



DOI: 10.14744/SEMB.2019.46656

Med Bull Sisli Etfal Hosp 2019;53(4):366–370

## Original Research

# Patients Lost after Anti-HCV-Positive Finding in a Tertiary Care University Hospital: Increased Awareness and Action is Necessary to Eradicate HCV

Mustafa Zanyar Akkuzu, Orhan Sezgin, Serkan Yaraş, Osman Özdoğan, İbrahim Yılmaz, Enver Üçbilek, Fehmi Ateş, Engin Altıntaş

Department of Gastroenterology, Mersin University Faculty of Medicine, Mersin, Turkey

### Abstract

**Objectives:** Though there is a global effort to eradicate hepatitis C infection (HCV), several obstacles remain. Many patients infected with the virus are not detected or go untreated. The goal of this study was to identify any barriers to treatment and any difficulties contributing to the elimination of HCV infection at a tertiary care university hospital.

**Methods:** This was a retrospective review. The hospital data system was searched for records of patients admitted to the hospital for any reason from between 2013 and 2018 who were screened for viral markers and determined to be anti-HCV positive. The follow-up performed was then analyzed.

**Results:** Viral marker testing was requested for 65,853 patients during the study period. Of those, 64,735 (98.3%) were found to be anti-HCV negative and 1118 (1.7%) were anti-HCV positive. In all, 392 (35.06%) were detected in the gastroenterology department, 417 (37.3%) were patients in the infectious diseases department, and 309 (27.64%) were identified in other clinics, including emergency services, the blood bank, and others. There were 30/392 (7.65%) patients admitted to the gastroenterology clinic who declined a biopsy and/or treatment. In other clinics, 88/309 (28.5%) patients were identified who were not treated for HCV and not followed up because they were not referred to the related specialty department.

**Conclusion:** It was determined that there was a significant gap in referring patients to the appropriate specialized department following an anti-HCV positive finding and thus to appropriate follow-up and treatment programs.

**Keywords:** Awareness; hepatitis C virus; knowledge.

Please cite this article as "Akkuzu MZ, Sezgin O, Yaraş S, Özdoğan O, Yılmaz İ, Üçbilek E, et al. Patients Lost after Anti-HCV-Positive Finding in a Tertiary Care University Hospital: Increased Awareness and Action is Necessary to Eradicate HCV. Med Bull Sisli Etfal Hosp 2019;53(4):366–370".

Hepatitis C virus (HCV) infection is a public health sector concern in both developed and developing countries. The World Health Organization (WHO) has estimated that about 71 million people have a chronic HCV infection and 399,000 die every year due to HCV-related cirrhosis or cancer.<sup>[1–3]</sup> The WHO described the burden of disease in different parts of the world in a 2017 report and reported the highest incidence of HCV infection in the Eastern Mediterranean Regional Office and European Regional Office areas.<sup>[3]</sup> In a study published in 2015, it was estimated that 514,000 people (0.7%) (range: 317,000–540,000) were infected with HCV

in Turkey as of 2013. In the same study it was estimated that 5500 (1.1%) were newly diagnosed patients and only 4200 (0.8%) patients were receiving treatment.<sup>[4]</sup>

Direct-acting antivirals have created a revolution in the treatment of HCV and the WHO goal is to eradicate HCV by 2030. These drugs are especially effective in the treatment of the genotype 1 variety, which was previously determined to be the most prevalent subtype in Mersin, Turkey.<sup>[5]</sup> Although health professionals have adopted goals of treatment and elimination, it remains a challenge. Many

**Address for correspondence:** Mustafa Zanyar Akkuzu, MD. Mersin Üniversitesi Tıp Fakültesi, Mersin, Turkey

**Phone:** +90 507 942 66 83 **E-mail:** zanyarakkuzu@gmail.com

**Submitted Date:** August 06, 2019 **Accepted Date:** August 29, 2019 **Available Online Date:** November 22, 2019

©Copyright 2019 by The Medical Bulletin of Sisli Etfal Hospital - Available online at [www.sislietfaltip.org](http://www.sislietfaltip.org)

**OPEN ACCESS** This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).



people may not have symptoms or know they are infected and the illness often goes undetected and untreated. Globally, approximately 50% to 80% of HCV-infected individuals remain undiagnosed and fewer than 20% of those diagnosed have been linked to appropriate care.<sup>[6-8]</sup> The HCV care continuum is often broken in the early stages.

