Original Article

Treatment initiation rates of patients with positive anti-hepatitis C virus results in tertiary hospitals in Turkey

Mustafa K Çelen¹, Buket Ertürk Şengel², Şafak Kaya³, Neşê Demirtürk⁴, Alpay Azap⁵, Hüsnü Pullukçu⁶, Esma Eroğlu⁷, Figen Yıldırım⁸, Hüseyin Ş Barut⁹, Esra Zerdali¹⁰, Ayşe Sağmak Tartar¹¹, Ayşe Ö Mete¹², Ahmet M Şahin¹³, Bedia Mutay Suntur¹⁴, Nagehan D Sarı¹⁵, Emel Yılmaz¹⁶, Aslıhan Candevisir¹⁷, Funda Şimşek¹⁸, Dilara İnan¹⁹, Sila Akhan²⁰, Ali Asan²¹, Özgür Günsal²², Onur Ural²³, Mehmet Parlak²⁴, Mehmet Çabalak²⁵, Selçuk Nazık²⁶, Kenan Hızel²⁷, Sami Kınıklı²⁸, Zehra Beştepe Dursun²⁹, Ayşe Batire³⁰, Çağdem Mermutluoğlu¹

¹ Department of Infectious Diseases, Dicle University Medical Faculty, Diyarbakır, Turkey
² Department of Infectious Diseases, Pendik Training and Research Hospital, İstanbul, Turkey
³ Department of Infectious Diseases, Sağlık Bilimleri University Diyarbakır Gazi Yaşargil Training and Research Hospital, Diyarbakır, Turkey
⁴ Department of Infectious Diseases, Afyonkaraşisar Sağlık Bilimleri University Medical Faculty, Afyonkaraşisar, Turkey
⁵ Department of Infectious Diseases and Clinical Microbiology, Ibn-i Sina Research and Application Hospital, Ankara University Medical Faculty, Ankara, Turkey
⁶ Department of Infectious Diseases and Clinical Microbiology, Ege University Medical Faculty, İzmir, Turkey
⁷ Department of Infectious Diseases, Konya Meram State Hospital, Konya, Turkey
⁸ Department of Infectious Diseases and Clinical Microbiology, Antalya Training and Research Hospital, Antalya, Turkey
⁹ Department of Infectious Diseases, Gaziosmanpaşa University Research and Application Hospital, Tokat, Turkey
¹⁰ Department of Infectious Diseases and Clinical Microbiology, Haseki Training and Research Hospital, İstanbul, Turkey
¹¹ Department of Infectious Diseases, Firat University Medical Faculty, Elaziğ, Turkey
¹² Department of Infectious Diseases, Gaziantep University Şahinbey Research and Application Hospital, Gaziantep, Turkey
¹³ Department of Infectious Diseases, Giresun University Prof. Dr. A. İlhan Özdemir Training and Research Hospital, Giresun, Turkey
¹⁴ Department of Infectious Diseases, Adana City Training and Research Hospital, Adana, Turkey
¹⁵ Department of Infectious Diseases and Clinical Microbiology, İstanbul Training and Research Hospital, İstanbul, Turkey
¹⁶ Department of Infectious Diseases and Clinical Microbiology, Bursa Uludağ University Medical Faculty, Bursa, Turkey
¹⁷ Department of Infectious Diseases and Clinical Microbiology, Adana Çukurova University Hospital, Adana, Turkey
¹⁸ Department of Infectious Diseases and Clinical Microbiology, Prof. Dr. Cemil Taşçıoğlu City Hospital, İstanbul, Turkey
¹⁹ Department of Infectious Diseases, Akdeniz University Hospital, Antalya, Turkey
²⁰ Department of Infectious Diseases and Clinical Microbiology, Kocaeli University Research and Application Hospital, Kocaeli, Turkey
²¹ Department of Infectious Diseases, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey
²² Department of Infectious Diseases and Clinical Microbiology, Sağlık Bilimleri University Samsun Training and Research Hospital, Samsun, Turkey
²³ Department of Infectious Diseases, Selçuk University Medical Faculty, Konya, Turkey
²⁴ Department of Infectious Diseases and Clinical Microbiology, Atatürk University Medical Faculty Hospital, Erzurum, Turkey
²⁵ Department of Infectious Diseases, Mustafa Kemal University Research and Application Hospital, Hatay, Turkey
²⁶ Department of Infectious Diseases, Kahramanmaraş Sütçü İmam University Research and Application Hospital, Kahramanmaraş, Turkey
²⁷ Department of Infectious Diseases, Gazi University Medical Faculty Hospital, Ankara, Turkey
Abstract

Introduction: The aim of this national, multicenter, cross-sectional, retrospective chart review study was to determine the proportion of patients in Turkey who received hepatitis C virus (HCV) treatment after receiving positive anti-HCV results during HCV screening.

