HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2025.24992
Haydarpasa Numune Med J 2025;65(1):91–97

hnhtipdergisi.com

ORIGINAL ARTICLE

Challenges in Anti-HCV Screening: A Retrospective Analysis and Pooled Data Review from Türkiye

Semiha Çelik Ekinci, Ercan Yenilmez, Feyza İslamoğlu Tıkır

Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Türkiye, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Türkiye

Abstract

Introduction: The availability of appropriate screening and diagnostic procedures for hepatitis C virus (HCV) is critical for early diagnosis, reduction in mortality and morbidity, and HCV elimination. In our study, we aimed to evaluate the appropriateness of HCV testing procedures and HCV prevalence both in our hospital and across Türkiye.

Methods: HCV screening and confirmation procedures performed in our hospital between 01.01.2021 and 01.12.2022 were retrospectively evaluated. In the literature review phase, a pooled analysis was conducted using data from studies performed in Türkiye between 01.01.2019 and 21.12.2024 with a methodology parallel to ours.

Results: A total of 25,137 patients underwent anti-HCV testing, with 181 positive cases (0.72%). After the exclusion process, 151 anti-HCV positive patients remained. Among them, one patient (0.6%) was HCV RNA positive, 76 patients (50.3%) were HCV RNA negative after a history of HCV treatment, and 74 patients (49%) were HCV RNA negative without any treatment history (false anti-HCV positive or HCV spontaneous clearance). The mean and median S/CO ratio in false-positive patients were 11.6±19.21 and 2.5 (IQR: 6.89), respectively. Additionally, the mean and median S/CO ratio in true-positive patients were 74.8±36.43 and 69.45 (IQR: 47.15), respectively. According to the pooled data analysis, the seropositivity rate was 1.3% (range: 0.21%-2.46%), with 13,992 of 1,079,492 anti-HCV tests testing positive. A reflex HCV RNA confirmation test was performed in 77.44% of anti-HCV positive patients, and the confirmed disease rate was 42.5%. In these patients, the minimum anti-HCV S/CO ratio ranged from 1.81 to 12.3, while the optimal S/CO threshold was between 5 and 15.85.

Discussion and Conclusion: Our results indicate that the probability of false anti-HCV positive results is very high, especially when the anti-HCV S/CO ratio is low. Although HCV endemicity remains low in our region, anti-HCV screening is inadequate, and clinicians should be more aware of this issue.

Keywords: HCV optimal S/CO threshold; HCV prevalence; pooled analysis.

Hepatitis C virus (HCV) is an important infectious disease that causes inflammation in the liver, leading to fibrosis, cirrhosis, and hepatocellular carcinoma. It is estimated that approximately 50 million people worldwide are infected with HCV, with approximately 1 million new infections occurring annually[1].

According to data reported by the World Health Organization (WHO), the total number of individuals infected with HCV was estimated to reach 20 million by the year 2022. This figure includes 1 million new cases and 240,000 projected deaths due to HCV during the same period. While it has been documented that only 36.4% of individuals living

Correspondence: Semiha Çelik Ekinci, M.D. Department of Infectious Diseases and Clinical Microbiology, University of Health Sciences Türkiye, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Türkiye
Phone: +90 506 357 49 80 **E-mail:** dr_semiha@hotmail.com
Submitted Date: 30.12.2024 **Revised Date:** 05.02.2025 **Accepted Date:** 14.02.2025
Haydarpaşa Numune Medical Journal

with HCV were diagnosed, only 20% received treatment[2]. The WHO's global strategy for the elimination of hepatitis aims to reduce new hepatitis infections by 90% and deaths by 65% between 2016 and 2030[3].

Although elimination efforts have been in place for many years, the development of direct-acting antiviral agents (DAAs) over the last two decades and the implementation of effective screening programs have made elimination targets more achievable[4].

