Virological and immunological status and comorbidities in elderly people living with HIV

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Summary

Background: Our study aims to assess the clinical, treatment and analytical characteristics of older HIV-positive patients, comparing patients aged 65–74 versus those aged ≥ 75 years.
Material and methods: Cross-sectional study in patients diagnosed with HIV, born before 1 August 1952, and followed at the General University Hospital of Alicante.
Results: We included 73 patients of the total 1280 patients in follow-up. Median age was 72 years (interquartile range [IQR] 65–87). 64 patients (87.7%) were men. 40 (54,8%) had a sexual transmission, 1 (1,5%) by intravenous drug use and 30 (41.1%) had an unknown transmission. 30 (41.1%) presented an advanced clinical stage of disease at diagnosis. Median Charlson index was 5 (IQR 1–11) [4 (65-74y) vs 8 (>75y) p=0,009]. Arterial hypertension (44,1% vs 77,3%, p= 0,007), isquemic cardiopathy (9,8% vs 31,8%, p=0,02) and chronic kidney disease (23,5% vs 50%, p=0,03) were significantly higher in the older subgroup. Most (88.6%) had a viral load < 50 copies, and median CD4/CD8 ratio was 0.70 without difference of the age.
Conclusions: The study population was generally diagnosed at an advanced stage of HIV with a plurality infected through sexual transmission. Patients had high levels of comorbidity, especially in older patients. Despite having good virological and immunological control, the inversion of the CD4/CD8 ratio persists.

Key words:
HIV. Cross-sectional study. Elderly. Comorbidity.

Situación virológica e inmunológica y comorbilidades en ancianos con infección por VIH

Resumen

Fundamentos: El objetivo de nuestro estudio fue analizar las características clínicas, terapéuticas y analíticas de nuestros pacientes VIH mayores de 65 años.
Material y métodos: Estudio transversal de pacientes en seguimiento en el Hospital General Universitario de Alicante con diagnóstico de infección por VIH y habiendo nacido antes del 1 de agosto de 1952.
Resultados: Se incluyeron 73 pacientes de un total de 1280 pacientes en seguimiento. La edad media fue 72 años (rango intercuartílico [RIC] 65-87). 64 pacientes (87,7%) fueron varones. 40(54,8%) tuvieron una transmisión sexual, 1 (1,5%) por administración de drogas parenterales y 30 (41.1%) tuvieron una transmisión desconocida. 30 (41,1%) presentaron un estadio clínico avanzado al diagnóstico. La mediana de índice de Charlson resultó en 5(RIC 1-11), estadísticamente superior en el grupo de más edad [4(65-75 años)vs 8(>75 años) p=0,009]. Predominan la hipertensión (44,1%vs77,3%, p= 0,007), la cardiopatía isquémica (9,8%vs31,8%, p=0,02) y la enfermedad renal crónica (23,5%vs50%, p=0,03). El 88,6% tenían una carga viral <50 copias y la mediana del cociente CD4/CD8 fue de 0,70 sin diferencias significativas por edad.
Conclusiones: La población analizada se caracteriza por un diagnóstico en estadio avanzado predominando el mecanismo de transmisión sexual. Existe elevada comorbilidad, la cual es mayor en los pacientes más añosos; y un buen control virológico e inmunológico, pero persiste inversión del cociente CD4/CD8.

Palabras clave:
VIH. Estudio transversal. Edad avanzada. Comorbilidad.

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Introduction

HIV was first discovered in 1983. Since then, medical and treatment advances —especially highly active antiretroviral therapy, which became available in 1997— have continued to extend the life expectancy of people living with HIV (PLHIV)[1-4].

In the general population, people over the age of 65 years are considered older adults, as this age threshold has traditionally been linked to social and work-life changes signalling a new stage in adult life[1,2]. In the population of PLHIV, age over 65 is regarded as very advanced[3]. These patients seem biologically older than their years would indicate, and they tend to have health problems associated with older subgroups[2,5].

In 2015, about 41,5% of PLHIV in Spain are at least 50 years old, and this figure is expected to reach 73% by 2030[3]. As the life expectancy of PLHIV continues to increase, it is important to understand the epidemiological characteristics of this population in order to offer them the best treatment and address their comorbidities in a holistic way[1,3].

Our study aims to assess the clinical, treatment, and analytical characteristics of older HIV-positive patients, comparing patients aged 65–74 versus those aged ≥75 years.

Material and methods

Study design

Observational retrospective cohort study.

Study setting

The General University Hospital of Alicante is a public hospital with a catchment area of 270,000 inhabitants; its cardiac surgery service is a reference center for the province of Alicante (approximately 1.9 million inhabitants) on the Mediterranean coast of Spain.

