Original Article

Effect of Baseline Symptom Manifestations on Retention in Care and Treatment among HIV-Infected Patients in Nigeria

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Abstract

Background: Symptom management is an important component of HIV care. But symptom patterns and how they affect engagement with HIV care and treatment services have not been adequately explored in the era of increased HIV treatment scale-up. We investigated the relationship between symptom patterns among people living with HIV (PLHIV) and 12 months retention in care, within the context of other clinical and demographic characteristics. **Methods:** Retrospective cohort analysis of 5114 PLHIV receiving care within a large HIV treatment program in Nigeria. We assessed the prevalence and burden of baseline symptoms reported during routine clinic visits from January 2015 to December 2017. Multivariable regression was used to identify relationships between 12-month retention and symptom dimensions (prevalence and burden) while controlling for demographic and other clinical variables. **Results:** Increasing symptom burden was associated with higher likelihood of retention at 12 months (adjusted odds ratio [aOR] = 1.19 [95% confidence interval, CI: 1.09-1.29]; $P < .001$) as was the reporting of skin rashes/itching symptom (aOR = 2.59 [95% CI: 1.65-4.09]; $P < .001$). Likelihood of retention reduced with increasing World Health Organization (WHO) Clinical staging, with CD4 ≥500 cells/mL and self-reported heterosexual mode of HIV transmission. **Conclusions**: Symptom dimensions and standardized clinical/immunological measures both predicted retention in care, but effects differed in magnitude and direction. Standardized clinical/immunological measures in HIV care (eg, WHO clinical staging and CD4 count categories) can mask important differences in how PLHIVs experience symptoms and, therefore, their engagement with HIV care and treatment. Symptom management strategies are required alongside antiretroviral treatment to improve outcomes among PLHIV, including retention in care.

Keywords

symptoms, antiretroviral therapy, retention, treatment outcomes

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Introduction

Nigeria has made significant progress in the fight against HIV/AIDS, and much of this progress is attributable to increased access to antiretroviral treatment (ART) services. At the end of 2018, 80% of known people living with HIV (PLHIV) in Nigeria were on ART.[1] This increased treatment coverage has increased optimism about Nigeria's ability to achieve global and national HIV goals by 2030.

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What Do We Already Know about This Topic?

Symptom management is an important component of HIV care and plays an important role in how people living with HIV engage with care and treatment.

How Does Your Research Contribute to the Field?

This research advances knowledge about HIV care by investigating the relationship between symptom patterns among people living with HIV and retention in care and treatment.

What Are Your Research's Implications toward Theory, Practice, or Policy?

To ensure maximum engagement with care, HIV care providers and health systems need to place equal emphasis on both symptom assessment/management and antiretroviral therapy.

Despite the scale-up of treatment services, treatment outcomes among PLHIV remain suboptimal. Recently conducted National AIDS Indicator and Impact Survey showed that less than half of PLHIVs on treatment are virologically suppressed.[2] Documented barriers to optimal treatment outcomes include poor adherence and retention in care, disruptions in the health services and drug delivery, health worker strikes, poor clinic experiences, suboptimal patient–provider relationships, and long wait times.[3-5] But beyond service delivery challenges, PLHIV also experience a high prevalence and burden of self-reported symptoms along the care cascade that has been shown to interfere with the effectiveness of ART toward optimal outcomes.[5-8] Studies have shown association between symptom burden and sexual risk taking,[9] poor adherence to treatment,[10,11] and viral rebound.[12] This shows that symptom management is an essential component of care alongside ART in every stage of HIV infection.[13]

In Nigeria, the relationships between symptoms and treatment outcomes among PLHIV have not been well explored. Most of the studies on treatment outcomes among PLHIV have focused on standardized clinical and laboratory measures (eg, World Health Organization [WHO] clinical staging and CD4 count) to assess the relationships between symptoms reporting, disease status, and treatment outcomes.[14-18] However, standardized measures such as WHO clinical staging and CD4 count are limited because such measures can mask important differences in how individuals within the same clinical or immunological categories experience symptoms. For instance, while some PLHIV with advanced WHO clinical stage and low CD4 count may feel very ill, others may feel relatively well, and such differences may be important for how individuals engage with HIV care and treatment.

