JACOBS PUBLISHERS

OPEN ACCESS

Jacobs Journal of Epidemiology and Preventive Medicine

Research Article

The -1Year Survival In Hiv-Infected People Receiving Antiretroviral Therapy Varies Across Location Of Health Care Facilities In Benin

C. Sossa Jerome[*1,2], Mt Agonnoudé[3], Ge. Sopoh[1], Ai Bah-Chabi[1], A.De Souza[1], M. Bachabi[1], G. Gbetowenonmon[1], V. Agueh[2], Em Ouendo[2], Lt Ouedraogo[2]

[1]*Programme National de Lutte contre le Sida et les IST(PNLS), 01 BP 882 Cotonou, Bénin*

[2]*Institut Régional de Santé publique, BP 384, Ouidah, Bénin*

[3]*ENATSE, Université de Parakou, BP123, Tél./Fax : (229)23 61 07 12; Fax : (229) Parakou, Bénin*

**Corresponding author: Dr. Sossa Jerome Charles, University of Abomey-Calavi, Regional Institute of Public Health, Route des esclaves, IRSP, BP 384, Ouidah, Benin (West Africa) Tel; (229) 66278085; E-mail: sossajero@yahoo.com*

Received: 12-15-2016

Accepted: 08-01-2017

Published: 08-11-2017

Abstract

The National Programme for Fight against (PNLS) of Benin has been providing free antiretroviral drugs since 2003. Two assessments of survival in HIV infected patients receiving antiretroviral treatment (ART) were previously done in 2006 and 2009. The objective of this study was to assess 1-year survival in persons living with HIV/AIDS (PLWHA) in Benin in 2014, to compare it with previous ones (2006 and 2009) and explore its association with locations of ART providing facilities. This retrospective study included 2176 Benin PLWHA under highly active antiretroviral therapy (HAART) as per 2006 WHO ART guidelines, selected in 46 ART providing facilities through all regions across the country. Selected participants were those who started ART from July, 1st 2011 to June, 30th 2012. Data on socio-demographics, ART care site location and deathwas collected. Survival analyses were performed to assess 1-year survival rate in PLWHA under HAART. During the study period, 50 patients (2.3%) died thereby yielding an estimated mortality rate of 2% at 12 months among 2176 PLWHA.. This mortality rate was lower than 11.5% and 6.6% reported in 2006 and 2009 respectively reflecting the increasing survival rate in PLWHA under HART in Benin. Location of ART providing facilities were associated with 1-year survival after ART initiation in PLWHA. Likelihood of 1-year death was higher in men [OR=1.93 95%CI = (1.07 - 3.48)] than in women, in PLWHA treated in Zou-Collines ART providing facilities [OR=2.89, 95% CI = (1.25-6.70)] compared to Ouémé-Plateau ones. Likelihood of 1-year death was lower in PLWHA under HART in Atlantique – littoral ART providing facilities [OR=0.270 95% CI = (0.09 - 0.783)] compared to Ouémé-Plateau ones. Efforts are needed to improve 1-year survival in regions where likelihood of death is high.

Keywords: Pwlha; Survival; Arv Therapy; Predictors; Benin

Introduction

Mortality reduction and improved quality of life due to the benefit of antiretroviral treatment (ART) for acquired immunodeficiency syndrome (AIDS) patients is well known. The efficacy of ART, as reflected by viral suppression. Cluster of differentiation 4 (CD4) lymphocyte repletion and durable reductions in AIDS related opportunistic diseases and death is similar among patients treated in high-income as well in low income countries [1, 2]. However, high early mortality after starting ART has been observed in the resource limited countries[2]. The impact of ART programs in resource poor setting[2] is, therefore, unlikely to be related to questions of drug efficacy, but rather to health system issues and programme effectiveness [3].

Factors that limit the success of ART include poor therapy adherence, regimen complexity, viral resistance, drug tolerance and toxicity, therapy costs, and presence of comorbid conditions such as substance abuse and addiction.