Study population

People diagnosed with HIV, born before 1 August 1952, and in follow-up as outpatients in the Infectious Diseases Unit of the General University Hospital of Alicante up to at least 1 August 2017.

Study variables

We collected variables related to epidemiology, route of transmission, drug treatments, antirretroviral therapy, underlying diseases (dyslipidemia, arterial hypertension, diabetes mellitus, chronic kidney disease, fractures, cancer, ischemic cardiopathy, osteopenia, chronic obstructive pulmonary disease, peripheral arterial disease, hepatitis C, stroke, venous insufficiency, hyperuricemia, dementia), Charlson comorbidity index[6], HIV stage and analytical and immunological parameters (estimated glomerular filtration rate, CD4 and CD8 cells, CD4/CD8 ratio and viral load).

Data collection

Patients' clinical records were retrieved from the informatics systems Abucasis® (Conselleria de Sanitat, Generalitat Valenciana, Spain) and Orion Clinic® (Conselleria de Sanitat, Generalitat Valenciana, Spain) systems to collect study variables

Data analysis

Data analysis was undertaken using IBM SPSS software (version 23.0). Patients aged 65 to 74 years were compared to those aged 75 or older by means of the chi-square statistic for categorical variables and the Mann-Whitney U test for continuous variables. P-values of less than 0.05 were considered statistically significant.

Ethical aspect

Data confidentiality and patient anonymity were maintained at all times, in accordance with Spanish regulations on observational studies. Patient identifiable information was deleted before the database was analyzed; thus, it is not possible to identify patients on an individual level either in this article or in the database. This study was carried out in accordance with the Declaration of Helsinki and was approved by the Institutional Research Ethics Committees of the hospital.

Results

Of the 1280 patients in follow-up at the Infectious Diseases Unit on 1 August 2017, 73 (5.7%) were aged 65 or older. Of these, 51 were aged 65 to 74, while 22 were 75 years old or older.

Table 1 presents patients' epidemiological, clinical, virological and immunological characteristics, both in the total sample and by age subgroup. 64 patients (87.7%) were men and 9 (13,3%) women. 30 (41.1%) presented a clinical stage C disease, according to the Centers for Disease Control and Prevention staging system[7]. The most frequent known route of transmission was sexual (38.4% homosexual and 16.4% heterosexual), only 1 (1.5%) was by intravenous drug use while 41.1% either did not know or did not admit it. Median time since diagnosis was 18 years (interquartile range [IQR] 15.0–20.5). Twenty (27.4%) patients were diagnosed between 1987 and 1997, 56 (53.4%) between 1998 and 2007, and 6 (8.2%) between 2008 and 2017.

Table 1. Epidemiological, clinical, analytical, and immunological characteristics of elderly patients with HIV.

