

Going Beyond Giving Antiretroviral Therapy: Multimorbidity in Older People Aging with HIV in Nigeria

Abimbola Margaret Obimakinde,¹ Lawrence Adebusoye,²
Chad Achenbach,³ Adesola Ogunniyi,⁴ and David Olaleye⁵

Abstract

“Graying of HIV epidemic” is observed globally, as people living with HIV (PLWH) are aging, due to effectiveness of antiretrovirals. The normal aging processes and HIV-induced immune dysfunction, are potential mechanisms, driving multimorbidity (MM) in PLWH. MM is the concurrent presence of two or more diseases in a single individual. Aging PLWH, are at increased risk of acute and chronic morbidities compared with counterpart without HIV. Despite increasing concern in Nigeria, research on correlates of MM in aging PLWH is lagging. This was a comparative study, of ≥ 60 years of age, age-matched (± 5 years) HIV-positive and HIV-negative patients. Patients were recruited, from the Infectious Disease Institute and Geriatric clinics of the University College Hospital, Ibadan, Nigeria, between April and June 2018. MM was defined as the occurrence of more than two morbidities in an individual, and it was considered acute, when within 30 days and chronic, when above 3-months duration. Data analysis was done using SPSS 23. We studied 186 individuals (62 HIV-positive and 124 HIV-negative). The PLWH had lower mean age (63.9 vs. 68.1 years, $p = .00$, $t = 5.68$), more chronic MM (2.0 vs. 1.3, $p = .004$, $t = 2.970$), which occurred earlier (4.7 vs. 9.6 years, $p = .003$, $t = 3.05$), more overall MM (3.6 vs. 2.8, $p = .015$, $t = 2.448$), and lower quality of life (82.7 vs. 86.2, $p = .002$, $t = 3.130$). Risk estimates for “any” MM revealed the odds are in favor of the older PLWH [69.4% vs. 46.8%, $p = .004$, odds ratio = 0.388 (95% confidence interval = 0.204–0.740)]. Logistic regression revealed, age > 64 years, higher total body fat, lower nadir CD4 counts, and longer duration of HIV infection, were significantly associated with MM in aging PLWH ($p = .019$). Older individuals with HIV on antiretrovirals in Ibadan, had a significantly greater burden of MM compared with those without HIV. HIV treatment programs in Nigeria will need to adapt a comprehensive health care plan for aging PLWH.

Keywords: PLWH, multimorbidity, ART, aging, quality of life

Introduction

THIS IS THE ERA of “graying of HIV epidemic,” where many people living with HIV (PLWH), are aging due to the effectiveness of combination antiretroviral therapy (ART).^{1,2} The increasing number of older PLWH can also be attributed to the incidence of HIV infection among older adults.^{1–3} Globally, there is an estimate of 34.5 million chronically HIV-infected PLWH and currently, they constitute 10% of adults above the age of 50 years.⁴ There has been an increase in PLWH 50 years of age and above in the last two

decades.¹ In the United States of America, 50% of PLWH are above 50 years and it is projected that by 2030 this will increase to 70%.^{4,5} Nigeria has a 4.0% HIV prevalence in people 50 years of age and above, which is very close to the prevalence of 5.0% among younger people 15–49 years of age, buttressing the concern about “graying of HIV epidemic” in Nigeria.^{2,5} HIV infection is reported to enhance the aging process in PLWH, which may predispose them to multimorbidity (MM), with consequent high disease burden, poor quality of life, and risk of premature death.^{4,6} The European General Practice Research Network (EGPRN)

¹Family Medicine Unit, Department of Community Medicine, College of Medicine University and Family Medicine Department, University College Hospital, Ibadan, Nigeria.

²Geriatric Center, University College Hospital, Ibadan, Nigeria.

³Division of Infectious Disease and Cancer Epidemiology, Department of Medicine and Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.

⁴Neurology Unit, Department of Medicine, College of Medicine, University of Ibadan, Ibadan, Nigeria.

