

Original Article



Aging with HIV: The Burden of Comorbidities, Polypharmacy, and Drug Interactions in Korean People Living with HIV Aged ≥ 50 Years

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ABSTRACT

Background: The life expectancy of people living with human immunodeficiency virus (PLWH) has significantly improved with advancements in antiretroviral therapy (ART). However, aging PLWH face a growing burden of non-communicable diseases (NCDs), polypharmacy, and drug-drug interactions (DDIs), which pose challenges in their management. This study investigates the prevalence of NCDs, polypharmacy, and DDIs among PLWH aged ≥ 50 years in Korea and their impact on quality of life (QOL).

Materials and Methods: A cross-sectional study was conducted among 243 PLWH aged ≥ 50 years receiving ART for at least three months at three university hospitals in Korea between January and July 2022. Data were collected through electronic medical records and personal interviews, assessing demographics, comorbidities, polypharmacy, ART adherence, and QOL using the Korean version of WHOQOL-HIV BREF scale. Potential DDIs were analyzed using the University of Liverpool HIV Drug Interaction Database, and potentially inappropriate medications (PIMs) were identified using the 2023 American Geriatrics Society Beers Criteria. We classified participants into three age groups: 50- <65 years, 65- <75 years, and ≥ 75 years.

Results: The prevalence of comorbidities was 71.6%, with older participants (≥ 75 years) showing a significantly higher burden, including bone diseases, osteoarthritis, and dementia ($P < 0.001$). Polypharmacy was observed in 28.4% of participants and increased with age, with 53.3% of those aged ≥ 75 years taking ≥ 10 pills daily.

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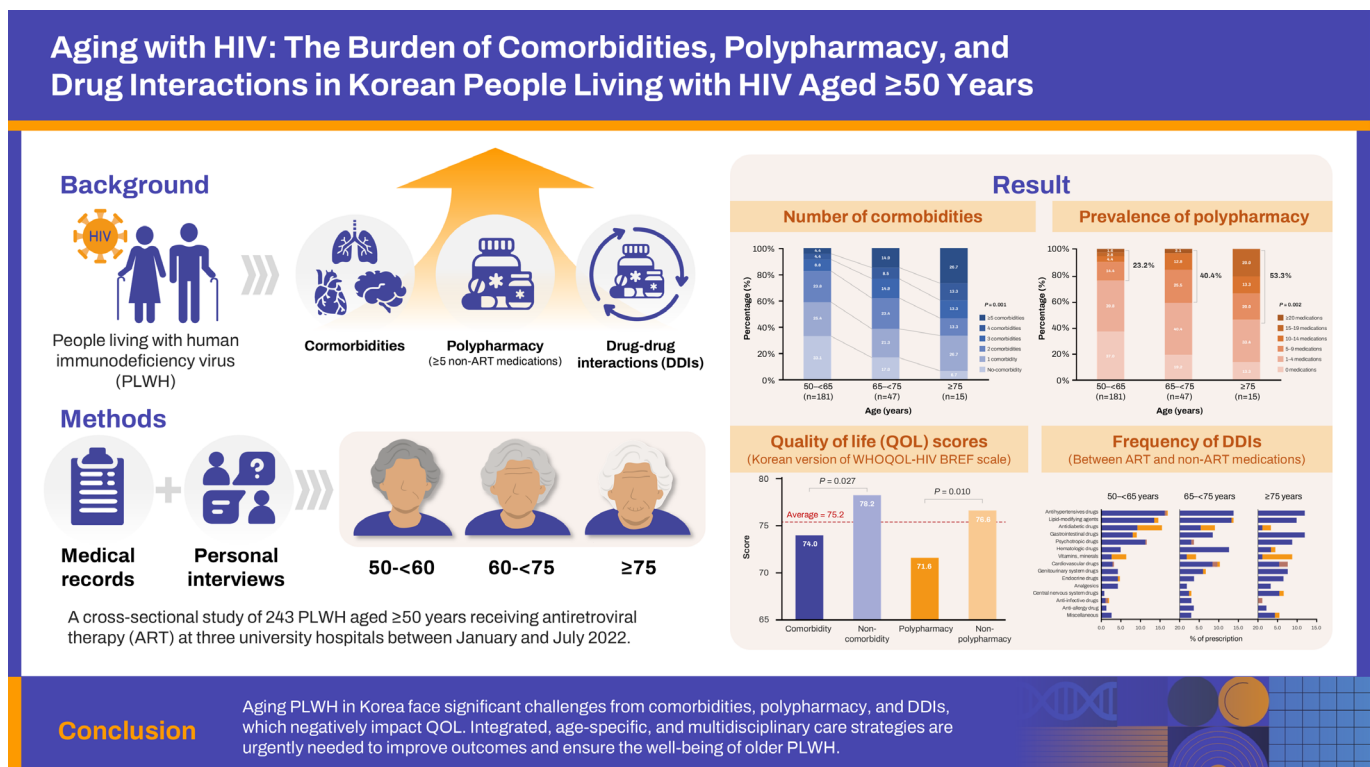
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Polypharmacy was associated with poorer QOL (71.6 vs. 76.6, $P=0.010$). Amber-flag DDIs were found in 81 participants (33.3%), most commonly involving metformin and divalent cations. No red-flag DDIs were identified. PIMs were observed in 6.6% of participants aged ≥ 65 years.

