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Characteristics and treatment outcomes of elderly people on antiretroviral therapy at two community health centres and a primary care facility, Potchefstroom, South Africa

Abstract

Background: South Africa (SA) has a high Human Immunodeficiency Virus (HIV) burden but little is known of older people living with HIV (PLWH). Its growth rate is accelerating in this age group and could put more strain on dwindling resources. Studies have been done in other provinces, but the North-West Province (NWP) has a paucity of information on HIV for this age group.

Objectives: This study aimed to describe characteristics and comorbidities of older people living with HIV in Potchefstroom. Viral load (VL) suppression was evaluated and relationships between patient characteristics and outcomes were explored.

Methods: A descriptive, retrospective file review was done. Descriptive statistics were described and associations between patient characteristics and treatment outcomes were explored. Statistically significant associations were tested in a logistic regression model.

Results: Out of 191 patients, female patients were in the majority (58.1%), < 70 years old (87.4%) and had been on antiretroviral therapy (ART) for ≤ 10 years (74.4%). Most patients were on first line ART (82.7%) and had VL suppression (81.9%). Hypertension was the most common comorbidity (55.5%). A high recent CD4 cell count (≥ 350 cells/mm^3) had positive relationships with suppressed VL (OR 2.3, $p = 0.037$), first line ART (OR 2.78, $p = 0.041$) and treatment duration ≥ 5 years (OR 3.15, $p = 0.009$)

Conclusion: There was room for improving the level of VL suppression in this cohort. More research is needed in older PLWH in the NWP so as to direct resources to optimise their well-being.

Keywords: HIV; Older adults; Characteristics; Treatment outcomes.

Introduction

The term "older persons" is defined by chronological age for research purposes, where persons aged ≥ 60−65 years belong to this category according to the United Nations (UN).[1] Moreover, South Africans are eligible for the older persons grant at 60 years of age, and this definition was used to define older persons in this study.[2] In a recent publication the UN recognised that the global ageing population is increasing, and sub-Saharan Africa is no exception, with a growth rate of 218% predicted from 32 million in 2019 to 101 million by 2050. This is the second highest expected growth rate globally in the older population surpassed only by northern Africa and western Asia at 226% respectively.[1]

Almost 8% of the South African population is ≥ 60 years and could reach 10.5% by 2030 and 15.4% by 2050.[3] The main drivers for these changes are: firstly, lower fertility rates because of better access to contraception, lower childhood mortality and changing gender perceptions; and secondly, lower death rates because of improved access to health care interventions across generations.[4] The ageing Human Immunodeficiency Virus (HIV)-positive population in South Africa (SA) might be attributed partly to the provision and expansion of treatment strategies for all people living with HIV (PLWH) countrywide since 2016 through the universal test and treat (UTT) policy.[5]

Literature shows a paucity of data for older PLWH, specifically in the South African context. For many years, researchers have focused their attention on broadly defined population groups with a myriad of non-communicable diseases, seeing as many of these diseases remain major causes of death and disability in SA.[6] In his foreword to the 2012 World Health Organisation/Human Research Council/National Department of Health study on global AGEing and adult health (SAGE) Wave 1 National Report, the then minister of health, Doctor Aaron Motsoaledi, stated the necessity of expanding preventive, curative and palliative programmes to address chronic diseases. He mentioned many diseases that commonly affect older people, but neglected to mention HIV. The proportion of PLWH was 12.4% in people ≥ 50 years in this study.[7]

Older people present to health facilities with complex illnesses, multimorbidity and polypharmacy. South African doctors are ill-equipped to deal with these challenges, as they

are not adequately trained in gerontology.[8] This could lead to suboptimal provision of care especially for older PLWH.

HIV has become a chronic disease in itself.[9] Benefits of identifying older PLWH include direct benefits such as reduced morbidity and mortality, as well as indirect economic benefits such as strengthening the labour force and home environment. Older people could care for children, allowing younger adults to enter the labour market. They may also become less financially dependent on younger family members if they are able to work longer and reduce their health care utilisation costs.[10]

It is well-established that even when viral load (VL) suppression is achieved in older PLWH, they have attenuated CD4 cell count responses to antiretroviral therapy (ART) and thus need to start treatment early on in the disease process to ensure a more robust immune response.[10] Malaza et al[11] found that the median CD4 cell count in older PLWH was 367 cells/mm^3 after a median duration of 2.3 years on ART. Similarly, Fatti et al[12] found that older PLWH had a median CD4 cell count of 377 cells/mm^3 after three years on ART.

Questions around the prevalence and outcomes of older PLWH in SA were answered in part by Cornell et al[13] and Dawood et al.[14] In the former study, data from three provinces in SA were analysed retrospectively to assess mortality, loss to follow-up (LTFU) and immunologic and virologic responses in 16–80 year old patients who started ART from 2004-2013. The proportion of adults aged ≥50 years comprised 9% of total ART enrolment and increased from 2004 to 2012/13. This study enrolled one of the largest cohorts of older people (> 7 000 patients aged ≥ 50 years) in SA to date, but did not include a cohort in all nine provinces, which poses a potential problem for generalising these findings nationally. The authors encouraged further research in different contexts, of which the North West Province (NWP) is one.

In the latter study, the older age group had a higher prevalence of diabetes mellitus (DM) (6.3%) and hypertension (HPT) (21.5%) which was statistically significant ($p < 0.001$) compared to the younger age group. These findings need to be explored further in other South African settings, including the NWP.

