



# Intravenous Drug Use Rates and Results of Direct-acting Antiviral Treatment in Prisoner Patients

Mahkum Hastalarda İntravenöz İlaç Kullanım Oranları ve Direkt Etkili Antiviral Tedavi Sonuçları

● Mehmet Çabalak, ● Tayibe Bal

Hatay Mustafa Kemal University Faculty of Medicine, Department of Infectious Disease and Clinical Microbiology, Hatay, Turkey

## ABSTRACT

**Objectives:** Intravenous drug use (IVDU) is more common in prisoner patients, and this is a global problem. Hepatitis C virus (HCV) infection is higher in prisoners than general population. In our study, we aimed to examine the IVDU rates and direct-acting antiviral (DAA) treatment results of the prisoners who applied to Hatay Mustafa Kemal University Clinic of Infectious Diseases.

**Materials and Methods:** In our study, IVDU rates and HCV treatment results of 85 prisoners who applied to Hatay Mustafa Kemal University Faculty of Medicine Clinic of Infectious Diseases between January 2017 and December 2019 were retrospectively analyzed. Treatment results were evaluated by performing modified intention to treat (mITT) and per protocol (PP) efficacy analysis, respectively.

**Results:** The rate of IVDU was 37.7% in prisoners who were positive for HCV. Although sustained virological response (SVR) rate was 100% in PP analysis, SVR rate was determined as 80.5% in mITT analysis. Viral genotype 3 (41.6%) and genotype 4 (39%) were the most common.

**Conclusion:** However, data on HCV screening and treatment in prisons in Turkey is inadequate or too low. We think that with the use of DAAs, patients' compliance to treatment will increase, it is an important step for HCV eradication and multicenter studies should be conducted.

**Keywords:** Chronic hepatitis C, prisoners, direct acting antiviral, IV drug user

## ÖZ

**Amaç:** Mahkum hastalarda intravenöz ilaç kullanımı (IVDU) sıklığı ve hepatit C virüs (HCV) enfeksiyonu prevalansı küresel olarak genel popülasyona göre daha yüksektir. Bu çalışmada Hatay Mustafa Kemal Üniversitesi Enfeksiyon Hastalıkları Kliniği'ne başvurup sağlık hizmeti alan mahkum hastalardaki IVDU oranlarının ve direkt etkili antiviral (DEA) tedavi sonuçlarının incelenmesi amaçlandı.

**Gereç ve Yöntemler:** Çalışmamızda Ocak 2017- Aralık 2019 yılları arasında Hatay Mustafa Kemal Üniversitesi Tıp Fakültesi Hastanesi Enfeksiyon Hastalıkları Kliniği'ne başvurup sağlık hizmeti alan toplam 85 mahkum hastanın IVDU oranları ve DEA tedavi sonuçları retrospektif olarak incelendi. Sırasıyla modifiye intention to treat (mITT) ve per protocol (PP) ile etkinlik analizi yapılarak tedavi sonuçları değerlendirildi.

**Bulgular:** HCV pozitif mahkum hastalarda intravenöz ilaç kullanım oranı %37,7 idi. PP analizinde kalıcı virolojik yanıt (KVY) %100 iken mITT analizinde bu oran %80,5 olarak saptandı. En sık viral genotip 3 (%41,6) ve genotip 4 (%39,0) saptandı.

**Sonuç:** Cezaevlerinde HCV taranması ve tedavisi açısından Türkiye'de yeterli veri yok veya çok azdır. DEA'ların kullanılması ile hastaların tedaviye uyumunun artacağını, HCV eradikasyonu için önemli bir adım olduğunu ve çok merkezli çalışmalar yapılması gerektiğini düşünmekteyiz.