The appropriateness of anti-HCV test ordering and evaluation processes is crucial for early diagnosis and the reduction of virus-related morbidity and mortality, thereby making a valuable contribution to global HCV elimination efforts.

In our study, we aimed to determine seropositivity and true disease rates, evaluate false positivity status by retrospectively analyzing the anti-HCV test results of patients who were tested for various reasons in our hospital, and assess the HCV prevalence in Türkiye during the DAA era by compiling published studies from the last five years.

Materials and Methods

Data Collection

A retrospective evaluation of all anti-HCV tests conducted in our hospital for various reasons over a two-year period (1.01.2021–31.12.2022) was undertaken. In the subsequent stage, the data of patients with anti-HCV positivity was accessed through the hospital automation system and E-pulse system. Patients with missing data or who were thought to have not undergone confirmatory testing with the HCV RNA test were approached via their contact information and were advised to apply to the hospital. Test results of more than one study in the same patient (duplication) were not evaluated. After the exclusion of duplicate tests, the proportion of anti-HCV positive tests among all tests was calculated. Patients whose data could not be accessed through the hospital and E-pulse system, and patients who did not present to the hospital despite being contacted by telephone because HCV RNA (PCR) confirmation was not performed, were excluded from the study. The exclusion process was conducted in a manner that was entirely devoid of any demographic or clinical bias. True positivity, false positivity, and previous infection status were determined by taking into account the patients' previous treatment with interferon-based or direct-acting agents or HCV-RNA positivity. The proportion of PCR-confirmed patients among all anti-HCV positive results was subsequently calculated.

Anti-HCV and HCV-RNA Tests

The presence of 'anti-HCV' antibodies, which are developed by the immune system against HCV, is utilized as a screening test. Enzyme immunoassays (EIA) and chemiluminescence microparticle immunoassays (CMIA) are employed for antibody detection, and the signal-to-cutoff (S/CO) ratio is a primary factor in determining the diagnostic reliability of CMIA tests. However, it should be noted that these tests are unable to differentiate between active and previous infection, and furthermore, the occurrence of false positive results is a possibility. Therefore, the validation of nucleic acid amplification tests (NAATs) is essential[5,6]. However, the utilization of NAAT as a screening test does not appear to be a cost-effective approach.

The unit S/CO was used for anti-HCV, and IU/mL for HCV RNA. The anti-HCV test was performed using the Roche Elecsys® Anti-HCV II Cobas e 602 module, with results considered negative for <0.9, borderline for ≥0.9 and <1.0, and positive for ≥1.0. The HCV-RNA assay was performed on the NeuMoDx 96 Molecular System with HCV Quant Test Strip kits. This test is an in-vitro diagnostic nucleic acid amplification assay for the detection and quantitation of HCV RNA in human plasma samples using real-time polymerase chain reaction (PCR). The quantitative measurement range of the test is 8-158,489,319 IU/mL.

Data Collection and Statistical Methods for Pooled Analysis

In the literature review phase of the study, studies revealing the prevalence of HCV and/or confirmed HCV patients with true anti-HCV threshold levels in Türkiye between January 1, 2019, and December 21, 2024, were reviewed and pooled analyzed. A literature search was performed in the TUBITAK ULAKBIM Database with the words "anti-HCV seropositivity" or "anti-HCV positivity" or "anti-HCV seroprevalence" or "anti-HCV false positivity" and also in the Turkish and Google Scholar Database with the same keywords.

Primary data from original research were obtained. After the pooled analysis data were collected, the data were handled with the fixed effect model. The period of data included, the number of anti-HCV total tests, the anti-HCV positivity rate, the rate of HCV-RNA tests requested from anti-HCV positive cases, the HCV-RNA positivity rate, the minimum anti-HCV level among confirmed patients, and the optimal threshold value among confirmed patients were recorded. The data were homogenized and presented in tables.

