

Awareness of chronic hepatitis C in the Western Black Sea Region

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Abstract. – OBJECTIVE: Chronic hepatitis C (CHC) can be cured with oral antivirals. Awareness of CHC is a substantial barrier to the World Health Organization's goal of eradicating HCV by 2030. This study aimed at evaluating CHC awareness among different departments in a Western Black Sea Region University Hospital.

PATIENTS AND METHODS: Anti-HCV and HCV RNA test results of all patients admitted to our center for whatever reason and who underwent anti-HCV screening between January 2017 and January 2022 were analyzed. CHC awareness has been defined as the presence of HCV RNA testing for anti-HCV positives.

RESULTS: Of the 63,963 patients who underwent anti-HCV testing, anti-HCV positivity was observed in 2%. HCV RNA was tested in 647 (48.8%) patients who had tested positive for anti-HCV. The HCV RNA was positive in 212 (32.7%) patients tested. Only 66 (29.7%) of those with positive HCV RNA test results had received antiviral therapy. The distribution of HCV RNA testing rates for patients with positive anti-HCV by different departments were as follows: 33% (n=78/232) in medical inpatient clinics, 78% (n=539/685) in medical outpatient clinics, 7% (n=16/223) in surgical inpatient clinics, 7% (n=14/183) in surgical outpatient clinics, and 0% in the emergency department.

CONCLUSIONS: The prevalence of anti-HCV positivity in our region was 2%. Less than half of the patients tested for anti-HCV had HCV RNA testing, and less than a third of the HCV RNA-positive patients received antiviral therapy. To meet the WHO's HCV eradication target by 2030, it is necessary to increase physicians' awareness of CHC.

Key Words:

Chronic hepatitis C, Anti-HCV, HCV RNA testing, Chronic hepatitis C awareness, Chronic hepatitis C eradication.

Introduction

A significant global public health concern, the hepatitis C virus (HCV) is one of the most

common causes of cirrhosis and hepatocellular carcinoma. An estimated 71.1 million chronically infected patients have been reported, accounting for 1% of the worldwide population^{1,2}. Its prevalence and transmission routes vary by country and continent. Moreover, HCV-related deaths will keep rising unless infected patients are recognized and treated appropriately³. In 2016, the World Health Organization (WHO) announced the first worldwide viral hepatitis plan to eradicate HCV, a public health problem, by 2030. The established strategy aims at reducing new HCV infections by 90% and HCV liver-related mortality by 65% and to diagnose and treat 90% of chronically infected people⁴. With current antiviral therapy, more than 95% of people with CHC can be cured. However, a low percentage of patients are diagnosed and treated⁵. Only 20% of CHC patients are aware of their diagnosis, and only 15% of patients with confirmed CHC have received treatment^{1,2}. In fact, only few nations currently have eradication policies, and while the instruments to achieve eradication are accessible, the necessary investments, commitments, and finances are absent⁶.

Anti-HCV antibodies, a serological test that identifies infected people, must first be assessed to determine the presence of HCV infection. If the anti-HCV antibody test is positive, an HCV ribonucleic acid (RNA) test is required to confirm a chronic infection. Approximately 30% of HCV patients resolve the infection spontaneously without treatment, and these patients are persistently positive for anti-HCV antibodies even if they are not infected².

Several factors contribute to the low rate of treatment access. One of the most important is the low awareness of physicians about HCV⁷. Clinicians should know that HCV RNA testing is necessary for diagnosing CHC and perform an HCV RNA test in patients with positive HCV antibody results. However, few studies⁸⁻¹¹ report that

general practitioners (GPs) or even specialists at tertiary care centers do not consider it necessary to screen for HCV-RNA in patients who have positive anti-HCV tests.

This study aimed at reflecting the rate of HCV RNA positivity in patients with positive anti-HCV tests, as well as the percentage of CHC patients who had access to antiviral therapy. Additionally, it aimed at emphasizing physician awareness of the significance of HCV RNA testing and to determine the rates of HCV RNA testing throughout the hospital's different departments.

Patients and Methods

The anti-HCV and HCV RNA test results of all patients admitted to our center for any reason and screened for anti-HCV between January 2017 and January 2022, were analyzed retrospectively. Patients under 18 years of age and repeated tests were excluded from the analysis.