Methodology: Data related to patients’ demographics, laboratory results, time interval from obtaining a positive anti-HCV result to treatment initiation, specialty of the physician requesting anti-HCV screening, and type of hospital were analyzed.

Results: Among 1,000 patients who received a positive anti-HCV result, 50.3% were male and 78.5% were screened for HCV-RNA. Among HCV-RNA screened patients, 54.8% (n = 430) had a positive result. Among patients who tested positive for HCV-RNA, 72.8% received HCV treatment in line with their positive anti-HCV results. The median time from obtaining a positive anti-HCV result to initiation of HCV treatment was 91.0 days (interquartile range 42.0 to 178.5). Non-surgical branches requested HCV-RNA testing more frequently than surgical branches (p < 0.001). The rate of access to HCV treatment was higher among patients screened in university hospitals than among patients screened in training and research hospitals (p < 0.001).

Conclusions: Our results indicate a higher rate of treatment initiation among patients with HCV infection than is described in the published literature. Furthermore, the time from screening to treatment initiation was considerably shorter compared with other international studies. However, since HCV-RNA testing was not requested in a significant portion of patients with a positive anti-HCV test result, there might be a large patient population with HCV who do not receive treatment.

Key words: Hepatitis C; anti-HCV; screening; treatment; Turkey.


Introduction

The World Health Organization (WHO) estimated in 2015 that 71 million people globally were living with hepatitis C virus (HCV) infection, accounting for 1% of the world population [1]. HCV infection is unevenly distributed in the world. The European and Eastern Mediterranean regions are affected more, but there are variations in HCV infection prevalence across and within countries [1]. In Turkey, HCV infection prevalence rates range between 0.95% and 2.4% [2-5].

Left untreated, hepatitis B virus (HBV) and HCV infection can lead to cirrhosis (720,000 deaths in 2015) and hepatocellular carcinoma (470,000 deaths in 2015) [1]. These long-term complications are life-threatening and account for 96% of the deaths due to viral hepatitis. Mortality from viral hepatitis has increased by 22% since 2000. Unless people with HBV and HCV infection are diagnosed and treated, the number of deaths due to viral hepatitis will continue to increase. However, currently available direct-acting antiviral (DAA) treatments can prevent these complications depending on the disease stage at which treatment is initiated. However, there are country-based variations in terms of accessibility to the treatments [1].

The virus is mainly acquired via percutaneous exposures to infected blood. Unsafe healthcare practices (including unsafe healthcare injections) and injection drug use remain the leading modes of transmission [1,6,7].

Areas with a high rate of HCV infection are located in the Eastern Mediterranean Region (62.5 per 100,000) and the European Region (61.8 per 100,000). In the Eastern Mediterranean Region, the most common cause of transmission of HCV infection is unsafe healthcare injections [8,9]. In the European Region, injection drug use accounts for a significant proportion of infection transmission [10].

According to WHO, only 20% of patients living with HCV infection have been diagnosed and are aware of their infection. Among those diagnosed, only 7.4% were receiving treatment in 2015 [1]. Recently, potent oral short-term antiviral treatment options have become available, and the success rate of these treatments in terms of HCV eradication and cure is reaching > 90% [11]. Well-designed screening policies may help to reduce the rate of undiagnosed and untreated patients. Preoperative hepatitis serology testing is regularly conducted in major surgical clinics; however, it cannot be generalized to all regions within the country. Furthermore, information regarding the results of these serology screenings is available only through sporadic reports (mostly reported as single-center reports), and
multicentral study results that would represent Turkey are not available yet. Among patients who receive positive anti-HCV results during preoperative anti-HCV screening, more than half are neither tested further for HCV-RNA nor notified with their HCV-RNA test results [12]. Therefore, most of these patients remain unaware of their HCV infection and do not receive antiviral treatment, which results in an inaccurate and low diagnosis rate of HCV infection.

