Non-Interventional Study (Non-PMOS)

Final Study Report

Title	Treatment initiation rates of patients with positive anti-HCV results in University and Training and Research Hospitals in Turkey: a retrospective chart review **(Lost-C Study)** H20-058
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1.0 Abstract

Title

Treatment initiation rates of patients with positive anti-HCV results in University and Training and Research Hospitals in Turkey: a retrospective chart review (Lost-C Study)

Keywords

Hepatitis C, treatment initiation, HCV, anti-HCV, HCV-RNA

Rationale and Background

World Health Organization (WHO) estimates that in 2015, globally 71 million people were living with hepatitis C virus (HCV) infection, accounting for 1% of the world population. Left untreated, hepatitis B virus (HBV) and HCV infection can lead to cirrhosis and hepatocellular carcinoma. These long-term complications are life-threatening and accounted for 96% of the deaths due to viral hepatitis. According to WHO, only 20% of patients living with HCV infection have been diagnosed and are aware of their infection. Among those diagnosed, only 7.4% were receiving treatment in 2015. Recently, there are anti-viral treatment options in the market and success rate of these treatment are almost 100%. Well-designed screening policies may help to reduce the rate of undiagnosed and untreated patients. Even though during the pre-operative anti-HCV screening, patients are being detected with positive anti-HCV results, more than half of the patients are not notified for HCV-RNA test results. Most of these patients remain unaware of their infection and do not receive treatment.

In this study, we aim to determine the rate of patients who receive HCV treatment after receiving positive anti-HCV results during HCV screening in Turkey during the last 3 years.

Research Question and Objectives

This study was aiming to find out the proportion of patients with positive anti-HCV results who receive treatment within university and training and research hospitals in Turkey.

The primary objective of this study was to determine the rate of initiation of hepatitis treatment in patients who received positive Anti-HCV results during routine anti-HCV screening for any reason.

The secondary objectives were as follows:

- To determine the proportion of patients who have positive anti-HCV results during the screening process but not screened for HCV-RNA
- To determine the proportion of patients who receive positive HCV-RNA results among patients for whom HCV-RNA screening was performed
- To determine the proportion of the patients who receive negative HCV-RNA results among patients for whom HCV-RNA screening was performed
- To determine the proportion of patients with positive HCV-RNA results who previously received HCV treatment in line with their positive anti-HCV results
- To determine the time interval from screening to treatment initiation
- To determine the specialty(ies) of the physician(s) who request anti-HCV screening

Study Design

This was a non-interventional, observational, multi-center, cross sectional and retrospective chart review study which included patients screened for anti-HCV.

Results

The study was conducted in 30 study centers which were either university hospitals or training and research hospitals located in various cities in Turkey. Data of 1000 patients were included in this retrospective chart review study and 50.3% of the patients were male. The majority of the patients (82.7%) were residing in cities or towns and only 15.6% were living in rural areas.

Most frequently anti-HCV test requesting specialty was infectious diseases (22.7%), followed by gastroenterology (14.4%) and internal medicine (13.6%).

Among 1000 patients who received a positive anti-HCV result, 78.5% were screened for HCV-RNA. Among HCV-RNA screened patients, 54.8% (n=430) had a positive result. Proportion of patients who received HCV treatment in line with their positive anti-HCV results in HCV-RNA positive patients was 72.8%. Considering all eligible anti-HCV positive patients, this proportion was corresponding to 31.3%. Patients who received HCV treatment following obtaining a positive HCV-RNA result were evaluated according to the screening departments within the surgical branches and non-surgical branches. Within the surgical branches, 49.0% of the patients reaching treatment were screened in general surgery department whereas only 2.0% of the patients who received HCV treatment were screened in department of ear nose and throat. Within the non-surgical branches, 46.2% of the patients reaching treatment were screened in infectious diseases department. Among patients who had access to treatment, the lowest rate of access to treatment within non-surgical branches was observed in chest diseases, endocrinology, family medicine and oncology departments.

Discussion

In general, the group of patients waiting to be treated is much more than those who receive treatment. Studies show that 50-80% of HCV-infected patients could not be diagnosed, and only less than 20% receive appropriate treatment. Similarly, treatment initiation was reported as 21% in a Danish study conducted in patients with chronic HCV infection. In our study a higher percentage of patients (31.3%) were able to initiate HCV treatment after obtaining a positive anti-HCV result. This could be due to high number of patients who were screened and followed-up in infectious disease and gastroenterology departments.

A similar retrospective chart-review study recently conducted in Mersin, Turkey included 1118 anti-HCV positive patients. Among these anti-HCV positive patients,

35% were screened in gastroenterology, 37% were screened in infectious diseases, and 28% were screened in other departments. Treatment was initiated in 91% of the patients who were identified in the gastroenterology department. This result shows a high rate of treatment initiation in the gastroenterology department and might be a possible reason for obtaining a high rate of treatment initiation in our study since 37% of our patients were screened in gastroenterology and infectious diseases departments.

