Emergency department contribution to HIV and HCV control in the Iberian Peninsula

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Research Article

Keywords: HIV, HCV, emergency department, screening, diagnosis

Posted Date: November 14th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2237854/v1
Abstract

**Background:** Undiagnosed cases of transmissible blood-borne viruses (HCV and HIV) result in significant morbidity and mortality, further spread of epidemics, and increased public health costs. Testing in emergency departments (EDs) is an opportunity for expanding HIV and HCV screening. The goal of this project was to increase the proportion of eligible patients screened for HIV and HCV in urban areas.

**Methods:** An opportunistic automated screening program for HIV and HCV was implemented in the EDs of 4 public hospitals in Spain and Portugal at different periods between 2018 and 2022. HIV and HCV prevalence was prospectively evaluated. In case of anti-HCV or anti-HIV reactive test results, reflex testing was done for confirmation.

**Results:** More than 90% of the population eligible for testing were screened in the participating centers. We found a seroprevalence rate of 0.7% for HIV and seroprevalence rates ranging from 0.6% to 3.9% for hepatitis C. Between 19% and 53% of individuals who tested positive for HCV antibodies were viremic.

**Conclusions:** Opportunistic HIV and HCV screening in EDs is feasible, does not disrupt ED activities, is highly effective in increasing diagnosis, and contributes to WHO goals for the elimination of HIV and hepatitis C.

Introduction

The human immunodeficiency virus (HIV) epidemic remains uncontrolled worldwide, with nearly a million people dying of HIV/AIDS every year [1]. Despite efforts by the Joint United Nations Program on HIV/AIDS (UNAIDS) to achieve its 90-90-90 target in HIV patients by 2020 (90% diagnosed, 90% treated, 90% with undetectable viral load) [2], countries in the Iberian peninsula (Spain and Portugal) have still not achieved the first goal of a diagnostic rate of 90%. Indeed, an estimated 19,600 and 2,800 people living with HIV in Spain and Portugal, respectively, are unaware of their infection, while one in two receive their diagnosis at a late stage [3-5]. Almost half (47.6% and 49.7%) of new HIV diagnoses in Spain and Portugal are detected late (CD4+ T cell count ≤350 cells/mm³ at diagnosis) [6-8]. Less than 4% of the eligible Portuguese population currently undergo screening in the country's primary healthcare system [9,10].

An estimated 58 million people have chronic hepatitis C infection (HCV), and about 1.5 million new infections are diagnosed annually worldwide [11]. The World Health Organization (WHO) estimated that in 2019 approximately 290,000 people died from hepatitis C, mostly as a result of cirrhosis and hepatocellular carcinoma (primary liver cancer) [11]. As part of the first global health sector strategy on viral hepatitis (2016-2021), the WHO aims to eliminate viral hepatitis as a public health problem by reducing new viral hepatitis infections by 90% and reducing viral hepatitis deaths by 65% by 2030 [11]. Reaching these objectives will require a substantial increase in the number of HCV screenings performed to diagnose and treat 80% of the estimated 58 million HCV-infected persons [11]. However, by 2017, only about 20% of this population were aware of their infection, and only 5 million of individuals diagnosed with HCV had received appropriate therapy [12]. In fact, an estimated 22,500 and 12,300 people living with chronic HCV in Spain and Portugal are unaware of their infection.

Although generally held by health systems as their strategy of choice, indicator condition guided testing is insufficiently implemented, resulting in significant levels of missed opportunities for diagnosis [13]. Underdiagnosis and late diagnosis of blood-borne viruses (BBVs) have 3 main consequences: 1) worse prognosis and loss of quality of life in patients with late diagnosis; 2) increased healthcare costs; and 3) greater spread of the epidemic. More effective and evidence-based models of BBV preventive care are needed.