⁵Department of Virology, College of Medicine, University of Ibadan, Ibadan, Nigeria.

defined MM as any combination of chronic disease with at least one other disease (acute or chronic) or biopsychosocial factor (associated or not) or somatic risk factor.⁷ MM has also been defined as the presence of at least two morbidities in a person, which imparts on functionality, and it is categorized as acute if it occurs within a 6-week period and chronic when the condition has persisted for more than 3 months.⁷⁻¹⁰ There is an increased predisposition to acute morbidities in people burdened with chronic MM, hence the inclusion of acute health conditions in the primary care concept of MM, in view of holistic health care.^{7,9} Additionally, while chronic MM has been defined as the occurrence of greater than or equal to two chronic diseases in an individual, acute MM is defined as the presence of greater than one acute health condition concurrently occurring in the same individual.¹¹

Aging PLWH can be affected by a variety of non-HIV-related acute and chronic MM, including ocular problems, joint pains, hypertension, diabetes, degenerative musculoskeletal diseases, and peptic ulcer disease.^{1,6,7,12} Studies among HIV-positive patients, mostly defined MM as the co-occurrence of more than two age-associated chronic morbidities such as diabetes, cardiovascular disorders, metabolic syndrome, hypercholesterolemia, chronic liver disease, chronic kidney disease, and non-AIDS-related cancer.^{1,8,13,14} However, the National Institute for Health and Care Excellence (NICE) recognizes acute MM as part of the complexity of MM in the older age group, since all morbidities add up to determine their health care needs.¹⁰

The mechanism contributing to higher risk of MM, in aging PLWH are immune dysfunction, chronic inflammation, medication toxicity, other conditions associated with HIV persistence, and coinfections (e.g., hepatitis B and C).^{1,13,14} Lower CD4 cell counts, especially nadir CD4 and higher HIV RNA

levels in PLWH, coupled with interruption in use of ART are also associated with burden of MM in aging PLWH.^{2,5,13,14}

Interestingly, despite the global attention being paid to HIV epidemic, beyond administration, and monitoring of ART, MM among aging PLWH in Sub-Saharan Africa, has not been adequately studied.^{2,15} Hence, the need to study aging PLWH bearing in mind acute and chronic morbidities, as MM is increasing in this population.¹³⁻¹⁵ Thus, we studied the factors associated with MM among aging PLWH compared with those aging without HIV, in Nigeria.

Materials and Methods

We performed a cross-sectional study of consenting HIV-positive and HIV-negative older adults, 60 years of age and above, using ratio 1:2 and age-matched on ± 5 years. We focused on this age group, according to the UN (United Nations) cutoff age for the "elderly." Participants were enrolled in the study, between April and June 2018. PLWH were recruited from the AIDS Preventive Initiative of Nigeria (APIN), clinic, of the Infectious Disease Institute of the College of Medicine, University of Ibadan (UI), Nigeria. The age-matched HIV-negative participants were recruited from the geriatric center of the University College Hospital (UCH) Ibadan. Informed consent was obtained from all participants and ethics clearance was obtained from the UI/UCH Institutional Review Board (IRB).

Information on sociodemographic characteristics and current medical history were obtained from the participants and health records. MM was categorized as acute when it occurred within 30 days and chronic when the duration was more than 3 months, from the time of encounter with the patients at these clinics.

