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Prevalence of hepatitis B and C, and their linkage to care among drug abusers attending psychiatric hospital in Hiroshima, Japan

Aya Sugiyama[1,2], Ariyuki Kagaya[3,4], Ko Ko[1,2], Zayar Phyo[1,2], Golda Ataa Akuffo[1,2], Tomoyuki Akita[1,2], Kazuaki Takahashi[1,2], Ryotaro Tsukue[3], Chika Shimohara[3], Junko Tanaka[1,2,*]

[1] Department of Epidemiology, Infectious Disease Control and Prevention Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan;

[2] Project Research Center for Epidemiology and Prevention of viral hepatitis and hepatocellular carcinoma, Hiroshima University, Hiroshima, Japan;

[3] Senogawa Hospital, Hiroshima, Japan;

[4] KONUMA Memorial Institute of Addiction and Mental Health, Senogawa Hospital, Hiroshima, Japan.

Abstract: Towards the WHO goal for hepatitis elimination, understanding the prevalence and management of hepatitis B and C viruses (HBV, HCV) among drug abusers is crucial. However, in Japan, where drug abuse is less prevalent than in other countries, there is a dearth of epidemiological studies on this topic. This study aimed to fill this gap by investigating virus prevalence and the testing and treatment landscape for drug abusers in Japan. We conducted a cross-sectional sero-epidemiological study at a psychiatric hospital in Hiroshima where approaching drug abusers was feasible. Blood samples and questionnaire on HBV/HCV testing and treatment were collected from drug abusers (n = 35, 85.7% male, mean age 55.4 years) and control group (n = 45, 71.1%, 48.2 years). Prevalence of HCV-Ab and HCV RNA in drug abusers was 60.0% (95% CI: 43.8–76.2%) and 28.6% (13.6–43.5%), respectively, which was significantly higher than in the control group (2.2%, 0.0%, respectively). All HCV-Ab positive drug abusers had undergone prior hepatitis virus testing, but only 42.9% of those eligible for HCV treatment were connected to it. For HBV, while prevalence of HBsAg was similar between groups (2.9% *vs*. 2.2%), prevalence of HBc-Ab was higher in drug abusers (34.3% *vs.* 17.8%), indicating a greater likelihood of exposure to HBV infection. In conclusion, HCV prevalence among drug abusers in psychiatric care is notably high. Although testing is accessible, a recognized challenge is the insufficient connection to treatment. Enhancing collaboration between psychiatric hospitals and hepatologists is crucial. Disregarding this issue is not an option for hepatitis elimination.

***Keywords*:** HBV, HCV, sero-epidemiology, drug abusers, micro-elimination, Japan

Introduction

Data from the World Health Organization (WHO) indicate that as of 2019, there were 296 million people globally living with chronic hepatitis B virus (HBV) infection and 58 million with chronic hepatitis C virus (HCV) infection, with 1.5 million new infections each year. HBV and HCV infections can lead to liver cirrhosis and hepatocellular carcinoma, resulting in over 820,000 deaths for HBV and 290,000 deaths for HCV (*1,2*).

In Japan, various initiatives have been implemented for the prevention and management of HBV and HCV infections (*3,4*). These include the screening system for blood donors for HBV and HCV, with hepatitis B surface antigen (HbsAg) screening in place since 1972 and HCV antibody (HCV-Ab) screening since 1989. Additionally, a national project has been established since 1986 to prevent mother-to-child transmission of HBV. Since 2002, there has been a nationwide screening program targeting residents aged 40 years and over for HBV and HCV. Furthermore, since 2007, regional core hospitals for the treatment of liver diseases have been established in every prefecture. This network aims to enhance the capacity for managing liver-related conditions across the country. Additionally, since 2008, a medical expense subsidy system has been in operation to support the antiviral treatment of individuals infected with HBV or HCV. The Basic Act on Hepatitis Measures was enacted in 2009, providing a legal framework for both the national government and local authorities to implement countermeasures based on this legislation. As a result of these measures, the number of individuals with sustained infections of HBV and HCV decreased from a range of 3.01 to 3.66 million people in the year 2000 to a range of 1.91 to 2.49 million people in 2015 (*5*). In Japan, the prevalence of HBsAg and HCV-Ab is controlled at 0.37% and 0.28%, respectively, indicating a globally low level of infection (*5,6*).

WHO has established assessment criteria related to incidence, mortality, and health service coverage associated with prevention and treatment for the goal of eliminating Viral Hepatitis by 2030. For HBV, as there is currently no curative treatment to eliminate the virus, achieving the goal by 2030 is anticipated to be challenging in all countries, including Japan and worldwide (*7*). Regarding HCV, it is anticipated that Japan will achieve elimination by 2030 (*7*). However, to achieve this target, special attention should be given to the detection and effective treatment of high-risk populations such as drug abusers, including people who inject drugs (PWID), people living with HIV (PLHIV), prisoners and the homeless (*8*).