The European Center for Disease Prevention and Control (ECDC) is promoting an increase in test coverage and uptake, especially for those most at risk, as an essential element of any strategy to eliminate HBV, HCV and HIV in the European Union and European Economic Area (EU/EEA) [14]. Additionally, in Spain, the “Guideline for Recommendations for Early Diagnosis of HIV in the Healthcare Sector” advocates performing serology under certain circumstances in various healthcare settings, including emergency departments (EDs) [15]. Indeed, urban EDs are well-positioned for detecting HIV/HCV infection and might be suitable places to reach patient profiles that could be difficult to access at other levels of care [16]. The aim of our project was to increase the proportion of eligible patients for HIV and HCV screening who undergo testing by implementing an opt-out testing strategy in the EDs of 4 hospitals in the Iberian Peninsula.

Methods

**Project design and intervention setting**

A prospective, observational study was conducted after implementing the TEST model for opportunistic screening in the ED of four public hospitals in Spain and Portugal. The TEST model was employed in participating hospitals to promote changes in care systems and broader uptake of screening and linkage to care, as previously described[17-21]. Briefly, TEST is based on 4 main pillars: testing and linkage integrated into the normal clinical workflow, using existing infrastructure and staff to generate efficiencies (T); electronic health record (EHR) modifications (E); systemic policy change (S); training, continuous quality enhancement and feedback by using program data to track progress, identify areas for improvement, and support staff training (T). Screening eligibility criteria and workflows were defined, and EHR modifications were used whenever possible to automate the identification of eligible patients. To ensure that opt-out language was used, consent procedures were adjusted, and refusal to participate in testing was noted in patients’
records. Following local ethics committee opinion and ECDC guidance [14], written consent forms were avoided whenever possible.

Laboratory request forms and profiles were updated, and EHR systems were adjusted to automate the population of requests whenever possible. Biological specimen collection workflows were defined and integrated into regular patient pathways. To guarantee reflex testing was used, laboratory testing procedures were updated. Patient notification procedures and linkage to care workflows were defined and assigned to specific individuals.

Each site incorporated the redesigned protocols into its systems, trained its staff on the new procedures, and maintained an implementation log for monitoring and evaluating indicators that was regularly reviewed to ensure adherence to each program objective. Positive feedback loops were fostered by sharing key intervention milestones with personnel. Patient education materials and posters were designed and visibly displayed.

Patients received appropriate clinical follow up until discharge, regardless of test results. Patients with positive tests were contacted by dedicated teams to ensure and monitor linkage to specialist medical care.

**Participating centers and inclusion criteria**

The EDs of four hospitals in Portugal and Spain participated in the study:

1. **Hospital de Cascais Dr José de Almeida (HJA)**, in Cascais, Portugal, where the intervention was implemented in the adult ED which receives 98,000 visits per year. Eligible patients for HIV and HCV screening consisted of individuals aged 18-64 seeking ED care with no record of previous serologies and no record of HIV/HCV infection or tests in the past 12 months, who needed a blood draw for any reason. Data were collected between September 2018 and December 2021 (40 months).

2. **Hospital Dr Nélio Mendonça (HNM)** in Funchal, Portugal, where the intervention was implemented in the adult ED which receives 99,000 visits per year. Eligible patients for HCV screening consisted of individuals aged 18-70 seeking ED care with no record of previous serologies and no record of HCV infection or HCV test within the previous year of presentation, who needed a blood draw for any reason. Data were collected between August 2020 and January 2022 (18 months).

3. **Hospital Vall d’Hebron (HUVH)** in Barcelona, Spain, where the intervention was implemented in the adult ED which receives 108,000 visits per year. Eligible patients for HCV screening consisted of individuals aged 18 and over seeking ED care, with no record of previous serologies in the past 3 months and no record of HCV infection or HCV test within the previous year of presentation, who needed a blood draw for any reason. Data were collected between February 2020 and February 2022 (24 months).

4. **Hospital Universitario Torrecárdenas (HUT)** in Almería, Spain, where the intervention was implemented in the adult ED which receives 92,000 visits per year. Eligible patients for HCV screening consisted of individuals aged 18-70 seeking ED care, with no record of previous serologies in the past 12 months and no record of HCV infection or HCV test during the same period, who needed a blood draw for any reason. Data were collected between August 2021 and June 2022 (11 months).

