Gut and Liver
https://doi.org/10.5009/gnl240581
pISSN 1976-2283 eISSN 2005-1212

Original Article

Temporal Dynamics and Treatment Outcomes of Hepatitis C Virus/Human Immunodeficiency Virus Coinfection: A Multicenter Retrospective Study from South Korea

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Article Info

Received December 7, 2024
Revised March 22, 2025
Accepted March 24, 2025
Published online July 18, 2025

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Background/Aims: Due to the very low incidence of human immunodeficiency virus (HIV) infection in South Korea, epidemiological data on hepatitis C virus (HCV)/HIV coinfection are limited. The aim of this study was to investigate the clinical characteristics and treatment outcomes of patients with HCV/HIV coinfection in South Korea.

Methods: We retrospectively collected data from patients diagnosed with HCV/HIV coinfection at 12 academic hospitals in South Korea from 2009 to 2020.

Results: A total of 124 patients were included in this study; most patients were males (n=112, 90.3%), and the mean age was 46.5±13.5 years. Among the study patients, 11 (8.9%) had cirrhosis, and seven (5.6%) tested positive for the hepatitis B surface antigen. During the follow-up period (mean period: 67.4 months), two patients (1.6%) developed hepatocellular carcinoma, and nine (7.3%) died. Of the 112 patients (90.3%) who underwent HCV genotype testing, most were infected with HCV genotype 2 (n=53, 47.3%) and genotype 1b (n=41, 36.6%). In particular, HCV genotype 1a was identified in 12.5% (n=14) of patients. Ninety-one patients (73.4%) received antiviral therapy, with 104 antiviral treatments administered overall. The sustained virologic response rate was significantly higher in patients treated with direct-acting antiviral agents (DAA) than in those receiving pegylated interferon-based treatment (89.0% vs 58.1%, p<0.001).

Conclusions: In South Korea, patients with HCV/HIV coinfection were predominantly male and younger and exhibited a higher prevalence of genotype 1a than those with HCV monoinfection. These patients demonstrated a significantly better treatment response to DAA treatment than to interferon-based therapy. **(Gut Liver, 2025;19:868-877)**

Key Words: Hepatitis C virus; HIV; Coinfection; Antiviral agents; Republic of Korea

INTRODUCTION

Chronic hepatitis C virus (HCV) infection is significantly more prevalent among individuals coinfected with the human immunodeficiency virus (HIV) due to overlapping transmission routes–parenteral, sexual, and perinatal.[1] The prevalence of HCV coinfection among HIV-positive individuals was estimated at 6.2% in a 2016 global systematic review and meta-analysis, with approximately 2.3 million out of 36.6 million HIV-infected individuals being coinfected with HCV.[2] In Japan, where the prevalence of HIV infection is similarly low as in South Korea, the seroprevalence of HCV antibodies among individuals with HIV infection is estimated at 3.3%.[3] The incidence of HCV coinfection varies by transmission mode; sexual transmission accounts for less than 10% of cases, while over 80% occur among people who inject drugs.[2] In patients with HCV/HIV coinfection, HIV is associated with higher HCV RNA levels, which contributes to the chronicity of HCV infection.[4,5] Moreover, coinfected patients experience a faster progression to advanced liver fibrosis and cirrhosis compared to those with HCV monoinfection, significantly increasing the risk of end-stage liver disease and hepatocellular carcinoma (HCC).[5]

Historically, patients with HCV/HIV coinfection were considered a distinct group with significantly poorer responses to interferon-based therapies.[6,7] However, since the introduction of direct-acting antiviral agents (DAA) in 2011, treatment outcomes have improved dramatically.[6,7] DAA have demonstrated similar sustained virologic response (SVR) rates in both coinfected and HCV monoinfected patients, with a meta-analysis reporting an SVR rate of approximately 94% among coinfected individuals.[8] As a result, the American Association for the Study of Liver Diseases/Infectious Diseases Society of America and the European Association for the Study of the Liver now recommend the same treatment regimens for HCV/HIV coinfected patients as those used for individual with HCV monoinfection.[9,10]

In South Korea, epidemiological data on HCV/HIV coinfection is limited, partly due to the relatively low incidence of HIV infections, which was reported at 2.08 new cases per 100,000 individuals annually in 2022.[11] The prevalence of HCV/HIV coinfection among HIV-positive individuals with detectable HCV antibodies ranges from 1.7% to 5.2%.[12,13] Prior research in South Korea has primarily been limited by single-center studies and small sample sizes, often relying on anti-HCV antibody rather than HCV-RNA polymerase chain reaction (PCR) positivity to define infection status.[12-14] These limitations have resulted in an inadequate understanding of the clinical characteristics of HCV/HIV coinfected patients. Additionally, there is a significant lack of studies examining the efficacy of antiviral treatment specifically in this population. To address these gaps, we conducted a multicenter study aimed at elucidating the clinical characteristics and treatment outcomes of patients with HCV/HIV coinfection in South Korea. Our study seeks to provide a comprehensive understanding of this population, ultimately contributing to improved clinical management and therapeutic strategies.

