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Older HIV-infected patients—an underestimated population in northern Greece: epidemiology, risk of disease progression and death

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SUMMARY

Objectives: HIV prevalence among older people is on the increase. The aim of this study was to evaluate the epidemiological and clinical features at diagnosis and survival of older patients.
Methods: This was a retrospective analysis of the data of 558 newly diagnosed antiretroviral-naïve patients between January 1998 and December 2008. Patients were divided into two groups according to their age at diagnosis: ≥50 years ($n = 103$) and 18–49 years ($n = 455$).
Results: The most common risk factor for older patients was heterosexual contact ($p < 0.013$). Older patients were more likely to suffer from hypertension (33.0% vs. 5.1%, $p < 0.0005$), cardiovascular disease (20.4% vs. 2.9%, $p < 0.0005$), neurological disorders (11.7% vs. 5.5%, $p = 0.02$), renal dysfunction (12.6% vs. 5.3%, $p = 0.01$), and infections (66.0% vs. 49.7%, $p = 0.003$) than their younger counterparts, and to have more hospital admissions during follow-up (47.5% vs. 19.6%, $p < 0.0005$). Older patients had a shorter survival time ($p < 0.0005$). A statistically significant increase in CD4+ cell number through time was observed in both groups ($p < 0.0005$). Younger patients reached higher magnitudes of absolute numbers of CD4+ cells during follow-up ($p < 0.0005$) after the initiation of antiretroviral therapy. The total number of patients with clinical AIDS from baseline throughout the study period was also higher in the older age group (35.9% vs. 25.0%).
Conclusions: HIV-infected people aged ≥50 years differ in epidemiological and clinical features to younger HIV-infected people. The issue of increasing prevalence of HIV infection is a matter of concern due to existing comorbidities, which probably lead to higher mortality rates and faster progression to clinical AIDS.

1. Introduction

In 2005, individuals aged ≥50 years accounted for 15% of new HIV/AIDS diagnoses and 24% of people living with HIV/AIDS.[1] The increased prevalence among older patients has been attributed to prolonged survival of those on highly active antiretroviral therapy (HAART), as well as an increasing proportion of people in midlife and late adulthood newly infected with HIV.[2–6] Given the dynamic epidemiology of HIV and the fact that HIV is nowadays considered as a chronic disease, it is important to understand the impact of age in these patients.[7]

Much attention has been paid to the prevention of HIV infection in the young population, though studies from Western Europe have presented alarming data concerning new infections in more aged people.[8] In 2007, 12.9% of newly confirmed HIV cases in Western Europe were in the population over 50 years of age, higher than in Central or Eastern Europe.[7] In Greece, the total HIV population aged over 50 years is 15.1%, as stated in the annual report of the Hellenic Center for Disease Control and Prevention (HCDCP). However, the patient's misperception of their risk and the low suspicion for this disease by clinicians may account for the underreporting of HIV cases among older people.[9,10] Currently, no previous studies have assessed the demographic and clinical characteristics of the more aged HIV-infected population in Greece. By 2015, individuals aged 50 years or more will comprise nearly half of HIV/AIDS patients in the USA.[11]

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Data from several studies have revealed conflicting results with regard to the clinical responses to HAART and HIV outcomes.[12–16] Similarly multiple studies have shown differences in the rates of HIV-1 RNA suppression, rates of CD4 cell recovery, and the magnitude between the age groups.[12,17,18] Some studies have implied that survival is significantly lower in elderly people due to deficiencies of the immune system,[19,20] while others have attributed this poor outcome to frequent late presentation of the aged people.[21,22] However, there are some large studies that have shown older people to respond similarly to HAART as their younger counterparts.[23,24] Physiological transformations attributed to ageing, including reduced immunocompetence, the presence of comorbidities that may affect the disease progress and make its management more complicated, and interactions among HAART and other co-administered drugs, underline the need for the development of age-related treatment strategies.[25]

Further research is certainly required to form and validate age-specific HIV treatment guidelines.[26] Currently, a few updated publications have summarized all the relevant issues with regard to the aged and aging HIV population and recommend general treatment strategies for integrated management of these patients.[27,28] These articles emphasize the HIV-associated non-AIDS conditions (HANA) and their association with advancing age. Moreover, they underline the need for studies that will help predict which patients are at high risk for certain complications or might need specific interventions in a multi-morbidity context and the need to enhance collaboration between HIV specialists and geriatricians.[27,28] The aim of this study was to assess the prevalence rates of comorbid conditions, mortality, survival, and immunological and virological responses in the ageing population and moreover to detect differences in clinical and epidemiological features at baseline between older and younger HIV patients.

2. Materials and methods

2.1. Study setting and design

Subjects were enrolled at the AHEPA University Hospital in Thessaloniki, Greece. This hospital provides primary and specialty care to approximately 1000 HIV-infected patients in its Infectious Diseases Division (IDD). The IDD of AHEPA Hospital is the only one in northern Greece and serves the majority of HIV-seropositive patients in this geographical area. This study was a retrospective cohort study (1998–2008).

