Impact of the COVID-19 Pandemic on the Management of Chronic Hepatitis C Infection: A Cross- Sectional Study

COVID-19 Pandemisinin Kronik Hepatit C Enfeksiyonunun Yönetimine Etkisi: Kesitsel Bir Çalışma

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ABSTRACT

Objectives: The coronavirus disease-2019 (COVID-19) pandemic have affected the chronic hepatitis elimination program globally. This study aimed to evaluate the effect of the COVID-19 pandemic on the rate of requesting hepatitis C virus (HCV) testing and the rate of initiating chronic HCV treatment, follow-up, and completion and compliance of treatment of chronic hepatitis C patients.

Materials and Methods: Between January 01, 2018 and December 12, 2021, the number of anti-HCV and HCV-RNA test requests and patients who started treatment were retrospectively evaluated. The rates of follow-up treatment compliance and treatment completion of the patients who were treated in the ınfectious diseases clinic were analyzed on a year basis.

Results: A positive anti-HCV test was found in 4,468 of 301,999 patients who underwent anti-HCV testing in 4 years. Significant reductions were observed in all three pandemic waves in both anti-HCV and HCV-RNA test requests. The data of 213 treated patients were analyzed. While the most common risk factor was intravenous drug usage, genotype 3 was determined to be the dominant genotype. While the rates of regular outpatient follow-up and completion of treatment were the lowest in 2020 (63.6% in both), no significant difference was found between years (p=0.118, p=0.087, respectively).

Conclusion: The pandemic affected the management of chronic hepatitis C. National microelimination programs should be rearranged to meet the elimination targets. In addition to the at-risk population, the whole population should be screened and training for awareness raising should be planned again for both society and physicians.

Keywords: Hepatitis C virus, chronic hepatitis C, COVID-19, management, elimination

ÖZ

Amaç: Koronavirüs hastalığı-2019 (COVID-19) salgını, küresel olarak kronik hepatit eliminasyon programını etkilemiştir. Bu çalışma ile, COVID-19 pandemisinin hepatit C virüsü (HCV) testi isteme oranına, kronik HCV tedavisine başlama, kronik hepatit C hastalarının takip ve tedavisini tamamlama ve tedaviye uyum oranlarına etkisinin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: 01 Ocak 2018-12 Aralık 2021 tarihleri arasında anti-HCV ve HCV-RNA testi istemi ve tedavi başlanan hastalar retrospektif olarak değerlendirildi. Enfeksiyon hastalıkları polikliniğinde tedavi gören hastaların takip-tedavi uyum oranları ve tedaviyi tamamlama oranları incelenerek yıl bazlı karşılaştırma yapıldı.

Bulgular: Dört yılda anti-HCV testi yaptıran 301.999 hastanın 4.468'inde anti-HCV testi pozitif bulundu. Hem anti-HCV hem de HCV-RNA test istemlerinde her üç pandemi dalgasında da önemli düşüşler tespit edildi. Tedavi edilen 213 hastaya ait veriler analiz edildi. En sık görülen risk faktörü intravenöz ilaç kullanımı iken, baskın genotip olarak genotip 3 saptandı. Poliklinikten düzenli takip ve tedaviyi tamamlama oranları 2020 yılında en düşük iken (her ikisinde de; %63,6) yıllar arasında anlamlı fark bulunmadı (sırasıyla; p=0,118, p=0,087).

Sonuç: Pandemi, kronik hepatit C yönetimini etkilemiştir. Ulusal mikro-eliminasyon programlarının eliminasyon hedeflerine ulaşacak şekilde yeniden düzenlenmesi gereklidir. Risk altındaki popülasyonun yanı sıra tüm popülasyon taranmalı ve hem toplum hem de hekimler için bilinçlendirme amaçlı eğitimler tekrar planlanmalıdır.

