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Infeção VIH – diagnóstico na população acima dos 50 anos

HIV diagnosis in people over 50 years

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/ Resumo

Introdução: A população com vírus de imunodeficiência humana (VIH) está a envelhecer em todo o mundo e é crescente o número de novas infeções em doentes com idade superior a 50 anos. Apesar do impacto positivo da terapêutica antirretroviral sobre morbilidade global e doenças relacionadas, estas são mais prevalentes nesta faixa etária. As condições crónicas associadas ao envelhecimento também aumentam em todos os pacientes com VIH.

Objetivo: Descrição de características clínicas e imunológicas, bem como comorbilidades numa amostra de doentes estratificada de acordo com a idade à data do diagnóstico.

Métodos: Caracterização de doentes VIH acompanhados na consulta externa de um hospital terciário em Lisboa durante 2014, através da revisão dos processos clínicos e avaliação retrospetiva dos parâmetros demográficos, epidemiológicos, clínico-laboratoriais e regimes terapêuticos.

Resultados: Dos 730 doentes, 105 foram diagnosticados com idade superior ou igual a 50 anos. A maioria foi do género masculino (66,7%), caucasiana (77,1%) e heterossexual (86,7%), tendo sido diagnosticada num estádio avançado da infeção (52,4%). À data de recolha de dados, considerando este grupo de doentes, 100 indivíduos encontravam-se sob tratamento antirretroviral e com supressão viral (90,5%). A prevalência de comorbilidades aumentou com a idade do diagnóstico ($p<0.001$).

Conclusões: Doentes diagnosticados mais tardiamente apresentaram uma maior prevalência de comorbilidades e polimedicação, estando expostos a um risco mais elevado de interações medicamentosas. Uma abordagem clínica abrangente e rigorosa configura-se primordial para a redução da morbilidade e mortalidade nesta população.

Palavras-chave: VIH, envelhecimento, comorbilidades

/ **Abstract**

Introduction: *The human immunodeficiency virus (HIV) epidemic is ageing worldwide with increasing numbers of newly diagnosed individuals being over 50 years old. In spite of the positive impact of antiretroviral treatment on overall morbidity and related diseases, these are more prevalent in this age group. Furthermore, it is well-recognized the association between accelerated ageing and HIV infection.*

Objectives*: Describe the immunological, clinical and comorbidity profile across a cohort of HIV-infected patients stratified according to age at time of diagnosis.*

Methods*: Characterization of HIV infected population attending the outpatient department of a tertiary hospital in Lisbon in 2014, through the review of medical records and retrospective evaluation of demographic, epidemiological, clinical, laboratorial and treatment parameters.*

Results*: Of 730 patients, 105 were aged 50 and older at the time of diagnosis. Most of these patients were male (66.7%), white (77.1%), heterosexual (86.7%) and were diagnosed with advanced stage of infection (52.4%). At the time of data collection, within this older group, 100 individuals were under antiretroviral treatment and with viral suppression (90.5%). The prevalence of comorbidities significantly increased with age of diagnosis ($p<0.001$).*

Discussion*: Older diagnosed patients had a higher prevalence of comorbidities and polypharmacy, being exposed to an increased risk of potential drug interactions. A comprehensive approach to clinical care plays a key role in reducing morbidity and mortality in this population.*

Keywords: *HIV; Ageing; Comorbidity*

/ Introduction

The infection by the human immunodeficiency virus (HIV) is a dynamic phenomenon. The classic segments of population affected at the beginning of the epidemic suffered important decline over time.[1] The present distribution worldwide depends on individual and collective behaviour, among other significant factors. In recent years, in all geographical areas a progressive increase in the average age of HIV and Acquired Immune Deficiency Syndrome (AIDS) diagnosis has been noted.

The improved survival of people with HIV results from progress in clinical diagnosis and treatment. This became particularly evident after the introduction of combination antiretroviral therapy (cART), which has radically changed the natural history of HIV disease. From diagnosis at an advanced stage of disease, with an invariably deleterious progression, to a chronic and controllable disease, there has been a drastic fall in morbidity and mortality.[2]

The overall morbidity of AIDS and related illnesses have declined significantly since the introduction of cART and the "full-blown" disease seems to develop with a higher CD4 cell count in comparison to what happened in the past.

