline variables were performed using chi square test, with P. Value at 0.05. Logistic regression analysis was performed to estimate the direction and magnitude of the association between individual variables and the outcome. Survival analysis was conducted to measure the average survival time since initiation of ART, the average time until lost to follow up, and the average time for retention in care. The data was described in average time, and survival functions were presented by the survival curves. Comparison between the different strata within each variable was conducted to those with significant findings, for both the average time till event and the behavior of the survival curve. Cox regression

analysis was conducted to variables which showed significant association with different treatment outcomes to measure the hazard ratios, and it is association with the treatment outcome.

3. Results

Total number of patient records included in the study was 547. The male sex represented 59.4%, and females were 40.6%. The average age for female and male were 38 and 35 years respectively, where 80.3% of the respondents were between 20 and 49 years old and 3.3% of the patients were less than nine years old. Regarding the marital status, 33.1% were married, 16.1% were single, 8% were divorced, and 2.9% were widowed. Literacy rate was 66%, and information was not available for 17.7%. Employment rate was 45.5%. Regarding alcohol use, 75.9% indicated no use, 0.9% were habitual alcohol drinkers, 0.5% social drinkers, while 22.7% of the records showed no information on alcohol intake. While 49.5% of study participants were enrolled in ART in the first 30 days, the average duration between diagnosis and initiation of ART was 5.57 months. The eligibility criteria for initiating ART was missing in 95.6% of patients records. The WHO staging at start of ART was mostly stage three 70.9%, followed by 12.4% in stage four, 8.8% stage one and only 5.9% stage two. The functional status at start of ART for patients who were working was 71.1%, ambulant were 22.5%, and those bedridden were 2.2%. Records were missing for 4.2%.

Table 1. Socio demographic characteristics, baseline clinical and functional status, and adherence to CTX.

Variable		number	percentage
sex	male	325	59%
	female	222	41%
literacy	Literate	361	80%
	illiterate	89	20%
Employment status	employed	222	51%
	un employed	214	49%
alcohol intake	habitual alcohol	8	2%
	no alcohol use	415	98%
marital status	single	88	27%
	married	181	55%
	divorced	44	13%
	widowed	16	5%
WHO stage at start of ART	WHO stage I	48	9%
	WHO stage II	32	6%
	WHO stage III	388	72%
	WHO stage IV	68	13%
Functional status at start of ART	working	389	74%
	ambulant	123	23%
TB status	bedridden	12	2%
	TB Pulmonary smear positive	119	27%
	Not a TB case	320	73%
CTX status	adherent to CTX	499	97%
	Not adherent to CTX	13	3%

The verified treatment outcome at the time of study was 45.3% on care, 9.9% dead, 7.7% transferred out, and 37.1%

true lost to follow up.

The average survival time since initiation of ART till the

end of study which was June 2017, was 116·232 weeks (95% CI 112·729 – 119·735 weeks), in months it was 27.33. The survival curve in general showed drop at the first 10 weeks of

initiation of ART, with cumulative survival function for the first year of initiation of ART was 0.9. Majority of the deaths occur during the first 13 weeks after initiation of treatment.

