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Editorial

Missed opportunities in HIV diagnosis: A need to close the gap

Oportunidades perdidas en el diagnóstico del VIH: es tiempo de actuar



In the mid-21st century, the fight against HIV/AIDS remains a global challenge, and despite medical and social advances, opportunities to diagnose and treat the infection continue to be missed. This editorial aims to shed light on the missed opportunities in HIV diagnosis in Spain, highlighting the crucial importance of early detection and the critical role of health systems and public awareness.

The lack of early detection represents one of the biggest missed opportunities in the fight against HIV. Persistent stigma and low awareness in some communities contribute to people avoiding testing. Lack of training of doctors who do not usually participate in the care of people living with HIV, who are unaware of HIV indicator situations or those possibly associated with a higher prevalence, the care overload, and the need for a consent process that can be cumbersome, are among the possible causes that make diagnosis difficult in the healthcare setting.

The result is late diagnosis, with serious consequences for people's health and the continued spread of the virus. Late diagnosis is a major problem both for the health of patients and for the health care system because of the increased costs associated with the severe immunosuppression that leads to opportunistic infections that characterise advanced HIV infection.¹ Hidden HIV infection, i.e. patients who are infected but undiagnosed, is a global problem that directly affects the ability to limit the spread of the HIV epidemic and to reduce its incidence. This group of patients constitutes the "reservoir" of the disease and is responsible for the vast majority of new HIV infections.^{2,3}

The WHO has set targets for 2025 that 95% of people living with HIV to be diagnosed, 95% to be on treatment and 95% to have an undetectable viral load.⁴ In this way, 86% of people living with HIV will have achieved virological suppression and the number of new infections will be drastically reduced as people living with HIV and an undetectable viral load cannot transmit the virus. These challenges must be overcome to reach the 2030 goal of ending AIDS as a public health threat as defined in the Agenda on Sustainable Development.

In Spain, according to the latest available report from the HIV, STI and Hepatitis Surveillance Unit (data from 31 December 2021),⁵ it is estimated that there are between 136,436 and 162,307 people living with HIV in Spain, corresponding to an HIV prevalence of

0.31% of the total Spanish population. Of these, 137,484 (95% CI: 126,220–149,542), or 92.5% of people with HIV infection, would know their diagnosis. This means that 7.5% (95% CI: 5.8%–10.4%) of people living with HIV in Spain (10,232–12,173) are unaware of their infection. Of those diagnosed, 132,809 people living with HIV are estimated to be receiving antiretroviral treatment, which represents 96.6% (95% CI: 95.7%–97.3%). Of these, 120,073 people would have a suppressed viral load, 90.4% (95% CI: 89.1%–91.7%) of people receiving antiretroviral treatment. Based on these results, it is estimated that 80.8% of all people living with HIV in Spain would have achieved viral suppression. Regarding late diagnosis and advanced disease, 88.8% of new HIV diagnoses in 2022 had information on the first CD4 lymphocyte count after diagnosis ($n = 2624$). The median CD4 count was 359 (RIC: 178–551). The percentage of cases with advanced disease was 27.6% and with late diagnosis was 48.6%. Late diagnosis was higher in women than in men (54.2% vs. 47.6%), increases with age, being 36.7% in those aged less than 25 years and 64.4% in those aged 50 years and over, with higher rates among those from sub-Saharan Africa, Latin America and North Africa. By mode of transmission, late diagnosis was higher among heterosexually transmitted cases in both men (59.9%) and women (54.6%) than among MSM (42.3%).

Spain is on its way to meet the WHO 2025 target for 95% of people living with HIV to be diagnosed but still behind it, so it is clear that any measure to promote and improve the diagnosis of hidden HIV infection is a necessity. It is paradoxical that a large number of patients diagnosed in Spain have often consulted different levels of care (emergency, hospital, primary care), and even when clinical or analytical indications recommend screening for HIV infection, this has not been done. Gargallo-Bernad et al.,⁶ showed that 44% of the late diagnoses in their study had previously been seen for one of the clinical indicator conditions associated to a higher prevalence of HIV infection. This study also showed that 71.5% of new diagnoses had more than one opportunity for diagnosis in the 3 years prior to diagnosis, while one in five new HIV/AIDS cases were hospitalised in the 3 years prior to diagnosis. In the same way, Hernández-Febles et al.⁷ described that more than 40% of patients with late missed had the opportunity to be diagnosed in the hospital environment in the three years prior to diagnosis.