The earliest and latest dates of the study periods were recorded. The number of anti-HCV total tests, the number of anti-HCV positive tests, the number of HCV-RNA tests, and the number of HCV-RNA positive tests were

summed and their percentages were taken. Values for the optimal threshold value among confirmed patients were mean-averaged. Calculations were made with the "Microsoft Excel 2016" program.

Ethical Approval

Our study was conducted in accordance with the Declaration of Helsinki, and the ethics committee approval was obtained from the Scientific Research Ethics Committee of Martyr Prof. Dr. İlhan Varank Training and Research Hospital (number 2022/159 dated 14.12.2022).

Results

Hospital Study Data

During the two-year study period, a total of 35,082 anti-HCV tests were performed in our hospital, 15,523 in 2021 and 19,529 in 2022. After excluding 9,945 tests performed more than once on the same patient (duplications), the study found that 25,137 patients had undergone anti-HCV testing, of whom 181 were positive for the virus, resulting in a two-year positivity rate of 0.72%. Of the 181 patients included in the study, 30 were excluded from the analysis due to incomplete data in the hospital system, inaccessibility of the E-pulse system, death, or inaccessibility by phone. The data of the remaining 151 patients was analyzed. Of these patients, only one (0.6%) had a confirmed diagnosis of HCV (HCV RNA positive), while 76 (50.3%) were HCV RNA positive but had received or were receiving treatment. In the remaining 74 patients (49%), HCV RNA was negative without a history of treatment; these patients were considered as false positive or spontaneous remission patients (Fig. 1).

In the present study, the mean S/CO value in false positive patients was 11.6±19.21, with a median value of 2.5 (interquartile range [IQR]: 6.89), while the mean S/CO ratio in true positive patients was 74.8±36.43, with a median value of 69.45 (IQR: 47.15). The highest S/CO ratio observed was 124 in false positive patients, while the lowest S/CO ratio was 15.3 in true patients. The S/CO ratios in true and false positive patients are presented in Figure 2, arranged in descending order.

Pooled Analysis of Literature Data

The studies conducted in Türkiye between 2019 and 2024 are presented in Table 1, and a total of 16 studies from 11 different cities were included in the review[7-22]. The data in these studies covered the years 2010 and 2023. A pooled data analysis of these studies revealed that out of 1,079,492

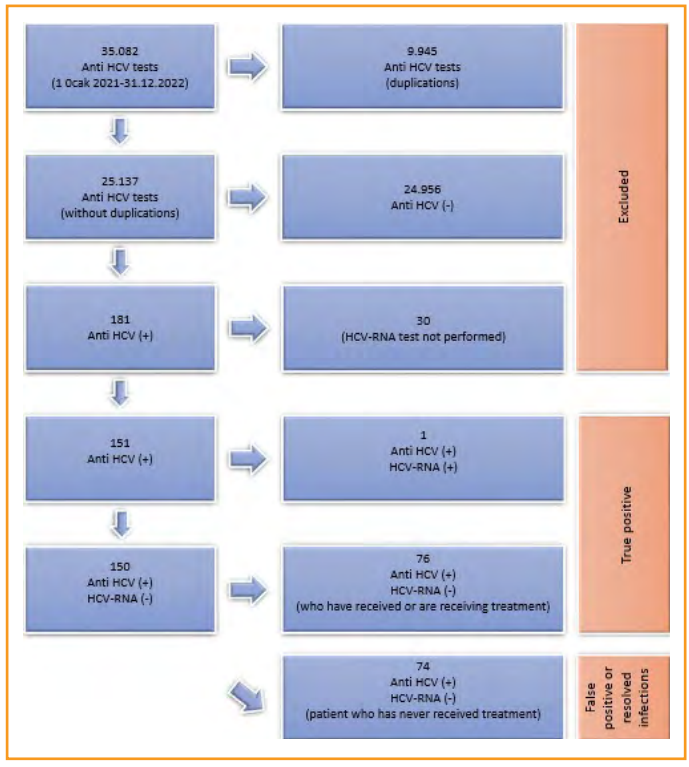

Figure 1. Diagnostic algorithm.