MATERIALS AND METHODS

1. Patients

We conducted a retrospective multicenter study and reviewed a medical records of HCV/HIV coinfected patients aged 19 years or older who visited 12 academic hospitals (Seoul St. Mary's Hospital, Kyungpook National University Hospital, Korea University Guro Hospital, Korea University Ansan Hospital, National Medical Center, Seoul National University Hospital, Severance Hospital, Ajou University Hospital, Asan Medical Center, Inha University Hospital, Chungnam National University Hospital, and Chonnam National University Hospital) in South Korea between January 2009 and December 2020. Of the 137 patients diagnosed with HCV/HIV coinfection, 13 were excluded due to ongoing HCV (n=2) treatment at another institution or insufficient medical records (n=11). Consequently, a total of 124 patients were ultimately enrolled in the study. To evaluate the prevalence of HCV/HIV coinfection among patients with HCV monoinfection or HIV monoinfection, we investigated the presence of HCV and HIV infections in each hospital. HCV infection was defined by positive result for HCV-RNA PCR, while HIV infection was defined by positive result for HIV-RNA PCR or by the patients receiving antiretroviral therapy.

2. Clinical and laboratory parameters

At the time of HCV/HIV coinfection diagnosis, we collected the following clinical and laboratory data: age, gender, nationality, comorbidities, serum platelet count, serum aspartate transaminase (AST), serum alanine transaminase (ALT), serum total bilirubin, serum albumin, serum creatinine, HCV RNA titer, HCV genotype, HIV RNA titer, CD4 cell count, hepatitis B surface antigen, presence of liver cirrhosis, history of anti-HCV treatment, type and duration of antiviral therapy, rate of SVR, and antiretroviral therapy status. HCV genotyping was conducted using PCR. Liver cirrhosis was diagnosed based on histological findings or radiological findings suggestive of cirrhosis, such as surface nodularity, splenomegaly, ascites, and esophageal

or gastric varices. Additionally, APRI (AST/upper limit of normal/platelet count [$\times 10^9$/L]×100) and fibrosis-4 (FIB-4) index ([age×AST]/[platelet count ($\times 10^9$/L)×√ALT]) were calculated to assess the degree of liver fibrosis. Based on previous literatures, the degree of fibrosis was classified using APRI with a cutoff of >1.5 and ≤1.5, and the FIB-4 index with a cutoff of >3.25 and ≤3.25.[15,16]

Concurrent infection was defined as the presence of HCV/HIV coinfection at the initial visit or an interval of less than 1 year between positive HCV PCR and positive HIV PCR after the initial visit. Sequential infection was defined as an interval of more than 1 year between positive HCV PCR and positive HIV PCR following the initial visit. Antiviral regimens were selected based on the individual treating physician's decision, in accordance with the guidelines of the Korean Association for the Study of the Liver.[17-19]

3. Patient follow-up and treatment efficacy

All patients were regularly monitored laboratory and imaging tests. Time to event was calculated from the date of HCV/HIV coinfection identification to the date of HCC development, death, the last follow date, or August 31, 2021. Treatment efficacy was assessed based on the SVR and the definition of SVR, following the Korean Association for the Study of the Liver guidelines. SVR12 or SVR24 was defined as the undetectable HCV RNA (<15 IU/mL) at 12 (in patients receiving DAA treatment) or 24 weeks (in those receiving pegylated interferon [PEG-INF] based treatment) after completion of the antiviral treatment.[17-19]

4. Statistical analysis

Categorical variables were expressed as frequencies (%), while continuous variables were presented as mean values with standard deviations for parametric data and median values with ranges for nonparametric data. Between-group differences were evaluated using the independent t-test or Wilcoxon rank sum test for continuous variables and the chi-square test or Fisher exact test for categorical variables. Changes of inflammation markers (AST and ALT) and fibrosis markers (APRI and FIB-4 index) from baseline after antiviral treatment (at the time of achieving SVR) were evaluated using paired t tests or Wilcoxon signed rank tests. The p-values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS statistics version 26.0 (IBM Corp., Armonk, NY, USA).

5. Ethical consideration

The present study protocol was reviewed and approved by institutional review boards or independent ethics committees at each site (National Medical Center Institution Review Board, NMC-2021-07-092). It is a retrospective investigation and informed consent was waived by the ethics committees.

