original article

Epidemiology of hepatitis B, hepatitis C, and syphilis co-infections in HIV-1 patients: a retrospective cross-sectional study of prevalence and viral load correlates

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Citation: Aydoğan S, Kirca F, Cozalan A, Aslan FG, Gürler M, Toyran A, et al. Epidemiology of hepatitis B, hepatitis C, and syphilis co-infections in HIV-1 patients: a retrospective cross-sectional study of prevalence and viral load correlates. Ann Saudi Med 2025; (45)5: 345-352. DOI: 10.5144/0256-4947.2025.28.08.1204

Received: May 2, 2025

Accepted: July 10, 2025

Epub ahead of print: August 28, 2025

Funding: None.

BACKGROUND: Co-infections with hepatitis B (HBV), hepatitis C (HCV) and syphilis complicate the clinical management of people living with HIV by influencing disease progression, treatment response, and transmission risk. Despite the growing HIV burden in Türkiye, data on the impact of these coinfections remain limited.

OBJECTIVES: To determine the prevalence of HBV, HCV, and syphilis coinfections in adults with HIV-1 and to examine their associations with demographics and HIV-1 viral load.

DESIGN: Retrospective cross-sectional study

SETTING: Single center, tertiary care hospital in Türkiye

PATIENTS AND METHODS: Adults diagnosed with HIV-1 between March 2019 and June 2024 at Ankara Bilkent City Hospital were included. Demographic information, HIV viral load measurements, and serological and molecular test results for HBV, HCV, and syphilis were retrieved from the institutional laboratory database. Coinfection status was assessed relative to age, gender, and HIV viral load.

MAIN OUTCOME MEASURES: Prevalence and distribution of HBV, HCV, and syphilis coinfections and their associations with demographic variables and HIV viral load.

SAMPLE SIZE: 724 patients

RESULTS: The study population was predominantly male (86%), with a median age of 40 years. Syphilis was the most common coinfection (25.6%), followed by HBV at 4.1% and HCV at 1.8%. Syphilis was significantly more prevalent among men (P=.001), and HBV coinfection was associated with older age (P=.005). No significant associations were observed between HIV viral load and any co-infection. Notably, a substantial proportion of patients, especially those newly diagnosed after 2019, had high HIV RNA levels, suggesting delayed diagnosis and treatment initiation. Triple coinfections were rare but remain clinically relevant.

CONCLUSIONS: The high prevalence of syphilis and delayed HIV diagnoses highlight the urgent need for improved screening protocols, timely initiation of antiretroviral therapy, and broader implementation of HBV vaccination programs. An integrated multisectoral approach is critical to address the overlapping clinical and public health burdens posed by these co-infections. Healthcare strategies must consider the impact of COVID-19-related service disruptions, which likely contrib-

uted to delays in diagnosis and treatment.
LIMITATIONS: Lack of data on patients' behavioral risk factors and no follow-up on treatment outcomes for syphilis
CONFLICT OF INTEREST: None.
KEYWORDS: HIV, viral load, HBV, HCV, syphilis, co-infections

HIV remains a significant global public health challenge due to its detrimental immunosuppressive effects, resulting in increased susceptibility to opportunistic infections and co-infections. Among these co-infections, hepatitis B virus (HBV), hepatitis C virus (HCV), and Treponema pallidum (syphilis) are particularly significant, as they can accelerate HIV disease progression, compromise the effectiveness of antiretroviral therapy (ART), and alter transmission dynamics. These coinfections complicate HIV management by contributing to liver toxicity, especially with HBV and HCV, impairing immune reconstitution, and creating diagnostic challenges due to overlapping serological responses or atypical clinical manifestations. Moreover, HBV co-infection has been associated with heightened oxidative stress and immune dysregulation, further worsening clinical outcomes in people living with HIV (PLWH).[1,2]

Although the epidemiological distribution of co-infections varies between countries, it is influenced by factors such as screening policies, access to risk groups, and availability of treatment.[3] In Türkiye, recent multicenter data with large, representative samples remain scarce, especially in low- and middle-income settings. This highlights the need for updated epidemiological assessments like this study and further research on how these coinfections relate to clinical and laboratory findings.