The diagnosis and treatment policies in Turkey are undergoing improvements. As per the existing protocol [13], the prescription of treatment requires a report from gastroenterology or infectious diseases specialists working at tertiary health institutions. This report includes information such as HCV-RNA positivity, the presence of cirrhosis, Child-Pugh classification of the cirrhosis, genotype in decompensated cirrhotic patients, previous HCV treatment, and the use of NS5A inhibitors in prior treatment. For treatment-naive or treatment-experienced patients without NS5A inhibitors who are non-cirrhotic or have compensated cirrhosis, the recommended treatments are sofosbuvir/velpatasvir/voxilaprevir or glecaprevir/pibrentasvir. If the patient has decompensated cirrhosis, ledipasvir/sofosbuvir + ribavirin may be prescribed based on the genotype results. In the case of treatment experience with NS5A inhibitors, patients are assessed on an individual basis with aforementioned medications.

In this study, we aimed to determine the rate of patients who received HCV treatment after receiving positive anti-HCV results during HCV screening in Turkey within the last 3 years.

Methodology

This study was designed as a national, non-interventional, observational, multicenter, cross-sectional, retrospective chart review study that included patients screened for anti-HCV.

The study was initiated after obtaining ethics committee approval from Gaziantep University Clinical Research Ethics Committee (reference number 2020/20, 04 November 2020) in conformation with the Declaration of Helsinki, and data collection took place between 24 December 2020 and 22 June 2021. Since this was a retrospective chart review study, obtaining informed consent was not necessary and a waiver of informed consent was obtained from the same ethics committee. A total of 30 tertiary study centers, which were university hospitals or training and research hospitals located in various geographic regions in Turkey, participated in this study. Investigators in the participating study centers retrospectively reviewed the charts of the patients who had undergone screening for anti-HCV for any reason. Adult (≥ 18 years of age) patients who received a positive anti-HCV result between 30 June 2016 and 30 June 2019 were considered eligible for this study. Laboratory result databases of the participating centers were used as the main data source for this study. All eligible patients were identified in each site from the laboratory database according to the inclusion criteria, and the treatment information was obtained from the patients’ charts. Data collection was anonymized, and a code number was assigned to each patient. The investigator or delegated staff entered the available data into the electronic case report form designed for this study.

Patient demographics (e.g., gender, place of residence), laboratory results for HCV screening, including anti-HCV and, where available, HCV-RNA results, the time interval from obtaining a positive anti-HCV result to treatment initiation (if treated), specialty of the physician who requested anti-HCV screening, and type of hospital (university hospital or training and research hospital) were among collected data. In addition, physician specialties were categorized into surgical or non-surgical specialty groups.

To prevent patient selection bias, a patient selection method was defined in the protocol for sites that had a high number of eligible patients. Initially, all patients meeting eligibility criteria were identified at each site in chronological order. If the number of eligible patients in a site exceeded the local limit allowed to enroll per site (n = 33), then the total number of eligible patients was divided by 33 to determine the selection factor (i.e., every third or fourth patient). Then the site continued with enrollment starting with the earliest treated patient using this selection factor until the total number of patients allowed per site was reached.

This study was exploratory in nature, and hypothesis testing was not applicable. Therefore, a formal sample size calculation with the estimation of statistical power was not performed. According to available data from Turkey, 30% of the patients who were detected with positive anti-HCV during screening for any reason and who were not screened for HCV-RNA received HCV treatment only after follow-up efforts of the clinical microbiologists [14]. With this assumption, we planned to enroll 1,000 patients, which would provide a two-sided 95% confidence interval rate of 5.6% (± 2.8%) for this study. Data were mainly analyzed using descriptive statistics. The normality assumption was determined using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Median and
interquartile range (IQR) were reported where a normal distribution was not obtained. The Mann-Whitney U test was used to compare the data of two quantitative groups that did not show normal distribution. Kruskal Wallis test was used to compare the data of three quantitative groups. Fisher's exact test was used for the comparison of two categorical groups. $p < 0.05$ was considered statistically significant. All analyses were performed using the SPSS for Windows, Version 16.0. Chicago, SPSS Inc.

Results

Data from 1,000 patients were included in this retrospective chart review study, and 50.3% of the patients were male. Most patients (82.7%) were residing in cities or towns; only 15.6% were living in rural areas. More than half of the patients ($n = 570, 57.0\%$) were included in the study from university hospitals, whereas 43.0% were included from training and research hospitals.