The prevalence of HIV infection in older people in Potchefstroom is unknown. In fact, the mid-year population estimates published by Statistics SA in July 2019 showed the prevalence estimations in terms of HIV for the 15–49 age group only.[15] No recent statistics have been available for other age groups in SA. During 2012, Shisana et al[16] reported that the prevalence of HIV was estimated to be around 7.6% (95% CI 6.5-8.8) for those ≥ 50 years. It is against this backdrop that the researcher studied what transpired in primary care HIV treatment facilities in Potchefstroom, SA, specifically relating to older PLWH.

The aim of the study was to describe patient characteristics and outcomes among older people on ART in Potchefstroom, SA.

The study objectives were:

1. To describe the sociodemographic, treatment, clinical and laboratory characteristics of older PLWH;
2. To describe comorbidities in older PLWH;
3. To evaluate VL suppression in older PLWH; and
4. To explore the relationships between patient characteristics and four treatment outcomes (virologic and immunologic response to treatment, LTFU and death) in older PLWH.

Research methods and design

Study design

A descriptive, retrospective study of older PLWH on ART for ≥ one year prior to the period under review (01 May 2017 – 30 April 2018).

Study setting

The study was conducted at three primary care sites (two community health centres and one primary care clinic) in Tlokwe, SA. The population of Tlokwe City Council is approximately 163 000 people comprising of: black people (71.3%), white people (20.6%); and other population groups (8.1%).[17] People ≥ 65 years comprise 5.7% of the total population. Tlokwe is situated in the Doctor Kenneth Kaunda District in the south-eastern region of the North-West Province (NWP).

Clinic A is a primary care clinic adjacent to the regional hospital in Tlokwe. It serves the population of the town area and caters predominantly for patients who are referred from the hospital outpatient clinics. The clinic renders all services as stipulated by the National Core Standards[18] and National Strategic Plan[19] on a primary care level to patients of all ages. These services include counselling, testing for, and treating HIV.

Clinic B is a community health centre in Ikageng situated just outside the Tlokwe central business district. It serves a predominantly Setswana-speaking community who attends the clinic for acute and/or chronic care.

Clinic C is a community health centre that caters for residents of Promosa. Here, mixed race people comprise just over 51% of the population, while black people represent almost 48% of the population. Afrikaans is the predominant language spoken by 54.8% of residents, while Setswana is spoken by 26%.[20]

Seeing as a diverse array of patients attend the three facilities, the researcher included them in the study so as to represent the population of Tlokwe as accurately as possible.

Study population

Older PLWH aged ≥ 60 years who received treatment for HIV at one of the three study sites from 01 May 2017 until 30 April 2018 and who had been receiving treatment for ≥ 12 months at file review.

Inclusion criteria

(i.) PLWH aged ≥ 60 years as per their last birthday on their last clinic visit date between 01 May 2017 and 30 April 2018. In other words, patients with birth dates prior to 30 April 1958 were evaluated, and then included in the study according to their latest clinic visit date. For example, if the last clinic visit date was 31 December 2017, the patient's date of birth had to be on or before 31 December 1957.

(ii.) PLWH and had been on ART for at least 12 months, so as to determine whether virologic suppression occurred when the second (12 months of treatment) VL was taken as per the 2015 South African HIV Clinical Guidelines.[21] The 2015 guidelines

were amended during the latter half of 2017, but outcomes were measured as per the 2015 guideline seeing as all patients in the cohort were initiated on treatment prior to July 2017.

(iii.) Patient/someone else (friend or family member)/the ward-based outreach team (WBOT) collected treatment at one of the study sites in the preceding three months during the study period to determine whether the patient was adherent to treatment. In primary care, treatment is generally dispensed for one to three months until the next follow-up date is scheduled.

Exclusion criteria

(i.) Patient file was missing for the study period under review, i.e. 01 May 2017–30 April 2018.

Definitions and outcomes

- **Previous defaulter**: Past single or serial failure by the patient or client regarding his or her treatment documented in the clinical record or on TIER.Net.
- **Self:** A patient who collected his or her own treatment in person at any time during the study period.
- **Other:** A family member or friend who collected treatment on the patient's behalf at any time during the study period.
- **Ward-based outreach team (WBOT)**: A clinic-bound team that collected treatment on the patient's behalf at any time during the study period. A patient could thus be categorised in one, two or three categories in terms of treatment collection during the study period.
- **Transfer out as per clinical record or TIER.Net:** A distinction was made as to whether the new treatment collection site was still the primary care facility or at a higher level of care.
- **Comorbidity as documented on ART stationery:** If the comorbidity was unstated but treatment was prescribed during the period under review at any time, the patient was considered as having a comorbidity. If the comorbidity was stated in the clinical record, this was recorded on the data collection sheet.
- **Recent hospitalisation**: A discharge summary recorded in the patient file or specified in clinical notes.

- **Suppressed VL:** A reading of ≤ 400 copies/ml.
- **Adequate immunological response**: A recent CD4 cell count ≥ 350 cells/mm^3. These values were based on previous studies that examined the same outcomes in SA.[12-14,22]
- **LTFU:** The patient's treatment not collected in the preceding three months during the study period; and the patient who could not be traced either telephonically or at his or her place of residence by community health workers during data collection period.
- **Died:** The patient's date of death documented in the clinical records or on TIER.Net.

Measuring tool

A data collection sheet developed by the researcher was used to capture data as per the study's aim and objectives. Previous studies [12-14,22] were perused to establish 'variable themes' that would be relevant and feasible to study. All information was captured solely by hand, by the researcher on the data collection sheet and transferred to Excel 2016 (Microsoft, US).

