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Genotype distribution, intravenous drug use rates and direct-acting antiviral treatment results in prisoner hepatitis C patients

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ABSTRACT:

— ***Objective:*** Hepatitis C is an important public health problem targeted for elimination by WHO. The prevalence of hepatitis C infection is higher in prisoner patients, compared to the general population. However, data on HCV infection in prisoners are extremely limited in Turkey. This study aimed to examine the genotype distributions, intravenous drug use rates, and treatment success with direct-acting antivirals in prisoner patients in a single center in Turkey.

— ***Patients and Methods:*** In this study, data from 64 HCV antibodies positive prisoner patients who were admitted to Kırıkkale University Hospital Infectious Diseases out-patient clinic between 2017-2021 were retrospectively analyzed. Negative HCV RNA in the first month of treatment and 12 weeks after treatment were accepted as early and sustained viral responses.

— ***Results:*** According to the pre-treatment results, HCV RNA was positive in 52 of the 64 patients who resulted positive to HCV screening. The most frequently detected viral genotypes were: genotype 1a (55.8%) and genotype 3 (26.9%). The rate of intravenous drug use in patients with chronic HCV infection was 61.5%. Forty-three patients received direct-acting antiviral therapy. Early viral response and sustained viral response were achieved in all patients.

— ***Conclusions:*** Active surveillance, timely treatment and prevention measures among inmates are essential in terms of HCV infection elimination targets. Direct-acting antivirals can be considered as milestones for the elimination of HCV due to their low side effects, short treatment course, and high viral response rates.

— ***Keywords:*** *Chronic hepatitis C, HCV genotypes, Intravenous drug use, Direct-acting antiviral, Prisoners.*

INTRODUCTION

Hepatitis C virus (HCV) is an enveloped RNA virus belonging to the *Hepacivirus* genus in the *Flaviviridae* family. HCV has 7 genotypes and 67 subtypes[1].

HCV infection can cause hepatitis, hepatic steatosis, cirrhosis, and hepatocellular carcinoma (HCC)[2]. According to the World Health Organization (WHO) data[3], 71 million people worldwide are chronically infected with HCV. In addition, new HCV infections develop in 1.75 million people each year, and approximately 400,000 patients develop HCV-induced cirrhosis and HCC each year. For these reasons, WHO aims at eliminating HCV by 2030 all over the world[4].

Intravenous drug use (IDU), transfusion of contaminated blood and blood products, sexual contact, surgery and other interventional procedures are the most common routes of HCV transmission. On the other hand, sharing tools such as toothbrushes, injectors during IDU, razor blades and tattooing patients cause the spread of HCV in

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prisons[5]. Furthermore, HCV is considered to be the main cause of death due to liver disease for prisoners caused by the increased risk of contracting the infections[6].

In Turkey, HCV screening and treatment data of prisoner patients are lacking. In this study, we aimed to examine the genotype distributions, IDU rates, and treatment success with direct-acting antiviral therapy (DAA) in prisoner patients diagnosed with chronic hepatitis C, and to compare the results with the data available in literature.

PATIENTS AND METHODS

In this study, data from prisoner patients who attended the Kırıkkale University Medical Faculty Hospital Infectious Diseases Clinic between January 2017 and January 2021 were analyzed retrospectively. Records from anti-HCV positive patients were exhamined. Patients with undetectable viremia, younger than 18 years old, and co-infected with hepatitis B virus and human immunodeficiency virus were not included in the study. All patients were Turkish citizens. Patients' age, gender, HCV-RNA level (before treatment, in the first month of treatment, at the end of treatment and, if available, at the third month after treatment), HCV genotype, IDU information, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alpha-fetoprotein (AFP) levels, liver ultrasonography examinations, liver biopsy pathology results were evaluated. Geno Sen's HCV Genotyping 1/2/3/4 Real Time PCR Reagents Kit (Corbett Research, Australia) was used for HCV RNA level and HCV genotyping. The patients who were diagnosed with chronic hepatitis C were treated with one of the DAAs. Available DAAs were PrOD [ombitasvir (OBV) + paritaprevir/ritonavir (PTV/r) + dasabuvir (DSV)] ± ribavirin (RBV), and glecaprevir + pibrentasvir. Treatment decision, treatment selection and treatment duration were decided according to the Turkish Social Security Institution Health Practice Notification guide[7].