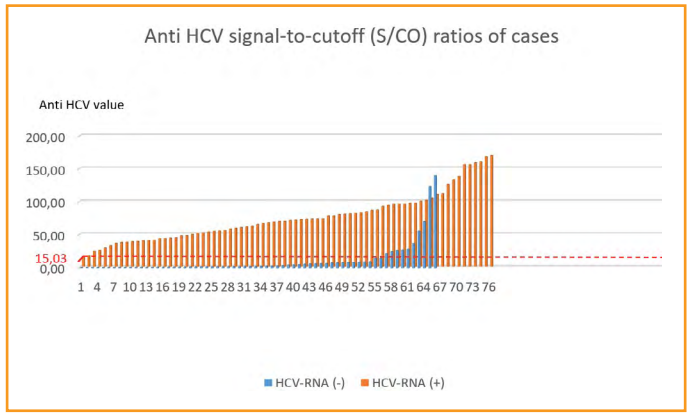

Figure 2. Anti-HCV signal-to-cutoff (S CO) ratios of cases.

anti-HCV tests performed during the study period, the total anti-HCV positive tests was 13,992 and the anti-HCV seropositivity rate was 1.3%, ranging from 0.21% to 2.46% depending on the center. Of the 13,992 anti-HCV-positive patients, 77.44% underwent a simultaneous (reflex) HCV RNA test, while the remainder did not undergo a confirmatory test. The rate of HCV RNA-confirmed disease among these patients was 42.5%. In the relevant studies, the minimum anti-HCV S/CO ratio in confirmed HCV patients ranged from 1.81 to 12.3, while the optimal S/CO threshold ranged from 5 to 15.85.

Table 1. Pooled analysis

Referance no	Study	Period of data included	Anti-HCV total test (n)	Anti-HCV positivity (n / %)	Reflex HCV-RNA testing (n / %)	Confirmed HCV disease (HCV RNA positive) (n / %)	Minimum Anti-HCV among confirmed patients	Optimal threshold value among confirmed patients
1	Türkoğlu, E. 2022 Tokat/Turkey	2010-2020	132,215	3,249 2.46%	2,297 70.70%	899 39.14%	No data	No data
2	Şenol, G. 2023 İzmir/Turkey	2016-2019	9,878	133 1.35%	58 43.61%	12 20.69%	8 (Architect i1000, Abbott, USA)	5
3	Dabanlıoğlu, B. 2024 Erzincan/Turkey	2018-2020	72,341	150 0.21%	150 0.21%	50 33.33%	5.1-10 (Architect i2000, Abbott, USA)	15.4 IU/ml
4	Demirci, M. 2022 Manisa/Turkey	2016-2018	10,944	109 1.00%	No data	No data	No data	No data
5	Suntur, B.M. 2020 Adana/Turkey	2016-2018	146,342	2,613 1.79%	1,761 67.39%	960 54.51%	No data (Architect SR2000i, Abbott, Germany)	No data
6	Sarıkaya, B. 2024 İstanbul/Turkey	2020-2023	96,515	602 0.62%	537 89.20%	130 24.21%	3 (Elecsys Anti-HCV II, Roche Diagnostics, Germany)	10.86
7	Işık, S.A. 2022 İstanbul/Turkey	2016-2019	36,019	428 1.19%	257 60.05%	84 32.68%	1.82 (Architect SR2000i, Abbott, Germany)	8.58
8	Kirişci, Ö. 2019 Kahramanmaraş/ Turkey	2013-2018	81,203	No data	559 No data	214 No data	1.99 (Elecsys Anti-HCV II, Roche Diagnostics, Germany)	12.27
9	Deniz, R. 2024 İstanbul/Turkey	2014-2017	77,783	943 1.21%	419 44.43%	309 38.28%	No data (Innogenetics HCV Ab IV; Belgium)	No data
10	Avcıoğlu, F. 2021 Bolu/Turkey	2017-2019	17,021	315 1.85%	315 100%	75 23.81%	No data (CMIA, Abbot®, Architect System)	No data
11	Şirin, M.Ş. 2019 Isparta/Turkey	2017-2018	21,035	297 1.41%	210 70.70%	94 44.76%	12.3 (Elecsys Anti-HCV II, Roche Diagnostics, Germany)	12.34
12	Gülseren, Y.D. 2023 Balıkesir/Turkey	2019-2021	No data	626	626 100%	31 4.95%	No data (Architect i2000, Abbott, USA)	8.9
13	Atalay, M.A. 2021 Kayseri/Turkey	2018-2021	No data	687	687 100%	302 43.96%	No data (Elecsys Anti-HCV II, Roche Diagnostics)	5.8
14	Yenilmez, E. 2019 İstanbul/Turkey	2017	20,038	220 1.10%	114 51.81%	36 31.58%	6.05 (Abbot®, Architect System)	14.05
15	Öcal, M. 2023 İstanbul/Turkey	2015-2019	199,516	2,039 1.02%	1419 69.59%	900 63.42%	3.1 (Elecsys Anti-HCV II, Roche Diagnostics, Germany)	15.85
16	Öztürk, S. 2021 İstanbul/Turkey	2015-2019	158,642	1,581 1.00%	727 45.98%	216 29.71%	5.2 (Architect i2000, Abbott, USA)	7.5
Pooled analysis of data		2010-2023	1,079,492	13,992 1.30%	10,136 77.44%	4,312 42.54%		Ort 10.60