**Data analysis**

The main outcomes reported were the number of HIV and HCV antibody tests performed, positive HIV/HCV patients identified by antibody testing, and confirmatory RNA or core antigen (cAg) tests performed for HCV. All data points were analyzed descriptively to determine percentages and increases in testing rates.

**Results**

**Testing rates before and after implementation of the screening intervention**

A summary of the main results is shown in Table 1. In HJA, 91% of individuals who were eligible for testing were screened between September 2018 and December 2021. A total of 38,357 HIV antibody tests (mean 1,051 tests/month) and 47,059 HCV antibody tests (mean 1,148 tests/month) were performed, resulting in an 833% and 4,159% increase in testing rates for HIV and HCV, respectively. At HNM, 96% of individuals eligible for testing were screened in the period between August 2020 and January 2022. The number of HCV tests increased by 1,686% after the implementation of the screening, with an uptake of 14,617 tests (mean 585 tests/month). In HUVH, 17,560 people completed HCV testing in a 24-month period, representing an increase in testing rates of more than 70,000,000%. Between August 2021 and June 2022 (11 months), HUT performed a total of 4,448 HCV antibody tests (mean 404 tests/month).
Table 1

<table>
<thead>
<tr>
<th>Hospital (period analyzed)</th>
<th>Virus screened</th>
<th>Number of tests before the intervention/month (mean)*</th>
<th>Number of tests after the intervention (mean)</th>
<th>Number of tests after the intervention/month (mean)</th>
<th>Increase in testing rate (%)</th>
<th>Seroprevalence rate (%)</th>
<th>Active infection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Dr. José de Almeida, Cascais (Sept 2018-Dec 2021)</td>
<td>HCV</td>
<td>27.6</td>
<td>47,059</td>
<td>1,148</td>
<td>1.5</td>
<td>1.5</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>HIV</td>
<td>126.1</td>
<td>38,357</td>
<td>1,051</td>
<td>0.7</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Hospital Dr. Nélio Mendonça, Madeira (Aug 2020- Jan 2022)</td>
<td>HCV</td>
<td>34.7</td>
<td>14,617</td>
<td>585</td>
<td>0.6</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Hospital Universitario Vall d’Hebron, Barcelona (Feb 2020-Feb 2022)</td>
<td>HCV</td>
<td>0.001</td>
<td>17,560</td>
<td>732</td>
<td>3.9</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Hospital Universitario Torrecárdenas, Almería (Aug 2021-Apr 2022)</td>
<td>HCV</td>
<td>15.5</td>
<td>4,448</td>
<td>404</td>
<td>1.5</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

*The monthly average of individuals tested within the previous 12 months prior to intervention implementation was calculated. In centers where screening was performed for less than 12 months before the intervention, monthly average of individuals tested was calculated for the available months.

HIV seroprevalence rate

HJA was the only study center that performed HIV testing. The seroprevalence rate for HIV was 0.7%.

HCV seroprevalence and active infection rates

In HJA, the HCV seroprevalence rate was 1.5%. Among those testing positive for HCV antibodies, 53% were confirmed positive by reflex testing for HCV RNA, with an overall 0.8% of patients presenting active HCV infection. We found a seroprevalence rate of 0.6% for HCV in HNM. Forty-seven percent of the diagnosed individuals were confirmed positive by reflex testing, of whom a total of 0.3% had active HCV infection. The HCV seroprevalence rate was 3.9% in HUVH, 19% of whom were HCV RNA positive, with an overall 0.7% of patients presenting active HCV infection. In HUT, the HCV seroprevalence rate was 1.5%, 31% of whom were confirmed HCV RNA positive; 0.5% of patients had active HCV infection.