Anahtar Kelimeler: Hepatitis C virüs, kronik hepatit C, COVID-19, yönetim, eliminasyon

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Introduction

Chronic hepatitis C virus (HCV) infection is one of the leading causes of chronic liver disease. It is estimated that around 71 million individuals worldwide are chronically infected with HCV (1). The coronavirus disease-2019 (COVID-19) pandemic has seriously affected the global health system, and it has been determined that programs related to the prevention and control of infectious diseases have been seriously affected all over the world (2,3). One of the affected prevention programs is the chronic HCV infection elimination program. The World Health Organization (WHO) has published a global action plan for the prevention and control of viral hepatitis, aiming to prevent the transmission of hepatitis viruses, reduce complications and deaths related to viral hepatitis, improve patient care, and reduce the socio-economic negative effects of viral hepatitis in social areas (4). In May 2016, WHO established a 2016-2021 global health sector strategy on viral hepatitis. With the introduction of direct-acting antivirals (DAA), the global health sector strategy will reduce the risk of new HCV infections by 80%, HCV-related deaths by 65%, the diagnosis rate from 5 to 80%, and the rate of eligible patients to be treated from 1 to 80%.

The main elements of a successful strategy to combat viral hepatitis are prevention measures, appropriate screening, and surveillance practices that allow timely and accurate diagnosis. The American Centers for Disease Prevention and Control recommends that pregnant women be screened for hepatitis C at every pregnancy and at least once in a lifetime for all adults aged 18 years and older in areas with HCV-RNA positivity ≥0.1% (5). Since vaccine has not yet been developed for HCV, it is important to increase the diagnosis rate for elimination and evaluate patients in terms of treatment. This may lead to higher morbidity and mortality rates in individuals living with undiagnosed HCV during the pandemic, which may later be diagnosed at later stages of the disease and complications cannot be avoided (6). In addition, individuals with undiagnosed HCV continue to be a source of transmission, resulting in both patient burden and increased cost. To catch up with the pre-pandemic period, a systematic approach and more effort should be made by increasing the screening and treatment targets by 200% (7).

In this study, we aimed to evaluate the effect of the COVID-19 pandemic on the rate of requesting anti-HCV and HCV RNA tests and the rate of initiating chronic HCV treatment, follow-up, and completion of treatment.

Materials and Methods

Study Design and Patient Selection

Between January 01, 2018 and December 12, 2021, the patients whose anti-HCV test was studied in the laboratories of our hospital were evaluated. Our hospital is a tertiary training and research hospital with 1,550 beds, and chronic hepatitis C treatment is carried out in certain centers in our country, and one of these centers is our hospital. The number of anti-HCV test requests, the number of HCV-RNA tests requested from those with a positive anti-HCV test, and the number of treatments started from those with a positive HCV-RNA test were obtained by retrospective screening through the hospital automation system. The data were evaluated annually and monthly during the study period. Outcomes of adult patients aged 18 years and older who applied to the ınfectious diseases and clinical microbiology outpatient clinics in the same period and were treated with positive anti-HCV and HCV-RNA were evaluated. Compliance with the follow-up periods and treatments and the sustained virological responses (SVR) of the patients were investigated.

Definitions

The "SVR" was defined as an undetectable HCV-RNA level in serum at 12 weeks after the completion of treatment (8). Patients who did not apply to the monthly outpatient clinic control during the treatment and after completion of treatment (on months 3 and 6) were considered as "not follow-up".

Data Collection

Data regarding the patients' demographical, clinical, and laboratory characteristics, comorbid status, treatment regimens, and outcomes were obtained by retrospective review of electronic patient records.

Statistical Analysis

The data were analyzed using SPSS Statistics version 22.0 software (IBM Corp, Armonk, NY, USA). Continuous variables were evaluated for the normal distribution using the Shapiro-Wilk test. Categorical variables were expressed as frequency (n) and percentage (%), continuous variables that met the assumptions for parametric tests were presented as mean and standard deviation, and those that did not were presented as median, minimum, and maximum values. Chi-square and Fisher's exact significance tests were used in the analysis of categorical variables.

Results

The Effect of the COVID-19 Pandemic on Anti-HCV and HCV-RNA Tests

Anti-HCV testing was performed on a total of 301,999 patients, and 4,468 of them were found to be positive in 4 years. It was determined that 4,256 (95.3%) of the anti-HCV-positive patients were tested for HCV-RNA. It was found that 383 of those with 886 positive HCV RNA results had started treatment. When evaluated on a yearly basis, it was found that the rate of requesting anti-HCV and HCV-RNA and starting treatment, which increased in 2019, decreased in 2020 with the pandemic (Figure 1). Details of monthly requested anti-HCV and HCV-RNA test for 4 years are shown in Figure 2, 3. When the anti-HCV test request was evaluated, it was determined that the number of tests started to decrease in March 2020, when the first wave of the pandemic started in Turkey. The lowest rates were observed in April and May 2020. While a decrease was observed in November and December 2020 when the 2nd wave started, it was seen to have an increasing trend again in January 2021. Between May and July 2021, when the 3rd wave of the pandemic was experienced and the Delta variant dominated, there was a decreasing trend again (Figure 2). When HCV-RNA test request rates were evaluated, it was found that there was a sharper decrease than the decrease observed in anti-HCV during the same time frame (Figure 3).

