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Original paper

Physician awareness of hepatitis C virus among different departments

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Abstract

Aim of the study: To determine the anti-hepatitis C virus (HCV) positivity in our region and to evaluate physician awareness of HCV among different inpatient and outpatient departments in a tertiary reference center in Turkey.

Material and methods: This retrospective study was conducted between January 2017 and January 2020. The patients tested for anti-HCV for any reason were enrolled from the data of all patients admitted to our hospital, which is the reference center of the region.

Results: A total of 121,492 anti-HCV assays were screened from the computerized database. Total number of patients with a positive anti-HCV result was 891 (0.81%). HCV RNA was positive in 147 (16.5%) of 891 patients and negative in 389 (43.7%) patients. Unfortunately HCV RNA was not tested in 355 (39.8%) patients. The percentages of the untested patients regarding the departments were 65.38% (n = 85/130) in medical inpatient clinics, 61.02% (n = 72/118) in surgical clinics, 16.67% (n = 88/528) medical outpatient departments, 96.8% (n = 91/94) in surgical outpatient departments, and 90.5% (n = 19/21) in the emergency department.

Conclusions: The prevalence of anti-HCV positivity was found to be 0.81% and was stable in Turkey. However, the level of physician awareness for HCV was unsatisfactory, and differed between departments. Because HCV is commonly asymptomatic, positive patients should not be overlooked and adequate treatment should be administered. Awareness of physicians should be increased to prevent delays in the diagnosis of hepatitis C and to reduce the number of untreated patients.

Key words: chronic hepatitis C, prevalence, awareness, HCV RNA, anti-HCV.

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Introduction

Chronic viral hepatitis C (HCV) is a common public health problem. It is estimated that approximately 71 million people worldwide are infected with HCV [1]. According to the most recent World Health Organization (WHO) global hepatitis report, 80% of these 71 million people are undiagnosed, mostly because they are asymptomatic, and 93% remain untreated [2]. Prevalence and transmission routes vary between countries and regions. Its prevalence is high in countries of Africa and Asia; however, its incidence is lower in areas such as North America and Europe. For example, the prevalence of infection is 1.3-1.6% in the USA, while it is 15% in Egypt. More than half of the patients with chronic HCV infections live in China, Pakistan, Nigeria, Egypt, India and Russia.

The TURHEP study including 5460 patients from the general population of Turkey reported that anti-HCV prevalence is around 1% [3]. In Turkey, the etiological role of HCV in chronic hepatitis has increased from 23% to 38.1% and the etiological rate of HCV in cirrhosis has increased from 25.2% to 45.9% [4]. According to the WHO data, only 7.4% of patients with chronic HCV have access to treatment. This percentage is 11.1% in America, but only 2.2% in Africa. The low rate of treatment accessibility depends on several factors, but the physician awareness of HCV is one of the most important parameters [5].

For the diagnosis of chronic HCV, both anti-HCV antibody and HCV RNA have to be determined. Because of that, it is recommended to test HCV RNA levels if anti-HCV antibodies are detected [1]. Physician awareness is important in the diagnosis, treatment and prevention of hepatitis C. Clinicians should have the knowledge that testing HCV RNA for the diagnosis of chronic HCV is essential and should be tested in patients with positive anti-HCV antibody tests. The aim of this study was to determine the anti-HCV antibody positivity, the HCV RNA results in patients with detected anti-HCV antibody levels and to establish physician awareness for the necessity of HCV RNA testing in the diagnosis of chronic HCV in our region.

Material and methods

Patient selection and data collection

Age, sex, laboratory and clinical data of all patients who were admitted to our hospital between January 2017 and January 2020 for any reasons and were screened for anti-HCV were analyzed retrospectively. Repeated requests from the same patient were excluded from the analysis.

During the study, samples were studied on the day they arrived. Anti-HCV assays were studied using a COBAS 6000 analyzer series (Roche Diagnostics, Switzerland) autoanalyzer. HCV-RNA assays were studied using a Magnesia2448 Nucleic Acid Isolation & PC Setup Robot and Montania 4896 Real-Time PCR Device (Anatolia Diagnostics and Biotechnology Products, Turkey) in accordance with the manufacturer recommendations. All laboratory analyses were performed in our laboratory with a biosafety level of 2.