Another retrospective chart review study conducted in United States in 2019 included 8407 individuals with chronic HCV infection. Of these patients, 830 initiated treatment with a DAA agent, whereas 7577 did not, suggesting a DAA treatment initiation rate of 9.9%. Median time to initiate DAA treatment was reported as 300 days. We detected a much shorter time to treatment duration in our study (median 91 days). Following categorization of screening hospitals into university or training and research hospitals, we found that time to treatment was even shorter in university hospitals (median 70 days). This difference could be due to different health care systems present in Turkey and United States.

In conclusion, our study results indicate a higher rate of treatment initiation in patients with HCV infection as compared to most of the published literature. Furthermore, we found that time from screening to treatment initiation was considerably shorter comparing to other international studies. On the other hand, despite these promising results, there might be a big patient population who cannot reach treatment, since HCV-RNA was not requested in a significant portion (22.5%) of anti-HCV positive patients.

2.0 List of Abbreviations

Abbreviation	Definition
CI	Confidence interval
DAA	Direct-acting antiviral
eDRF	Electronic Data Recording Form
HBV	Hepatitis B virus
HCV	Hepatitis C Virus
Max	Maximum
Min	Minimum
NA	Not applicable
Q1	Lower quartile
Q3	Upper quartile
SD	Standard deviation
WHO	World Health Organization

3.0 Responsible Parties

This study was designed and sponsored by AbbVie.

4.0 Milestones

Milestone	Date
Start of Data Collection:	24 December 2020
End of Data Collection:	22 June 2021
Final Report of Study Results:	26 November 2021

5.0 Rationale and Background

World Health Organization (WHO) estimates that in 2015, globally 71 million people were living with hepatitis C virus (HCV) infection, accounting for 1% of the world population. HCV infection is unevenly distributed in the world. The European and Eastern

Mediterranean regions are affected more, but there are variations in prevalence across and within countries [WHO, 2017]. In Turkey, HCV prevalence rates range between 0.5 and 1.0% [Ministry of Health, 2018].

Left untreated, hepatitis B virus (HBV) and HCV infection can lead to cirrhosis (720 000 deaths) and hepatocellular carcinoma (470 000 deaths). These long-term complications are life-threatening and accounted for 96% of the deaths due to viral hepatitis. Mortality from viral hepatitis has increased by 22% since 2000. Unless people with HBV and HCV infection are diagnosed and treated, the number of deaths due to viral hepatitis will continue to increase [WHO, 2017].

The virus is mainly acquired via percutaneous exposures to infected blood. Unsafe health-care practices (including unsafe healthcare injections) and injection drug use remain the leading modes of transmission [WHO, 2017; Chou, 2013; Yawn 2002].

Areas with high rates of infection are located in the Eastern Mediterranean Region (62.5 per 100 000) and the European Region (61.8 per 100 000). In the Eastern Mediterranean Region, the most common cause of transmission of infection is unsafe health-care injections [Mohsen, 2015; Khan, 2000]. In the European Region, injection drug use accounts for a substantial proportion of new infections [Mitruka, 2015]

According to WHO, only 20% of patients living with HCV infection have been diagnosed and are aware of their infection. Among those diagnosed, only 7.4% were receiving treatment in 2015 [WHO, 2017]. Recently, there are anti-viral treatment options in the market and success rate of these treatment are almost 100% [Pham, 2018]. Well-designed screening policies may help to reduce the rate of undiagnosed and untreated patients. Anti-HCV testing is requested in hospitals during routine clinical practice for various reasons, including preoperative testing. However, information regarding the results of these serology screenings is available only through sporadic reports (mostly reported as single center reports) and currently multi-central study results that can represent Turkey are not available. Even though during the pre-operative anti-HCV screening, patients are being detected with positive anti-HCV results, more than half of the patients are not

notified for HCV-RNA test results [Yoshioka, 2017]. Most of these patients remain unaware of their infection and do not receive treatment. This population, unaware of their infection, has the potential to reduce the rate of HCV infection, moreover it is an opportunity for HCV elimination efforts.

In Turkey, hospital laboratory results medical records database systems underwent major renovations recently and especially during the last 3 years access to reliable retrospective data improved significantly. In this study, we aim to determine the rate of patients who receive HCV treatment after receiving positive anti-HCV results during HCV screening in Turkey during the last 3 years.

6.0 Research Questions and Objectives

This study was aiming to find out the treatment initiation rates of patients with positive anti-HCV results in university and training and research hospitals in Turkey. Due to exploratory nature of the study, descriptive results were obtained, and hypothesis testing was not applicable to this study.

The primary objective of this study was to determine the rate of initiation of hepatitis treatment in patients who received positive Anti-HCV results during routine anti-HCV screening for any reason.

The secondary objectives were as follows:

- To determine the proportion of patients who have positive anti-HCV results during the screening process but not screened for HCV-RNA
- To determine the proportion of patients who receive positive HCV-RNA results among patients for whom HCV-RNA screening was performed
- To determine the proportion of the patients who receive negative HCV-RNA results among patients for whom HCV-RNA screening was performed

- To determine the proportion of patients with positive HCV-RNA results who previously received HCV treatment in line with their positive anti-HCV results
- To determine the time interval from screening to treatment initiation
- To determine the specialty(ies) of the physician(s) who request anti-HCV screening

7.0 Amendments and Updates

Number	Date	Amendment	Reason
1	26 November 2021	Not applicable	First version

8.0 Research Methods

8.1 Study Design

This was a non-interventional, observational, multi-center, cross sectional and retrospective chart review study which included patients screened for anti-HCV.