As for PWID, approximately 15.6 million PWIDs worldwide are between 15 and 64 years of age (*9*), and more than half of them (52.3%) are HCV-Ab positive and 9.0% are HBs-Ag positive, according to a previous systematic review (*9*). In the United States, 2.6% of adults report a history of injection drug use, with over 50% testing positive for HCV-Ab (*10*). In most countries, the risk of HCV infection among PWID is a major concern due to insufficient awareness and widespread unsafe injection practices (*11*).

Compared to the global situation, Japan has a significantly lower number of PWID. For example, while the estimated PWID population in the United States was over 3.7 million in 2018 (*12*), Japan had 0.5 million in 2011 (*13*). Consequently, little attention has been paid to this group, and their infection and treatment status remain unknown. PWID in Japan are either in prison or hidden in society, making it difficult to conduct a survey among them.

This study conducted within a psychiatric hospital setting offers a feasible approach to reach this hidden population. It provides an opportunity to collect data and investigate a sero-epidemiological investigation among psychiatric patients with a history of drug abuse at a psychiatric hospital, with a control group of patients without a history of drug abuse. Our goal was to clarify the current sero-epidemiological status of hepatitis viruses among them and to assess the linkage to care conditions of HCV treatment-eligible patients with a history of drug abuse.

Patients and Methods

We conducted a cross-sectional sero-epidemiological study from November 2021 to March 2022 to estimate the prevalence of HBV and HCV infections among patients at a psychiatric hospital in Hiroshima City, including those with and without a history of drug abuse. Additionally, we explored their history of treatment for HBV or HCV using a self-administered questionnaire.

Ethics approval and patient informed consent

This study was approved by the Hiroshima University Epidemiological Ethics Review Committee and the Senogawa Hospital Ethics Committee (E-2634, R03). Informed consent was obtained from all participants before any study procedure was conducted. All study activities were performed following the Declaration of Helsinki and relevant guidelines and regulations in Japan.

Study population

For this study, we recruited psychiatric patients with or without a history of drug abuse. The control group consisted of patients without a history of drug abuse. Participants were included if they expressed a desire to participate and provided written consent. Exclusions comprised individuals with an unknown history of drug abuse or those with severe mental illness lacking the capacity to provide consent. We used a voluntary convenient sampling method and recruited a total of 80 psychiatric patients, including 35 with a history of drug abuse and 45 without.

Samples collection and sero-molecular analysis of HBV and HCV

A questionnaire was administered to the subjects using a survey form consistently employed by the Ministry of Health, Labour and Welfare research group for general populations (*14*). This comprehensive questionnaire covered aspects such as past hepatitis virus tests and treatment history in the event of a positive result. Notably, a section on drug abuse history was incorporated into the questionnaire specifically for this study. The survey questionnaire was self-administered by clinically stable psychiatric patients; however, individuals with visual impairments or handwriting difficulties due to tremors, for instance, had a physician read the questionnaire, and the individual verbally responded while the physician recorded the answers.

We collected 10 ml of intravenous blood samples from each participant. All blood samples collected were tested for hepatitis B, C, and liver function tests (AST and ALT). HCV-Ab (Lumipulse II Ortho HCV antibody, Fujirebio Inc, Tokyo, Japan) was detected by a chemiluminescent immunoassay (CLIA) with a signal to cutoff ratio of 1. Hepatitis B serological tests were done using Lumipulse Presto HBsAg-HQ (Fujirebio Inc, Tokyo, Japan) for HBsAg with cutoff at 0.005 IU/mL, Lumipulse Presto HBs-Ab-III (Fujirebio Inc, Tokyo, Japan) for HBs-Ab with cutoff at 10.0mIU/mL, and Lumipulse Presto HBc-Ab-III (Fujirebio Inc, Tokyo, Japan) for HBc-Ab with cutoff at 1.0 cutoff index.

All serum samples positive for HBsAg or HCV-Ab were underwent further molecular analysis. The viral titer was determined for HBV DNA and HCV RNA using Taqman Fast advanced master mix (Thermo Fisher

Scientific, MA, USA) and Fast 1 Step Mix (Thermo Fisher Scientific, MA, USA) on Applied Biosystems StepOne (Thermo Fisher Scientific, MA, USA). The positive PCR samples were then employed for amplification of surface polymerase gene for HBV and core gene for HCV by first and second rounds of nested PCR followed by Sanger sequencing as per previous reports (*15-17*). The genotypes of both HBV and HCV were determined after the phylogenetic tree analysis of sample genomes and retrieved reference genomes from GeneBank was constructed by the Neighbor-joining method with Molecular Evolutionary Genetic Analysis 10 (MEGA-X, Pennsylvania State University, PA, USA).