TABLE 1. CHARACTERISTIC OF STUDY PARTICIPANTS

N = 186 Characteristics	HIV-positive elderly (n = 62)	HIV-negative elderly (n = 126)	t-test/ χ^2	p
	Mean (\pm SD)	Mean (\pm SD)		
Mean age (in years)	63.9 (4.0)	68.1 (5.6)	5.68	.000
Gender, n (%)				
Female	39 (62.9)	98 (79.0)		
Male	23 (37.1)	26 (21.0)	5.54	.019
Marital status, n (%)				
Widowed/widower	28 (45.2)	38 (30.6)		
Married/separate/divorced	34 (54.8)	88 (69.4)	3.81	.051
Number of acute morbidities	1.6 (1.2)	1.5 (1.5)	0.317	.752
Number of medications for acute morbidities	1.6 (0.7)	2.5 (1.8)	2.74	.009
Chronic morbidities	2.0 (1.8)	1.3 (0.8)	2.972	.004
Years living with chronic morbidities	4.7 (4.6)	9.6 (9.0)	3.05	.003
Number of medications for chronic morbidities	2.2 (1.0)	3.2 (1.5)	3.32	.001
All MM (number of both acute and chronic MM)	3.6 (2.1)	2.8 (2.0)	2.448	.015
Total body fat (% body weight)	33.2 (11.8)	41.6 (9.2)	4.81	.000
Visceral fat (% body weight)	9.5 (4.2)	12.0 (4.5)	3.84	.000
BMI (kg/m ²)	25.7 (5.1)	29.5 (5.2)	4.78	.000
Systolic blood pressure (mmHg)	141.0 (24.8)	139 (12.6)	0.59	.000
Diastolic blood pressure (mmHg)	77.99 (14.1)	80.1 (5.9)	1.18	.244
PCV (%) ^a	12.8 (4.7)	36.7 (5.5)	31.08	.000
Fasting Plasma Glucose (mg/dL)	103.7 (26.6)	119.5 (31.9)	1.38	.185
WHOBref Quality-of-life Scores	82.7 (8.9)	86.2 (6.5)	3.130	.002

^aHemoglobin concentration; Hb (g/dL) = (PCV/3) (%).

BMI, body mass index; MM, multimorbidity; PCV, packed cell volume; SD, standard deviation.

The operational definition for MM used in this study, is in accordance with the NICE concept and the EGRN definition of MM. These organizations define MM as the presence of at least two chronic medical conditions in combination with at least one acute medical condition.⁷⁻⁹ Hence, for this study, chronic MM was taken as the presence of greater than or equal to two chronic diseases and acute MM was taken as the presence of greater than or equal to two acute diseases for uniformity and in the embrace of holistic primary care management of the elderly.

The details of the duration of HIV infection and treatments received, inclusive of records of HIV-RNA levels and CD4 counts, were obtained from the APIN clinic database. HIV-related opportunistic infections or diseases, for which the older PLWH were managed, within 6 months of data collection, were retrieved from the APIN database. All elderly patients, recruited from the geriatric center had HIV voluntary counseling and testing to confirm their HIV-negative status. All participants had the following measurements and tests done; weight, height, body mass index (BMI), estimated percentage of total body fat and visceral fat, blood pressure, packed cell volume (PCV; a measure of hemoglobin concentration) and fasting plasma glucose (FPG). Hypertension was defined as blood pressure >140/90 mmHg over two consecutive measurements, whereas FPG level >126 mg/dL was defined as diabetes mellitus. The estimated percentage total body fat (%TBF) and visceral fat were measured using the Omron HBF 510 body composition monitor machine.^{16,17} This is an inexpensive machine that uses dual electrical impedance technology for the estimation of percentage total body and visceral fat and it has been validated as a tool that can predict the metabolic syndrome.¹⁶⁻¹⁹

The quality of life was assessed using the brief version of the WHO quality of life instrument (WHOQL BREF). The WHOQOL-BREF is a 26-item instrument, which is scored on a response scale from 1 to 5, and the scores were transformed linearly to a 0-100 scale. It has excellent reliability (Cronbach's $\alpha=0.86$), and the lower the score on the WHOQOL-BREF, the poorer the quality of life.²⁰

Data management

Data were analyzed using SPSS version 23. Frequency table was used to present the morbidity patterns. The *t*-test was used for analysis and comparison of continuous variables between the two groups. The 2x2 risk estimation and logistic regression were done to compare and evaluate associations between participant characteristics and MM. A multivariate model of predictors of MM, among aging PLWH was conducted. All analyses were reported at a statistically significant level of *p*-value <.05.