In line with sexually transmitted infection screening being one of the most prevalent clinical indicator conditions associated to HIV diagnosis,⁸ García de Lomas-Guerrero et al.⁹ present in the current issue of EIMC a retrospective cross-sectional descriptive

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study under real-life conditions, analyzing all patients treated in the health area of the Costa del Sol hospital in Marbella during 2018, whose physician requested a PCR for *Chlamydia trachomatis*, *Neisseria gonorrhoeae* or *Trichomonas vaginalis*. The authors studied how many patients had been tested for HIV antibodies at the time of screening for sexual transmitted infections. The study included 1896 patients, with 2141 samples processed. *C. trachomatis* was detected in 169 (7.89%) samples, 68 (3.18%) were positive for *N. gonorrhoeae* and 22 (1.03%) were positive for *T. vaginalis*. Of the 1896 patients, 78 had known HIV infection. Of the remaining 1818, HIV serology was performed only on 812 (44.66%) finding a 1.72% prevalence of occult HIV infection (OHI), within the 0.8%–3% range of prevalence of occult HIV infection previously reported in patients with STIs.¹⁰ In the study newly diagnosed people living with HIV (PWHIV) had a mean CD4 count of 566.76 cells per microliter, with only two patients in the late diagnosis range (<350 CD4 cells per microliter). The authors conclude that the high prevalence of hidden HIV infection in people with STIs and the high level of suspicion advocate to strengthen early diagnosis strategies that will allow to reduce the number of hidden infections. Measures should include education and training in the early detection of HIV infection, through missed opportunity markers and alert criteria, training courses, awareness campaigns and interdisciplinary clinical sessions.

Although with the limitation that risk factors associated with a higher level of clinician suspicion of occult HIV infection and leading to the request or non-request of the diagnostic test were not analysed, some interesting aspects arise from these data. First, it is striking to know that more than 50% of the patients were not screened for HIV; assuming the 1.72% prevalence of hidden infection found for those patients that have been screened would also be true for this population, 17 more patients could have been diagnosed. Second, late diagnosis between those patients that were newly diagnosed was lower (14%) than previously described (40%–50%),¹¹ meaning that HIV screening of all patients with a suspected STI clearly may reduce HIV late diagnosis.

Fortunately, in Spain there are ongoing initiatives that are contributing to lower missed opportunities and to increase the number of patients that are diagnosed. The Spanish Society of Emergency Medicine (SEMES), in collaboration with the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), and its AIDS Study Group (GESIDA) have launched a programme to encourage physicians in Spanish hospital emergency departments to request non-urgent HIV serology when attending patients aged 18–65 with 6 specific conditions associated with an increased prevalence of HIV infection: STIs, chemsex, mononucleosis syndrome, herpes zoster, community-acquired pneumonia or those prescribed post-exposure prophylaxis against HIV¹² (<https://dejatuhuella.semes.org/>). This programme has brought about a cultural change among emergency physicians and their involvement in this public health problem. In this way, 1124 new diagnoses were made in 30 months in the 136 hospitals currently involved in this project.

The efficiency of HIV screening in the ED has been demonstrated in multiple studies.¹³ An economic study showed that the implementation of DTH recommendations requires an investment of €20 million over the next 20 years, but would result in potential savings of €4411 billion.¹⁴ Regarding STIs, a recent study evaluated the pre- and post-implementation of the DTH program, showed an increase in HIV testing in patients attended in the emergency department (ED) due to STIs from 36.21% to 66.79% (relative increase of 84.4 (95% CI 75.9–93.5)). The percentage of positive results for HIV respect to the STIs condition was 1.52 (95% CI 1.15–1.98).¹⁵