It is well established that survival among patients on antiretroviral (ARV) therapy is associated with good adherence [4-6], a high CD4 cell count at baseline, young age [4, 5, 7, 8], world health organization (WHO) classification of HIV infection stages [5,7]. Studies reported that coinfection or comorbidity (especially tuberculosis), the marital status [5,7], ARV combination, occupation and body mass index (BMI) were predictor of death [7]. Another influence of sex was uncovered at Dar es Salam in Tanzania, where researchers reported that one-year after ART initiation, women have a better immunologic response with high rate of undetectable virus load [8].

In Benin the estimated prevalence of HIV/AIDS was 1.2 % in 2012 (1.6 % in urban setting and 0.9 % in rural area) [9], ART began in Benin since February 2002 in three sites. In scaling up according to 3 by 5 initiative, National Programme for Fight against HIV/AIDS (PNLS) opted for decentralized health centers for HIV/AIDS care [10]. Two 1-year survival after stating ART were performed and the rate varied from 88.5% (2006-2007) to 93.4% (2008-2009). In order to assess changes in the performance of ART caregivers and to improve program's quality of services to persons living with HIV/AIDS (PLWHA), PNLS needed to assess 1-year in 2014. Furthermore, PNLS needed to identify regions where the likelihood of death during the first year of ART initiation is high in order to improve the quality of services in these area. Comparing the survival of patients treated in health facilities across health regions can inform HIV/AIDS program managers for actions. The objective of this study was to assess 1-year survival in PLWHA receiving ART in Benin in 2014, to compare it with survival rate reported from 2006-2007 and 2008-2009 studies and explore its association with health regions.

Material and Methods

We conducted a retrospective study in PLWHA under ART in the National HIV/AIDS program. Patients were enrolled from 46 HIV/AIDS care sites in all parts of Benin. Forty two ART centers with more than 100 patients were randomly selected out of all 86 centers available in Benin in 2014. In order to take into account representativeness of sites, four complementary sites with fewer than 100 patients were randomly selected. PLWHA whose medical records include complete information on 1-year survival after ART initiation participated in the study.

The study population was HIV/AIDS patients aged 15 and over receiving ART according to 2006 WHO guidelines for antiretroviral therapy (ART for all HIV-positive patients with CD4 counts <350 cells / mm3, regardless of clinical symptoms) [11]. The criteria for inclusion were: - being HIV positive; - starting antiretroviral therapy from July, 1st 2011 to June, 30th 2012. The exclusion criterion was being pregnant receiving ART for preventing mother to child HIV transmission.

Sample size

A total of 3080 patient's records enrolled from July, 1st 2011 to June 30th 2012 were reviewed.

The independent variables studied were patients sociodemographic (sex and age) ART care site (size of attendance) and on region in which ART care sites were located. The main dependent variable was the time of death.

Data collection

Investigators were divided in teams of two; each team was responsible for one or more centres of HIV/AIDS management according to the number of patients receiving ART in the centres and the distance between sites. Data were collected through a documentary review of the medical records of patients and the periodic reports from the centres of HIV/AIDS management. At each centre, data collectors extracted information regarding the variables from these documents. Investigators were enrolled for two days training to be familiar with study procedure. National supervision of data collection was also set. Deaths were verified by professional or site mediator information, if possible, and were otherwise verified by a death certificate in the patient file, by a death record in the death register, or by a phone call using the phone number in the patient file. National supervision of the data collection was set up by the principal investigator and PNLS's monitoring evaluation representatives.

Statistical analysis

Data was collected from regular patients' medical records in each site and were analyzed using SPSS version 20.0 (SPSS Inc, Chicago, IL, USA). Univariate analyses were performed to describe patients' baseline characteristics.

For survival analysis, patient lost of follow up for three months were censored unless it was verified that patient was died. Verification was done by professional or site mediator information, or by a phone call using the phone number in the patient file. Kaplan Meier estimation was used to estimate survival function with two main principles [12, 13]: -survival function was hypothesized to be stable between two death time intervals; - survival function is estimated at each observed death time. Cox proportional hazards regression models [13] were used to investigate associations between regions associated with survival takin Ouémé-Plateau as reference (the capital of Benin is located in this region). Interactions between factors were also explored. The level of significance was fixed at $p < 0.05$.