Nevertheless, the population affected by AIDS-associated diseases remains similar. Most AIDS patients aged 50 or older either find out about their infection in a late stage or have continuously shown poor treatment compliance.[3,4]

The increasing average age at AIDS diagnosis has progressed alongside with the gradual increase in mean age of HIV infected patients. This situation, already noticeable even before cART introduction, is probably related to a prolonged delay in seeking medical help by patients who were not aware of their condition and progressive change of HIV transmission risk behaviour.[5]

Taking into account the unquestionable effectiveness of cART in extending life expectancy, it is understandable that the number of people over 50 years old living with HIV is expected to rise in the coming decades.

In addition, it is important to be aware of the risk of HIV primary infection in this age group, which is often neglected.[6] Several factors contribute to this scenario: most people aged 50 years and older do not consider themselves at risk of contracting HIV infection, unlike younger groups; advertising campaigns rarely target individuals over 50 years; health care professionals tend to

undermine the risk and undertake less frequent screenings; incipient HIV infection can mimic age-related symptoms, significantly delaying diagnosis; in Western countries prolonging life expectancy and improving quality of life facilitate the use of pro-erectile drugs and increase exposure to sexually transmitted diseases; barrier methods are generally less used by many older people who remain sexually active; physiological changes in the vaginal mucosa after menopause leads to greater infection risk.[7]

The majority of these patients present with symptomatic HIV disease and some even with AIDS defining illnesses at time of diagnosis.[8]

Regardless of the individual immunological status, clinical course and outcome are additionally conditioned by ageing, which is an independent predictor of disease progression.[9] Several theories have been presented to explain this rapid evolution of the infection, such as: small T cells reserve; increased viral entry into cells; reduced IL-2 leading to immunosenescence.

Physiological changes caused by ageing also interfere with drug metabolism and pharmacokinetics, resulting in increased susceptibility to potential side effects.[9]

Of special importance are the neuropsychiatric symptoms associated with efavirenz, osteoporosis and kidney damage related to tenofovir, gastrointestinal intolerance and hepatotoxicity. The increased cardiovascular risk – namely through dyslipidemia and other metabolic alterations – and probability of certain malignancies should also prompt particular awareness.[9]

Regarding Portugal, since the first available data (1983), 74% of new infections have occurred within the age group 20-44 years. However, patients above 50 years old already account for 14.4% of all cases, similarly to other reports showcasing a remarkable growth of diagnosis in this population. In 2013 there were 1416 new cases of HIV-infection, a decrease of 2.1% comparing to the previous year. The Portuguese incidence was at the time 13.6/100.000 population, which was still considerably high among western European countries.[10,11]

/ General Objective

The aim of this study was to describe the immunological, clinical and comorbidity profile across a cohort of patients with HIV infection, stratified according to age of diagnosis, followed up in an outpatient center in Lisbon during the year 2014.

/ Methods

Characterization of HIV infected patients followed at an outpatient department of a tertiary hospital in Lisbon. Data was collected through review of clinical reports and laboratory test results.

For this retrospective study, 730 patients over 18 years old who have had at least one appointment between January 1st 2014 and December 31st 2014 were included. Patients were stratified into two groups: "Diagnosis before 50 years" and "Diagnosis at or after 50 years".

A retrospective evaluation was made considering the following parameters: age at diagnosis, gender, race, region of origin, transmission category, HIV type, years of HIV infection, immune and virological status, type and duration of antiretroviral therapy and associated comorbidities.