Eligible patients had to have entered HIV care at AHEPA IDD between January 1, 1998 and December 31, 2008, and had to have available CD4 cell counts and HIV-RNA levels, and to have attended for at least one visit each year during the follow-up. Other inclusion criteria were age $\geq$18 years, to be antiretroviral-naïve, and to have a complete clinical record during the follow-up. Five hundred fifty-eight patients from the IDD who met the inclusion criteria were included and analyzed in this study. Two age groups were defined according to the age at the time of diagnosis. The first group consisted of HIV-infected people aged 18–49 (n = 455), and the second group consisted of patients aged $\geq$50 years (n = 103) at diagnosis. The cut-off for the age (50 years) was decided on the basis of the data of previous HIV studies, since most significant immunological diversities take place at that time.[29–32]

2.2. Variables evaluated

Demographic parameters included gender, sex, race (Greek and non-Greek), age at diagnosis, HIV transmission risk factors (heterosexual contact, men who have sex with men (MSM), and injecting drug use (IDU)), number of hospitalizations after diagnosis, cause of hospitalization, HAART intake (initiation of HAART regimen) and time to HAART initiation from HIV diagnosis, HIV-defining morbidity (hairy leukoplakia, lymphadenopathy, oral thrush, thrombopenia, prolonged diarrhea, herpes zoster, etc.), HANA (progression to cirrhosis, cardiovascular disorders, lipoatrophy and dyslipidemia, blood disorders, infection-related cancers, peripheral neuropathy, dementia, osteoporosis, and nephropathy), AIDS-defining diseases, and data of death. Clinical variables also collected by review of inpatient and outpatient medical records were: other comorbid conditions, including hepatitis B and C, diabetes mellitus, hypertension, psychological dysfunctions, malignancy history, and all infections other than those that are HIV-defining.

The selection of HANAs and other comorbid conditions to be included in our analysis was based upon the most common interactions with HIV infection and the side effects of antiretroviral agents, according to the literature. We characterized cardiovascular disease as the presence of hypertension requiring medication, any existing ischemic cardiovascular disorder, or former angioplasty. Diabetes mellitus referred to hyperglycemia treated either with insulin or oral hypoglycemic drugs. Neurological dysfunctions included peripheral neuropathy, epilepsy, dementia, and residual clinical manifestations of a central nervous system attack (infection, tumors), while psychological impairment was defined as any condition requiring continuous treatment (psychotropics or antidepressants) or psychological support.

Blood disorders refer to thrombocytopenia (relative decrease of platelets in blood below 150×10^9 platelets per liter) or anemia (hemoglobin thresholds: women $<$12 g/dl, men $<$13 g/dl). Liver impairment/damage includes severe acute chronic viral hepatic infections (liver inflammation due to hepatitis B virus (HBV) or hepatitis C virus (HCV)) or dysmetabolic function (inflammation of the liver with concurrent fat accumulation in the liver in the context of alcoholic liver disease or metabolic syndrome) and renal damage/dysfunction refers to chronic renal insufficiency with creatinine clearance $\leq$80 ml/min or proteinuria (presence of an excess of serum protein in the urine, over 30 mg/dl) or nephrotic syndrome (proteinuria at least 3.5 g per day per 1.73 m^2 body surface area, hypoalbuminemia, hyperlipidemia, and edema) or any glomerular disease (inflammation of the glomeruli or small blood vessels in the kidneys, regardless of cause). Hyperlipidemia refers to high blood lipids (total cholesterol above 200 mg/dl, triglycerides above 150 mg/dl, or both). High blood uric acid (hyperuricemia) is considered as a blood level of uric acid above 6 mg/dl for women and 6.8 mg/dl for men.

Moreover, we evaluated the observed AIDS-free interval (time period from HIV diagnosis to AIDS progression) and mortality (time from HIV diagnosis to death). The 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults, as well as the HIV and Aging Consensus Project were used to specify HANAs and AIDS-associated morbidities. Clinical AIDS refers to the onset of an infection or a malignancy that defines the progression to the integrated AIDS syndrome, irrelevant of CD4 cell count. Laboratory screening included CD4 cell counts and HIV-1 RNA levels at entry and throughout the follow-up time. Changes in the CD4 cell count from baseline were measured at clinic visits every 6 months. CD4 counts at these intervals were estimated by averaging all CD4 cell counts recorded within 8 weeks before and after that time period. Late presentation or late diagnosis was considered as a CD4 cell count $<$350 cells/ml at baseline visit.

2.3. Statistical analysis

Age group comparisons were performed using the Chi-square test for qualitative data. However, if a cell of the table had few expected cases ($<$5), Fisher's exact test was used. All continuous