



Epidemiological trends of HBV and/or HCV infections in HIV-infected adults in Guangzhou: A 2017-2020 retrospective analysis

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Abstract

Objective: To investigate the contemporary epidemiological trends of hepatitis B (HBV) and C (HCV) virus coinfection among people living with HIV (PLWH) in southern China.

Methods: This study was conducted from January 2017 to December 2020 at the largest government-designated referral hospital in Guangzhou, Guangdong Province, southern China. Serum samples from PLWH were tested for HBV and HCV coinfection. Risk factors associated with HIV-HBV, HIV-HCV, and HIV-HBV-HCV coinfections were subsequently analyzed.

Results: A total of 1277 HIV-infected adults were included in this study. The mean age was 28.71 years (range: 18-66), with the majority being young adults (45.8% aged 20-31 years). The overall seroprevalence of HBV, HCV, and HBV-HCV coinfection was 2.0%, 3.1%, and 0.8%, respectively. Intravenous drug use was identified as a significant risk factor for HBV-HIV (12.2%), HCV-HIV (7.8%), and triple infection (2.1%).

Conclusions: Our findings indicate that HBV and HCV coinfection rates among adults with HIV did not escalate in Guangzhou. Notably, intravenous drug use remains a predominant contributor to hepatitis coinfection within this demographic.

Keywords: Hepatitis B virus, hepatitis C virus, human immunodeficiency virus

Introduction

Human immunodeficiency virus (HIV) remains a major global public health challenge. Since China's reform and opening-up, rapid socioeconomic transformations have heightened the risk of a widespread HIV epidemic. Nationwide surveillance data up to 2016 documented 780,368 diagnosed HIV cases, including 164,082 recorded deaths [1]. Due to shared routes of transmission-including injection drug use, unprotected sexual contact, commercial blood/plasma donation, blood transfusion, and mother-to-child transmission- the coinfection of chronic hepatitis B (HBV) and/or hepatitis C (HCV) among people living with HIV (PLWH) has emerged as a significant public health concern. Due to shared routes of transmission-including injection drug use, unprotected sexual contact, and iatrogenic exposures (e.g., blood transfusion and commercial plasma donation)-the high burden of chronic hepatitis B (HBV) and/or hepatitis C (HCV) coinfection among people living with HIV (PLWH) has emerged as a major public health concern. Chronic hepatitis B and C virus infections have been reported in 6-14% and 25-30% of people living with HIV (PLWH) in Western Europe and the United States, respectively [2]. Furthermore, data from seven Chinese provinces (municipalities) with high HIV prevalence, collected between May 2007 and September 2008, revealed that the overall prevalence of HBV and/or HCV coinfection among HIV-positive individuals reached up to 49.1% [3]. Coinfection with HBV and/or HCV virus is

increasingly recognized as a major contributor to morbidity and mortality among PLWH, and has been consistently associated with an accelerated progression to advanced liver disease [4]. Recognizing the significance of these challenges, the Chinese central and local governments have allocated 680 million yuan (approximately US\$98 million) to establish and improve disease prevention and control mechanisms at the provincial level. Guangzhou has allocated an annual special fund of over 200 million yuan (US\$24 million) to HIV/AIDS prevention, care, and treatment. Previous studies have demonstrated that effective preventive interventions significantly reduced the frequency of risky drug use and sexual behaviors compared to non-participants [5]. However, data regarding the recent epidemiological trends of HBV and HCV infections among people living with HIV (PLWH) remain scarce. Therefore, this study aimed to investigate the prevalence and temporal trends of HBV and/or HCV coinfection among HIV-positive individuals at a major HIV/AIDS referral center in Guangzhou, Guangdong Province, China.

Materials and Methods

Study population

This study was conducted at Guangzhou Eighth People's Hospital, a 2000-bed governmental referral center and the largest specialized infectious disease hospital in Guangzhou, Guangdong Province, Southern China. Adult patients (aged ≥ 18 years) living with HIV were consecutively recruited

from January 2017 to December 2020. All participants provided written informed consent after receiving a thorough explanation of the study procedures. Ethical approval was obtained from the Institutional Review Board (IRB) of Guangzhou Eighth People's Hospital.