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Figure 1. Evaluation of anti-hepatitis C virus (HCV), HCV-RNA test request, HCV-RNA test positivity, and chronic hepatitis C treatment initiation rates by years

*HCV-RNA was positive in 263 patients in 2018, 316 in 2019, 169 in 2020, and 212 in 2021. Patients who died before the test result and who could not start antiviral treatment because of taking immunosuppressive therapy were excluded
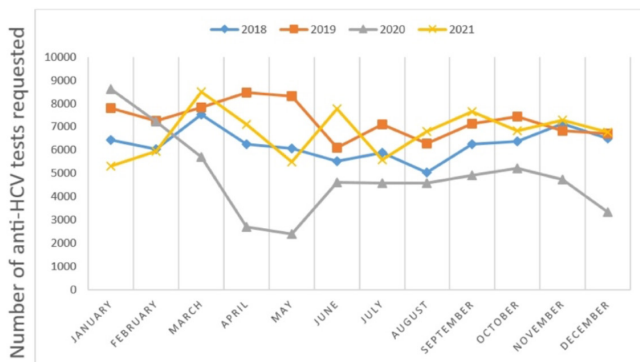
Figure 2. Monthly evaluation of anti-HCV test requests for 4 years

HCV: Hepatitis C virus
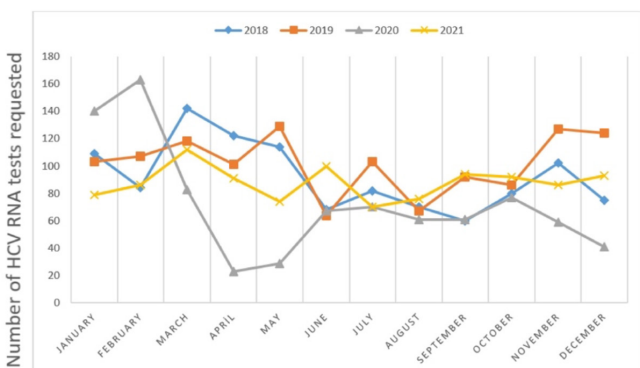
Figure 3. Monthly evaluation of HCV-RNA test requests for 4 years

HCV: Hepatitis C virus

Effect of the COVID-19 Pandemic on Treatment Management

The data of 213 patients who were treated in the infectious diseases and clinical microbiology clinic were analyzed. The median age of the patients was 30 (18-84) and 180 (4.5%) of them were male. The most common comorbid diseases were hypertension in 29 (13.6%) patients, chronic pulmonary disease in 16 (7.5%), and diabetes mellitus in 14 (6.6%). Intravenous drug usage was found to be the most common risk factor (n=151, 70.9%). The transmission route of 41 (19.2%) patients was unknown. Of the 213 patients, 151 (70.9%) were intravenous drug users (IVDUs) and 63 (29.6%) were prisoner individuals (Table 1). 40 (65.6%) patients in 2018, 69 (80.2) patients in 2019, 10 (90.9%) in 2020, and 32 (58.2) patients in 2021 were IVDU. When the genotype distributions were examined, it was determined that 93 (43.7%) patients were genotype 3, 47 (22.1) patients were genotype 1B, 29 (13.6%) were genotype 2, and 21 (9.9%) were genotype 1A. Infection with two different genotypes was detected in 22 patients. In one patient, there were 3 different genotypes as 1A, 2, and 3.

When the rates of compliance with the regular outpatient clinic controls of the patients whose treatment was initiated were analyzed yearly, it was found that it was at the lowest level in 2020 compared to other years (63.6%). However, no statistically significant difference was found between years in compliance rates (p=0.118). When the rate of completion of antiviral treatment was evaluated, there was no statistically significant difference between years (p=0.087), while the rate was lower in 2020 (63.6%) compared to other years (Table 2).

