ORIGINAL ARTICLE

Frequency, sociodemographic and clinical characteristics of adults with HIV and HBV coinfection in Peru, 2017-2021

Sebastian Hidalgo[1,a]; Rodrigo Cueva[1,a]; Mary Reyes[2,b]; Pablo Renjifo[2,c]; César Gutiérrez[1,b]

1 Universidad de Piura, School of Human Medicine. Lima, Peru.
2 Ministry of Health, Centro Nacional de Epidemiología, Prevención y Control de Enfermedades (National Center for Epidemiology, Prevention and Disease Control). Lima, Peru.
[a] Medical student; [b] Doctor of Medicine, master's degree in Epidemiology; [c] Professional degree in Nursing, master's degree in Health Services Management.

ABSTRACT

Objective: To describe the frequency and the sociodemographic and clinical characteristics of human immunodeficiency virus (HIV) and hepatitis B virus (HBV) coinfection. **Materials and methods:** A cross-sectional study was conducted by cross-matching the HIV/AIDS and HBV infection databases of the Peruvian epidemiological surveillance system between 2017 and 2021. Individuals aged 18 years and older who were diagnosed with HIV and HBV coinfection were included. We collected data on variables such as age, sex, region of residence, AIDS stage, HIV transmission route, year of HIV diagnosis, year of HBV diagnosis, antiretroviral use and year of antiretroviral initiation. A bivariate analysis and a multiple correspondence analysis (MCA) were carried out. The databases of the Peruvian epidemiological surveillance system include the entire available population in that country. **Results:** A total of 106 adults with HIV and HBV coinfection were included. The median age at diagnosis was 32 years, and 77.88 % were between 18 and 39 years old, 87.62 % were male. Out of these patients, 68.57 % were diagnosed between 2018 and 2019; 66.02 % lived on the coast of Peru, and 10.87 % were treated in a department other than their department of residence. In addition, 64.76 % were diagnosed with both infections in less than one year, 23.58 % were in the AIDS stage, and 44.34 % were using antiretrovirals. **Conclusions:** Most individuals with HIV and HBV coinfection in Peru have a median age of 32 years, live on the coast, are male, and were diagnosed in less than 12 months. MCA associations can be explained by access to the healthcare system, availability of screening tests, comprehensiveness of clinical record, and natural history of HIV.

Keywords: Coinfection; HIV Infections; Hepatitis B virus; Public Health Surveillance; Peru (Source: MeSH NLM).

INTRODUCTION

In 2020, the global prevalence of hepatitis B virus (HBV) infection among individuals living with human immunodeficiency virus (HIV) ranged from 7.40 % [1] to 8.40 % [2]. The prevalence in Latin America and the Caribbean was 5.10 % [2]. Patients coinfected with HIV and HBV have a higher incidence of hepatocellular carcinoma [3] and a higher risk of death from it [4]. On the other hand, tenofovir-based antiretroviral treatment reduces the progression to end-stage liver disease [5] and the degree of liver fibrosis [6].

According to Prussing et al., 79.00 % of the individuals coinfected with HIV and HBV in New York are male, and sexual route transmission is a risk factor [7]. We have found few publications on the description of HIV and HBV coinfection in Peru. Lama et al. reported a prevalence of 9.50 % among men who have sex with men [8]. Cabezas et al. observed a prevalence of 0.50 % in an HBV-endemic area of Amazonia [9].

The description of the sociodemographic and clinical characteristics, as well as the temporal evolution of the frequency of HIV and HBV coinfection will contribute to the understanding of the epidemiology of this population in Peru. The objective of this research is to describe the frequency, sociodemographic and clinical characteristics of HIV and HBV coinfection in adults between 2017 and 2021, using data from the Peruvian epidemiological surveillance system.