**Anahtar Kelimeler:** Kronik hepatit C, mahkum, direkt etkili antiviral, IV ilaç kullanımı

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## Introduction

Hepatitis C virus (HCV) is a major global epidemic, and estimated 71 million people worldwide are chronically infected. Approximately 399,000 people die annually due to HCV-related liver failure and cancer in the world (1,2). In the developed countries, intravenous drug use (IVDU) is the main transmission route of HCV (2). In the literature, unsafe IVDU, sharing of drug paraphernalia, toothbrushes and shavers, tattooing have been identified as a risk factor for HCV infection transmission in prisoners (3,4,5,6). The prevalence of HCV in prisoners worldwide is up to 26%, and the incidence in prisoners who using intravenous drugs is up to 64% (3). Due to the physical conditions and psychological characteristics of prisoners, it is difficult for them to access and benefit from health services (7,8). Prisoners may have better access to health care and lower mortality rates in prisons than when they return to society (7,9). HCV treatment can be performed similar or better than the normal population in prisoners (10,11). All prisoners in prisons should be tested for HCV infection (12). HCV is now a preventable and treatable infection, but difficulties remain in reaching infected people (9,13). Prisons can provide a good opportunity to overcome these difficulties. Prison-based screening and treatment should be essential. However, data on HCV screening and treatment in prisons in Turkey is inadequate or too low. In our study, We aimed to discuss the treatment results and IVDU rates of prisoners who were followed up in our clinic due to HCV, by comparing them with other literature data in our country and in the world.

## Materials and Methods

This retrospective, observational, single-center study was performed in prisoners who were followed up by Hatay Mustafa Kemal University Faculty of Medicine Hospital, Clinic of Infectious Diseases. Patients' ages, genders, demographic data, previous treatment experience, drug use, liver biopsy if available, viral load (HCV-RNA levels at 4<sup>th</sup> week of treatment and after the treatment, 12<sup>th</sup> and/or 24<sup>th</sup> week post-treatment) and viral genotype data were obtained from the hospital automation system and patient files retrospectively. Patients younger than 18 years old, who were coinfecting with HBV and human immunodeficiency virus were not included in the study. The cases were treated with one of the direct-acting antiviral (DAA) drugs. The drugs used in the treatment are as follows; sofosbuvir ± ribavirin (SOF ± RBV), ombitasvir + paritaprevir/ritonavir (OBV + PTV/r) ± RBV, PrOD [(OBV + PTV/r) ± dasabuvir (DSV)] ± RBV, glekapravar + pibrentasvir and ledipasvir + SOF. RBV dose was determined according to the patient's weight. DAA drug selection and treatment decisions were made according to the Health Application Communique of the Turkish Social security institution guideline and the decision of physician responsible for treatment (14). HCV genotype and plasma HCV-RNA levels were determined by a real-time PCR assay, using either the COBAS AmpliPrep/COBAS Taqman (Roche Molecular Systems Inc., Pleasanton, CA, USA) or the Bosphore HCV Quantification Kit V2 (Anatolia Geneworks, Turkey) with a detection limit of 15 IU/mL and 25 IU/mL, respectively.

The primary outcome was the proportion of patients achieving a sustained virological response (SVR), which define as an undetectable HCV viral load at 12 weeks after completion of

therapy. Effectiveness assessments other than SVR12 included: early virological response (EVR) (undetectable serum HCV-RNA at 4 weeks of therapy), virologic breakthrough (detectable HCV-RNA during treatment when previously undetectable) and relapse (detectable HCV-RNA after treatment when previously undetectable at the end of therapy).

The study was carried out with the approval of Hatay Mustafa Kemal University Faculty of Medicine Retrospective Ethics Committee (approval number: 10, date: 13.02.2020). Due to the retrospective design of the study informed consent was not obtained.

## Statistical Analysis

Treatment efficacy analyzes were performed with both modified intention to tract (mITT) and per protocol (PP). PP analysis includes the level of HCV-RNA both post-treatment and after completing 12 weeks of follow-up. For mITT analysis, in addition to the HCV-RNA value measured prior to treatment, patients had to have a measured HCV-RNA value at least in the first month of treatment and all patients whose SVR12 was unknown were accepted as unresponded when conducting mITT analysis. For statistical analysis, IBM SPSS version 23.0 statistical package program (SPSS Inc, Chicago, IL, USA) was used. The compatibility of variables to normal distribution was tested using the Kolmogrov-Smirnov test and histogram. Median and interquartile intervals were used for variables that do not fit the normal distribution.