Laboratory analysis

Our laboratory adheres to the World Health Organization (WHO) diagnostic strategies for HIV testing. HIV screening was performed in duplicate using an enzyme-linked immunosorbent assay (ELISA) (AIKANG, China), and positive results were confirmed by HIV-1/2 Western blot immunoassay (MP Biomedicals, USA). A definitive HIV-positive diagnosis required concordant positive results from both assays. Only these confirmed positive serum samples were included in this study and were tested anonymously. Hepatitis B surface antigen (HBsAg) and hepatitis C virus (HCV) antibodies were screened by ELISA according to the manufacturer's instructions, using kits from AIKANG (China), and all positive samples were retested using the same method. Lymphocyte subsets, specifically CD4⁺ T-cell counts, were quantified by flow cytometry using monoclonal antibodies and a FACScan instrument (Becton Dickinson, USA). For the evaluation of biochemical characteristics, patients were stratified into three groups based on their CD4⁺ count: Group 1 (CD4⁺ ≤ 200 cells/μL), Group 2 (200 < CD4⁺ < 500 cells/μL), and Group 3 (CD4⁺ ≥ 500 cells/μL).

Statistical analysis

Statistical analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). Participant characteristics, infection statuses of HIV, HBV, and HCV, and CD4⁺ cell counts were analyzed. Continuous variables were compared using Student's t-test, non-parametric tests, or one-way analysis of variance (ANOVA), as appropriate. Categorical variables were analyzed using the chi-square test or Fisher's

exact test to identify independent risk factors associated with positive test results for each infection. A two-tailed P-value of < 0.05 was considered statistically significant.

Results

Over the four-year study period, 1,302 individuals were screened at the hospital. Among them, 25 patients were excluded due to poor health status (n = 16) or lack of interest (n = 9). Consequently, a total of 1,277 people living with HIV (PLWH) completed the study, and their data were available for analysis. Demographic characteristics revealed a male predominance (1,019, 79.8% vs. 258, 20.2%). The mean age was 28.71 years (range: 18–66 years). The majority of participants were aged 21–30 years (45.8%), followed by 31–40 years (22.6%), 41–50 years (16.4%), 51–60 years (8.5%), and >60 years (6.7%) (Figure 1).

The overall prevalence of HBV and HCV among PLWH was 2.0% (26/1277) and 3.1% (40/1277), respectively (Table 1). No significant sex-based differences were observed in the rates of HBV-HIV coinfection (2.3% in males vs. 3.1% in females; P = 0.16) or HCV-HIV coinfection (3.1% in both sexes; P = 0.97). Notably, all 8 cases of triple infection (HBV/HCV/HIV) occurred exclusively in female patients (0.8% of the total cohort). The prominent mode of HIV transmission in our study was unsafe sex with multiple partners 461 of 1277 (36.1%); followed by intravenous drug use (IDU) 335 of 1277 (26.2%); homosexuality 214 of 1277 (16.8%); blood transfusion 180 of 1277 (8.7%) (Table 2).

Compared with individuals infected through other transmission routes, people who inject drugs (PWID) exhibited the highest prevalence of HBV (12.2%), HCV (7.8%), and HBV/HCV co-infection (2.1%), respectively. Furthermore, no significant association was observed between the seroprevalence of HBV, HCV, or HBV/HCV co-infection and CD4⁺ T-cell counts among PLWH (Figure 2).

Table 1: Seroprevalence of HBV and HCV in HIV positive patients.

Coinfection with HIV	Male (n = 1019)	Female (n = 258)	P Value
HBV, n(%)	18(2.3%)	8(3.1%)	P = 0.16
HCV, n(%)	32(3.1%)	8(3.1%)	P = 0.97
HBV-HCV, n(%)	0(0%)	8(3.1%)	P < 0.001

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

Table 2: Prevalence of HBV, HCV according to the route of transmission of HIV

Route of HIV Transmission	No of patients (%)	HBV	HCV	HBV plus HCV	P Value
Blood transfusion, n(%)	180(8.7%)	5(2.7%)	5(2.7%)	2(1.1%)	P = 0.60
Unsafe Sex (multiple sexual partners), n(%)	461(36.1%)	25(5.4%)	16(3.5%)	8(1.3%)	P < 0.001
Homosexuality, n(%)	214(16.8%)	7(3.3%)	11(5.1%)	0(0%)	P = 0.236
Intravenous drug use, n(%)	335(26.2%)	22(12.2%)	14(7.8%)	8(2.1%)	P < 0.001
Other/unknown, n(%)	87(6.8%)	0(0%)	0(0%)	0(0%)	NS
Total	1277 (100%)	26(2.0%)	40(3.1%)	8(0.6%)	

