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NEUROCOGNITIVE IMPAIRMENT IN AGING PEOPLE LIVING WITH HIV; A COMPARATIVE STUDY OF ELDERLY PATIENTS ATTENDING THE UNIVERSITY COLLEGE HOSPITAL IBADAN, NIGERIA.

DÉFICIENCE NEUROCOGNITIVE CHEZ LES PERSONNES ÂGÉES VIVANT AVEC LE HIV ; UNE ÉTUDE COMPARATIVE DES PATIENTS ÂGÉS FRÉQUENTANT L'HÔPITAL UNIVERSITAIRE D'IBADAN, NIGÉRIA.

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ABSTRACT

Background

Ageing People Living with HIV (PLWH) can experience an exacerbation of age-associated Neurocognitive impairment (NCI) and decline compared to HIV- uninfected counterpart. This study aimed to evaluate age-associated cognitive impairment in ageing PLWH in contrast to age-matched HIV-uninfected older adults.

Method

A survey of 186 persons (≥60years) was conducted at the University College Hospital, Ibadan Nigeria, in April-June 2018. Participants were selected at ratio 1:2 for HIV-positive and HIV-negative status and age-matched at ±5 years. The Montreal Cognitive Assessment (MoCA), and Trail Making Test (TMT) A & B were conducted for cognitive assessment and other clinical data were collected and analyzed with SPSS 23.

Results

Ageing PLWH, had the poorer cognitive ability (p=0.000) and a higher burden of Chronic Non-Communicable Diseases (NCDs) (p=0.000). Many (71%) of the PLWH, had cognitive-impairment, with 32 cases of Mild Cognitive Impairment (MCI) and 12 cases dementia. Of the HIV-infected cohort, the cognitively-impaired, ageing PLWH had higher viral-load and poorer HAARTs-compliance. Risk factors for cognitive impairment among ageing-PLWH are ≥8years duration of HIV-infection (p=0.032), poor HAARTs-compliance (p=0.039), type-1 HIV (p=0.057) and higher viral-load (p=0.076).

Conclusion

Ageing People living with HIV(PLWH) are more at risk of developing early-onset dementia because of HIV-related factors. Early screening for dementia can be recommended as part of HIV-care plan for adult persons living with HIV in low and middle-income countries like Nigeria**.**

RESUME

Introduction

Les personnes âgées vivant avec le VIH (PVVIH) peuvent connaître une exacerbation de la déficience neurocognitive associée à l'âge par rapport à leurs homologues non infectés par le HIV. Cette étude visait à évaluer la déficience cognitive liée à l'âge chez les PVVIH vieillissants par rapport aux adultes plus âgés non infectés par le VIH de même âge.

Méthode

Une enquête auprès de 186 personnes (≥ 60 ans) a été menée à l'Hôpital Universitaire d'Ibadan au Nigéria entre avril et juin 2018. Les participants ont été sélectionnés selon un ratio de 1 : 2 pour le statut séropositif et séronégatif et appariés selon l'âge à ± 5 ans. L'évaluation cognitive de Montréal (MoCA) et le Trail Making Test (TMT) A & B ont été menés à des fins d'évaluation cognitive et d'autres données cliniques ont été collectées et analysées avec le logiciel SPSS 23.0.

Résultats

Le PVVIH vieillissant avait une capacité cognitive plus faible (p=0.000) et un fardeau plus élevé des maladies non transmissibles chroniques (MNT) (p=0.000). Beaucoup (71%) de PVVIH, ont eu un affaiblissement cognitif, avec 32 cas de troubles cognitifs modérés (MCI) et 12 cas de démence. Sur la cohorte infectée par le VIH, ceux ayant une déficience cognitive avaient une charge virale plus élevée et une compliance plus faible aux ARVs. Les facteurs de risque de troubles cognitifs chez les personnes âgées vivant avec le VIH étaient la durée de l'infection par le VIH ≥8 ans (p=0,032), la mauvaise observance aux ARVs (p=0,039), le VIH de type 1 (p=0,057) et la charge virale plus élevée (p=0,076).

Conclusion

Les personnes âgées vivant avec le VIH/ SIDA sont plus à risque de développer une démence précoce en raison de facteurs liés au VIH lui-même. Le dépistage précoce de la démence peut être recommandé dans le cadre du plan de soins contre le HIV pour les adultes vivant avec le VIH dans les pays à revenu faible ou intermédiaire comme le Nigéria.