Data collection

A sample size was not calculated prior to the commencement of the study seeing as the researcher set out to use information for all patients fulfilling inclusion criteria at the three study sites. All relevant files were manually and electronically retrieved with the help of data capturers and clerks at the research sites. Electronic retrieval was facilitated by TIER.Net., the electronic patient management system used for information capturing about HIV and tuberculosis (TB) services in SA since 2011.[23] Files that met inclusion criteria were scrutinised individually and relevant data were extracted and documented on the data collection sheet. Reasonable measures were taken to account for missing data by cross-referencing information in the files with information on TIER.Net. Patient files and the National Health Laboratory Services (NHLS) results tracking website (TrakCare) designed for clinicians to find results relating to creatinine (creat), haemoglobin (Hb) and total cholesterol (chol) were scrutinised using the advanced search option. If the most recent result was ≥ one year old, it was excluded from the analysis as it was deemed to be non-representative of the patient's current clinical status. Finding VL and CD4 cell count results were similarly approached and if values were outdated on TIER.Net for the study period, it was updated on the system.

Data analysis

Stata/IC 16.0 software (STATA Corporation, LLC, TX, US 2019) was used to analyse data. For descriptive statistics numbers, percentages, medians, minimum and maximum values and interquartile ranges (IQR) were used. For evaluating associations between demographic, clinical and laboratory characteristics with four treatment outcomes (most recent VL and CD4 cell count, LTFU and death), Pearson's chi-square, Fisher's exact, Mann-Whitney (Wilcoxon rank-sum), Kruskall-Wallis or Spearman's correlation tests were used where appropriate. Most values for the continuous variables were shown to be non-normally distributed as per the Shapiro-Wilk normality test. Even after logarithmic transformation, the data were non-normally distributed. All variables were initially assessed individually against the treatment outcomes. If p values were ≤ 0.05 or there were > 0.5 correlations for measures of association, these predictors were entered into a linear or logistic regression model where appropriate. Again, a level of ≤ 0.05 was considered statistically significant.

During the initial analysis, the VL and latest CD4 cell count outcomes were assessed as continuous variables as well as categorised into clinically meaningful categories. Whenever there was a statistically significant relationship between any continuous or categorical outcome and characteristic in the initial analysis, it was used in the binomial logistic regression model provided that the number of observations were ≥ 10 per cell and where the VL was suppressed (≤ 400 copies/ml) and the latest CD4 cell count high (≥ 350 cells/mm^3).

Ethical consideration

Ethical clearance was granted by both the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg (M180304) and the North-West Health Research Committee (NW_2018_006). The Tlokwe subdistrict Office of the Primary Health Care Manager also granted permission for the research. Owing to the sensitive nature of the research (that is, by possibly 'exposing' older PLWH in the community) a decision was made to access patient records for data extraction. All data were de-identified and thus informed consent was waived for this study.

Results

In Clinic A, some 39 patients were eligible for the study but one patient was a duplicate from Clinic C and thus excluded from Clinic A's cohort (100% file availability). Clinic B had 107 eligible patients but 11 files were not found (89.7% file availability). There were 69 eligible

patients in Clinic C but 12 files were missing (82.6% file availability). Data could thus be collected for a total of 191 patients: Clinic A (38:19.9%); Clinic B (96:50.2%); and Clinic C (57:29.8%). An overview of the sociodemographic, treatment, clinical and laboratory characteristics is provided in Table 1 (objective 1). The table also depicts comorbidities (objective 2) and VL suppression (objectives 3).

TABLE 1: Sociodemographic, treatment, clinical and laboratory characteristics, comorbidities and VL suppression

	n	%	Minimum	Maximum	Median	IQR
SOCIODEMOGRAPHIC CHARACTERISTICS						
Female sex	111	58.1				
Age (years)			60	78	63	61−66
60–69	167	87.4				
Marital status						
Married/Partner/Cohabitation	53	27.8				
Single/Widowed	39	20.4				
Unknown	99	51.8				
Living arrangements						
Lives alone	11	5.8				
≥ 2 people in the home	27	14.1				
Unknown	153	80.1				
TREATMENT CHARACTERISTICS						
Treatment collected by						
Self	169	88.4				
Self, Other	5	2.6				
Self, Other, WBOT	5	2.6				
Self, WBOT	7	3.7				
Other	2	1.1				
WBOT	3	1.6				
ART initiated at current site	106	55.5				
Previously defaulted treatment	18	9.4				
Transferred out						
Higher level of care	4	2.1				
Primary care	4	2.1				
ART regimen						
Tenofovir/emtricitabine/efavirenz	158	82.7				
Zidovudine/lamivudine/lopinavir/ritonavir	10	5.2				
Abacavir or zidovudine/lamivudine/efavirenz	21	11				
Tenofovir/emtricitabine/nevirapine	2	1.1				
Duration on ART (months)			12	205	74	40−110
12–60	76	39.8				
61–120	66	34.6				
≥ 121	39	20.4				
Unknown	10	5.2				