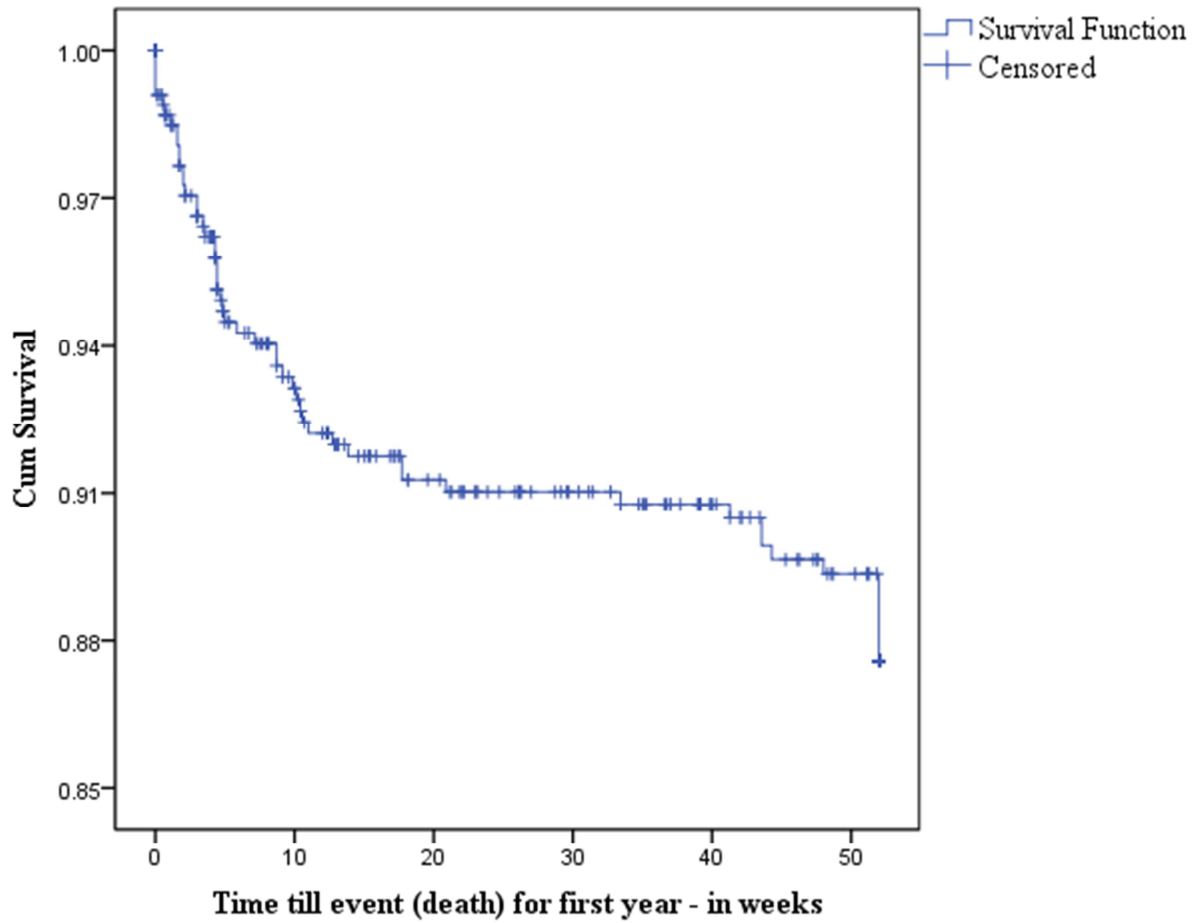


Figure 1. Survival function.

Average survival time for the first year since initiation of ART was 47.718 week (95% CI 46.509 - 48.928). Death rate in the first year was 8%. The average survival time by the end of the second year of initiation of ART to 2015 cohort was 93.814 weeks (95% CI 91.129 - 96.499). Death rate by the end of the second year of initiation of ART was 9%.

Survival time was significantly longer among those literate, those who do not drink alcohol, on Cotrimoxazole, ambulant and working functional status, WHO clinical stage one and two and time between diagnosis and initiation of ART. The sex differences, marital statuses, age groups and employment status, did not show statistically significant effect on average survival time.

Survival time was significantly longer among those literate,

Table 2. Distribution of treatment outcome, average survival time by the first and second year since initiation of ART.

Variables	Treatment outcome in the first year of initiation of ART		survival analysis by the first year of initiation of ART				P.value	
	Death (%)	Alive (%)	mean survival time in week		95% Confidence Interval			
			Estimated mean	Std. Error	Lower Bound	Upper Bound		
Sex	male	9.85%	90.15%	48.13	0.76	46.64	49.63	.979
	female	9.91%	90.09%	47.11	1.05	45.05	49.17	
literacy	yes	6.65%	93.35%	49.25	0.61	48.03	50.46	.000*
	no	16.85%	83.15%	44.14	2.11	39.99	48.28	
Employment	employed	8.56%	91.44%	49.02	0.83	47.38	50.66	.724
	unemployed	7.94%	92.06%	48.04	0.93	46.21	49.88	
Alcohol Use	habitual	25.00%	75.00%	37.2	8.90	19.80	54.69	0.034*
	no use	8.67%	91.33%	48.39	0.65	47.11	49.68	
marital status	single	7.95%	92.05%	49.66	1.13	47.44	51.88	.476
	married	11.60%	88.40%	46.54	1.22	44.14	48.95	
	divorced	15.91%	84.09%	45.36	2.76	39.94	50.79	
	widowed	12.50%	87.50%	45.81	4.04	37.88	53.75	