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

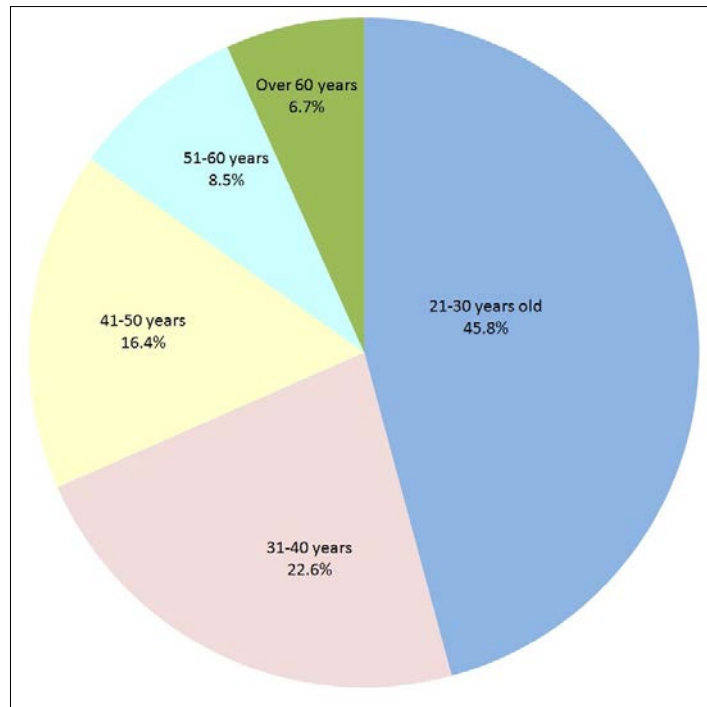


Fig 1: Prevalence by age in HIV positive patients.

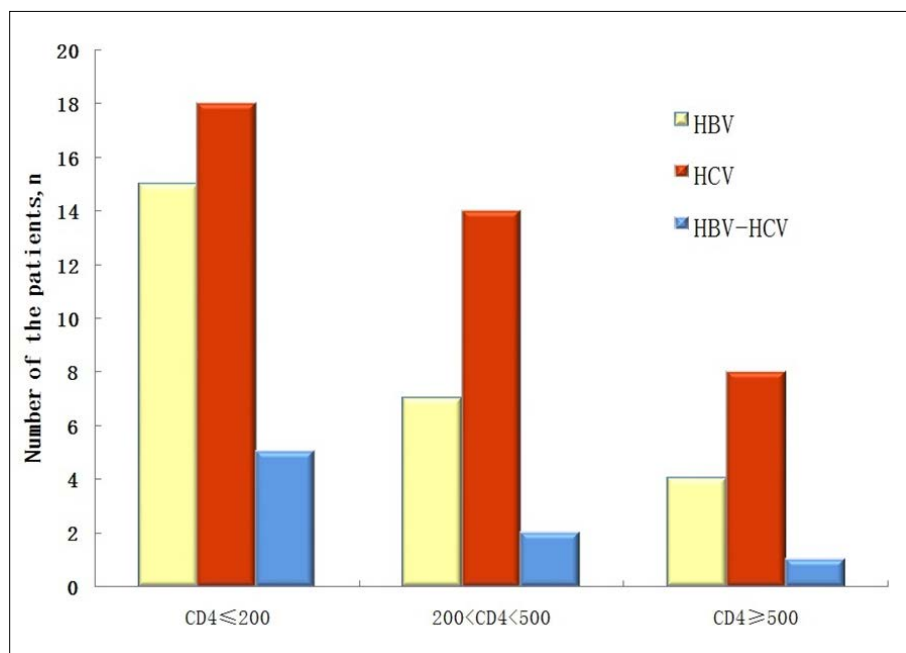


Fig 2: Prevalence of HBV, HCV and HBV-HCV in HIV positive patients by CD4 count.