Treatment efficacy, relapse rates and HCV RNA levels were determined at the first month, at the end and 12 weeks after the treatment. Negative HCV RNA in the first month of treatment was accepted as early viral response (EVR), and negative HCV RNA 12 weeks after treatment was accepted as sustained viral response (SVR12). Since the study was retrospective, informed consent was not obtained.

Statistical Analysis

Statistical analyses were performed using SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). The conformity of the variables to the normal distribution was examined using the histogram and Kolmogorov-Smirnov test. Descriptive statistics were given as numbers and percentages for categorical variables, and as mean ± standard deviation, minimum and maximum value for numerical variables. The Kruskal-Wallis' test was used to compare numerical variables between multiple groups that did not fit the normal distribution. Cases where the *p*-value was below 0.05 were considered as statistically significant results.

RESULTS

Overall, 64 records of patients with anti-HCV positive test were analyzed. Out of these, 52 patient had a detectable HCV-RNA. All patients in the study were male. The mean age of the patients was 27.96 ± 5.6 (min: 20, max: 53), the mean AST was 44.77 U/L ± 29.26 (min: 12, max: 142), the mean ALT was 86.96 U/L ± 60.7 (min: 12, max: 293), the mean AFP was 3.32 (min: 1.2, max: 10.8) ng/ml.

Regarding genotypes, 29/52 (55.8%) were genotype 1a, 14/52 (26.9%) genotype 3, five/52 (9.6%) genotype 1b, three/52 (5.8%) genotype 2, and one/52 (1%) was identified as genotype 4. There was no statistically significant difference between the HCV RNA levels of the patients according to their HCV genotypes (p=0.245).

Of 52 patients with detectable viremia, 43 patients received DAA treatment. All patients were treatment naive. Although HCV RNA and genotypes were detected in nine patients, a treatment plan could not be made for these patients because these patients did not apply for follow-up due to their release from prison or transfer to another prison. Overall, 24/43 patients (46.2%) received glecaprevir + pibrentasvir, 15/43 (28.8%) PrOD (OBV + PTV/r + DSV) + RBV, 4/43 (7.7%) received PrOD (OBV + PTV/r + DSV). Of 43 patient starting treatment, 36 had follow-up visits at the first month of treatment and after the treatment was completed. All 36 patients were found to be HCV-RNA negative at the end of treatment. Only 24 patients complied to the 12 weeks follow-up visits and all of them were found to be HCV-RNA negative.

The rate of IDU in HCV RNA positive patients was 61.5% (32/52). There was no statistically significant difference between IDU and others according to their HCV genotypes (p=0.5). Genotype distribution is reported in Table 1. Of 32 IDU patients, 26 HCV-RNA positive patients received treatment. Of these, 21 complied to the first month and the end of treatment follow-up. EVR was achieved in all patients. Only 12 patients complied to follow-up at week 12, and SVR12 was reached in all of them.

All patients underwent liver ultrasound exhamination, with no cirrhosis observed. No patient underwent a liver biopsy. No cases of treatment termination due to side effects or drug incompatibilitywere reported.

DISCUSSION

The prevalence of HCV in the world is estimated to be over 2.8%[8]. In a study[9] conducted in Turkey, the prevalence of HCV has been reported to be between 0.4% and 1.5%. HCV infections are more common in prisoner patients than in the general population. The prevalence of HCV in prisoner patients varies depending on the geographic region, IDU, age, length of stay in prison, and

Table 1. IDU distributions of prisoner patients according to HCV genotypes.

HCV genotypes	Number of patients with intravenous drug use	Number of patients without intravenous drug use	Total number of patients
Genotype 1a	15	14	29
Genotype 1b	4	1	5
Genotype 2	2	1	3
Genotype 3	11	3	14
Genotype 4	-	1	1

p-value = 0.5.

the history of the patient[10]. It has been reported that the prevalence of HCV in prisoner patients is between 2% and 58% worldwide[11,12].