Nearly 70% of the anti-HCV screening requests were made by the non-surgical specialties. Infectious diseases (33.3%) was the specialty that most frequently requested anti-HCV tests in the non-surgical specialty group, followed by gastroenterology (20.9%) and internal medicine (19.8%). On the other hand, general surgery (27.6%) was the specialty that most frequently requested anti-HCV tests in the surgical group.

Among the 1,000 patients who received a positive anti-HCV test result, 78.5% were further screened for HCV-RNA (Figure 1). More patients were admitted to non-surgical versus surgical branches, and non-surgical branches requested HCV-RNA testing more frequently than surgical branches ($p < 0.001$). HCV-RNA screening rates were similar in university hospitals and training and research hospitals ($p = 0.313$). A statistically significant difference was observed between the ratios of surgical and non-surgical branches requesting anti-HCV screening in different types of hospitals. Non-surgical branches requested anti-HCV screening more frequently in training and research hospitals ($p = 0.001$). Among patients screened for HCV-RNA, 54.8% ($n = 430$) had a positive result (Figure 1). The proportion of patients with a positive HCV-RNA result was higher among patients screened by physicians in the non-surgical group ($p = 0.001$). The ratio of patients with positive HCV-RNA results was similar in university hospitals and training and research hospitals ($p = 0.663$).

Among patients testing positive for HCV-RNA, 72.8% (Figure 1) received HCV treatment in line with their positive anti-HCV test result. Considering all eligible patients with a positive anti-HCV test, this percentage corresponded to 31.3%. No statistical difference was detected in terms of access to treatment in patients screened by physicians in the surgical or non-surgical group ($p = 0.051$). Frequencies of screening and treatment of the patients according to the screening departments within the surgical branches and non-surgical branches. Within the surgical branches, 49.0% of the patients who received treatment were screened in the general surgery branches.

![Figure 1](image-url) Distribution of enrolled patients with positive anti-HCV test results.

Table 1. Frequency of screening and treatment of the patients according to the branches and hospital type.

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>$p$ value$^\dagger$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screening for HCV-RNA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical branches</td>
<td>192 (61.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non-surgical branches</td>
<td>593 (86.2)</td>
<td>0.313</td>
</tr>
<tr>
<td>Training and research hospitals</td>
<td>331 (77.0)</td>
<td>0.663</td>
</tr>
<tr>
<td>University hospitals</td>
<td>454 (79.6)</td>
<td></td>
</tr>
<tr>
<td><strong>HCV-RNA positivity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical branches</td>
<td>80 (41.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non-surgical branches</td>
<td>350 (59.0)</td>
<td>0.663</td>
</tr>
<tr>
<td>Training and research hospitals</td>
<td>178 (53.8)</td>
<td></td>
</tr>
<tr>
<td>University hospitals</td>
<td>252 (55.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Receiving HCV treatment in line with positive results</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical branches</td>
<td>51 (63.8)</td>
<td>0.051</td>
</tr>
<tr>
<td>Non-surgical branches</td>
<td>262 (74.9)</td>
<td></td>
</tr>
<tr>
<td>Training and research hospitals</td>
<td>103 (57.9)</td>
<td></td>
</tr>
<tr>
<td>University hospitals</td>
<td>210 (83.3)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

$^\dagger$ Fisher’s exact test; HCV: hepatitis C virus.
department, whereas only 2.0% of the patients who received HCV treatment were screened in the department of ear, nose, and throat surgery. Within the non-surgical branches, 46.2% of the patients receiving HCV treatment were screened in the infectious diseases department. Among patients who had access to HCV treatment, the lowest rate of access to treatment within non-surgical branches was observed in chest diseases, endocrinology, family medicine, and oncology departments. Considering the type of hospital, the rate of access to HCV treatment was higher in patients screened in a university hospital than in patients screened in a training and research hospital ($p < 0.001$).

The median time from obtaining a positive anti-HCV result to initiation of HCV treatment was 91.0 days (IQR 42.0 to 178.5). Time from anti-HCV screening to treatment initiation was categorized according to the physician’s specialty, and no statistical difference was observed in terms of access to HCV treatment among patients who were examined by different specialties ($p = 0.230$). With a similar categorization for patient residence, no statistical difference was observed in terms of access to HCV treatment among patients who were living in different residential categories such as city/town, village/rural area, or closed community areas ($p = 0.250$, Table 2). No statistical difference was detected in terms of time to reach HCV treatment in patients screened by physicians in the surgical or non-surgical group ($p = 0.942$, Table 2). However, the time to reach HCV treatment was shorter in patients screened in university hospitals than in those screened in training and research hospitals (median 70 vs. 98 days, $p = 0.006$, Table 2).