INTRODUCTION

People Living with HIV(PLWH) have increased longevity and are ageing with HIV since the advent of combined Highly Active Antiretroviral (HAARTs) (1). HIV-infection in ageing PLWH coexists as a chronic disease and moderates the morbidity pattern. Globally and most especially in Africa, researches on HIV and ageing are not robust despite the growing concerns (2). It was reported at the end of 2012, that 10% of the adults PLWH, in Lower and Middle-Income Countries (LMICs) were aged 50 years or older and they experience a higher burden of diseases (3). Likewise, it had been projected that in Africa, HIV-infected patients aged 50 and over, will triple by the year 2040 due to "greying of HIV epidemic" (1,2,4). Therefore, there is an expedient need to bridge the research gap on ageing PLWH (1,2,4).

Cognitive impairment is an expectation of the ageing modern society due to many risk factors. HIV is known to exacerbate age-associated cognitive impairment, with ageing PLWH having cognitive decline akin to that of much older non-HIV infected adults (4). HIV reproduces in the brain microglia with resultant central nervous system inflammation which causes a spectrum of progressive cognitive impairments referred to as HIV Associated Neurocognitive disorders (HANDs) (5). HANDs ranges from Asymptomatic Neurocognitive Impairment (ANI) through Mild Cognitive Impairment(MCI) to dementia (5). Advancing age, age-associated chronic diseases and HIV- related morbidities and infections like Hepatitis B and Hepatitis C, are common risk factors to neurocognitive impairment in ageing PLWH, hence the concern for cognitive impairment in PLWH (5).

Mild neurocognitive disorder occurs in the early stages of HIV and the symptoms are usually subtle and elusive (5,6). Unrecognized or untreated, neurocognitive impairments in PLWH may eventually progress to

dementia at a later stage, with memory and executive function problems (5–8). Dementia, the extreme of neurocognitive impairment, is projected to quadruple by 2050 worldwide, with a higher burden in Low and Middle-Income Countries (LMICs) especially due to "triple-burden-of-diseases" (5–7). Triple burden of diseases, in LMICs, explains the phenomenon where, the high burden of poverty, is superimposed on the double burden of communicable and non-communicable diseases (9,10). People living and ageing with HIV are prone to early onset MCI and dementia by virtue of their clinical condition. This risk is heightened in middle income country like Nigeria where neurocognitive assessment of PLWH is not a routine despite the tendency for triple burden of disease in PLWH. This study aimed to evaluate age-associated cognitive impairment in ageing PLWH in contrast to age-matched HIV-uninfected older adults.

METHODS

Study design:

This was a cross-sectional survey of 186 persons aged 60 years and above. The participants were selected, using ratio 1:2, 64 HIV-positive and 124 HIV-negative patients were recruited in April-June 2018.

Study population:

The HIV-positive participants were recruited from the APIN (AIDs Preventive Initiative of Nigeria) clinic of the Infectious Disease Institute of the College of Medicine, University of Ibadan Nigeria. The HIV-negative participants were selected from the Chief Tony Aneni Geriatric Center (CTAC) of the University College Hospital, Ibadan Nigeria.

Sampling:

Consecutive consenting eligible patients encountered at the APIN and geriatric clinics were selected to participate in the study. For every selected person living with HIV, 2 (two) patients of the geriatric center were selected after matching for age at ± 5 years. The presumed HIV-negative participants selected from the geriatric center of the University College Hospital (UCH) Ibadan had Voluntary Counselling and Testing (VCT) for HIV, after which they are recruited on confirmation of negative HIV-screening test results.