MATERIALS AND METHODS

Study design and population

A cross-sectional study was conducted using data from HIV epidemiological surveillance database and the HBV epidemiological surveillance database from 2017 to 2021. Both belong to the Directorate of Public

Corresponding author:
Sebastián Antonio Hidalgo Gallosa
hidalgogallosa.sebastian@gmail.com

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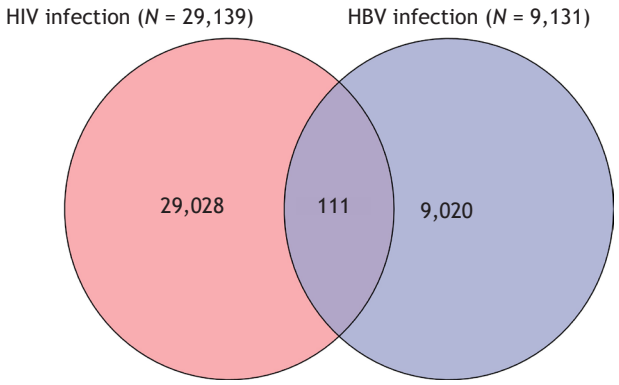
Health Surveillance at the Centro Nacional de Epidemiología, Prevención y Control de Enfermedades (CDC) - Perú (National Center for Epidemiology and Disease Prevention and Control [CDC] - Peru). Epidemiological surveillance of HIV and HBV infections is passive; and reporting is carried out by means of a clinical-epidemiological form, on a mandatory, individual and nationwide basis. This article was written according to the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement [10].

Adults aged 18 years and older diagnosed with HIV and HBV between 2017 and 2021 were included. The CDC-Peru databases include the entire available Peruvian population; therefore, a sample size was not calculated. Participant identification and cross-matching were performed by CDC-Peru. Participants were identified using ICD-10 codes B20 and B24 in the HIV infection database and B16 in the HBV infection database. Cross-matching of the databases was done via ID card number. Figure 1 depicts the cross-matching process. The CDC–Peru routinely cleans its databases, including the search for duplicate entries and the verification of data consistency. The authors accessed the HIV and HBV coinfection database in May 2022.



HIV: human immunodeficiency virus. HBV: hepatitis B virus.

Figure 1. Cross-matching of the HIV and HBV infection databases

Variables and measurements

The following variables were collected: *year of birth*, *sex*, *place of residence*, *AIDS stage*, *HIV transmission route*, *year of HIV diagnosis*, *year of HBV diagnosis*, *antiretroviral (ARV) use*, and *year of ARV initiation*.

Year of HIV and HBV coinfection diagnosis was defined as the year of the most recent reported infection. Age at coinfection diagnosis was calculated by subtracting the year of birth from the year of diagnosis. Order of diagnosis was defined according to the temporal relationship between the year of HIV diagnosis and the year of HBV diagnosis, respectively. This variable had the following categories: same year of diagnosis, first diagnosis HBV and first diagnosis HIV. Time to diagnosis was calculated by subtracting the year of first reported infection from the year of coinfection diagnosis. It was categorized into < 12 months, 12-23 months and ≥ 24 months. Time to antiretroviral initiation was defined as the time from HIV diagnosis to antiretroviral initiation and was categorized into < 12 months, 12-23 months, 24-35 months and ≥ 36 months.

Statistical analysis

The median and interquartile range (IQR) were calculated for age at diagnosis as it did not follow a normal distribution. Qualitative variables were expressed as absolute frequency and percentage. Bivariate analysis was performed using the chi-square test of independence, Fisher's exact test, Mann-Whitney *U* test and Kruskall-Wallis test. Missing data were not considered in the statistical analysis. A result was considered statistically significant when the *p* value was < 0.050.

A multiple correspondence analysis was performed with the variables *age at diagnosis*, *sex*, *place of residence*, *year of coinfection diagnosis*, *AIDS stage*, *HIV transmission route* and *antiretroviral use*. *Age at diagnosis* was categorized into 18-29 years, 30-39 years, 40-49 years, 50-59 years and 60-69 years. Participants with any missing data were excluded from this analysis.