RESULTS

1. Prevalence of HCV/HIV coinfection

A total of 124 patients with HCV/HIV coinfection were enrolled in the study. Geographically, the majority of patients were from the metropolitan area, with 105 individuals (83.9%). During the study period, 25,261 patients were diagnosed with HCV infection, and 8,608 patients were diagnosed with HIV infection. Consequently, the prevalence of HCV/HIV coinfection among HCV-infected individuals was 0.49% (124/25,261), while the prevalence among HIV-infected individuals was 1.44% (124/8,608).

2. Baseline characteristics and sequential infection

The clinical and laboratory characteristics of patients with HCV/HIV coinfection are shown in Table 1. The mean age at the time of coinfection diagnosis was 46.5 years, with the predominance of male patients (90.3%) and 10 foreign nationals (8.1%). Liver cirrhosis was present in 11 patients (8.9%), and during the mean follow-up period of 67.4 months, two patients developed HCC (Supplementary Table 1), while nine patients died. A total of seven cases of extrahepatic malignancies were identified. One case (cervical cancer) was diagnosed before the date of coinfection diagnosis or the first visit, whereas six cases (lymphoma [n=2], breast cancer [n=2], gastric cancer [n=1], and liposarcoma [n=1]) were diagnosed after the date of coinfection diagnosis or the first visit. Hepatitis B virus (HBV) coinfection was observed in seven patients (5.6%), who exhibited relatively good liver function. At the time of HBV/HCV/HIV coinfection diagnosis, HCV predominated over HBV in all cases. Among them, six patients were receiving antiretroviral therapy that included an antiviral agent for HBV (2 with lamivudine, 3 with tenofovir disoproxil fumarate, and 1 with tenofovir alafenamide). Spontaneous clearance of HCV infection occurred in two patients. When comparing patients who received antiviral treatment to those who did not, the treated group was younger, had higher hemoglobin and albumin levels, whereas they had a lower FIB-4 index and a lower proportion of patients with cirrhosis (Table 1).

Among the 124 patients, 112 patients (90.3%) confirmed HCV genotypes, as shown in Table 2. The majority had common genotypes found in South Korea, with 53 patients (47.3%) classified as genotype 2, 41 patients (36.6%) as genotype 1b, and 14 patients (12.5%) as geno-

Table 1. Characteristics of the Patients with HCV/HIV Coinfection (n=124)

Characteristics	Total patients (n=124)	Treatment (n=91)	No treatment (n=33)	p-value
Clinical characteristics				
Age, yr	46.5±13.5	44.7±11.7	51.4±16.6	0.039
Male sex	112 (90.3)	84 (92.3)	28 (84.8)	0.214
Foreigner	10 (8.1)	6 (6.6)	4 (12.1)	0.454
BMI, kg/m^2 (n=103)	22.5±3.0	22.7±3.1	21.9±2.9	0.241
Diabetes	15 (12.1)	12 (13.2)	3 (9.1)	0.757
Hypertension	15 (12.1)	10 (11.0)	5 (15.2)	0.530
Hyperlipidemia	6 (4.8)	6 (6.6)	0	0.340
Cirrhosis	11 (8.9)	5 (5.5)	6 (18.2)	0.028
Laboratory characteristics				
HBsAg (+)	7 (5.6)	6 (6.6)	1 (3.0)	0.674
HCV RNA, IU/mL	$6.5\times10^6\pm1.1\times10^7$	$6.9\times10^6\pm1.0\times10^7$	$5.3\times10^6\pm1.3\times10^7$	0.498
HIV RNA, copies/mL	$4.3\times10^4\pm9.1\times10^4$	$4.2\times10^4\pm9.8\times10^4$	$4.8\times10^4\pm6.8\times10^4$	0.714
CD4+ cell, cells/μL (n=113)	424±245	418±253	440±225	0.684
Hemoglobin, g/dL	13.8±2.1	14.2±1.8	12.9±2.6	0.009
Platelet count, ×10^3/mm^2	194±78	195±69	191±102	0.823
AST level, IU/L	79.0±129.8	80.3±143.0	75.1±84.6	0.845
ALT level, IU/L	123.2±291.9	144.4±336.0	64.7±72.1	0.180
Total bilirubin, mg/dL	1.25±2.28	1.11±1.64	1.61±3.50	0.285
Albumin, g/dL	4.00±0.66	4.15±0.50	3.58±0.85	0.001
Creatinine, mg/dL	0.86±0.21	0.87±0.17	0.84±0.30	0.482
APRI	1.66±4.40	1.30±2.42	2.66±7.51	0.315
APRI >1.5	27 (21.8)	16 (17.6)	11 (33.3)	0.060
FIB-4	3.38±6.28	2.42±4.39	6.03±9.36	0.039
FIB-4 >3.25	29 (23.4)	15 (16.5)	14 (42.4)	0.003

Data are presented as mean±SD or number (%).
HCV, hepatitis C virus; HIV, human immunodeficiency virus; BMI, body mass index; HBsAg, hepatitis B surface antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; APRI, AST level to platelet ratio index; FIB-4, fibrosis-4.