HCV antibody was detected using an ELISA kit (Abbott Laboratories, USA), while two distinct real-time polymerase chain reaction systems – Rotor-Gene 6000 (Corbett Research, UK) and Cobas Taqman (Roche Diagnostic, Basel, Switzerland) were used to quantify HCV-RNA.

Demographic data, such as age and gender of patients with positive anti-HCV tests, were recorded from the hospital database. The proportion of HCV RNA testing in patients who tested anti-HCV positive, as well as the distribution of this test among departments, were evaluated. Additionally, it was documented whether patients with positive HCV RNA tests received direct-acting antiviral therapy. CHC awareness has been defined as the presence of HCV RNA testing for anti-HCV positives and evidence of these patients' access to treatment.

Statistical Analysis

The SPSS (Statistical Package for Social Sciences) version 22 (IBM Corp., Armonk, NY, USA) was employed for statistical assessment. Data were presented as numbers (%), medians (interquartile ranges), or means \pm standard deviations. The χ^2 (Chi-square) test was used to compare categorical data. The Kolmogorov-Smirnov test was utilized to evaluate if the data were normally distributed. Parametric tests (Student's *t*-test) were used to assess normally distributed data. Statistical significance was defined as a *p*-value of less than 0.05.

Ethics Committee

Zonguldak Bulent Ecevit University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee approved the present study (Protocol No.: 2022/07, Approval date: 06/04/2022). The study protocol adheres to the Ethical criteria of the 1964 Declaration of Helsinki.

Results

Between January 2017 and January 2022, 92,785 anti-HCV tests were performed in our tertiary center. 26,486 anti-HCV tests were excluded because of repetition, and 2,336 patients were excluded from the study because under 18. Thus, a total of 63,963 patients were included in the study. Of the 63,963 patients who underwent anti-HCV testing, anti-HCV positivity was observed in 1,325 (2%). HCV RNA was tested in 647 (48.8%) patients who had tested positive for anti-HCV. The HCV RNA test was positive in 212 (32.7%) patients who were tested. Unfortunately, it was determined that only 66 (29.7%) of those with positive HCV RNA test results had received direct-acting antiviral therapy (Figure 1).

The mean age of the overall patient population was 50.55 ± 18.47 . The mean age of anti-HCV-positive patients (62.34 ± 15.92) was significantly higher than that of negative patients (50.30 ± 18.44) ($p < 0.001$). The gender distribution was similar in patients with anti-HCV positive and negative ($p = 0.378$). The mean age of HCV RNA-positive patients (65.81 ± 14.63) was significantly higher than that of negative patients (60.82 ± 13.43) ($p < 0.001$). The HCV RNA test positivity rate

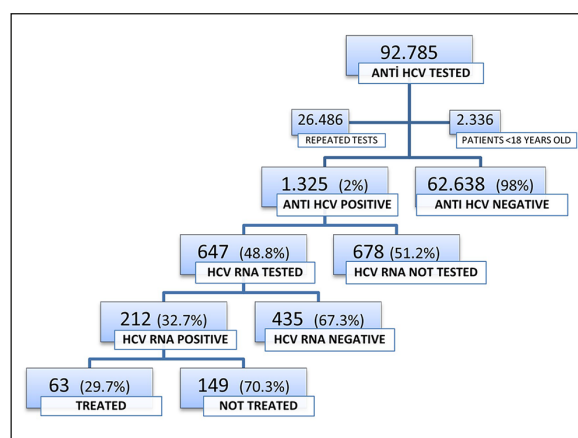


Figure 1. Flow chart of the patients included in the study.

Table I. Demographic characteristics and laboratory parameters of the study participants.