This study aims to determine the prevalence of HBV, HCV, and syphilis co-infections among PLWH aged 18 and above diagnosed between March 1, 2019, and June 30, 2024. It also explores associations with demographic factors and supports clinical management through comparison with national and international data. The study period, starting from the hospital's opening in March 2019, spans both the COVID-19 pandemic and post-pandemic phases, ensuring a comprehensive and adequately powered cross-sectional analysis.

PATIENTS AND METHODS

In this retrospective cross-sectional study, a total of 724 individuals aged 18 years or older who were diagnosed with HIV-1 infection and followed at our institution between March 2019 and June 2024 were included. Exclusion criteria were missing or incomplete medical records and those not under regular follow-up at the time of data collection. No control group (HIV-negative individuals) was included in this study. Instead, comparisons were made between HIV-positive individuals with and without coinfections (HBV, HCV, or syphilis) to evaluate the impact of coinfections on laboratory parameters.

Testing was conducted following the national HIV guidelines in Türkiye, which align with international standards. HBV and HCV are tested at baseline, while syphilis screening is recommended at baseline and annually or based on clinical indications. In our center, patients were tested at diagnosis and re-evaluated annually or as needed. Therefore, coinfections reported in this study may have been identified either at baseline or during the longitudinal follow-up from March 2019 to June 2024.

Based on the patients' year of diagnosis and date of initial presentation, data on age, gender, HIV viral load, viral hepatitis markers (HBsAg, anti-HBs, anti-HBc Total, HBV DNA, anti-HCV, HCV RNA, hepatitis D virus [HDV] Ag, anti-HDV), and syphilis test results (Rapid plasma reagen [RPR], Treponema pallidum hemagglutination assay [TPHA]) were retrospectively documented using the laboratory information system.

Viral hepatitis serology was performed using Siemens Advia Centaur® (Tarrytown, NY, USA), Siemens Atellica® IM (Tarrytown, NY, USA), and BioMerieux VIDAS® 3 (Marcy-l'Étoile, France). Nucleic acid testing was conducted using real-time polymerase chain reaction (PCR) on the Rotor-Gene Q device following extraction with the QIAsymphony SP system (artus HIV-1 QS RGQ, artus HBV QS RGQ, and artus HCV QS RGQ; Qiagen QIAGEN GmbH, Hilden, Germany). Syphilis tests were carried out using Tulip Diagnostics Carbogen RPR and Atellica™ IM while VDRL/TPHA tests were conducted at the Microbiology Reference Laboratory of the Turkish Public Health Institution. No modifications were made to the laboratory testing methods throughout the study period.

Ethical considerations

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was

obtained from the Ankara Bilkent City Hospital Scientific and Ethical Evaluation Board for Medical Research (TABED 1-24-487, Approval Date: 28.08.2024). All data were anonymized.

Statistical analysis

All data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD) or median (min–max), after testing for normality using histogram and Kolmogorov-Smirnov test. Categorical variables were presented as frequencies (n) and percentages (%). For comparisons between groups, Pearson's Chi-square test or Fisher's exact test was used for categorical variables, and independent Student's T-test or Mann–Whitney U test was applied for continuous variables. A *P* value of <.05 was considered statistically significant.

RESULTS

A total of 724 patients were included. The median age was 40 years (IQR: 21; age range: 18–85 years). Among the patients, 101 (14%) were females (mean age: 43.5 years [IQR: 14]) and 623 (86%) were males (median age: 39 years, [IQR: 22]). A statistically significant difference in age was observed with females being significantly older than males (*P*<.001). Hepatitis B and hepatitis C serological test results were available for all patients. Syphilis testing was performed in 588 patients (81.2%).

A total of 11 pregnant women were included in the study cohort. Eight were diagnosed during pregnancy, while three became pregnant while on antiretroviral therapy (ART). Four pregnant women were found to be immune to hepatitis B, whereas seven were susceptible. None of the patients had HCV coinfection, although syphilis was detected in one pregnant woman who was incarcerated.

