RESEARCH / ARAŞTIRMA
DOI: 10.26650/IUITFD.1401786
İst Tıp Fak Derg 2024 / J Ist Faculty Med 2024

IS ONLY REQUESTING AN ANTI-HCV TEST SUFFICIENT FOR HEPATITIS C SCREENING?

HEPATİT C TARAMASI İÇİN SADECE ANTİ-HCV TESTİ İSTEMEK YETERLİ MİDİR?

Rabia DENİZ[1], Seda KARSLI[1], Ömer Burak EKİNCİ[1], Ilkane KALANTAROVA[1], Alp ATASOY[2], Mustafa ÖNEL[3], Ali AĞAÇFİDAN[3], Filiz AKYÜZ[2], Kadir DEMİR[2], Fatih BEŞIŞIK[2], Sabahattin KAYMAKOĞLU[2]

[1]İstanbul University, İstanbul Faculty of Medicine, Department of Internal Medicine, İstanbul, Türkiye
[2]İstanbul University, İstanbul Faculty of Medicine, Department of Internal Medicine, Division of Gastroenterohepatology, İstanbul, Türkiye
[3]İstanbul University, İstanbul Faculty of Medicine, Department of Medical Microbiology, İstanbul, Türkiye

ORCID IDs of the authors: R.D. 0000-0003-4537-894X; S.K. 0000-0003-0765-0770; Ö.B.E. 0000-0002-2018-0980; I.K. 0009-0007-4852-8532; A.A. 0000-0003-1791-897X; M.Ö. 0000-0002-3987-6611; A.A. 0000-0002-5470-296X; F.A. 0000-0001-7498-141X; K.D. 0000-0002-5226-3705; F.B. 0000-0001-5184-376X; S.K. 0000-0003-4910-249X

Cite this article as: Deniz R, Karslı S, Ekinci ÖB, Kalantarova I, Atasoy A, Önel M, et al. Is only requesting an anti-HCV test sufficient for hepatitis C screening? J Ist Faculty Med 2024;87(3):215-219. doi: 10.26650/IUITFD.1401786

ABSTRACT

Objective: Unless treated, a hepatitis C virus (HCV) infection is associated with high morbidity and mortality. The study investigates anti-HCV screening efficacy and treatment access rates for patients.

Material and Method: This cross-sectional study screened all anti-HCV tests requested between January 2014-June 2017 from hospital records. Patient interviews were conducted by telephone-based interview.

Result: The overall number of anti-HCV tests requested was 77,783, 1,373 of which were positive. Among these, the study interviewed 488 patients (266 females, 222 males; mean age=52.81±16.5 years) and analyzed their tests. Further investigation with HCV-RNA had not been done in 69 (14.1%) anti-HCV positive patients. HCV-RNA was positive in 309 patients, 268 of whom were treated (86%), while 41 were not (14%). The main reasons for remaining untreated are: unknown (21%), no patient follow up (28%), or physician didn't indicate (19%).

Conclusion: In order to successfully eliminate HCV, the anti-HCV test alone is not enough. Informing patients about the results of the anti-HCV test and, if positive, referring them for the HCV-RNA test are important. When considering the high amount of untreated patients, linkage to care should be encouraged in HCV-RNA positive patients unless an absolute contraindication is present.

Keywords: Hepatitis C virus infection, anti-HCV antibody, HCV-RNA, screening

ÖZET

Amaç: Hepatit C Virüs (HCV) enfeksiyonu, tedavi edilmediği sürece yüksek morbidite ve mortalite ile ilişkilidir. Bu çalışmada anti-HCV tarama etkinliği ve tedaviye erişim oranları araştırılmıştır.

Gereç ve Yöntem: Bu kesitsel çalışmada Ocak 2014 ile Haziran 2017 tarihleri arasında istenen tüm anti-HCV testleri hastane kayıtlarından tarandı. Hasta görüşmeleri telefon ortamında gerçekleştirildi.

Bulgular: İstenilen toplam anti-HCV testi sayısı 77,783 olup, bunların 1,373'ü pozitif çıkmıştır. Bunlardan 266'sı kadın, 222'si erkek; yaş ortalaması 52,81±16,5 yıl olan 488 hastayla görüşme yapılmıştır. Anti-HCV pozitif hastaların 69'una (%14,1) HCV-RNA ile ileri araştırma yapılmadığı saptandı. Üç yüz dokuz hastada HCV-RNA pozitifti ve 268'i tedavi almışken (%86), 41'i (%14) tedavi edilmemişti. Tedavisiz kalmanın temel nedenleri ise bilinmeyen (%21), takip edilmeyen hasta (%28) ve hekimin endikasyon göstermemesi (%19) olarak belirlendi.