Variables	Age			P value
	≥ 65 years	65-74 years	≥ 75 years	
Men, n (%)	64 (87.7)	43 (84.3)	21 (95.5)	0.18
Years since HIV diagnosis, median (IQR)	18 (15-20.5)	18 (15-22)	18 (13-19)	0.40
Number of follow-up visits in previous year, median (IQR)	5 (2.25-7.0)	5 (2.5-8.0)	5 (3.0-7.0)	0.75
Route of transmission				
Homosexual, n (%)	28 (38.4)	19 (37.3)	9 (40.9)	0.62
Heterosexual, n (%)	12 (16.4)	10 (19.6)	2 (9.1)	0.33
Transfusion, n (%)	2 (2.7)	1 (2.0)	1 (4.5)	1.00
Intravenous drug use, n (%)	1 (1.4)	1 (2.0)	0 (0.0)	1.00
Unknown, n (%)	30 (41.1)	20 (39.2)	10 (34.5)	0.76
Drug treatments				
Number of prescriptions, median (IQR)*	5 (3-8)	4 (3-7)	7 (3-10)	0.001
Antirretroviral therapy				
Integrase inhibitors, n (%)	27 (37.0)	17 (33.3)	10 (45.5)	0.23
NNRTIs, n (%)	20 (27.4)	17 (33.3)	3 (13.6)	0.083
Protease inhibitors, n (%)	13 (17.8)	7 (13.7)	6 (27.3)	0.24
Protease and integrase inhibitors, n (%)	12 (16.4)	9 (17.6)	3 (13.6)	0.92
General drug treatments				
Hypolipidemics, n (%)	43 (59.7)	29 (58.0)	14 (63.6)	0.65
Antihypertensives, n (%)	37 (51.4)	21 (42.0)	16 (72.7)	0.016
Antidiabetics, n (%)	21 /29.2)	14 (28.8)	7 (31.8)	0.74
Psychotropic drugs, n (%)	21 (29.2)	14 (28.0)	7 (31.8)	0.74
Stomach protector, n (%)	17 (23.6)	10 (20.0)	7 (31.8)	0.28
Antiplatelet, n (%)	15 (20.8)	6 (16.0)	7 (31.8)	0.13
Analgesics, n (%)	10 (13.9)	6 (12.0)	4 (18.2)	0.49
Steroids, n (%)	3 (4.29)	2 (4.0)	1 (4.5)	1.00
Anticoagulants, n (%)	6 (8.3)	3 (6.0)	3 (13.6)	0.36
Underlying diseases				
Dyslipidemia, n (%)	54 (74.0)	37 (72.5)	17 (77.3)	0.67
Arterial hypertension, n (%)	39 (53.4)	22 (43.1)	17 (77.3)	0.007
Diabetes mellitus, n (%)	23 (31.5)	15 (29.4)	8 (34.8)	0.56
Chronic kidney disease, n (%)	23 (31.5)	12 (23.5)	11 (50.0)	0.032
Fractures, n (%)	18 (24.7)	10 (19.6)	8 (36.4)	0.13
Cancer, n (%)	17 (23.3)	11 (21.6)	6 (27.3)	0.57
Ischemic cardiopathy, n (%)	12 (16.4)	5 (9.8)	7 (31.8)	0.020
Osteopenia, n (%)	11 (15.1)	6 (11.8)	5 (22.7)	0.39
COPD, n (%)	11 (15.1)	6 (72.6)	5 (22.7)	0.23
Peripheral arterial disease, n (%)	10 (13.7)	4 (7.8)	6 (27.3)	0.057
Hepatitis C, n (%)	8 (11.0)	7 (13.7)	1 (4.5)	0.42
Stroke, n (%)	7 (9.6)	1 (5.9)	4 (18.2)	0.19
Venous insufficiency, n (%)	6 (8.2)	3 (5.9)	3 (13.6)	0.36
Hyperuricemia, n (%)	4 (5.5)	3 (5.9)	1 (4.5)	1.00
Dementia, n (%)	2 (2.7)	1(2.0)	1 (4.5)	1.00
Active tobacco use, n (%)	18 (24.7)	14 (27.5)	4 (18.2)	0.38
Charlson comorbidity index, median (IQR)	5 (1-11)	4 (1-9)	8 (3-12)	0.009
HIV stage				
A, n (%)	31 (42.5)	26 (51,0)	5 (22,7)	0.02
B, n (%)	12 (16.4)	6 (11,8)	6 (27,3)	0.16
C, n (%)	30 (41.1)	19 (37,3)	11 (50,0)	0.31
Nadir CD4 cells/µL				
<200, n (%)	41 (56.2)	28 (54,9)	13 (59,1)	0.91
200-499, n (%)	27(37.0)	20 (39,2)	7 (31,8)	0.81
>500, n (%)	5 (6,8)	3 (5,9)	2 (9,1)	0.92
Analytical and immunological parameters				
eGFR, median (IQR)	71 (56-83)	76 (61.5-86)	61 (45-79)	0.012
CD4 cells/µL, median (IQR)	663 (353-847)	703 (491-832)	581 (429-882)	0.55
CD8 cells/µL, median (IQR)	852 (620-852)	893 (693-1450)	716 (536-1147)	0.072
CD4/CD8 ratio, median (IQR)	0.70 (0.48-0.93)	0.67 (0.45-0.90)	0.71 (0.51-0.93)	0.38
Viral load < 50 copies/mL**, n (%)	62 (88.6)	44 (89.8)	18 (85.7)	0.69

*missing values (1/1/0), ** (3/2/1)

In bold, statistically significant differences. COPD: chronic pulmonary obstruction disease; eGFR: estimated glomerular filtration rate; IQR: interquartile range; NNRTI: non-nucleoside reverse transcriptase inhibitors.

Regarding comorbidities, median Charlson index was 5 (IQR 1–11). Fifty-four (74.0%) patients presented dyslipidemia; 39 (53.4%), arterial hypertension; 23 (31.5%), diabetes mellitus; 23 (31.5%), chronic kidney disease (defined as an estimated glomerular filtration rate [eGFR] of < 60 mL/min); 12 (16.4%), ischemic cardiopathy; and 10 (13.7%), peripheral arterial disease. The rest of the comorbidities are presented in Table 1.