Study tools:

Cognitive assessment of each participant was conducted using the Montreal Cognitive Assessment (MoCA) questionnaire and the Trail Making Test (TMT) A and B (11). The Montreal Cognitive Assessment examination (MoCA) is a valid and reliable screening test for early cognitive impairment in older adults, as it evaluates multiple cognitive domains in one sitting even in absence of obvious physical and behavioural abnormality (5,11). The MoCA is a 30-point screening tool that can be administered within 10 minutes, to ages 49 years to ≥ 85 years and it evaluates aspects of attention, orientation, language, verbal memory, visuospatial, and executive function (11). The MoCA scores for all participants was adjusted for education using a one-point correction for participants with less than 12 years of formal education (11,12). There are a published MoCA score cutoffs, with a score of < 26 points taken as cognitive impairment (11,12). Specifically, the MoCA score range of 19-25.2 is taken as Mild Cognitive Impairment (MCI) and the score range of 11.4-21 is taken as dementia (11,13,14). However, due to the known differences in MoCA scores by ethnic groups, the mean and S.D scores of the study population was utilized for classifying patients in the study. Mild Cognitive impairment (MCI) for this study was defined by MoCA score of +1 SD below the mean, and MoCA score of +2 S.D below the mean was used to define dementia, as previously validated (11,13,14).

The Trail Making Test (TMT) A and B, are known to readily identify cognitive impairment in persons 15-89 years of age, as it measures attention, speed, mental flexibility, visuospatial organization, sequencing, abstraction, recall, recognition and task shifting (15,16). People, especially older adults with a cognitive deficit lacks mental flexibility and often have difficulty in performing timed and repetitive activities (5,6). The Trail Making Test is sensitive and useful in assessing cognitive impairment and has high predictive power, although the specificity has been debated (15,16). The Trail Making Test -B specifically measures the cognitive domain of executive functioning with the ability to maintain two trains of thoughts, modify an action plan, psychomotor speed and cognitive flexibility (15,16). Both components of Trail Making Test are timed and the score represents the amount of time an individual completes each of the tasks (15,16). The expected time for cognitively competent individual averages 29 seconds for trail A and 75 seconds for trail B, trail

completion time above 90 seconds and 3 minutes respectively for trail A and B, signifies cognitive impairment (17,18). Trail Making Test, has also been found to be effective in the identification of mild neurocognitive disorder and HIV associated Dementia with a sensitivity of 86 % and specificity of 79 % when combined with other neuropsychometry tools (15–18). The raw completion time scores of Trail Making Test was utilized in this study, with higher TMT completion time (scores) interpreted as worse cognitive assessments.

Information on sociodemography, clinical and laboratory parameters were obtained from the participants and their medical records. The socio-economic classification was done using the Wealth Index questionnaire. Relevant records of HIV-management including viral titer and CD4-counts were obtained from APIN medical records.

Data management:

Collected data were analyzed with the Statistical Package for Social Sciences (SPSS) version 23 using Chi-square test, T-test, correlation analysis and logistic regression.

RESULTS

Ageing people living with HIV, in contrast to the HIV-uninfected cohort had lower mean age (63.5yrs; p=0.000) and poorer cognitive ability [lower MoCA-scores (p=0.000) and longer TMT A & B completion-time (p=0.001 & 0.006)] (Table 1). There was female preponderance in both groups and more of the ageing PLWH were widowed (p=0.051), had lower education attainment (p=0.000) and more chronic Non-Communicable Diseases (NCDs) (p=0.000). The ageing PLWH had lower mean BMI despite which they had higher markers of cardiovascular and metabolic disorder [i.e. higher Systolic Blood Pressure (SBP) and Fasting Blood Sugar (FBS)].

Using the validated mean MoCA scores with the S.D variations, 71% (44) of the ageing PLWH, had cognitive impairment, of which 51.6% (32) had MoCA scores indicating Mild Cognitive Impairment (MCI) and 19.4% (12) had scores in keeping with dementia. The female PLWH had lower MoCA score compared to the males (19.4 vs 21.9, p=0.045, t=2.046). The average duration of HIV-infection was 8.79 (±3.52) years at a range of 1-14 years, mode of 13 years and median of 9 years.

The cognitively impaired ageing PLWH had lower MoCA scores, especially for the visuospatial functioning which correlates negatively with the TMT completion time (TMT A; rs-0.358, p-0.004 and TMT B; rs-0.208, p-0.104). The cognitively impaired PLWH were younger, had fewer years of HIV 1-infection, higher viral titer and poorer compliance with Highly Active Antiretroviral (HAARTs) prescriptions. (Table 2). In contrast to the cognitively unimpaired PLWH, the cognitively impaired ageing PLWH had a higher burden of chronic NCDs and socioeconomic disadvantages. Additionally, all (100%) the ageing PLWH with Hepatitis B (2.2% prevalence) or C (3.2% prevalence) were cognitively impaired.