Regulatory approvals

The study was approved by Benin National Health Research Ethics Committee before the operational stage beginning. Confidence and anonymity were ensured regarding collected information.

Results

Participants' characteristics

A total of 3080 patient's records enrolled from July, 1st 2011 to June 30th 2012 were reviewed.

Among 3080 patient's records reviewed, 2176 (70.67%) had all data complete with possibility of survival estimation. We don't find any difference between social demographic characteristics (sex an age) of patients with incomplete data and those with complete ones. The mean age at initiation of ART was 36.9 ± 10.4 years and the mean hemoglobin level was 10.3±2.7g/dl. Table I shows that 68.9% of the patients were female, 42.2% of subjects lived in Atlantic-littoral region and 95.5% had CD4 cells count less than 500 per mm^3. The mean of CD4 cells count was 196.4±176.8 cells/mm^3.

Variables		Absolute frequency	Relative frequency
Sex	Male	676	31.1
	Female	1500	68.9
Age (years)	15 to < 30	546	25.1
	30 to < 50	1349	62.0
	≥ 50	281	12.9
CD4 *	< 500	1910	95,5
	≥ 500	90	4,5
ART Site attendance	<50	110	5.1
	50 – 100	503	23.1
	> 100	1563	71.8
Health Regions	Alibori-Borgou	234	10.8
	Atacora-Donga	157	7.2
	Atlantique-Littoral	918	42.2
	Mono-Couffo	242	11.1
	Ouémé-Plateau	336	15.4
	Zou-Collines	289	13.3

*Data available in 2000 participants

Table 1. Participants' characteristics: socio sociodemographic and region of residence, PLWHA aged 15 and over on HART, Benin 2014.

1-year survival of PLWHA

The mortality rate was estimated at 2% at 12 months among 2176 PLWHA included in the study (Figure 1). The total patient-time contributed was 32253 patient-months. The maximum observed exit time was approximately 38 months, and the last death was observed at 25 months. During the first year follow up, 42 patients (1.9%) died and the estimated mortality rate were 2% at 12 months.

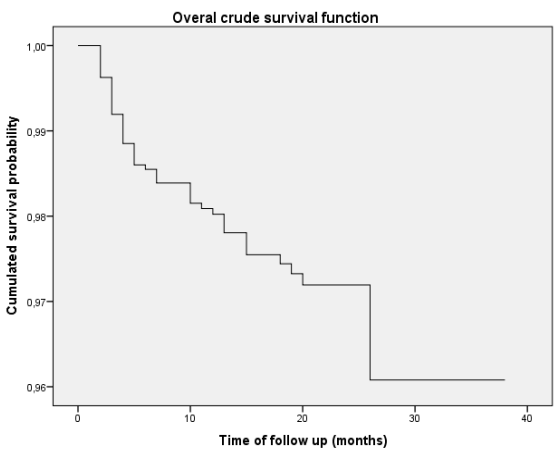
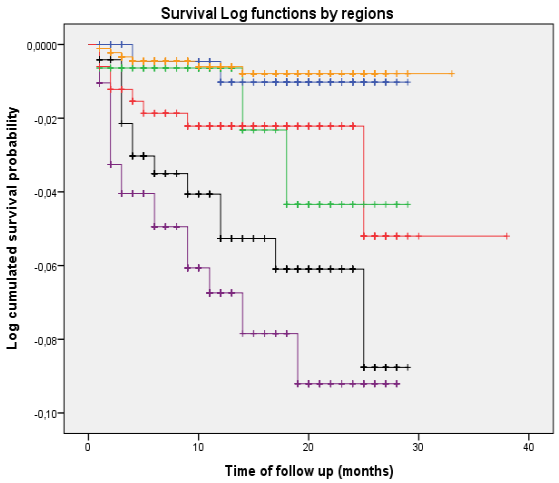


Figure 1. Overall crude survival curve in PLWHA aged 15 and over under HART, Benin 2014, n=2176