Patient distribution by year

Among the patients, 277 out of 724 were diagnosed between 2008 and 2018, with available records indicating either ongoing or past treatment histories. The remaining 447 (61.7%) patients received their diagnoses upon admission between 2019 and 2024. Of these, 308 (68.9%) were newly diagnosed, while 139 (31.1%) were detected incidentally with their initial diagnosis dates undetermined, and prior treatment information was unavailable. Of the 447 patients diagnosed at our hospital since 2019, the yearly distribution is as follows: 74 (10.2%) in 2019, 69 (9.5%) in 2020, 113 (15.6%) in 2021, 115 (15.9%) in 2022, 49 (6.8%) in 2023, and 27 (3.7%) in the first half of 2024.

HIV viral load distributions

Among the 277 patients diagnosed before 2019, no viral load was detected in 159 (57.4%) patients. Viral loads of 37–1000 copies/mL were observed in 92 (33.2%) patients, 1001–10 000 copies/mL in 10 (3.6%) patients, 10 001–100 000 copies/mL in 7 (2.5%) patients, 100 001–1 000 000 copies/mL in 6 (2.2%) patients, and >1 000 000 copies/mL in 3 (1.1%) patients. Among the 447 patients newly diagnosed between 2019 and 2024: no viral load was detected in 25 (5.6%) patients; viral loads of 37–1000 copies/mL were found in 17 (3.8%) patients; 1001–10 000 copies/mL in 28 (6.3%) patients; 10 001–100 000 copies/mL in 87 (19.5%) patients; 100 001–1 000 000 copies/mL in 159 (35.6%) patients; and >1 000 000 copies/mL in 131 (29.3%) patients. The overall median log HIV viral load was 5.48 copies/mL. The distribution of patient numbers and viral loads by year is presented in **Table 1**.

Hepatitis B serology

Among the 724 patients evaluated, 299 (41.3%) were susceptible to hepatitis B virus (HBV) infection, whereas 366 (50.6%) were found to be immune—219 (30.3%) due to prior vaccination and 147 (20.3%) due to resolved natural infection. Isolated anti-HBc reactivity was observed in 29 patients (4.0%), chronic HBV infection was identified in 27 patients (3.7%), and acute HBV infection was detected in 3 patients (0.4%). Among those with isolated anti-HBc positivity, HBV DNA was detectable at a low level (<32 IU/mL) in one patient, while it remained undetectable in the others.

Yearly distribution of HBV co-infection

The prevalence of HBV coinfection was 5.1% before 2019, 6.8% in 2019, 5.8% in 2020, 1.8% in 2021, and 4.4% in 2022. No cases of HBV coinfection were detected in 2023 and 2024. Overall, the prevalence of HBV coinfection after 2019 was 3.8%. Additionally, no serological evidence of hepatitis D virus (HDV) coinfection or superinfection was identified among HBsAg-positive patients.

Relationship between HBV status, HIV viral load, and age

Overall comparison of mean log HIV viral loads between HBsAg-positive (3.1834) and HBsAg-negative (3.5232) individuals revealed no significant difference (*P*=.458). HBV coinfection was not significantly associated with gender (*P*=.595), with males accounting for 83.3% and females for 16.7% of coinfected patients. However, patients with HBV coinfection were significantly older (47 years) than those without coinfection (41.6 years) (*P*=.005).

Table 1. Annual distribution of HIV-1 viral load categories in PLWH (n=724).

Years	<2019	2019	2020	2021	2022	2023	2024[b]	Total
Viral load[a]	159 (57)	11 (15)	2 (3)	7 (6)	3 (3)	1 (2)	1 (4)	184 (25)
37-1000	92 (33)	2 (3)	4 (6)	6 (5)	3 (3)	1 (2)	1 (4)	109 (15)
1001-10000	10 (4)	6 (8)	6 (9)	3 (3)	10 (9)	3 (6)	0 (0)	38 (5)
10001-100000	7 (3)	18 (24)	12 (17)	21 (19)	22 (19)	8 (16)	6 (22)	94 (13)
100001-1000000	6 (2)	25 (34)	25 (36)	45 (40)	43 (37)	15 (31)	6 (22)	165 (23)
>1000000	3 (1)	12 (16)	20 (29)	31 (27)	34 (30)	21 (43)	13 (48)	134 (19)
Total	**277 (100)**	**74 (100)**	**69 (100)**	**113 (100)**	**115 (100)**	**49 (100)**	**27 (100)**	**724 (100)**

Data is presented as n (%). [a]Copies /ml [b]First six months.