Table 2. HCV Genotype Distribution in the Patients with HCV/HIV Coinfection (n=112)

Genotype	No. of patients (%)
Genotype 1	55 (49.1)
1a	14 (12.5)
1b	41 (36.6)
Genotype 2	53 (47.3)
2	26 (23.2)
2a	23 (20.5)
2a/c	4 (3.6)
Genotype 3	4 (3.6)
3	2 (1.8)
3a	2 (1.8)

HCV, hepatitis C virus; HIV, human immunodeficiency virus.

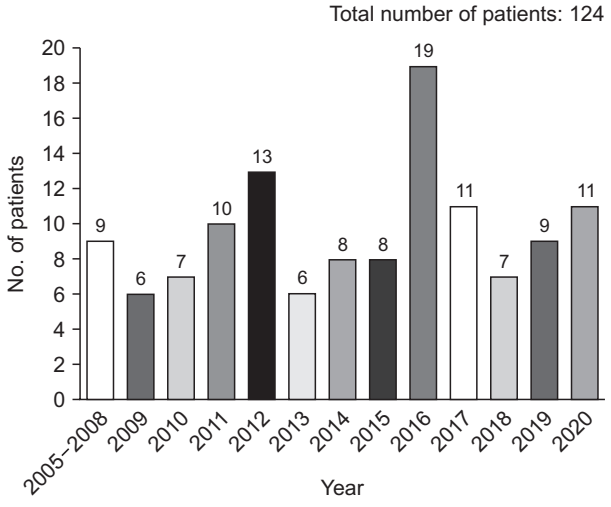

Fig. 1. Annual number of diagnoses of hepatitis C virus/human immunodeficiency virus coinfection.

type 1a. When comparing patients with genotype 1a to those with other genotypes, those with genotype 1a were significantly younger (genotype 1a vs other: 35.9±7.3 years vs 47.70±12.9 years, p<0.001). However, there was no difference based on nationality (Koreans vs foreign nationals: 12.5% [13/104] vs12.5% [1/8], p=1.000).

The annual incidence of HCV/HIV coinfection is shown in Fig. 1. In terms of simultaneous or sequential infections, 69 patients (55.6%) were already coinfected at the time of admission. The remaining 55 patients (44.4%) initially presented HIV monoinfection and later developed HCV coinfection, with an average interval of 82.7 months. Notably, no patients experienced a sequential HIV infection following an HCV monoinfection.

3. Treatment outcomes

Among the 124 patients with HCV/HIV coinfection, 91 patients (73.4%) received antiviral treatment for HCV at least once, with a total of 104 antiviral treatments administered (Table 3). Fig. 2 demonstrates the annual uptake of HCV treatment. Prior to 2015, the number of patients receiving PEG-IFN-based therapy remained stable. However, following the introduction of DAA in 2015, the number of patients receiving DAA treatment has increased each year since 2016.

When the patients were divided into groups–those who received PEG-INF based treatment (n=31) and those who received DAA treatment (n=73)–it was observed that the DAA-treated patients were significantly older than those treated with PEG-INF based treatment (PEG-INF based treatment vs DAA: 41.5±8.8 years vs 49.2±12.1 years, p<0.001). Aside from the age difference, there were no significant differences in other baseline characteristics, although the DAA-treated group had a higher rate of retreatment with antiviral agents (Table 3).

Out of the 104 antiviral treatments, 83 achieved SVR. The SVR rate was higher in the DAA-treated group compared to those treated with PEG-INF based therapy (PEG-INF vs DAA: 58.1% [n=18] vs 89.0% [n=65], p<0.001). After excluding five antiviral treatments for which SVR could not be confirmed, an analysis of 99 antiviral treatments showed a statistically higher SVR in the DAA group compared to the PEG-INF group (PEG-INF based treatment vs DAA: 60.0% [n=18] vs 94.2% [n=65], p<0.001) (Fig. 3). Examining the SVR rates for cases treated with different DAA regimens revealed the followings results: sofosbuvir+ledipasvir±ribavirin (19/19), sofosbuvir+daclatasvir (3/3), grazoprevir+elbasvir (5/5), ombitasvir+paritaprevir+ritonavir+dasabuvir (1/1), and glecaprevir+pibrentasvir (16/16) all achieved a 100% SVR rate. The SVR was 77.8% (7/9) for daclatasvir+asunaprevir and 87.5% (14/16) for sofosbuvir+ribavirin.