We, therefore, conducted this study to examine the relationships between symptom dimensions and retention in care among PLHIV in Nigeria. The objective was to determine symptom prevalence among PLHIV and to determine whether symptom burden was associated with retention in care within the context of other clinical and demographic characteristics. We hypothesized that there are important differences in symptom types that may explain observable differences in retention among Nigerian PLHIV. We also hypothesized that increasing symptom burden is associated with higher likelihood of being retained in care.

Given ongoing efforts at ART scale-up, and the limited knowledge on the role that patient symptoms play in treatment outcomes, findings from this study will be relevant in assisting treatment and care services to better respond to needs and concerns of PLHIV.

Methods

Setting

This study was conducted within selected comprehensive HIV clinics supported by the APIN Public Health Initiatives Ltd/Gte treatment network (known as APIN). APIN, a United States President's Emergency Plan for AIDS Relief (PEPFAR) implementing partner, provides technical and programmatic support to 285 comprehensive HIV care and treatment health-care facilities, located within 95 local government areas (LGAs) in 8 states in Nigeria (the country has a total of 774 LGAs distributed across 36 states). APIN-supported comprehensive sites provide care for adults and children; prevention of mother-to-child-transmission services; laboratory services including viral load, CD4 count, and routine safety and monitoring laboratory test results; and pharmacy services for ART dispensing. The study was conducted at 5 of these comprehensive clinics located in Lagos, Oyo, and Plateau states. All sites had provided adult HIV prevention, care, and treatment services for at least 1 year at the time of the study and had the infrastructure to electronically document symptoms data and administer on-site viral load testing. Stable patients on ART, defined as asymptomatic patients who have been virologically and/or immunologically suppressed, had monthly visits for ART pick-up and 6 monthly clinic follow-up visits unless otherwise indicated.

Study Design

We conducted a retrospective cohort study of adults enrolled in HIV care and treatment at eligible APIN sites between January 1, 2015, and December 31, 2017. Participants were included in this study if they met the following inclusion criteria: (1) greater than 15 years of age, (2) enrolled in HIV care and initiated treatment at the selected study sites, and (3) known to be alive during the 12 months following ART initiation. Patients were excluded if (1) they were pregnant at the time of enrollment, (2) became pregnant during the 12-month follow-up period, (3) were on second-line ART, (4) were self-referred for care, or (5) had stopped and restarted ART.

Exclusion was to ensure uniformity in the standard of care received, as the excluded patient groups had a treatment protocol that differed from the standard treatment protocol within the APIN program.

The exposure of interest was symptom reporting at baseline. The symptoms were recorded by clinicians using the following questions from the clinical encounter visit form: (1) "any symptoms (current or since last visit)?" and (2) "if yes, specify symptoms." The patients then identified specific physiological and psychiatric symptoms that they were experiencing, which were then verified by a clinician following an assessment (see Supplementary material for symptom assessment tool). Patients were classified as having symptom manifestations if they answered yes to the first question and had 1 or more symptoms reported at ART initiation. The main outcome of interest was retention in care at 12-month post-ART initiation. Retention was defined as keeping the last scheduled appointment within 12 months post-ART initiation, evidenced by documented clinic visit and/or drug pickup.

Data Collection and Analysis

Baseline characteristics. All data were collected on nationally approved program and developed structured data entry forms. These forms were then entered into the electronic database. Demographic characteristics included age, sex, level of education, occupation, employment, and marital status. Clinical and immunological characteristics included baseline WHO clinical staging and baseline CD4 count, respectively.

Symptom prevalence and burden. We computed symptom burden by adding the number of self-reported symptoms at baseline for each patient. Symptom prevalence was measured by calculating the proportion of symptom-reporting patients who reported a specific symptom at baseline.