The test results were communicated to individual patients by a hospital doctor and a record card of the hepatitis virus test was issued to all study participants, regardless of their results. Patients who tested positive for the hepatitis virus were referred to the Hiroshima Prefecture Liver Disease follow-up system and advised to undergo medical examinations.

Data analysis

Statistical analyses were performed by using JMP software (SAS Institute, California, USA). Chi-square (X2) test was used, and a p-value < 0.05 was considered statistically significant.

Results

Participant characteristics

The mean age of psychiatric patients with a history of drug abuse (n = 35) was 55.4 ± 11.0 years, and 85.7% were male (Table 1). One person had an occupation related to medical and nursing care. The mean age of psychiatric patients without a history of drug abuse (n = 45) was 48.2 ± 14.9 years, and 71.1% were male. Among them, 18 (40.0%) had occupations related to medical and nursing care.

Status of HCV infections

In this study, 22 out of 80 psychiatric patients were found to be positive for HCV-Ab, with 21 having a history of drug abuse and one without. We showed their individual characteristics in Table 2. All patients had undergone hepatitis virus testing prior to their involvement in this study. Four of the patients were unaware of their past testing status but were considered to have been tested based on their history of surgery, childbirth, and blood donation. Among the 21 HCV-Ab positive psychiatric patients with a history of drug abuse, 7 (33.3%) were HCV RNA negative without any treatment history (infection eliminated naturally), 4 (19.0%) were HCV RNA negative with a treatment history (successfully treated cases), 8 (38.1%) were HCV RNA positive without a treatment history (cases lacking necessary treatment), and 2 (9.5%) were HCV RNA-positive with a treatment history (unsuccessfully treated cases, Case 4, and Case 10 in Table 2). Among the 14 patients eligible for HCV treatment, 6 (42.9%) were linked to the care, and 8 (57.1%) were not linked to the care (Figure 1).

In contrast, among psychiatric patients without a history of drug abuse, only one case tested positive for HCV-Ab. This patient had a history of HCV treatment, and HCV RNA was not detected (Case 22 in Table 2).

The prevalence of HCV-Ab and HCV RNA among psychiatric patients with a history of drug abuse was 60.0% (21/35, 95% CI: 43.8–76.2%) and 28.6% (10/35, 95% CI: 13.6–43.5%), respectively, which was significantly higher than in psychiatric patients without a history of drug abuse (HCV-Ab 2.2%, 95% CI: 0–6.5%, p < 0.0001; HCV RNA 0.0%, 95% CI: 0–8.2%, p = 0.0001, Figure 2).

Status of HCV RNA-positive patients

In this study, we identified 10 patients who were HCV RNA-positive, all of whom had a history of drug abuse. Among these patients, 7 were male and 3 were female, and their ages ranged from 40 to 78 years. Moreover, 6

Table 1. Age and sex distribution of psychiatric patients stratified by drug abuse history

Characteristics	Total (n = 80)		Psychiatric patients with history of drug abuse (n = 35)		Psychiatric patients with no history drug abuse (n = 45)	
	n	%	*n*	%	*n*	%
With history of drug abuse	35	43.8%				
With no history of drug abuse	45	56.3%				
Gender						
Male	62	77.5%	30	85.7%	32	71.1%
Female	18	22.5%	5	14.3%	13	28.9%
Age						
Median (IQR)	50.5 (19.0)		54 (25.8)		47 (21.0)	
Mean age (SD)	51.4 (13.8)		55.4 (11.0)		48.2 (14.9)	

IQR, interquartile range; SD, standard deviation.