Among patients who achieved SVR after antiviral treat-

Table 3. Characteristics of the Patients Receiving Antiviral Therapy among the Patients with HCV/HIV Coinfection

Characteristics	Total patients (n=104)	PEG-INF (n=31)	DAA (n=73)	p-value
Clinical characteristics				
Age, yr	46.9±11.7	41.5±8.8	49.2±12.1	<0.001
Male sex	95 (91.3)	28 (90.3)	67 (90.3)	0.537
Foreigner	7 (6.7)	2 (6.5)	5 (6.8)	1.000
BMI, kg/m^2 (n=86)	22.6±3.0	22.5±3.0	22.6±3.0	0.899
Diabetes	14 (13.5)	3 (9.7)	11 (15.1)	0.547
Hypertension	13 (12.5)	6 (19.4)	7 (9.6)	0.168
Hyperlipidemia	7 (6.7)	2 (6.5)	5 (6.8)	1.000
Cirrhosis	8 (7.7)	1 (3.2)	7 (9.6)	0.431
ART	101 (97.1)	28 (90.3)	73 (100)	0.025
Naïve treatment	90 (86.5)	31 (100)	59 (80.8)	0.009
SVR	83 (79.8)	18 (58.1)	65 (89.0)	<0.001
Laboratory characteristics				
HBsAg (+)	6 (5.8)	0	6 (8.2)	0.175
HCV RNA, IU/mL	$6.4\times10^6\pm1.3\times10^7$	$5.6\times10^6\pm7.3\times10^6$	$6.7\times10^6\pm1.5\times10^7$	0.698
HIV RNA, copies/mL	$8.7\times10^4\pm7.6\times10^5$	$2.7\times10^5\pm1.4\times10^6$	$1.1\times10^4\pm3.8\times10^5$	0.316
CD4+ cell, cells/μL (n=98)	416±258	397±233	424±269	0.647
Hemoglobin, g/dL	14.6±1.5	13.9±1.4	14.9±1.5	0.002
Platelet count, ×10^3/mm^2	188±66	183±62	190±68	0.633
AST level, IU/L	63.7±58.2	61.9±48.7	64.5±62.1	0.832
ALT level, IU/L	96.1±129.3	89.0±75.6	99.2±146.6	0.713
Total bilirubin, mg/dL	0.88±0.55	1.03±0.72	0.81±0.44	0.116
Albumin, g/dL	4.20±0.47	4.00±0.48	4.29±0.44	0.003
Creatinine, mg/dL	0.88±0.16	0.87±0.15	0.88±0.16	0.854
APRI	1.13±1.93	1.06±1.17	1.17±2.19	0.802
APRI >1.5	21 (20.2)	6 (19.4)	15 (20.5)	0.890
FIB-4	2.43±4.12	1.97±2.06	2.62±4.72	0.464
FIB-4 >3.25	14 (13.5)	3 (9.7)	11 (15.1)	0.547

Data are presented as mean±SD or number (%).

HCV, hepatitis C virus; HIV, human immunodeficiency virus; PEG-INF, pegylated interferon; DAA, direct-acting antiviral agent; BMI, body mass index; ART, antiretroviral therapy; SVR, sustained virologic response; HBsAg, hepatitis B surface antigen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; APRI, AST level to platelet ratio index; FIB-4, fibrosis-4.

ment, one experienced HCV reinfection. This patient initially had genotype of 1b and achieved SVR following PEG-INF based therapy. However, approximately 4 years later, the patient was reinfected with genotype 1a and subsequently achieved SVR again after receiving DAA treatment (grazoprevir+elbasvir).

For the 69 patients with available data who achieved SVR, we compared the AST, ALT, APRI, and FIB-4 levels before and after antiviral treatment (Fig. 4). Significant reduction were observed in pre-treatment levels: AST

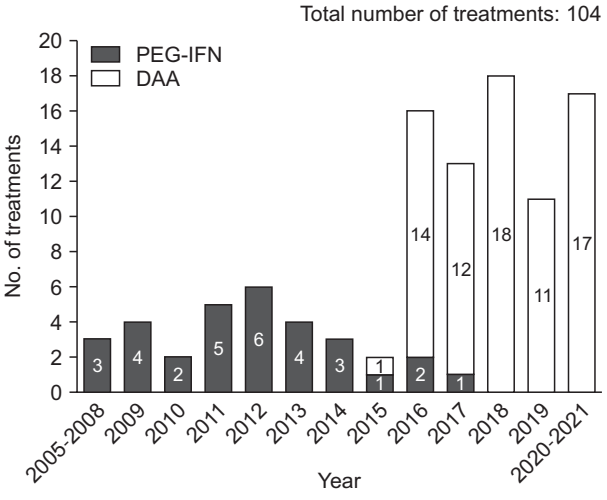

Fig. 2. Hepatitis C virus treatment uptake by year. PEG-INF, pegylated interferon; DAA, direct-acting antiviral agents.