Differences in symptom burden and retention. We summarized baseline demographics, clinical, and immunological characteristics and symptoms of the cohort. We regrouped some variables as follows: baseline CD4 variable into 4 categories (<200 cells/mL, ≥200-349 cells/mL, ≥350-499 cells/mL, and ≥500 cells/mL); HIV risk factor was recategorized from 7 groups (heterosexual, intravenous drug users, men who have sex with men, mother to child transmission, occupational exposure, transfusion, and unknown) into 3 categories (heterosexual, unknown, and other) due to small numbers in some of the subgroups. We used bivariate analysis to assess demographic and clinical differences in symptom burden and to explore the association between patient characteristics and retention in care. We used multivariable logistic regression to measure the independent associations between symptom characteristics and retention in care, accounting for sociodemographic (sex, level of education, occupation, employment, and marital status), clinical, and immunological characteristics (baseline CD4 count and/or WHO stage) of study participants. Factors were included in the multivariable model if they were significant ($P < .10$) in bivariate analysis. Individual symptoms with a prevalence of at least 10% were also included in the multivariable model. A process of backward elimination using likelihood ratio tests was then used to build the final adjusted multivariable model.

Approval of Institutional Review Board

We obtained approval to conduct this secondary data analysis from the National Health Research Ethics Committee in Nigeria.

Results

Baseline Characteristics of Study Population

A total of 5114 HIV-positive patients met our inclusion criteria and were included in the analysis. The cohort was predominantly female (64.45% versus 35.55%). The median age was 37 (interquartile range [IQR]: 30-45) at ART initiation, with the median age higher among males 40 (IQR: 33-48) compared to females, 35 (IQR: 29-43). Over a third (35.53%, n = 1817) of the cohort attained at least secondary education, and most (63.47%, n = 3246) were either self-employed/artisans or owned a business. Half (50.33%, n = 2574) of the population reported being married. Almost half (48.26%, n = 2060) of the population had CD4 <200, with 23.57% (n = 796) being at advanced WHO clinical stages 3 and 4. The majority (72.23%) reported having acquired HIV through heterosexual transmission (Table 1).

Symptom Prevalence and Burden

A total of 1347 (26.3%) patients reported symptoms at baseline. Among these symptom-reporting patients, most (93.32%, n = 1257) were 25 years and above; there were fewer males compared to females (36.45% versus 63.55%), and most were educated up to either primary (25.17%, n = 339) or secondary level (38.23%, n = 515). More than half (51.15%, n = 689) were married and most were self-employed or owned a business (73.72%, n = 993). Majority (60.72%, n = 719) had a baseline CD4 count less than 200 cells/mL, with fewer presenting at advanced WHO clinical stages 3/4 (33.5%, n = 257), compared to stages 1/2 (66.5%, n = 510).

Of the total of 28 symptoms reported, the most prevalent symptoms were cough (29.84%); ear, nose and throat symptoms (20.34%); constipation/diarrhea (19.82%); itching/rash (19.38%); pains (17.89%), and headache (15.81%; Table 2). Individuals reported a range of 1 to 14 symptoms at baseline, but more than half (54.68%) of those reporting any symptoms reported only 1 (Table 3).

Symptom burden was unrelated to baseline CD4 count. However, symptom burden was lower in patients with advanced WHO clinical stage 3 (odds ratio [OR]: 0.8, $P < .05$) or stage 4 (OR: 0.65, $P < .05$) compared to those with WHO stage 1 disease. Females had a higher symptom burden than men (OR: 1.26; $P < .05$), people who were married or had an "other" designated marital status had increased symptom

Table 1. Patient Demographic and Baseline Characteristics.