Conclusion: Aging PLWH in Korea face significant challenges from comorbidities, polypharmacy, and DDIs, which negatively impact QOL. Integrated, age-specific, and multidisciplinary care strategies are urgently needed to improve outcomes and ensure the well-being of older PLWH.

Keywords: HIV; Comorbidity; Polypharmacy; Drug interaction; Quality of life

GRAPHICAL ABSTRACT



INTRODUCTION

The survival rate of people living with human immunodeficiency virus (PLWH) has improved significantly, with life expectancy for these individuals now approaching that of the general population, thanks to advancements in antiretroviral therapy (ART) and increased access to these treatment [1]. However, PLWH often face non-communicable diseases (NCDs) earlier than those without human immunodeficiency virus (HIV), resulting in complex healthcare needs [2]. Korea, with one of the longest-standing universal health coverage systems, has enhanced healthcare accessibility nationwide and provided universal ART access via its health insurance

system since 1997 [3]. As a result, the HIV-positive population in Korea is aging, and the prevalence of comorbidities among PLWH is rising [4]. This increase in comorbidities has contributed to a substantial prevalence of NCDs in PLWH, which raises critical concerns about drug-drug interactions (DDIs) [5].

Polypharmacy in PLWH can lead to overlapping toxicities and pharmacokinetic changes that may diminish the effectiveness of treatments or exacerbate adverse effects from ART and other medications [6]. Compounding these challenges, HIV-related stigma and discrimination persist in Korean healthcare settings, especially in non-HIV specific services [7]. Many PLWH do not disclose their

HIV status when seeking non-HIV related medical care, thereby heightening the risk of unrecognized DDIs or potentially inappropriate medication (PIMs). According to a 2016 survey, 76.2% of PLWH reported difficulty in revealing their HIV status during non-HIV healthcare visits due to fear of discrimination [8].

Currently, data on the prevalence of polypharmacy and DDIs among PLWH in Korea remain scarce. This study aims to assess the prevalence of NCD, the use of co-medications, and DDIs with ART in individuals over 50 living with HIV. Additionally, it seeks to explore the impact of increased medication on their overall quality of life.

MATERIALS AND METHODS

1. Study population and setting

This study included individuals aged ≥ 50 years with HIV who had been on ART for at least 3 months, recruited from three university hospitals between January and July 2022. Patient data were obtained from electronic medical records and included information on age, gender, health insurance status, alcohol use more than once a month, comorbidities, date of HIV diagnosis, CD4+ T cell count, HIV-1 viral load, ART regimens, and ART duration at the last visit during the study period. Body mass index (BMI) measurements from the last follow-up visit were also recorded.

A personal interview collected additional information on living environments, the number and types of medications currently being taken (including medications prescribed by other hospitals and over-the-counter), knowledge about these medications, self-reported adherence within the 3 months preceding the interview, and quality of life (QOL). Medications analysis about DDIs were based on those taken continuously for one year, and prescriptions were checked or medications were brought in by the participants. Medications were classified using the Korea Food and Drug Safety Ministry [9]. Oral medications and injections were included, but topical ointments were excluded. The level of knowledge about the medications were assessed by asking each participant the purpose of each medication with response classified into four categories based on similarity to the intended purpose.

2. Ethics statement

This study was approved by the Institutional Review Board of Chonnam National University Hospital (IRB no. CNUH-

2021-452), and written informed consent was obtained from all participants.