8.2 Setting

The study was conducted in 30 study centers which were university hospitals or training and research hospitals in Turkey. Participating centers reviewed the charts of the patients who have undergone screening for anti-HCV for any reason during the past 3 years between 30 June 2016 and 30 June 2019. Patients with positive anti-HCV results were verified whether HCV-RNA test was performed or not. Results of HCV-RNA tests were recorded where available and number of patients who received or did not receive HCV treatment were obtained from available hospital records.

8.3 Subjects

Data of patients who have undergone screening for anti-HCV were reviewed in the hospital laboratory results database and data of eligible patients according to the following criteria were collected.

- Male or Female
- Adult (18 years or older) ≥18
- Patient who received a positive anti-HCV result during screening for any reason between 30 June 2016 and 30 June 2019

No exclusion criteria were implemented in this study.

8.4 Variables

Patient demographics, laboratory results for HCV screening as well as treatment data were retrospectively collected by chart review. In particular, the following variables were collected.

- Demographics: gender, place of residence, age at HCV screening and gender
- Laboratory results for HCV screening including anti-HCV and HCV-RNA results, where available
- Information on treatment related to HCV infection (e.g., time interval from obtaining anti-HCV positive test result at routine HCV screening to treatment initiation
- Specialties of the physicians who requested anti-HCV screening

8.5 Data Sources and Measurement

This study was planned as a patient chart review. Hospital laboratory results database were used as the main data source for this study. Data of patients who were screened for anti-HCV during the period mentioned in the inclusion criteria were collected from the laboratory results database and the treatment information was obtained from the patient charts.

Data collection was anonymized, no linking of any sort was kept that would enable someone to look up a code number assigned to a patient and determine the identity of that patient. The investigator or delegated staff completed the case report forms.

Neither AbbVie nor any agents acting on behalf of AbbVie were allowed to record data on the anonymized case report forms.

Each center documented patient data in electronic Data Recording Forms (eDRFs) designed for this study. Laboratory results and available HCV treatment information present in the patient file were entered by the physician or staff under his/her supervision into the eDRFs provided by AbbVie, in line with the protocol.

Only data specified in the protocol were submitted to AbbVie.

8.6 Bias

In order to prevent patient selection bias, a patient selection method was defined in the protocol for sites that have high number of eligible patients. Initially all patients meeting eligibility criteria were selected at each site. Sites with a high number of eligible patients, which exceeds the local limit allowed to enroll per site, divided the total number of eligible patients by the number allowed to enroll to determine the selection factor (i.e., every 3rd or 4th patient). They continued with the selection process using this selection

factor until the number of patients allowed to enroll is identified. For example, a site which had 120 eligible patients enrolled every 4th patient, starting with the earliest treated patient and continue in chronological order to reach the allowed number of patients for each site (n=30).

8.7 Study Size

This study was exploratory in nature and hypothesis testing was not applicable for this study. Therefore, a formal sample size with estimation of statistical power was not performed.

According to available data from Turkey [Gülmez, 2017], 30% of the patients who were detected with positive anti-HCV during screening for any reason and who were not screened for HCV-RNA, received HCV treatment only after follow-up efforts of the clinical microbiologists. In this study, with 30 sites, we expected to collect data of 1000 patients recorded between 30.06.2016 and 30.06.2019. With 1000 patients, the width of a two-sided 95% confidence interval for the rate would be 5.6% (+/-2.8%) if an underlying rate of 30% was assumed. If the underlying rate would be higher, say 40%, then the width would be 6% (+/-3%). Therefore, approximately 1000 patients were enrolled in this study.

8.8 Data Management

Each center documented patient data in electronic Data Recording Forms (eDRFs). User names and passwords were provided by the electronic system to the investigators in each site. The eDRF system provided a unique patient number automatically and each center documented patient data in the eDRF. Following cleaning, the data base was locked for final statistical analysis.

8.9 Statistical Methods

All data was summarized descriptively for all eligible patients. The quantitative variables were summarized using, mean, standard deviation, minimum, median, maximum, lower and upper quartiles (Q1 and Q3). Qualitative variables will be summarized using frequencies and percentages with two-sided 95% confidence intervals.

8.10 Quality Control

This observational study was run in compliance with local laws and regulations. Submissions and notifications to the responsible Ethics Committee and/or Competent Authorities were also done as required by local laws. To maintain subject confidentiality, no demographic data that could identify the patient was collected (e.g., initials, date of birth). In order to protect patient's identity, a unique number was assigned to each patient and related study records.

The participating site was asked to fill out the eDRF prepared in English. Examinations, diagnostic measures, laboratory results and information regarding the treatment of the patients was entered by the researcher or staff under his/her supervision into the eDRFs provided by AbbVie, according to the research plan.