		Total Study Population, N = 5114		Patients Without Symptoms at Baseline, n = 3767)		Patients With Symptoms at Baseline, n = 1347	
Variable	Category	Number	Percentages (95% CI)	Number	Percentages (95% CI)	Number	Percentages (95% CI)
Sex	Female	3296	64.45 (63.13-65.76)	2440	64.77 (63.22-66.28)	856	63.55 (60.94-66.08)
	Male	1818	35.55 (34.25-36.87)	1327	35.22 (33.71-36.77)	491	36.45 (33.92-39.06)
Age, years	15-24	529	10.34 (9.54-11.21)	439	11.65 (10.67-12.72)	90	6.68 (5.46-8.15)
	25 & above	4585	89.66 (88.79-90.46)	3328	88.35 (87.28-89.33)	1257	93.32 (91.85-94.54)
Education	None	798	15.6 (14.63-16.63)	574	15.24 (14.12-16.42)	224	16.62 (14.73-18.71)
	Primary	1106	21.63 (20.52-22.78)	767	20.36 (19.1-21.68)	339	25.17 (22.92-27.56)
	Secondary	1817	35.53 (34.23-36.85)	1302	34.56 (33.06-36.09	515	38.23 (35.67-40.86)
	Tertiary	1393	27.24 (26.04-28.48)	1124	29.83 (28.4-31.32)	269	19.97 (17.92-22.19)
Marital status	Married	2574	50.33 (48.96-51.7)	1885	50.04 (48.44-51.64)	689	51.15 (48.47-53.82)
	Single	1364	26.67 (25.48-27.9)	1094	29.04 (27.61-30.51)	270	20.04 (17.99-22.27)
	Others	1176	23 (21.86-24.17)	788	20.92 (19.65-22.25)	388	28.80 (26.45-31.29)
Occupation	Own business/ Self-employed	3246	63.47 (62.14-64.78)	2253	59.81 (58.23-61.36)	993	73.72 (71.29-76)
	Employee	956	18.69 (17.65-19.79)	768	20.38 (19.18-21.76)	188	13.96 (12.2-15.91)
	Student	459	8.98 (8.22-9.79)	389	10.33 (9.39-11.34)	70	5.19 (4.13-6.52)
	Unemployed	453	8.86 (8.11-9.67)	357	9.48 (8.58-10.46)	96	7.12 (5.87-8.63)
HIV risk factor	Heterosexual	3,694	72.23 (70.99-73.44)	2,682	71.19 (69.72-72.62)	1,012	75.13 (72.75-77.37)
	Others	187	3.66 (3.18-4.21)	153	4.06 (3.48-4.74)	34	2.52 (1.81-3.51)
	Unknown	1,233	24.11 (22.96-25.3)	932	24.74 (23.39-226.15	301	22.35 (20.19-24.65)
Baseline CD4 count, cells/mL	<200	2060	48.26 (46.77-49.77)	1341	43.48 (41.74-45.24)	719	60.72 (57.91-63.47)
	200-349	951	22.28 (21.06-23.56)	738	23.92 (22.46-25.47)	213	17.98 (15.9-20.29)
	350-499	568	13.31 (12.32-14.36)	444	14.39 (13.2-15.68)	124	10.47 (8.86-12.35)
	>500	689	16.14% (15.07-17.28)	561	18.19 (16.87-19.59)	128	10.81 (9.16-12.71)
Baseline WHO Stage	Stage 1	1822	53.97 (52.28-55.65)	1537	58.91 (57.01-60.79)	285	37.16 (33.79-40.64)
	Stage 2	758	22.45 (21.07-23.89)	533	20.43 (18.93-22.02)	225	29.34 (26.21-32.66)
	Stage 3	635	18.8 (17.53-20.16)	437	16.75 (15.36-18.23)	198	25.81 (22.83-29.04)
	Stage 4	161	4.77 (4.10-5.54)	102	3.91 (3.22-4.72)	59	7.69 (6-9.8)

Abbreviations: CI, confidence interval; WHO, World Health Organization.

burden compared to those who were single (OR: 1.93, $P < .01$). Compared to no education, higher levels of education were associated with higher symptom burden (primary education OR: 2.12, $P < .001$; secondary education OR: 1.79, $P < .001$). Business owners and employees reported significantly higher symptom burden compared to students (OR: 2.53, $P < .001$ versus OR: 1.39, $P = .06$). Older age (>25) was significantly associated with increasing symptom burden (OR: 1.33, $P < .05$). Patients with known HIV risk factor reported higher symptom burden than those whose risk factor was unknown (heterosexual OR: 4.54, $P < .001$, other OR: 2.9, $P < .001$; Table 4).