Compared to patients aged 65 to 74 years, patients over 75 showed a statistically higher Charlson index (8, IQR 3–12 versus 4, IQR 1–9; p = 0.009) along with greater prevalence of hypertension (n = 17, 77.3% versus n = 22, 43.1%; p = 0.007) and ischemic cardiopathy (n = 7, 31.8% versus n = 5, 9.8%; p = 0.020). There were also more older patients with a low eGRF (n = 11, 50.0% versus n = 12, 23.5%; p = 0.032).

With respect to pharmacological treatments, patients were prescribed a median of 5 drug treatments (IQR 3–8), with this number higher in the older group (7, IQR 3–10 versus 4, IQR 3–7; p = 0.001). In terms of which drugs they were taking, 43 (59.7%) were on hypolipidemics, and 37 (51.4%) on anti-hypertensives; the latter drug treatment was more common in patients over 75 (n = 16, 72.7% versus n = 21, 42.0%; p = 0.016). Other prescribed treatments are listed in Table 1.

The antiretroviral treatment regimen was classified according to the third drug treatment. Twenty-seven patients (37.0%) were on integrase inhibitors and 20 (27.4%) on non-nucleoside reverse transcriptase inhibitors (NNRTIs). Older patients were less likely to use the latter drugs (n = 3, 13.6% versus n = 17, 33.3%; p = 0.083).

Median CD4 lymphocyte count was 663 cells/µL (IQR 653–847), while the median CD8 count was 852 cells/µL (IQR 620–852). The median CD4/CD8 ratio was 0.70, and it was similar in both age groups. Most patients (n = 62, 88.6%) had a viral load of less than 50 copies/mL, and this was unrelated to the number of pills taken, the length of antiretroviral treatment, or age.

Discussion

The results of our study show a notably low percentage of adults aged 65 or older (5.7%) among HIV-positive patients. Among these, very few acquired the infection through intravenous drug use. These results can be explained by the premature mortality among PLHIV due to the higher morbidity associated with intravenous drug use[8]; and the timing of the HIV/AIDS epidemic worldwide, as people who were infected under the age of 35 and who also had access to antiretroviral treatment could probably not have turned 65 yet[9,10].

Our patients showed a high burden of comorbidities, indicating a high demand for care and healthcare resources. Cardiovascular comorbidity was the most prevalent: three of four patients presented dyslipidemia and more than half arterial hypertension, which is consistent with the literature[11]. A higher prevalence of cardiovascular disease was seen in literature and values are similar to our study[11,12]. The prevalence of chronic kidney disease is high in HIV-infected people and grows with age, similar than other studies.

Polymedication in our group of patients was high and increased with age and it`s correlated with the literature[11]. The risk of interactions and poor treatment compliance increases exponentially to greater drug consumption. It is therefore a relevant factor to be taken into account in patients with HIV[2].

Despite the high percentage of patients with a previous diagnosis of AIDS and the high median years since diagnosis, 88.6% of the patients showed an HIV viral load of less than 50 copies/mL at the assessment time point. However, even with this virological success, the median CD4/CD8 ratio was lower in our study population than in the unit as a whole. The inversion of the CD4/CD8 ratio is a marker of immunosenescence, and it has been associated with a greater presence of comorbidities and premature death[13]. We also observed that advanced age did not affect virological and immunological status.

The study has some limitations. First, it is an observational, retrospective study developed in a single centre with a specific population and a reduced number of patients which could limit the generalization of our results. Other factors are showing great relevance when studying elder HIV patients such as frailty, quality of life or sarcopenia[14,15]; however, they weren't study. Nowadays frailty is a trendy topic to explain that. It is an aged related syndrome of decreased physiological reserve which is indepently associated with HIV infection. Frailty seems to be a predictor of adverse health outcomes, such as comorbidities, falls and disability, and can be measured in people aging with HIV by frailty index and frailty phenotype[16,17]. It is necessary to study differences between patients aged 65 to 74 years and over 75 to know the changes with ageing.

In conclusion, the study population was generally diagnosed at an advanced stage of HIV or AIDS, with a plurality infected through sexual transmission. Patients had high levels of comorbidity, especially cardiovascular disease and chronic kidney disease; which are significantly higher in patients older than 75. Despite having good virological and immunological control, the inversion of the CD4/CD8 ratio persists.

Due to the improvements in virological treatments and HIV-patients' healthcare`s quality, the life expectancy of this population is growing dramatically and thus comorbidities and health problems related to ageing[3]. This is a novel paradigm

which physicians are going to face on in a short period of time. So that, according Negredo *et al*[2] the ageing of PLHIV population constitutes a new challenge for clinicians who treat people with this disease, and it will compel health professionals and researchers to reevaluate the care that these patients will need in the not-so-distant future.

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