Results

We enrolled 186 participants, 62 HIV-positive and 124 HIV-negative older adults, above 60 years of age. There were female preponderance in both groups, at prevalence of 62.9% and 79% in HIV-positive and HIV-negative group, respectively (Table 1). The duration of HIV infection, in the older PLWH was at a mean of 8.29 (± 3.5) years, a median of 9 years and on a range of 1-14 years. The majority (79%) of the older PLWH were diagnosed with HIV-1 infection, 3.3% had HIV-2 infection, whereas 17.7% were diagnosed with HIV-

TABLE 2. PATTERN OF MULTIMORBIDITIES AND OPPORTUNISTIC DISEASES/INFECTIONS AMONG THE PARTICIPANTS

	HIV (n = 62) %	Non-HIV (n = 126) %	Chronic morbidity	HIV (n = 62) %	Non-HIV (n = 126) %	Opportunistic diseases/infection	HIV (n = 62) %
<i>Acute morbidity</i>							
Malaria	41.9	21.8	Diabetes	3.2	21.0	Oropharyngeal candidiasis	11.3
Cough	11.3	8.9	Hypertension	29.0	46.8	Vaginal candidiasis	1.6
Common cold	3.2	7.3	Heart disease	0	1.6	Tinea corporis	1.6
Headache	6.5	12.1	Arthritis	27.4	21.8	Enteritis/diarrhea	22.6
Toothache	3.2	3.2	Cancer	0	0.8	Pneumonia	27.4
Joint pains	27.4	33.9	Tuberculosis	12.4	0	Herpes zoster	1.6
Backache	6.5	13.7	Asthma	1.6	1.6	Cheilitis	3.2
Dizziness	9.7	4.0	Hemorrhoids	1.6	0	Postherpetic neuralgia	1.6
Weight loss	3.2	1.6	Peptic ulcer	3.2	6.5	HIV-associated dermatitis	28.7
Heartburns	3.2	0.8	Chronic obstructive pulmonary diseases	1.6	0	HIV-related anemia	4.3
Eye problems	4.8	5.6	Hepatitis B	6.5	0	Genital wart	1.6
Anxiety	3.2	3.2	Hepatitis C	9.7	0	HIV peripheral neuropathy	19.4
Skin diseases	1.6	0.8	Others: prostate disease, cataract etc.	8.1	10.5	Lymphadenopathy	1.6

TABLE 3. RISK ESTIMATES OF MULTIMORBIDITY IN ELDERLY HIV POSITIVE AND HIV NEGATIVE

	HIV (n=62), %	Non-HIV (n=126), %	χ^2	p	OR	95% CI of OR
Acute MM						
Yes	37.1	33.9	0.189	.664	0.869	0.460–1.640
No	62.9	66.1				
Chronic MM						
Yes	51.6	26.6	11.363	.001	0.340	0.180–0.643
No	48.4	73.4				
Any MM						
Yes	69.4	46.8	8.498	.004	0.388	0.204–0.740
No	30.6	53.2				

CI, confidence interval; OR, odds ratio.

dual (1&2). Most (83.9%) of the older PLWH, were on first-line ART, whereas fewer (16.1%) were on second-line ART.

More (45.2%) of the HIV-positive elderly were widow or widowers, compared with fewer (30.6%) of HIV-negative older adults (Table 1). Of the widowed HIV-infected older PLWH, 17.9% were diagnosed within 1–4 years of the demise and clinical disclosure of the HIV-positive status of their spouses and they were commenced on ART thereafter. Of the HIV-positive elderly, 51.7% had chronic MM, compared with 26.6% of HIV-negative elderly, on a range of 1–6 chronic diseases (likelihood ratio [LR]=11.16, $p=.001$). While on a range of 1–7 acute diseases, 37.1% of HIV-positive elderly had acute non-HIV-related MM, compared with 33.9% of HIV-negative elderly (LR=0.188, $p=.664$). The HIV-positive elderly had lower mean age (63.9 vs. 68.1 years, $p=.00$, $t=5.68$) and shorter duration of chronic MM (4.7 vs. 9.6 years, $p=.003$, $t=3.05$), despite which they significantly had more overall (acute and chronic) MM (3.6 vs. 2.8, $p=.015$, $t=2.448$) especially chronic MM (2.0 vs. 1.3, $p=.004$, $t=2.970$) and significantly lower quality of life (82.7 vs. 86.2, $p=.002$, $t=3.130$) (Table 1).