Factors Associated with Retention

Baseline CD4 count was predictive of retention, as those having baseline CD4 of 500 and above were less likely to be retained (adjusted OR [aOR] = 0.55 [95% confidence interval, CI: 0.43-0.71]; $P < .001$). Similarly, patients with higher WHO baseline clinical staging were less likely to be retained, reaching statistical significance at WHO stage 3 (aOR = 0.44 [95% CI: 0.35-0.54]; $P < .001$) and stage 4 (aOR = 0.31 [95% CI: 0.21-0.45]; $P < .001$). The type of HIV risk factor was also predictive as heterosexuals (aOR = 0.67 [95% CI: 0.53-0.83]; $P < .001$), and other categories of HIV transmission (aOR = 0.57[95% CI: 0.35-0.92]; $P < .05$) had a reduced likelihood of retention. Among individual symptoms included in the multivariate model, itching/rash was associated with an increased likelihood of retention at 12 months (aOR = 2.59 [95% CI: 1.65-4.09]; $P < .001$). Symptom burden also predicted retention; the higher the number of symptoms reported, the higher the likelihood of being retained by 12 months (aOR = 1.19[95% CI: 1.09-1.29]; $P < .001$; Table 5).

Discussion

Our study shows that symptom reporting is fairly common among PLHIV and is associated with advanced clinical disease. We also show that symptom dimensions within the context of clinical and individual sociodemographic characteristics can influence retention in care. In terms of most prevalent symptoms among PLHIVs, our findings are comparable to what has been reported in the literature, although our proportions were generally lower than those from other studies.[19-27] For example, some African studies showed cough prevalence as 53% (versus 29.84%), itching and skin changes 52% to 67% (versus 19.38%), and pain 76% (versus 17.89%).[20,29] Those studies, however, had much smaller sample sizes and were conducted

Table 2. Symptom Prevalence.

Symptom	Prevalence, n = 1347
Cough	29.84%
Ear, nose and throat symptoms	20.34%
Constipation/diarrhea	19.82%
Itching/rashes	19.38%
Pains	17.89%
Headaches	15.81%
Loss of appetite	9.43%
Genitourinary symptoms	7.28%
Malaise	5.64%
Psychiatric symptoms	5.57%
Fever	5.27%
Weight loss	4.97%
Dizziness	4.68%
Nausea/vomiting	4.16%
Cardiovascular symptoms	4.01%
Heartburn/indigestion	4.01%
Fatigue	3.12%
Night sweats	2.82%
Fat maldistribution	2.52%
Aches	1.93%
Swollen lymph nodes	1.93%
Difficulty walking	1.71%
Anal/rectal symptoms	1.04%
Difficulty in swallowing	0.97%
Rigors	0.89%
Poor sleep	0.74%
Memory loss	0.37%

Table 3. Symptom Burden.

Symptom Burden (Number of Symptoms/Person)	Number of Patients	Proportion
0	3767	73.66%
1	718	14.04%
2	331	6.47%
3	147	2.87%
4	64	1.25%
5	32	0.63%
6	27	0.53%
7	15	0.29%
8	5	0.10%
9	4	0.08%
10	1	0.02%
11	1	0.02%
13	1	0.02%
14	1	0.02%
	5114	100%

among PLHIV at advanced stages of clinical disease. Nevertheless, the similarity in types of prevalent symptoms between our study and previous studies support the emerging emphasis on symptom clustering among PLHIV.[29] We also found that sociodemographic factors (female, higher education up to secondary level, nonsingle marital status, and increasing age) were all associated with increased symptom burden. Contrary to what might be expected, WHO clinical stages 3 and 4 were associated with lower symptom burden, while CD4 count at baseline was not related to symptom burden.

Table 4. Associations between Symptom Burden and Demographic/Clinical Characteristics of Participants.

Variable	Category	OR (95% CI)	*P* Value
Sex	Male	Ref	
	Female	1.26 (1.1-1.44)	.01
Education	No education	Ref	
	Primary	2.12 (1.71-2.62)	.00
	Secondary	1.79 (1.47-2.19)	.00
	Tertiary	1.03 (0.83-1.28)	.77
Marital Status	Single	Ref	
	Married	1.93 (1.64-2.27)	.00
	Others	1.93 (1.6-2.32)	.00
Occupation	Student	Ref	
	Employee	1.39 (0.99-1.94)	.06
	Unemployed	1.27 (0.94-1.72)	.11
	Business/Self-employed	2.53 (1.95-3.29)	.00
HIV risk factor	Unknown	Ref	
	Heterosexual	4.54 (3.72-5.55)	.00
	Others	2.91 (1.98-4.28)	.00
Age group	15-24	Ref	
	25 & above	1.33 (1.08-1.65)	.01
Baseline CD4	<200	Ref	
	200-349	0.96 (0.81-1.15)	.69
	350-499	1.08 (0.87-1.33)	.48
	500 and above	1.16 (0.96-1.4)	.13
WHO Stage	Stage 1	Ref	
	Stage 2	1.01 (0.85-1.22)	.84
	Stage 3	0.80 (0.66-0.98)	.04
	Stage 4	0.65 (0.44-0.95)	.03