Discussion

Human immunodeficiency virus (HIV) is a single-stranded RNA retrovirus that primarily targets CD4⁺ T lymphocytes [6]. Hepatitis B virus (HBV), a member of the Hepadnaviridae family, is an enveloped, partially double-stranded DNA virus that exhibits a unique tropism for hepatocytes [7]. Hepatitis C virus (HCV) is an enveloped positive-sense single-stranded RNA virus classified within the genus Hepacivirus and family Flaviviridae [8]. Although HBV, HCV, and HIV possess distinct virological characteristics, they share common transmission risk factors and have evolved diverse strategies to evade host immunity, thereby establishing chronic infection [2]. Moreover, HIV

infection has been shown to increase the viral loads of both HBV and HCV [9, 10]. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), approximately one-third of people living with HIV (PLWH) globally die from liver-related complications, including cirrhosis and hepatocellular carcinoma [11]. Therefore, this 4-year study aimed to extend previous findings by updating the latest trends of HBV/HCV infection and associated risk factors among people living with HIV (PLWH) in Southern China. Based on a cohort of 1,277 HIV-positive patients, our study provides a precise estimation of the seroprevalence of HBV and HCV markers. HBV coinfection is common in individuals with HIV. Previous studies have reported

HIV/HBV coinfection rates of 8.7% in Thailand and 6%–16% in India [12–14]. Similar coinfection rates have been reported in the USA and Europe, ranging from 6% to 14% [15, 16]. However, in sub-Saharan Africa, where endemicity ranges from intermediate to high (10%–20.4%), infection is acquired predominantly through perinatal transmission and early childhood exposure [17]. In 2010, a multicenter study involving 4,306 HIV-infected patients across 31 Chinese provinces reported an HBV-HIV coinfection prevalence of 12.5% [18]. Notably, the incidence of HIV-HBV coinfection observed in this study (2%) was substantially lower than that documented in previous reports [12–16, 18]. These discrepancies may be attributable to demographic shifts within the cohort. Specifically, the mean age of HIV-infected patients was 28.71 years, with a notably higher proportion of new infections occurring among younger individuals (aged 21–30 years). Advanced age has been associated with accelerated clinical progression in individuals living with HIV [19]. Secondly, our study demonstrated that blood transfusion was not a major contributing factor to HBV/HIV coinfection. Routine HBV screening among blood donors contributes to the low HBV coinfection rate in HIV-positive individuals with a history of blood transfusion. Specifically, the widespread adoption of HBV nucleic acid amplification testing (NAT) in urban China has substantially improved transfusion safety beyond what serological assays can achieve [20]. In 2009, Shang et al [21] reported that mini-pool nucleic acid testing (NAT) identified only two hepatitis B virus (HBV) DNA-positive blood donors among 41,301 HBsAg-negative, anti-HCV-negative, and anti-HIV-negative donations with normal alanine transaminase (ALT) levels in Shenzhen, China. In 2010, NAT screening of 178,447 blood donations yielded no HIV-1-positive results, but identified 169 HBV NAT-yield cases (0.095%) [22]. Thirdly, both universal HBV vaccination and hepatitis B immunoglobulin have markedly reduced the prevalence of chronic HBV infection [23, 24]. Since 2002, the hepatitis B vaccine has been included in China's National Expanded Programme on Immunization (EPI), prioritizing the administration of a timely birth dose (within 24 h of birth). Finally, and most importantly, targeted interventions—including health education and harm reduction strategies—should be implemented in these high-risk populations.

HCV-HIV coinfection has been reported at varying rates (18.7%–53.4%) among patients in China, the United States, and Europe [25, 28]. Fortunately, the prevalence of HCV-HIV coinfection observed in our study (3.1%) was substantially lower than that reported in previous studies. This discrepancy may reflect the effectiveness of local harm-reduction education programs in preventing HIV transmission, or it may indicate a critical window of opportunity for implementing targeted HIV prevention strategies among individuals with HCV infection [29]. Furthermore, routine screening for HCV has been mandatory for blood donors, which has effectively curtailed the transmission of HCV via blood/plasma collection and transfusion. More specifically, HBV-HCV coinfection was

predominantly observed in eight female HIV-positive individuals, all of whom had a history of intravenous drug use and sexually transmitted infections. Drug use is a proxy indicator for high-risk sexual practices and contributes to HIV acquisition through enhanced susceptibility to ulcerative sexually transmitted diseases [30]. Female drug users face a dual risk: they are susceptible to HIV and other sexually transmitted infections (STIs), while also acting as a bridge population for transmitting these infections to clients and the broader community. Recent studies in China and elsewhere have reported that 21% to 60% of female intravenous drug users are concurrently engaged in sex work [31, 35].