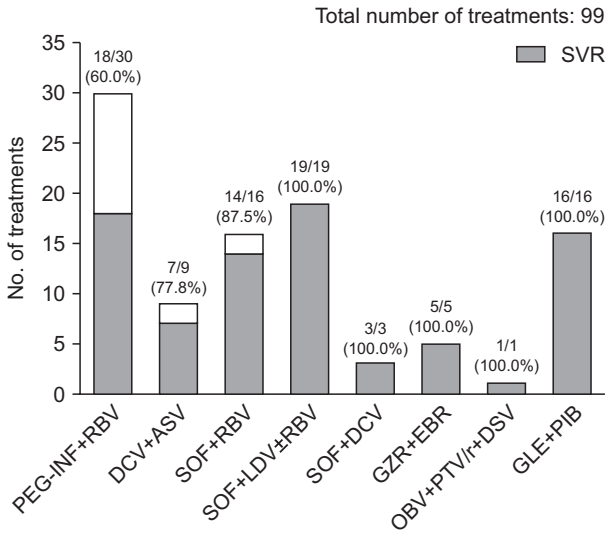

Fig. 3. Number of patients and sustained virologic response (SVR) rates according to hepatitis C treatment. PEG-INF, pegylated interferon; RBV, ribavirin; DCV, daclatasvir; ASV, asunaprevir; SOF, sofosbuvir; LDV, ledipasvir; GZR, grazoprevir; EBR, elbasvir; OBV, ombitasvir; PTV/r, paritaprevir/ritonavir; DSV, dasabuvir; GLE, glecaprevir; PIB, pibrentasvir.

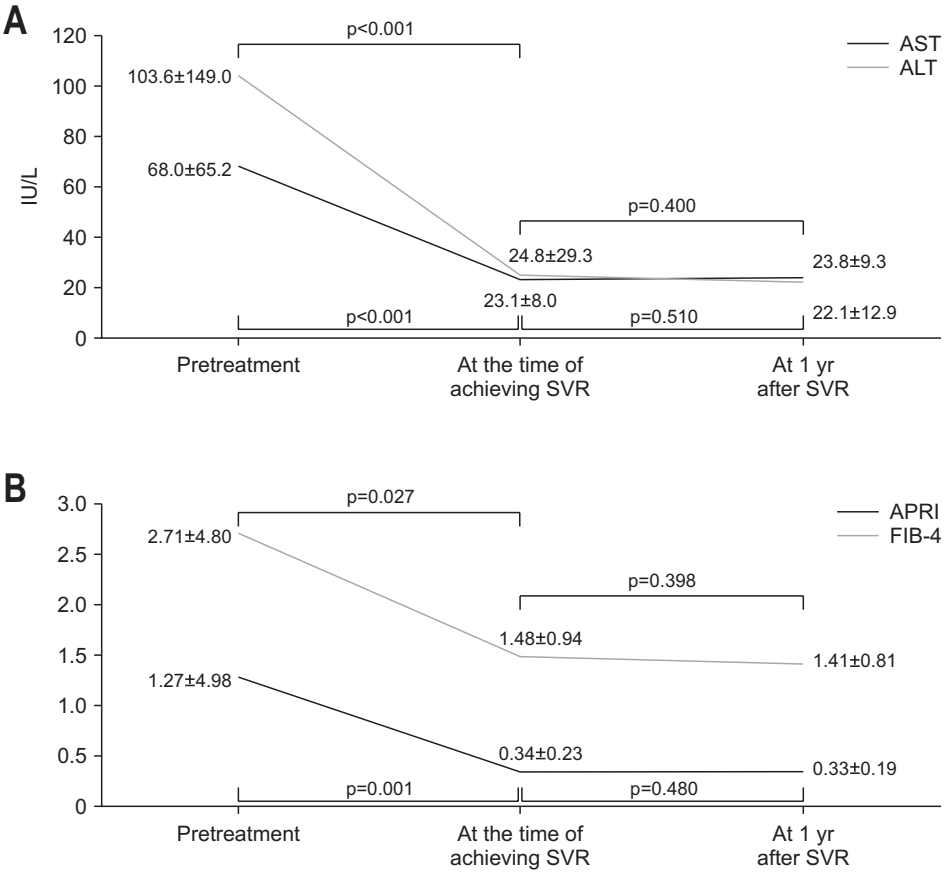

Fig. 4. Changes in inflammation (A) and fibrosis (B) markers from baseline to after antiviral treatment. AST, aspartate aminotransferase; ALT, alanine aminotransferase; SVR, sustained virologic response; APRI, AST level to platelet ratio index; FIB-4, fibrosis-4