There are many factors that can prevent patients from being identified or treated. The general public has insufficient knowledge about HCV and unfortunately, there is also often insufficient knowledge among primary healthcare workers.<sup>[9]</sup> Patients may not be referred to the relevant department or given detailed information necessary for follow-up. This should be resolved and the patient or related physician must be convinced of the need to pursue appropriate treatment after detection of HCV infection. The aim of this study was to evaluate potential obstacles to treatment of HCV-infected patients at a university hospital that is also an important hepatology center of the region.

### Methods

This was a retrospective record review study. The hospital data system was searched and patients from the period of 2013 to 2018 who had an analysis of viral markers performed and were determined to be anti-HCV positive were included. These patients were grouped according to the clinic: gastroenterology, infectious diseases, and other clinics (emergency service, blood bank center, preoperative preparation, etc.). Patients with an anti-HCV positive result who were not directed to the relevant follow-up and patients with an HCV RNA-positive result but who were not treated were identified and counted and the distribution was calculated according to clinic of origin. The patients determined to be anti-HCV positive by the infectious diseases clinic were not included in the final study analysis. Ethics committee approval was granted by Mersin University Ethical Committee with the decision number 106 dated 06/03/2019.

### Results

Viral marker screening was requested in 65,853 cases. In all, 64,735 (98.3%) were found to be anti-HCV negative and 1118 (1.7%) were anti-HCV positive. Of the anti-HCV positive subjects, 392 (35.06%) were from the gastroenterology department, 417 (37.3%) were from the infectious disease department, and 309 (27.64%) were from other clinics (Table 1). Among those with an anti-HCV negative result, 35,527 of the patients were male (54.88%; mean age: 42.15 years) and 29,208 were female (45.12%; mean age: 43.6 years). Analysis of the group of 1118 (1.7%) anti-HCV positive patients revealed a mean age and sex distribu-

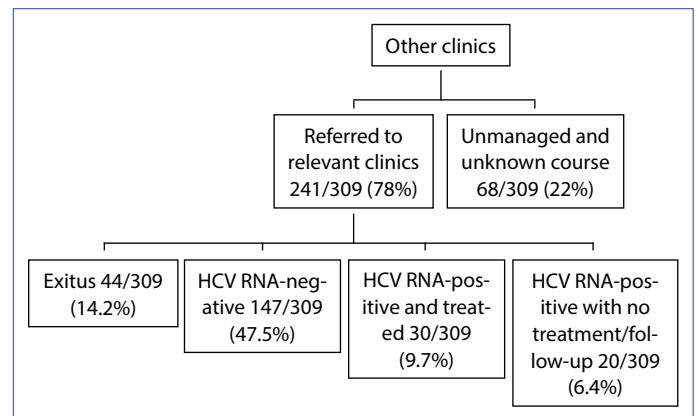
tion of 547 (48.92%) male (mean age: 55.45 years) and 571 (51.08%) female (mean age: 52.71 years). The significant age difference between the positive and negative groups was an important finding.

Of the 309 anti-HCV positive patients detected in various clinics, 241 (78%) were referred to the appropriate department. In all, 44 (14.2%) died due to diverse major diseases. Thirty (9.7%) patients with an HCV RNA-positive result initiated treatment, while 20 (6.4%) patients referred to the related department did not have follow-up care. In the group of 309, 147 (47.5%) patients were subsequently found to be HCV RNA-negative. Following an anti-HCV positive determination, 68 (22%) of the 309 patients were not directed to the related department and no evaluation of HCV was conducted. In all, 88 (28.5%) patients remained unfollowed and untreated (Fig. 1).

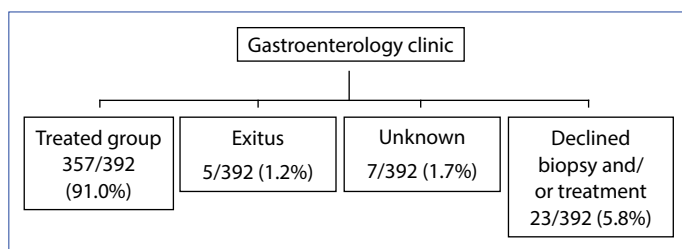
In the gastroenterology clinic, 385 of 392 (98%) patients who had an anti-HCV positive result were followed up and the necessary planning for treatment was performed. Of these, 357 (91.0%) patients were treated, but 23 (5.8%) patients refused a biopsy and/or treatment despite being positive for HCV RNA. Five (1.2%) patients were admitted to hospital for the first time and subsequently died of cirrhosis complications. Seven of the 392 (1.7%) patients with anti-HCV positivity were called but they did not present for further evaluation and we have no knowledge of their condition (Fig. 2).