**Discussion**

In this study, we evaluated the rate of initiation of HCV treatment in patients who received positive anti-HCV results during routine anti-HCV screening for any reason. Among patients with a positive anti-HCV test, 31.3% received HCV treatment. HCV-RNA was tested in 78.5% of patients who had a positive anti-HCV result; among patients with active HCV infection, 72.8% received treatment for HCV.

HCV infection is one of the most common causes of liver cirrhosis and hepatocellular carcinoma (HCC), which has an insidious course because it is asymptomatic in its early stages, and 60%-80% of the infected cases become chronic. Globally, 27% of cirrhosis cases and 25% of HCC cases are caused by HCV infection [15]. Studies have shown that HCV is the second most common cause of both liver cirrhosis and HCC in Turkey [16,17]. Today, HCV infection is a disease that can be successfully treated. With the use of DAA drugs, the success rate in the treatment of HCV infection has improved tremendously [18]. When the disease is caught at earlier stages, infected patients benefit more from the HCV treatment [19]. Published studies also indicate that HCV eradication with the use of DAA drugs reduces not only hepatic complications but also the risk of cardiovascular disease and has a positive effect on glycemic control [20,21].

The WHO aims to reduce the number of new cases of HCV by 90% and mortality due to HCV by 65% worldwide by 2030 [22]. In general, the group of patients waiting to be treated is much more than those who receive treatment. Studies show that 50%-80% of patients with HCV infection are not diagnosed, and < 20% of those who are diagnosed receive appropriate treatment [23]. Similarly, treatment initiation was reported as 21% in a Danish study conducted in patients with chronic HCV infection [24]. In our study, a higher percentage of patients (31.3%) were able to initiate HCV treatment after obtaining a positive anti-HCV result, which could be due to the high number of patients who were screened and followed up in infectious disease and gastroenterology departments.

A similar retrospective chart review study recently conducted in Mersin, Turkey, included 1,118 patients who tested positive for anti-HCV, among which, 35% were screened in gastroenterology, 37% were screened in infectious diseases, and 28% were screened in other departments. Treatment was initiated in 91% of the

<table>
<thead>
<tr>
<th>Branch type/ geographical region/ type of hospital</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
<th>Median</th>
<th>Q1-Q3</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>313</td>
<td>157.8</td>
<td>185.3</td>
<td>7.0</td>
<td>917.0</td>
<td>91.0</td>
<td>42.0-178.5</td>
<td>-</td>
</tr>
<tr>
<td>Surgical branches</td>
<td>71</td>
<td>157.0</td>
<td>183.4</td>
<td>14.0</td>
<td>693.0</td>
<td>91.0</td>
<td>35.0-175.0</td>
<td>0.942†</td>
</tr>
<tr>
<td>Non-surgical branches</td>
<td>242</td>
<td>158.0</td>
<td>186.3</td>
<td>7.0</td>
<td>917.0</td>
<td>91.0</td>
<td>42.0-182.0</td>
<td>-</td>
</tr>
<tr>
<td>City/town</td>
<td>265</td>
<td>21.6</td>
<td>25.8</td>
<td>1.0</td>
<td>131.0</td>
<td>11.0</td>
<td>5.00-11.00</td>
<td>0.250‡</td>
</tr>
<tr>
<td>Village/rural area</td>
<td>46</td>
<td>27.8</td>
<td>30.1</td>
<td>2.0</td>
<td>99.0</td>
<td>16.0</td>
<td>6.00-39.00</td>
<td>-</td>
</tr>
<tr>
<td>Closed community areas</td>
<td>2</td>
<td>27.0</td>
<td>25.5</td>
<td>9.0</td>
<td>45.0</td>
<td>27.0</td>
<td>9.00 - NA</td>
<td>-</td>
</tr>
<tr>
<td>Training and research hospitals</td>
<td>110</td>
<td>174.4</td>
<td>187.3</td>
<td>14.0</td>
<td>917.0</td>
<td>98.0</td>
<td>63.0-203.0</td>
<td>-</td>
</tr>
<tr>
<td>University hospitals</td>
<td>203</td>
<td>148.8</td>
<td>184.1</td>
<td>7.0</td>
<td>693.0</td>
<td>70.0</td>
<td>35.0-161.0</td>
<td>0.006‡</td>
</tr>
</tbody>
</table>