Table 2. Characteristics of 22 HCV-Ab positive psychiatric patients

Basic information				Testing and treatment history for HCV				HCV					HBV		
Case	History of drug abuse	Age	Sex	Testing	Detailed examination	HCV treatment	Hope for HCV treatment	HCV-Ab titer (C.O.I.)	RT-qPCR (Ct)	Viral Load (copies/mL)	Nested PCR	HCV Genotype	HBs-Ag	HBs-Ab	HBc-Ab
1	Yes	43	M	Yes (Before surgery, unrecognized)	No	No	Hope	91.0	23.36	1,008,743	(+)	1b	(-)	(-)	(-)
2	Yes	78	M	Yes (Hospital)	No	No	Hope	78.4	30.01	9,547	(+)	1b	(+)	(-)	(+)
3	Yes	40	F	Yes, (Before surgery and childbirth, unrecognized)	No	No	Hope	88.0	22.47	4,355,578	(+)	2b	(-)	(-)	(-)
4	Yes	54	M	Yes (Hospital)	Yes	Yes	Hope	100.0	31.89	2,345	(+)	2b	(-)	(-)	(-)
5	Yes	49	M	Yes (Hospital)	No	No	Hope	62.8	29.45	45,998	(+)	2a	(-)	(-)	(-)
6	Yes	51	F	Yes (Hospital)	No	No	Don't know	68.5	32.01	1,267	(+)	2a	(-)	(+)	(+)
7	Yes	67	M	Yes (Hospital)	No	No	Hope	75.1	28.75	23,567	(+)	1b	(-)	(+)	(+)
8	Yes	52	M	Yes (Hospital)	No	No	Don't know	88.7	21.11	40,385,056	(+)	1b	(-)	(-)	(-)
9	Yes	53	F	Yes (Hospital)	No	No	Hope	26.9	25.35	651,379	(+)	2a	(-)	(+)	(+)
10	Yes	60	M	Yes (Hospital)	Yes	Yes	Hope	5.3	29.26	14,322	(+)	1b	(-)	(+)	(+)
11	Yes	60	M	Yes (Hospital)	No	No	Hope	55.9	-	Undetermined	(-)	-	(-)	(-)	(+)
12	Yes	53	M	Yes (Hospital)	No	No	Don't know	80.5	-	Undetermined	(-)	-	(-)	(-)	(-)
13	Yes	45	M	Yes (Hospital)	Yes	Yes	Hope	21.2	-	Undetermined	(-)	-	(-)	(-)	(-)
14	Yes	58	M	Yes (Hospital)	Yes	Yes	Hope	38.8	-	Undetermined	(-)	-	(-)	(-)	(-)
15	Yes	61	M	Yes (No answer)	Yes	Yes	Hope	11.8	-	Undetermined	(-)	-	(-)	(-)	(-)
16	Yes	50	M	Yes (Hospital)	No	No	Hope	17.0	-	Undetermined	(-)	-	(-)	(-)	(-)
17	Yes	60	M	Yes (Hospital)	No	No	Hope	5.0	-	Undetermined	(-)	-	(-)	(-)	(+)
18	Yes	73	M	Yes (Hospital)	No	No	Hope	5.5	-	Undetermined	(-)	-	(-)	(+)	(+)
19	Yes	61	M	Yes (Hospital)	Yes	Yes	Hope	3.2	-	Undetermined	(-)	-	(-)	(-)	(-)
20	Yes	65	F	Yes (Before surgery, unrecognized)	No	No	Hope	18.2	-	Undetermined	(-)	-	(-)	(+)	(+)
21	Yes	71	M	Yes (Before surgery, blood donation, unrecognized)	No	No	Don't want	45.2	-	Undetermined	(-)	-	(-)	(-)	(-)
22	No	42	M	Yes (Hospital)	Yes	Yes	Hope	47.8	-	Undetermined	(-)	-	(-)	(-)	(-)

HBV, hepatitis B virus; HCV, hepatitis C virus; HCV-Ab, hepatitis C virus antibody; C.O.I, cut off index; RT-qPCR, reverse transcriptase quantitative polymerase chain reaction; Ct, cycle threshold; HBs-Ag, hepatitis B surface antigen; HBs-Ab, hepatitis B surface antibody; HBc-Ab, hepatitis B core antibody; LFT, liver function test; AST, aspartate transferase; ALT, alanine transferase; U/L, unit per liter. [†]HCV screening for donated blood has been introduced since 1989 in Japan.

Table 2. Characteristics of 22 HCV-Ab positive psychiatric patients (continued)