**Table 1.** Total patient distribution

	Anti-HCV positive, (%)	Anti-HCV negative, (%)	Total
Gastroenterology clinic	392 (35.06)	8248 (12.75)	8640 (13.12)
Other clinics	309 (27.64)	50718 (77.88)	50727 (77.03)
Infectious disease clinic	417 (37.3)	6069 (9.37)	6486 (9.85)
Total	1118 (1.7)	64735 (98.3)	65853



**Figure 1.** Documentation of anti-hepatitis C positive patients identified by other clinics.



**Figure 2.** Documentation of anti-hepatitis C positive patients identified by the gastroenterology clinic.

## Discussion

We found that in the 5-year period examined, the anti-HCV antibody positivity rate in our hospital was 1.7%. In our gastroenterology clinic, the necessary procedures were performed for all patients. However, 1.7% of those patients who were called after an anti-HCV positivity result did not pursue treatment. Another 5.8% of the patients came to the control and were positive for HCV RNA, but declined a biopsy and/or treatment and they were not followed up. In other words, 7.5% of patients did not accept follow-up and treatment despite hospital observance of the procedures.

In other clinics, (emergency service, blood bank center, preoperative preparation, etc.) 22% of the patients were not referred to the relevant department after the anti-HCV positivity finding and 6.5% were properly referred and the HCV RNA test result was positive, but no follow-up was initiated. In total, 28.5% of patients did not participate in follow-up or treatment.

The most important limitation to our study is the retrospective design. We do not have an objective result indicating why patients were not referred to the related department or why patients declined treatment. Physicians may have made a later referral to the relevant department; however, the data indicated that 22% of the patients from other clinics who were positive for anti-HCV were not referred to the appropriate specialty branch in the hospital, and unfortunately, even if the patient was told immediately, the likelihood of the patient pursuing that recommendation is low. Similarly, in a study conducted in the USA, it was determined that 42% of patients with a positive HCV infection result had not pursued treatment.<sup>[10]</sup>

The need to increase the knowledge and sensitivity of physicians about HCV infection and the importance in terms of public health is clear. In our earlier study conducted with 440 general practitioners working in Mersin, it was observed that their knowledge and awareness of HCV was low.<sup>[9]</sup> This likely contributes to reduced referrals and a lack of detailed information about the infection. His-

torically, primary care physicians (PCPs) have had a role in HCV detection and counseling.<sup>[11]</sup> However, many PCPs, the gatekeepers of the healthcare system, have limited HCV knowledge. Some systematic reviews have identified significant knowledge gaps among PCPs and internal medicine residents related to the natural history, diagnostic approaches, and treatment of HCV.<sup>[11-13]</sup>

In addition, the awareness of patients and the general community about HCV infection is unfortunately low. This leads to reduced screening for the disease and less effective treatment. Similar problems are common around the world. In a study from Egypt, the level of knowledge and available sources of information about HCV infection among HIV-infected Egyptians was very low.<sup>[14]</sup>

It is for these reasons that we have been providing information and support to local patients with hepatitis twice a year for the last 8 years. At these information and morale meetings, the patients and their relatives are informed about treatment processes and diseases by doctors from our center at an informal breakfast event. All questions are answered and misconceptions are corrected. As far as we know, there is no similar public meeting format in use anywhere else. This informative and supportive meeting has significantly increased the compliance of the patients with treatment and follow-up and contributed to the development of trust.<sup>[15]</sup> Among participants, 95% stated that they felt better after the meetings and that the negative psychological impact of the disease had decreased. They became more optimistic, they understood that it is a treatable disease, and that there is a group of doctors who care about them. Numerous patients stated that they used their drug treatment regularly after the meeting. In all, 99% of patients and their relatives wanted the meetings to continue and recommended them to other patients.

Despite the high prevalence of hepatitis C in France (about 1.2%), it was observed that the majority of people infected with HCV were unaware of their status and that physicians had little information.<sup>[16]</sup> Similar results have been identified in China.<sup>[17]</sup> This lack of information at a global level reinforces the potential benefit of holding educational public meetings.

A percutaneous liver biopsy can be performed safely and effectively when the rules of sedoanalgesia and biopsy are observed.<sup>[18, 19]</sup> However, following the screening, 5.8% of our patients evaluated by the gastroenterology department did not wish to have a biopsy performed or pursue treatment. Although a liver biopsy is the gold standard in the diagnosis and follow-up of diffuse liver diseases at times it is not welcomed by patients or even embraced by

physicians because of the invasive nature and the risk of complications. The health insurance system in Turkey requires a biopsy for treatment and we observed that this biopsy requirement prevented some patients from obtaining treatment.