Discussion

Before the COVID-19 pandemic, the national elimination program in our country was created with the joint action of the Ministry of Health of the Republic of Turkey and associations, and in this context, practices such as awareness training for family physicians and screening of prisoners were initiated. In 2019, it was observed that the effects of these practices emerged, and increases in the rate of diagnosis and treatment were obtained (9). The hepatitis elimination program has been disrupted because of COVID-19 causing a major worldwide epidemic, and the vast majority of healthcare practices and opportunities are being used to combat this disease. With the COVID-19 pandemic, the delay in the diagnosis and treatment of hepatitis C is predicted to cause approximately 44,800 liver cancer and 72,300 HCV-related deaths by 2030 (6).

In our study, the year 2021 was evaluated and the pre-pandemic and early period of the pandemic. Our evaluation is not only based on tests but also on the rates of starting treatment, applying for regular follow-up, and completing treatment. In other words, the management of chronic hepatitis C was evaluated as a whole from a different perspective. Although it is a single center, it is seen that the number of cases included in our study is substantial.

With the introduction of national HCV microelimination programs in 2019, it is obvious that the rates of test requests and treatment initiation increased in our center compared to 2018. In 2020, with the effect of the pandemic, a decrease in test request rates was detected, and the negative effect of the pandemic

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Table 1. Demographic and clinic characteristics of patients treated in infectious diseases clinic (n=213)

The number of patients by year, n (%)	
2018	61 (28.6)
2019	86 (40.4)
2020	11 (5.2)
2021	55 (25.8)
Age, median (minimum-maximum)	30 (18-84)
2018	28 (18-77)
2019	31.5 (20-84)
2020	27 (22-59)
2021	33 (21-83)
Sex, n (%)	
Male	180 (84.5)
Female	33 (15.5)
Transmission route, n (%)	
Opioid/intravenous drug usage	151 (70.9)
Surgical procedure	6 (2.8)
Dental procedure	6 (2.8)
Blood/blood product transfusion	3 (1.4)
Hemodialysis	3 (1.4)
Occupational	3 (1.4)
Unknown route	41 (19.2)
HBV co-infection, n (%)	5 (2.3)
Comorbid diseases, n (%)	
Hypertension	29 (13.6)
Chronic pulmonary disease	16 (7.5)
Diabetes mellitus	14 (6.6)
Coronary artery disease	10 (4.7)
Cardiac failure	4 (1.9)
No comorbidity	167 (78.4)
Treatment, n (%)	
Naive	202 (94.8)
Non-naive	11 (5.2)
The treatment regimen, n (%)	
Glecaprevir + pibrentasvir	133 (62.4)
Sofosbuvir + ribavirin	31 (14.6)
Ombitasvir/paritaprevir/ritonavir + dasabuvir	27 (12.7)
Ombitasvir/paritaprevir/ritonavir + dasabuvir + ribavirin	14 (6.6)
Sofosbuvir + ledipasvir + ribavirin	3 (1.4)
Sofosbuvir + ledipasvir	3 (1.4)
Ombitasvir/paritaprevir/ritonavir + ribavirin	2 (0.9)
The sustained virological response[*], n (%)	
2018	56 (91.8)
2019	75 (84.3)
2020	7 (63.6)
2021	51 (92.7)

[*]The virological response of 4 patients each year could not be evaluated. HBV: Hepatitis B virus

on the diagnosis, treatment, and management of chronic HCV infection has been shown in many studies (10,11,12,13). In the study of Mandel et al. (10), it was shown that there was a serious decrease in the number of anti-HCV and HCV-RNA tests in all three waves of the pandemic. Similar findings were obtained in our study. In particular, the decrease in the number of HCV-RNA tests in the first and second waves of the pandemic was remarkable. Especially in the first wave of the pandemic, the postponement of elective surgical interventions and the low rate of admission to outpatient clinics outside the emergency services are thought to directly affect the number of anti-HCV and HCV-RNA test requests. In another study, Schorr et al. (14) conducted a modeling study on the chronic hepatitis C microelimination program, and they predicted that in one scenario, there might be a 50% increase in HCV-related mortality in 2030, with the decrease in the number of patients to be treated with the effect of COVID-19 in the long term. In a survey conducted by the European Association for the Study of the Liver in Europe and non-European countries, it has been shown that there is a significant decrease in the number of HCV consultations, HCV RNA test requests, and HCV treatment initiation during the pandemic period (15). In a study from our country, it was found that the number of anti-HCV and HCV-RNA tests requested from different clinical disciplines decreased during the COVID-19 period (16).