Discussion

It is imperative to emphasize the significance of HCV screening in facilitating early diagnosis, thereby reducing morbidity and mortality and ultimately leading to the eradication of the disease. Such screening should be conducted periodically for specific high-risk groups. In our country, the implementation of HCV screening is not limited to high-risk groups; it is also routinely conducted prior to blood donation, pre-operatively, pre-marriage, during employment, and as part of periodic health examinations.

However, in low-risk groups, the prevalence of false positive results is high, leading to a significant number of unnecessary hospital visits, additional tests, blood sample collections, and financial burdens. These consequences persist until the false positive result is ruled out, causing considerable psychological distress for the patient.

The primary method of screening for HCV infection is the detection of anti-HCV antibodies. Enzyme-linked

immunosorbent assay (ELISA), chemiluminescence immunoassay (CLIA), and rapid diagnostic tests (RDTs) are the main diagnostic tools used for this purpose. When an anti-HCV antibody positive result is obtained, confirmation must be performed via HCV polymerase chain reaction (PCR) detection by molecular methods or by detecting the presence of HCV core antigen using ELISA methods[23].

In the present pooled analysis, 22.56% of anti-HCV positive cases did not undergo simultaneous HCV-RNA testing. The most common reason for this was that the anti-HCV test was requested from high-traffic clinical areas, such as emergency departments or surgical clinics, without further consultation from an infectious diseases specialist. In some centers, it has been observed that even cases with high S/CO values may be overlooked without proper diagnostic confirmation.

Notably, publications from the same centers in consecutive years have shown an increasing rate of reflex test requests, suggesting that the recently added alert system in hospital information systems may be contributing to improvements in follow-up procedures[7,8,12,13,20].

The HCV seropositivity rate, defined as the ratio of all anti-HCV tests to anti-HCV positivity, was determined to be 1.3% in the pooled analysis study. In our hospital-based study, the anti-HCV seropositivity rate was calculated as 0.72%. Comparatively, global HCV prevalence has been reported as follows: 0.8% in Africa, 0.5% in the Americas, 1.3% in Europe, 1.6% in the Eastern Mediterranean Region, 0.5% in Southeast Asia, and 0.5% in the Western Pacific Region. These findings indicate that our study results align with existing global literature[24].