Basic information				LFT		Risk factors for infection					Awareness of infection risk by sharing needle		
Case	History of drug abuse	Age	Sex	AST (U/L)	ALT (U/L)	Frequency of sharing syringes or needles with others	History of blood transfusions before 1989[†]	Tattoos	Piercing	Medical staff	HBV	HCV	HIV
1	Yes	43	M	42	45	1–49 times	No	Yes	Yes	No	Know	Know	Know
2	Yes	78	M	26	18	> 100 times	Yes	No	No	No	Don't know	Don't know	Don't know
3	Yes	40	F	37	37	1–49 times	No	No	Yes	No	Know	Know	Know
4	Yes	54	M	39	38	1–49 times	No	No	No	No	Don't know	Know	Don't know
5	Yes	49	M	47	56	1–49 times	No	Yes	Yes	No	Don't know	Don't know	Don't know
6	Yes	51	F	74	34	50–99 times	No	No	No	No	Don't know	Know	Don't know
7	Yes	67	M	14	6	> 100 times	No	Yes	No	No	Don't know	Know	Know
8	Yes	52	M	82	87	> 100 times	No	No	No	No	Don't know	Know	Don't know
9	Yes	53	F	16	8	Don't want to answer	No	Yes	Yes	No	Know	Don't know	Don't know
10	Yes	60	M	16	6	> 100 times	Yes	No	Yes	No	Know	Know	Know
11	Yes	60	M	27	19	50–99 times	No	Yes	No	No	Don't know	Know	Don't know
12	Yes	53	M	20	18	1–45 times	Yes	No	No	No	Don't know	Know	Don't know
13	Yes	45	M	21	13	> 100 times	No	Yes	Yes	No	Don't know	Don't know	Don't know
14	Yes	58	M	21	10	50–99 times	No	No	No	No	Know	Know	Know
15	Yes	61	M	13	8	> 100 times	No	Yes	No	No	Know	Know	Know
16	Yes	50	M	14	11	50–99 times	No	Yes	Yes	No	Don't know	Know	Don't know
17	Yes	60	M	18	16	> 100 times	No	No	Yes	No	Know	Know	Know
18	Yes	73	M	16	12	> 100 times	No	Yes	No	No	Know	Know	Know
19	Yes	61	M	29	21	> 100 times	No	No	No	No	Don't know	Know	Don't know
20	Yes	65	F	22	14	50–99 times	No	No	Yes	No	Don't know	Don't know	Know
21	Yes	71	M	38	20	> 100 times	No	Yes	No	No	Don't know	Don't know	Don't know
22	No	42	M	18	11	-	No	No	Yes	No	Don't know	Don't know	Don't know

HBV, hepatitis B virus; HCV, hepatitis C virus; HCV-Ab, hepatitis C virus antibody; C.O.I, cut off index; RT-qPCR, reverse transcriptase quantitative polymerase chain reaction; Ct, cycle threshold; HBs-Ag, hepatitis B surface antigen; HBs-Ab, hepatitis B surface antibody; HBc-Ab, hepatitis B core antibody; LFT, liver function test; AST, aspartate transferase; ALT, alanine transferase; U/L, unit per liter. [†]HCV screening for donated blood has been introduced since 1989 in Japan.

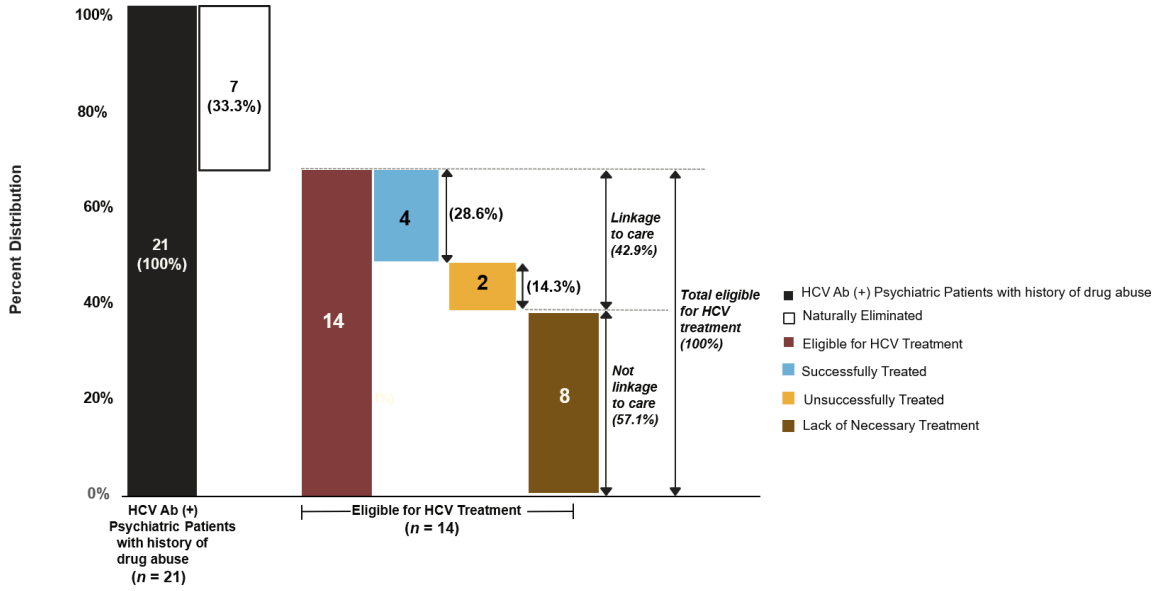

Figure 1. Percent distribution of linkage to care among HCV-Ab positive psychiatric patients with history of drug abuse. This figure represents among the 14 patients eligible for HCV treatment, 6 (42.9%) were linked to the care, and 8 (57.1%) were not linked to the care.