HCV coinfection

Anti-HCV reactivity was detected in 11 patients (1.5%). Of these, four were already on HIV treatment, while seven were newly diagnosed. The prevalence of HCV coinfection was 1.1% before 2019, 2.7% in 2019, 1.5% in 2020, 1.8% in 2021, and 2.6% in 2022. No cases were identified in 2023 and 2024. Overall, the prevalence of HCV coinfection after 2019 was 1.8%. The mean age was 41.0 years in HCV-positive individuals and 41.8 years in HCV-negative individuals. The mean log HIV viral load was 3.8162 in patients with HCV coinfection and 3.5044 in those without. No differences were observed between HCV coinfection status and age (*P*=.859) or HIV viral load (*P*=.695).

Syphilis coinfection

Syphilis serology was performed in 588 patients, with one patient excluded due to a false-positive RPR result. Among the tested individuals, 83 (14.1%) were positive for both RPR and TPHA, while 67 (11.4%) were RPR-negative but TPHA-positive. RPR titers were distributed as follows: 1:2 (n=2), 1:4 (n=6), 1:8 (n=12), 1:16 (n=10), 1:64 (n=22), 1:128 (n=2), 1:256 (n=6), and 1:640 (n=1).

The prevalence of syphilis coinfection was 31.6% before 2019 and ranged between 19.2% and 27.3% annually thereafter, with an overall post-2019 prevalence of 22.3%. Syphilis coinfection was more common in males (27.7%) than females (9.0%) (*P*=.001). There were no differences in mean HIV log viral load (3.4830 vs. 3.7859; *P*=.487) or mean age (40.9 vs. 41.0 years; *P*=.970) between patients with and without syphilis coinfection.

Combined co-infections

HIV+HBV+HCV co-infection was detected in only two patients. In the first patient, the HIV RNA level was 117 321 copies/mL, HBV DNA was 380,397,240 IU/mL, and no HCV RNA viremia was detected. In the second patient, HIV RNA was <37 copies/mL, HBV DNA was <32 IU/mL, and HCV RNA was measured at 2 593 250 IU/mL.

HIV+HBV+syphilis coinfection was observed in nine patients (1.5%), while HIV+HCV+syphilis coinfection was identified in two patients (0.3%). The yearly distribution of combined coinfections is summarized in **Table 2**. **Figure 1** shows the course of coinfections over the years in PLWH.

DISCUSSION

In our study, 724 patients diagnosed with HIV-1 infection were evaluated. The majority of the patients were males, with females accounting for 14% of the cohort. A statistically significant difference in age was observed between genders. Transmission route data was not comprehensively available for all patients in our cohort. According to the Turkish Ministry of Health and published surveillance reports, heterosexual contact remains the most reported transmission route, followed by men who have sex with men (MSM). Injection drug use is relatively uncommon in Türkiye. According to the 2024 data of our country's Ministry of Health, 81.8% of reported HIV cases were males and 18.2% were females, with the most affected age groups being 25–29 and 30–34 years.[4]

The finding that women were significantly older than males in our study may suggest that HIV infection is diagnosed later in women or that they are exposed to transmission risks at older ages. In Türkiye, HIV screening for women is often limited to the pregnancy period or performed incidentally, which may partly explain this age difference.

Of the total cohort, 447 patients were newly diagnosed between 2019 and 2024. Among these, 308 were identified during clinical admission, while 139 were di-

Table 2. Epidemiological trends in HBV, HCV, and syphilis coinfections in PLWH: A year by year analysis.

