Risk factors for loss to follow-up in human immunodeficiency virus care in the Greater Accra Regional Hospital in Ghana: a retrospective cohort study

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Background: Loss of human immunodeficiency virus (HIV)-positive patients to follow-up increases HIV-related morbidity and mortality. This study identified the factors associated with loss to follow-up (LTFU) in an urban health facility in Ghana.

Methods: A 12-y retrospective study was conducted using routinely collected data from the National Acquired Immune Deficiency Syndrome (AIDS) Control Programme (NACP) on persons living with HIV/AIDS (PLWHA) who initiated antiretroviral therapy (ART) from 2006 to 2017 at the Greater Accra Regional Hospital. Convenience sampling was used to select the study area. All gathered data were exported to Stata 14 statistical software for analysis.

Results: A total of 4330 PLWHA initiated ART between January 2006 and December 2017. Of these, 1166 (26.9%) were lost to follow-up over the 12-y period. The factors associated with LTFU included being a Muslim (adjusted hazard ratio [aHR] 1.31 [95% confidence interval {CI} 1.05 to 1.65]), having CD4 <250 cells/ml (aHR 1.45 [95% CI 1.21 to 1.76]) and completing adherence counselling (aHR 1.58 [95% CI 1.31 to 1.92]). Having other sources of health care funding and disclosure of one's disease status were found to be protective (aHR 0.74 [95% CI 0.58 to 0.94] and 0.80 [95% CI 0.65 to 0.98], respectively).

Conclusions: Some of the determinants of LTFU in the hospital are comparable to those found in other parts of Africa and could be addressed using existing interventions.

Keywords: Africa, antiretroviral therapy, Ghana, HIV/AIDS, loss to follow-up

Introduction

The burden of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) continues to increase worldwide with an estimated 36.9 million people living with the disease in 2017 and approximately 2% dying within the same period.[1] Africa, particularly sub-Saharan Africa (SSA), bears a disproportionately high burden of the disease, accounting for about two-thirds of the global disease burden.[1] In Ghana, the national and urban prevalence of the disease was estimated to be 1.8% and 2.4%, respectively, in 2015.[2] The disease is known to affect the physical, social and economic lives of those affected and their families, communities and respective countries of residence as a whole.[3–5]

Patient monitoring, defined as 'routine collection, compilation, and analysis of data on patients over time and across service delivery points, using information either collected from paper forms or entered into a computer', ensures that appropriate care is given to patients.[6] It allows for assessment of the patients' response to therapy, monitoring of side effects, encouragement of adherence to management plans and eventually prevention of drug resistance.[7,8] The World Health Organization (WHO) recommends the use of unique identifiers to link HIV patient records with their health records as a way of strengthening their monitoring and moving towards the provision of patient-centred care.[9] Losing patients to follow-up results in disruption of the monitoring process, is likely to lead to unfavourable outcomes for the patient and causes setbacks in HIV programmes.

Loss to follow-up (LTFU) has been defined differently in different studies. The WHO recommends a period of 90 d after a patient misses his/her last appointment, but also acknowledges that patients labelled as LTFU may include those who have died

or transferred themselves without notifying their care centres.[9] A study conducted using data from 19 countries in Asia, Latin America and Africa suggests a patient can be considered as LTFU if she/he has missed his/her clinic appointment for ≥180 d.[10] Another study conducted in Mozambique recommended considering the local context and clinic appointments in the definition of LTFU.[11] Despite the definition given, the several factors that are associated with LTFU can be categorized into individual-level factors, interpersonal, institutional and community-level factors.[8] These factors have been identified through studies conducted mostly in East African countries and may differ based on the setting. A study conducted in Malawi identified individual factors such as age, sex, body mass index at the start of antiretroviral therapy (ART), clinical stage at presentation and poor adherence to ART as being predictors of LTFU. This study also identified a decreased risk in clinics with low patient load and patients in urban areas.[12] Another study assessing facility-level factors associated with LTFU in Kenya, Uganda and Tanzania found an increased risk in facilities that provided a secondary level of care to patients, those unable to provide monitoring tests (such as CD4 testing) in the facilities and those that opened less than four mornings within a week.[13] Studies from West Africa have shown a high level of LTFU among patients within this region.[14,15] For instance, a study describing LTFU at all stages of an HIV programme in Guinea-Bissau found more than half of the patients on ART were LTFU over 7 y of follow-up and a CD4 count <200 cells/ml was the strongest contributor to LTFU.[16]