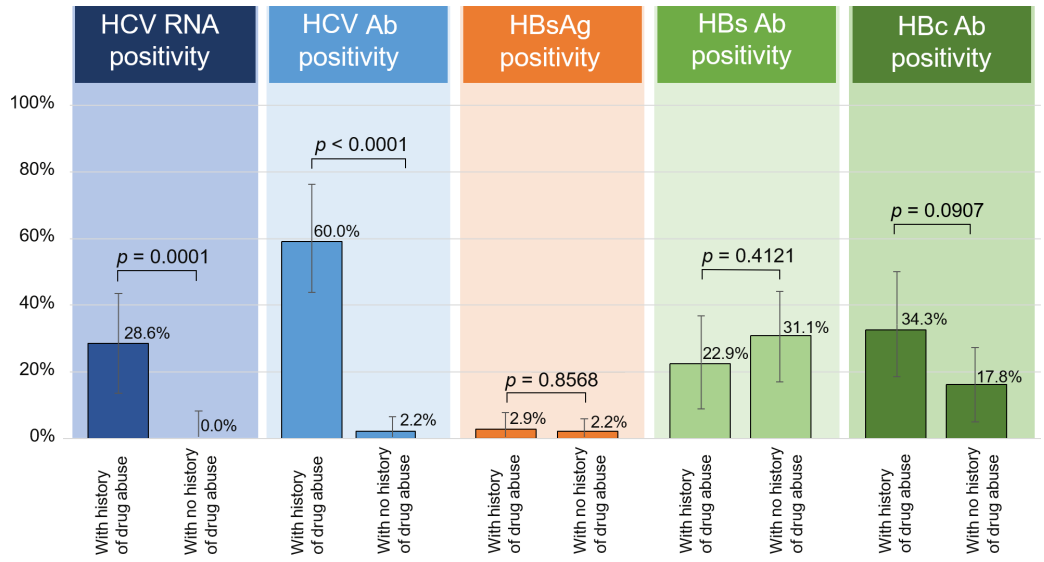

Figure 2. Hepatitis B and C virus infection status of psychiatric patients with history of drug abuse (n = 35) and no history of drug abuse (n = 45). This figure represents the prevalence of HCV-Ab and HCV RNA among psychiatric patients with a history of drug abuse was 60.0% (21/35, 95% CI: 43.8–76.2%) and 28.6% (10/35, 95% CI: 13.6–43.5%), respectively, which was significantly higher than in psychiatric patients without a history of drug abuse (HCV-Ab 2.2%, 95% CI: 0–6.5%, $p < 0.0001$; HCV RNA 0.0%, 95% CI: 0–8.2%, $p = 0.0001$). The prevalence of HBs-Ab was 22.9% (8/35, 8.9-36.8%), and that of HBc-Ab was 34.9% (12/35, 18.6–50.0%) among psychiatric patients with a history of drug abuse. There was no significant difference in the HBsAg positive rate between the two populations ($p = 0.8568$). However, the HBc-Ab positive rate tended to be higher in psychiatric patients with a history of drug abuse than in those without a history of drug abuse ($p = 0.0907$).

patients (60.0%) showed abnormal results for ALT and AST. (Table 2).

According to the questionnaire results, 8 out of 10 patients (80.0%) reported undergoing hepatitis virus screening tests during their hospital visits. The remaining 2 patients (20.0%) indicated that they had never undergone hepatitis virus testing before, but it was discovered that they had been tested without their knowledge due to their history of surgery or childbirth. Therefore, all HCV RNA-positive psychiatric patients with a history of drug abuse had undergone hepatitis virus testing at some point prior to their involvement in this study. Among them, 30.0% (3/10) received a detailed examination, while 20.0% (2/10) received HCV treatment.

HCV genotype

Out of the 10 patients who tested HCV RNA-positive, 5 were found to have genotype 1b (50%), 3 had genotype

2a (30%), and 2 had genotype 2b (20%) (Table 2). The HCV sequences of the 2 patients with genotype 2b (Case 3 and Case 4 in Table 2) showed a high degree of similarity at 98.8%.