Abbreviations: CI, confidence interval; WHO, World Health Organization.

Results from this study suggests that symptom dimensions within the context of clinical and individual sociodemographic characteristics can influence retention in care. Most of the predictors for retention in our study were more of immunologic/clinical factors (WHO stage, CD4 count, and symptom dimensions) than sociodemographic factors (HIV risk factors). However, we found differing magnitude and direction of effect for these predictors. For example, while advanced WHO Clinical stages (stages 3 and 4) and CD4 count >500 cells/mL reduced the likelihood of retention, symptom burden and symptom type (itching/rash) increased the likelihood of retention. In line with previous studies, our findings show that low retention is common among PLHIVs at both extremes of the clinical spectrum (the very sick with WHO stages 3 and 4, and the very healthy with CD4 >500 cells/mL). Our findings suggest that, in-between these 2 clinical extremes, symptom dimensions are important determinants of retention in care. However, studies have shown that providers often miss up to two-thirds of patient-reported HIV-related symptoms when providing care, particularly when these symptoms are not associated with extreme clinical illness.[26] In such scenario, broad clinical categorizations (eg, WHO clinical staging or CD4) mask important differences in patient symptom experiences that may affect retention.

Table 5. Multivariable Regression Parameters for Factors Associated with Retention at 12 Months.

Variable and Categories		Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Sex	Male	Ref			
	Female	1.03 (0.86-1.24)	.73		
Education	No education	Ref			
	Primary	1.12 (0.86-1.48)	.85		
	Secondary	1.09 (0.85-1.41)	.49		
	Tertiary	1.30 (0.97-1.74)	.08		
Marital Status	Single	Ref			
	Married	0.89 (0.71-1.13)	.35		
	Others	1.09 (0.83-1.44)	.52		
Occupation	Student	Ref			
	Employee	0.80 (0.50-1.28)	.36		
	Unemployed	0.88 (0.56-1.36)	.55		
	Owns business/Self-employed	0.87 (0.57-1.31)	.49		
HIV risk factor	Unknown	Ref			
	Heterosexual	0.67 (0.54-0.85)	.00	0.67 (0.53-0.83)	.00
	Others	0.55 (0.34-0.91)	.02	0.57 (0.35-0.92)	.02
Age group	15-24	Ref			
	25&above	0.96 (0.68-1.36)	.83		
Baseline CD4	<200	Ref			
	200-349	1.09 (0.88-1.36)	.43	1.11 (0.89-1.39)	.32
	350-499	1.03 (0.79-1.34)	.82	1.05 (0.81-1.36)	.71
	500 and above	0.53 (0.41-0.68)	.00	0.55 (0.43-0.71)	.00
WHO Stage	Stage I	Ref			
	Stage2	0.92 (0.74-1.15)	.47	0.92 (0.73-1.14)	.44
	Stage3	0.43 (0.35-0.55)	.00	0.44 (0.35-0.54)	.00
	Stage4	1.3 (0.97-1.74)	.00	0.31 (0.21-0.45)	.00
Cough	No cough	Ref			
	Cough	0.98 (0.65-1.45)	.91		
Headache	No headache	Ref			
	Headache	1.67 (0.98-2.85)	.06		
Pains	No pains	Ref			
	Pains	1 (0.65-1.56)	.98		
Constipation/Diarrhea	No constipation/diarrhea	Ref			
	Constipation/diarrhea	0.84 (0.56-1.26)	.41		
Itching/rashes	No itch/rashes	Ref			
	Itching/rashes	2.62 (1.65-4.19)	.00	2.59 (1.65-4.09)	.00
ENT	No ENT symptoms	Ref			
	ENT symptoms	0.79 (0.54-1.16)	.24		
Symptoms	No symptoms	Ref			
	Have symptoms	0.94 (0.69-1.28)	.69		
Symptom burden		1.21 (1.11-1.33)		1.19 (1.09-1.29)	.00

Abbreviations: ENT, ear, nose and throat; CI, confidence interval; OR, odds ratio; WHO, World Health Organization.