3. Definitions

Comorbidity was defined based on guidelines-defined criteria [10], and polypharmacy was defined as the use of ≥ 5 concomitant drugs, excluding ART [6]. Adherence to ART and non-ART medications was assessed using the Simplified Medication Adherence Questionnaire (SMAQ), which has a dichotomous structure [11]. Adherence was classified as 'not good' if there was a 'positive' response to any of the four qualitative questions, if two or more doses were missed in the previous week, or if there were two or more days in the past 3 months when no medication taken [10].

QOL was assessed using the Korean version of the World health organization's quality of life-human immunodeficiency virus brief scale (WHOQOL-HIV BREF) [12, 13]. This tool comprises 31 items, including two general questions about overall quality of life and health status, and 29 items representing six domains. Each item is scored on a 25-point Likert scale from 0 (very bad) to 100 (very good), with seven reverse-scored items (3, 4, 5, 8, 9, 10, and 31). The six domains evaluated are physical, psychological, independence, social relationships, environment, and spiritual/personal beliefs [11]. The total score of the 31 items is converted to a scale ranging from a minimum of 0 to a maximum of 100, with higher scores indicating better quality of life.

Potential DDIs between ART and non-ART medications were determined using the University of Liverpool HIV Drug Interaction Database [14]. If a medication contained two or more pharmacologically active agents, each substance was assessed individually. The interactions were categorized from "no interaction" (green) to "weak interaction not requiring additional action" (yellow), "clinically relevant DDI requiring dose adaptation or monitoring" (amber), and "contraindicated" (red). PIMs were identified using the 2023 American Geriatrics Society (AGS) Beers criteria [15]. The criteria assess PIM use based on drug-disease interactions, the need for cautious use in older adults, clinically important DDIs to avoid, and required dosage modifications for varying kidney function. However, due to lack of data on timely kidney function, dosage modifications for renal adjustments could not be assessed.

4. Statistical analysis

Participants were stratified by age into three groups: 50-<65 years, 65-<75 years and ≥ 75 years. Demographic and clinical characteristics were summarized using median (interquartile range; [IQR]), mean (standard deviation; [SD]) or percentage with frequency values by age group. Continuous variables were compared using analysis of variance, followed by Tukey's post hoc test for normally distributed data. Normality was assessed with the Kolmogorov-Smirnov test. Categorical variables were evaluated using Pearson's chi-square test. All significance tests were two-tailed, with P -values < 0.05 considered statistically significant. Analyses were conducted using SPSS (version 27.0, IBM Corp., Armonk, NY, USA).

RESULTS

1. Demographic and clinical characteristics of the participants

Of the 519 PLWH aged ≥ 50 years invited to participate, 243 (46.8%) were enrolled. By age group, 181 (48.5%) were 50-<65 years, 47 (49.0%) were 65-<75 years, and 15

(30.0%) were ≥ 75 years, with percentages indicating the proportion of participants within each age group. **Table 1** summarizes the demographic and clinical characteristics by age group. The median age was 59.0 years (IQR, 55.0-65.0), and 92.2% of the participants were male. Living arrangements varied, with 55.6% living with family and 37.9% living alone. All participants had medical insurance, while 24.3% received medical aid. Alcohol use was more prevalent in younger participants ($P=0.001$). The median CD4+ T cell count was 538 cells/mm³, and 95.9% had undetectable HIV RNA levels (<40 copies/mL). The median ART duration was 9.0 years (IQR, 5.0-13.0), and most participants (92.2%) were on INSTI-based regimens. ART adherence, as assessed by SMAQ, was high (88.1%) and consistent across age groups ($P=0.201$).

2. Comorbidity and polypharmacy

The prevalence of comorbidities was 71.6%, increasing significantly with age ($P<0.001$, **Table 2**, **Fig. 1A**). The median number of comorbidities rose from 1 (IQR: 0-2) in participants aged 50-<65 years to 3 (IQR, 1-5) in those aged ≥ 75 years ($P<0.001$). Common comorbidities included dyslipidemia (33.7%), hypertension (31.3%),

Table 1. Demographic and clinical characteristics of people living with human immunodeficiency virus aged ≥ 50 years