CLINICAL CHARACTERISTICS						
Hospitalised in the previous 12 months	8	4.2				
Weight (kg)			29	138	63.5	53–76
< 40	5	2.6				
40–59	68	35.6				
60–79	78	40.8				
≥ 80	33	17.3				
Unknown	7	3.7				
LABORATORY CHARACTERISTICS						
Initial CD4 cell count (cells/mm³)			6	1118	279.5	167–433
< 200	67	35				
200–349	54	28.3				
350–499	26	13.6				
≥ 500	37	19.4				
Unknown	7	3.7				
Latest CD4 cell count (cells/mm³)			51	1873	536	337.5–703.5
< 200	19	9.9				
200–349	30	15.7				
350–499	31	16.2				
≥ 500	104	54.5				
Unknown	7	3.7				
Creatinine (µmol/L)			29	632	81	65–98
≤ 99	121	63.4				
≥ 100	**36**	**18.8**				
Unknown	34	17.8				
Haemoglobin (g/dL)			4.3	16.5	13	11.05–14.65
< 12	7	3.7				
≥ 12	17	8.9				
Unknown	167	87.4				
Total Cholesterol (mmol/L)			2.55	6.89	4.9	4.4–5.68
≤ 5	40	21				
> 5	35	18.3				
Unknown	116	60.7				
COMORBIDITIES						
Comorbidity present	123	64.4				
TB						
Current	6	3.2				
Previous	5	2.6				
Hypertension	106	55.5				
Diabetes Mellitus	15	7.9				
Chronic Kidney Disease	7	3.7				
Hypercholesterolaemia	18	9.4				
VL SUPPRESSION						
VL (copies/ml)			LTDL	394143	≤ 20	0–157.5
< 400	154	81.9				
400–1000	16	8.5				

> 1000	18	9.6	

IQR, interquartile range; WBOT, ward-based outreach team; ART, antiretroviral therapy; TB, tuberculosis; VL, viral load; LTDL, lower than detectable level.

The current treatment collection facility was the site of treatment initiation for 106 patients (55.5%). Other sites of treatment initiation included the regional Wellness clinic (18.9%), another local primary care clinic (5.2%), clinics outside the catchment area (1.6%), private care providers (1.1%), psychiatric hospital, a mining company, correctional facility or the inpatient ward at the regional hospital (0.5% each). The initiation sites were unknown for 30 patients (15.7%). These characteristics were deemed to be treatment characteristics.

Four patients were referred to a higher level of care or a different primary care facility respectively during the study period, thus only 4.2% of patients were documented as having been transferred out of the three facilities to continue treatment elsewhere. Eight patients were hospitalised in the preceding year (4.2%).

ART regimens in relation to renal function

Out of 157 patients for whom the ART regimen and the latest creat were available, some 25/129 patients (19.4%) had a creat of ≥ 100 μmol/L while on first line ART. Those on second-line ART showed a high creat in 3/7 patients (42.9%) and in those on an abacavir or zidovudine-based regimen in 8/19 patients (42.1%).

Comorbidities

One hundred and twenty-three patients (64.4%) had one or more comorbidity. Eighty-four patients (44%) had one chronic condition, a number of 34 patients (17.8%) had two chronic conditions and five patients (2.6%) had three chronic conditions. Most patients (55.5%) had HPT. The following other comorbidities were found: hypercholesterolaemia (9.4%), DM (7.9%), CKD (3.7%), mental health problem (3.1%), asthma (2.6%), post-herpetic neuralgia (1.0%), epilepsy and chronic obstructive airway disease (0.5% respectively). Six patients (3.1%) had TB during the study period and five patients (2.6%) previously had TB. Comorbidities were reflected as proportions of the total cohort.

Virologic suppression

The VL results were available for all but three patients in the cohort (98.4%). Female patients showed 81.7% VL suppression rates compared to 82.3% for male patients. The overall VL

suppression rate was 81.9%. Table 2 depicts the proportion of patients with VL suppression considering their most recent CD4 cell counts. Nineteen percent of patients still had a CD4 cell count of < 350 cells/mm³, even when they were found to have VL suppression.

TABLE 2: VL suppression (recent VL) in relation to recent CD4 cell counts.

	CD4 < 350 cells/mm³ n (%)	**CD4 ≥ 350 cells/mm³ n (%)**	**Total n (%)**
VL < 400 cells/ml n (%)	35 (19)	115 (62.5)	150 (81.5)
VL ≥ 400 cells/ml n (%)	14 (7.6)	20 (10.9)	34 (18.5)
Total n (%)	49 (26.6)	135 (73.4)	184 (100)

VL, viral load

CD4 cell count changes

The median CD4 cell count improved from a baseline of 279.5 cells/mm³ (IQR 167−433) to 536 cells/mm³ (IQR 337.5−703.5) at the most recent CD4 cell count monitoring visit, resulting in a median improvement of 256.5 cells/mm³. Moreover, some 33% of the cohort had a CD4 cell count of ≥350 cells/mm³ at baseline compared to 70.7% at the most recent CD4 cell count monitoring visit.

Relationships between patient characteristics and outcomes

There were no strong correlations or meaningful linear regression results amongst the most recent VL, latest CD4 cell count and other continuous variables (age, duration of ART in months, weight, baseline CD4 count, creat, Hb and chol). During the study period, six patients were LTFU (3.1%) and four died (2.1%) with a mean age of 65.5 years at death. No statistically significant relationships were evident for the outcome LTFU. Table 3 shows the statistically significant relationships that were apparent between patient characteristics and outcomes (objective 4).

Hospitalisation in the past year was positively correlated with dying (50% of patients who died during the study period also had been hospitalised in that year). Moreover, patients with lower Hb levels had a greater association with dying than those with higher Hb levels where there were no mortalities.