A particularly concerning finding was that 30 (16.7%) of the 181 anti-HCV positive patients did not receive confirmatory testing. This is especially significant when compared to the 22.56% rate observed in similar studies conducted in Türkiye. This suggests that a substantial proportion of patients who underwent anti-HCV testing may not have received proper clinical follow-up or may have declined further evaluation. This highlights the need for enhanced patient follow-up strategies to ensure the proper management of individuals with suspected HCV infection, ultimately contributing to the broader goal of disease elimination.

In a study investigating the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the Elecsys test, which is also utilized in our hospital, these values were 99.30%, 99.86%, 88.04%, and 99.99%, respectively, while the prevalence of HCV infection was 1.0%. Furthermore, the AUROC value of the Elecsys test for detecting "true HCV infection" cases was 0.9980 (95% CI=0.9944-1.0017), and the optimal S/CO cut-off value indicating maximum diagnostic performance was 0.93, with 99.53% sensitivity and 99.85% specificity[25]. However, within immunocompetent populations exhibiting anti-HCV prevalence of less than 10% (for instance, voluntary blood donors, active duty and retired military personnel, the general population, healthcare workers, or patients attending sexually transmitted disease [STD] clinics), analogous to the general screening population in our country, the prevalence of anti-HCV false positive results ranges from 15% to 60%[26].

The prevalence of false positive anti-HCV test results in studies conducted in Türkiye ranged from 36.58% to 95.05%, with an average of 47.46% in the pooled data. In the present study, this rate was observed to be similar to the overall average, with a percentage of 49%. However, it is important to note that all studies included patients with spontaneously resolved infection during the acute phase of infection, and no threshold value was established for the differentiation of these cases (Table 1 for further details). A significant challenge in the management of anti-HCV positive and HCV RNA negative patients pertains to the differentiation between a previous infection and false positivity. The minimum anti-HCV S/CO ratio in confirmed HCV patients in studies from Türkiye ranged from 1.81 to 12.3, while the optimal S/CO threshold ranged from 5 to 15.85 (Table 1). In the study by Choi et al.,[27] the evaluation of patients for active, previous infection, and false positivity with CMIA, Recombinant Immunoblot Assay (RIBA), and NAAT was conducted, with the aim of investigating the place of Architect test results. Although the sensitivity was found to be very high (96.7%) for the optimal S/CO ratio of 5.2, the positive predictive value was not high enough (52.1%). Furthermore, the mean S/CO ratio was determined to be 12.96±2.90, 5.29±4.53, and 1.81±1.31 for active HCV infection, previous infection, and false positivity, respectively. In a different study, the sensitivity of the Architect Anti-HCV test for an S/CO ratio of 1.0 was found to be very high (100%), while the specificity was low (36.1%). However, the diagnostic accuracy of the test was reported to be much higher when the S/CO ratio was increased to 8.0. Thus, it was concluded that although this test is good as a screening test due to its high sensitivity, values between 1.0 and 8.0 must be confirmed[28]. Consequently, it can be anticipated that the level of positivity will be highest in cases of active infection, moderate levels will be observed in previous infections, and low levels will be seen in false positive test results. It is imperative that clinicians

receive comprehensive education through national awareness initiatives or informational brochures. It is crucial to emphasize that even in cases where S/CO ratios are intermediate, they must be confirmed through the utilization of HCV-RNA testing. Furthermore, it is essential to ensure that anti-HCV test positivity is systematically documented as a warning within hospital information systems. This measure must be designed to ensure that clinicians do not miss the indication and that they are guided towards the confirmation of the disease and referral to the relevant department.

Conclusion

In conclusion, our data showed that Türkiye is still a low-endemic country for HCV. Our study results and the studies conducted in Türkiye mainly show that anti-HCV screening is incomplete and that there is a significant proportion of patients with positive anti-HCV test results who have not been confirmed, indicating that patient follow-up is not at the desired level. Our results also show that almost half of the anti-HCV positive results do not result in a true HCV patient and that particularly low levels of S/CO ratio positivity do not eliminate the need for HCV RNA confirmation, but the probability of false positives is very high.

