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Late presentation of HIV infection:

# **Situation in Spain**

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#### **INTRODUCTION**

Human immunodeficiency virus (HIV) infection is a chronic condition that gradually weakens the patient's immune system and, if left untreated, leads to AIDS and death. Although the primary infection produces a series of symptoms, they are highly non-specific and frequently go unnoticed; thus, in many cases the diagnosis is made only after the affected person has experienced considerable damage to the immune system, or has already developed AIDS.

HIV infected persons who are unaware of their situation are of great concern to public health authorities and clinicians, for several reasons. First, because they do not benefit from highly active antiretroviral treatment (HAART), and consequently are much more likely to develop AIDS and to die than patients who are diagnosed and treated early. Second, because these persons can unknowingly transmit the infection: some American studies show that 54% of new infections are due to the 25% of persons who did not know they were infected (1). Finally, the cost of treating and caring for patients with late presentation is much higher than if they had been diagnosed early (2).

For these reasons, the detection of HIV infected persons who are unaware of their status, what has been called the "hidden epidemic", has become a priority for those responsible for controlling HIV throughout the world.

### UNDIAGNOSED HIV INFECTION: CURRENT SITUATION

In the United States, where various studies have been conducted to determine the proportion of undiagnosed HIV infection, the figures have varied (ranging between 21% and 44%) depending on the year, methodology and population group studied (1,3,4). In a study by the Centers for Disease Control (CDC) in 2008 in men who have sex with men (MSM) who frequented gay venues in 21 cities throughout the country, the overall prevalence of undiagnosed HIV infection was 44%, with marked differences by age and ethnic group; the most affected groups were young MSM and those belonging to ethnic minorities (4). In the WHO European Region, including the European Union (EU), little information is available on the magnitude of this phenomenon. An article published in 2008 estimated that the proportion of undiagnosed HIV infections in the EU overall was 30%, ranging from 15% (Norway) to over 50% (Poland). In the rest of the countries that comprise the WHO European Region, excluding the EU, the proportion of undiagnosed HIV infection may reach 65% (5).

In Spain, it is estimated that around 30% of persons with HIV do not know they are infected. In an anonymous unlinked study conducted in 1998-2000 in persons requesting care in centres for sexually transmitted infections (STI), it was found that 38% of all persons infected with HIV were unaware of their status (6). In a subsequent work it was observed that, among cases of infectious syphilis and gonorrhoea diagnosed between July 2005 and December 2008 in 15 STI and correctional centres, 11.1% were co-infected with HIV and, of these, 34.1% were unaware of their status with respect to the infection (7). After adjusting for sex and place of origin, it was found that lack of awareness of HIV status was more common in persons under 35 years of age (under 29 years: OR: 3.3, 95% CI: 1.3-8.4; 29-35 years: OR: 2.7, 95% CI: 1.1-6.5) compared with those aged 40 and over, and in bisexuals males compared with homosexuals males (OR: 4.6; 95% CI: 0.9-23.9); the number of persons in this group was small, however, therefore the estimates are unstable. Conversely, those with a history of STI had a higher probability of having been diagnosed with HIV before the current episode of syphilis and/or gonorrhoea (OR: 0.2; 95% CI: 0.07-0.32). This underlines the importance of offering the HIV test to all persons seeking medical consultation for any type of STI.

## LATE PRESENTATION OF HIV INFECTION: CURRENT SITUATION

CD4 level at HIV diagnosis is used as an indicator of late presentation. The new treatment guidelines recommend starting treatment when the CD4 level is below 350 cells/ $\mu$ l (8), therefore this threshold is used to define late presentation; likewise, when the CD4 count at diagnosis is below 200 cells/ $\mu$ l or

when HIV and AIDS are diagnosed at the same time, the term "advanced disease" is used.

An important problem in the EU when estimating late diagnosis is the lack of information in many countries on the CD4 level when HIV is diagnosed. Spain and Slovenia have the most complete information on this variable. In countries where this information is available for at least 50% of new HIV diagnoses, the percentage of late presentation is between 24% and 64% (Figure 1).