Our findings suggest better retention/engagement with care due to higher symptom burden. However, in the current HIV policy climate of "test and start" where CD4 and WHO clinical staging are no longer eligibility requirements for initiating patients on ART, unintended changes to clinical assessment processes may occur in order to accommodate faster ART initiations. Ongoing rapid scale-up of ART services in the face of severe human resource for health shortages also place care providers under pressure, resulting in the tendency to underemphasize symptom assessment and management in favor of quick ART provision for PLHIV. These kinds of adjustments in care provision can precipitate self-care strategies and predispose PLHIV to poor retention. Unaddressed symptoms may also reverse previous improvements in health-care outcomes and health-seeking behavior. While ART is no doubt an important component of clinical management of PLHIV, studies have shown that ART alone is insufficient in reversing some HIV-associated symptom burden/experience.[21]

Notably, we also found that itching/body rash symptoms independently increase the likelihood of being retained in care. Although dermatological/image-related and other stigma-predisposing symptoms (eg, weight loss and body rashes) are typically associated with advanced stages of the HIV course, our study suggests, in line with other studies, that stigma concerns can drive care engagement for PLHIV at every stage of the clinical disease spectrum.[20,21,28,29] This is very relevant in the context of test and start where majority of PLHIVs are more likely to present before advanced stage of the clinical disease

spectrum. While treatment and/or palliation from symptoms is a basic human right and requires no further justification, our study point to adherence and retention in care as important reasons to pay attention to and monitor symptoms among PLHIV.

Taken together, our study suggests that in order to derive maximum engagement and outcomes in care, providers and health systems need to place equal emphasis on both symptom assessment/management and ART. As HIV is fast becoming a chronic disease due to increasing life expectancy, need-based attention to symptom management has become more necessary, not less. Recorded progress may be hampered or even reversed if PLHIV perceive self- or alternative care to outweigh the benefits of being retained in care.

We note some limitations in this study. First, our study used only symptoms reported at baseline; we did not investigate how symptoms evolved over the period of follow-up, or how the side effects of ART could have affected symptom evolution and retention in care. Second, our study did not have a comparison cohort of PLHIVs not on ART and/or people not HIV-infected. We also did not collect information on or control for HIV-associated comorbidities, which may have biased our findings. Also, the different education levels of the study population could have influenced health literacy and the accuracy of symptom self-reporting, which could have impacted study findings. As a retrospective cohort study, our findings were also limited by missing data, which was expected given that data collection was in the context of routine service delivery. We attempted to control for missing data in analysis through listwise deletion method, but it is possible that patients missing certain information (and therefore excluded from certain analysis) differ from those analyzed, and this may have introduced some bias into our findings. Finally, our study may be limited in generalizing our findings, as it was conducted in health-care facilities that are funded by PEPFAR, which may differ in patient outcomes from health facilities not funded by PEPFAR.

Conclusion

Symptom dimensions are important determinants of PLHIV engagement with care and need to receive more attention alongside other known demographic, clinical, and immunological factors. Rather than relying only on standardized clinical/immunological measures, HIV care providers should target inquiries to patients regarding symptom burden and identify bothersome symptoms for management as a way to improve outcomes, including retention in care.

Authors' Note

J.A. conceived the study, conducted the analysis, wrote the first draft. O.A.B. assisted with analysis and writing of subsequent drafts. A.A., M.M., and L.P. provided critical reviews of all drafts. P.O., P.A.A., C.T.E., I.A., and T.J. contributed to study conception, oversight for study implementation, and critical reviews of all draft versions. B.L.A., I.O., R.M., P.A., J.M., P.A., and D.K. assisted with data analysis/interpretation and writing and critical reviews of manuscript drafts. All authors reviewed and approved the final draft of the manuscript.

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