In Ghana, the national policy on HIV/AIDS recommends treatment of persons living with HIV/AIDS as a way of reducing HIV-related morbidity and mortality. The policy further encourages monitoring of patients to avoid drug toxicity, improve their retention in care and slow the development of resistant strains of HIV.[17] These are done through scheduled visits to health facilities/centres that offer treatment and follow-up for persons living with HIV/AIDS (PLWHA) under the HIV management programme, supervised by the National AIDS/STI (sexually transmitted infection) Control Programme. Adherence to care is therefore important in reducing the morbidity and mortality associated with the disease. This study identifies the probability of retention in care over a specified follow-up period and the factors associated with LTFU among HIV-positive patients receiving care at an urban ART centre in Ghana and recommends measures to curb the phenomenon.

Materials and methods

Aim, design and setting of the study

The study sought to explore the risk factors for LTFU among HIV/AIDS patients in the Greater Accra Regional Hospital in Ghana. A retrospective study design was adopted using routinely collected data from the National HIV/AIDS/STI Control Programme (NACP) on PLWHA who initiated ART care from 2006 to 2017 at the facility.
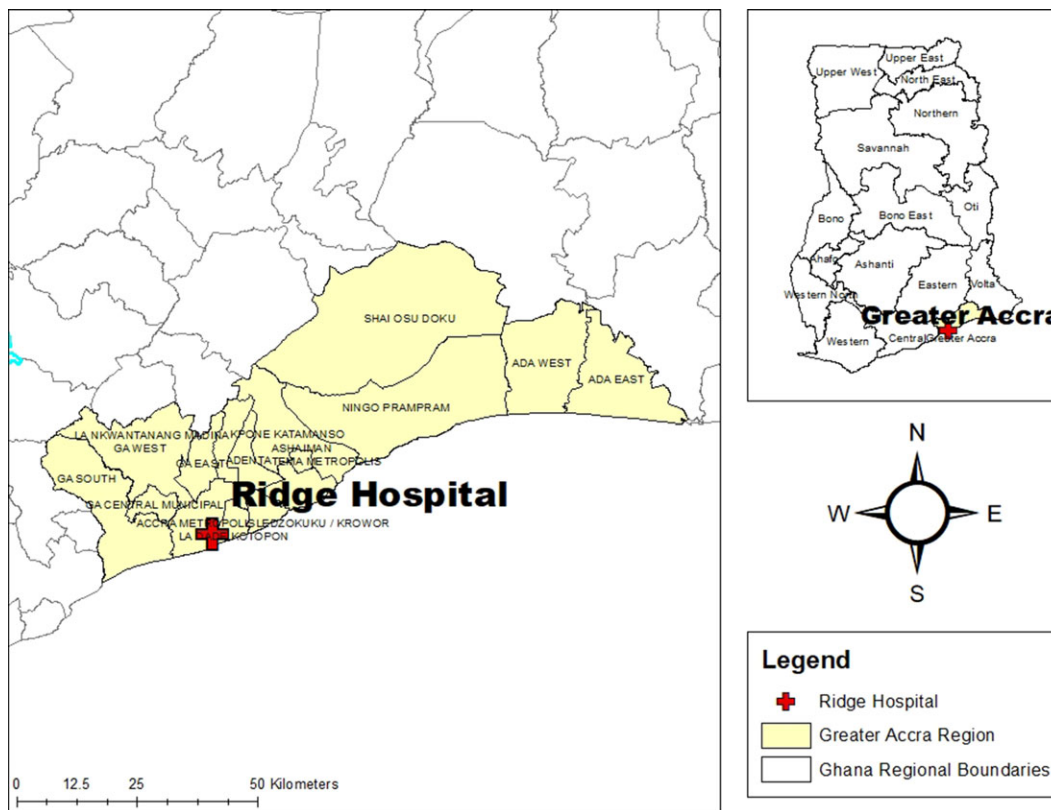
Figure 1. A map of the study site.

