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Prevalence of comorbidities in a cohort of women living with HIV

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ABSTRACT:

— ***Background:*** Women are usually under-represented in HIV studies, representing only 20% of the individuals enrolled in clinical trials. Even if most studies have found no gender-related differences in clinical outcomes, evidence is limited by the heterogeneity of studied cohorts and by the low number of reports specifically addressing this issue.

— ***Patients and Methods:*** In this short report, we focus on the characteristics of the female cohort attending the Outpatient HIV Clinic of the Garibaldi Nesima Hospital of Catania, with a particular emphasis on the prevalence of comorbidities in this population. 89 women were included in our analysis, median age was 47 (43-52) years. Median time since HIV diagnosis was 180 (101-242) months.89.9% were on cART, median CD4+ T-cell count was 544 (385-729) cells/μl. 17.9% of women were coinfected with hepatitis C.

— ***Results****:* The prevalence of diabetes was 4.5%. 15.7% of women had hypertension, 24.7% hypercholesterolemia. Hypovitaminosis D was highly prevalent, with 40.9% of patients having vitamin D levels <20 ng/ml. Median Frax® score was 4.3 (3-6.5)%.

— ***Conclusions****:* The aging of the HIV population implies the need to address the increased prevalence of multiple comorbidities. Women, especially older ones, have been poorly represented in clinical studies. Considering that gender differences may have a significant impact on several clinical outcomes, more research should specifically focus on this population.

— ***Key words:*** Aging, cART, Comorbidity, Gender, HIV, Women.

INTRODUCTION

The introduction of combination antiretroviral therapy (cART) has deeply improved the quality of life of individuals with HIV infection, causing a significant decline in the morbidity and mortality rates associated with AIDS-defining events. However, HIV-infected cohorts are aging and experiencing a significant increase in the prevalence of the so-called non-AIDS defining diseases, including malignancies, bone, cardiovascular and renal disease[1-5].

Women are usually an under-represented population in HIV studies. According to a recent meta-analysis[6], women account for only 20% of the enrolled population in HIV clinical trials. Although most studies reported no gender-related differences in viro-immunological outcomes, some authors described better CD4+ recovery and lower baseline HIV RNA in women; other studies have found reduced tolerability of cART and lower adherence in women compared to men. However, data are inconsistent across studies and largely affected by the different characteristics of the studied cohorts[7].

In this short report, we aimed at describing the characteristics of the female cohort attending the Outpatient HIV Clinic of the Garibaldi Nesima Hospital of Catania, with a particular focus on the prevalence of comorbidities in this population.

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PATIENTS AND METHODS

Study population

In this cross-sectional study, we consecutively enrolled HIV-positive women attending the HIV Outpatient Clinic of the Division of Infectious Diseases in Catania, Italy. All participants provided a written informed consent to participate in the study. We extracted the following parameters from medical records: patient demographics, body mass index (BMI), time since HIV diagnosis and initiation of cART, antiretroviral regimen, HCV coinfection, presence of comorbidities, such as diabetes mellitus, hypertension, smoking, menopausal status, most recent CD4+ T-cell count, plasma HIV RNA, vitamin D, parathyroid hormone (PTH) levels, calcium, phosphorus, vitamin B12, folic acid, total and HDL cholesterol levels. Glomerular filtration rate (GFR) was calculated by using the chronic kidney disease (CKD)-epidemiology collaboration equation. Vitamin D deficiency was defined as a value below 20 ng/ml, whereas secondary hyperparathyroidism was defined as a PTH higher than 65 pg/ml, with normal calcium levels. We also extracted from medical record data on bone status, which was assessed using heel QUS (Hologic Sahara®), a non-invasive radiation-free ultrasound-based technique. QUS evaluates heel stiffness, providing a "stiffness" index, called quantitative ultrasound index (QUI). A QUI threshold >83 has been suggested to identify patients with a low likelihood of osteoporosis, a QUI <59 those with a high likelihood of osteoporosis[8].

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences version 22.0 (SPSS, Chicago, IL, USA). For our descriptive analysis, we used N (percentage) for nominal data and median [interquartile range (IQR)] for continuous data, as appropriate.

RESULTS

Subject characteristics

The characteristics of the study population are summarized in Table 1. In our analysis, we included 89 women, accounting for around 20% of the HIV cohort attending our Outpatient Clinic. Median age was 47 (43-52) years. Most of them (87.6%) were Caucasian. 39.3% were in menopause, one third were smokers.

Viro-immunological characteristics

83.1% of women were infected through heterosexual exposure. Median time since HIV diagnosis was 180 (101-242) months. 89.9% were on cART, of them 78.8% had an undetectable viral load. Median CD4+ T-cell count was 544 (385-729) cells/µl. 54% with a CD4+ T-cell count >500 cells/µl. Only 9% had a CD4+ count < 200 cells/µl. Median CD4/CD8 T-cell ratio was 0.96 (0.6-1.32). Median time since cART initiation was 148 (96-218) months. 60% of subjects was receiving tenofovir (TDF), 20% raltegravir, 52.5% a PI-based regimen. Only 33.8% of individuals were on their first- or second-line regimen. More than one third were highly treatment-experienced (sixth line or more).