In the study of Larney et al[5], the prevalence of HCV was found to be 26% in prisoner patients, while this rate was reported to be 64% in prisoners with IDU. In the study of Çabalak and Bal[13] in Hatay prisoner patients, the rate of IDU was reported to be 37.6% among HCV infected patients. In this study, the IDU rate of prisoners diagnosed with chronic hepatitis C was 61.5% (32/52).

Genotype determination in chronic HCV infection is important for treatment options, prognosis and epidemiological data. Worldwide, genotype 1 is the most common (46%), followed by genotype 3 (30%)[14]. In Turkey, the most common genotype is 1b, but other genotypes have started to be reported due to mass migration movements and touristic travels[15]. In the study of Özger et al[16], genotype 3 (66.7%) was the most common genotype. In the study of Çabalak et al[13], genotype 3 was the most common genotype (41%), and genotype 4 (39%) was following. In this study, genotype 1a was the most common (55.8%) in prisoner patients with HCV, followed by genotype 3 (26.9%). We think that this may be due to the number of patients in the study and the geographical region difference.

Regarding treatment, success rate has increased with the use of DAAs. DAAs have become preferable to interferon-based therapies, as they have fewer side effects, are better tolerated, shorten the duration of treatment up to 8-12 weeks, and are easy to use due to oral formulation[17]. In the study of Daniel et al[18], 15,720 chronic hepatitis C patients who received DAA treatment were examined, and SVR was 92%. It has been reported that the rate of SVR at six months after treatment in prisoner patients receiving peg-interferon (IFN)+RBV treatment is between 28% and 69%[10]. In the study conducted by Özger et al[16] in our country, Peg-IFN + RBV treatment was initiated in 99 prisoner patients, and it was reported that SVR at six months was reached in 33 patients. In a study conducted by Çabalak and Bal[13] in Turkey, it was reported that DAA treatment was started in 77 prisoner patients, SVR12 was reached in all 60 patients who complied to their follow-ups. In our study, 43 patients received DAA treatment. Of these, 24 were evaluated for SVR12, which was achieved in all 24 patients. In our study, there was no patient whose treatment was terminated due to side effects or drug incompatibility in prisoner patients who were started on DAA.

The rate of accessing and benefiting from health services of prisoner patients in prisons is higher than that of being in the community, due to the fact that they have a health file and are followed by the prison. After being released, these patients have difficulty in accessing health services and receiving treatment due to their psychological characteristics and physical conditions in the community[11]. It has been reported that the HCV treatment of prisoner patients in prisons can be done similarly or better than in the case of being in the community[19]. In the study of Çabalak and Bal[13], 17 prisoner patients with HCV infection whose DAA treatment was started, could not be evaluated because they did not apply for follow-up after their release[13]. Similarly, in this study, the treatment status of 19 prisoner patients with HCV infection, who were started on DAA treatment, could not be evaluated because they did not apply for follow-up due to reasons such as release or transfer to another prison.

Limitations

The most important limitation of this study is that it is a single-centered cross-sectional study and includes a single prison. Also, all patients were male and Turkish citizens living in Kırıkkale. Also, we could not access the transferred or released prisoner information. Moreover, we reported data from a limited sample size. The results of the study cannot be generalized to the whole country, as this limitation may affect the results.

CONCLUSIONS

Diagnosing prisoner patients with HCV infection, arranging their treatments, applying preventive measures, especially ptargeting IDU, is extremely important in terms of HCV infection elimination targets.

DAAs are giving a crucial contribution towards HCV infection elimination targets due to the low side effects, good tolerance, shorter treatment duration, ease of oral treatment and high SVR12 rates.

Mapping HCV prevalence and challenges among prisoners is crucial to design targeted prevention and treatment campaigns, which together with drug addiction treatment programs constitute an important step towards reaching the 2030 elimination target.

Conflict of Interest:
No competing interests to declare.

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Ethics Approval:
This study was approved by Kırıkkale University Non-Interventional Research Ethics Committee (Date: 28.09.2022, decision no.: 2022.09.19).

Informed Consent:
Since the study was retrospective, informed consent was not required.

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