Sonuç: HCV'nin başarılı bir şekilde eradike edilmesi için anti-HCV testi tek başına yeterli değildir. Hastaların anti-HCV testi sonuçları hakkında bilgilendirilmesi; pozitif ise HCV-RNA testine başvurulması önemlidir. Tedavi edilmeyen hasta sayısının yüksek olduğu göz önüne alındığında, mutlak bir kontrendikasyon olmadığı sürece HCV-RNA pozitif hastalarda tedaviye yönlendirilme teşvik edilmelidir.

Anahtar Kelimeler: Hepatit C enfeksiyonu, anti-HCV antikoru, HCV RNA, tarama

Corresponding author/İletişim kurulacak yazar: Rabia DENİZ – dr.rabiadeniz@gmail.com

Submitted/Başvuru: 13.12.2023 • **Revision Requested/Revizyon Talebi:** 16.02.2024 •
Last Revision Received/Son Revizyon: 28.02.2024 • **Accepted/Kabul:** 22.03.2024 • **Published Online/Online Yayın:** 27.05.2024

INTRODUCTION

Acute hepatitis C virus (HCV) infection has a chronicity rate of 75-80%, and is one of the most common reasons for chronic liver disease and hepatocellular carcinoma (1, 2). Chronic HCV infection is a common public health issue associated with high all-cause morbidity and mortality if left untreated (1). Around 71 million cases of HCV infection are found all around the world (2). The introduction of direct-acting antiviral agents (DAA) makes HCV a curable disease in a shorter time with less adverse effects and more than 95% sustained viral response (SVR) rates (3). Thus, the World Health Organization (WHO) announced the target of eliminating HCV by 2030 (4). To achieve this 2030 target, around 300,000 viremic HCV patients have been waiting to be diagnosed and treated since 2016 in Türkiye (5). However, the success of this elimination plan will only be possible if infected patients are detected and get treatment on time, thus indicating the importance of HCV screening. An effective screening and treatment policy is not only important for diagnosis and treatment success but also for decreasing disease incidence and prevalence by avoiding transmission among individuals (4).

To investigate the effectiveness of the HCV screening policy regarding hospital care settings and treatment administration rates, the study evaluates the patient pathway, which starts with anti-HCV monitorization and continues with the treatment of HCV RNA positive patients, and identifies key markers for each step.

MATERIALS and METHODS

This study was conducted cross-sectionally and identifies all patients screened for HCV between January 1, 2014-June 30, 2017 at a single tertiary center based on the medical records of the hospital archive, with a total of 77,783 patients being included. To gather data, a telephone-based interview was performed with the patients themselves.

Virologic tests were performed using the routine enzyme-linked immunosorbent assay (ELISA) method for the anti-HCV test (Innogenetics HCV Ab IV; Innogenetics N.V, Belgium) and quantitative real-time polymerase chain reaction (qt RT-PCR) for the HCV-RNA test in a microbiology laboratory (COBAS Ampliprep/COBAS Taqman HCV Quantitative Test V2.0, Roche Diagnostics Mannheim, detection range 15-100 000 000 IU/mL).

All participants gave informed consent and volunteered to be interviewed. The study was approved by the İstanbul Faculty of Medicine Clinical Research Ethics Committee (Date: 22.09.2023, No: 19). Data are presented as mean values for continuous variables and as percentages for qualitative variables.

Statistical analysis

Due to only patient group data being defined, mean and standard deviations have been given for the quantitative data and frequencies for the qualitative variables. Statistical analyses were performed using SPSS Statistics for Windows, version 28.0 (IBM SPSS Corp., Armonk, NY, USA).

RESULTS

Study population characteristics

A total of 77,783 patients were enrolled in the study. Among these, 1,373 had tested positive for anti-HCV (1.76%). Duplicated requests (n=430, 31.3%) were removed, and the remaining 943 patients were reviewed. After obtaining consent, the 943 patients were interviewed. Among these, 200 patients' telephone numbers could not be found, 157 did not respond to repeated calls, 73 patients had died, and 25 refused to give information. As a result, the study interviewed 488 patients (266 females, 222 males; mean age = 52.81±16.5 years) via a telephone-based interview.