1-year survival and ART care site location

Log survival curves using Kaplan-Meier technique showed differences between regions. Khi-Square of Log Rank (Mantel-Cox) was 47.9 with p<0.001. Using Cox regression model, location (department or health region) of ART providing facilities was associated with 1-year survival in PLWHIV after ART initiation. Likelihood of 1-year death was higher in men [OR=1.93 95%CI = (1.07 - 3.48)] than in women and in PLWHA treated in Zou-Collines ART providing facilities [OR=2.89, 95% CI = (1.25-6.70)] compared to Ouémé-Plateau ones. Likelihood of 1-year death was lower in PLWHA under HART in Atlantique – littoral ART providing facilities [OR=0.270 95% CI = (0.09 - 0.783)] compared to Ouémé-Plateau ones.



Legend: AB=Alibori-Borgou, AD=Atacora-Donga, AL=Atlantique-Littoral, ZC=Zou-Collines, MC=Mono-Couffo, OP=Ouémé- Plateau

Figure 2. Log survival crude functions by regions in PLWHA under HART in Benin, 2014.

Variables		HR	95% CI	p
ART site attendance				
	100 and over	1		
	0-49	1.234	0.42 - 3.606	0.701
	50-100	1.029	0.50 - 2.12	0.939
Health regions	Ouémé - Plateau	1		
	Borgou - Alibori	0.333	0.07 - 1.64	0.177
	Atacora - Donga	0.555	0.11 - 2.69	0.464
	Atlantique - Littoral	**0.270**	0.09 - 0.783	**0.016**
	Zou - Collines	**2.892**	1.25 - 6.70	**0.013**
	Mono - Couffo	2.009	0.80 - 5.08	0.140
Sex	Women	1		
	Men	**1.931**	1.07 - 3.48	**0.029**
Age (years)	50 and over	1		
	15-29.9	0.818	0.33 - 2.03	0.665
	30-49.9	0.736	0.36 - 1.52	0.407

Table 2. Cox regression 1-year survival of PLWHA aged 15 and over with socio-demographic, ART care site attendance and location, Benin 2014, n=2176

Discussion

This 1-year survival study in PLWHA receiving ART showed an estimated survival rate at 98% at 12 months, meaning a continuous improvement of survival rate among PLWHA under HART in Benin since 2006 (88.5 % in 2006, 93.4% in 2009, and 98% in the present study). Using sex an age adjusted Cox regression HR, we found that location of ART providing facilities influenced and patients' 1-year survival.

Continuous improvement of 1-year survival

Findings in this study were in accordance with those worldwide who reported that the introduction of ART has significantly reduced morbidity and mortality in HIV-infected patients in various developed and developing countries [13,15]. In contrast, Chakravarty et al. reported in India that [16], the mortality in patients on ART was 14/100 person-years which was higher than results from in a study from eastern India [17] but similar to another study from western part of the country [18]. Indeed, the goal of universal access to ART adopted at the June 2006 General Assembly High-Level Meeting on HIV/AIDS, has a positive impact on survival in PLWHA [19]. Mahy and al. [20] in a study on estimating the impact of antiretroviral therapy: regional and global estimates of life-years gained among adults reported that 14.4 million life-years have been gained among adults globally between 1995 and 2009 as a result of ART. According to authors, 54 % of these years were gained in Western Europe and North America, where ART has been available for over 10 years. In recent years the growth in life-years has occurred more rapidly in sub-Saharan Africa and Asia [20]. The benefits of highly active antiretroviral therapy in the treatment of HIV infection have been well described including viral suppression, CD4 lymphocyte repletion, and durable reductions in AIDS related opportunistic diseases and death [21,22].

In organizational context, the large size of ARV site (ART site attendance) was associated with decreased mortality rate in PLWHA, but we didn't point out this link. This may be due to low number of ART sites with high attendance included in the study, reflecting the general characteristics of ART sites attendance in Benin. According to Megerso et al. [23] the antiretroviral treatment outcome among ART naïve adult patients was not significantly different among patients treated at the primary health care centers and from those treated at hospital. In the study we didn't explore survival differences between PLWHA receiving ART in primary health care centers versus those treated in hospitals.