Statistical analysis was performed using the R programming language version 4.2.1 [11] and the RStudio environment [12]. The R packages gtsummary [13] and flextable [14] were used for descriptive and bivariate analysis, while FactoMineR [15] and factoextra [16] were used for the MCA. The analysis code can be retrieved from Harvard Dataverse. The data generated are available from the corresponding author upon request.

Ethical considerations

This study was approved by the Institutional Review Board of the Universidad de Piura (No.: PREMED0820213). No intervention of human subjects or biological samples was required. No information was collected that would allow the identification of participants.

RESULTS

The initial database included 111 individuals. Five participants were excluded for not meeting the eligibility criteria: four were under 18 years of age, and one was from 2022. In total, 106 participants with HIV and HBV coinfection were included in the study.

A total of 87.62 % (*n* = 93) of the participants were male. The median age at the time of diagnosis was 32 years (Table 1), and 77.88 % (*n* = 81) were between 18 and 39 years old. Of the participants, 66.02 % (*n* = 68) resided on the Peruvian coast. Additionally, 10.87 % (*n* = 10) received care in a department different from their place of residence. A majority of diagnoses, i.e., 68.57 % (*n* = 72), occurred in 2018 and 2019. In 2017, most participants resided in the highlands (61.54 % [*n* = 8], whereas in 2018, 2019, and 2020, the majority resided on the coast (64.86 %–81.25 %).

The most frequent route of HIV transmission was sexual contact (90.57 % [*n* = 96]) (Table 1). A total of 23.58 % (*n* = 25) of participants were at the AIDS stage. In 64.76 % (*n* = 68) both infections were diagnosed in less than 12 months. Among those whose time to diagnosis was greater than 12 months, 89.61 % (*n* = 19) were initially diagnosed with HIV (*p* < 0.001).

Table 1. Characteristics of participants with HIV and HBV coinfection by sex

Variables [a]	Global *N* = 106 *n* (%)	Male *n* = 93 *n* (%)	Female *n* = 13 *n* (%)	*p* value
Age [b]	32.0 (27.0-38.2)	33.0 (27.5-39.0)	29.0 (24.0-32.0)	0.083 [c]
Year of diagnosis				0.038 [d]
2017	13 (12.38)	9 (9.78)	4 (30.77)	
2018	34 (32.38)	31 (33.70)	3 (23.08)	
2019	38 (36.19)	35 (38.04)	3 (23.08)	
2020	16 (15.24)	15 (16.30)	1 (7.69)	
2021	4 (3.81)	2 (2.17)	2 (15.38)	
Time to diagnosis (months)				0.077 [d]
< 12 months	68 (64.76)	63 (68.48)	5 (38.46)	
12-23 months	28 (26.67)	22 (23.91)	6 (46.15)	
≥ 24 months	9 (8.57)	7 (7.61)	2 (15.38)	
Region of residence				0.057 [d]
Coast	68 (66.02)	63 (70.00)	5 (38.46)	
Highlands	30 (29.13)	23 (25.56)	7 (53.85)	
Jungle	5 (4.85)	4 (4.44)	1 (7.69)	
VIH transmission route [e]				1.000 [d]
Sexual	96 (90.57)	84 (90.32)	12 (92.31)	
Unknown	10 (9.43)	9 (9.68)	1 (7.69)	
Order of diagnosis				0.038 [d]
The same year	68 (64.76)	63 (68.48)	5 (38.46)	
First diagnosis HBV [f]	14 (13.33)	10 (10.87)	4 (30.77)	
First diagnosis HIV	23 (21.90)	19 (20.65)	4 (30.77)	
Antiretroviral use	47 (44.34)	40 (43.01)	7 (53.85)	0.461 [g]

[a] Missing data: for age, data were missing one value in female and one in male sex; for year of diagnosis, one in male sex; for time to diagnosis, one in male sex; for region of residence, three in male sex.

[b] Median (IQR).

[c] Mann-Whitney *U* test.

[d] Fisher's exact test.