The pandemic has affected not only the test request for HCV but also the number of patients in whom treatment was initiated and the compliance of patients with treatment (17,18,19). In our study, in which we obtained similar results, the number of patients who received treatment and adherence to treatment, regular outpatient visits, and completion of treatment was found to be lower in 2020, even if there was no statistically significant difference. When we examined the distribution of the ages of the treated patients by years, it was determined that the age range in 2020 consisted of younger patients. In the study of Barutçu et al. (16), HCV test requests were grouped according to age, and it was determined that the number of tests in patients aged 65 and over decreased significantly during the pandemic period (p=0.004). Restrictions and curfews for the 65-year-old and older group in our country for a long time and the elderly patients' unwillingness to apply to the hospital except for emergencies have reduced the number of applications to health institutions. When we evaluate 2021, although it is thought that the pandemic affected 2020, its effects continued in 2021 as well. With the resumption of elective surgeries that could not be performed in 2020, there has been an increase in anti-HCV test requests, but this increase was not reflected in HCV-RNA test requests in 2021. Since the surgical intervention of these patients was prioritized, there was a disruption in requesting HCV-RNA testing and directing the patients to the relevant branches. In the same year, although the HCV-RNA test request was low, the number of patients who started treatment, followed up, and obtained SVR increased, and compliance with treatment was found to be higher. Awareness training was planned to canalize patients with positive anti-HCV results to relevant clinics such as ınfectious diseases and gastroenterology.

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Table 2. Evaluation of patients who started treatment in the ınfectious diseases clinic in terms of regular follow-up and completion of treatment

	The regular follow-up, n (%)	p-value	Completing the treatment, n (%)	p-value
2018, (n=61)	51 (83.6)		54 (88.5)	
2019, (n=89)	69 (80.2)	0.118	71 (82.6)	0.087
2020, (n=11)	7 (63.6)		7 (63.6)	
2021, (n=55)	50 (90.9)		50 (90.9)	

70.9% of the patients we treated consisted of IVDU patients. A study evaluating IVDUs found higher rates of syringe reuse, alcohol consumption, and greater reductions in syringe utility programs and buprenorphine use during the pandemic (20). Therefore, the reflection of the pandemic, especially in IVDUs, is expected to emerge more clearly in the future. The fact is that a significant portion of our patients are prisoners (29.6%) and that they were isolated in solitary cells for 15 days after the hospital examination, especially in the first and second waves of COVID-19. This situation caused these individuals not to want to go to the hospital, and this contributed to the decrease in the number of patients who applied for and received treatment in 2020. Unless the risky behavior was stopped, either the treatment of the patients can not be completed or reinfection were observed. These patients should first be provided with professional support for addiction therapy and cooperate with an experienced psychiatrist/psychiatrist and their family.

Although we were caught unprepared for the COVID-19 pandemic, there are also studies showing that chronic hepatitis C treatment and patient follow-up can be successfully carried out with telemedicine application in this process (21,22). In one of these studies, telemedicine application in the follow-up and treatment of 41 chronic hepatitis C patients during the lockdown period in Romania achieved 100% success in the rate of treatment compliance and SVR. When compared with the results in 2019, it is seen that there is a statistically significant difference in terms of adherence to treatment (p<0.0001) (22). Considering the disruptions experienced in the follow-up and treatment of these patients during the pandemic, similar action plans should be created for adverse situations that may occur in the health system.

Study Limitations

There are some limitations to this study. It was single-centered, retrospective and had a relatively small sample size.

Conclusion

The pandemic had a negative impact on the diagnosis, treatment, and management of chronic hepatitis C, and it was predicted that the planned elimination targets would not be realized until 2030. It is a clear fact that more effort is required to meet the elimination targets. For this, national microelimination programs should be reviewed and rearranged, awareness training should be emphasized again, and the effectiveness of DAA treatments should be emphasized. Both technical and financial support should be provided to the health system in this regard. Conducting surveillance on the whole population as well as on risky groups such as IVDUs and prisoners will achieve the elimination target.

Ethics

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