	N (%)	Mean age \pm SD	p-value	Gender		p-value
				Female (%)	Male (%)	
Anti-HCV	63963					
Positive	1,325 (2%)	62.3 \pm 15.9	< 0.001	764 (2.1%)	561 (2%)	0.37
Negative	62,638 (98%)	50.3 \pm 18.4		35,358 (97.9%)	27,280 (98%)	
HCV RNA	647					
Positive	212 (32.7%)	65.8 \pm 14.6	< 0.001	119 (29.1%)	93 (39.1%)	0.009
Negative	435 (67.3%)	60.8 \pm 13.4		290 (70.9%)	145 (60.9%)	
Antiviral Treatment	212					
Treated	63 (29.7%)	70.9 \pm 15.3	0.001	31 (26.1%)	32 (34.4%)	0.186
Not treated	149 (70.3%)	63.6 \pm 13.8		61 (65.6%)	88 (73.9%)	

was significantly higher in male patients than in females ($p=0.009$). The mean age of patients receiving direct-acting antiviral therapy (70.9 \pm 15.3) was significantly higher than the mean age of untreated patients (63.6 \pm 13.8) ($p=0.001$). The gender distribution was similar in the treated and non-treated patients ($p=0.186$) (Table I).

The distribution of HCV RNA testing rates for patients with positive anti-HCV by different departments were as follows: 33% ($n=78/232$) in medical inpatient clinics, 78% ($n=539/685$) in medical outpatient clinics, 7% ($n=16/223$) in surgical inpatient clinics, 7% ($n=14/183$) in surgical outpatient clinics, and 0% ($n=0/2$) in the emergency department (Table II).

Discussion

This is the first study to evaluate the awareness of CHC among different medical departments in the Western Black Sea Region in Turkey. In the present study conducted in a tertiary center, the rate of anti-HCV positivity was 2% in patients who underwent anti-HCV testing for any reason. The hepatitis C virus may cause acute and chronic hepatitis, with symptoms ranging from mild to life-threatening, including liver cirrhosis

Table II. Distribution of HCV RNA testing rates in anti-HCV positive patients by departments.

	Anti-HCV positive	HCV RNA tested
Medical inpatient clinics	232	78 (33%)
Medical outpatient clinics	685	539 (78%)
Surgical inpatient clinics	223	16 (7%)
Surgical outpatient clinics	183	14 (7%)
Emergency department	2	0 (0%)

and malignancy. To diagnose HCV infection, HCV antibody tests must first be performed. Those positive for HCV antibodies should then be tested for HCV RNA². In the TURHEP study¹² from Turkey, the anti-HCV prevalence was reported to be between 0.5% and 1%. The higher rate of anti-HCV positivity in our study can be explained by the fact that the TURHEP study included healthy population data obtained through home visits. Another reason is that, although the TURHEP study included data from 23 provinces throughout Turkey, our analysis contains data reflecting the Western Black Sea Region. WHO recommends that all individuals have access to and be offered HCV testing related to prevention, care, and treatment services in countries where HCV antibody seroprevalence in the general population is high (2% or 5% HCV antibody seroprevalence)⁵. According to the WHO definition, our results show that our region has a high anti-HCV seroprevalence. In a population-based study¹³ conducted in the Central Black Sea region, the prevalence of anti-HCV was determined to be 2.1%, in accordance with our results. About 15 years ago, the seroprevalence of hepatitis C virus was 2.2% in healthy people admitted to the university hospital for routine health examinations in West-Central Turkey for a check-up¹⁴.

In the present study, approximately half (48.8%) of the Anti-HCV positive patients were tested for HCV RNA, and about one-third (32.7%) of the HCV RNA test had a positive result. Only less than one-third (29.7%) of patients with a positive HCV RNA test were treated with direct-acting antiviral therapy. Between 2014 and 2018, the Anti-HCV positivity rate of the patients admitted to a university hospital was 2.3% in the Marmara region. HCV RNA was tested in 71% of those patients and positive in

23%¹⁵. Although that study was conducted in a university hospital, the HCV RNA test rate was higher, the HCV RNA positivity rate lower, and the rate of treated patients higher in that study compared to our research. These differences may be due to regional variations. Unlike our region, the rates of HCV RNA testing were 60.2% and 29%, respectively, in studies^{9,10} conducted in two different tertiary centers in Central Anatolia and Southeast Anatolia. Anti-HCV positivity decreased from 3.1% to 0.6% from 2000 to 2015 and then plateaued, according to a recent study¹¹ conducted in a university hospital that serves as a reference center in Turkey, evaluating the change in hepatitis C awareness throughout the last two decades. Besides, the overall percentage of RNA testing among Anti-HCV positive patients was 53.1% (range, 20-70%), which stabilized at around 50% after 2010. Even in a tertiary reference center, the testing rate for HCV RNA was only half of the anti-HCV-positive patients in the last two decades. Increasing diagnosis and treatment connectivity through cost-effective diagnostic tests and universal access to pan-genotypic direct-acting antiviral therapy is vital to achieving the WHO's 2030 eradication targets. Ideally, HCV infection should be diagnosed in asymptomatic infected patients before developing cirrhosis and cirrhosis-related complications. Early treatment would improve clinical outcomes and reduce transmission likelihood, reducing healthcare costs.