9.0 Results

9.1 Demographic Characteristics

The study was conducted in 30 study centers which were either university hospitals or training and research hospitals located in various cities in Turkey. Participating study centers and number of patients enrolled from each site are presented in Table 1. Data of 1000 patients were included in this retrospective chart review study and 50.3% of the patients were male (Table 2). The majority of the patients (82.7%) were residing in cities

or towns and only 15.6% were living in rural areas (Table 3). Istanbul, the largest city in Turkey, was declared as city of residence by 14.0% of the patients, and it was followed by Ankara (7.5%) which is the capital city of Turkey. Thirteen patients (1.3%) were living abroad, and they were in Turkey at the time of their hospital visit (Table 4). More than half of the patients (n=570, 57.0%) were included in the study from university hospitals whereas 43.0% were included from training and research hospitals.

Table 1 Participating study sites and number of patients in each site

Site name	n	%
Dicle University Faculty of Medicine	43	4.3%
Adana Cukurova University Hospital	33	3.3%
Adana City Training and Research Hospital	33	3.3%
Afyonkarahisar Health Sciences University Faculty of Medicine	33	3.3%
Akdeniz University Hospital	33	3.3%
Ankara Training and Research Hospital	33	3.3%
Ankara University Faculty of Medicine	33	3.3%
Antalya Training and Research Hospital	33	3.3%
Ataturk University Medical Faculty Hospital	33	3.3%
Bursa High Specialization Training and Research Hospital	33	3.3%
Diyarbakir Gazi Yasargil Training and Research Hospital	33	3.3%
Ege University Faculty of Medicine	33	3.3%
Firat University Faculty of Medicine	33	3.3%
Gazi University Faculty of Medicine Hospital	33	3.3%
Gaziantep University Şahinbey Research and Application Hospital	33	3.3%
Gaziosmanpaşa University Research and Application Hospital	33	3.3%
Giresun University Prof. Dr. A. İlhan Özdemir Training and Research Hospital	33	3.3%
Haseki Training and Research Hospital	33	3.3%
Istanbul Training and Research Hospital	33	3.3%
Istanbul Pendik Training and Research Hospital	33	3.3%
Kahramanmaraş Sutcu Imam University Health Practice and Research Hospital	33	3.3%
Kartal Dr. Lütfi Kirdar City Hospital	33	3.3%

Site name	n	%
Kayseri City Training and Research Hospital	33	3.3%
Kocaeli University Research and Application Hospital	33	3.3%
Konya Meram State Hospital	33	3.3%
Mustafa Kemal University Research and Application Hospital	33	3.3%
Prof. Dr. Cemil Taşcıoğlu City Hospital	33	3.3%
Health Sciences University Samsun Training and Research Hospital	33	3.3%
Selcuk University Faculty of Medicine	33	3.3%
Uludag University Faculty of Medicine	33	3.3%
Total	1000	100.0%

Table 2 Distribution of gender

Gender	n	%	95% CI
Male	503	50.3%	1.47-1.53
Female	497	49.7%	
Total	*1000*	*100.0%*	

Table 3 Distribution of patient residence

Patient residence	n	%	95% CI
City/town	827	82.7%	1.16-1.22
Village/ rural area	156	15.6%	
Closed community areas (incarcerated, hospices, military units)	17	1.7%	
Total	*1000*	*100.0%*	

Table 4 Distribution of city of residence

City of residence	n	%
Istanbul	140	14.0%
Ankara	75	7.5%
Antalya	67	6.7%

City of residence	n	%
Konya	65	6.5%
Bursa	64	6.4%
Adana	55	5.5%
Diyarbakir	55	5.5%
Afyon	36	3.6%
Giresun	34	3.4%
Kayseri	34	3.4%
Hatay	33	3.3%
Kahramanmaras	33	3.3%
Kocaeli	33	3.3%
Elazig	32	3.2%
Tokat	30	3.0%
Izmir	29	2.9%
Samsun	28	2.8%
Gaziantep	27	2.7%
Erzurum	16	1.6%
Out of Turkey	13	1.3%
Batman	10	1.0%
Mardin	8	0.8%
Osmaniye	8	0.8%
Sanliurfa	8	0.8%
Agri	6	0.6%
Aksaray	5	0.5%
Amasya	5	0.5%
Igdir	5	0.5%
Sakarya	4	0.4%
Bartin	3	0.3%
Kars	3	0.3%
Kirikkale	3	0.3%
Sinop	3	0.3%
Siirt	3	0.3%
Yalova	3	0.3%
Balikesir	2	0.2%

City of residence	n	%
Cankiri	2	0.2%
Duzce	2	0.2%
Tekirdag	2	0.2%
Ardahan	1	0.1%
Bayburt	1	0.1%
Bilecik	1	0.1%
Bingol	1	0.1%
Isparta	1	0.1%
Icel	1	0.1%
Karaman	1	0.1%
Kirsehir	1	0.1%
Manisa	1	0.1%
Mugla	1	0.1%
Mus	1	0.1%
Ordu	1	0.1%
Sivas	1	0.1%
Trabzon	1	0.1%
Usak	1	0.1%
Yozgat	1	0.1%
Total	*1000*	*100.0%*