One of the most important causes of patient reluctance to treat HCV or noncompliance with follow-up was the difficulty associated with pegylated interferon-based therapies used prior to direct-acting antiviral drugs, the frequency of side effects, long duration, and low efficacy. In a multicenter study conducted in China in 2015, patients still thought that HCV treatment would be interferon-based. This was seen as the main reason for patients not wanting to receive treatment.<sup>[20]</sup> It is now possible to achieve a curative treatment of around 95% with short-term treatment using all-oral direct-acting antiviral drugs.<sup>[21–23]</sup> Prior to the introduction of these medications, we did not treat patients other than those who needed emergency treatment because of similar reservations.<sup>[24]</sup>

The rapid change in the HCV treatment environment requires health professionals to adopt a new attitude in order to combat HCV infection effectively. We need to do more screening for HCV and the knowledge level of both society and physicians must be elevated. Public forums have proven to be useful and we believe that once informed, patients will be more willing to volunteer for hepatitis screening. As in other parts of the world, community-based healthcare education programs will both improve the diagnosis and treatment compliance and success of efforts to eradicate the disease.<sup>[25–28]</sup>

## Conclusion

In conclusion, we found that there was a significant gap in referring patients with a positive finding to specialized departments and thus to the appropriate follow-up and treatment programs, with the exception of clinics that specialized in HCV infection. Training programs about hepatitis should be implemented to address and correct this, as it presently constitutes an important obstacle to the eradication of HCV infection.

## Disclosures

**Ethics Committee Approval:** Ethics committee approval was granted by Mersin University Ethical Committee with the decision number 106 dated 06/03/2019.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – O.S.; Design – O.S.; Supervision – O.S.; Materials – Z.A.; Data collection &/or processing – Z.A.; Analysis and/or interpretation – O.S.; Literature search – O.S., Z.A.; Writing – Z.A., O.S.; Critical review – O.S.

## References

1. Lavanchy D. Evolving epidemiology of hepatitis C virus. *Clin Microbiol Infect* 2011;17:107–15. [\[CrossRef\]](#)
2. Alberti A, Chemello L, Benvegnù L. Natural history of hepatitis C. *J Hepatol* 1999;31 Suppl 1:17–24. [\[CrossRef\]](#)
3. World Health Organization. Hepatitis C, fact sheet. 2017. Available at: [www.who.int/mediacentre/factsheets/fs164/en](http://www.who.int/mediacentre/factsheets/fs164/en). Accessed Jun, 2018.
4. 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;21:1020–6. [\[CrossRef\]](#)
5. Tezcan S, Ulger M, Aslan G, Yaraş S, Altıntaş E, Sezgin O, et al. Determination of hepatitis C virus genotype distribution in Mersin province, Turkey. *Mikrobiyol Bul* 2013;47:332–8. [\[CrossRef\]](#)
6. Thomas DL, Cannon RO, Shapiro CN, Hook EW 3rd, Alter MJ, Quinn TC. Hepatitis C, hepatitis B, and human immunodeficiency virus infections among non-intravenous drug-using patients attending clinics for sexually transmitted diseases. *J Infect Dis* 1994;169:990–5. [\[CrossRef\]](#)
7. Mehta SH, Astemborski J, Kirk GD, Strathdee SA, Nelson KE, Vlahov D, et al. Changes in blood-borne infection risk among injection drug users. *J Infect Dis* 2011;203:587–94. [\[CrossRef\]](#)
8. Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition Examination Survey 2001–2008. *Hepatology* 2012;55:1652–61. [\[CrossRef\]](#)
9. Nayır E, Sezgin O, Altıntaş E, Üçbilek E. Knowledge levels of general practitioners employed in Mersin province about hepatitis B and hepatitis C. *Academic Gastroenterology* 2012;11:58–62.
10. Irvin R, McAdams-Mahmoud A, Hickman D, Wilson J, Fenwick W, Chen I, et al. Building a Community - Academic Partnership to Enhance Hepatitis C Virus Screening. *J Community Med Health Educ* 2016;6. pii: 431. [\[CrossRef\]](#)
11. Zickmund SL, Brown KE, Bielefeldt K. A systematic review of provider knowledge of hepatitis C: is it enough for a complex disease? *Dig Dis Sci* 2007;52:2550–6. [\[CrossRef\]](#)
12. Johnson S, Aluzaitė K, Taar A, Schultz M. Identifying barriers to treatment of HCV in the primary care setting. *Hepatol Int* 2019;13:58–65. [\[CrossRef\]](#)
13. Khalid M, Dahal S, Gayam V, Mandal A, Hossain MR, Mukhtar O, et al. Assessment of Knowledge, Attitudes, and Practices Regarding Chronic Hepatitis C Treatment and Its Challenges: A Survey of Internal Medicine Residents in a Community Hospital. *Gastroenterology Res* 2018;11:31–5. [\[CrossRef\]](#)
14. Sultan NY, YacoobMayet A, Alaqeel SA, Al-Omar HA. Assessing the level of knowledge and available sources of information about hepatitis C infection among HCV-infected Egyptians. *BMC Public Health* 2018;18:747. [\[CrossRef\]](#)