Characteristic	Total (N=243)	Age 50-<65 Years (N=181)	Age 65-<75 Years (N=47)	Age ≥ 75 Years (N=15)	P-value
Age, median (IQR), years	59 (55-65)	57 (54-60)	68 (66-71)	79 (77-81)	<0.001
Male, N (%)	224 (92.2)	171 (94.5)	44 (93.6)	9 (60.0)	<0.001
Living arrangement, N (%)					0.689
Living alone	92 (37.9)	69 (38.1)	18 (38.3)	5 (33.3)	
With family	135 (55.6)	98 (54.1)	27 (57.4)	10 (66.7)	
With friend/colleague	16 (6.6)	14 (7.7)	2 (4.3)	0	
Health insurance service, N (%)					0.243
Medical aid	59 (24.3)	47 (26.0)	11 (23.4)	1 (6.7)	
Social health insurance	184 (75.7)	134 (74.0)	36 (76.6)	14 (93.3)	
Alcohol use, n (%)	126 (51.9)	105 (58.0)	19 (40.4)	2 (13.3)	0.001
BMI (kg/m ²), median (IQR)	24.3 (22.5-26.2)	24.3 (22.5-26.4)	24.0 (22.6-25.2)	25.1 (21.5-26.9)	0.565
CD4+ T cell count (cells/mm ³), median (IQR)	538.0 (390.0-805.0)	550.0 (377.5-820.0)	536.0 (444.0-749.0)	553.0 (317.0-658.0)	0.651
HIV RNA (copies/mL), N (%)					0.484
<40 copies/mL	233 (95.9)	172 (95.0)	46 (97.9)	15 (100)	
≥ 40 copies/mL	10 (4.1)	9 (5.0)	1 (2.1)	0	
Duration of ART (years), median (IQR)	9.0 (5.0-13.0)	9.0 (4.0-13.0)	9.0 (6.0-12.0)	11.0 (8.0-18.0)	0.054
ART regimens, N (%)					0.034
NRTI(s)+INSTI	224 (92.2)	168 (92.8)	41 (87.2)	15 (100)	
NRTIs+PI	8 (3.3)	4 (2.2)	4 (8.5)	0	
PI+INSTI	7 (2.9)	7 (3.9)	0	0	
PI+INSTI+NNRTI	2 (0.8)	2 (1.1)	0	0	
NRTIs+NNRTI	2 (0.8)	0	2 (4.3)	0	
ART adherence, N (%)					0.201
Good	214 (88.1)	160 (88.4)	39 (83.0)	15 (100)	
Not-good	29 (11.9)	21 (11.6)	8 (17.0)	0	

N, number; IQR, interquartile range; BMI, body mass index; HIV, human immunodeficiency virus; ART, antiretroviral therapy; NRTI, nucleoside reverse transcriptase inhibitor; INSTI, integrase strand transfer inhibitor; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor.

diabetes mellitus (20.2%), and bone diseases including osteopenia, osteoporosis, and bone fracture (14.0%). Bone diseases, osteoarthritis, and dementia were notably more prevalent in the oldest age group ($P<0.01$). Drugs for hypertension and lipid modification were the most commonly prescribed, but there was a sharp increase in the use of gastrointestinal and psychiatric medications among participants aged ≥ 75 years compared to younger age groups (Fig. 1B). Older participants visited healthcare facilities more frequently for comorbidity management (median: 5 visits/year for those aged ≥ 75 years, $P=0.022$).

Polypharmacy, defined as the use of ≥ 5 non-ART medications, was more common among participants aged ≥ 65 years (43.5%) compared to those aged <65 years (23.2%, $P=0.006$, Table 2). The number of non-ART medications and pill burden also increased with age, with 53.3% of participants aged ≥ 75 years taking ≥ 10 pills daily

(Fig. 1C). Knowledge about non-ART medications declined significantly with age ($P=0.002$), although adherence to non-ART medications remained high (80.0%).

3. Quality of life

The overall WHOQOL-HIV BREF score was lowest in participants aged 65- <75 years ($P=0.030$, Table 3). Most domain scores, except for physical and independence, followed a similar trend. Participants with at least one comorbidity had significantly lower QOL scores compared to those without comorbidities (74.0 vs. 78.2, $P=0.027$, Fig. 2). Likewise, polypharmacy was associated with worse QOL (71.6 vs. 76.6, $P=0.010$).