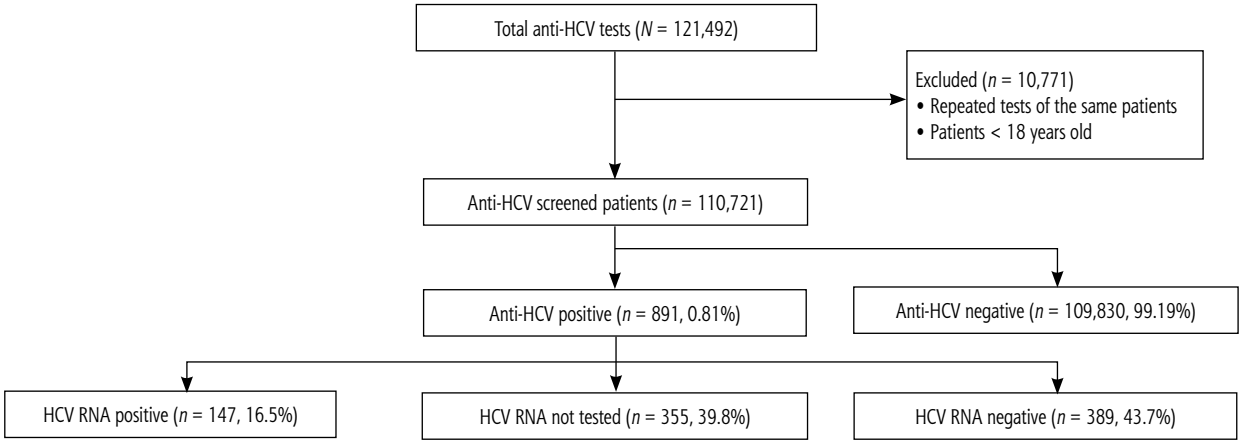
Demographic and laboratory data of patients with anti-HCV positivity were recorded from the hospital computer database. In addition, we analyzed the rates of HCV RNA assays of the patients with anti-HCV positivity and the distribution of the departments. Testing of HCV RNA in patients with detectable anti-HCV antibody was determined as physician awareness.

Statistical analysis

Statistical analyses were performed using SPSS software (SPSS, version 15.0, SPSS Inc., Chicago, IL, USA). Descriptive statistics (frequency distributions, percentage, mean, median, standard deviation) of the study group were determined. The data were evaluated for normal distribution by Kolmogorov-Smirnov test and by visual parameters (histogram, variation coefficient, skewness, kurtosis etc.). Student's t and Mann-Whitney U tests were used for comparisons. The χ^2 test was used to analyze categorical data. $P < 0.05$ was considered statistically significant.

Results

A total of 121,492 anti-HCV assays were requested in our hospital within three years. Exclusion criteria were: repeated assays on the same patient and patients younger than 18 years old. Overall, a total of 110,721 patients were included in the study (Fig. 1). The total number of patients with positive anti-HCV results was 891 (0.81%) (Table 1). The mean age of the whole patient group was 49.11 ±19.91. The mean ages of patients with anti-HCV positive and negative assays were 56.51 ±19.20 and 49.05 ±19.90 respectively ($p < 0.001$). HCV RNA was tested in 536 patients and was positive



HCV – hepatitis C virus, RNA – ribonucleic acid

Fig. 1. Patient enrollment and classification

Table 1. Demographic and laboratory characteristics of the study population

	n (%)	Age (mean)	*P*-value	Sex		*P*-value
				Female (*n*, %)	Male (*n*, %)	
Anti-HCV	110,721	49.11 ±19.91		59,242	51,499	
Positive	891 (0.81)	56.51 ±19.20	< 0.001*	450 (0.76)	441 (0.86)	0.154
Negative	109,830 (99.19)	49.05 ±19.90		58,792	51,008	
HCV RNA						
Positive	147 (16.5)	56.49 ±21.95	0.359**	64 (14.2)	83 (18.9)	0.149**
Negative	389 (43.7)	54.63 ±18.13		206 (45.8)	183 (41.5)	
Not screened	355 (39.8)	58.59 ±18.95		180 (40)	175 (39.6)	