Status of HBV infections

Only one psychiatric patient with a history of drug abuse (a 78-year-old male) was found to be positive for HBsAg (2.9%, 1/35, 95% CI: 0–8.4%). This patient was co-infected with HCV (Case 2 in Table 2), negative for hepatitis B surface antibody (HBs-Ab), and positive for hepatitis B core antibody (HBc-Ab), but HBV DNA was undetectable. The patient had undergone a hepatitis virus test during a previous medical visit and a subsequent detailed examination but did not meet the eligibility criteria for treatment. The prevalence of HBs-Ab was 22.9% (8/35, 8.9–36.8%), and that of HBc-Ab was 34.9% (12/35, 18.6–50.0%) among psychiatric patients with a history of drug abuse (Figure 2).

Among the non-drug abuser group, only one patient (female, 41 years old) was positive for HBsAg, with a prevalence of 2.2% (1/45, 95% CI: 0–6.5%). This patient tested negative for HBs-Ab and HBc-Ab and had undetectable levels of HBV DNA. She reported receiving a hepatitis virus test during a past visit to a medical institution but did not receive treatment due to the eligibility criteria not requiring further detailed examination. The positive rates of HBs-Ab and HBc-Ab were 31.1% (14/45, 95% CI: 17.6–44.6%) and 17.8% (8/45, 95% CI: 6.6–28.9%), respectively.

There was no significant difference in the HBsAg positive rate between the two populations (p = 0.8568). However, the HBc-Ab positive rate tended to be higher in psychiatric patients with a history of drug abuse than in those without a history of drug abuse (p = 0.0907, Figure 2).

Results from questionnaire

In this study, 62.9% (22/35) of psychiatric patients with a history of drug abuse and 37.8% (17/45) of psychiatric patients without a history of drug abuse reported prior HCV testing. Among psychiatric patients with no history of drug abuse (n = 27, after excluding 18 healthcare workers), the awareness of needle sharing as a route of transmission for HBV, HCV, and HIV was 51.9%, 48.1%, and 59.3%, respectively. In comparison, the corresponding figures for patients with a history of drug abuse were 42.9%, 65.7%, and 48.6%, respectively (p = 0.4816, p = 0.1646, p = 0.4030).

Discussion

We conducted a cross-sectional sero-epidemiological study at a psychiatric hospital in Japan to determine the prevalence of HBV and HCV infections among psychiatric patients with a history of drug abuse. This is crucial not only for their individual health but also for public health efforts in controlling the spread of viral hepatitis within their community. The prevalence of HCV-Ab and HCV RNA among patients with a history of drug abuse was found to be 60% and 28.6%, respectively, which were significantly higher than those in the control group without a history of drug abuse. The control group in this study had a high percentage of healthcare workers (40%). Despite healthcare professionals having a higher risk of HBV and HCV, their infection rate was lower, possibly due to increased infection prevention measures. In contrast, PWID may use drugs without prevention due to strong cravings.

Compared to studies conducted in Japan between 1992 and 1995, our study showed a decreased prevalence of HCV-Ab among drug users, with 60% in our study compared to 78.9% in 1992 and 74.5% in 1995 (*18-20*). According to an annual survey conducted from 1998 to 2017 in recovery support facilities for drug abusers, the HCV-Ab positivity rate was reported to be 30–50% (*20*). However, when compared to other countries, the prevalence of HCV-Ab in the Stockholm needle exchange program was reported to be 77%, and that of HCV RNA was 57% in 2018 (*21*). Our finding is consistent with a nationwide study conducted in Germany in 2020, where the prevalence of anti-HCV and HCV RNA among 2,466 opioid stimulation therapy (OST) patients was 58.8% and 27.3%, respectively (*22*).

According to studies conducted between 1995 and 2016, the prevalence of HCV-Ab among the general population in Japan was less than 1% (*6,23-25*). Therefore, our study revealed that the rate of HCV infection is extremely high among the population with a history of drug abuse in Japan. To achieve HCV elimination, a cascade of measures including awareness of hepatitis virus infection, risk reduction, access to screening and confirmatory testing, as well as linkage to treatment, are generally required to interrupt the chain of HCV transmission. As mentioned earlier, in Japan, measures such as hepatitis virus screening and subsidy programs for treatment have been implemented, effectively controlling infections in the general population (*3*).

However, has there been an opportunity for PWIDs to be tested and treated in Japan? There have been no reports on this matter. In our study, 21 out of 22 HCV-Ab positive patients were drug abusers, and all of them had been previously tested. Four of them were unaware that they had been tested, but it was determined based on their history of surgery, childbirth, or blood donation. In Japan, 60% of the general population have been tested for HCV, and 70% have been tested for HBV, including those who were unaware of it (*26*). Our study population of drug abusers receiving psychiatric treatment may not be representative of all drug abusers in Japan, as they have had access to medical care.