This study substantiates the observed epidemiological shifts. While China has made substantial strides in combating HIV over recent decades, ongoing efforts are required to optimize public health education and awareness. A multifaceted approach is needed: strengthening health education to improve condom utilization rates—the cornerstone of preventing sexual HIV transmission and fostering intercity cooperation to mitigate drug smuggling while simultaneously enhancing anti-drug education across the general population and educational sectors. These findings differ from earlier Chinese studies, potentially due to the varying prevalence of HIV-HBV-HCV coinfection (5.23%–19.1%) reported between 2010 and 2011 [18, 36–38]. Compared to HIV monoinfection, HIV/HBV, HIV/HCV, and HIV/HBV/HCV coinfections markedly elevate the risk of liver fibrosis and cirrhosis. However, data regarding the effects of these viral coinfections on HIV-associated liver disease, which is a major driver of morbidity and mortality, are scarce. Further investigation is thus needed.

Conclusion

Although HBV remains endemic in China, our findings indicate that the prevalence of HBV/HCV coinfection among people living with HIV (PLWH) in Guangzhou did not increase substantially between 2017 and 2020.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

None.

References

1. Ma Y, Dou Z, Guo W, et al. The Human Immunodeficiency Virus Care Continuum in China: 1985–2015. *Clin Infect Dis.* 2018;66(6):833–839.
2. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol.* 2006;44(1 Suppl):S6–S9.
3. Yan YX, Gao YQ, Sun X, et al. Prevalence of hepatitis C virus and hepatitis B virus infections in HIV-positive Chinese patients. *Epidemiol Infect.* 2011;139(3):354–360.
4. Thimme R, Spangenberg HC, Blum HE. Hepatitis B or hepatitis C and human immunodeficiency virus infection. *J Hepatol.* 2005;42 Suppl(1):S37–S44.