Although, some of the acute and chronic morbidities were more prevalent in the HIV-negative elderly, of concern was the higher occurrence of, either or both acute and chronic MM in the HIV-positive elderly (Table 2). Of note, is the prevalence of 41.9% versus 21.8% for malaria, arthritis at 27.4% versus 21.8%, tuberculosis (TB) at 12.4% versus 0%, chronic obstructive pulmonary diseases (COPD) at 1.6% versus 0%, hepatitis B at 6.5% versus 0%, and hepatitis C at 9.7% versus 0%, with higher prevalence of these diseases, in the HIV-positive elderly. Aside the comparable acute and chronic MM between the two study groups, the HIV-positive elderly had the additional burden of HIV-related opportunistic diseases or infections, which are extraneous morbidities, exclusive to this group (Table 2).

The risk estimates for acute MM in HIV-positive elderly was higher but not significant while that for chronic MM revealed significantly higher odds for HIV-positive patients, compared with HIV-negative patients. The risk estimates for the presence of any MM revealed higher odds for the HIV-positive elderly at $\chi^2=8.498$, $p=.004$, odds ratio=0.388 (95% confidence interval=0.204–0.740), compared with HIV-negative elderly (Table 3).

Binary logistic regression at 90.5% correct prediction for presence of any MM, indicates that age >64 years, higher total body fat, lower nadir CD4 and longer duration of HIV-infection, at a mean of >8.29 years, were significant predictors

of the presence of any MM, in HIV-positive elderly [chi-square=22.795, $df=11$ and $p=.019$ (<0.05)]. The predictive coefficients were: total body fat—wald=4.857, $p=.028$; Nadir CD4 count—wald=4.735, $p=.030$; years living with HIV—wald=4.301, $p=.038$; and age—wald=4.623, $p=.032$. All the 11 predictors “explained” 43.9% variability of the presence of any MM in the HIV-positive elderly cohort. The model correctly predicted 52.6% of cases, where there was no MM and 90.5% of cases where there was any-MM, with an overall percentage correct prediction rate of 78.7% (Table 4).

Table 5, depicts the results of multivariate analysis on the predictors of MM in older PLWH at R -squared=0.113, $F=1.808$, and $p=.140$. These four variables predicted MM, in 11.3% of cases. Increasing age and duration of HIV infection can increase risk of MM by 22.7% and 7.6%, respectively, decreasing nadir CD4 counts can increase risk of MM by 14%, and increase in %TBF can increase risk of MM by 3.9%.

TABLE 4. PARTICIPANTS’ CHARACTERISTICS ASSOCIATED WITH MULTIMORBIDITY AMONG THOSE WITH HIV

Variables	OR (95% CI)	Sigf.
Age group (years)		
60–64 years vs. 65–74 years	0.113 (0.016–0.825)	0.032
Gender		
Female vs. male	0.098 (0.005–2.024)	0.133
Total body fat (% of body wt.)	1.237 (1.024–1.494)	0.028
Visceral fat (% of body wt.)	0.906 (0.693–1.183)	0.467
Systolic BP (mmHg)	0.987 (0.950–1.025)	0.482
Diastolic BP (mmHg)	0.967 (0.903–1.036)	0.340
Nadir CD4 count <199 $\mu\text{g}/\text{dL}$ vs. $\geq 200 \mu\text{g}/\text{dL}$	0.038 (0.002–0.723)	0.030
Current CD4 count <199 $\mu\text{g}/\text{dL}$ vs. $>200 \mu\text{g}/\text{dL}$	0.139 (0.014–1.367)	0.091
Mean of years living with HIV <8 years vs. ≥ 8 years	0.141 (0.022–0.898)	0.038
Line of HAART 1st line vs. 2nd line	1.572 (0.634–1.5420)	0.696
BMI Normal wt. vs. over wt./obese	10.678 (0.555–205.561)	0.117

TABLE 5. MULTIVARIATE ANALYSIS OF PREDICTORS OF CHRONIC MULTIMORBIDITY IN OLDER PEOPLE LIVING WITH HIV

<i>Predictors of chronic multimorbidities</i>	<i>HR</i>	<i>95% CI</i>	<i>p</i>
Age in years	0.227	0.856 to 0.403	.474
Years living with HIV	0.076	0.063 to 0.215	.279
Nadir CD4	-0.140	-0.624 to 0.345	.566
Total body fat (%)	0.039	0.000 to 0.078	.051

HR, hazard ratio.