Variables		Treatment outcome in the first year of initiation of ART		survival analysis by the first year of initiation of ART				P.value	
		Death (%)	Alive (%)	mean survival time in week		95% Confidence Interval			
				Estimated mean	Std. Error	Lower Bound	Upper Bound		
WHO stage at start of ART	Stage I	0.00%	100.00%	Stage I, II	50.63	0.89	48.86	52.40	0.044*
	Stage II	9.38%	90.63%						
	Stage III	10.05%	89.95%	stage III, IV	47.24	0.707	45.86	48.63	
	Stage IV	14.71%	85.29%						
Functional status at start of ART	working	4.11%	95.89%	50.56	0.437	49.70	51.42	0.000*	
	ambulant	26.83%	73.17%	39.24	2.067	35.19	43.30		
	bedridden	25.00%	75.00%	36.05	7.631	21.09	51.01		
TB	TB	8.40%	91.60%	48.20	1.359	45.54	50.87	.729	
	not TB	10.31%	89.69%	47.69	0.791	46.14	49.24		
CTX	on CTX	9.22%	90.78%	47.89	0.629	46.66	49.13	0.004*	
	not on CTX	23.08%	76.92%	41.40	8.508	24.73	58.08		

Cox regression model for mortality significantly confirmed that the functional status at start of ART (hazard ration HR 4.765 time higher among those bed ridden and ambulant compared to working). The hazard with Alcohol use 4.392 higher compared those who do not. WHO clinical stage III and IV at start of ART has hazard of 1.859 times higher

compared to stage I and II.

Being literate was significantly associated with longer survival time compared to illiteracy, the hazard ratio HR was 0.338. Adherence to cotrimexazole followed the same manner (HR: 0.013).

Table 3. Results of Cox regression analysis, for each variable individually.

Independent variables	B	Sig.	Exp(B)	95.0% CI for Exp(B)	
				Lower	Upper
Sex	0.001	0.998	1.001	0.581	1.722
Literacy	- 1.086	0.001*	2.962	1.553	5.652
Employment	-0.131	0.696	0.878	0.456	1.689
Alcohol	-0.740	0.042*	0.477	0.234	0.974
CTX	1.480	0.013*	4.393	1.360	14.190
Functional status at start of ART	1.561	0.000*	4.765	3.197	7.104
WHO clinical stage at start of ART	0.620	0.009*	1.859	1.171	2.951
Initiating ART in first month of diagnosis versus more than one month	-0.795	0.006*	0.452	0.256	0.796

4. Discussion

Death rate in this study [9%] was similar to the rate in Ethiopia [11] which was around 10.3%. Survival probability was higher than countries in sub-Sahara such as Cameroon which had survival probability of 77% at first year on initiation of ART [12], this can be justified by the lower burden of disease that affects Sudan compared to other Sub Saharan countries.

The average survival time in the first year after initiation of ART was (47.718 week) was longer compared to 2014 mortality analysis in Sudan (35.99 weeks) [5], this can be explained by the increased engagement of the PLHIV in the national response including activation of adherent supporters by MoH, such as including adherent supporters and PLHV peer educators, in addition to the socio economic impact mitigating measures targeting the PLHIV in addition to activation of ART active tracing of patients who were lost to follow up [3].

Majority of deaths occurred in the first three months of initiation of ART, which can be attributed to the advanced disease stage at time of initiation; as majority of the patients were at WHO clinical stage III and IV at time of initiation. The literature indicated that the advanced disease stage, the

delayed the immune response to the ART. This finding is similar to what was reported in similar other studies [11, 13 - 15]

Moreover, the average survival time for non-alcohol users is longer than those who use alcohol. This is consistent with what is reported in the literature. Alcohol use is known to negatively impact individual's health condition. The impact is increased with the infection with HIV, contributing to poor health seeking behaviours, reducing adherence to ART, and poor treatment outcomes [11, 23 - 25].

The WHO staging at start of ART showed significant association with survival, as those at stage III and IV had shorter average survival time compared to those at stage I and II. In addition, the functional status at start of ART significantly associated with shorter survival time was among bedridden PLHIV compared to ambulant and working study participants. This can be explained by poor immunologic response mainly failure to restore CD4 cells to 500 cells/ μ L despite being virally suppressed [29]. Both findings were consistent with previous studies [11- 14].

Early initiation of ART in the first 30 days from diagnosis showed longer survival time compared to those whom ART was later initiated, as early initiation is associated with increased viral suppression [26, 29]. This was consistent with similar studies from China [27], and Uganda [28].

5. Conclusion and Recommendation

Average survival time for the first year is relatively longer. The following were identified as determinants of shorter survival time within the first year since initiation of ART: illiteracy, alcohol consumption, initiation of ART more than one month after diagnosis, advanced WHO clinical staging (III & IV), bedridden functional status, and poor adherence to CTX.

It is recommended that care providers should modify existing follow up mechanisms to ensure provision of needed care to the patients with the identified determinants. In addition, the national HIV guidelines should intensify its effort towards shortening the duration between diagnosis and linkage to care and early initiation of ART.

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