†Data were available for 313 patients; ‡Mann-Whitney U test; §Kruskal-Wallis test. HCV: hepatitis C virus; max: maximum; min: minimum; Q1: first quartile; Q3: third quartile; SD: standard deviation.
patients identified in the gastroenterology department [25]. This result shows a high rate of treatment initiation in the gastroenterology department and might be a possible reason for obtaining the high rate of treatment initiation in our study since 37% of our patients were screened in gastroenterology and infectious diseases departments. Gastroenterology and infectious diseases are the primary departments for screening HCV infection in Turkey, and in our study, the overall treatment initiation rate in these two departments is 51.2%.

A recent single-center study conducted in Istanbul, Turkey, investigated treatment responses for chronic HCV infection. Among 1,808 patients with positive anti-HCV results, HCV-RNA was tested in 1,286 (71%) patients, and 23% of the patients (n = 291) had positive HCV-RNA results. Among these patients, only 44% (n = 129) received treatment for HCV [26]. Results of similar studies conducted in Turkey indicate that HCV-RNA was not investigated in 30%-40% of the patients who had positive anti-HCV results [27,28]. Investigation of HCV screening in a tertiary care hospital in Turkey showed that 95 patients were positive for anti-HCV and that HCV-RNA was not investigated in 47% of these patients [29]. Similarly, the results of another Turkish study showed that HCV-RNA was not tested in 51% of the patients who had positive anti-HCV results [30]. Furthermore, the studies reported higher rates of HCV-RNA negativity, ranging from 70% to 80%, among the patients with positive anti-HCV results [26,27,30]. Results of these studies may suggest that diagnosis and treatment rates of HCV infection are not sufficient in Turkey. In another study by Lee et al., 53.5% of the patients had positive HCV-RNA results, and the authors suggested considering transaminase and albumin levels in conjunction with anti-HCV results to enhance the prediction of HCV infection [31]. In contrast, our study observed a lower rate of HCV-RNA negativity (45%). HCV-RNA negative results with reactive antibody may indicate either a past HCV infection, or a false-positive antibody test. However, due to the lack of enzyme and albumin levels in our study, further investigation is not possible.

We detected higher screening and treatment ratios in our study. In the present study, among 1,000 patients with a positive anti-HCV result, 78.5% were screened for HCV-RNA, 31.3% received HCV treatment, and among patients with active HCV infection, 72.8% received treatment for HCV. Nevertheless, it is crucial to investigate the reasons behind patients missing the screening and treatment. In a recent single-center study, a total of 3,249 patients with positive anti-HCV results were evaluated, and among the subset of patients who tested positive for HCV-RNA (n = 899), only half of them were initiated on treatment [32]. The authors of the study highlighted that treatment failure could be attributed to various patient-related factors, including comorbidities, non-compliance with clinic appointments, or refusal of treatment. Furthermore, inadequate follow-up of test results by physicians and a lack of proper communication to patients regarding their positive results should also be considered. While there have been promising improvements in reimbursement conditions in Turkey, the process of assessing patients and initiating treatment were time-consuming, primarily due to the limited availability of medications in various centers, as well as the reimbursement being conditioned based on genotype results in patients with decompensated cirrhosis.

Another retrospective chart review study conducted in the United States in 2019 included 8,407 individuals with chronic HCV infection [33]. Of these patients, 830 initiated treatments with a DAA agent, whereas 7,577 did not, suggesting a DAA treatment initiation rate of 9.9%. The median time to initiate DAA treatment was reported as 300 days. We detected a higher treatment rate and shorter time to treatment in our study (median 91 days). However, this difference could be due to different healthcare systems present in Turkey and the United States. In the United States, despite the benefits of medicare drug coverage, studies have shown that the patients can experience escalating financial burdens associated with the HCV treatments [34]. While the exact payment figures cannot be determined in Turkey, the coverage of HCV medications through reimbursement may offer an advantage in assessment of the patients. Following categorization of screening hospitals into university or training and research hospitals, we found that the time to treatment was shorter in university hospitals (median 70 days).