## Results

In our study, a total of 85 prisoner patients used DAA treatment between 2017-2019. Six of these patients were excluded from the study because they had never used the treatment and did not come to follow-up, and two patients were excluded from the study because their medication was just started. All of the patients were male. The rate of IVDU in HCV positive prisoners was 37.7% (29/77). To evaluate the effectiveness, mITT in 77 cases and PP analysis in 60 cases were used. While SVR was 100% in PP analysis, this rate was 80.5% in mITT analysis.

In our study, the average age of 77 patients who evaluated by mITT efficacy analysis was 30 [interquartile range (IQR): 25-33.5]. Eighteen cases (23.4%) in 2017, 21 cases (27.3%) in 2018, 38 cases (49.4%) in 2019 were included in our study. The number of prisoner patients whose treatment is started by years was shown in Figure 1.

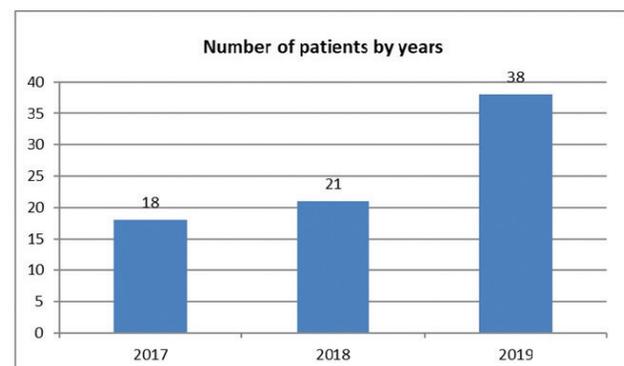


Figure 1. Number of patients by years

The genotype distribution of the patients is as follows; genotype 1a: 5 cases (13%), genotype 1b: 2 cases (2.6%), genotype 2: 7 cases (9.1%), genotype 3: 32 cases (41.6%), genotype 4: 30 cases (39.0%), mixed genotype: 1 case (1.3%). Viral genotype distribution in prisoner patients was shown in Figure 2. The treatments that patients receive are as follows; 22 patients SOF ± RBV (28.6%), 28 patients OBV + PTV/r (36.4%), 7 patients PrOD (OBV + PTV/r + DSV) ± RBV (9.1%), 19 patients glecapravir + pibrentasvir (24.7%), 1 patient SOF + LED (1.3%). RBV (71.4%) was used in 55 cases. No virological exacerbation and relapse were detected during treatment. EVR was obtained in 72 cases (93.5%). Only one case was treatment experienced.

Only 17 of 29 patients with a history of IVDU was achieved SVR. The rate of SVR in patients with IVDU was 17/29 (58.6%). There was a significant difference between with and without IVDU in terms of SVR ( $p=0.000$ ). In our study, headache, bloating, weight loss and insomnia were observed as side effects in patients who were followed-up regularly. Especially in three patients using OBV + PTV/r + DSV ± RBV, minimal aspartate aminotransferase/alanine aminotransferase elevation and isolated bilirubin elevation were detected, but no treatment was discontinued due to serious adverse effects. In our study, liver biopsy was performed in six patients and no cirrhotic patient was detected.

## Discussion

In studies evaluating the response of peg-interferon (IFN) + RBV therapy, SVR at the end of treatment was determined between 28% and 69% in prisoner patients with hepatitis C (1,15,16,17,18,19,20,21,22,23). In the study conducted by Ozger et al. (24), only 33 of the 99 patients who started Peg-IFN + RBV treatment had SVR at the 6<sup>th</sup> month after treatment. DAAs' used in HCV treatment are more effective, reliable and tolerable drugs compared to interferon-based regimens (25). In our study, SVR12 was obtained in 60 of 77 patients whose treatment was started. In patients who completed the treatment, SVR12 was 100%. Although they received DAA treatment, it was thought-provoking that SVR12 was not examined in 17 patients. Second-generation DAAs are a great improvement in the completion of the treatment and follow-up of prisoners, as their short course of treatment is reliable and tolerable (26). However, in our study, the most important reason for not continuing to treatment and follow-up was determined as the fact that prisoners did not come to follow-