Definitions used:

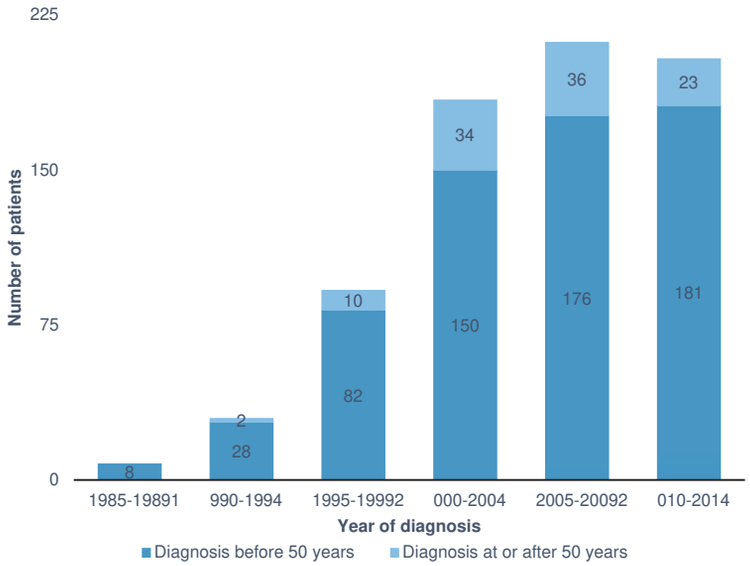
- "Years of HIV infection" – period between the first HIV positive test available and 31st December 2014.
- "Viral suppression" – viral load less than 50 HIV RNA copies/µL in the last assessment performed in 2014.
- "Last CD4 cells/µL" – the last CD4 count available until 31st December 2014.
- "Nadir CD4 cells/µL" – the lowest CD4 count available until 31st December 2014.
- "Comorbidities" such as: hypertension (values ≥ 140 mmHg and/or ≥ 90mmHg); CVD (ischemic heart disease and/or cerebrovascular disease); diabetes (HbA1c ≥ 6.5%, or fasting plasma glucose ≥ 126mg/dL); dyslipidemia (total cholesterol ≥ 200mg/dL, LDL cholesterol ≥100mg/dL HDL cholesterol < 40mg/dL, triglycerides ≥ 150mg/dL); chronic renal failure (glomerular filtration rate lower than 60mL/min); depression (if under specific drug intervention).
- "AIDS staging", "AIDS defining illness" and "non-AIDS defining cancer" were defined according to CDC criteria.
- "Advanced HIV disease" – patients presenting with a CD4 count below 200 cells/µL or presenting with an AIDS defining event, regardless of the CD4 cell count.
- "Alcohol abuse" – pattern of drinking that results in harm to one's health, interpersonal relationships or ability to work.

Statistical comparison of quantitative variables across groups was accomplished using parametric test (T-student) and non-parametric test (Chi-square and Wilcoxon test). For all tests, the threshold for statistical significance was set at 5%. Analyses were done using Excel software 2013 edition.

All data were collected with patient consent and were treated under confidentiality.

/ Results

Through 12 months, 730 patients were evaluated at our outpatient clinic with a mean follow-up of 8.7 years. At the time of diagnosis, 105 patients (14.4%) were aged 50 or more and 625 patients (85.6%) were under 50 years old. *Graphic I* displays the



Graphic I – Patient distribution by age of diagnosis

number of patients diagnosed by year, distributed according to the two previously defined groups.

Table I shows clinical and laboratorial parameters, distributed according to age of the diagnosis. There was no significant difference in duration of HIV infection between the two groups.

In both groups there was a higher prevalence of male (overall average of 70%), white (overall average of 77%) and European patients (overall average of 71%). In terms of region of origin there was a relevant prevalence of Africa (overall average 20.8%), reflecting the standing relation between Portuguese-speaking countries. Interestingly, Brazil accounted for most American patients (61 in 63), representing exclusively the group diagnosed before age 50.

Regarding HIV-transmission, sexual contacts were the most common ($p<0.001$). The proportion of heterosexual and men who have sex with men (MSM) differed between age groups. In general terms, heterosexual transmission was the barely the most common (50.7%), having in the older group a statistically significance higher prevalence, which contrasted with MSM (86.7 and 8.6%, respectively). Active intravenous drug users were found exclusively in the younger group (15.4%).