The setting of the study was the Greater Accra Regional Hospital (also known as the Ridge Hospital). It is a 620-bed hospital situated in Ridge, Accra. It was commissioned in 1928 by the British and upgraded to the status of a regional hospital in 1997. It provides services to about 4 283 322 people living in and around Accra, the nation's administrative capital (Figure 1).

Characteristics of participants

The study participants included all PLWHA who had initiated ART in the hospital from 1 January 2006 to 31 December 2017. The data for these patients had been entered into the NACP database. Participants were classified as LTFU if they had not attended the clinic 90 d after their last appointment date.

Ethics and processes

Ethical approval for the study was obtained from the Ensign College of Public Health Ethical Review Board. In addition, permission to access the data was sought from the NACP. Administrative permission was also sought from the ART clinic prior to data collection. The data covering 1 January 2006 to 31 December 2017 were then extracted by the data officer from the NACP database at the Greater Accra Regional Hospital. The data were then cleaned and exported into the Stata 14 statistical software package (StataCorp, College Station, TX, USA) for analysis.

Statistical analysis

The data were extracted in XPS format and converted to XLs for cleaning in Excel (Microsoft, Redmond, WA, USA). The cleaned data were then transferred into Stata version 14 for analysis. Multiple imputation approaches were used to impute missing observations. Multiple imputation by chain equations (MICE) was used to impute age (mlogit), marital status (mlogit), weight (mlogit), CD4 count <250 cells/ml (logit), counselling (logit) and disclosure status (logit) as categorical variables. The predicting variables included lost to follow-up (failure indicator/outcome), duration in years (the survival time), cumhaz (the Nelson–Aalen cumulative baseline hazard), gender, education background, employment status, source of funding and religion. Fifty datasets were created since the proportion of missing values was relatively high (ranging from 1.0% to 60.9%).

Descriptive analyses were performed and presented as frequencies, proportions and median values for continuous variables. The time to loss to follow-up was calculated as the difference between the date a patient initiated ART and 90 d since his/her last visit and the patient had not been classified as 'died' or 'transferred out' in the database. Patients who were transferred out or died were considered as not LTFU. The patients' data were censored on 31 December, 2017. A bivariate Cox regression proportional analysis was used to determine candidates for the multivariate Cox regression proportional model that was carried out to identify the determinants of LTFU. Candidate variables with p-values ≤0.25 or variables with a known association with LTFU were selected using a backward selection procedure.

Kaplan–Meier estimates were used to compute the probability of retention in care and 95% confidence intervals (CIs)

Table 1. Baseline characteristics of the study participants (N=4330)