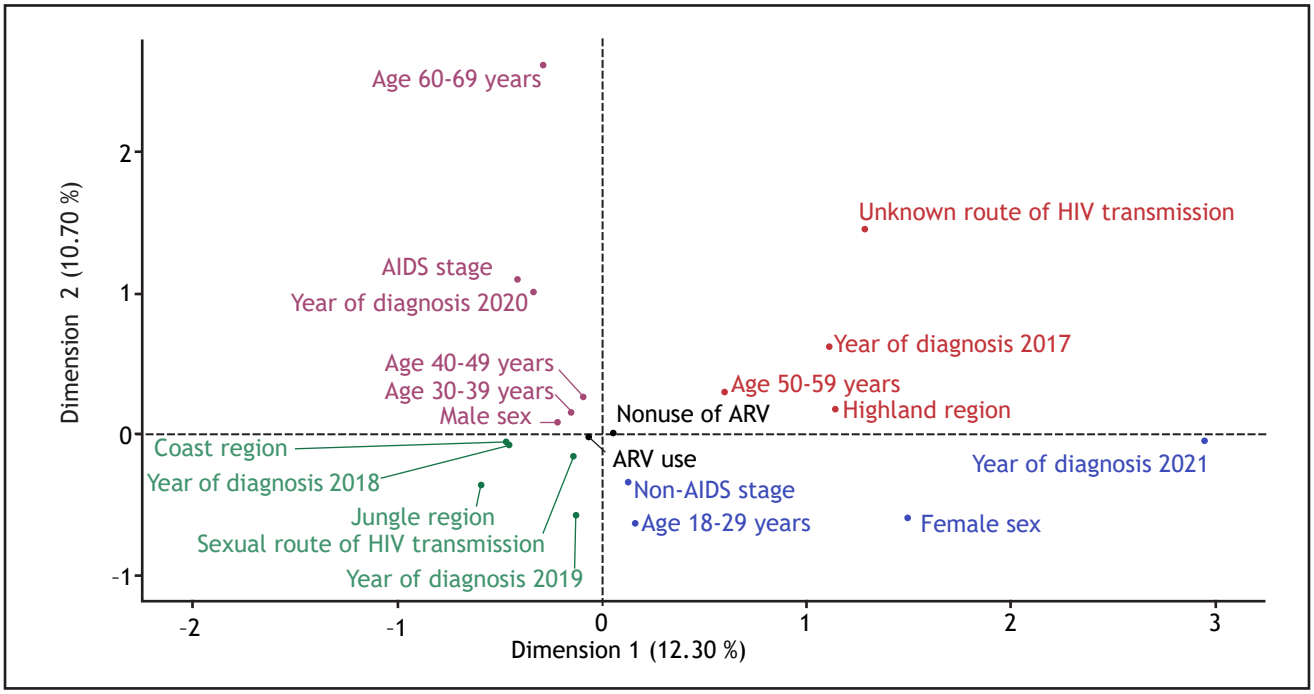
[e] HIV: human immunodeficiency virus.

[f] HBV: hepatitis B virus.

[g] Chi-square test of independence.

Multiple correspondence analysis (MCA)

Four participants were excluded due to missing data, and 102 participants were included in this analysis. The category year of diagnosis 2020 was associated with the categories male sex, AIDS stage, and age groups 30–39, 40–49, and 60–69 years. Similarly, the category year of diagnosis 2017 was associated with the categories region of residence in the highlands, age 50–59 years and unknown route of HIV transmission. On the other hand, the category year of diagnosis 2021 was associated with the categories age 18-29 years, non-AIDS stage and female sex. Finally, the category year of diagnosis 2019 was associated with the categories year of diagnosis 2018, region of residence in the coast, region of residence in the jungle, and sexual route of HIV transmission. The categories ARV use and nonuse of ARV were not associated with other categories (Figure 2).