4. Potential drug-drug interactions and potentially inappropriate medications

For the 165 participants taking non-ART medications, 689 drug interaction analyses were performed. No red-flag

Table 2. Prevalence of comorbidities and polypharmacy in people living with human immunodeficiency virus aged ≥ 50 years

Variables	Total (N=243)	Age 50- <65 Years (N=181)	Age 65- <75 Years (N=47)	Age ≥ 75 Years (N=15)	P-value
Comorbidity, N (%)	174 (71.6)	121 (66.9)	39 (83.0)	14 (93.3)	0.014
Number of comorbidities, median (IQR)	1.0 (0.0-2.0)	1.0 (0.0-2.0)	2.0 (1.0-3.0)	3.0 (1.0-5.0)	<0.001
Type of comorbidities, N (%)					
Dyslipidemia	82 (33.7)	58 (32.0)	19 (40.4)	5 (33.3)	0.556
Hypertension	76 (31.3)	51 (28.2)	18 (38.3)	7 (46.7)	0.170
Diabetes mellitus	49 (20.2)	38 (21.0)	9 (19.1)	2 (13.3)	0.762
Cardiovascular disease (including stroke)	36 (14.8)	16 (8.8)	16 (34.0)	4 (26.7)	<0.001
Bone disease ^a	34 (14.0)	19 (10.5)	7 (14.9)	8 (53.3)	<0.001
Osteoarthritis	30 (12.3)	16 (8.8)	9 (19.1)	5 (33.3)	0.006
Mental health	21 (8.6)	14 (7.7)	4 (8.5)	3 (20.0)	0.267
Dysuria	21 (8.6)	9 (5.0)	9 (19.1)	3 (20.0)	0.002
Dermatologic diseases	17 (7.0)	9 (5.0)	6 (12.8)	2 (13.3)	0.107
Liver diseases	16 (6.6)	12 (6.6)	4 (8.5)	0	0.511
Solid tumor	7 (2.9)	5 (2.8)	2 (4.3)	0	0.680
Dementia	3 (1.2)	0	1 (2.1)	2 (13.3)	<0.001
Lung diseases	3 (1.2)	2 (1.1)	1 (2.1)	0	0.771
Kidney diseases	3 (1.2)	2 (1.1)	1 (2.1)	0 (0.0)	0.771
Eye diseases	3 (1.2)	0	2 (4.3)	1 (6.7)	0.009
Alopecia	2 (0.8)	2 (1.1)	0	0	0.708
Number of visits to medical institutions for comorbidities/year, median (IQR)	4.0 (0.0-6.0)	2.0 (0.0-6.0)	4.0 (0.0-10.0)	5.0 (3.0-12.0)	0.022
Polypharmacy, N (%)	69 (28.4)	42 (23.2)	19 (40.4)	8 (53.3)	0.006
Number of patients with non-ART medication, N (%)	165 (67.9)	114 (63.0)	38 (80.9)	13 (86.7)	0.018
Pill burden of non-ART medication, median (IQR)	2 (0-5)	2 (0-4)	4 (1-7)	5 (2-14)	0.004
Non-ART Medication knowledge, N=165 (%)					0.002
All	115 (69.7)	86 (75.4)	22 (57.9)	7 (53.8)	
Most of	25 (15.2)	16 (14.0)	9 (23.7)	0	
A little	15 (9.1)	9 (7.9)	2 (5.3)	4 (30.8)	
Not at all	10 (6.1)	3 (2.6)	5 (13.2)	2 (15.4)	
Non-ART Medication Adherence, N=165 (%)					0.170
Good	132 (80.0)	89 (78.1)	30 (78.9)	13 (100)	
Not good	33 (20.0)	25 (21.9)	8 (21.1)	0	

^aOsteopenia, osteoporosis, bone fracture.

N, number; IQR, interquartile range; ART, antiretroviral therapy.