Discussion

Our multicenter prospective study shows that the implementation of opportunistic screening for HCV and HIV in EDs is viable, does not disrupt the normal workflow of the emergency services, and is highly effective in increasing the diagnosis of both HCV and HIV infections, with viremic seroprevalence rates ranging from 0.3% to 0.8% for HCV and 0.7% for HIV.

The identification of individuals with BBV infections provides a critical opportunity for linkage to care, particularly when patients are in contact with the hospital for other conditions. Furthermore, if patients are aware of their serostatus, they reduce individual actions that contribute to viral transmission [22]. EDs are an important healthcare setting for efficiently testing patients for BBVs. In the case of HIV, the burden of the disease is increasingly carried by racial and ethnic minorities, the elderly, young people in low and middle-income countries, and socioeconomically disadvantaged people [23]. Many individuals in these groups have limited access to primary care and use the ED as their unique source of medical care. These data highlight both the need for and the importance of promoting BBV screening programs in EDs.

Many studies have previously demonstrated the impact of opportunistic, automated screening programs for HIV and HCV in EDs. Retrospective BBV seroprevalence studies in the US, where routine opt-out screening for HIV has been recommended for individuals aged 13-64 years in all healthcare settings since 2006 [24], have shown high levels of infection in tests performed in EDs [25,26]. In the UK, a prospective, real-world study performing opt-out testing for BBVs in nine urban EDs identified 54 viral hepatitis infections in a single week, nearly half of which were newly diagnosed infections [27]. In Dublin, a 10-month pilot study of BBV testing in the ED in an urban hospital showed a seroprevalence of 5.1% for HCV and 1.1% for HIV [28]. The seroprevalence rates found in our study were lower (0.7% for HIV and up to 3.9% for HCV). Many factors could explain these differences. On one hand, the period in which the screenings were performed might have affected the data, especially considering that our study was conducted during the COVID-19 pandemic. Also, the size of the EDs and local population prevalence of BBVs should be considered. Although the EDs in the UK and Ireland receive fewer visits per year than some of the participating centers in our study (46,000 vs 100,000 respectively), they are located in regions with a very high population prevalence of HIV/HCV [27,28]. In any case, when all the data are considered together, they strongly suggest that BBV testing in urban EDs is an efficient intervention.
Several studies have evaluated the economic feasibility of performing routine HCV and HIV tests in EDs [29-34]. They demonstrated that a prevalence of viremic infection above 0.1% for HIV and 0.13% for HCV marks the cost-effectiveness threshold for such interventions [29,35-37]. Some studies have also analyzed the effect of opportunistic screening programs in the general population. In Spain, a study performed in a primary care setting in Valencia found a prevalence of HIV antibodies of ≥0.1% and an HCV RNA prevalence of 0.5% (manuscript submitted for publication). An economic evaluation of the implementation of BBV screenings in Spain showed that a prevalence of 0.13% for HCV is considered cost-effective [38], while in the United Kingdom, for screening to be considered a cost-effective intervention, the prevalence for HIV should be ≥0.2%, and ≥0.26% for HCV [39]. On the basis of these data, one could extrapolate that screening for HCV would be cost-effective in the Valencia region, but possibly not screening for HIV. However, it is important to point out that there are differences that possibly limit these conclusions. Country-level epidemiology differs, affecting cost-effectiveness analyses and calculations. On the other hand, unit testing and treatment costs are lower in Spain than in the UK. In fact, HIV screening in the UK is often based on point-of-care and rapid diagnostic tests, while with the TEST model, screening is performed using laboratory-based ELISA, resulting in significant cost savings. Therefore, given both countries’ similar societal willingness to pay at average currency conversion rates, along with the lower test costs in Spain, a cost-effectiveness analysis would likely also favor universal HIV screening if calculations were adapted to Spain.