(baseline vs at SVR: 68.0±65.2 IU/mL vs 23.1±8.0 IU/mL, p<0.001), ALT (baseline vs at SVR: 103.6±149.0 IU/mL vs 24.8±29.3 IU/mL, p<0.001), APRI (baseline vs at SVR: 1.27±4.98 vs 0.34±0.23, p=0.001), and FIB-4 (baseline vs at SVR: 2.71±4.80 vs 1.48±0.94, p=0.027). Furthermore, AST, ALT, APRI, and FIB-4 levels measured 1 year after SVR showed no significant difference compared to the levels at the time of achieving SVR.

DISCUSSION

In this retrospective multicenter study, we examined the clinical characteristics and treatment outcomes of HCV/HIV coinfected patients in South Korea. The prevalence of HCV coinfection among HIV patients was approximately 1.44%. Patients with HCV/HIV coinfection were predominantly male, younger, and exhibited a higher prevalence of genotype 1a compared to those with HCV monoinfection. Additionally, HCV/HIV coinfected patients showed higher SVR rates with DAA-based treatment compared to PEG-IFN-based treatment.

Globally, the estimated population of HCV/HIV coinfected individuals is approximately 2.3 million, with prevalence varying across different regions.[2] In HIV-infected individuals, HCV infection is approximately six times more common than in the HIV-negative population.[2] However, data on HCV/HIV coinfection in South Korea are limited due to the limited number of HIV patients. This study found an HCV coinfection rate of 1.44% among HIV-infected individuals, which is notably lower than the rates reported in previous studies, which ranged from 1.7% to 5.2%.[12,13] This discrepancy may be attributed to the small sample sizes and inclusion of HCV antibody-positive individuals in previous studies.[12,13]

In South Korea, individuals infected with HCV typically have a mean age ranging from 53.8 to 57.3 years, with a relatively balanced gender distribution.[20,21] However, in this study, HCV/HIV coinfected patients had a younger mean age of 46.5 years and were predominantly male, consistent with the demographic profile commonly observed in HIV-infected populations. Additionally, due to their younger age, HCV/HIV coinfected patients exhibited a lower prevalence of cirrhosis (8.9%) and relatively preserved liver function, resulting in only two cases of HCC development during the follow-up period.

This study observed a distinct distribution of HCV genotypes in HCV/HIV coinfected patients compared to those with HCV monoinfected. While the predominant genotypes in South Korea, 1b and 2, accounted for the majority (83.9%) in this study, genotype 1a represented 12.5% (n=14). In contrast, a previous prospective multicenter study on HCV patients in South Korea reported a much lower prevalence of genotype 1a by 2.4%.[21] Additionally, a study on HCV/HIV coinfected patients at a large HIV clinic in Busan found no cases of genotype 1a among the 19 individuals analyzed.[12] Although not definitive, it is hypothesized that the prevalence of genotype 1a among the patients in this study may have been influenced by their frequent interactions with individuals from Western countries.[6] This speculation is based on the observation that a majority of the study participants were from the metropolitan area, where there is likely increased contact with individuals from regions where genotype 1a is more prevalent.[6] Additionally, a shift in HCV genotype distribution based on birth cohort effects should be considered.[22] A study from the United States reported a decreasing proportion of genotype 1b and an increasing proportion of genotypes 1a and 3 over successive birth decades, likely reflecting changes in HCV transmission routes—from medical exposure to injection drug use.[22,23] The findings of this study may also reflect the evolving pattern of HCV transmission.

In HCV/HIV coinfected patients who did not undergo antiviral therapy, advanced age, higher FIB-4 index, and a higher prevalence of cirrhosis were observed. These factors contributed to the challenges of antiviral therapy during previous DAA era, particularly in cases with compromised liver function, such as those with decompensated cirrhosis.[24] However, in the advent of DAA therapy, various antiviral agents have shown excellent SVR rates even in patients with advanced or decompensated cirrhosis, leading to notable improvement in liver function.[25] Studies on the DAA treatment uptake have shown that a higher FIB-4 index is a significant factor influencing treatment uptake.[26,27] Consequently, there is now greater optimism regarding antiviral therapy for a broader population of hepatitis C patients.