Discussions

The older adults living and aging with HIV in this study had a greater burden of MM than the age-matched counterparts without HIV. The presence of chronic MM was associated with older age, higher total body fat, lower nadir CD4 counts, and longer duration of HIV infection. It is noteworthy that, more of the HIV-positive older adults were widowed and diagnosed shortly after the death of their spouses. This suggested that they contracted the HIV infection later in life as attested by some of the elderly PLWH in this study. This finding buttresses one of the reasons for the occurrence of “graying of HIV epidemic,” which is seroconversion at older ages.^{1-4,6} The higher female representation in both groups may be a reflection of the better health care-seeking behaviors of female across all ages, which is heightened in older ages.²¹

The HIV-positive elderly in this study, who were of lower mean age and had lived with HIV for a mean of 8 years, had more MM than the HIV-negative elderly cohort. This corroborates the knowledge that HIV infection may highlight the aging process, which can encourage higher incidence and prevalence of a variety of age-related MM at a much younger age.^{1,2,4,6,22} However, due to the cross-section nature of the collected data, we could only measure burden of MM and was unable to determine causality of MM in the HIV-infected elderly.^{1,13} The HIV-negative elderly cohort had higher mean age, but fewer MM, therefore, one may ascribe the higher risk of MM in HIV-positive elderly to their HIV sero-status. Additionally, the HIV and Aging Working Group of the NIH Office of AIDS Research had stated that, MM may occur earlier in life and more frequently in older PLWH, in contrast to the HIV-negative counterpart, as we observed in this study.¹³ The study also revealed a significantly higher risk for MM in the HIV-positive elderly compared with HIV-negative elderly. This result is similar to that which was discovered in the Modena HIV Metabolic Clinic cohort study, which revealed that older HIV-infected people had a higher risk for MM than their age-matched HIV-negative group.¹ Studies have reported also, that older PLWH in contrast to age-matched HIV-negative counterpart experiences higher prevalence of MM like chronic anemia (as measured by low PCV), hypertension, COPD, and chronic liver diseases like hepatitis B and C, as exemplified in this study.¹³ It is postulated that aging PLWH have greater immunosenescence, “inflamm-aging,” and ART toxicity, mediating the development of non-HIV-related morbidities.^{13,23} The “inflamm-aging” of older PLWH that predisposed them to MM is explained as, persistent immune activation and systemic inflammation due to several mechanisms.²³ Likewise, several ART medications have cardiovascular, lipid, and metabolic complications.⁹ The

forementioned mechanisms we speculate as explanations for the observed higher mean systolic blood pressure in older PLWH, despite a close estimate of total body fat and a much lower BMI. Lipodystrophy, which is a side effect of some ART, together with the age-related redistribution of fat which is heightened in older PLWH predisposes them to early development of NCDs (noncommunicable diseases).²³ The total body fat significantly predicted MM in HIV-positive elderly in this study, hence active monitoring and evaluation of this parameter, which is at the root cause of some NCDs, can be recommended as part of the routine care of older PLWH. This is because it has been documented that within 3 years of commencement of some ART, there is fat redistribution with eventual development of metabolic syndrome and increased risk of hypertension and other NCDs.^{6,19} Generally, MM is seen in HIV-infected people, earlier in their old ages, due to the extra “hit” to the body metabolism, by HIV viremia and or ART, which can facilitate the aging process.^{1,5,6,22} It has been documented that in spite of longevity of HIV-infected older person due to effectiveness of combination ART, they have a poorer quality of life in contrast to their HIV-uninfected counterpart due to burden of MM, as revealed in this study.^{4,24}

