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## **Dynamics of HIV resistance, and factors associated with its development, and maintenance at a large reference university hospital in Valencia, Spain, from 2003 to 2014**

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**Background:** HIV-1 drug resistance compromises the success of ART. We evaluated the epidemiological behaviour of this resistance according to specific risks and clinical factors.

**Material/methods:** This is a pooled, cross-sectional study. Our objective was to describe the trends of HIV-1 resistance mutations to protease and reverse transcriptase inhibitors according to; type of resistance (transmitted/acquired), risk group, ART, and immune status, among a University Hospital in Spain over 2003 and 2014. Treatment histories, viral sequences, demographic, and clinical data were retrieved from our centre database. All patients with a genotypic resistance test were included.

**Results:** 852 subjects were included. Overall we found a declining trend (OR=0.38 [95% CI: 0.28-0.51]) of resistance mutations from ≈90% in 2003, to ≈20% in 2011-2014 (OR=1.04 [1.02-1.05]). Roughly, resistance mutations in heterosexuals, MSM, and IDU risk groups followed the same overall trend, although IDU showed mutations more frequently in last years. The odds ratio of presenting resistance was 1.33 (0.79-2.27) and 2.33 (1.30-3.47) times more often for MSM and IDU, respectively, than heterosexuals. Both acquired and transmitted resistance declined statistically as separate trends, from 87% to 30%, and from 45% to 5%, respectively, for the period 2003-2014 (OR=8.96 [5.88-13.64]).

After declining markedly from 2003 to 2011, there was a statistically significant upward trend of NRTI-resistance from 2012 to 2014 (OR=1.01 [1.00-1.02]), and NNRTI-resistance (OR 1.01 [1.00-1.01]), but not for PI-resistance, which remained very low in the last years.

From 2003 to 2014, 1000+ viral copies per millilitre were associated with less resistance, compared with <1000 copies/ml; although a declining trend was evident for both groups. Also, for the same period, CD4 cell counts above 100/mm<sup>3</sup> were associated with a declining trend of resistance mutations from 93% to 13%, respectively. However, CD4 cell counts below 100/mm<sup>3</sup> tended to stabilise around 30% from 2010 to 2014 (OR=1.19 [1.04-1.36]).

**Conclusions:** HIV-1 drug resistance has declined and shows a stabilising trend with a prevalence of around 20%. This trend was also shown according to risk groups and CD4 cell counts below 100/mm<sup>3</sup>. Resistance to NRTI and NNRTI showed an upward trend that guaranteed further studies. There was a higher risk to develop resistance mutations by acquired resistance, IDU, MSM and viral loads <1000 copies/ml. There is a need for ongoing HIV-1 drug resistance control, especially by risk groups and virological failure under RTI, with viral loads <1000 copies/ml, and in high immunosuppressed patients.

**Figure 1. Trends of HIV-1 resistance mutations to protease and reverse transcriptase inhibitors according to; antiretroviral treatment, type of resistance, risk group, and immune status, among a University Hospital in Spain over 2003 and 2014.**