9.2 Physician and Hospital Characteristics

In addition to individual specialty types, specialties were categorized into surgical or non-surgical specialties. Almost 69% of the anti-HCV screening requests were made by the non-surgical specialties. Most frequently anti-HCV test requesting specialty was infectious diseases (33.3%) in the non-surgical specialty group, followed by gastroenterology (20.9%) and internal medicine (19.8%). On the other hand, general surgery was the most frequently anti-HCV requesting specialty in the surgical group with 27.6%. The distribution of physician specialties requesting anti-HCV screening according to surgical and non-surgical specialty groups are presented in Table 5.

Table 5 Distribution of physician specialties

Specialty of the physician requesting anti-HCV screening	Surgical		Non-surgical	
	n	%	n	%
General surgery	86	27.6%	-	-
Gynecology	48	15.4%	-	-
Anesthesiology	35	11.2%	-	-
Infectious diseases	-	-	227	33.3%
Gastroenterology	-	-	144	20.9%
Internal medicine	-	-	136	19.8%
Other	143	45.8%	181	26.3%
Urology	*34*	*23.8%*	-	-
Ophthalmology	*33*	*23.1%*	-	-
Orthopedics And Traumatology	*33*	*23.1%*	-	-
Neurosurgery	*14*	*9.8%*	-	-
Ear Nose Throat	*13*	*9.1%*	-	-
Plastic Surgery	*13*	*9.1%*	-	-
Dental Surgeon	*1*	*0.7%*	-	-
Thoracic Surgery	*1*	*0.7%*	-	-
Intensive Care Medicine	*1*	*0.7%*	-	-
Psychiatry	-	-	*39*	*21.5%*
Cardiology	-	-	*36*	*19.9%*
Hematology	-	-	*18*	*9.9%*
Emergency Medicine	-	-	*14*	*7.7%*
Dermatology	-	-	*14*	*7.7%*
Neurology	-	-	*14*	*7.7%*

Specialty of the physician requesting anti-HCV screening	Surgical		Non-surgical	
	n	%	n	%
Chest Diseases	-	-	*13*	*7.2%*
Rheumatology	-	-	*11*	*6.1%*
Oncology	-	-	*8*	*4.4%*
Physical Therapy and Rehabilitation	-	-	*5*	*2.8%*
Family Medicine	-	-	*5*	*2.8%*
Endocrinology	-	-	*3*	*1.7%*
Radiology	-	-	*1*	*0.6%*
Total	*312*	*100.0%*	*688*	*100.0%*

9.3 Patient Characteristics Related to Hepatitis-C

Retrospective data of patients who received a positive anti-HCV result in the participating study center between 30 June 2016 and 30 June 2019 were included in the study. Participating study centers reviewed the patient charts and recorded patient data on the eDRF between 24 December 2020 and 22 June 2021.

Among 1000 patients who received a positive anti-HCV result, 78.5% were screened for HCV-RNA (Table 6). Physicians who are specialized in the non-surgical branches requested HCV-RNA testing more frequently than surgical branches ($p<0.001$, Table 7). HCV-RNA screening rates were similar in university hospitals and training and research hospitals ($p>0.05$, Table 8). A statistically significant difference was observed between ratios of surgical and non-surgical branches requesting anti-HCV screening in different types of hospitals. In university hospitals non-surgical branches, whereas in training and research hospitals surgical branches were requesting anti-HCV screening more frequently ($p=0.001$, Table 9). Among HCV-RNA screened patients, 54.8% (n=430) had a positive result (Table 10). Proportion of patients with a positive HCV-RNA result was higher in

patients screened by physicians in non-surgical group (p=0.001, Table 12). Ratio of patients with positive HCV-RNA results were similar in university hospitals and training and research hospitals (p>0.05, Table 13).

Proportion of patients who received HCV treatment in line with their positive anti-HCV results in HCV-RNA positive patients was 72.8% (Table 14). Considering all eligible anti-HCV positive patients, this proportion was corresponding to 31.3% (Table 15). No statistical difference was detected in terms of reaching treatment in patients screened by physicians in surgical or non-surgical group (p>0.05, Table 16). Patients who received HCV treatment following obtaining a positive HCV-RNA result were evaluated according to the screening departments within the surgical branches and non-surgical branches. Within the surgical branches, 49.0% of the patients reaching treatment were screened in general surgery department whereas only 2.0% of the patients who received HCV treatment were screened in department of ear nose and throat (Table 17). Within the non-surgical branches, 46.2% of the patients reaching treatment were screened in infectious diseases department. Among patients who had access to treatment, the lowest rate of access to treatment within non-surgical branches was observed in chest diseases, endocrinology, family medicine and oncology departments (Table 18). Considering the type of hospital, the rate of access to HCV treatment was higher in patients screened in a university hospital than in patients screened in a training and research hospital (p<0.001, Table 19).