HCV – hepatitis C virus, RNA – ribonucleic acid, n – number
**p < 0.05 is considered significant*
**p values represent HCV RNA positive and HCV RNA negative groups*

Table 2. Distribution rates of non-tested HCV RNA in the patients with anti-HCV positivity according to departments

	Anti-HCV positive patients (*N* = 891)	
	HCV RNA tested (*n* = 536)	HCV RNA not tested (*n* = 355)
Medical inpatient clinics	45	85 (65.38%)
Medical outpatient clinics	440	88 (16.67%)
Surgical inpatient clinics	46	72 (61.02%)
Surgical outpatient clinics	3	91 (96.8%)
Emergency department	2	19 (90.48%)

HCV – hepatitis C virus, RNA – ribonucleic acid

in 147 (27.4%) and negative in 389 (72.6%) patients. HCV RNA was not tested in 355 (39.8%) patients with anti-HCV positivity. The percentages of these patients regarding the departments were: 65.38% (*n* = 85/130) in medical inpatient clinics, 61.02% (*n* = 72/118) in surgical clinics, 16.67% (*n* = 88/528) in medical outpatient departments, 96.8% (*n* = 91/94) in surgical outpatient departments, and 90.5% (*n* = 19/21) in the emergency department (Table 2).

Discussion

The incidence of chronic HCV is expected to decrease towards the 2030s. The WHO adopted a resolution declaring that viral hepatitis should be eliminated by 2030. Currently, few countries have elimination programs in place, and even though the tools to achieve elimination are available, the right resources, commitments and allocations are lacking [6].

Medical procedures unsafely performed and use of intravenous drugs result in the development of new HCV infection. While the incidence of HCV infection decreased in several countries in 2015, there may be increases in various geographical regions [2]. For example, the incidence of HCV infection has decreased over the years in the USA, but after that decrease the incidence increased twofold between 2010 and 2014 due to intravenous drug addiction [7]. Similarly, because of intravenous drug addiction, HCV cases started to appear in rural areas where its incidence was low in the past. HCV transmission has also been reported in HIV-infected homosexual patients in Europe, Australia and the USA [8]. 5.6 million (8%) chronic HCV patients worldwide are still intravenous drug users [2].

In a study by Tozun *et al*. from Turkey, anti-HCV prevalence was reported to be 0.5% to 1% [3]. We found a prevalence of 0.81% of anti-HCV positivity, which is consistent with Turkey's formerly published data. In addition, in a prevalence study conducted by Yıldırım *et al*. in 2009 [9], the number of anti-HCV positive cases among 1095 participants was 23 (2.1%), with no statistically significant difference between male and female genders. This study was performed approximately 10 years ago in a region close to our hospital, so we find it interesting that our study showed a lower prevalence. These data may support the knowledge that the HCV prevalence has been decreasing gradually within years for our region. Similarly, in a 2006 study involving 1320 individuals who were admitted to a tertiary hospital for checkup, anti-HCV positivity was 2.2% and anti-HCV positivity in the patients over 50 years old was found to be significantly higher [10]. Our study showed no significant difference by sex in anti-HCV positive patients, but we found that the mean age of anti-HCV positive patients was significantly higher than that of negative patients. The mean age of anti-HCV positive and negative patients was 56.5 and 49, respectively. Similarly, in a study performed in Turkey in 2015, the only significant parameter to predict anti-HCV positivity was age over 50 years [3].

The aforementioned epidemiological Turkish studies did not evaluate HCV RNA levels [3, 9, 10]. Among the patients tested for HCV RNA, 147/536 (27.4%) of the patients had chronic hepatitis C, and the HCV RNA positive ratio for the whole population was 147/110,721 (0.13%). HCV RNA positive patients are fewer than negatives; we think that this result may be due to patients who have been treated and have a sustained viral response, patients who have recovered from the disease spontaneously and false-positivity of anti-HCV. Especially in populations with low HCV prevalence, false-positive results are common in anti-HCV tests used for screening purposes [11]. Therefore, it is recommended to repeat the test with a new sample two weeks later in patients with low-titer anti-HCV reactivity, to evaluate the patient's clinical condition, and to study HCV RNA if anti-HCV is still positive [12]. We consider that a considerable amount of our patients had false positive anti-HCV results since our laboratory's anti-HCV threshold value was kept low (1 S/Co) and thus HCV RNA tests expanded.