Years	HBV Seropositivity	HCV Seropositivity	Test number	Syphilis Seropositivity	Test number
<2019	14 (5.1)	3 (1.1)	227	65 (31.6)	206
>2019	16 (3.8)	8 (1.8)	447	85 (22.3)	381
2019	5 (6.8)	2 (2.7)	74	14 (21.9)	64
2020	4 (5.8)	1 (1.5)	69	12 (23.1)	52
2021	2 (1.8)	2 (1.8)	113	22 (23.7)	93
2022	5 (4.4)	3 (2.6)	115	20 (19.2)	104
2023	0	0	49	11 (23.9)	46
2024[a]	0	0	27	6 (27.3)	22
Total	**30 (4.1)**	**11 (1.8)**	**724**	**150 (25.6)**	**587[b]**

Data is presented as n (%). [a]First six months [b]Not all patients were tested for syphilis, see Patients and Methods section for details.

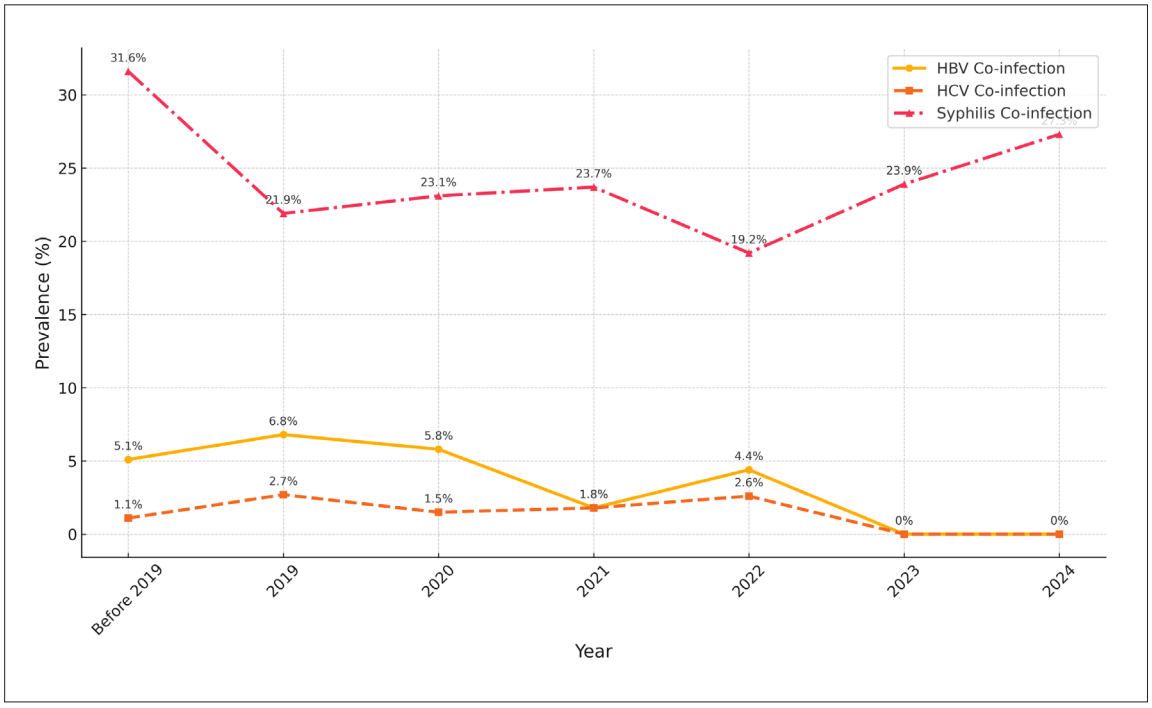

Figure 1. Yearly distribution of HBV, HCV, and syphilis co-infections rates in PLWH.

agnosed incidentally. This underscores the persisting challenge of undiagnosed asymptomatic infections and limited routine screening programs in Türkiye. WHO estimates indicate that more than one in four PLWH globally remain unaware of their status, and many others are diagnosed at later stages of disease.[5] Moreover, the observed decline in new diagnoses in 2023 and 2024 could be attributable to pandemic-related healthcare disruptions, consistent with findings from global surveillance data which highlight significant setbacks in HIV testing and access to services during COVID-19.