Table 6 Distribution of patients screened for HCV-RNA

Has the patient been screened for HCV-RNA?	n	%	95% CI
Yes	785	78.5%	0.76-0.81
No	215	21.5%	
Total	*1000*	*100.0%*	

Table 7 HCV-RNA screening comparison results by surgical and non-surgical branches

Has the patient been screened for HCV-RNA?	Surgical		Non-surgical		95% CI	p*
	n	%	n	%		
Yes	192	61.5%	593	86.2%	1.72-1.79	<0.001
No	120	38.5%	95	13.8%	1.37-1.51	
Total	*312*	*100.0%*	*688*	*100.0%*		

** Fisher's Exact Test*

Table 8 HCV-RNA screening comparison results by type of hospital

Has the patient been screened for HCV-RNA?	Training and Research hospital		University hospitals		95% CI	p*
	n	%	n	%		
Yes	331	77.0%	454	79.6%	1.54-1.61	0.313
No	99	23.0%	116	20.4%	1.47-1.61	
Total	*430*	*100.0%*	*570*	*100.0%*		

** Fisher's Exact Test*

Table 9 Comparison of branches requesting anti-HCV testing in different types of hospitals

Hospital type	Surgical		Non-surgical		95% CI	p*
	n	%	n	%		
Training and Research hospital	159	51.0%	271	39.4%	1.47-1.57	0.001
University hospitals	153	49.0%	417	60.6%	1.48-1.56	
Total	*312*	*100.0%*	*688*	*100.0%*		

** Fisher's Exact Test*

Table 10 Distribution of results among patients screened for HCV-RNA

Did the patient have positive HCV-RNA results?	n	%	95% CI
Yes	430	54.8%	0.51-0.58
No	355	45.2%	
Total	*785*	*100.0%*	

Table 11 Distribution of HCV- RNA results among all eligible patients

Did the patient have positive HCV-RNA result?	n	%	95% CI
Yes	430	43.0%	0.51-0.58
No	355	35.5%	
Missing	215	21.5%	
Total	*1000*	*100.0%*	

Table 12 Comparison of HCV-RNA results by branches

Did the patient have positive HCV-RNA results?	Surgical		Non-surgical		95% CI	p*
	n	%	n	%		
Yes	80	41.7%	350	59.0%	1.78-1.85	<0.001
No	112	58.3%	243	41.0%	1.64-1.73	
Total	*192*	*100.0%*	*593*	*100.0%*		

** Fisher's Exact Test*

Table 13 Comparison of HCV-RNA results by type of hospital

Did the patient have positive HCV-RNA results?	Training and Research hospital		University hospitals		95% CI	p
	n	%	n	%		
Yes	178	53.8%	252	55.5%	1.54-1.63	0.663
No	153	46.2%	202	44.5%	1.52-1.62	
Total	*331*	*100.0%*	*454*	*100.0%*		

Fisher's Exact Test

Table 14 Distribution of patients who received treatment among patients with positive HCV-RNA results

Has the patient received an HCV treatment in line with his/her positive HCV-RNA results?	n	%	95% CI
Yes	313	72.8%	0.69-0.77
No	117	27.2%	
Total	*430*	*100.0%*	

Table 15 Distribution of patients who received treatment among all eligible patients

Has the patient received an HCV treatment in line with his/her positive HCV-RNA results?	n	%	95% CI
Yes	313	31.3%	0.69-0.77
No	117	11.7%	
Missing	570	57.0%	
Total	*1000*	*100.0%*	

Table 16 HCV treatment comparison by branches

Has the patient received an HCV treatment in line with his/her positive HCV-RNA results	Surgical		Non-surgical		95% CI	p*
	n	%	n	%		
Yes	51	63.8%	262	74.9%	1.80-1.88	0.051
No	29	36.3%	88	25.1%	1.67-1.83	
Total	*80*	*100.0%*	*350*	*100.0%*		

** Fisher's Exact Test*

Table 17 Distribution of patients receiving HCV treatment in surgical branches

Department	n	%
General surgery	25	49.0%
Anesthesiology	9	17.6%
Gynecology	2	3.9%
Other	15	29.4%
Urology	*4*	*7.8%*
Orthopedics And Traumatology	*3*	*5.9%*
Plastic Surgery	*3*	*5.9%*
Neurosurgery	*2*	*3.9%*
Ophthalmology	*2*	*3.9%*
Ear Nose Throat	*1*	*2.0%*
Total	*51*	*100.0%*

Table 18 Distribution of patients receiving HCV treatment in non-surgical branches

Department	n	%
Infectious diseases	121	46.2%
Gastroenterology	69	26.3%
Internal medicine	37	14.1%
Other	35	13.4%
Psychiatry	*11*	*4.2%*
Hematology	*5*	*1.9%*
Dermatology	*5*	*1.9%*
Emergency medicine	*3*	*1.1%*
Cardiology	*2*	*0.8%*
Neurology	*2*	*0.8%*
Rheumatology	*2*	*0.8%*
Chest diseases	*1*	*0.4%*
Endocrinology	*1*	*0.4%*
Family medicine	*1*	*0.4%*
Oncology	*1*	*0.4%*
Physical therapy and rehabilitation	*1*	*0.4%*
Total	*262*	*100.0%*