When we evaluated HCV RNA testing in anti-HCV-positive patients among hospital departments, we noticed that physician awareness was insufficient, especially in surgical clinics (7%). Although a relatively high rate of HCV RNA testing was observed in outpatient clinics in medical departments (78%), it was observed that this test was neglected in approximately two-thirds of anti-HCV-positive patients in inpatient medical clinics. Surprisingly, no HCV RNA testing has been performed in the emergency department in the last five years. Our findings are consistent with studies conducted in a tertiary university hospital in the Central Anatolia region^{9,11}. Tertiary hospitals play a critical role in the early diagnosis and treatment of CHC. Those institutions' low level of HCV awareness highlights the critical need for physician education, particularly in surgical clinics. To reach more patients, it is essential to raise primary care physicians' awareness as well^{8,16}. Because of the importance of comprehensive

HCV awareness in promoting HCV screening, initial physician-targeted education programs are required if global HCV eradication is to be achieved¹⁷. As part of Scotland's Hepatitis C Action Plan, during 2008-2011, several public awareness efforts were held to encourage testing by a GP. Surveys were used to evaluate HCV testing practices among GPs before and after these campaigns, and government awareness campaigns were shown to have a limited impact on GP testing. It was also emphasized that an electronic reminder encouraging the GP to ask questions about the patient's risk factors for HCV might eliminate the need for the GP to investigate them actively. It has been emphasized that such technique can be used to overcome the barriers perceived by the physician as reported by the physician's "poor awareness" and "limited knowledge of testing protocols"¹⁸. According to a national strategy and action plan to guide HCV eradication activities in Kuwait¹⁹, it has been proposed to establish a coordination mechanism among hepatitis working committees that prioritizes micro-elimination in prisons, rehabilitation centers, and primary care centers to tertiary institutions. Education for awareness of HCV infection was highlighted, and the development of a national HCV registry was recommended to monitor the compliance of viral hepatitis programs toward national and global goals. It has been observed that 60.5% of CHC patients could access treatment by applying an easy risk-based screening program for patients in the emergency department²⁰.

Finally, in the present study, anti-HCV positive and HCV RNA positive patients were older than negative patients. These results can be explained by the possible increase in HCV exposure with advancing age. While the gender distribution was similar in anti-HCV positive and negative patients, the HCV RNA test positivity rate was significantly higher in male patients than in females. Due to the more robust immune response in females, the infection's seroclearance may be higher. Our results on the age and gender distribution of the patients are consistent with the literature^{9,20}.

Limitations

The most important limitation of our study was that based on data from a single center. Our results are not generalizable, since geographical and socio-cultural differences in our region might affect the results. Another limitation of our study was

that patients with positive HCV RNA tests were not considered for acute hepatitis C infection.

Conclusions

The prevalence of anti-HCV positivity was 2% in this retrospective cohort conducted in a tertiary center between 2017-2022 in the Western Black Sea region, which is in the high seroprevalence category according to WHO. We also showed that less than half of anti-HCV-positive patients had undergone HCV RNA testing, and less than a third of HCV RNA-positive patients had received antiviral therapy. To meet the WHO's HCV eradication target in Turkey by 2030, educational and electronic warning systems should be implemented for physicians for screening purposes.

Conflict of Interest

The author declares that they have no conflicts of interest.

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Ethics Approval

This study was approved by the local Ethics Committee of Zonguldak Bulent Ecevit University (Date: 06/04/2022, Decision number: 2022/07).

Informed Consent

Not applicable.

Authors' Contribution

ZGS: Concept and design of study or acquisition of data or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, final approval of the version to be published.

Availability of Data and Materials

The data supporting the findings of this study are included within the manuscript and are available upon reasonable request to ZGS (corresponding author).

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