Conclusions

In conclusion, our study results indicate a higher rate of treatment initiation among patients with HCV infection compared with the data in most of the published literature. Furthermore, we found that the time from screening to treatment initiation was considerably shorter compared with other international studies. We did not investigate why treatment is initiated earlier in university hospitals than in training and research hospitals since this was not among the objectives of this study. However, further research investigating factors affecting treatment initiation may help to shorten the time to treatment initiation. Despite
these promising results, there might be a considerably
large population of patients with HCV who do not
receive HCV treatment because further HCV-RNA
testing is not requested in a significant portion of
patients who test positive for anti-HCV. Raising
awareness among healthcare professionals and the
general population about HCV screening and treatment
options, ensuring that individuals are receiving proper
counseling, establishing effective communication
channels with patients, and continued improvement of
reimbursement policies are key recommendations for
the future.

Acknowledgements
This study was funded entirely by AbbVie. Statistical
analysis, writing support, and editing services in the
development of this manuscript were provided by
MonitorCRO (Istanbul, Turkey) and funded by AbbVie.
The design and study conduct for the LOST-C study were
provided by AbbVie. AbbVie participated in the
interpretation of data, review, and approval of the
publication. All authors, except Çiğdem Mermutluoğlu,
received payments from AbbVie to participate in this study.

Author contributions
All authors contributed equally for the design, data
collection, analysis, preparation, and review of this
manuscript.

References
2. Örmeçi N, Malhan S, Balık I, Ergör G, Razavi H, Robbins S
(2017) Scenarios to manage the hepatitis C disease burden
and associated economic impact of treatment in Turkey. Hepatol
3. Yıldırım M, Çakır S, Geyik MF, Özdemir D, Güclü E, Çakır
M (2014) Seroprevalences and associated risk factors of
factors for higher anti-HCV positivity in a border city in
southern Turkey with unique population characteristics. Turk J
5. Thomas DL, Mahley RW, Badur S, Palaoglu E, Quinn TC
Screening for hepatitis C virus infection in adults: a systematic
review for the US Preventive Services Task Force. Ann Intern

Development and maintenance of a community-based hepatitis
8. Mohsen A, Bernier A, LeFouler L, Delarocque-Astagneau E,
El-Daly M, El-Kafrawy S, El-Mango S, Abdel-Hamid M,
Hepatitis C virus acquisition among Egyptians: analysis of a
10-year surveillance of acute hepatitis C. Trop Med Int Health
Unsafe injections and the transmission of hepatitis B and C in
a periurban community in Pakistan. Bull World Health Organ
78: 956-963.
10. Mitruka K, Tsetsrvadze T, Butashvili M, Gamkrelidze A,
Sabelashvili P, Adamia E, Chokheli M, Drobeniuc J, Hagan L,
Harris AM, Jiaqia T, Kasradze A, Ko S, Qerashvili V,
Sharvadze L, Tskhomelidze I, Kvartskhelia V, Morgan J,
classification program - Georgia, April 2015. MMWR Morb
11. Pham TT, Keast SL, Farmer KC, Thompson DM, Ratbun RC,
Nesser NJ. Holderread BP, Skrepek GH (2018) Sustained
virologic response and costs associated with direct-acting
antivirals for chronic hepatitis C infection in Oklahoma
Medicaid. J Manag Care Spec Pharm 24: 664-676. doi:
12. Yoshioka N, Okumura A, Yamamoto Y, Yamaguchi K, Kaga
A, Yamada K, Hirosaki T, Ishikawa D, Kunii S, Watanabe K,
Utsunomiya S, Hayashi K, Ishigami M, Goto H, Hirooka Y
(2017) Promoting notification and linkage of HBs antigen and
anti-HCV antibody-positive patients through hospital alert
system. BMC Infect Dis 17: 330. doi: 10.1186/s12879-017-
2438-1.
13. Social Security Institution (2022) Amendments to healthcare
implementation communication. Available: https://www.resmigazete.gov.tr/eskiler/2022/06/20220601-
evaluation of patients who were found positive for anti HCV
antibodies and were lost to follow-up with laboratory data. In:
4. National Clinic Microbiology Congress - 2017 Abstract PS-
Turkish].
Z, Gumussoy M, Er R, Ozercan M, Duman S, Toruner M,
Cinar K, Soykan I, Beyler AR, Ozkan H (2021) Natural history
of cirrhosis: changing trends in etiology over the years. Dig Dis
17. Arhan M, Akdoğan M, İbiş M, Kaçar S, Tunç B,
Şaşmaz N (2009) Data of hepatocellular carcinoma from a
single center: a retrospective study. Akad Gastroenteroloji
Derg 8: 18-23. [Article in Turkish].