The nadir CD4 count was found to be significantly associated with MM in older PLWH in our study. It is known that the persistence of chronic immune activation and low-grade inflammation, engendered by lowest-ever CD4 count is a major contributor to MM in PLWH through expedited immunologic aging compared with aged-matched HIV-negative individuals.²⁴ Nadir CD4 is documented as a predictor for the development of MM, which is indicative of a higher immune dysfunction initially induced by high levels of HIV RNA.^{1,22,24} Likewise, it has been proven that, even after recovery of CD4 cells on ART, the CD4 T cells do not reconstitute their normal functionality.²⁴ Additionally, immunologic abnormality and senescence that contributes to the development of MM in older PLWH can also be determined by the current CD4 count, but more significantly by the nadir CD4 count, as we observed in this study.²⁴ The dysfunctional CD4 T cells, as determined by prior nadir CD4 before ART, contributes greatly to MM in those aging with HIV.^{6,24} Therefore, it might be beneficial to consider starting ARTs, at a relatively higher CD4 count level, in the older PLWH in low and middle income countries (LMIC), like Nigeria, to reduce the risk of development of MM.

The age, 64 years, which is an approximation of the mean age of the older PLWH in this study, seemed to be predictive of the onset of chronic MM. Therefore, early active screening for non-HIV-related morbidities in older PLWH can be recommended. The study also showed that, at about 8 years of HIV infection, older PLWH may begin to experience chronic MM, hence there should be a high index of suspicion for MM within this time frame. This is corroborated by a study that reported a median age of 56 years for higher risk of MM in older PLWH, which is comparable to three decades older HIV-negative elderly.⁶ This observation was attributed to immunosenescence from continuous immune stimulation by HIV virus and conjoint viral infection like hepatitis B and C, even at good viral suppression and normal current CD4 counts,⁶ as similarly observed in this study.

Overall, in considerations of the factors associated with MM in elderly PLWH, it is important to ensure a high index of suspicion for acute non-HIV-related morbidities and screen early for non-HIV-related chronic MM. Adopting the

forementioned management approach could support enhanced quality of life, in combination with optimal use of ART.¹³ To prevent undue MM, superimposed on the burden of living with HIV and predisposition to opportunistic infections, as seen in this study, there is a need to have a comprehensive health care plan for middle-aged and older PLWH in LMICs.

The recommendation from this study, as previously suggested from a similar¹ study, is to have a structured clinical evaluation and follow-up of non-HIV-related morbidities that may prevail in people aging with HIV.

Limitations

The cross-sectional design of this study limits our ability to draw strong inferences from the results. There is an ongoing plan for a longitudinal study design, which will include more detailed measurements of confounders and factors associated with MM in both study groups. Prospectively, we hope to categorically state predictors and psychosocial factors that can contribute to MM in aging PLWH.

Conclusion

This study provided pieces of evidence that HIV-positive older adults may be more at risk of MM, which may be facilitated by their sero-status. Therefore, beyond the administration and monitoring of ART, it is important to evaluate for and manage other non-HIV-related morbidities in people aging with HIV, which can afford them a comparable quality of life to people aging without HIV.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

Funding was received from the NIH Fogarty Center, D43TW010140, which sponsors the UI MEPI-J research training program of the University of Ibadan, Nigeria.