The group ≥ 50 years old had a lower nadir and last CD4 cell count ($p<0.05$). The proportion of treatment naïve patients has significantly decreased with age ($p<0.05$).

Viral suppression was found in higher proportion in patients diagnosed after 50 years of age ($p<0.05$).

The mean time on cART was similar in both groups, overall 7.5 years (*Table II)*. There was a significant difference in protease inhibitors based regimens between the two groups ($p<0.001$): 62% in the group aged 50 or more, compared to 55.4% in the younger group. For all other regimens there was a similar distribution.

In relation to HIV staging, differences with statistical significance were also found: more frequent A1 stage in the group diagnosed before 50 years ($p<0.001$); more frequent C3 stages in the group diagnosed after 50 years ($p<0.001$). Advanced HIV disease was more frequent in the group diagnosed over 50 years old (52.4%; $p<0.001$) compared with the younger group (30.1%).

For AIDS defining illnesses, *Mycobacterium tuberculosis* infection was the most common in both. On the other hand, older diagnosed individuals had more *Pneumocystis jirovecii* pneumonia and oesophageal candidiasis ($p<0.05$).

Table III illustrates the comorbidities, which significantly increased with greater age ($p<0.001$). The same pattern was observed for the majority of the comorbidities, including hypertension, diabetes, dyslipidemia, CVD, chronic renal failure, chronic obstructive pulmonary disease and also for non-AIDS related cancers ($p<0.001$). This trend was also present for the number of medicines ($p<0.001$).

Depression was slightly more observed in the group diagnosed over 50 years old (12.4%), however without statistical significance when compared with younger group (7.4%). Use of medication concerning central nervous system (antidepressants, anxiolytics and antipsychotics) was similar, being 14.3% over 50 years and 12.6% under 50 years.

There was a significant difference in relation to hepatitis C virus (HCV) co-infection: 17.8% in the younger group, compared to the 4.8% for older patients.

TABLE I - DEMOGRAPHIC AND LABORATORY PARAMETERS			
VARIABLES	DIAGNOSIS BEFORE 50 YEARS	DIAGNOSIS AT OR AFTER 50 YEARS	p-VALUE
Nº Patients (n;%)	625 (85.6%)	105 (14.4%)	
Age at HIV diagnosis, years			
Median (IQR)	32 (26-38)	57 (52-63)	p<0.001
Gender			
Male (n;%)	441 (70.6%)	70 (66.7%)	p=0.42
Female (n;%)	184 (29.4%)	35 (33.3%)	p=0.42
Race			
White (n;%)	478 (76.5%)	81 (77.1%)	p=0.88
Black (n;%)	147 (23.5%)	24 (22.9%)	p=0.88
Region of origin			**p<0.05**
Europe (n;%)	432 (69.1%)	79 (75.2%)	
Africa (n;%)	127 (20.3%)	25 (23.8%)	
America (n;%)	63 (10.1%)	-	
India (n;%)	2 (0.3%)	-	
Oceania (n;%)	1 (0.2%)	1 (1%)	
HIV Transmission Category			**p<0.001**
Heterosexual (n;%)	279 (44.6%)	91 (86.7%)	
MSM (n;%)	225 (36%)	9 (8.6%)	
IV Drug user (n;%)	96 (15.4%)	-	
Vertical (n;%)	10 (1.6%)	-	
Blood transfusion (n;%)	7 (1.1%)	2 (1.9%)	
Unknown (n;%)	8 (1.3%)	3 (2.8%)	
HIV type			
HIV 1 (n;%)	607 (97.1%)	96 (91.4%)	p<0.05
HIV 2 (n;%)	14 (2.2%)	6 (5.7%)	p<0.05
HIV 1 + 2 (n;%)	4 (0.7%)	3 (2.9%)	p<0.05
Years of HIV infection			
Median (IQR)	8 (4-13)	8 (5-12)	p=0.69
Viral suppression (n;%)	**483 (77.3%)**	**95 (90.5%)**	**p<0.05**
Last CD4 cells/µL			
Median (IQR)	570 (418-748)	504 (338-679)	p<0.05
Nadir CD4 (cells//µL)			
Median (IQR)	238 (120-360)	180 (74-314)	p<0.05
cART naïve (n;%)	**80 (12.8%)**	**4 (3.8%)**	**p<0.05**