Table 3 shows the result of logistic regression (Chi sq-24.137, df=11, p=0.019) at 75.8% overall prediction with 81.1% correct prediction for cognitive impairment. The prediction for cognitive impairment among ageing PLWH, revealed that the duration of HIV-infection (wald=4.588 p=0.032), HAARTs-compliance (wald=4.255, p=0.039), type-1 HIV infection (wald=3.636 p=0.057) and viral titers (wald=3.138, p=0.076) are important risk factors.

Table 4 showed results of multivariate analysis (R=0.449; R squared=0.201; adjusted R squared =0.114; F=2.310, p=0.046) of predictors of cognitive impairment. The analysis revealed that an increase in the age and duration of HIV-infection can decrease MoCA scores (decrease MoCA scores=poorer cognition) by 2.0% and 8.9% respectively. Likewise, an increase in the number of chronic Non-Communicable Diseases (NCDs) and HIV viral titer can decrease MoCA scores by 53.4% and 16.1% respectively. However, an increase in the percentage HAART-compliance and CD4-count can increase MoCA scores (increased MoCA scores=better cognition), by 10.5% and 0.7% respectively.

DISCUSSIONS

HIV-infection is a common cause of preventable Neurocognitive-Impairment (NCI) and young- onset dementia (dementia under 65years), which readily occurs, as a comorbidity in ageing PLWH (11,13,14). This

is evident in this study, where the ageing PLWH at a mean age of 63.5years significantly had poorer cognitive measures in contrast to the HIV-uninfected counterpart at mean age 68.5years. The prevalence of HAND in Sub-Saharan Africa (SSA) varies widely between 17% to 88%, depending on the nomenclature used (11,13,14). This study revealed a 71% prevalence of cognitive impairment among the ageing PLWH with 51.6% prevalence of Mild Cognitive Impairment (MCI) and 19.4% prevalence of dementia. In tandem with this study, it was reported that the prevalence of MCI and dementia in ageing PLWH may be as high as 60% and 29% respectively (5). It was also theorized that mild neurocognitive impairment does not necessarily progress to dementia but a longitudinal cohort study reported progressively severe cognitive impairment in PLWH despite viral suppression and immune reconstitution, as can be inferred from the results of this study (5,20). HIV associated dementia (HAD) was commoner in the pre HAART era, while MCI is commoner since the advent of combined HAART, but it has been said that the longer people live with HIV infection, the more the possibility of an increase in dementia prevalence (21). The aforementioned can be drawn from the results of this study.

Neurocognitive impairment is commonly associated with HIV-1 infection, and it is one of the most feared complications in ageing PLWH, due to the chronic immune activation driven by viral titer and central nervous system (CNS) viral infection (6). This study revealed that many of the cognitively impaired ageing PLWH had HIV-1 infection with significantly higher plasma viral titer, and both are important predictors of neurocognitive impairment. It is known that in PLWH, the brain act as a sanctuary site for the latent slowly replicating virus (6). HIV-1 infection induces neurodegeneration due to deposition of amyloid and precursor protein such as the toxic viral products called tat protein, in the brain, which produces changes similar to that seen in Alzheimer's disease (6,7). There is a postulation that neurocognitive impairment in ageing PLWH results from HIV-induced aggravated immunosenescence which accelerates the premature expression of dementia (7). These can explain the reason why the ageing PLWH in this study had worse cognitive measures despite being significantly younger than the HIV-negative cohort. However, the exact mechanism by which HIV-1 provoke neuronal injury and death is controversial but there is evidence of multiple risk factors and mechanisms contributing to neurocognitive impairment in PLWH (7,21). Aside from the synergistic effect of age-related and direct HIV-related immunosenescence in PLWH, there are other indirectly related factors, which facilitate the early presentation of neurocognitive impairment (6,7). For instance in this study, compared to the HIV-negative elderly, anemia, a higher burden of chronic NCDs and metabolic markers (elevate blood pressure and sugar) of cardiovascular disease, supports premature pathogenesis of neurocognitive impairment in ageing PLWH (6,7). The cognitively impaired ageing-PLWH in this study were of lower mean age compared to the cognitively unimpaired ones, which is in agreement with the fact that HIV and ageing are independent risk factors for cognitive impairment (22). HIV infection is known to accentuate brain ageing as found in a study that reported a higher predicted brain age relative to chronological age in PLWH (22). Likewise, although the cognitively impaired ageing PLWH were younger than the unimpaired PLWH, they had higher risk factors for a metabolic disorder which had been linked to earlier and poorer cognitive function in ageing PLWH (23). Additionally, it is important to note that in this study, an increase in the age of older PLWH significantly increase the cognitive impairment, as previously published (6,7).