HIV: human immunodeficiency virus. HBV: hepatitis B virus. AIDS: acquired immunodeficiency syndrome.
Figure 2. MCA of the categories of variables of participants with HIV and HBV coinfection

DISCUSSION

We found that 87.62 % of those coinfected were male, a finding compatible with different cross-sectional studies based on secondary data sources and carried out in people living with HIV/AIDS (PLWHA), a range that oscillates between 82.00 % and 97.70 % [17-19]. A prospective study reported a frequency of 92.10 % [20]. Among studies based on PLWHA with primary data sources, the frequency range was 71.40 % to 97.40 % [21-23]. In 2019, a cross-sectional study in Ghana reported that 56.00 % of participants were women [24]. The median age in this study was lower than that reported in cross-sectional PLWHA studies, which documented median ages of 39 [17], 40 [21] and 41 years [19].

Fewer diagnoses were made in 2020 than in 2019 (16 vs. 38) (Supplements S1 and S2). One study reported that in 2020 HIV diagnoses were reduced by 42.10 % compared to 2019 [25] during the first wave of COVID-19 infections. In this study, individuals initially diagnosed with HIV in 2019 were 39.13 % and, in 2020, 8.70 % of the total. One study reported that in 2020, there was a 33.0 % decrease in the use of tests to detect HBV compared to 2019 [26]. In our study, 42.86 % of cases were diagnosed in 2019, compared to only 14.29 % in 2020. This difference may be attributed to the impact of lockdown during the COVID-19 pandemic on access to health services.

Our results are consistent with several studies [19,20,22,23,27] that report sexual route as the most common mode of HIV transmission. We found 23.58 % of participants in AIDS stage, a figure that is within the reported range of 8.4 % [20] and 50 % [23]. ARV use (43.81 %) is less than half compared to 90.40 % and 99.00 % [19,20,22,28] of other studies. According to UNAIDS, 79.00 % of patients living with HIV in Peru receive ARV treatment [29]. We collected information on ARV use at the time of reporting; therefore, some patients may have initiated treatment after the report. Consequently, the actual ARV use in this population may be higher than 43.81 %.

Concerning the MCA, the relationships between male sex, AIDS stage, and age 30-39, 40-49 and 60-69 years can be explained by early HIV transmission during adulthood and the progression to AIDS between the 30 and 69 years of age. Male sex is associated with these categories as it is the most prevalent segment with HIV infection in Peru [29]. The

association between an unknown route of HIV transmission and region of residence in the highlands could be explained by the fact that this population may not report the transmission route due to social stigma or because they are unaware of the time of exposure. The relationship between the non-AIDS stage and age 18-29 years could be attributed to recent infection and early diagnosis. The associations between sexual route of HIV transmission, region of residence in the jungle and coast regions could be explained by better access to the healthcare system in these areas. These conditions allow the identification of the most common HIV transmission route, i.e., sexual contact. However, we were unable to explain the relationships between age 50-59 years, female sex and years of diagnosis.

The limitations of passive surveillance [30] of HIV and HBV infections, such as underestimation of cases and delays in data collection processes, could affect our study. Other limitations would be the amount of missing data and the impact of COVID-19 on the healthcare system and the epidemiological surveillance system. We were unable to collect immunological variables and data on liver fibrosis and mortality. Moreover, our main strength is the use of databases that encompass the entire epidemiological surveillance system. Likewise, we did not limit the study to the population with risk factors, which allows us to extrapolate the results to the Peruvian population aged 18 years and older.

In conclusion, data from the epidemiological surveillance system indicate that individuals with HIV and HBV coinfection are predominantly males aged 18-39 years living on the coast of Peru. One-third are in the AIDS stage, and fewer than half are using ARV treatment for HIV at the time of reporting. This characterization is important because literature regarding this population is scarce in Peru. Therefore, our research helps expand knowledge on the epidemiology of HIV-HBV coinfection in the country. It is recommended to broaden the description of HIV and HBV coinfection in populations with risk factors or in other settings, to verify the factors associated with coinfection and to describe the impact of the SARS-CoV-2 pandemic on the reporting of HIV and HBV coinfection.