up after release. According to the study of Larney et al. (3), the prevalence of anti HCV in prisoners is 26%, while it can be up to 64% in IV drug addicted prisoners. In the same study, while anti HCV was 1.4% in the general population, anti HCV was found to be 16.4% in IV drug addicts (3). In our study, the rate of IVDU in prisoners with HCV infection was 37.6% (29/77). We think that this may be due to the low number of patients and geographical region differences. In the study conducted by Zampino et al. (25), The prevalence of anti HCV in convicted patients reported between 3% and 38% according to geographic region, IV drug use, age, duration of imprisonment, and prisoners' history. The most common genotypes in studies are genotype 1 and 3 (25,27). In Turkey, there are very few studies on prisoner patients. In the study conducted by Keten et al. (28), the most common genotype among prisoners in Turkey is genotype 3(68.1%). In the study of Ozger et al. (24), Genotype 3a is 66.7% (66/99). Unlike the literature, the remarkable result in our study was that genotype 4 was found to be 39% (30/77). However, we found the most common genotype is genotype 3, as 41.6% (32/77). We think that this difference may be due to geographical region difference. Only 17 of 29 patients with a history of IVDU reached SVR-12. SVR-12 was not known in 12 cases. The rate of SVR-12 in patients with a history of IVDU was 17/29 (58.6%). When patients with and without IVDU history were compared in terms of SVR, there was a significant difference. The antiviral treatment response in prisoners is similar to the general population (10,11). Unfortunately, treatment compliance is low in prisoners because treatment follow-up and management are difficult. In our study, it was found that treatment compliance was low, especially in patients with a history of IVDU. The most important reason for not continuing to treatment and follow-up was determined as the fact that prisoners did not come to follow-up after release. Side effects are an important factor affecting treatment results and continuation of the treatment, but in our study, no patient was discontinued their drugs due to drug-related side effects.

## Study Limitations

The limitation of our study is that it is a retrospective study, the data is regional and the number of cases is low.

## Conclusion

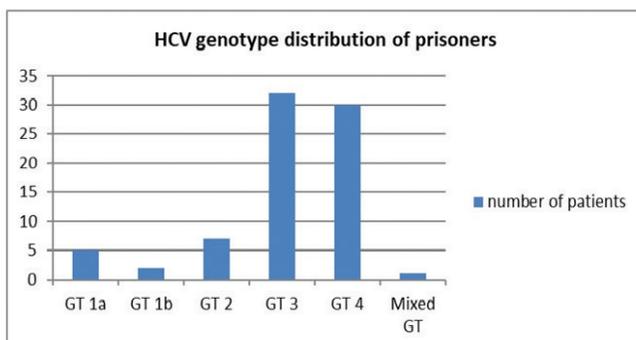
We think that prisoners provide a good opportunity to increase the diagnosis and treatment of HCV infection. We think that the compliance of patients to treatment will increase with the use of second-generation DAA drugs and it is an important step for HCV eradication and we suggest that multicenter studies should be conducted in our country.

## Ethics

**Ethics committee approval:** The study was carried out with the approval of Hatay Mustafa Kemal University Faculty of Medicine Retrospective Ethics Committee (approval number: 10, date: 13.02.2020).

**Informed Consent:** Due to the retrospective design of the study informed consent was not obtained.

**Peer-review:** Externally peer-reviewed.



**Figure 2.** Viral genotype distribution in prisoner patients  
HCV: Hepatitis C virüs, GT: Genotype

### Authorship Contributions

Concept: M.Ç., T.B., Design: M.Ç., T.B., Data Collection or Processing: M.Ç., Analysis or Interpretation: T.B., Literature Search: M.Ç., Writing: M.Ç.

**Conflict of Interest:** The authors declare no conflict of interest.

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