| Variable	Before imputation		After imputation	
	n	%	n	% (95% CI)
Age group (years)				
10–24	440	10.2	445	10.3 (9.4 to 11.2)
25–39	2560	59.1	2586	59.7 (58.3 to 61.2)
40–53	1000	23.1	1011	23.4 (22.1 to 24.6)
≥54	285	6.6	288	6.6 (5.9 to 7.4)
Missing observation	45	1.0		
Gender				
Female	3148	72.7	3148	72.7 (71.4 to 74.0)
Male	1182	27.3	1182	27.3 (26.0 to 28.6)
Marital status				
Single	889	20.5	913	21.1 (19.9 to 22.3)
Married/cohabiting	2665	61.5	2766	63.9 (62.4 to 65.3)
Separated/divorced	343	7.9	353	8.1 (7.3 to 9.0)
Widow(er)	289	6.7	297	6.9 (6.1 to 7.6)
Missing observation	144	3.3		
Education				
No formal education	700	16.2	700	16.2 (15.1 to 17.3)
Primary	595	13.7	595	13.7 (12.7 to 14.8)
JSS/middle school	1825	42.2	1825	42.2 (40.7 to 43.6)
Sec/tech/vocational	793	18.3	793	18.3 (17.2 to 19.5)
Tertiary	417	9.6	417	9.6 (8.8 to 10.5)
Employment status				
Not employed	564	13.0	564	13.0 (12.0 to 14.0)
Employed	3766	87.0	3766	87.0 (86.0 to 88.0)
Religion				
Christianity	3971	91.7	3971	91.7 (90.9 to 92.5)
Islam	248	5.7	248	5.7 (5.0 to 6.4)
Other	111	2.6	111	2.6 (2.1 to 3.0)
Weight (kg)				
<45	186	4.3	462	10.7 (9.4 to 12.0)
46–60	577	13.3	1447	33.4 (31.3 to 35.6)
≥61	929	21.5	2420	55.9 (53.6 to 58.2)
Missing observation	2638	60.9		
CD4 count <250 cells/ml				
No	764	17.6	2004	46.3 (43.9 to 48.6)
Yes	1001	23.1	2326	53.7 (51.4 to 56.1)
Missing observation	2565	59.2		
Source of funding				
Out of pocket	2937	67.8	2937	67.8 (66.4 to 69.2)
Medical insurance	248	5.7	248	5.7 (5.0 to 6.4)
Special project	823	19.0	823	19.0 (17.8 to 20.2)
Other	322	7.4	322	7.4 (6.6 to 8.2)
Completed counselling				
No	1692	39.1	3371	77.9 (77.9 to 79.9)
Yes	475	11.0	959	22.1 (20.1 to 24.2)
Missing observation	2163	49.9		
Disclosure status				
Yes	505	30.4	3104	71.7 (69.4 to 74.0)
No	1316	11.7	1226	28.3 (26.0 to 30.6)
Missing observation	2509	57.9		
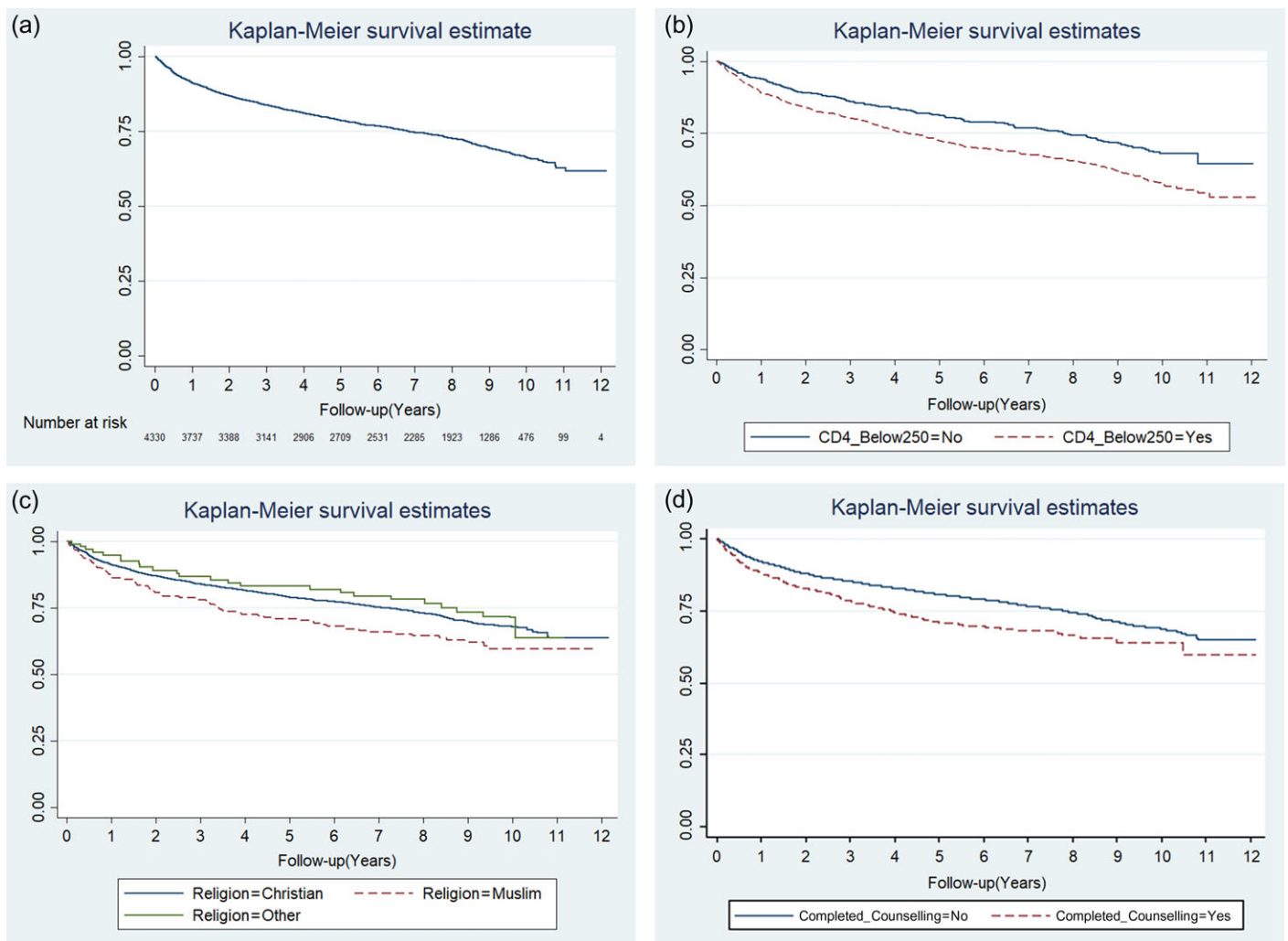
Figure 2. (**A**) Kaplan–Meier survival estimate of patients receiving HIV/AIDS care and LTFU. Those with a CD4 count <250 cells/ml had a significantly lower retention rate throughout the follow-up period compared with those with a CD4 count >250. (**B**) Logrank test: χ^2=946.57, p<0.001, having a CD4 count <250 cells/ml (HR 1.47 [95% CI 1.23 to 1.75]). Muslims had a significantly lower retention rate throughout the follow-up period compared with Christians. (**C**) Logrank test: χ^2=428.66, p <0.001, being a Muslim (HR 1.31 [95% CI 1.05 to 1.63]). Those who had completed adherence counselling had a significantly lower retention rate throughout the follow-up period compared with those who had not completed adherence counselling. (**D**) Logrank test: χ^2=1295.8, p<0.001, having completed adherence counselling (HR 1.45 [95% CI 1.23 to 1.72]).