Statistically significant relationships for VL were: firstly, patients tended to have higher CD4 cell counts when their VL were suppressed; and secondly, post-herpetic neuralgia (PHN) was

associated with an unsuppressed VL, although only two patients in the cohort were noted to have PHN.

Patients on first line ART had 2.78 greater odds of having higher CD4 cell counts, whereas those on ART for > 5 years had 3.15 greater odds of having higher CD4 cell counts. Although not statistically significant in the logistic regression model, it is still worth noting that female patients had 2.24 times higher odds of having higher CD4 cell counts than male patients and that the odds of having a lower creat was 1.67 times more likely in those with higher CD4 cell counts. A high baseline CD4 cell count was associated with a high recent CD4 cell count, and current TB infection was associated with lower recent CD4 cell counts.

TABLE 3: Relationships between patient characteristics and treatment outcomes.

Outcome	**Alive**	**Dead**	**Chi-square/Fisher exact**	**Logistic regression**
Characteristic	**n**	**n**	***p* value**	***p* value, OR (95% CI)**
Hospitalised in the past year	6	2	0.009	n/a†
Haemoglobin < 12 g/dL	3	4	0.017	n/a†
Outcome	**VL ≤ 400 copies/ml**	**VL > 400 copies/ml**		
Characteristic	**n**	**n**		
Current CD4 ≥ 350 cells/mm^3	115	20	0.034	0.037, 2.3 (1.05–5.02)
Post-herpetic neuralgia	0	2	0.032	n/a†
Outcome	**CD4 < 350 cells/mm^3**	**CD4 ≥ 350 cells/mm^3**		
Characteristic	**n**	**n**		
Patient on first-line ART	35	116	0.023	0.041, 2.78 (1.04–7.42)
Patient on ART > 5 years	19	83	0.007	0.009, 3.15 (1.34–7.40)
Baseline CD4 ≥ 350 cells/mm^3	8	54	0.002	n/a†
Female gender	19	89	0.001	0.059, 2.24 (0.97–5.18)
Current tuberculosis	4	1	0.018	n/a†
Creatinine ≤ 99 µl/L	23	96	0.012	0.277, 1.67 (0.66–4.18)

†Cells contain ≤ 10 observations, thus findings were omitted from the logistic regression model.

OR, odds ratio; CI, confidence interval; VL, viral load; ART, antiretroviral therapy.

Discussion

According to our knowledge, this study was the first to describe patient characteristics and outcomes of PLWH ≥ 60 years old on ART in Tlokwe. Patients 60–69 years old and female patients comprised the largest proportion of our sample. Most patients were on ART for ≤ 10 years, collected their own treatment and few patients had been transferred to other facilities for

further care. The VL suppression rates and CD4 cell response to treatment were fair and almost two-thirds of our sample had one or more comorbidity. Seeing as a small proportion of patients were LTFU or had died during the study period, it is unsurprising that there were few significant relationships between these outcomes and patient characteristics. A low Hb and recent hospitalisation were associated with death, and in this cohort a suppressed VL was associated with a good CD4 cell response. A good CD4 cell response was also associated with first line ART and longer treatment duration.

Female gender seemed to predominate in South African studies evaluating older PLWH from the age of 50 years old.[12,14,22] Although the present study consisted of a smaller cohort of women living with HIV, they represented a similar demographic from the age of 60 and older. One study reported on age sub-categories: 60–64 years and ≥ 65 years where 50% in both groups were women.[13] Interestingly, the only other study in sub-Saharan Africa which showed a female predominance (60.3%) was a recent Ugandan study. Similar to the current study, the aforementioned had a smaller sample size of 244 HIV positive patients.[24] Studies from other sub-Saharan African countries painted a slightly different picture. In 2014, Auld et al[25] pooled data from seven countries situated below the Sahara. With regard to gender, male patients aged ≥ 50 years formed the majority of the cohort in six of the seven countries (51–62%) that were studied. Nigeria was the exception, where 51% of older patients aged ≥ 50 years were female patients.[25] In Burkina Faso, female patients comprised 47.5%[26] of the cohort and in Malawi female patients were also in the minority of the cohort at 41%.[27] Both studies used the age ≥ 50 years to define older adults. Even further afield, Asher et al[28] had a 41% female cohort in Israel, but the older cohort consisted of only 89 patients. European studies also showed a male predominance.[29,30] This could be ascribed to the fact that the principal mode of HIV transmission in these countries is not by heterosexual sexual contact, but by needle transmission in people who inject drugs and between men who have sex with men.

In 2012, the SA National HIV prevalence, incidence and behaviour survey reported a higher HIV prevalence in female patients aged 55–60 years but male patients still predominated in the age categories of 50–55 and ≥ 60, in contrast to our findings. In the aforementioned survey, the proportion of men who reported having more than one sexual partner was eight times that of women. Older men also reported low condom use during their last sexual encounter. These factors may explain why men are more likely to be HIV-infected when they are older. On the other hand, women are known to test for HIV more readily than men and are more aware of

their status, which could influence their HIV incidence. This was reiterated in the report.[16] There is scope to explore sex-specific HIV incidence and prevalence further in SA, especially in the older population.

The majority of this study cohort had been on ART for ≤ 10 years. It was evident from the file reviews that changing treatment guidelines over the years have had an influence on ART initiation in this population, as they were more likely to be initiated in line with their CD4 cell count values at a later stage of infection. Dates of HIV diagnoses were unavailable for many patients that made it impossible to report on the timeline from receiving a diagnosis of HIV and initiating treatment.