**Figure 1.** Percentage of new HIV diagnoses with information on CD4 count and percentage of late presentation in EU countries, 2008

In Spain, the information systems on new HIV diagnoses in the Autonomous Regions of Aragon, Asturias, Balearic Islands, Canary Islands, Cantabria, Castilla and Leon, Catalonia, Ceuta, Extremadura, Galicia, La Rioja, Madrid, Melilla, Navarre and the Basque Country provide information that is fundamental for knowing HIV late presentation, its magnitude and the characteristics of affected persons (9).

In 2009, 30.4% of new HIV diagnoses had a CD4 count below 200 cells/ $\mu$ l at the time the infection was diagnosed, and 19.8% had a CD4 count between 200 and 350 cells/ $\mu$ l. This means that 50.2% of new HIV diagnoses were eligible for antiretroviral treatment at the time they were diagnosed with HIV infection (Figure 2).



Figure 2. Late presentation of HIV infection. Information systems on new HIV diagnoses. 15 Autonomous Regions, 2009

Analysis of the factors associated with late presentation (for the period 2003-2008, data from 12 Autonomous Regions), found it to be higher in men (OR: 1.4; 95% CI: 1.2-1.6); in persons aged 30-39 years (OR: 1.6; 95% CI: 1.5-1.9), 40-49 years (OR: 2.6; 95% CI: 2.2-3.0) and 50 years or over (OR: 4.7; 95% CI: 3.9-5.7); in persons from Latin America (OR: 1.5; 95% CI: 1.3-1.7) and Sub-Saharan Africa (OR: 1.7; 95% CI: 1.4-2.1); and in persons attributing their HIV infection to shared use of injection material (OR: 1.8; 95% CI: 1.5-2.1) or to homosexual relations (OR: 1.9; 95% CI: 1.7-2.2). Furthermore, the probability of late presentation was higher in those diagnosed in 2003 (OR: 1.4; 95% CI: 1.2-1.7), 2004 (OR: 1.3; 95% CI: 1.1-1.6) and 2005 (OR: 1.3; 95% CI: 1.1-1.5) as compared to those diagnosed in 2008 (10). However, observation of the trend in

late presentation by mechanism of HIV transmission in the period 2004-2009 shows that it decreased in MSM whereas it remained stable in the other groups (9) (Figure 3).



**Figure 3.** Late presentation by transmission mechanism and year of diagnosis. 9 Autonomous Regions, 2004-2009

The higher percentage of late presentation in men versus women is seen in all the developed countries, and is attributed to the fact that HIV testing is routinely offered to all pregnant women. This underlines the importance of disseminating and standardising implementation of HIV testing to detect the infection in its earliest stages.

### **HIV TESTING**

Unfortunately, until 2009, not all Autonomous Regions routinely collected data on the number of HIV tests performed. According to the Survey of HIV Prevention Activities in the Autonomous Regions (Spanish acronym, ICAP), in the 9 regions that provided this information from 2002 to 2008 a marked increase is seen in the number of tests carried out, from 392,054 to 637,315 (11).

With regard to patterns of HIV testing, there is some information in this respect. Of new HIV diagnoses detected between 2003 and 2008 in a network of 19 HIV/STI centres located in the principal cities in Spain, 67% had received a test before the one in which the infection was diagnosed (12). In examining the factors associated with previous testing (adjusted for age, sex, year and centre of diagnosis, and history of STIs), it was found that the probability of having been tested was lower in persons with lower educational level (OR: 0.8; 95% CI: 0.6-1.0), those from Eastern Europe (OR: 0.6; 95% CI: 0.4-1.1) and those who acquired the infection through heterosexual relations (OR: 0.3; 95% CI: 0.2-0.4).

### **INTERVENTION MEASURES**

Reduction of the proportion of undiagnosed HIV infection is a priority for controlling the epidemic in Spain. Improvement of this situation requires implementation of a series of actions that are listed below:

- Development of guidelines to scale-up HIV testing in Spain
- Actions aiming to increase the perception of risk, both in health professionals and groups most affected by late presentation.
- Actions aiming to increase accessibility to HIV testing
- Actions aiming to guaranty confidentiality and quality HIV counselling
- Actions aiming to assure linking of newly diagnosed HIV patients to quality treatment and support programmes.

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