There was female preponderance in this study and the females in the HIV-infected cohort significantly had poorer cognitive scores, in keeping with the fact that the female gender is a risk factor for HAND, especially for dementia (5,24).Majority of the cognitively impaired PLWH were of lower social status, suggesting the possibility of the inherent poverty, malnutrition and limited access to health care may underscore the poorer cognitive ability, observed (1). It can be deduced that among people of lower social status malnutrition supports anemia, a higher level of percentage total body fat, visceral fat and dyslipidemia as observed in the cognitively impaired ageing PLWH in this study (1). The association of "triple burden of disease'' with neurocognitive impairment is evident in this study because aside socioeconomic disadvantage and a higher burden of chronic NCDs, all ageing PLWH with Hepatitis B and Hepatitis C were cognitively impaired (7).

Majority of the cognitively impaired PLWH in this study were on first-line HAART. A study compared neurocognitive impairment between the pre-HAART and post-HAART era, and found out that NCI was associated with being on HAART only in the HAART era (8). This raises the question of whether some of the newer ARV medications may have toxic effects on the CNS (8). The first line group of HAART are very effective, well-tolerated and therefore preferred, but some of them are neurotoxic. Ritonavir, Zidovudine and Etravirine which are components of the cART prescribed for this studied PLWH has been linked to neurotoxicity and consequent NCI (21). Likewise, Efavirenz and Nevirapine are neurotoxic, particularly Efavirenz which have been linked to neurocognitive impairment (21). Additionally, it was reported that some neurotoxic HAART can increase the production of brain lymphocytes that can cause cognitive disorder (5).

There were higher levels of triglyceride, percentage total body fat and visceral fat in the cognitively impaired ageing PLWH compared to the cognitively unimpaired PLWH. It has been documented that adipose tissues alteration (ATA) is common with the use of HAART especially with first-line HAART (24). Dyslipidemia and adipose tissue alteration in ageing PLWH can aid the pathogenesis of neurocognitive impairment, as can be inferred from the results of this study (1,24). Abdominal or visceral fat accumulation is the predominant type of adipose tissues alteration which worsens with a longer duration on HAART, as the person living with HIV ages (1,24). This study showed a significant difference in visceral fat between the PLWH, with higher levels in the cognitively impaired PLWH. Adipose tissues alteration starts around two years of HAART initiation and increases as PLWH age and increases the risk of cognitive impairment (24). This could be the reason the cognitively impaired PLWH in this study, at fewer years of HIV-infection, had cognitive impairment due to higher fat deposition enhanced by 1st-line HAART (1,24). Adipose tissues alteration invokes metabolic alteration which expedites cognitive impairment, which is exponential in the presence of Hepatitis infection and this may be another explanation for the observation of cognitive impairment in all PLWH who had hepatitis coinfection (1,24). Stavudine, one of the commonly used HAART among the studied ageing PLWH, has been linked to increased risk of ATA and indirectly can contribute to the development cognitive impairment (24).

Chronic non-communicable conditions were important comorbidity and predictor of neurocognitive impairment among PLWH in this study. In sub-Saharan Africa, chronic non-communicable conditions are prevalent in ageing PLWH compared to non-HIV infected counterpart as demonstrated in this study (23). Additionally, this study revealed that cognitive impairment in ageing PLWH was significantly associated with a higher burden of the risk factors for chronic non-communicable diseases (NCDs). These, included elevated systolic blood pressure (SBP), elevated blood glucose, dyslipidemia and elevated body fat. In accordance, studies have reported that chronic NCDs and these multiple risk factors for chronic non-communicable diseases are covariates of cognitive impairment in PLWH (7,11,25). A study reported that cardiovascular disease markers like elevated blood pressure and elevated blood sugar, are more strongly associated with neurocognitive impairment in ageing PLWH compared to HIV-disease markers like current viral load and CD4 counts (7). This study showed evidence of this, where the effect of chronic NCDs on neurocognitive impairment supersede that of HIV-disease markers. Likewise, chronic NCDs, high body fat and dyslipidemia as found among cognitively impaired PLWH in this study, are documented modifiable risk factors for NCI in PLWH (7,11,25).