Viral load patterns in this cohort reflected significant clinical distinctions. Among patients diagnosed before 2019, 57.4% had undetectable viral loads, suggesting effective ART use. Conversely, 65.2% of patients diagnosed after 2019 had viral loads ≥100001 copies/mL, and nearly one-third had levels exceeding 1000000 copies/mL. The higher viral loads observed in patients

diagnosed after 2019 may be attributed to several factors. First, late presentation and delayed initiation of ART could result in elevated baseline viral loads. Second, the impact of the COVID-19 pandemic likely disrupted healthcare access, delayed testing, and interfered with early ART initiation in newly diagnosed individuals. Third, differences in adherence levels or follow-up continuity between cohorts diagnosed before and after 2019 could also contribute to these findings. These findings align with WHO treatment targets that aim for viral suppression in 95% of patients receiving ART; however, this benchmark remains difficult to achieve without robust early diagnosis and linkage-to-care strategies.[6]

Our findings on syphilis coinfection are consistent with trends observed in both national and international literature. The overall prevalence of syphilis among HIV-positive individuals in our cohort was 25.6%. Previous studies conducted in Türkiye have reported prevalence rates ranging from 8% to 30%, varying by population and region.[7-11] In China, the prevalence of syphilis among PLWH was 19.9%, increasing to 21.9% among MSM.[12] In sub-Saharan Africa, the AFRICOS study reported a 5.3% prevalence, with confirmed cases at 3.1%.[13]

Our findings further substantiate the gender disparity in syphilis coinfection, with 27.7% of males affected compared to 9.0% of females. The male predominance was also reported in a global scoping review by Varshney et al, which highlighted structural, behavioral, and biological risk factors contributing to higher co-infection rates among men. The significant difference in coinfection rates reinforces the need for gender-responsive interventions.[14]

RPR titer variability observed in our study suggests diagnoses at diverse stages of syphilis. A considerable number of patients demonstrated moderate-to-high titers, indicating active infection or inadequate treatment response. These patterns raise concerns about reinfection, treatment failure, or serofast status. In such scenarios, clinical follow-up and symptom-based assessment are crucial. The lack of consensus regarding serological response to syphilis treatment in PLWH is well documented. Ren et al note that delayed serological resolution is more common in this population, prompting current guidelines to recommend extended follow-up periods.[15]

Although no statistically significant association was found between syphilis coinfection and HIV viral load in our study, previous research has suggested that syphilis may transiently increase HIV replication. Jarzebowski et al, in the ANRS CO4 cohort, reported that plasma HIV RNA levels increased during syphilis coinfection but returned to baseline after treatment.[16] Similarly, Fan et al documented viral rebounds coinciding with active syphilis episodes.[17] However, Chan et al demonstrated no meaningful viral load fluctuation in individuals with effective ART during syphilis coinfection.[18] These varying findings suggest that the virological impact of syphilis may depend on ART adherence, immune status, and infection stage.

The low prevalence of triple coinfections in our cohort is notable. HIV+HBV+syphilis was present in 1.5%, while HIV+HCV+syphilis was found in 0.3%. In contrast to our findings, where triple coinfection involving HIV, HBV, and either HCV or syphilis was found to be rare, a study from West China Hospital reported a notably high prevalence of triple coinfections, along with a low rate of effective hepatitis B vaccination among PLWH.[19] These differences may reflect variations in regional epidemiology, risk behaviors, and preventive healthcare strategies such as vaccination coverage and STI screening programs. Although uncommon in Türkiye, each form of triple coinfection may contribute to challenges such as the requirement for alternative treatment regimens, potential drug interactions, and an elevated risk of opportunistic infections.[20,21]

HBV coinfection rates in our study were 5.1% before 2019 and 3.8% after 2019, with no new cases detected in 2023 and 2024. These figures are lower than those reported in some African countries, such as Ethiopia, where Teame et al found a 10% prevalence.[22] The decrease over time may reflect the success of HBV vaccination programs in Türkiye, especially among younger age groups. Supporting this, our study found that HBV coinfection was significantly more common among older PLWH.

Though HBV coinfection was not significantly associated with HIV viral load in our cohort, it still poses long-term clinical risks. Chronic HBV in PLWH may accelerate liver disease progression, especially in the absence of dual-active ART regimens. Ruta et al emphasize that liver-related morbidity and mortality are substantially higher in coinfected patients, advocating for close monitoring using fibrosis indices and virological assays.[23] In our cohort, 41.3% of patients remained susceptible to HBV, highlighting a missed opportunity for immunization. While isolated anti-HBc reactivity was detected in 4.0% of patients, only one showed detectable HBV DNA, suggesting a low burden of occult infection, but ongoing monitoring remains prudent.