When we examined the patient group (39.8%) who were anti-HCV positive without HCV RNA testing, we found that the awareness level of physicians was not at the desired level. Generally the percentage of overlooking HCV RNA was high, and the highest rate was in the outpatient departments of surgical clinics. In this context, the Lancet Gastroenterology & Hepatology Commission reported that the patients and physicians have insufficient information on chronic viral hepatitis [5]. Studies on this subject are generally survey studies. A survey study performed by Tiftikçi *et al.* found that the awareness levels of patients and physicians about transmission routes of hepatitis C infection was low [13]. Feng *et al.*'s survey study on 1362 Chinese general practitioners revealed that 44% of the participants thought that anti-HCV positive cases do not need to be referred for further examination, 62% of the participants did not know that anti-HCV had been tested in routine controls in the hospital and 71% of the participants were not aware of the new treatments of hepatitis C [14]. A study performed in China reported that the patients educated for HCV had increased compliance with the follow-ups and treatments [15]. A study from Argentina also showed that the success of the physicians at follow-up increased with the new education models [16]. In the survey study of 125 family physicians and 76 internal medicine physicians by Kayar *et al.* it was found that the awareness of physicians about transmission routes and the patient groups needing to be screened for anti-HCV was low [17]. Another study revealed that the success of the disease treatment is associated with the knowledge of primary care physicians on the diagnosis and screening of HCV [18].

A recent study conducted in Turkey indicated that the awareness of physicians was low and the mean delay in the diagnosis of hepatitis C might reach 74.88 weeks following anti-HCV positivity [19]. The authors stated that only 248 of 855 patients (29%) with anti-HCV positivity were tested for HCV RNA, whereas this ratio was 60.2% in our study [19]. Our study obtained better results compared to this study, but is still under the desired level. To the best of our knowledge our study is the first study determining the HCV RNA studying awareness among different departments in Turkey. We found that physician awareness is low in inpatient clinics, the emergency department and surgical outpatient clinics and patients with anti-HCV antibody are not tested for HCV RNA at an adequate level in these clinics. Our results give us the ability to determine a target for physician education.

If HCV patients are left untreated, the disease burden and mortality are expected to increase gradually in the next 20 years, and furthermore most of the patients infected with HCV are not aware of this condition. Studies on the treatment of infection have reached high success rates in the last years thanks to the development of highly effective new oral anti-viral drugs – also called direct acting antivirals (DAAs) [20]. The eradication of HCV thanks to DAA-based treatments results in improved hepatic functions and disease course, decreased cirrhosis and associated complications and hepatocellular cancer development [20].

The introduction of highly effective treatments for HCV created an unprecedented opportunity to cure almost all patients, reduce HCV transmission and eliminate the disease [21]. However, more effort is needed for screening. In order to achieve the stated goal of elimination of HCV by 2030, Hasan *et al.* [22] pointed out that raising awareness about HCV infection was essential and a national HCV registry should be developed to help monitor the implementation of viral hepatitis plans and progress towards achieving national and international targets. Also Samuel *et al.* reported that hepatitis C virus knowledge improves HCV screening practices [19]. The authors also noted that HCV-related knowledge gaps must be addressed in order to increase the HCV workforce, leading to increased opportunities for HCV screening and engagement in care. Finally, one of the most important factors in the fight against HCV is to increase awareness [5]. Our study revealed that the awareness of physicians is not at the desired levels and should be increased immediately.

In conclusion, the prevalence of anti-hepatitis C virus positivity is found to be 0.81% and appears to be stable in Turkey. However, the level of physician awareness for HCV was unsatisfactory, and differed between departments. Identification of new infections is very important to prevent complications, deaths or transmission of HCV. Most of the people with the disease do not have any signs and symptoms, most of the people do not see themselves in the risk groups, and physicians may overlook these patients. The level of physician awareness should be raised to prevent delay in the diagnosis and treatment of hepatitis C. Potentially, adding warnings and information about HCV diagnosis and treatment to hospital computer systems may be beneficial for physicians.

Disclosure

The authors declare no conflict of interest.

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