Low levels of CD4 count are known risk factor for neurocognitive impairment in ageing PLWH (4). A lower current CD4 count was associated with NCI in ageing PLWH in this study, and it has been debated whether nadir rather than current CD4 tracks better with neurocognitive impairment in PLWH and many controversies abound (26). The association between CD4-count and NCI in this study was weak. A plausible explanation is that regardless of good immune recovery on combined HAART other risk factors contributes to the occurrence of HANDs ageing PLWH (26). Likewise, high rates of neurocognitive impairment are known to persist at all stages of HIV-infection in PLWH, especially in the presence of other risk factors regardless of immune recovery (8). Poorer HAART compliance and use of neurotoxic HAART are HIV-related factors while dyslipidemia, anaemia and impaired blood sugar are non-HIV related factors, as shown from this results of this study and confirmed by other researches (1,8,24). Lower education attainment, seen in the setting of lower social status as found more prevalent, amongst the PLWH in this study is a sociodemographic factor that can support the development of NCI regardless of CD4 counts (8). A study reported a 20% prevalence of hepatitis co-infection among PWLH and this usually occurs at lower CD4-count (4). Regardless of immune recovery and current CD4-count, hepatitis coinfection persists and contributes to the development of neurocognitive impairment in ageing PLWH. Although in this study the prevalence of hepatitis B and C was minimal, all ageing PLWH with hepatitis co-infection had cognitive impairment at not too low CD4 count.

The cognitively impaired ageing PLWH had lower percentage HAART compliance and increase in HAART compliance in this study is associated with better cognition function. There were higher incidence and prevalence of HAND in the pre and early HAART era (8). However, HAND prevails mostly in developing countries especially in ageing PLWH, in the presence of poor HAART compliance and other risk factors like anemia and lower social status, as discovered in this study (5). Long-term use of HAART is said to have an undetermined effect on the course of HIV associated dementia, however, HAART compliance has been proven to delay the course of HAND (5). Viral titers were significantly higher in cognitively impaired PLWH in this study, although not a significant predictor like HAART compliance. This is in tandem with the report that HAND is known to be associated with higher viral titer which can occur in PLWH with reduced HAART adherence (26).

STRENGTH, LIMITATION AND RECOMMENDATION

This study provides current information on ageing PLWH and attempts to bridge some research gap on neurocognitive impairment in people living and ageing with HIV in Nigeria. However, the cross-sectional nature limits stronger inferences on the associations between neurocognitive impairment and HIV related factors in ageing PLWH. It can be recommended that a longitudinal cohort studies between HIV and non HIV infected older adult be conducted to establish stronger causalities of earlier neurocognitive impairment and dementia in HIV infected older adults.

CONCLUSION

This study showed that ageing PLWH are at risk of developing neurocognitive impairment due to HIV-related factors and non-HIV factors engendered by HIV induced aggravated immunosenescence. Routine evaluation of cognitive function can facilitate early detection of mild neurocognitive impairment, which is more manageable than burdensome dementia.

The cognitively impaired ageing PLWH were females of lower social status with type 1 HIV and were significantly younger with shorter duration of HIV infection, higher viral titer and had more risk factors for metabolic syndrome and chronic NCDs. These may be the factors to consider in the evaluation and management of HAND in ageing PLWH. The importance of delaying the onset or modifying the progress of neurocognitive impairment in ageing PLWH cannot be overemphasized. Therefore, there is a need to actively monitor and reduce the risk of neurocognitive impairment in ageing PLWH.