Location of ART providing facilities was associated with mortality. In Benin context, according to household consumption surveys, the evolution of poverty by department between 2006 and 2011 shows that poverty has decreased in Ouémé-Plateau region, increased in Zou-Collines, Mono-Couffo and remained virtually unchanged in Atlantic-Littoral [24]. House hold food insecurity prevalence ranged from 3-6% in Oueme Plateau, 1-5% in Atlantique Littoral, 7-10% in Zou-Collines and 28-29% in Mono-Couffo [25]. These information may explain, partly these findings. Ensuring food security in Zou Collines departments may help in reducing mortality in PLWHA in Zou Collines. In contrast, mortality did not increase in Mono-Couffo where it was expected (due to poverty and food insecurity rate) to be worsened compared to Oueme-Plateau. High early mortality after starting ART has been observed in the resource poor setting by Braitstein et al. [26]. The impact of ART programmes in low-income countries is, therefore, unlikely to be related to questions of drug efficacy, but rather to health system issues and programme effectiveness [27] that needs to be take into account by AIDS programme manager.

This study of survival in PLWHIV receiving ART had some limitation including incomplete patients' medical record.

Conclusion

The study shows that one-year survival of patients initiated to ART is in a continuous improvement in Benin since 2006. This improvement reflects efforts made by the national Aids Control Programme of Benin in ART has positive impact on patients. The 1-year survival in HIV-infected people receiving antiretroviral therapy varies across location of health care facilities. Efforts are needed to strength health system in regions were survival in PLWHA was low.

Acknowledgements

We thank all ARV cares sites managers and Benin Information and PLWHA cares centers (CIPEC) managers for their contributions to data collect in this study.

Funding: We thank Global fund for Malaria, HIV/AIDS and tuberculosis Representative in Benin and its partner PNLS for funding this study as periodic evaluation of ART care for PLWHA.

Competing interest

None

References

1. Braitstein P, Brinkhof MW, Dabis F, Schechter M, Boulle A, Miotti P et al. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. Lancet. 2006, 367(9513):817–824.

2. Ivers LC, Kendrick D, Doucette K. Efficacy of antiretroviral therapy programs in resource-poor settings: a meta-analysis of the published literature. Clin Infect Dis. 2005,41(2):217–224.

3. Lawn SD, Myer L, Wood R. Efficacy of antiretroviral therapy in resource poor settings: are outcomes comparable to those in the developed world? Clin Infect Dis. 2005,41(11):1683–1684.

4. Abaasa AM, Todd J, Ekoru K, Kalyango JN, Levin J, Odeke E et al. Good adherence to HAART and improved survival in a community HIV/AIDS treatment and care programme: the experience of The AIDS Support Organization (TASO), Kampala, Uganda. BMC Health Serv Res. 2008,8:241.

5. Gezahegn A. Survival status among patient living with HIV AIDS who are on ART treatment in Durame and Hossana hospitals: A restrospective longitudinal study. Addis Ababa: Faculty of Health Science, ADDIS ABABA University; 2011.

6. Glass TR, Sterne JAC, Schneider M-P, De Geest S, Nicca D, Furrer H et al. Self-reported nonadherence to antiretroviral therapy as a predictor of viral failure and mortality. AIDS. 2015,29(16):2195-2200.

7. Kouanda S, Meda IB, Nikiema L, Tiendrebeogo S, Doulougou B, Kaboré I et al. Determinants and causes of mortality in HIV-infected patients receiving antiretroviral therapy in Burkina Faso: a five-year retrospective cohort study. AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV. 2012,24:(4):478-490.

8. Mosha F, Muchunguzi V, Matee M, Sangeda RZ, Vercauteren J, Nsubuga P et al. Gender differences in HIV disease progression and treatment outcomes among HIV patients one year after starting antiretroviral treatment (ART) in Dar es Salaam, Tanzania. BMC Public Health. 2013,13:38, 1-7.

9. Institut National de la Statistique et de l'Analyse Économique (INSAE) et ICF International, 2013. Enquête Démographique et de Santé du Bénin 2011-2012. Calverton, Maryland, USA : INSAE et ICF International.