among various characteristics. Log-rank tests were used to test for significance between the survival curves the Kaplan–Meier estimates produced.

Variables

The outcome of interest was LTFU status. An individual was classified as LTFU when she/he did not visit the clinic 90 d after their appointment date and had not been classified as 'died' or 'transferred out' in the database. The independent variables included sex, age, marital status, educational background, employment status, religion, weight at baseline, CD4 count at registration, the source of health care funding, completion of adherence counselling sessions prior to ART initiation and disclosure of disease status.

Results

Sociodemographic and clinical characteristics of patients

A total of 4330 PLWHA were registered to receive ART follow-up care from 1 January 2006 to 31 December 2017. The study participants had a median age of 34 years (interquartile range [IQR] 28–42) with majority being female (73% [n=3148]). About two-thirds (64% [n=2766]) were married or cohabiting and 7% (n=297) were widowed. Most participants (64% [n=2766]) had a basic education (junior high or middle school) and 10% had a tertiary education (n=417). The majority (87% [n=3766]) were employed and most were Christians (92% n=3971]) (Table 1).

The study participants had a median baseline weight of 64 kg (IQR 54–99) and the majority (54% [n=2326]) had a baseline CD4

Table 2. Factors associated with LTFU among patients receiving HIV/AIDS care at Accra Regional Hospital, 2006–2017