Table 1: Characteristics of study participants N=186

	Variables	HIV n=62	Non-HIV n=124	x^2/t-test	P
1	**Mean Age (years)**	63.5(4.0)	68(5.6)	5.68	0.000
2	**Gender; n(%)**				
	Female	39(62.9)	98(79.0)		
	Male	23(37.1)	26(21.0)	5.54	0.019
3	**Educational attainment; n(%)**				
	≤12 years of formal education	46(74.2)	59(47.6)		
	>12years of formal education	16(25.8)	65(52.4)	11.9	0.001
4	**Socioeconomic status; n(%)**				
	Lower class	51(82.3)	61(49.2)		
	Upper class	11(17.7)	63(50.8)	0.066	0.797
5	**Cognitive assessment; mean(sd)**				
	MoCA score	20.3(4.8)	21.9(1.7)	3.166	0.000
	TMT A completion (in seconds)	158.5(90.8)	113.1(56.8)	4.174	0.001
	TMT B completion (in seconds)	254.9(120.6)	212.8(83.5)	2.780	0.006
7	**Dementia (MoCA score);n(%)**				
	Present	12(19.4)	1(0.8)		
	Absent	50(80.6)	123(99.2)	30.89	0.000
8	**Numbers of chronic NCDs;mean (s.d)**	1.98(1.8)	1.25(0.9)	3.643	0.000

Table 2: Covariates of cognitive impairment in Ageing People Living with HIV (N=62)

	Variables	Cognitive Impaired n=44	Cognitive Unimpaired n=18	x^2/t-test	p
1	**Cognitive assessment**				
	+MoCA total scores	18.3	25.3	6.938	0.000
	Visuospatial MoCA score	2.3	3.7	3.474	0.001
2	**Age (in years)**	63.5	64.9	1.222	0.033
3	**Gender**				
	Female	29	10		
	Male	15	8	0.587	0.444
4	**Socioeconomic status**				
	Lower status	37	14		
	Upper status	7	4	0.349	0.715
5	**Type of HIV infection**				
	HIV-1	32	17		
	HIV-2	2	0		
	HIV-Dual	10	10	4.739	0.094
6	**Line of HAART**				
	1st line	38	14		
	2nd line	6	4	0.404	0.696
7	**Current CD4 count (cells/µl)**	475.8	519.3	0.542	0.547
8	**Plasma Viral titer (copies/ml)**	380732.8	183822.2	1.1413	0.022
9	**cART compliance(%)**	89.9	97.9	1.949	0.013
10	**Duration of HIV infection (years)**	8.18	10.28	2.190	0.032
11	**Numbers of Chronic NCD;**	3.7	3.3	0.498	0.682
12	**Packed cell volume (PCV) (%)**	12.4	13.9	1.123	0.249
13	**Triglyceride**	120.3	96.9	1.435	0.079
14	**Total body fat (% body weight)**	34.3	30.7	1.083	0.925
15	**Visceral fat (% body weight)**	9.6	9.2	0.329	0.088
16	**Systolic Blood pressure (mmHg)**	166.7	163.6	0.422	0.674

Hemoglobin concentration; Hb (g/dl) = (PCV÷ 3) (%) +(MoCA score correlates positively with CD4 count and negatively with Viral Load)

Table 3 : Predictors of Cognitive impairment in ageing PLWH

		Odds of predictors		
	Variables	**Wald**	**Exp(0R)**	**p**
1	Age <63.5yrs vs >63.5years)	0.149	0.967	0.699
2	Gender(female vs male)	0.034	0.847	0.854
3	Plasma Viral titer (copies/ml)	3.434	1.000	0.064
4	Current CD4 count (cells/µl)	0.470	0.999	0.493
5	*cART compliance(%)	4.255	0.872	0.039
6	Duration of HIV-infection (in years) <8yrs vs ≥ 8yrs	4.588	0.906	0.032
7	Type of HIV(HIV 1 vs other types)	3.636	0.879	0.057
8	Chronic NCDs	2.894	1.877	0.089

*cART-Combined Antiretroviral

Table 4; Multivariate analysis of predictors of cognitive impairment (MoCA scores) in ageing PLWH

		MoCA scores		
	Predictors	**Hazard Ratio**	**T**	**p**
1	Age	-0.020	1.866	0.067
2	Duration of HIV-infection	-0.089	1.469	0.148
3	cART compliance(%)	0.105	0.623	0.536
4	Chronic NCDs	-0.534	-1.863	0.068
5	Current CD4 count (cells/µl)	0.007	1.279	0.206
6	Plasma Viral titer (copies/ml)	-0.161	-1.309	0.196

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