Among the 488 anti-HCV positive patients, 69 (14.1%) had not been monitored for HCV-RNA testing. Among the 419 HCV-RNA results, 110 were negative (false positive for anti-HCV), while 309 were confirmed positive through qt RT-PCR (Figure 1). No significant differences were observed regarding age or gender for the patients tested positive for anti-HCV and HCV-RNA.

Reasons for HCV screening and transmission route according to groups

Based on the patient interviews, Table 1 presents the major reasons for anti-HCV screening for the HCV-RNA tested (n=419) and non-tested (n=69) groups. The main indication for screening was general screening in study population (32%), and pre-operative screening was the most common reason in patients who'd not been referred for HCV-RNA testing (42%).

The main routes of HCV transmission were declared as unknown (37%), blood transfusion (23%), surgery (12%), dental care (9%), hemodialysis (14%), tattoo-piercing (1%), risky sexual behavior (1%), intravenous drug abuse (1%), and positive family history for viral hepatitis (1%).

Treatment status

Positivity for HCV-RNA was detected in 309 patients, of whom 268 received treatment (86%) and 41 who did not (14%). The given treatments involved interferon-based regimen (46%), DAA (27.4%), multiple therapy (21.5%), and unknown (5.1%). Patients declared the reasons for remaining untreated as: unknown (21%), no patient follow up (28%), clinician's decision to not consider treatment without a contraindication (19%), physician perceiving the patient as too young or too old for treatment (12%),

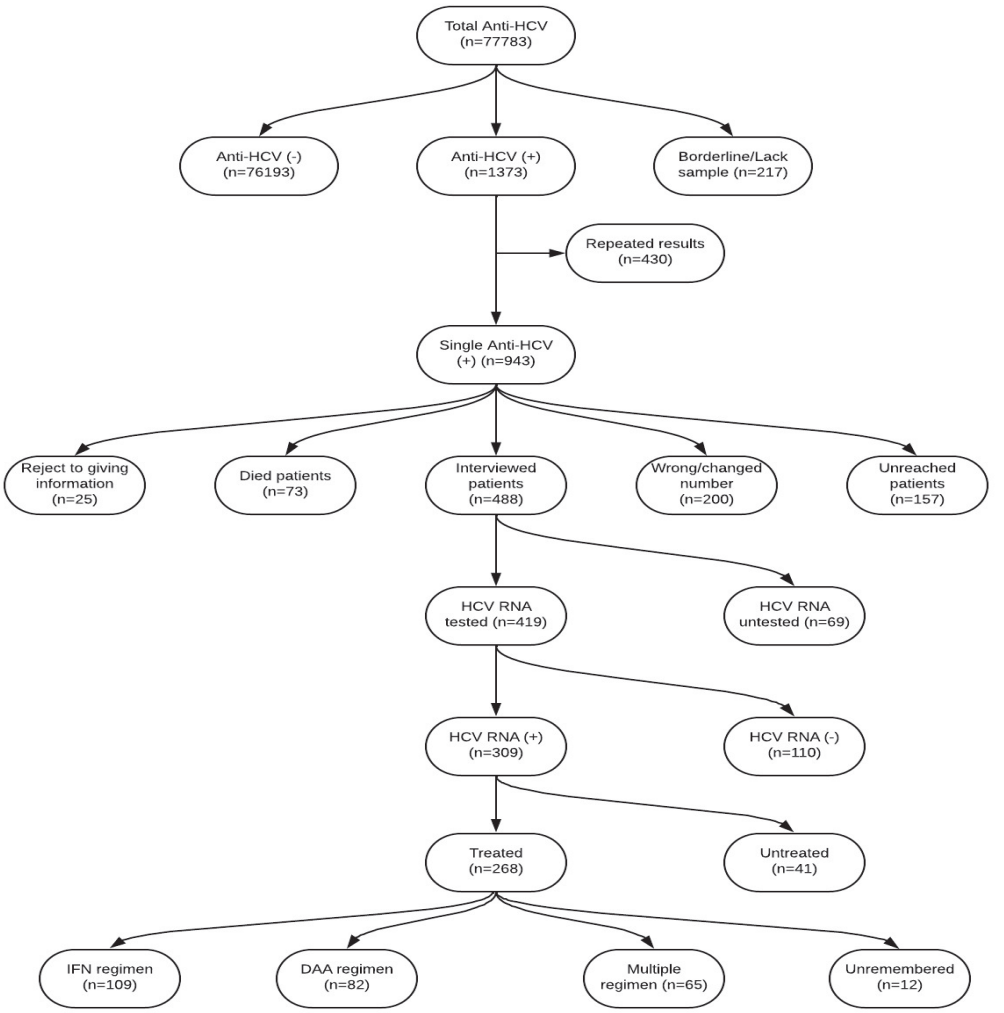

Figure 1: Study flowchart
HCV: Hepatitis C virus, IFN: Interferon, DAA: Directly acting antivirals