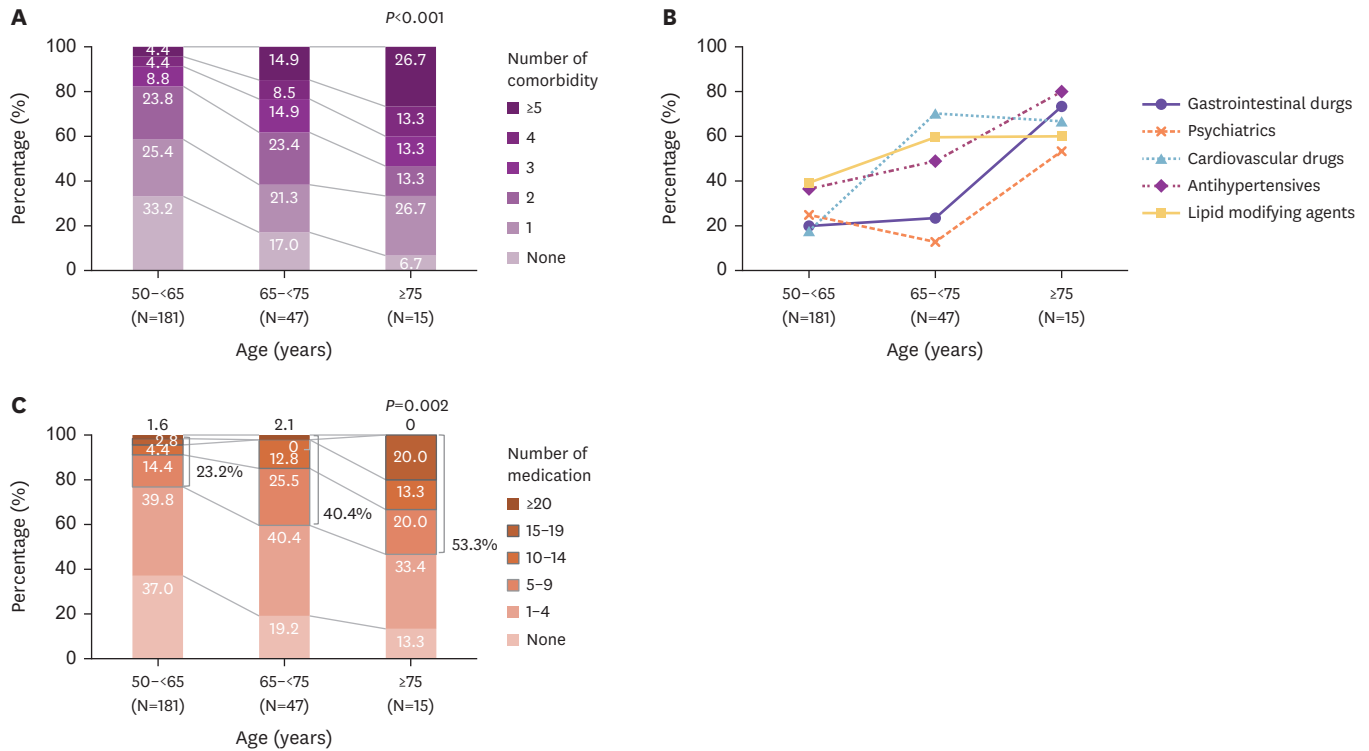


Figure 1. Comorbidity and polypharmacy among people with human immunodeficiency virus.

(A) Number of comorbidities according to age group. Comorbidities in participants, stratified by age groups (50-65 years, 65-75 years, and ≥75 years). (B) Percentage of non-antiretroviral therapy (ART) medications by therapeutic class among people living with HIV with comorbidities. Distribution of commonly used non-ART medications (e.g., antihypertensives and lipid-modifying agents) among participants with comorbidities. (C) Prevalence of polypharmacy according to age proportion of participants with ≥5 non-ART medications, stratified by age groups, highlighting the increasing prevalence with age. Polypharmacy was 53.3% in participants aged ≥75 years, 40.4% in those aged 65-75 years, and 23.2% in those aged 50-65 years.

Table 3. Quality of life of people living with human immunodeficiency virus aged ≥50 years

WHOQOL-HIV BREF categories	Total (N=243)	Age 50-65 Years (N=181)	Age 65-75 Years (N=47)	Age ≥75 Years (N=15)	P-value
WHOQOL-HIV BREF score, median (IQR)	75.2 (65.5-86.2)	76.3 ^a (67.2-86.6)	70.5 ^a (61.4-80.0)	76.7 (60.7-91.0)	0.030
General quality of life	72.4 (60.0-100.0)	74.5 ^a (60.0-100.0)	62.1 ^{a,b} (40.0-80.0)	78.7 ^b (60.0-100.0)	0.001
General Health	70.5 (60.0-100.0)	71.3 (60.0-100.0)	66.4 (60.0-80.0)	73.3 (60.0-100.0)	0.415
Physical	76.0 (65.0-90.0)	77.5 (65.0-95.0)	72.3 (65.0-85.0)	68.7 (55.0-85.0)	0.053
Psychological	73.4 (60.0-88.0)	74.3 (62.0-88.0)	68.0 (56.0-80.0)	78.7 (72.0-96.0)	0.035
Independence	74.0 (65.0-85.0)	75.9 ^b (65.0-85.0)	68.6 ^b (60.0-80.0)	68.3 (50.0-80.0)	0.005
Social relationships	69.9 (60.0-80.0)	71.4 ^b (60.0-80.0)	63.3 ^b (50.0-75.0)	72.3 (50.0-90.0)	0.010
Environment	77.7 (67.5-87.5)	78.6 ^a (68.8-90.0)	72.6 ^{a,b} (65.0-80.0)	83.3 ^b (75.0-97.5)	0.011
Spirituality	77.3 (65.0-95.0)	77.2 (65.0-95.0)	75.2 (65.0-90.0)	85.0 (80.0-100.0)	0.207