Variable	Unadjusted			Adjusted		
	HR	95% CI	p-Value	aHR	95% CI	p-Value
Age group (years)						
10–24	Ref					
25–39	0.98	0.80 to 1.20	0.86			
40–53	0.97	0.78 to 1.21	0.82			
≥54	1.04	0.78 to 1.39	0.80			
Gender						
Female	Ref					
Male	1.03	0.91 to 1.17	0.63			
Marital status						
Single	Ref					
Married/cohabiting	0.99	0.86 to 1.16	0.95			
Divorced/separated	1.11	0.88 to 1.41	0.36			
Widow(er)	0.88	0.67 to 1.15	0.36			
Religion						
Christian	Ref			Ref		
Muslim	1.31	1.05 to 1.63	0.02*	1.31	1.05 to 1.65	0.02*
Other	0.87	0.60 to 1.27	0.47	0.97	0.66 to 1.42	0.89
Weight (kg)						
<45	Ref			Ref		
46–60	1.10	0.82 to 1.47	0.51	1.15	0.85 to 1.56	0.35
≥61	0.85	0.63 to 1.14	0.28	0.96	0.71 to 1.31	0.80
CD4 count <250 cells/ml						
No	Ref			Ref		
Yes	1.47	1.23 to 1.75*	0.00	1.45	1.21 to 1.76	0.00*
Source of funding						
Out of pocket	Ref			Ref		
Medical insurance	1.17	0.83 to 1.67	0.37	1.03	0.72 to 1.48	0.87
Special project	0.98	0.84 to 1.13	0.76	1.05	0.90 to 1.21	0.56
Other	0.74	0.58 to 0.93*	0.01	0.74	0.58 to 0.94	0.01*
Completed counselling						
No	Ref			Ref		
Yes	1.45	1.23 to 1.72	0.00*	1.58	1.31 to 1.92	0.00*
Disclosure status						
No	Ref			Ref		
Yes	0.96	0.79 to 1.18	0.73	0.80	0.65 to 0.98	0.05*

*p-Value ≤0.05.
Ref: reference.

cell count >250 cells/ml. Most paid for health care services out of pocket (68% [n=2937]), 19% (n=823) were on a special project funded by Global Fund that paid for their health care delivery services and 6% (n=248) used some kind of medical insurance. Seventy-eight percent (n=3371) had completed adherence counselling sections and 72% (n=3104) had disclosed their status (Table 1).

Retention in care

The participants were followed up for a median of 7.4 y (IQR 2.6–9.3), contributing 26 677 person-years of follow-up. Approximately 91%, 87%, 84% and 81% of patients were retained in care at 12, 24, 36 and 48 months, respectively, during the follow-up period. By the end of the study period, 196 had died (4.5%), 312 (7.2%) were transferred out and 1166 were LTFU (26.9%).

The probability of survival is shown according to overall retention (Figure 2a), baseline CD4 count (Figure 2b), religion (Figure 2c) and counselling status (Figure 2d).

Factors associated with follow-up status using the Cox proportional regression model

The participants' reported religious belief, laboratory-confirmed CD4 cell count, completion of adherence counselling, source of

health care funding and disclosure of HIV status were predictive of LTFU. Factors associated with an increased risk of LTFU, after adjusting for all other covariates, included being a Muslim compared with being Christian (adjusted hazard ratio [aHR] 1.31 [95% CI 1.05 to 1.65]), having a CD4 count <250 cells/ml compared with having a CD4 count >250 cells/ml (aHR 1.45 [95% CI 1.21 to 1.76]). Participants who paid for ART services with 'other' sources of funding (other than medical insurance or the special project) compared with those who paid out of pocket were less likely to be lost to follow-up (aHR 0.74 [95% CI 0.58 to 0.94]) holding all other variables constant.

After adjusting for marital status, religion, CD4 count and source of funding, those who had completed counselling were more likely to be lost to follow-up (aHR 1.58 [95% CI 1.31 to 1.92]), whereas those who had disclosed their HIV status were less likely to be lost to follow-up (aHR 0.80 [95% CI 0.65 to 0.98]) (Table 2).

Discussion

This study assessed the effect of selected sociodemographic and clinical factors with LTFU among PLWHA receiving HIV/AIDS care at the Greater Accra Regional Hospital. After 12, 24, 36 and 48 months approximately 91%, 87%, 84% and 81% of patients, respectively, were retained in care. These figures are generally higher than the overall retention in other low- and middle-income countries as found by Fox and Rosen[15] in their systematic review on retention of adult patients on ART in care. In that study, retention after 12, 24, 36 and 48 months in Africa was 81%, 71%, 65% and 60%, respectively. This may be because the figures found in the latter study are an average of a number of African countries, which may have higher or lower retention rates.