Table 1: The reasons for HCV screening overall and by patient group

Screening indications	All patient groups (n=488), %	Patients not screened for HCV-RNA (n=69), %	HCV-RNA positive patients not referred and untreated (n=41), %
General screening	32	32	43
Surgery	26	42	22
Impaired liver biochemistry	21	10	15
Hemodialysis	7	3	N/A
Don't remember	5	9	10
Blood donation	3	3	2
Self-interest	2	N/A	N/A
Risky behavior	1	N/A	3
Job application	1	N/A	3
Marriage screening	1	1	N/A
Family history	1	N/A	2

improper general health status (5%), patient rejected (10%), and being under a treatment plan (5%). Therefore, 29 (71%) of the 41 untreated HCV-RNA positive patients (i.e., the ones excluding those as non-indicated by physicians, with improper health status, and under a treatment plan) were also eligible for treatment. Overall, 14% of anti-HCV positive patients (n=69) and 13% of HCV-RNA positive patients (n=41), namely a total of 110 of the 488 interviewed patients at the time of that research, were unable to access treatment.

DISCUSSION

Chronic hepatitis C virus (HCV) infection is a worldwide public health problem and one of the reasons for preventable morbidity and mortality if left untreated (1). Therefore, early screening, diagnosis, and linkage to care have crucial importance. The generally accepted method for HCV screening is the testing of anti-HCV antibodies in peripheral venous blood using the enzyme-linked immunosorbent assay (ELISA) method. Anti-HCV positivity frequency varies from region to region and also from the general population to special groups, including HIV comorbidity and among people who inject drugs (PWID) (2, 4, 6). WHO data showed anti-HCV positivity in Western countries as 1.10%, while studies from Eastern regions demonstrated even higher anti-HCV rates. Naz et al. declared 1.56% in Pakistan, while Turkish HCV epidemiology data reveal an anti-HCV positivity rate of 1% (7, 8). This study found an anti-HCV positivity rate of 1.76%, higher than in most studies that include the general population. However, because this study was performed in a tertiary hospital, high-risk subgroups were probably recruited at a greater frequency than in the general population as a one-center study bias. This is consistent with previous hospital-based studies that found a higher prevalence of anti-HCV positivity than expected for the general population (9-11). During the calculation of anti-HCV positivity, those who had negative HCV RNA tests (n=110) were not excluded; they had either been treated previously or had a false positive anti-HCV test with no actual infected status. However, even in the patients requesting the HCV RNA test, being tested once is necessary to exclude active infection and need for treatment.

The high number of repeated tests and the gap between anti-HCV positivity and a referral for the HCV-RNA test were the main results of low awareness among physicians. Repeated tests not only increase the cost of managing the disease but also the emotional stress for patients with false positives or who've been cured owing to the lifelong positivity of anti-HCV in both situations. Although studies have shown an increased effort to screen special groups, such as patients with risky behaviors, HCV-HBV, HCV-HIV coinfections, and PWIDs, they also show screening, referrals for HCV-RNA testing, and active infection rates to be lower in the general population (6, 12). However, studies have also shown cost effectivity for screening high-risk populations vs general populations owing to decreased transmission and higher treatment success rates with DAAs (13). In addition, the lack of evaluation regarding the HCV-RNA test results for proper linkage to care and the lack of education among patients about disease outcomes and the importance of being treated decreased the rate of treatment initiation. The results from this study have revealed a lack of knowledge on how to manage HCV infection to be present among patients and physicians, such as informing anti-HCV positive patients who'd already been indicated as positive in the healthcare databases about test results, as well as the need to refer these patients for HCV-RNA testing to determine viremia.

One of the limitations of this study is its retrospective design, which has led to an important loss for the cohort due to the inability to contact patients. Another limitation is the basis on a single tertiary center. Data from tertiary centers may include more risky and complicated patient groups compared to the general population.