Table 19 HCV treatment comparison by type of hospital

Has the patient received an HCV treatment in line with his/her positive HCV-RNA results	Training and Research hospital		University hospitals		95% CI	p*
	n	%	n	%		
Yes	103	57.9%	210	83.3%	1.62-1.72	<0.001
No	75	42.1%	42	16.7%	1.27-1.45	
Total	*178*	*100.0%*	*252*	*100.0%*		

** Fisher's Exact Test*

9.4 Time to Treatment

Time from anti-HCV screening to treatment initiation is presented in Table 20. Median time from obtaining positive anti-HCV result to initiation of HCV treatment was 91.0 days (IQR 42.0 to 178.5). The same duration corresponds to 13.0 weeks (IQR 6.0-25.5) or 3.3 months (IQR 1.5-6.4).

Time from anti-HCV screening to treatment initiation was categorized according to the physician's specialty and no statistical difference was observed in terms of access to treatment in patients who were examined by different specialties (p=0.230, Table 21).

A similar categorization was done for patient residence and similarly no statistical difference was observed in terms of access to treatment in patients who were living in different residential categories such as city/town, village/rural area, or closed community areas (p=0.250, Table 22).

No statistical difference was detected in terms of time to reach HCV treatment in patients screened by physicians in surgical or non-surgical group (p>0.05, Table 23). However, time to reach HCV treatment was shorter in patients screened in university hospitals than in patients screened in training and research hospitals (median 70 vs. 98 days, p=0.006, Table 24).

Table 20 Time interval from HCV screening to treatment initiation in days, weeks, and months

Time Interval	n	Min.	Max.	Mean	SD	Median	Q1-Q3
Time from screening to treatment initiation (days)	313*	7.0	917.0	157.8	185.3	91.0	42.0-178.5
Time from screening to treatment initiation (weeks)	313*	1.0	131.0	22.5	26.5	13.0	6.0-25.5
Time from screening to treatment initiation (months)	313*	0.3	32.8	5.6	6.6	3.3	1.5-6.4

**Data available for 313 of 1000 patients.*

Table 21 Time interval from anti-HCV screening to treatment initiation by physician specialty (weeks)

Specialty of the physician requested anti-HCV screening	n	Mean	SD	Min	Max	Median	Q1-Q3	p*
Anesthesiology	10	17.1	19.4	5.0	69.0	13.0	5.00-.19.00	
Gastroenterology	52	22.3	28.0	2.0	99.0	10.0	5.00-24.50	
Infectious diseases	98	16.5	16.7	2.0	99.0	10.0	5.00-21.25	
Internal medicine	44	27.0	34.2	1.0	131.0	13.0	5.25-26.00	0.230
General surgery	25	22.2	27.1	5.0	99.0	9.0	5.00-24.00	
Gynecology	9	11.3	7.1	5.0	23.0	9.0	6.00-18.50	
Other	75	30.1	30.7	2.0	99.0	18.0	7.00-45.00	

**Kruskal-Wallis Test*

Table 22 Time interval from anti-HCV screening to treatment initiation by patient residence (weeks)

Patient residence	n	Mean	SD	Min	Max	Median	Q1-Q3	p*
City/town	265	21.6	25.8	1.0	131.0	11.0	5.00-11.00	0.250
Village/ rural area	46	27.8	30.1	2.0	99.0	16.0	6.00-39.00	
Closed community areas	2	27.0	25.5	9.0	45.0	27.0	9.00 - NA	

** Kruskal-Wallis Test*

Table 23 Time to reach HCV treatment by surgical or non-surgical branches

Time/Branch	n	Mean	SD	Min	Max	Median	Q1-Q3	p*
Day								
Surgery	71	157.0	183.4	14.0	693.0	91.0	35.0-175.0	0.942
Non surgery	242	158.0	186.3	7.0	917.0	91.0	42.0-182.0	
Week								
Surgery	71	22.4	26.2	2.0	99.0	13.0	5.0-25.0	0.942
Non surgery	242	22.6	26.6	1.0	131.0	13.0	6.0-26.0	
Month								
Surgery	71	5.6	6.6	0.5	24.8	3.3	1.3-6.3	0.942
Non surgery	242	5.6	6.7	0.3	32.8	3.3	1.5-6.5	

** Mann-Whitney U Test*

Table 24 Time to reach HCV treatment by type of hospital

Time/Hospital	n	Mean	SD	Min	Max	Median	Q1-Q3	p*
Day								
Training and Research hospitals	110	174.4	187.3	14.0	917.0	98.0	63.0-203.0	**0.006**
University hospitals	203	148.8	184.1	7.0	693.0	70.0	35.0-161.0	
Week								
Training and Research hospitals	110	24.9	26.8	2.0	131.0	14.0	9.0-29.0	**0.006**
University hospitals	203	21.3	26.3	1.0	99.0	10.0	5.0-23.0	
Month								
Training and Research hospitals	110	6.2	6.7	0.5	32.8	3.5	2.3-7.3	**0.006**
University hospitals	203	5.3	6.6	0.3	24.8	2.5	1.3-5.8	

** Mann-Whitney U Test*

10.0 Discussion

In this study we evaluated the rate of initiation of HCV treatment in patients who received positive anti-HCV results during routine anti-HCV screening for any reason. Among anti-HCV positive patients, 31.3% received HCV treatment. HCV-RNA was tested in 78.5% of patients who had a positive anti-HCV result and among patients with active HCV infection, 72.8% received treatment for HCV.