5. Qian HZ, Hao C, Ruan Y, et al. Impact of methadone on drug use and risky sex in China. *J Subst Abuse Treat.*,2008;34(4):391-397.
6. Xiao SY, Lu L, Wang HL. Fibrosing cholestatic hepatitis: clinicopathologic spectrum, diagnosis and pathogenesis. *Int J Clin Exp Pathol.*,2008;1(5):396-402.
7. Schaefer S. Hepatitis B virus taxonomy and hepatitis B virus genotypes. *World J Gastroenterol.*,2007;13(1):14-21.
8. Kato N. Genome of human hepatitis C virus (HCV): gene organization, sequence diversity, and variation. *Microb Comp Genomics.*,2000;5(3):129-151.
9. Ragni MV, Belle SH. Impact of human immunodeficiency virus infection on progression to end-stage liver disease in individuals with hemophilia and hepatitis C virus infection. *J Infect Dis.*,2001;183(7):1112-1115.
10. Wang H, Li Y, Zhang C, et al. Immunological and virological responses to cART in HIV/HBV co-infected patients from a multicenter cohort. *AIDS.*,2012;26(14):1755-63.
11. Global AIDS Monitoring 2023. [Online] December [cited 2023 January]; Available from: URL: <https://www.aidsdatahub.org/sites/default/files/resource/unaid-global-aids-monitoring-2023.pdf>, 2022.
12. Sungkanuparph S, Vibhagool A, Manosuthi W, et al. Prevalence of hepatitis B virus and hepatitis C virus co-infection with human immunodeficiency virus in Thai patients: a tertiary-care-based study. *J Med Assoc Thai.*,2004;87(11):1349-1354.
13. Sud A, Singh J, Dhiman RK, et al. Hepatitis B virus co-infection in HIV infected patients. *Trop Gastroenterol.*,2001;22(2):90-92.
14. Kumarasamy N, Solomon S, Flanigan TP, et al. Natural history of human immunodeficiency virus disease in southern India. *Clin Infect Dis.*,2003;36(1):79-85.
15. Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol.*,2006;44(1 Suppl):S6-S9.
16. Rockstroh JK. Management of hepatitis B and C in HIV co-infected patients. *J Acquir Immune Defic Syndr.*,2003;34(Suppl 1):S59-S65.
17. Nyirenda M, Beadsworth MB, Stephany P, et al. Prevalence of infection with hepatitis B and C virus and coinfection with HIV in medical inpatients in Malawi. *J Infect.*,2008;57(1):72-77.
18. Yan YX, Gao YQ, Sun X, et al. Prevalence of hepatitis C virus and hepatitis B virus infections in HIV-positive Chinese patients. *Epidemiol Infect.*,2011;139(3):354-360.
19. GBD 2017 HIV collaborators. Global, regional, and national incidence, prevalence, and mortality of HIV, 1980-2017, and forecasts to 2030, for 195 countries and territories: a systematic analysis for the Global Burden of Diseases, Injuries, and Risk Factors Study 2017. *Lancet HIV.*,2019;6(12):e831-e859.
20. Wu D, Feng F, Wang X, et al. The impact of nucleic acid testing to detect human immunodeficiency virus, hepatitis C virus, and hepatitis B virus yields from a single blood center in China with 10-years review. *BMC Infect Dis.*,2022;22(1):279.
21. Shang G, Yan Y, Yang B, et al. Two HBV DNA+/HBsAg- blood donors identified by HBV NAT in Shenzhen, China. *Transfus Apher Sci.*,2009;41(1):3-7. doi: 10.1016/j.transci.2009.05.001.
22. Dong J, Wu Y, Zhu H, et al. A pilot study on screening blood donors with individual-donation nucleic acid testing in China. *Blood Transfus.*,2014;12(2):172-179.
23. Wong GL, Hui VW, Yip TC, et al. Universal HBV vaccination dramatically reduces the prevalence of HBV infection and incidence of hepatocellular carcinoma. *Aliment Pharmacol Ther.*,2022;56(5):869-877.
24. Wei KP, Zhu FC, Liu JX, et al. The efficacy of two different dosages of hepatitis B immunoglobulin combined with hepatitis B vaccine in preventing mother-to-child transmission of hepatitis B virus: A prospective cohort study. *Vaccine.*,2018;36(2):256-263.
25. Zhang C, Li X, Liu Y, et al. Co-infections of tuberculosis, hepatitis B or C viruses in a cohort of people living with HIV/AIDS in China: predictors and sequelae. *AIDS Care.*,2017;29(8):974-977.
26. Zhang C, Yang R, Xia X, et al. High prevalence of HIV-1 and hepatitis C virus coinfection among injection drug users in the southeastern region of Yunnan, China. *J Acquir Immune Defic Syndr.*,2002;29(2):191-196.
27. Jia J, Zhu Q, Deng L, et al. Treatment outcomes of HIV patients with hepatitis B and C virus co-infections in Southwest China: an observational cohort study. *Infect Dis Poverty.*,2022;11(1):7.
28. Ahmadi Gharaei H, Fararouei M, Mirzazadeh A, et al. The global and regional prevalence of hepatitis C and B co-infections among prisoners living with HIV: a systematic review and meta-analysis. *Infect Dis Poverty.*,2021;10(1):93.
29. Zhang JY, Li ZB, Zhang L, et al. DOES IT WORK? -a randomized controlled trial to test the efficacy of HCV and HIV-related education on drug users in MMT, China. *BMC Infect Dis.*,2019;19(1):774.
30. Wu J, Huang J, Xu D, et al. Infection status and risk factors of HIV, HBV, HCV, and syphilis among drug users in Guangdong, China--a cross-sectional study. *BMC Public Health.*,2010;10:657.
31. Bao YP, Liu ZM. Systematic review of HIV and HCV infection among drug users in China. *Int J STD AIDS.*,2009;20(6):399-405.
32. Lau JTF, Gu J, Tsui HY, et al. Anticipated suicidal ideation among female injecting drug users who are sex workers of negative or unknown HIV status in China. *Women Health.*,2018;58(7):774-789.
33. Ge L, Li D, Li P, et al. HIV and HCV Infection Status Among Drug Users - China, 2010-2018. *China CDC Wkly.*,2020;2(7):109-112.
34. Srirak N, Kawichai S, Vongchak T, et al. HIV infection among female drug users in Northern Thailand. *Drug Alcohol Depend.*,2005;78(2):141-145.

35. Liu L, Wang L, Zhang H, et al. Changing Epidemiology of Hepatitis B Virus and Hepatitis C Virus Coinfection in a Human Immunodeficiency Virus-Positive Population in China: Results From the Third and Fourth Nationwide Molecular Epidemiologic Surveys. *Clin Infect Dis.*,2021;73(4):642-649.
36. He Y, Zhao QX, Ren YJ, et al. Coinfection with HBV and HCV in 128 AIDS patients infected through blood transmission. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao.*,2006;28(5):662-664.
37. Zhou YH, Liu FL, Yao ZH, et al. Comparison of HIV-, HBV-, HCV- and co-infection prevalence between Chinese and Burmese intravenous drug users of the China-Myanmar border region. *PLoS One.*,2011;6(1):16349.
38. Chen X, He JM, Ding LS, et al. Prevalence of hepatitis B virus and hepatitis C virus in patients with human immunodeficiency virus infection in Central China. *Arch Virol.*,2013;158(9):1889-1894.