^{a,b}Significant statistical differences between groups determined by Turkey post hoc analysis ($P < 0.05$).

WHOQOL-HIV BREF, World Health Organization's quality of life-human immunodeficiency virus brief scale; N, number; IQR, interquartile range.

DDIs were identified, but amber-flag DDIs were observed in 81 cases (Supplementary Fig. 1). Amber-flag DDIs most commonly involved metformin (43.2%, $n=35$) and divalent cations (33.3%, $n=27$) (Supplementary Table 1). INSTI-based regimens accounted for 84.0% of amber-flag DDIs. In the ≥75 age group, amber-flag DDIs with vitamins/minerals were most frequent (7.7%, Supplementary Fig. 1).

Among participants aged ≥65 years, 27.4% (17/62) had PIMs according to the Beers criteria. Common PIMs included antidepressants with strong anticholinergic effects and zolpidem tartrate (Table 4). There were no contraindicated DDIs.

Table 4. Potentially inappropriate medications (PIMs) identified by Beers criteria in people living with human immunodeficiency virus aged ≥65 years (N=62)

PIM category	Number, (%)
PIMs use	N=14
Antidepressants with strong anticholinergic activity, alone or in combination (risk of anticholinergic effects, high risk of orthostatic hypotension)	4 (23.5)
Non-benzodiazepine, benzodiazepine receptor agonist hypnotics (have adverse events similar to those of benzodiazepines in older adults, e.g., delirium, falls, fractures)	4 (23.5)
First generation antihistamines (risk of anticholinergic effects)	3 (17.6)
Proton-pump inhibitors (risk of <i>Clostridioides difficile</i> infection, pneumonia, gastrointestinal malignancies, bone loss, and fractures)	2 (11.7)
Non-selective peripheral alpha-1 blockers for the treatment of hypertension (high risk of orthostatic hypotension)	1 (5.8)
PIMs due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome	N=2
Non-dihydropyridine calcium channel blockers in patients with history of heart failure	1 (5.8)
Non-selective peripheral alpha-1 blockers in patients with urinary incontinence (all type) in women	1 (5.8)
PIMs to be used with caution	N=1
Trimethoprim-sulfamethoxazole (may increase risk of hyperkalemia)	1 (5.8)

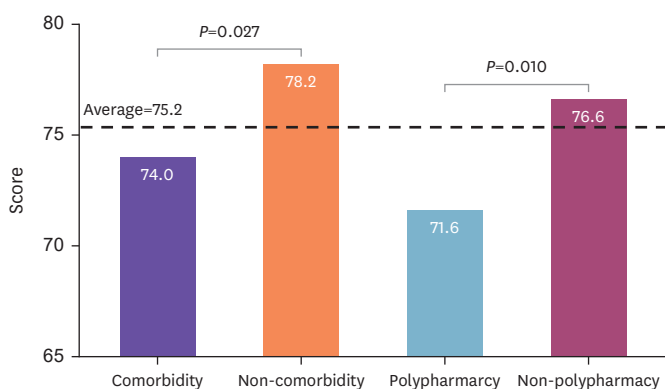


Figure 2. Quality of life scores according to comorbidity and polypharmacy.

The average quality of life (QOL) score for all participants was 75.2, with higher scores indicating better quality of life. A comparison of WHOQOL-HIV BREF scores between participants with and without comorbidities or polypharmacy revealed that those with comorbidities or polypharmacy had lower QOL scores.

WHOQOL-HIV BREF, World Health Organization's quality of life-human immunodeficiency virus brief scale.