HCV infection is one of the most common causes of liver cirrhosis and hepatocellular carcinoma (HCC), which has an insidious course because it is asymptomatic in its early stages, and 60-80% of the infected cases become chronic. Globally, 27% of the cirrhosis cases and 25% of HCC cases are caused by HCV infection [Alter, 2007]. Studies have shown that HCV is the second most common cause of both liver cirrhosis and HCC in Turkey [Idilman, 2020; Arhan, 2009]. Today, HCV infection is a disease that can be successfully treated. With the use of direct-acting antiviral (DAA) drugs, the success rate in the treatment of HCV infection has approached almost to 100% [Hezode, 2018]. When the disease is caught at earlier stages, infected patients' benefit more from the treatment [Calvaruso]. Published studies also indicate that HCV eradication with use of DAA drugs not only reduces hepatic complications, but also reduces the risk of cardiovascular disease and has a positive effect on glycemic control [Butt, 2019; Graf, 2020].

WHO aims to reduce new hepatitis C patients by 90% and mortality due to hepatitis C by 65% worldwide by 2030 [Waheed, 2018]. In general, the group of patients waiting to be treated is much more than those who receive treatment. Studies show that 50-80% of HCV-infected patients could not be diagnosed, and only less than 20% receive appropriate treatment [Denniston, 2012]. Similarly, treatment initiation was reported as 21% in a Danish study conducted in patients with chronic HCV infection [Hansen, 2009]. In our study a higher percentage of patients (31.3%) were able to initiate HCV treatment after obtaining a positive anti-HCV result. This could be due to high number of patients who were screened and followed-up in infectious disease and gastroenterology departments.

A similar retrospective chart-review study recently conducted in Mersin, Turkey included 1118 anti-HCV positive patients [Akkuzu 2019]. Among these anti-HCV positive patients, 35% were screened in gastroenterology, 37% were screened in infectious diseases, and 28% were screened in other departments. Treatment was initiated in 91% of the patients who were identified in the gastroenterology department. This result shows a high rate of treatment initiation in the gastroenterology department and might be a possible reason for obtaining a high rate of treatment initiation in our study since 37% of our patients were screened in gastroenterology and infectious diseases departments.

A recent single center study conducted in Istanbul, Turkey, investigated prevalence of chronic hepatitis C [Şengel, 2020]. Serum samples of 76413 patients were analyzed and only 2.4% of the patients were screened for anti-HCV. HCV-RNA was tested in 1286 patients and 23% of the patients (n=291) had positive HCV-RNA results. Among these patients only 44% (n=129) received treatment for HCV. Results of a similar study conducted in Turkey indicate that among 121492 patients, 0.8% had positive anti-HCV results and HCV-RNA was not investigated in 40% of the patients with positive anti-HCV results [Düzenli, 2020]. Hepatitis C screening was investigated in a tertiary care hospital in Turkey and results of 32803 anti-HCV tests were evaluated [İskender, 2020]. Results showed that 0.3% of the patients were positive for anti-HCV and HCV-RNA was not investigated 47% of these patients. Similarly, Yiş et al. [2020] reported that HCV-RNA was not tested in 51% of the patients who had positive anti-HCV results. Results of these studies suggest that diagnosis and treatment rates of HCV infection are not sufficient in Turkey.

Another retrospective chart review study conducted in United States in 2019 included 8407 individuals with chronic HCV infection [Kwo, 2019]. Of these patients, 830 initiated treatment with a DAA agent, whereas 7577 did not, suggesting a DAA treatment initiation rate of 9.9%. Median time to initiate DAA treatment was reported as 300 days. We detected a much shorter time to treatment duration in our study (median 91 days). Following categorization of screening hospitals into university or training and research hospitals, we found that time to treatment was even shorter in university hospitals (median 70 days). This difference could be due to different health care systems present in Turkey and United States.

11.0 Conclusion

In conclusion, our study results indicate a higher rate of treatment initiation in patients with HCV infection as compared to most of the published literature. Furthermore, we found that time from screening to treatment initiation was considerably shorter comparing

to other international studies. On the other hand, despite these promising results, there might be a big patient population who cannot reach treatment, since HCV RNA was not requested in a significant portion (22.5%) of anti-HCV positive patients.

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AbbVie Inc. (AbbVie)

Non-Interventional Study (Non-PMOS)

Protocol (H20-058)

Treatment initiation rates of patients with positive anti-HCV results in University and Training and Research Hospitals in Turkey: a retrospective chart review

(Lost-C Study)

Final Study Report

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