In this study, patients who did not receive antiviral treatment were older compared to those who received treatment, which contrasts with previous studies where older age was found to be a significant factor associated with treatment uptake.[26,28] However, as higher income is also associated with DAA treatment uptake, it is likely that the financial burden of DAA therapy plays a more critical role in influencing treatment uptake than age.[26,27] In fact, among the 33 patients who did not receive treatment in this study, 18 had no documented reason for not receiving treatment, six were unable to undergo HCV treatment due to impaired liver function or severe comorbidities, and two had spontaneous clearance. Of the remaining seven, four patients were unable to receive treatment due to financial constraints. Therefore, to achieve the goal of HCV elimina-

tion by 2030,[29] it will be essential to identify the group unable to receive treatment due to the economic burden and develop strategies to support them.

In this study, approximately 56% of patients were already coinfected with HCV/HIV at the time of admission, while about 44% sequentially acquired HCV infection after HIV infection. Notably, there were no cases where HIV infection occurred following HCV infection. The prevalence of HCV coinfection among HIV-infected individuals varies by transmission route, ranging from 4.0% to 6.4% in heterosexual individuals and men who have sex with men, to over 80% in IV drug users.[2] Therefore, regular HCV testing is recommended for all HIV-infected individuals, with a particular emphasis on high-risk patients involved in activities such as high-risk sexual behavior and illicit drug use.[9]

In the era of interferon-based therapy, HCV/HIV coinfection was regarded as a risk factor for poor SVR.[30] However, with the advent of DAA, the treatment outcome of HCV in individuals coinfected with HIV has become comparable to those without HIV.[9,10] Currently, key determinants of treatment success include factors such as drug adherence, the presence of decompensated cirrhosis, and active HCC.[31] In this study, patients treated with PEG-INF achieved an SVR of 60%, while those treated with DAA showed an SVR of 94.2%. Notably, patients receiving regimens other than daclatasvir+asunaprevir and sofosbuvir+ribavirin achieved SVR in all cases. A meta-analysis indicated that sofosbuvir+ribavirin, compared to other regimens, resulted in SVR rates 10% to 20% lower in the treatment of HCV/HIV coinfection, thus recommending against the continued use of sofosbuvir+ribavirin in these patients.[8]

Previous studies have demonstrated that liver fibrosis can reverse following HCV elimination, with similar outcomes noted in individuals with HIV coinfection.[32,33] In this study, we observed significant improvements in inflammation and fibrosis markers when comparing pre- and posttreatment levels, and these improvements were maintained even 1 year after treatment.

This study had several limitations. First, this study is subject to potential biases, including recall bias and selection bias, due to its retrospective design. Additionally, its retrospective nature inherently limits the collection of sensitive data, particularly concerning sexual behaviors and illicit drug use, which are critical factors for understanding the epidemiology of HCV/HIV coinfection. Second, the predominance of patients sourced from metropolitan areas may limit the generalizability of our findings, as this demographic may not accurately represent the broader population of HCV/HIV coinfected individuals across South Korea. Despite these limitations, this study represents the largest documented cohort of HCV/HIV coinfected patients documented in published literature in South Korea, contributing valuable insights into this understudied population. Third, the lack of data on HCV monoinfected patients precludes a direct comparison between HCV monoinfection and coinfection, limiting our ability to draw definitive conclusions regarding the differential impact of HIV on HCV disease progression and treatment outcomes. Future studies should adopt a prospective design and aim to address these limitations by including a broader and more diverse patient population, including those from non-metropolitan areas, and incorporating appropriate comparison groups.

In conclusion, this study found that patients with HCV/HIV coinfection in South Korea were predominantly male, younger, and had a higher prevalence of genotype 1a compared to those with HCV monoinfection. Notably, HCV/HIV coinfection typically developed after HIV infection. The efficacy of DAA was significantly superior to that of interferon-based therapy. Additionally, improvement in liver inflammation and fibrosis was observed following the achievement of SVR. Therefore, greater efforts are necessary to enhance HCV linkage to care through regular screening for HCV in HIV-infected individuals, particularly among high-risk populations.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

This study was supported by the Research Supporting Program of The Korean Association for the Study of the Liver and The Korean Liver Foundation (KASL2021-02). The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

AUTHOR CONTRIBUTIONS

Study concept and design: J.Y.J., S.S.K., T.Y.K., S.J.Y. Data acquisition: all authors. Data analysis and interpretation: all authors. Drafting of the manuscript J.Y.J. Critical revision of the manuscript for important intellectual content: J.Y.J., T.Y.K., S.J.Y. Statistical analysis: J.Y.J. Obtained funding: J.Y.J. Administrative, technical, or material sup-

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SUPPLEMENTARY MATERIALS

Supplementary materials can be accessed at https://doi.org/10.5009/gnl240581.

DATA AVAILABILITY STATEMENT

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

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