Table 1. Demographics and clinical characteristics of the study population.

Variable	N=89
Age (years)	47 (43-52)
Risk factors	
IDU	11 (12.4)
Heterosexual	74 (83.1)
Time since HIV diagnosis (months)	180 (101-242)
Current CD4+ T-cell count (cells/µl)	544 (385-729)
HIV viral load <50 copies/ml	65 (73)
Patients on cART	80 (89.9)
Time on cART (months)	148 (96-218)
Current use of PI	42 (52.5)
Current use of TDF	48 (60)
Current use of raltegravir	16 (20)
N therapeutic lines (≥6)	28 (35)
Menopause	35 (39.3)
BMI	23.2 (20.7-26.4)
Current smoking	25 (29)
eGFR (ml/min/1.73 m^2)	101 (89-109)
Heel QUI value	81 (69-99)
Frax® score (%)	4.3 (3-6.5)

Data are n. (%) of patients or median (interquartile range)
BMI: body mass index; cART: combination antiretroviral therapy; eGFR: estimated glomerular filtration rate; HIV: human immunodeficiency virus; IDU: intravenous drug user; MSM: men having sex with men; PI: protease inhibitor; QUI: quantitative ultrasound index; TDF: tenofovir

Prevalence of comorbidities

In our cohort, 17.9% of women were coinfected with hepatitis C. The majority of them reported previous intravenous drug use, none had cirrhosis. The prevalence of diabetes was 4.5%. Median BMI was 23.2 (20.7-26.4). 24.7% of women were overweight, 12.4% obese. 15.7% of women had hypertension. Although 24.7% of patients had hypercholesterolemia, only 16.9% were on statins. Median CKD-EPI value was 101 (89-109) ml/min, with 6.7% of them having CKD-EPI values <60 ml/min. The majority of women had vitamin B12 levels (325 (239-467) ρg/ml), as well as folic acid values (3 (1.9-5) ng/ml) within the normal range. Hypovitaminosis D was highly prevalent, with 40.9% of patients having vitamin D levels <20 ng/ml. 31.5% of women had secondary hyperparathyroidism. Serum calcium and phosphorus levels were within the normal range in all patients. Median heel QUI value was 81(69-99). Only 47.2% of women had normal QUI values. 11.2% of individuals had a QUI value <59, whereas 41.6% had a QUI value between 59 and 83. For women aged ≥40 years, which represented 84% of the cohort, median Frax® score was 4.3 (3-6.5)% (Table 2).

Table 2. Prevalence of comorbidities in the study population.

Variable	N=89
Obesity	11 (12.4)
Hepatitis C coinfection	16 (17.9)
eGFR <60 ml/min	6 (6.7)
Diabetes mellitus	4 (4.5)
Hypertension	14 (15.7)
Hypercholesterolemia	22 (24.7)
Vitamin D insufficiency (<20 ng/ml)	36 (40.9)
Heel QUI value <59	10 (11.2)

Data are n. (%)
eGFR: estimated glomerular filtration rate; QUI: quantitative ultrasound index

DISCUSSION

In this study, we found that the large majority of women attending our Outpatient HIV Clinic were virologically suppressed and with high CD4+ count. The long duration of HIV infection (median time 15 years) may explain why most of them were highly treatment-experienced patients. In fact, a significant proportion of women in our cohort were diagnosed before the introduction of well-tolerated antiretroviral drugs and were therefore more likely to change regimen, not only because of virological failures, but also as a consequence of poor tolerability and toxicities.

A significant number of women had low QUI values, suggesting increased risk of osteoporosis and fragility fractures; moreover, we found a high prevalence of hypovitaminosis D. Low vitamin D levels have been extensively reported in HIV-infected cohorts [4]. Considering that vitamin D has several important functions, including not only bone health but also immunomodulation, more efforts should be made to promote vitamin D supplementation among women, especially post-menopausal ones. A healthy lifestyle (i.e. smoking cessation, physical activity, and increased calcium dietary intake) may also help reducing the risk of osteoporosis in this at-risk population[9].

Of note, almost one fifth of the patients were coinfected with hepatitis C. HIV-infected individuals have an increased risk of fibrosis progression and hepatic decompensation. With the introduction of new highly effective direct-acting antivirals, this coinfected population should be specifically targeted in order to eradicate HCV and block the risk of progression to advanced liver disease[10].

CONCLUSIONS

The aging of the HIV population implies the need to address the increased prevalence of multiple comorbidities. Women, especially older ones, have been poorly represented in clinical studies. Considering that gender differences may have a significant impact on several clinical outcomes, more research should specifically focus on this population in order to obtain data that can be applied to HIV-positive women.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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