MSM Men who have sex with men; cART Combination antiretroviral therapy; SD Standard deviation; IQR Interquartile range

TABLE II - CLINICAL PARAMETERS			
VARIABLES	**DIAGNOSIS BEFORE 50 YEARS**	**DIAGNOSIS AT OR AFTER 50 YEARS**	**p-VALUE**
Duration of cART, Years			
Median (IQR)	6.6 (3-11.2)	7.5 (4.1-10.3)	p=0.29
Current cART treatment			
NNRTI based (n;%)	208 (38.2%)	31 (31%)	p=0.50
PI based (n;%)	302 (55.4%)	62 (62%)	p<0.001
Integ. Inhibitors based (n;%)	8 (1.5%)	1 (1%)	p=0.99
PI + Integ. Inhibitors (n;%)	22 (4%)	5 (5%)	p=0.58
Others (n;%)	5 (0.9%)	1 (1%)	p=0.91
Stage at diagnosis			
A1 (n;%)	198 (31.7%)	13 (12.3%)	p<0.001
A2 (n;%)	212 (33.9%)	30 (28.5%)	
A3 (n;%)	87 (13.9%)	26 (24.8%)	
B1 (n;%)	10 (1.6%)	-	
B2 (n;%)	17 (2.7%)	4 (3.8%)	
B3 (n;%)	22 (3.5%)	3 (2.9%)	
C1 (n;%)	8 (1.3%)	-	
C2 (n;%)	11 (1.8%)	3 (2.9%)	
C3 (n;%)	60 (9.6%)	26 (24.8%)	p<0.001
Advance HIV disease (n;%)	**188 (30.1%)**	**55 (52.4%)**	**p<0.001**
AIDS defining illnesses (no. of cases;%)			
Mycobacterium tuberculosis	75 (37.5%)	14 (30.4%)	p=0.70
Oesophageal candidiasis	28 (14%)	10 (21.7%)	p<0.05
Pneumo jiroveci pneumonia	27 (13.5%)	10 (21.7%)	p<0.05
Kaposi sarcoma	18 (9%)	6 (13%)	p=0.14
CMV	11 (5.5%)	2 (4.4%)	p=0.92
Toxoplasmosis	8 (4%)	-	-
PML	7 (3.5%)	1 (2.2%)	p=0.84
Mycobact. avium complex	6 (3%)	1 (2.2%)	p=0.99
Cryptococcosis	6 (3%)	-	-
HIV Encephalopathy	4 (2%)	1 (2.2%)	p=0.72
Herpes simplex	3 (1.5%)	-	-
Isosporiasis	2 (1%)	-	-
Lymphoma	2 (1%)	1 (2.2%)	p=0.35
Cervical cancer	2 (1%)	-	-
Pneumonia, recurrent	1 (0.5%)	-	-

cART Combination antiretroviral therapy; NNRTI Non-Nucleoside reverse transcriptase inhibitors; PI Protease inhibitors; PML Progressive multifocal leukoencephalopathy; SD Standard deviation; IQR Interquartile range