15. Sezgin O, Altıntaş E, Üçbilek E, Ateş F, Yaraş S, Sarıtaş B, et al. P1278: Effects of “chronic hepatitis patients information and morale meetings” on patient compliance and treatment success. *Journal of Hepatology* 2015;62:S263–864. [\[CrossRef\]](#)
16. Rotily M, Loubière S, Prudhomme J, Portal I, Tran A, Hofliger P, et al. Factors related to screening of hepatitis C virus in general medicine. [Article in French]. *Gastroenterol Clin Biol* 2002;26:261–9.
17. Wei L, Li J, Yang X, Wang G, Feng B, Hou J, et al. Nationwide survey of specialist knowledge on current standard of care (Peg-IFN/RBV) and barriers of care in chronic hepatitis C patients in China. *J Gastroenterol Hepatol* 2016;31:1995–2003. [\[CrossRef\]](#)
18. Sezgin O, Altıntaş E, Üçbilek E, Tombak A. Percutaneous Liver Biopsies: Safety and Efficacy *Turkiye Klinikleri J Med Sci* 2010;30:1287–91. [\[CrossRef\]](#)
19. Sezgin O, Yaras S, Ates F, Altintas E, Saritas B. Effectiveness of Sedoanalgesia in Percutaneous Liver Biopsy Premedication. *Euroasian J Hepatogastroenterol* 2017;7:146–9. [\[CrossRef\]](#)
20. Bian DD, Zhou HY, Liu S, Liu M, Duan C, Zhang JY, et al. Current treatment status and barriers for patients with chronic HCV infection in mainland China: A national multicenter cross-sectional survey in 56 hospitals. *Medicine (Baltimore)* 2017;96:e7885. [\[CrossRef\]](#)
21. Örmeci N, Gülşen M.T, Sezgin O et al. Treatment of HCV infection with direct acting antiviral agents. Real life experiences. *ApasI Single Topic Conference September 2018 İstanbul*, S-002
22. Demir M, Danis N, Kani HT, Sezgin O et al. Real world data on safety and efficacy of ledispavir+sofosbuvir±RBV, ombitasvir/paritaprevir/ritonavir ±dasabuvir±RBV combination therapy for chronic hepatitis C. *A Turkey experience ApasI Single Topic Conference September 2018 İstanbul*, S-001
23. Yaraş S, Üçbilek E, Özdoğan O, Ateş F, Altıntaş E, Sezgin O. Real-life results of treatment with ombitasvir, paritaprevir, dasabuvir, and ritonavir combination in patients with chronic renal failure infected with HCV in Turkey. *Turk J Gastroenterol* 2019;30:331–5.
24. Koksall I, Aladağ M, Koklu S, Sezgin O. The Demographic Aspects of Turkish Chronic Hepatitis C Patients And The Treatment Initiation From A Physician’s & Patient’s Point of View. *First Interim Analysis of Turkish Data From Mosaic Study. Value Health* 2015;18:A631.
25. Shiha G, Metwally AM, Soliman R, Elbasiony M, Mikhail NNH, Easterbrook P. An educate, test, and treat programme towards elimination of hepatitis C infection in Egypt: a community-based demonstration project. *Lancet Gastroenterol Hepatol* 2018;3:778–89. [\[CrossRef\]](#)
26. Samuel ST, Martinez AD, Chen Y, Markatou M, Talal AH. Hepatitis C virus knowledge improves hepatitis C virus screening practices among primary care physicians. *World J Hepatol* 2018;10:319–28.
27. Rogal SS, McCarthy R, Reid A, Rodriguez KL, Calgaro L, Patel K, et al. Primary Care and Hepatology Provider-Perceived Barriers to and Facilitators of Hepatitis C Treatment Candidacy and Adherence. *Dig Dis Sci* 2017;62:1933–43. [\[CrossRef\]](#)
28. Lubega S, Agbim U, Surjadi M, Mahoney M, Khalili M. Formal hepatitis C education enhances HCV care coordination, expedites HCV treatment and improves antiviral response. *Liver Int* 2013;33:999–1007. [\[CrossRef\]](#)