Our findings suggest that drug abusers who have had access to medical institutions in Japan have had good opportunities for hepatitis testing. However, access to treatment for those who test positive remains a concern. In our study, 33.3% of the 21 HCV-Ab positive drug abusers were considered to have naturally eliminated the virus, while the remaining 14 patients required treatment, but only 42.9% of them had been linked to medical care. In contrast, among HCV RNA positive individuals in the general population in Japan who survived from 2000 to 2015, 63.4–85.6% were linked to medical care by 2015 (*5*). In Japan, the introduction of direct-acting antiviral agents (DAAs) treatment in 2014 has led to a significant increase in the number of people receiving treatment as of 2022 (*27*). However, drug abusers still have a lower linkage to medical care compared to the general population. To meet the WHO target of hepatitis elimination by 2030, 80% of all eligible HCV patients must receive treatment (*2*). Worldwide, as of the end of 2019, it was estimated that only 21% of persons living with HCV knew their diagnosis, and among those diagnosed with chronic HCV infection, around 62% had been treated with DAAs (*2*). Linkage to treatment remains a challenge globally in achieving the WHO target, particularly among PWID. A study from Spain in 2018 found that only 45.9% of HCV patients with a history of drug use started treatment among 122 eligible patients (*28*), while an Italian focus group assessment reported that only 20.7% of HCV-positive patients among 3,796 eligible patients from 27 drug dependency centers were treated in 2019 (*29*).

For PWID, reinfection after treatment with DAAs has been a problem (*30-32*). To prevent new infections and reinfections, it is important to raise awareness about the risks of sharing needles. From this survey, 65.7% of psychiatric patients with a history of drug abuse recognized the risk of HCV infection due to sharing injection needles. Although it was slightly higher than the control group excluding healthcare workers, further improvement is desired. Many countries have implemented harm reduction programs recommended by WHO, such as syringe service programs (*33*). While such programs have not yet been introduced in Japan, there is a need for consideration in the future.

In this study, the prevalence of HBsAg positivity among individuals with a history of drug abuse was found to be 2.9%, which is higher than the reported prevalence of HBsAg positivity in the general population (0. 37%) (*5,6*). Although one patient each from those with history of drug abuse and those without was found to be HBsAg positive, our study is restricted to conduct the comparison between drug abusers and their control group in relation to HBsAg positivity and linkage to treatment. Meanwhile, HBsAg positivity did not change according to the presence or absence of drug abuse history, but the HBc-Ab positive rate was slightly higher in the drug abusers group, consistent with the previous report (*34*). It was suggested that the sharing of injection needles may have caused acute hepatitis B infection. Notably, awareness of the risks of needle sharing for HBV is slightly lower than for HCV, indicating a need for increased educational efforts to promote knowledge of these risks.

This study has several limitations. First, the study population consisted of individuals receiving treatment for drug addiction at a psychiatric hospital, which may introduce a bias towards those with a higher motivation for their own health. However, because PWID in Japan are often incarcerated or hidden in society, it can be challenging to conduct sero-epidemiological surveys, making drug users in psychiatric hospitals a feasible survey population. Additionally, the small sample size and single-center design are limitations of this study. Nevertheless, the absolute number of drug users in Japan is small and the psychiatric hospital included in this survey is one of the leading addiction treatment institutions in Japan. In situations where the target population is limited, small sample size studies can still provide valuable insights and serve as a starting point for further research in this underexplored area. With regards to the question of whether people with a history of drug abuse have access to hepatitis testing and treatment, the findings from this study cannot be completely generalized. Nonetheless, it was found that these individuals had been tested for hepatitis during their medical visits. However, these populations tend to have a lower linkage to treatment than the general population, which remains a challenge. Improving post-screening referral to treatment is crucial for them, going beyond the strategies employed for the general population. Additional efforts are needed to enhance the continuum of care for this rare and limited group, ensuring that they receive appropriate treatment and support. Despite the limitations described above, this study is a rare and valuable report that provides insights into the infection status of a population with a history of drug abuse in Japan.

Conclusion

Despite the small population of drug abusers in Japan, the high prevalence of HCV among them underscores the importance of addressing viral hepatitis in this group. Our study found that medical institutions in Japan provide opportunities for HBV/HCV testing for psychiatric patients with a history of drug abuse, but linkage to treatment is lower compared to the general population. Therefore, it is crucial to improve post-screening referral to treatment for drug abusers, beyond that of the general population. Strengthening collaboration between psychiatric hospitals and hepatologists is desirable. Overlooking this issue is not an option in the pursuit of hepatitis elimination.

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**Address correspondence to*:
Junko Tanaka, Department of Epidemiology, Infectious Disease Control and Prevention, Graduate School of Biomedical and Health Sciences Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima, 734-8551, Japan.
E-mail: jun-tanaka@hiroshima-u.ac.jp