Unfortunately, height and thus body mass index (BMI) and/or mid-upper arm circumference (MUAC) measurements were not routinely gathered for this study sample. The weight (median and IQR) nevertheless correlated well with that of participants in another South African study.[13] A comprehensive geriatric assessment (CGA) is a tool which includes 11 components which address biomedical, social and economic concerns for HIV care providers in the context of older patients seeking care. Nutritional status is one of the components that needs to be assessed in all older PLWH.[31] Knowing the nutritional status of a patient might affect 21–82% of treatment decisions, with poor nutritional status strongly associated with mortality. Recent hospitalisation is a known risk factor for dying in older PLWH, and was echoed in our study. A meta-analysis showed that those who underwent a CGA while hospitalised were more likely to be alive after 12 months than those who did not.[32] Hence, there are ample reasons for incorporating anthropometric data (not only weight) into the CGA, but even clinicians in better resourced settings are struggling to adhere to CGA recommendations.[33] Although this is a novel tool in HIV care, it has been successfully used in other disciplines and may prove to be an essential tool in the HIV sphere pertaining to the aging population in years to come.[13]

It may be challenging to comment on the current ART regimen of this cohort, as it was unclear as to if and when regimens were changed from a stavudine-based regimen for those taking treatment for longer as per evolving guidelines. It was clear, however, that an efavirenz-based regimen was the most common treatment prescribed for these patients in line with guidelines used at the time. The tenofovir component was substituted in 16.2% of patients but 18.8% of the cohort had renal dysfunction (creat ≥ 100 µl/L) as evident from the latest creat blood result. Renal dysfunction was especially evident in those on second line treatment and those on

411 abacavir or zidovudine-based regimens. Only 3.7% of the cohort was classified with CKD. One
412 explanation for the low prevalence of CKD may be that renal function improved when
413 tenofovir was substituted with an agent that is known to be renal protective and these patients
414 were subsequently not classified as having CKD, but this does not explain the high percentage
415 of renal dysfunction in this cohort. Another explanation may be that primary care clinicians
416 simply did not diagnose or document CKD in this cohort. The prevalence of CKD was one in
417 five PLWH aged ≥ 60 years in a study conducted in 12 French hospitals. CKD was
418 independently associated with five-year mortality (aHR = 2.25, 95% CI 1.58–2.21) along with
419 cardiovascular disease (aHR = 2.40, 95% CI 1.64–3.52).[29] These findings may warrant more
420 rigorous screening and documentation of kidney function in our setting, especially as
421 cardiovascular deaths and CKD walk hand-in-hand.[34]
422
423 Even in this reasonably small cohort, the prevalence of HPT and DM were high compared with
424 other studies.[14,24] In these studies, the prevalence of HPT ranged from 21.5–33.3%, the latter
425 percentage for patients aged ≥ 70 years. In our study population, there was 55.5% of older
426 PLWH on treatment for HPT. The differences may be due to the other studies actively
427 measuring participants' blood pressure at ART initiation, whereas the current study relied on
428 clinical records and could not account for what might have come first: HIV or HPT. The same
429 could be said about DM, where prevalence ranged from 2.2–6.3% in the other cohorts,
430 compared to 7.85% in the current cohort. Again, conclusive interpretation of these results is
431 elusive because the current study inception was not at ART initiation.
432
433 The VL suppression in this cohort was lower than previously reported in SA.[12-14] Moreover,
434 VL suppression was attained in 86%–89.5% of older adults in other settings after 12–60 months
435 of treatment. It was perturbing that only 81.9% of this cohort had a suppressed VL, especially
436 as a larger proportion of them were on second-line treatment than those found in other South
437 African cohorts. Female patients had lower VL suppression rates, despite historically better
438 treatment adherence rates. This may hamper the 90–90–90 UNAIDS target of achieving a 90%
439 VL suppression rate in all age groups globally by 2030. South Africa currently stands at 87%
440 VL suppression in 54% of all PLWH.[35] More attention should be given to older age groups in
441 order to attain the UNAIDS goals.
442
443 The median CD4 cell count increased by 256.5 cells/mm^3 from baseline in this cohort.
444 Similarly, Fatti et al[12] found that the median CD4 cell count increased from about 100

cells/mm^3 after six months and to over 300 cells/mm^3 after 48 months, since ART initiation. It is well-established that CD4 cell recovery is attenuated in older PLWH compared to younger PLWH.[11,12] In this study, it was evident that higher recent CD4 cell counts were more likely in those who had been taking ART for ≥ 5 years (OR = 3.15, 95% CI 1.34-7.40, p = 0.009) and those on first-line ART (OR = 2.78, 95% CI 1.04–7.42, $p = 0$.041). The former may have been an obvious finding, but further work may be needed to evaluate the latter, especially at the dawn of a new first-line regimen roll-out in SA, which will replace the drug efavirenz with dolutegravir.[36]

Strengths and limitations

Most previous studies in the field of older PLWH have defined them to be aged ≥ 50 years. However, seeing as assumptions of life expectancy without HIV and total fertility rates were estimated to be 61.5 years for males and 67.7 years for females in 2019,[16] it was imperative to assess older age groups and exclude those still eligible to work for future planning of care interventions for these individuals. This is one of the first local studies to use this novel approach. Also, a paucity of data were available on the subject in the NWP according to the researcher's knowledge, and this is the first study to begin to address this gap. Most previous studies published about older PLWH have compared their response since ART initiation to younger cohorts. The current study did not address this. The sample was chosen conveniently and thus could have introduced selection bias. Also, the retrospective design has disadvantages. Previous prospective studies on the subject could compare baseline characteristics and outcomes in terms of ART initiation and follow-up. This approach was not possible in the current study due to time constraints in terms of data collection, and there were many missing files as well as data missing within files (e.g. sociodemographic, treatment, clinical and laboratory information, reporting of comorbidities) which could have influenced study findings. The sample size was small and this could perhaps be seen as a pilot study for future studies on older PLWH in the NWP. Generalizability was affected by limited patient numbers and the exclusion of a more rural cohort. Unmeasured covariates could have resulted in hidden bias.