This study has some limitations. Firstly, there is significant heterogeneity between the study centers. Their linkage to care practices and eligibility criteria for screening before the application of the intervention was heterogenous, as was the degree of implementation of the TEST model. Thus, it is difficult to compare the resulting data among the different institutions. Furthermore, the period in which we analyzed the impact of the opportunistic screening program was different for each center. The COVID-19 pandemic in particular might have affected the volume of tests performed. This is particularly evident in HJA, where the intervention was implemented long before March 2020, allowing for a before-and-after comparison. Visits to EDs decreased both in Spain and Portugal after the beginning of the pandemic [40,41]. In our study, we observed a marked decline in the number of screenings conducted from March to June 2020 in HJA (989 test/month), as compared with the pre-pandemic period (1,443 tests/month from January 2019 to February 2020). Some factors may be associated with the fewer numbers of HCV/HIV tests performed during this period, including universal screening for COVID-19 at the time of admittance, changes in the ED workflow, and healthcare personnel stress levels associated with the heavy burden of the COVID-19 pandemic and fear of contracting the new virus. As long as COVID-19 remains a problem, albeit a potentially seasonal one, its impact on health services, especially in EDs, must continue to be monitored to reduce disruption of services and maintain the progress in tackling HIV/HCV transmission achieved so far. Another limitation is the lack of a formal cost-effectiveness analysis. Such an analysis, while critically important, is beyond the scope of this study. Moreover, as previously mentioned, recent publications have demonstrated the cost-effectiveness of non-targeted screening, although these were based on the general population and on not specific ED interventions.

Conclusion

Our prospective multicenter study has shown that opportunistic HIV and HCV screening in EDs is feasible, does not disrupt ED activities, and is highly effective in increasing diagnosis. Considering the prevalence rates found in our program, we posit that adults seeking emergency care in high-prevalence urban settings should be considered candidate populations for robust BBV screening policies.

Declarations

Ethics approval and consent to participate

BBV screening and linkage to care is considered standard medical practice according to both Spanish and Portuguese healthcare policies. When enhanced screening and linkage to care practices required modifying consent procedures from written opt-in consent to oral opt-out consent, the formal opinion of the local ethics committee or local public health authorities was requested. The study was conducted according to the World Medical Association Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

Diogo Medina owns stock in and is an employee of Gilead Sciences. Alba Carrodeaguas is an employee of Gilead Sciences. Dr. Buti and Dr. Esteban declare having received honoraria for providing consultancy on advisory board meetings and speaking at symposiums from Gilead Sciences and Abbvie. Dr. Casado received honoraria for lectures and advisory boards from Gilead Sciences, Abbvie and Intercept. Dr. Vaz Pinto states having received lecture and advisory fees from Gilead, Janssen and ViiV. Dr. Camelo-Castillo has received travel grants and conference fees from Gilead. The remaining authors declare no conflicts of interest regarding the research, authorship, and publication of this article. Data collection and management were conducted independently, with additional oversight from independent data monitoring agencies.

Funding
Gilead Sciences’ FOCUS program provides funding to support HIV and viral hepatitis screening and linkage to the first medical appointment after diagnosis. FOCUS is a public health initiative that enables partner organizations to develop and share best practices in BBV screening, diagnosis, and linkage to care in accordance with screening guidelines recommended by country guidelines, scientific societies, and initiatives such as Fast-Track Cities. FOCUS aims to reduce the stigma of viral testing and diagnosis and increase HIV and HCV screening and linkage to care. FOCUS funding does not support activities beyond the first medical appointment and is agnostic to how organizations handle subsequent patient care and treatment.

Authors’ contribution

MB, IV-P, VMP and MC contributed to the conception and design of the work; JL, AB, CE, MG, AG, TM, LJ, APR, NF, EX, BF, GA, AC-C and MAR-M were responsible for data acquisition; MB and DM contributed to the analysis and interpretation of data and drafted the manuscript; MB, IV-P, VMP, MC CE, MG, AG, TM, EX, LJ, APR, NF, BF, GA, AC-C, MAR-M, AC, DM and RE reviewed the manuscript critically for important intellectual content and provided final approval of the version to be published.

Acknowledgements

We thank Vanessa Marfil at Medical Statistics Consulting, Spain for assisting in the writing and editing of this manuscript.

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