In addition, clinical microbiology services are proposing initiatives to identify patients with conditions that may be indicative of HIV infection, which could help to minimise missed diagnostic

opportunities. Hernández et al. have evaluated the effectiveness of an automated opportunistic HIV screening strategy in the hospital setting. HIV testing was performed on all patients in whom a hospital admission analytical profile, a pre-surgical profile and several pre-designed serological profiles (fever of unknown origin, pneumonia, mononucleosis, hepatitis, infection of sexual transmission, rash, endocarditis and myopericarditis) was requested. Preliminary results reported at the SEIMC Congress in 2023¹⁶ showed that of 2849 HIV tests carried out on the profiles, 9 (0.3%) cases were diagnosed (23.1% of those diagnosed in the health area); three patients included in a routine hospital admission and pre-surgery profile and six in a serological profile requested for indicator entities (fever of unknown origin, sexually transmitted infection) of HIV occult infection. This opportunistic screening was profitable since the positive rate of 0.3% is cost-effective.

Last but not least, the support of community agencies and NGOs working in the field of HIV is essential to continue the push to diagnose people with HIV as early as possible to improve their prognosis and prevent new infections.

Healthcare professionals play a vital role in the early detection of HIV. However, in many cases, lack of training, resources and cultural sensitivity can limit their ability to respond effectively. Additionally, public awareness remains a key component in overcoming the stigma associated with HIV and encouraging testing. Educational campaigns should focus on the importance of knowing one's HIV status, dispelling myths and combating discrimination associated with HIV infection. In our opinion, measures that may enhance universal availability and accessibility of HIV testing, ensuring that the patient rights are guaranteed and receive adequate information about his or her clinical situation, should include:

- Training of health professionals involved in the care of people with a condition indicating or possibly associated with HIV infection (because of its association with increased prevalence of HIV infection). In these settings, diagnosis of HIV infection is indicated and is part of good medical practice.
- Implementing new innovative care processes adapted to the characteristics of our hospitals and electronic medical record systems to minimise loss of diagnostic opportunities, such as prioritising protocols and alert systems for performing HIV serology in a group of clinical situations with a high prevalence of HIV, based on their frequency in each service.
- Promoting safe strategies that respect patients' rights so that microbiology services can turn situations of lost opportunities into gained ones. The clinical microbiologist, as a physician involved in the patient's care process, has the opportunity to identify patients at high risk of HIV infection in whom serology has not been requested, but in whom other microbiological diagnostic tests related to the conditions have been requested, as long as that the patient rights are guaranteed.
- Involvement of associations of people living with HIV and community organisations in the design and evaluation of programmes, so that they are part of the necessary change, so that lost diagnostic opportunities are gained, as they are a key part of the change process to reduce hidden infection in Spain.

There are experiences in some European countries using an opt-out strategy in the ED, in which every patient who is requested to undergo an analysis is tested for HIV, unless the patient indicates otherwise, allowing the identification and linkage to care to a significant number of infected people in the ED.¹⁷ Information about performing the test is transmitted through multilingual information flyers to patients at the time of admission in the ED and posters available throughout the service. We must point out that at this time it is mandatory in Spain to request oral informed consent and leave it reflected in the patient's clinical history, but the dynamics

that are spreading in Europe and the results obtained should serve as a reflection for the Spanish health authorities and to the patients associations about the opportunity that this strategy represents in terms of public health and individual benefit.

In conclusion, closing the HIV diagnostic gap requires a concerted effort by governments, health organisations, medical professionals and society at large. Early detection not only saves individual lives, but is also key to controlling the spread of the virus at the community level. It is time to redouble our efforts to ensure that no one is left behind in the fight against HIV and that all opportunities for early diagnosis are fully exploited.

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Federico García^{a,b,c,*}, M^a José Pena^d, Juan González del Castillo^e

^a Servicio de Microbiología Clínica, Hospital Universitario Clínico San Cecilio, 18008, Granada, Spain

^b Ciber de Enfermedades Infecciosas, CIBERINFEC (www.ciberinfec.es), Spain

^c Instituto de Investigación Biosanitaria Ibs.GRANADA (www.ibsgranada.es), Spain

^d Servicio de Microbiología, Hospital Universitario de Gran Canaria Dr. Negrín, Spain

^e Emergency Department, Hospital Clínico San Carlos, IdISSC, Madrid, Spain

* Corresponding author.

E-mail address: fegarcia@ugr.es (F. García).