The most important step for the establishment of WHO's global strategy for the elimination of hepatitis in our country is to develop national algorithms for the early diagnosis of patients with HCV, ensure that screening reaches the desired standards, communicate test positivity to clinicians with in-hospital alert systems and to patients through other innovative technologies, and increase the sensitivity and awareness of clinicians with educational activities.

Ethics Committee Approval: The study was approved by Martyr Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (No: 2022/159, Date: 14.12.2022).

Use of AI for Writing Assistance: Not declared.

Peer-review: Externally referees.

Authorship Contributions: Concept – S.Ç.E., E.Y.; Design – S.Ç.E., E.Y.; Supervision – S.Ç.E., E.Y.; Fundings – S.Ç.E.; Materials – S.Ç.E., F.İ.T.; Data collection &/or processing – S.Ç.E., F.İ.T.; Analysis and/or interpretation – S.Ç.E., E.Y., F.İ.T.; Literature search – S.Ç.E., E.Y., F.İ.T.; Writing – S.Ç.E., E.Y.; Critical review – S.Ç.E., E.Y.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. World Health Organization. Hepatitis C. Available at: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c. Accessed on Feb 18, 2025.
2. World Health Organization. Hepatitis. Available at: https://www.who.int/data/gho/data/themes/chronic-viral-hepatitis. Accessed on Feb 18, 2025.
3. World Health Organization. Elimination of hepatitis by 2030. Available at: https://www.who.int/health-topics/hepatitis/elimination-of-hepatitis-by-2030#tab=tab_1. Accessed on Feb 18, 2025.
4. Torre P, Festa M, Sarcina T, Masarone M, Persico M. Elimination of HCV infection: Recent epidemiological findings, barriers, and strategies for the coming years. Viruses 2024;16:1792. [CrossRef]
5. Omata M, Kanda T, Wei L, Yu ML, Chuang WL, Ibrahim A, et al. APASL consensus statements and recommendations for hepatitis C prevention, epidemiology, and laboratory testing. Hepatol Int 2016;10:681–701. [CrossRef]
6. Kamili S, Drobeniuc J, Araujo AC, Hayden TM. Laboratory diagnostics for hepatitis C virus infection. Clin Infect Dis 2012;55:S43–8. [CrossRef]
7. Türkoğlu E, Parlak Z, Barut HŞ. Assessment of HCV-RNA test results and access rates to antiviral treatment in patients with anti-HCV positivity—A 10-year analysis. Turk J Med Sci 2022;52:1984–990. [CrossRef]
8. Şenol G, Coşkun M, Kaftan O, Biçmen C, Gündüz AT, Demirel MM, et al. Determination of confirmation rate of anti-HCV test positivity with HCV-RNA. Anatol J Gen Med Res 2023;33:316–21. [CrossRef]
9. Dabanlıoğlu B, Yılmaz A, Akyüz S, Gülhan B. The best anti-HCV S/Co values for reflecting HCV infection in a university hospital in the eastern part of Turkey. J Infect Dev Ctries 2024;18:131–5. [CrossRef]
10. Demirci M, Çınar C, Eslek A, Orhan M, Akar ŞŞ. Evaluation of anti-HCV positivity in patients receiving inpatient treatment in a mental health hospital in Turkey. J Tepecik Educ Res Hosp 2022;32:279–82. [CrossRef]
11. Suntur BM, Kaya H, Eker HB, Şahin B, Kara B, Bozok T, et al. A cross-sectional study of real-life data of HCV from Turkey south region. J Infect Dev Ctries 2020;14:380–6. [CrossRef]
12. Sarıkaya B, Yatar İD, Yılmaz S, Tiryaki Y, Sarıkaya VA, Çetinkaya RA, et al. The usefulness of anti-HCV signal to cut-off ratio in predicting hepatitis C viremia and the effect of genotype differences on signal to cut-off ratio. Rev Assoc Med Bras 2024;70:e20240370. [CrossRef]
13. Akkaya Işık S, Tural E, Yenilmez E, Çetinkaya RA, Baylan O, Görenek L. Diagnostic reliability of Architect anti-HCV tests and diagnostic cost of false positivity. South Clin Ist Euras 2022;33:136–41.
14. Kirişci Ö, Calıskan A. Threshold value of the anti-HCV test in the diagnosis of HCV infection. J Infect Dev Ctries 2019;13:914–9.
15. Deniz R, Karslı S, Ekinci ÖB, Kalantarova İ, Atasoy A, Önel M, et al. Is only requesting an anti-HCV test sufficient for hepatitis C screening? J Istanbul Fac Med 2024;87:215–9. [CrossRef]