Çelen et al. – Treatment initiation in patients with HCV

447


Corresponding author
Çiğdem Mermutluoğlu, MD
Department of Infectious Diseases, Dicle University, 21280, Sur, Diyarbakır, Turkey.
Tel: +90 (505) 225 27 00
Fax: +90 (412) 241 10 00
Email: cigdemmermut@gmail.com

Conflict of interests: Mustafa K Çelen has served as a consultant for AbbVie, Gilead, MSD, Pharmactive, İlko, GSK, and Abdi İbabrahim; as a speaker for Gilead, MSD, Pharmactive, İlko, and GSK; and has received research funding from AbbVie, Gilead, MSD, and GSK. Bukuert Ertük Şengel has served as a consultant for AbbVie, and has received research funding from AbbVie. Şafak Kaya has served as a consultant for AbbVie; as a speaker for Gilead, Abdi İbabrahim, and Pharmactive; and has received research funding from AbbVie. Neşe Demirtürk has served as a speaker for Nobel, Gilead, and Abdi İbabrahim; and has received research funding from AbbVie. A. Ayşap Azap has served as a consultant for AbbVie, and has received research funding from AbbVie. Hüsnü Pulkuçu has served as a consultant for AbbVie, Gilead, GSK, and MSD; as a speaker for AbbVie, Gilead, GSK, İlko, and MSD; and has received research funding from AbbVie. Esma Erdoğlu has received research funding from AbbVie. Figen Yıldırım has served as a consultant for AbbVie, Gilead, GSK, Santa Farma, and İlko; as a speaker for Gilead, GSK, Santa Farma, and İlko; and has received research funding from AbbVie. Hüseyin Ş Barut has received research funding from AbbVie. Esra Zerdali has served as a consultant for Gilead, GSK, and MSD; as a speaker for Gilead, İlko, and GSK; and has received research funding from AbbVie, and Gilead. Ayşe Sağmak Tartar has served as a speaker for Pharmactive, Pfizer, and Astellas; and has received research funding from AbbVie. Ayşel Ö Mete has served as a consultant for AbbVie, and Gilead; has served as a speaker for AbbVie, Gilead, Pharmactive, Pfizer, GSK, and Abdi İbabrahim; has received research funding from AbbVie, and Gilead. Esma Erdoğlu has received research funding from AbbVie, Pfizer, and Neutec; and has received congress participation support from Gilead, and Pfizer. Ahmet M Şahin has served as a consultant and a speaker for AbbVie, and has received research funding from AbbVie. Bedia Mutay Suntur has served as a speaker for AbbVie, and has received research funding from AbbVie. Emel Yılmaz has served as a speaker for AbbVie, İlko, and Abdi İbabrahim; and has received research funding from AbbVie. Aslıhan Candevir has served as a consultant and a speaker for AbbVie, Gilead, Pfizer, GSK, Pharmactive, and Santa Farma. Funda Şimşek has served as a consultant and speaker for Gilead, and has received research funding from AbbVie. Dilara İnan has served as a consultant for Gilead, GSK, and MSD; as a speaker for AbbVie, Gilead, İlko, and MSD; and has received research funding from AbbVie. Sıla Akhan has served as a consultant for AbbVie, and has received research funding from AbbVie. Ali Asan
has served as a consultant for AbbVie; as a speaker for AbbVie and Gilead; and has received research funding from AbbVie, and Gilead. Özgür Günal has served as a consultant and a speaker for AbbVie, and has received research funding from AbbVie. Onur Ural has received research funding from AbbVie. Mehmet Parlak has received research funding from AbbVie. Mehmet Çabalah has served as a consultant and a speaker for AbbVie, Gilead, MSD, and Pharmactive; and has received research funding from AbbVie. Selçuk Nazik has served as a consultant for AbbVie; as a speaker for İlko; and has received research funding from AbbVie. Kenan Hızel has received research funding from AbbVie. Sami Kınıklı has served as a speaker for Gilead, and has received research funding from AbbVie. Zehra Beştepe Dursun has received research funding from AbbVie. Ayşe Batrel has served as a consultant and a speaker for Gilead, Pfizer, and Santa Farma; and has received research funding from AbbVie. Çiğdem Mermutluoğlu has no conflict of interest to declare.