DISCUSSION

This study highlights the significant impact of aging on the health and treatment complexities faced by elderly PLWH aged ≥50 years in Korea. The prevalence of comorbidities increased substantially with age, with older participants exhibiting a higher burden of conditions such as bone diseases, osteoarthritis, and dementia. Polypharmacy was observed in nearly half of participants aged ≥65 years and was associated with higher pill burdens and poorer quality of life. Although no red-flag DDIs were identified, amber-flag DDIs involving ART and commonly prescribed medications, such as metformin and

divalent cations, were prevalent, particularly in those on INSTI-based regimens.

Most elderly PLWH are affected by multiple comorbidities. Previous studies report comorbidity rates ranging from 48% to 84%, with the average number of comorbidities per individual ranging from 2.4 to 3.6 [16-21]. Similarly, our study found that 71.6% of participants had at least one comorbidity, with the burden increasing with age. This trend aligns with global findings, where the interplay between HIV-related inflammation and aging accelerates the onset of age-associated diseases. Common comorbidities included dyslipidemia, hypertension, diabetes mellitus, and bone diseases. Older participants, particularly those aged ≥75 years, showed a higher prevalence of bone diseases, osteoarthritis, and dementia compared to younger age groups. These findings underscore the need for comprehensive geriatric assessments in routine HIV care to identify and manage comorbidities early, minimizing their impact on overall health outcomes.

Comorbidities were a major driver of polypharmacy in this study, as observed in previous research [17]. Reports of polypharmacy prevalence vary widely, ranging from 15% to 94% across studies [6, 16]. In this study, the overall prevalence of polypharmacy was relatively low at 28.4%, but it increased significantly with age, with over half of those aged ≥75 years taking 10 or more pills daily. The polypharmacy was associated with poorer QOL and the substantial pill burden likely contributed to this decline. While polypharmacy is often necessary to manage multiple comorbidities, it also increases the risk of medication non-adherence, adverse drug reactions, and DDIs. As fourth “90” target of UNAID’s 95-95-95

framework emphasizes achieving good health-related QOL, strategies such as deprescribing and tailored medication regimens are critical for mitigating these risks and improving quality of life for older PLWH.

Despite these challenges, adherence to ART and non-ART medications was remarkably high across all age groups, reflecting the effectiveness of Korea's robust healthcare infrastructure and universal ART access. However, as the population continues to age, cognitive decline and medication complexity could pose future barriers to adherence.

Amber-flag DDIs were prevalent, with INSTI-based regimens most commonly involved. INSTI, currently recommended as first-line therapy [10, 22], have a more favorable DDI profile compared to boosted PIs or NNRTIs [23-25]. However, due to the widespread use of INSTI in this cohort, amber-flag DDIs involving metformin and divalent cations were more frequent than in other studies, such as a Swiss cohort [25]. Metformin requires close monitoring for adverse effects, while divalent cations can reduce INSTI absorption if taken concurrently. Patient education and clear medication instructions are vital to managing these interactions effectively. PIMs were identified in 6.6% of PLWH aged ≥ 65 years, which is notably lower than the 16.0% reported in an Italian study [26]. The low rate of PIMs may be attributed to Korea's Drug Utilization Review system, which provides real-time information to doctors and pharmacists regarding drug safety, likely filtering out red-flag medications, as well as the counseling programs for PLWH in Korean health care facilities [27].

This study had several limitations. First, the cross-sectional design limits the ability to establish causal relationships between variables, such as comorbidities, polypharmacy, and quality of life. While the WHOQOL-HIV BREF instrument was used to assess quality of life, it may not fully capture the nuanced experiences of elderly PLWH, especially in relation to stigma, social support, and cognitive decline. Second, the study population consisted of PLWH voluntarily recruited from three university hospitals, which may not fully represent the general population of elderly PLWH in Korea. Third, the study relied on electronic medical records and self-reported medication use, which may have resulted in underreporting of certain PIMs or DDIs. Over-the-counter medications and traditional remedies, which were not captured, could also have influenced the results. Finally, while the findings

provide valuable insights into the Korean context, they may not be directly applicable to other countries with different healthcare systems or access to ART.

In conclusion, there are the increasing burden of comorbidities, polypharmacy, and DDIs in aging PLWH. These findings emphasize the need for comprehensive, age-specific HIV care strategies to further improve outcomes and ensure the well-being of older PLWH.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Cases with amber flag drug-drug interaction according to antiretroviral therapy classes

Supplementary Figure 1

Frequency of drug-drug interactions (DDIs) between ART and non-ART medications by interaction severity.

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Conflict of Interest

No conflict of interest.

Author Contributions

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