The overall HCV coinfection rate in our cohort was 1.5%, consistent with previous studies from Türkiye.[24,25] No significant differences were found in age or HIV viral load between co-infected and non-co-infected individuals. In contrast, in Western Europe and North America,

where intravenous drug use is more prevalent, HCV coinfection rates in PLWH range from 10% to 30%.[26] The low rate in our study reflects the characteristics of the general Turkish HIV-positive population, where injection drug use is relatively uncommon.

Despite the apparent minimal clinical impact of HCV in our cohort, caution is warranted. Gobran et al highlighted that HCV may contribute to HIV persistence by impairing immune clearance and sustaining latent reservoirs.[27] Therefore, interpretation of clinical outcomes should include detailed virological data such as liver transaminases, and fibrosis markers.

Two individuals with HIV+HBV+HCV triple co-infection were detected. One exhibited high HIV and HBV viral loads with undetectable HCV RNA, suggesting resolved or treated HCV infection but active replication of the other two viruses. The second patient demonstrated suppressed HIV and HBV viremia alongside high HCV RNA levels, indicating effective ART but active HCV infection. These contrasting virological profiles underscore the importance of individualized management and full-spectrum virological evaluation in triple co-infected patients.

The observed decline in reported coinfection rates after 2019, followed by a subsequent increase post-2023, may be partially attributed to the effects of the COVID-19 pandemic. During the pandemic, restrictions on movement, reduced access to routine healthcare services, and limitations on sexual and social interactions likely contributed to decreased testing and diagnosis of sexually transmitted infections (STIs). The increase observed after 2023 may reflect a rebound in transmission dynamics and resumption of routine screening activities.[3]

Although the absolute prevalence rates differ, HBV and HCV coinfections followed similar year-to-year trends in our cohort. This is likely due to shared transmission routes—such as bloodborne and sexual exposure—and the fact that both infections are typically screened together during HIV follow-up.

Among 11 pregnant women in the cohort, eight were diagnosed with HIV during pregnancy, and three were already on ART. Four were immune to HBV, while seven remained susceptible. No cases of HCV coinfection were observed, and one woman (incarcerated) was co-infected with syphilis. In a meta-analysis by Kafeero et al, HBV coinfection was reported to be significantly higher in HIV-positive pregnant women than those in the general population.[28] Wu et al found a pooled prevalence of HBV, HCV, and syphilis in pregnant women of 4.8%, 1.0%, and 0.8%, respectively, with rates highest in low-income settings.[29] Incarceration is a known risk factor for coinfection, as demonstrated in the study by Anteneh et al, which reported a 9.3-fold increased risk of HIV+syphilis coinfection among imprisoned women.[30]

Coinfection screening and vaccination are critical for maternal and fetal health in PLWH. Although none of the pregnant women in our cohort had HBV infection, the high rate of susceptibility signals a gap in preventive care. Early vaccination and screening should be standard practice during antenatal visits, particularly in high-risk populations. Furthermore, co-infection with syphilis poses a serious threat of vertical transmission, emphasizing the need for universal syphilis screening in pregnant women living with HIV.

Limitations of our study include the lack of assessment of patients' risk behaviors and the absence of follow-up data regarding treatment response in syphilis cases. Although our study had a single-center and retrospective design, our hospital has a capacity of 4050 beds and, due to its geographic location, serves patients from all regions of Türkiye as a major city hospital. Therefore, our data are considered representative of the national population. Moreover, our dataset covers an extensive time period and includes specific subgroups such as pregnant individuals.

In conclusion, coinfections with HBV, HCV, and syphilis remain a clinically significant concern among PLWH which may impact treatment strategies and outcomes. Future studies with larger, multicenter cohorts are needed to explore causal relationships, long-term effects of coinfections on immune recovery, and the effectiveness of integrated screening and prevention protocols in diverse populations. Finally, lessons learned from pandemic-related care disruptions must guide efforts to strengthen healthcare continuity and resilience in vulnerable populations.

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