References

- Guaraldi G, Zona S, Brothers TD, *et al.*: Aging with HIV vs. HIV seroconversion at older age: A diverse population with distinct comorbidity profiles. *PLoS One* 2015;10:e0118531.
- Negin J, Cumming RG: HIV infection in older adults in sub-Saharan Africa: Extrapolating prevalence from existing data. *Bull World Health Organ* 2010;88:847–853.
- Mpondo BCT: HIV infection in the elderly: Arising challenges. *J Aging Res* 2016;2016:1–10.
- Wing EJ: HIV and aging. *Int J Infect Dis* 2016;53:61–68.
- Nguyen N, Holodniy M: HIV infection in the elderly 2008; 3:453–472.
- Pathai S: Is HIV a model of accelerated or accentuated aging. *J Gerontol Ser A* 2017;69:833–842.
- Yves J, Reste L, Nabbe P, Rivet C, Lygidakis C: The European general practice research network presents the translations of its comprehensive definition of multimorbidity in family medicine in ten European languages. *PLoS One* 2015;10:e0115796.
- Aguiar R, Moreira H, Durand M, Sprinz E: International Journal of Infectious Diseases Comorbidity is more common and occurs earlier in persons living with HIV than in HIV-uninfected matched controls, aged 50 years and older: A cross-sectional study. *Int J Infect Dis [Internet]* 2018;70:30–35.
- WHO: *Multimorbidity: Technical Series on Safer Primary Care*. Department of Service Delivery and Safety World Health Organization, Geneva, Switzerland, 2016.
- Yarnall A, Sayer A, Clegg A, Rockwood K, Parker S, Hindle J: New horizons in multimorbidity in older adults. *Age Ageing* 2017;46:882–888.
- Acute and chronic diseases as part of multimorbidity in acutely hospitalized older patients. *Eur J Intern Med* 2016;27:68–75.
- Smith S, Soubhi H, Fortin M, Hudon C, O'Dowd T: Managing patients with multimorbidity: Systematic review of interventions in primary care and community settings. *BMJ [Internet]* 2012;345:e5205.
- Rodriguez-Penney AT, Iudicello JE, Riggs PK, *et al.*: Comorbidities in persons infected with HIV: Increased burden with older age and negative effects on health-related quality of life. *AIDS Patient Care STDS* 2013;27:5–16.
- Smith C, Ryom L, Weber R, *et al.*: Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): A multicohort collaboration. *Lancet* 2014;384:241–248.
- Salisbury C: Multimorbidity: Redesigning health care for people who use it. *Lancet* 2012;6736:7–9.
- Baudrand R, Dom JM, Tabilo C, *et al.*: The estimation of visceral adipose tissue with a body composition monitor predicts the metabolic syndrome. *J Hum Nutr Diet* 2013;26:154–158.
- Pribyl MI, Smith JD, Grimes GR: Accuracy of the Omron HBF-500 body composition monitor in male and female college students. *Int J Exerc Sci* 2011;4:93–101.
- Zhang L, Wang Z, Chen Z, Wang X, Zhu M: Association of body composition assessed by bioelectrical impedance analysis with metabolic risk factor clustering among middle-aged Chinese. *Prev Med Rep* 2017;6:191–196.
- Cho S-A, Yoo H, Cho J-Y, *et al.*: Visceral fat area and serum adiponectin level predict the development of metabolic syndrome in a community-based asymptomatic population. *PLoS One* 2017;12:e0169289.
- Vahedi S: World Health Organization Quality-of-Life Scale (WHOQOL-BREF): Analyses of their item response theory properties based on the graded responses model. *Iran J Psychiatry* 2010;5:140–153.
- Evert J, Lawler E, Bogan H, Perls T: Morbidity profiles of centenarians: Survivors, delayers, and escapers. *J Gerontol A Biol Sci Med Sci* 2003;58:232–237.
- Horvath S, Levine A: HIV-1 infection accelerates age according to the epigenetic clock. *J Infect Dis* 2015;212:1563–1573.
- Guaraldi G, Lonardo A, Maia L, Palella FJ: Metabolic concerns in aging HIV-infected persons: From serum lipid phenotype to fatty liver. *AIDS* 2017;31(Suppl. 2):S147–S156.
- Nasi M, De Biasi S, Gibellini L, *et al.*: Ageing and inflammation in patients with HIV infection. *Br Soc Immunol Exp Immunol* 2016;187:44–52.

Address correspondence to:
 Abimbola Margaret Obimakinde
 Family Medicine Unit
 Department of Community Medicine
 College of Medicine
 University of Ibadan
 Ibadan 200212
 Oyo State
 Nigeria

E-mail: magbimlucy@gmail.com
 tolutammy@yahoo.com