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BIBLIOGRAPHIC REFERENCES

1. Platt L, French CE, McGowan CR, Sabin K, Gower E, Trickey A, et al. Prevalence and burden of HBV co-infection among people living with HIV: A global systematic review and meta-analysis. J Viral Hepat [Internet]. 2020;27(3):294–315.
2. Leumi S, Bigna JJ, Amougou MA, Ngouo A, Nyaga UF, Noubiap JJ. Global burden of hepatitis B infection in people living with human immunodeficiency virus: A systematic review and meta-analysis. Clin Infect Dis [Internet]. 2020;71(11):2799–806.
3. Sun J, Althoff KN, Jing Y, Horberg MA, Buchacz K, Gill MJ, et al. Trends in hepatocellular carcinoma incidence and risk among persons with HIV in the US and Canada, 1996-2015. JAMA Netw Open [Internet]. 2021;4(2):e2037512.
4. Rajbhandari R, Jun T, Khalili H, Chung RT, Ananthakrishnan AN. HBV/HIV coinfection is associated with poorer outcomes in hospitalized patients with HBV or HIV. J Viral Hepat [Internet]. 2016;23(10):820–9.
5. Klein MB, Althoff KN, Jing Y, Lau B, Kitahata M, Lo Re V, et al. Risk of end-stage liver disease in HIV-Viral hepatitis coinfected persons in North America from the early to modern antiretroviral therapy eras. Clin Infect Dis [Internet]. 2016;63(9):1160-7.
5. Audsley J, Robson C, Aitchison S, Matthews GV, Iser D, Sasadeusz J, et al. Liver fibrosis regression measured by transient elastography in human immunodeficiency virus (HIV)-Hepatitis B virus (HBV)-Coinfected individuals on long-term HBV-Active combination antiretroviral therapy. Open Forum Infect Dis [Internet]. 2016;3(1):ofw035.
6. Prussing C, Chan C, Pinchoff J, Kersanske L, Bornschlegel K, Balter S, et al. HIV and viral hepatitis co-infection in New York City, 2000–2010: prevalence and case characteristics. Epidemiol Infect [Internet]. 2015;143(7):1408–16.
7. Lama JR, Agurto HS, Guanira JV, Ganoza C, Casapia M, Ojeda N, et al. Hepatitis B infection and association with other sexually transmitted infections among men who have sex with men in Peru. Am J Trop Med Hyg [Internet]. 2010;83(1):194–200.
8. Cabezas C, Trujillo O, Balbuena J, Marin L, Suárez M, Themme M, et al. Prevalencia de infección por los virus de la hepatitis B, D y por retrovirus en la etnia Matsés (Loreto, Perú). Rev Peru Med Exp Salud Pública [Internet]. 2020;37(2):259–64.
9. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, et al. The REporting of studies conducted using observational routinely-collected health data (RECORD) statement. PLoS Med [Internet]. 2015;12(10):e1001885.
10. Global Biodiversity Information Facility. R: A language and environment for statistical computing [Internet]. Copenhagen: GBIF; 2015. Available from: https://www.gbif.org/tool/81287/r-a-languageand-environment-for-statistical-computing
11. Posit. The most trusted IDE for open source data science [Internet]. Boston: Posit; 2022. Available from: https://posit.co/products/open-source/rstudio/
12. Sjoberg DD, Whiting K, Curry M, Lavery JA, Larmarange J. Reproducible summary tables with the gtsummary package. The R Journal [Internet]. 2021;13(1):570–80.
13. Gohel D, Skintzos P. Flextable R package [Internet]. Francia: Ardata; 2023. Available from: https://davidgohel.github.io/flextable/
14. Lê S, Josse J, Husson F. FactoMineR: An R Package for Multivariate Analysis. J Stat Soft [Internet]. 2008;25(1):1–18. doi:10.18637/jss.v025.i01
15. Kassambara A, Mundt F. Factoextra: Extract and Visualize the Results of Multivariate Data Analyses [Internet]. Alemania: Factoextra; 2020. Available from: http://www.sthda.com/english/rpkgs/factoextra
16. Rana U, Driedger M, Sereda P, Pan S, Ding E, Wong A, et al. Characteristics and outcomes of antiretroviral-treated HIV-HBV co-infected patients in Canada? BMC Infect Dis [Internet]. 2019;19(1):982.