Conclusion

To our knowledge, this was the first study to assess characteristics and outcomes in older PLWH in the NWP. There is an urgent need for South African clinicians to consider the implementation of standardised CGA in all older PLWH, as they have proved to be a unique

population in terms of HIV care and clinicians have experienced difficulties in assessing and managing them. CKD needs to be actively excluded in older PLWH as it has major implications, especially in the context of high cardiovascular morbidity and mortality. Mortality and LTFU were however low in this cohort. Further research in the NWP is necessary to confirm or refute the findings of low VL suppression rates in older PLWH and intervene as and if necessary, so as to assist the Department of Health to reach the UNAIDS targets.

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Competing interests

The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.

Authors' contributions

This article was submitted by Mareike Rabe (M.R) as a requirement for partial fulfilment of MMed (Family Medicine). M.R. was the main author. Carien Lion-Cachet (C.L.C.) was the primary supervisor and Melaku Eyassu (M.E.) the secondary supervisor. All authors commented on drafts of the article and approved the final version to be published.

REFERENCES

1. UN. World Population Ageing 2019: Highlights (ST/ESA/SER.A/430) [homepage on the internet]. Department of Economic and Social Affairs, Population Division: The United Nations; 2019 [cited 2019 Dec 03]. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Highlights.pdf
2. SASSA. Grants for Older Persons [homepage on the internet]. South African Department of Social Development; no date [cited 2019 Oct 23] Available from: https://www.sassa.gov.za/Pages/Older-Persons-Grant.aspx
3. UN. World Population Ageing 2015 (ST/ESA/SER.A/390) [homepage on the internet]. Department of Economic and Social Affairs, Population Division: The United Nations; 2015[cited 2019 Dec 03]. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2015_Report.pdf
4. WHO. World Report on Ageing and Health [homepage on the internet]. World Health Organisation; 2015 [cited 2019 Dec 03]. Available from: http://apps.who.int/iris/bitstream/10665/186463/1/9789240694811_eng.pdf?ua=1
5. NDoH. Implementation of the universal test and treat strategy for HIV positive patients and differentiated care for stable patients [homepage on the internet]. South African National Department of Health; 2016 [cited 2019 Mar 03]. Available from: http://www.sahivsoc.org/Files/22%208%2016%20Circular%20UTT%20%20%20Decongestion%20CCMT%20Directorate%20(2).pdf
6. STATSSA. Media release: Mortality and causes of death, 2015: Findings from death notification [homepage on the internet]. Department Statistics South Africa; 2017 [cited 2019 Dec 3]. Available from: http://www.statssa.gov.za/?p=9604
7. Phaswana Mafuya N, Peltzer K, Schneider M, et al. Study on Global Ageing and Adult Health (SAGE), South Africa 2007 – 2008. Geneva. World Health Organization; 2011
8. Tanyi PL, Pelser A. The missing link: finding space for gerontology content into university curricula in South Africa. Gerontology & Geriatrics Education. 2018;40(4): 491-507. https://doi.org/10.1080/02701960.2018.14285799
9. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. Lancet. 2013;382(9903):1525-1533. https://doi.org/10.1016/S0140-6736(13)61809-7

10. Bendavid E, Ford N, Mills EJ. HIV and Africa's elderly: the problems and possibilities. AIDS. 2012; 26(Suppl 1):S85-S91. https://doi.org/10.1097/QAD.0b013e3283558513
11. Malaza A, Mossong J, Bärnighausen, T, et al. Population-based CD4 Counts in a rural area in South Africa with high HIV prevalence and high antiretroviral treatment coverage. PLoS One. 2013;8(7):e70126. https://doi.org/10.1371/journal.pone.0070126
12. Fatti G, Mothibi E, Meintjies G, et al. Antiretroviral treatment outcomes amongst older adults in a large multicentre cohort in South Africa. PLoS One. 2014;9(6):e100273. https://doi.org/10.1371/journal.pone.0100273
13. Cornell M, Johnson LF, Schomaker M, et al. Age in antiretroviral therapy programmes in South Africa: a multicentre observational cohort study. Lancet HIV. 2015;2(9):pe368-e375. https://doi.org/10.1016/S2352-3018(15)00113-7
14. Dawood H, Hassan-Moosa R, Zuma N-Y, et al. Mortality and treatment response amongst HIV-infected patients 50 years and older accessing antiretroviral services in South Africa. BMC Infect Dis. 2018;**18**(168). https://doi.org/10.1186/s12879-018-3083-z
15. STATSSA. Mid-year population estimates [homepage on the internet]. Department Statistics South Africa; 2019 [cited 2019 Oct 22]. Available from: http://www.statssa.gov.za/publications/P0302/P03022019.pdf
16. Shisana O, Rehle T, Simbayi L, et al. South African National HIV prevalence, incidence and behaviour survey, 2012. Cape Town: HSRC Press; 2014
17. STATSSA. Statistics South Africa. Tlokwe City Council [homepage on the internet]. Department Statistics South Africa; no date [cited 2019 Oct 23]. Available from : http://www.statssa.gov.za/?page_id=993&id=tlokwe-city-council-municipality
18. NDoH. National Core Standards for Health Establishments in South Africa [homepage on the internet]. South African National Department of Health; 2011 [cited 2019 Oct 23]. Available from: http://www.rhap.org.za/wp-content/uploads/2014/05/National-Core-Standards-2011-1.pdf
19. NPC. National Development Plan 2030. Our future-make it work. South Africa: National Planning Commission; 2012 [cited 2019 Oct 23]. Available from: https://www.poa.gov.za/news/Documents/NPC%20National%20Development%20Plan%20Vision%202030%20-lo-res.pdf
20. STATSSA. Promosa [homepage on internet]. Department Statistics South Africa; no date [cited 2019 Oct 23]. Available from: http://www.statssa.gov.za/?page_id=4286&id=11135