Having 26.9% of participants lost to follow-up falls within the prevailing rates of LTFU in Africa, which ranges from 15% to 45%.[18] The 26.9% observed in our study is higher than the 22.6% found in the Pawi General Hospital in northwest Ethiopia and the 23.4% seen in the Tshepang Clinic in South Africa.[19,20] On the other hand, it is lower than the 33.6% witnessed in the Nkongsamba Regional Hospital and the 31.4% observed in the University of Gondar Hospital, both in Cameroon.[21,22] The differences could be accounted for by the different periods of study and operational definitions for LTFU. Despite the relatively low rate of LTFU in our study, it is imperative to aim at retaining all patients on treatment since LTFU is linked to negative health outcomes such as the spread of HIV infection and deaths.[18,23]

Although Muslims constituted only 5.7% of the study participants, they were at higher risk of LTFU compared with Christians, who constituted 91.7%. This may be a result of the greater stigma in Islamic communities, which attribute acquisition of HIV infection to involvement in illicit sex and drug-related activities.[24] Muslims found to have engaged in illicit sex and drugs are publicly punished[24] and hence those infected with HIV may be less motivated to receive care in public places where they can be identified. In addition, the facility studied has some large Muslim settlements nearby and is utilized by members of these communities, increasing the likelihood of being identified by a familiar person. Also, the finding may be a reflection of how the clinic appointment system is organized. Booking Muslim patients for follow-up care on Fridays, which is their day of worship, might make it difficult for them to honour appointments. A review of the last appointment dates suggests about 41% of the 84 Muslims who were LTFU were assigned to the Friday clinic for their follow-up care.

Our findings corroborate literature from Kenya, Cote D'Ivoire, Malawi, Zambia, Guinea-Bissau and South Africa indicating that decreasing CD4 cell count elevates the risk of LTFU.[16,25,26] Patients with a CD4 cell count <250 cells/ml were 1.5 times as likely to be lost to follow-up compared with those with a CD4 cell count >250 cells/ml. This may be accounted for by the fact that some patients die and relatives do not inform their caregivers in the clinic. Also, relatives at home may not know patients need support to report for treatment, because the patient has not disclosed his/her status. Similarly, patients with high CD4 cell counts have high LTFU rates because they do not feel sick and therefore do not feel the need to go for medical consultations.

The study found that patients who were on medical insurance, special project or relied on other sources of funding were less likely to be LTFU relative to those who paid for services out of their own pockets. However, only patients who relied on other sources of funding were significantly associated with a lower risk of LTFU compared with those who paid out of pocket. The other sources of funding included support from families, friends, communities and undisclosed sources. These sources of funding may cover other benefits not covered under the national health insurance and special project.

Prior to testing, people are offered counselling to provide them with information on HIV/AIDS and its management.[27] Those diagnosed positive are initiated into lifetime counselling on HIV/AIDS treatment. However, our findings suggest that clients who completed the initial counselling process were at higher risk of LTFU. Further research is recommended to explore the underlying reason(s) for this finding.

Disclosing one's status was strongly associated with a lower risk of LTFU. This corroborates literature indicating that disclosing one's HIV/AIDS status could be beneficial for patients, partners and families.[28] Disclosure may alleviate the stressful burden of concealment, enhance material and emotional support and facilitate self-acceptance of one's condition as well as shared responsibility for safer sex practices.[29,30] Patients in our study might have disclosed their status to people who provided them with support.

Our study has limitations worth sharing. The proportion of LTFU might have been overestimated due to self-transfers, which are likely but could not be measured in this study. Some patients might have switched treatment facilities without observing the protocol for transfer. Some of the deaths and those transferred out might be misclassified since follow-up contacts were not made to confirm the outcomes, which might be a threat to internal validity. Prior to 2011, the NACP was using a CD4 cut-off of 250 cells/ml with 'yes' or 'no' categories, making it difficult to compare with many studies. Also, data with missing values might have introduced bias. Similarly, variables such as treatment regimen, comorbidity and distance to facilities were not covered in the study. Therefore, care should be taken in generalizing the findings.

Conclusions

The study demonstrates that the probability of retention in ART follow-up care decreases over time. The risk factor for LTFU included being a Muslim, having a lower CD4 cell count and having completed counselling. In contrast, disclosing HIV/AIDS status and other funding sources were protective of LTFU. It is therefore recommended that the hospital should adopt an appointment system that allows patients to select suitable days for the clinic. Similarly, patients with lower CD4 cell counts should be provided with extra care and further studies should be conducted regarding the approach to counselling in the facility.

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