17. Bosh KA, Coyle JR, Hansen V, Kim EM, Speers S, Comer M, et al. HIV and viral hepatitis coinfection analysis using surveillance data from 15 US states and two cities. Epidemiol Infect [Internet]. 2018;146(7):920–30.
18. Choy CY, Ang LW, Ng OT, Leo YS, Wong CS. Factors associated with hepatitis B and C co-infection among HIV-Infected patients in Singapore, 2006–2017. Trop Med Infect Dis [Internet]. 2019;4(2):87.
19. Sterling RK, Wahed AS, King WC, Kleiner DE, Khalili M, Sulkowski M, et al. Spectrum of liver disease in hepatitis B virus (HBV) patients coinfected with human immunodeficiency virus (HIV): results of the HBVHIV cohort study. Am J Gastroenterol [Internet]. 2019;114(5):746–57.
20. Demosthenes JP, Sachithanandham J, Fletcher GJ, Zachariah UG, Varghese GM, John Daniel HD, et al. Characteristics of treatment-naïve HBV-Infected individuals with HIV-1 coinfection: A cross-sectional study from South India. Indian J Med Microbiol [Internet]. 2019;37(2):219–24.
21. Pérez-Latorre L, Berenguer J, Micán R, Montero M, Cifuentes C, Puig T, et al. HIV/HBV coinfection: temporal trends and patient characteristics, Spain, 2002 to 2018. Euro Surveill [Internet]. 2021;26(25):2000236.
22. Ranin J, Salemovic D, Brmbolic B, Marinkovic J, Boricic I, Pesic Pi, et al. Comparison of demographic, epidemiological, immunological, and clinical characteristics of patients with HIV Mono-infection versus patients co-infected with HCV or/and HBV: A Serbian cohort study. Curr HIV Res [Internet]. 2018;16(3):222-30.
23. Boateng R, Mutocheluh M, Dompreh A, Obiri-Yeboah D, Anto EO, Owusu M, et al. Sero-prevalence of Hepatitis B and C viral co-infections among HIV-1 infected ART-naïve individuals in Kumasi, Ghana. PLoS ONE [Internet]. 2019;14(4):0215377.
24. Romero-Hernández B, Martínez-García L, Rodríguez-Dominguez M, Martínez-Sanz J, Vélez-Díaz-Pallarés M, Pérez Mies B, et al. The negative impact of COVID-19 in HCV, HIV, and HPV surveillance programs during the different pandemic waves. Front Public Health [Internet]. 2022;10:880435.
25. Mandel E, Peci A, Cronin K, Capraru CI, Shah H, Janssen HLA, et al. The impact of the first, second and third waves of covid-19 on hepatitis B and C testing in Ontario, Canada. J Viral Hepat [Internet]. 2022;29(3):205–8.
26. Ireland G, Simmons R, Balogun K, Kirwan P, Sabin CA, Ramsay M, et al. HIV coinfection among persons diagnosed with hepatitis B in England in 2008-2014. HIV Med [Internet]. 2019;20(4):255–63.
27. Weitzel T, Rodríguez F, Noriega LM, Marcotti A, Duran L, Palavecino C, et al. Hepatitis B and C virus infection among HIV patients within the public and private healthcare systems in Chile: A cross-sectional serosurvey. PLoS One [Internet]. 2020;15(1):e0227776.
28. UNAIDS. UNAIDS Data 2021 [Internet]. Geneva: UNAIDS; 2021. Available from: https://www.unaids.org/sites/default/files/media_asset/JC3032_AIDS_Data_book_2021_En.pdf
29. Centers for disease control and prevention. Principles of epidemiology in public health practice [Internet]. Atlanta: CDC; 2006. Available from: https://www.cdc.gov/csels/dsepd/ss1978/SS1978.pdf