CONCLUSION

In conclusion, requesting an anti-HCV test is not adequate as a single screening tool with regard to the strategy for eliminating HCV. Further investigation of HCV-RNA in positive patients is so crucial and a complementary portion of the screening strategy. Therefore, physicians' awareness of screening and linkage to care become more important. The wide use of electronic patient record systems and digital warnings may decrease the number of unnecessary duplicated test requests. Despite being easily treated with DAAs, approximately one in four patients lose the chance of being successfully referred to treatment. Therefore, the healthcare system should be evolved to treat every patient who tests positive for HCV-RNA unless an absolute contraindication is present.

Ethics Committee Approval: The study has ethical approval from the İstanbul Faculty of Medicine Clinical Research Ethics Committee (Date: 22.09.2023, No: 19).

Informed Consent: All participants gave informed consent and volunteered to be interviewed.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- R.D., S. Kaymakoğlu; Data Acquisition- R.D., S.Karslı, Ö.B.E., İ.K., A.A., M.Ö., A.Ağaçfidan; Data Analysis/Interpretation- R.D., F.A., K.D., F.B., S.Kaymakoğlu; Drafting Manuscript- R.D.; Critical Revision of Manuscript- F.A., K.D., F.B., S.Kaymakoğlu; Final Approval and Accountability- R.D., S.Karslı, Ö.B.E., İ.K., A.A., M.Ö., A.Ağaçfidan, F.A., K.D., F.B., S.Kaymakoğlu

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study received no financial support.

Data availability statement: Data available on request from the authors. The data that support the findings of this study are available from the corresponding author upon reasonable request and all authors have access the all data.

REFERENCES

1. Westbrook RH, Dusheiko G. Natural history of hepatitis C. J Hepatol 2014;61(1 Suppl):S58-68. [CrossRef]
2. World Health Organization. Global hepatitis report 2017. Geneva SWhttps://www.who.int/publications/i/item/9789241565455 .
3. Pawlotsky JM. New hepatitis C therapies: the toolbox, strategies, and challenges. Gastroenterology 2014;146(5):1176-92. [CrossRef]
4. World Health Organization. Combating hepatitis B and C to reach elimination by 2030. 28 Feb 19. http://apps.who.int/iris/bitstream/10665/206453/1/WHO_HIV_2016.04_eng.pdf?ua=1.
5. Idilman R, Razavi H, Robbins-Scott S, Akarca US, Örmeci N, Kaymakoglu S, et al. A micro-elimination approach to addressing hepatitis C in Turkey. BMC Health Serv Res 2020;20(1):249. [CrossRef]
6. Radwan D, Cachay E, Falade-Nwulia O, Moore R, Westergaard R, Mathews WC, et al. HCV Screening and Treatment Uptake Among Patients in HIV Care During 2014-2015. J Acquir Immune Defic Syndr 2019;80(5):559-67. [CrossRef]
7. Naz A, Mukry SN, Naseer I, Shamsi TS. Evaluation of efficacy of serological methods for detection of HCV infection in blood donors: A single centre experience. Pak J Med Sci 2018;34(5):1204-8. [CrossRef]
8. Tozun N, Ozdogan O, Cakaloglu Y, Idilman R, Karasu Z, Akarca U, et al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clin Microbiol Infect 2015;21(11):1020-6. [CrossRef]
9. Bielen R, Kremer C, Koc OM, Busschots D, Hendrickx D, Vanelderen P, et al. Screening for hepatitis C at the emergency department: Should babyboomers also be screened in Belgium? Liver Int 2019;39(4):667-75. [CrossRef]
10. Orkin C, Leach E, Flanagan S, Wallis E, Ruf M, Foster GR, et al. High prevalence of hepatitis C (HCV) in the emergency department (ED) of a London hospital: should we be screening for HCV in ED attendees? Epidemiol Infect 2015;143(13):2837-40. [CrossRef]
11. Bert F, Rindermann A, Abdelfattah MA, Stahmeyer JT, Rossol S. High prevalence of chronic hepatitis B and C virus infection in a population of a German metropolitan area: a prospective survey including 10 215 patients of an interdisciplinary emergency unit. Eur J Gastroenterol Hepatol 2016;28(11):1246-52. [CrossRef]
12. Crowley D, Van Hout MC, Murphy C, Kelly E, Lambert JS, Cullen W. Hepatitis C virus screening and treatment in Irish prisons from a governor and prison officer perspective-a qualitative exploration. Health Justice 2018;6(1):23. [CrossRef]
13. Buti M, Dominguez-Hernandez R, Casado MA, Sabater E, Esteban R. Healthcare value of implementing hepatitis C screening in the adult general population in Spain. PLoS One 2018;13(11):e0208036. [CrossRef]