10. Programme National de Lutte contre le Sida (PNLS). Termes de référence: Recrutement d'un consultant pour réaliser l'étude intitulée: Évaluation de la prévention de la transmission du VIH de la mère à l'enfant au Bénin. Cotonou: PNLS, Ministère de la Santé du Bénin; 2014. 4p.

11. World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents. 2006,OMS, Geneva, 132p

12. Golmard JL, Mallet A, Morice V. Biostatistique. 2006-2007. Paris: Université Pierre et Marie CURIE, Paris-VI; 161-73.

13. Kestenbaum B. Survival Analysis. 2009. In: Epidemiology and Biostatistics: An Introduction to Clinical Research. Dordrecht Heidelberg London New York: Springer, 215-28.

14. Severe P, Leger P, Charles M, Noel F, Bonhomme G, Bois G et al. Antiretroviral therapy in a thousand patients with AIDS in Haiti. N Engl J Med. 2005, 353: 2325-2334.

15. Stringer JS, Zulu I, Levy J, Stringer EM, Mwango A, Chi BH et al. Rapid scale-up of antiretroviral therapy at primary care sites in Zambia: feasibility and early outcomes. JAMA. 2006, 296(7): 782-793.

16. Chakravarty J, Narendra K, Shashi T, Prasad R, Shukla S, Tiwari A et al. Determinants of survival in adult HIV patients on antiretroviral therapy in Eastern Uttar Pradesh: A prospective study. Indian J Med Res. 2014, 140(4): 491-500.

17. Bhowmik A, Bhandari S, De R, Guha SK. Predictors of mortality among HIV-infected patients initiating anti retroviral therapy at a tertiary care hospital in Eastern India. Asian Pac J Trop Med. 2012, 5 : 986-990.

18. Ghate M, Deshpande S, Tripathy S, Godbole S, Nene M, Thakar M et al. Mortality in HIV infected individuals in Pune, India. Indian J Med Res. 2011, 133 : 414-420.

19. World Health Organization, UNAIDS, UNICEF" Towards universal access : scaling up priority HIV/AIDS interventions in the health sector : progress report. 2007. World Health Organization. 92p

20. Mahy M, Stover J, Stanecki K, Stoneburner R, Tassie JM. Estimating the impact of antiretroviral therapy: regional and

global estimates of life-years gained among adults.Sex Transm Infect. 2010,86:(2):67-71.

21. Nieuwkerk PT, Sprangers MA, Burger DM, Hoetelmans RM, Hugen PW, Danner SA et al. Limited patients adherence to highly active antiretroviral therapy for HIV-1 infection in an observational cohort study. Arch Intern Med. 2001, 161: 1962-1968.

22. Abaasa AM, Todd J, Kenneth JE, Kalyango JN, Levin J, Odeke E et al. Good adherence to HAART and improved survival in a community HIV/AIDS treatment and care programme: the experience of The AIDS Support Organization (TASO), Kampala, Uganda. BMC Health Serv Res. 2008, 8: 241.

23. Megerso A, Garoma S. Comparison of survival in adult antiretroviral treatment naïve patients treated in primary health care centers versus those treated in hospitals: retrospective cohort study; Oromia region, Ethiopia. BMC Health Serv Res. 2016,(1): 16: 581.

24. République du Bénin. Evaluation de la pauvreté au Bénin. Cotonou, 2013, INSAE. 218p

25. Programme Alimentaire Mondial. Analyse globale de la vulnérabilité et de la sécurité alimentaire (AGVSA 2013) - rapport de synthèse par commune. Cotonou (2014), PAM. 14p)

26. Braitstein P, Brinkhof MW, Dabis F, Schechter M, Boulle A, Miotti P et al. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low income and high-income countries. Lancet. 2006, 367(9513): 817- 824.

27. Lawn SD, Myer L, Wood R. Efficacy of antiretroviral therapy in resource poor settings: are outcomes comparable to those in the developed world? Clin Infect Dis 2005, 41(11): 1683-1684.