21. NDoH.. National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults [homepage on the internet]. South African Department of Health; 2015 [cited 2019 Dec 5]. Available from: https://sahivsoc.org/Files/ART%20Guidelines%2015052015.pdf
22. Butler I, MacLeod W, Pappie P, et al. Human immunodeficiency virus infection and older adults: A retrospective single-site cohort study from Johannesburg, South Africa. South African Journal of HIV Medicine. 2018;19(1):a838. https://doi.org/10.4102/sajhivmed.v19i1.838
23. Osler M, Hilderbrand K, Hennessey C, et al. A three-tier framework for monitoring antiretroviral therapy in high HIV burden settings. J Int AIDS Soc. 2014;17:18908. https://doi.org/10.7448/IAS.17.1.18908
24. Mugisha JO, Schatz EJ, Randell M, et al. Chronic disease, risk factors and disability in adults aged 50 and above living with and without HIV: findings from the wellbeing of Older People Study in Uganda. Global Health Action. 2016;9(1):31098. https://doi.org/10.3402/gha.v9.31098
25. Auld AF, Agolory SG, Shirashi RW et al. Antiretroviral therapy enrolment characteristics and outcomes among HIV-infected adolescents and young adults compared with older adults – Seven African countries, 2004 – 2013 [homepage on the internet]. MMWR Morb Mortal Wkly Rep. 2014 [cited 2019 Dec 12];63(47):1097-1103. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5779521/
26. Diallo I, Meda N, Quédraogo S et al. Profiles of elderly people infected with HIV and response to antiretroviral treatment in Burkina Faso: A retrospective cohort study. J Int Assoc Provid AIDS Care. 2017;16(4):405-411. https://doi.org/10.1177/2325957417709088
27. Tweya H, Feldacker C, Heller T, et al. Characteristics and outcomes of older HIV-infected patients receiving antiretroviral therapy in Malawi: A retrospective observation cohort study. PLoS One. 2017;12(7):e0180232. https://doi.org/10.1371/journal.pone.0180232
28. Asher I, Guri K, Elbirt D, et al. Characteristics and outcome of patients diagnosed with HIV at older age. Medicine. 2016;95(1):e2327 https://doi.org/10.1097/MD.0000000000002327
29. Hentzien M, Dramé M, Allavena C, et al. Impact of age-related comorbidities in five-year overall mortality among elderly HIV-infected patients in the late HAART era – role of

chronic renal disease. J Nutr Health Aging. 2016;**20**:408-414. https://doi.org.10.1007/s12603-015-0608-7

30. Gimeno-Gracia M, Crusells-Canales MJ, Rabanaque-Hernández MJ. Clinical characteristics and antiretroviral treatment of older HIV-infected patients. Int J Clin Pharm. 2014;**36**:1190-1195. https://doi.org/10.1007/s11096-014-0015-x
31. Singh HK, Carmen TD, Freeman R, et al. From one syndrome to many: incorporating geriatric consultation into HIV care. Clinical Infectious Diseases. 2017;65(3):501-506. DOI: https://doi.org/10.1093/cid/cix311
32. Ellis G, Whitehead MA, O'Neil D et al. Comprehensive geriatric assessment for older adults admitted to hospital. Cochrane Database of Systematic Reviews 2011, Issue 7. Art. No. CD006211. https://doi.org/10.1002/14651858.CD006211.pub2.
33. Bitas C, Jones S, Singh HK, et al. Adherence to recommendations from comprehensive geriatric assessment of older individuals with HIV. J Int Assoc Provid AIDS Care. 2019;18:1-8. https://doi.org/10.1177/2325958218821656
34. Davids MR, Chothia MY. Chronic kidney disease for the primary care clinician. S Afr Fam Pract [serial on the internet]. 2019 [cited 2019 Dec 11];61(5):19-23. Available from: https://safpj.co.za/index.php/safpj/article/view/4941/5837
35. Avert. South Africa 90-90-90 progress [homepage online]. 2019 [cited 2019 Dec 12]. Available: https://www.avert.org/infographics/south-africa-90-90-90-progress-2019
36. DOH e-Library. 2019 ART clinical guidelines for the management of HIV in adults, pregnancy, adolescents, children, infants and neonates [homepage on the internet]. South Africa: Department of Health; 2019 [cited 2019 Dec 11]. Available from: https://www.knowledgehub.org.za/elibrary/2019-art-clinical-guidelines-management-hiv-adults-pregnancy-adolescents-children-infants