TABLE III - ASSOCIATED COMORBIDITIES			
VARIABLES	**DIAGNOSIS BEFORE 50 YEARS**	**DIAGNOSIS AT OR AFTER 50 YEARS**	**p-VALUE**
Prevalence of comorbidities			
Number patients (n;%)	229 (36.6%)	91 (86.7%)	p<0.001
Comorbidities			
Hypertension (n;%)	55 (8.8%)	39 (37.1%)	p<0.001
Dyslipidemia (n;%)	164 (26.2%)	66 (62.8%)	p<0.001
Diabetes mellitus (n;%)	18 (2.9%)	18 (17.1%)	p<0.001
Cardiovascular disease	20 (3.2%)	13 (12.4%)	p<0.001
Chronic renal failure (n;%)	13 (2.1%)	14 (13.3%)	p<0.001
COPD (n;%)	9 (1.4%)	9 (8.6%)	p<0.001
Depressive disorder (n;%)	46 (7.4%)	13 (12.4%)	p=0.08
Non AIDS related cancer (n;%)	14 (2.2%)	18 (17.1%)	p<0.001
Co-Infection			
Hepatitis B (n;%)	22 (3.5%)	5 (4.8%)	p=0.54
Hepatitis C (n;%)	111 (17.8%)	5 (4.8%)	p<0.001
Hepatitis B and C (n;%)	3 (0.5%)	-	
Medication			
Anti-Hypertensive (n;%)	45 (7.2%)	37 (35.2%)	p<0.001
Cardiovascular (n;%)	32 (5.1%)	24 (22.9%)	p<0.001
Lipid lowering drugs (n;%)	110 (17.6%)	50 (47.6%)	p<0.001
Anti-diabetic (n;%)	20 (3.2%)	19 (18.1%)	p<0.001
CNS (n;%)	79 (12.6%)	15 (14.3%)	p=0.64
Inhalers (n;%)	13 (2.1%)	9 (8.5%)	p<0.001
Tobacco use	**144 (23.0%)**	**12 (11.4%)**	**p<0.05**
Alcohol abuse	**86 (13.8%)**	**17 (16.2%)**	**p=0.50**

COPD Chronic obstructive pulmonary disease; CNS Central nervous system

Overall, 21.4% (156 individuals) were current smokers. There was a significant difference on smoking status by age group: 23% before 50 years (p<0.05). Alcohol abuse was identical.

/ Discussion

The results display considerable variations in several aspects related to HIV infection in the two groups. In our cohort, 14.4% of patients were diagnosed after 50 years old, which is similar to epidemiological data from Centers for Disease Control and Prevention (CDC) that described as far as 17% and in Western Europe 12.9% in newly diagnosed HIV cases.[8,12]

Gender distribution was similar in both groups, nevertheless, the ratio male/female was slightly higher in the group diagnosed in an early age. Women over 50 years were more vulnerable to HIV infection and are an emergent trend in developed countries.[13,14]

Men over 50 reported less MSM exposure as HIV risk category when compared to younger men. The same results have been observed in other studies in Spain and the United States of America.[14] This is probably related to cultural issues as elderly individuals may be less comfortable to refer their MSM sexual practices.[15]

There was no difference in duration of HIV infection in both groups (overall 8.7 years). These values were lower than the one

found in the Swiss cohort (15.7 years),[16] which is most likely due to the fact that our outpatient clinic was only established in 1995.

Older HIV infected patients presented with more advanced disease, lower nadir cell count and often manifesting AIDS defining illnesses. This probably reflects a lack of HIV awareness in general population, but also a lower degree of clinical suspicion by physicians among older patients.

We observed a higher proportion of viral suppression in older diagnosed patients with cART, as described in other cohorts. This could probably be credited to better adherence to cART.[17]

Both groups had a similar follow-up period and time of exposure to cART.

In contrast to the updated 2018 Portuguese Guidelines[18,19] – which recommend a nucleoside reverse transcriptase inhibitors (NRTI) backbone (abacavir/lamivudine or tenofovir/emtricitabine) in association with integrase inhibitors as first-line regimen – the previous version of these guidelines (2012)[20] favoured a backbone with either non-nucleoside reverse transcriptase inhibitors (NNRTI) or protease inhibitors (PI).

As this study focuses on a 2014 cohort, it has to be emphasised that the followed recommendations were distinct from the current orientations.

The preferred regimens in the studied population were PI based, mainly boosted atazanavir and darunavir, followed by NNRTI based – predominantly efavirenz (EFV), which was available at the time in coformulation as single tablet regimen (tenofovir/emtricitabine/efavirenz).

The difference found between the groups relatively to PI based regimens (the most used antiretroviral therapy class between patients ≥ 50 years) could probably be explained by the potentially increased susceptibility to the side effects associated with EFV, specially before an underlying neuropsychiatric disturbance.[9]

As in 2014 the indications to start treatment were restricted to specific conditions, in the group ≥ 50 years old 5 patients were undergoing cART: 4 did not fulfil the criteria and one abandoned all therapy.