16. Avcıoğlu F, Behçet M, Kalaycıoğlu O. Comparison of anti-HCV signal-to-cutoff ratio with HCV RNA results. Clin Lab 2021;67:376–80. [CrossRef]
17. Sirin MC, Cicioglu Aridogan B, Sesli Cetin E, Sirin FB. Evaluation of biochemical, hematological, RIBA and PCR assays in predicting viremia in anti-HCV positive patients. J Infect Dev Ctries. 2019;13:736–43. [CrossRef]
18. Gülseren YD, Sığ AK, Yarar M. Optimizing signal-to-cutoff values (S/Co) of anti-HCV in prediction of viremia: A retrospective analysis with HCV-RNA. J Acad Res Med 2023;13:95–9. [CrossRef]
19. Atalay MA, Sağıroğlu P, Oskay M, Emir B. Comparison of samples found positive by anti-HCV screening test with line immunoassay and determination of threshold value. Rev Assoc Med Bras 2021;67:1480–4. [CrossRef]
20. Yenilmez E, Çetinkaya RA, Sarıkaya B, Akkaya Işık S, Baylan O, Görenek L. Diagnostic reliability of Architect anti-HCV tests in a low-risk population. Bozok Med J [Article in Turkish] 2019;9:127–31.
21. Ocal M, Bulut ME. Determination of anti-HCV signal to cut-off value in patients with hepatitis C virus infection and the variety of antibody responses. Eur Res J May 2023;9:484–94. [CrossRef]
22. Oztürk S, Ağalar C. Updating the signal-to-cutoff level to reduce anti-hepatitis C virus false positivity. Jundishapur J Microbiol 2021;14:e119110. [CrossRef]
23. European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C: Final update of the series. J Hepatol 2020;73:1170–218. Erratum in: J Hepatol 2023;78:452. [CrossRef]
24. Fleurence RL, Alter HJ, Collins FS, Ward JW. Global elimination of hepatitis C virus. Annu Rev Med 2025;76:29–41. [CrossRef]
25. Kim B, Ahn HJ, Choi MH, Park Y. Retrospective analysis on the diagnostic performances and signal-to-cut-off ratios of the elecsys Anti-HCV II assay. J Clin Lab Anal 2018;32:e22165. [CrossRef]
26. U.S. Centers for Disease and Prevention. Guidelines for laboratory testing and result reporting of antibody to hepatitis C virus. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5203a1.htm. Accessed on Feb 18, 2025.
27. Choi MS, Lee K, Hong YJ, Song EY, Kim DS, Song J. The role of the signal-to-cutoff ratio in automated anti-HCV chemiluminescent immunoassays by referring to the nucleic acid amplification test and the recombinant immunoblot assay. Ann Lab Med 2018;38:466–72. [CrossRef]
28. Fletcher GJ, Raghavendran A, Sivakumar J, Samuel P, Abraham P. Diagnostic reliability of architect anti-HCV assay: Experience of a tertiary care hospital in India. J Clin Lab Anal 2018;32:e22245. [CrossRef]