HIV infected individuals aged 50 or above had nearly four times more chronic comorbid conditions than those younger and these illnesses could have a clinical presentation up to a decade earlier than in uninfected persons, being in accordance with the aforementioned theory about HIV-related premature ageing.[21]

This cohort showed elderly patients had more dyslipidemia (62.8%) and use of lipid-lowering agents (47.6%) with a higher prevalence than the one demonstrated in the Swiss Cohort.[16] This could be a consequence of the preferred PI based approach.[9]

In Portugal the occurrence of diabetes is estimated in 11.7% overall,[23] less than in this ≥50years old population(17.1%).

According to an US study the prevalence of diabetes mellitus among HIV infected patients under cART has been reported to be more than 4 times higher than in HIV negative control groups.[24]

On the other hand, the prevalence of arterial hypertension was similar to general population (approximately 40%).[22]

Patients with HIV have a higher risk of CVD in the long-term.[25] In this cohort, there was a higher prevalence of CVD among the older diagnosed patients compared to the younger diagnosed. In general there was a lower prevalence compared to European studies that describe 13% in Spain and 16% in Italy.[13,21]

Glomerular filtration rates usually decrease with age, hence the group diagnosed later had higher prevalence. As expected, there was a significant difference between the two groups consistent with what was observed in other cohorts. Appropriate comorbidity management and renal toxicity monitoring are crucial measures to preserve renal function among HIV patients.[14,21]

Chronic obstructive pulmonary disease is a progressive disorder with recognised increase with ageing and a very heterogeneous worldwide distribution. In Portugal it is estimated at 14.2%.[11] Facing the natural course of disease, it was shown a larger prevalence in the later diagnosed group, despite the lower active smoking habits.

The consumption of CNS medication, mainly anxiolytics, was similar in both groups. This highlights the additional burden related to HIV infection and its impact on the quality of life.[27]

Non-AIDS defining cancers have an increased risk of development and are currently the leading cause of morbidity and mortality in these patients.[28] Malignancy prevalence in this study was higher among patients later diagnosed. The most frequently diagnosed cancers consisted of lung, bladder and prostate. At 50 years old or more group it was seen that HIV raised the risk of lung cancer in 70%, even after taking in account the impact of smoking.[29] Therefore, it is essential to develop screening strategies to prevent the development of malignancies.[30]

Polypharmacy was frequent at ≥ 50 years old and increases the risk of therapeutic interactions with deleterious effect on associated comorbidities and HIV management.[27]

The higher prevalence of HCV before 50 years old is understandable considering the main route of transmission (intravenous drugs).

The prevalence of active smokers was lower than in the general portuguese population (21.4% vs 28%).[11] The prevalence of smoking is usually higher in HIV patients than in the HIV negative population,[31] however this result was probably due to under notification on clinic files. The significant difference on smoking status, more frequent on the diagnosed before 50 years, in accordance with national data that shows reduced smoking habit with age.[32]

Portugal is the eleventh country in Europe with the highest alcohol consumption per capita (12.9L/Year), and a prevalence of 34%.[33] We found a smaller prevalence in our cohort, probably due to underestimation. Alcohol consumption may pose as a problem for patients to adhere to complex therapeutic regimens, contributes to liver disease and negatively impact progression of HIV infection.

Older diagnosed patients have a higher prevalence of advanced stage of disease at time of diagnosis, AIDS defining illnesses, non-AIDS defining malignancies and comorbidities, such as hypertension, diabetes, dyslipidemia, CVD, chronic renal disease. Newly diagnoses over 50 years old are an emerging group in HIV epidemic. They live with a high burden of comorbidities, which makes a comprehensive approach to their clinical management absolutely fundamental.[9]

HIV infection is a "greying" epidemic. New strategies are needed to prevent new cases particular in this age group, improve screening procedures and promote a more efficient control of risk factors.

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