



Genotype Distribution of Hepatitis C Virus in Patients with Chronic Hepatitis C in Muğla, Türkiye (2019-2024)

Kronik Hepatit C'li Hastalarda Hepatit C'nin Genotip Dağılımı, Muğla, Türkiye (2019-2024)

✉ Mehmet Karabey, ✉ Alper Aksözek

Muğla Training and Research Hospital, Clinic of Medical Microbiology, Muğla, Türkiye

ABSTRACT

Objectives: Hepatitis C virus (HCV) continues to be an increasingly significant public health concern due to its substantial impact on morbidity and mortality. This study aims to determine the dynamic genotype (GT) distribution of HCV among HCV infections admitted to Muğla Training and Research Hospital and to evaluate the relationship between HCV GTs and factors such as gender and age.

Materials and Methods: A total of 230 patients with chronic HCV were included in the study between January 2019 and October 2024. Quantitative HCV-RNA polymerase chain reaction (PCR) tests were performed using the Rotor-Gene Q real-time PCR system, and HCV genotyping was conducted with the PyroMark Q24 pyrosequencing system.

Results: Among the 220 patients analyzed for HCV GTs, 69.5% were male, and 30.5% were female. The most prevalent GT was GT1, observed in 66.4% of cases. In females, the most common GT was 1b (58.2%), while in males, GT3a was the most frequent (35.9%). Of the patients, 90.9% (200) were Turkish, while 9.1% (20) were foreign nationals. The most common GT was GT1b, with frequencies of 34.0% and 70.0% respectively. On a yearly basis, GT1b was detected at the highest rates in 2021, 2022, 2023, and 2024. In contrast, GT1a was most common in 2019, and GT3a was predominant in 2020. Regarding age groups, the highest prevalence was observed in the 18-30 age range (30.9%; 68 cases), while the lowest was in individuals under 18 years, with only one case.

Conclusion: In our study, among patients tested for HCV GTs, GT1 was the most common GT, with a prevalence of 66.4%. This finding is consistent with many studies worldwide. The GT distribution was found to be associated with the patients' gender. The GT distribution was statistically significantly higher in the 18-30 age group among all age groups.

Keywords: Hepatitis C virus, hepatitis C virus genotypes, chronic hepatitis C, hepatitis C virus subtypes

ÖZ

Amaç: Hepatit C virüsü (HCV), morbidite ve mortalite üzerindeki önemli etkisi nedeniyle giderek artan bir halk sağlığı sorunu olmaya devam etmektedir. Bu çalışmanın amacı, Muğla Eğitim ve Araştırma Hastanesi'ne başvuran HCV enfeksiyonlu olguların HCV'nin dinamik genotip (GT) dağılımını belirlemek ve HCV GT'si ile cinsiyet ve yaş gibi faktörler arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntemler: Ocak 2019 ile Ekim 2024 tarihleri arasında 230 kronik HCV'li hasta çalışmaya dahil edildi. Kantitatif HCV-RNA polimeraz zincir reaksiyonu (PCR) testleri, Rotor-Gene Q gerçek zamanlı PCR cihazında ve HCV GT'lendirme, PyroMark Q24 pyrosekans cihazında yapıldı.

Bulgular: HCV GT'leri araştırılan 220 hastanın, %69,55'i erkek ve %30,5'i kadındı, en yaygın GT %66,4 ile GT1 idi. Kadınlarda, %58,2 ile GT1b, erkeklerde ise %35,9 ile GT3a idi. Hastaların %90,9 (200)'u Türk, %9,1 (20)'i ise yabancı idi, en sık görülen GT sırasıyla, %34,0 ve %70,0 ile GT1b idi. Yıllara göre; 2021, 2022, 2023 ve 2024 yıllarında GT1b, 2019'da GT1a ve 2020'de ise GT3a en yüksek oranda saptanmıştır. Yaş gruplarına göre; en yüksek %30,9 (68) ile 18-30 yaş arasında, en düşük ise 1 olgu ile 18 yaş altında görüldü.

Sonuç: Çalışmamızda HCV GT'leri araştırılan hastada, %66,4 ile GT1 en yaygın görülen GT'ydı, bu bulgu, dünya genelindeki birçok çalışmayla paralellik göstermektedir. GT dağılımının hastaların cinsiyetiyle ilişkili olduğunu göstermiştir. Yaş gruplarına arasında GT dağılımları 18-30 yaş arasında istatistiksel olarak anlamlı ölçüde yüksek idi.

Anahtar Kelimeler: Hepatit C virüsü, hepatit C virüsü genotipleri, kronik hepatit C, hepatit C virüsü alt tipleri

Address for Correspondence: Mehmet Karabey MD, Muğla Training and Research Hospital, Clinic of Medical Microbiology, Muğla, Türkiye

E-mail: karamehmetbey@gmail.com **ORCID ID:** orcid.org/0000-0002-7394-186X

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Introduction

Hepatitis C virus (HCV) is responsible for a significant proportion of chronic liver diseases worldwide (1). Due to its substantial impact on morbidity and mortality, HCV continues to be a significant public health concern (2). Unlike hepatitis A and B, there is currently no vaccine available to prevent HCV infection (3). It is estimated that HCV accounts for 27% of cirrhosis cases and 25% of hepatocellular carcinoma cases globally (1). HCV can be detected in blood and body fluids, with transmission primarily occurring through contact with infected blood or blood products. In developed countries, the most common route of transmission is needle sharing among people who inject drugs. Perinatal transmission from mother to child and sexual transmission among men who have sex with men have also been documented (4). The World Health Organization (WHO) has set a goal to eliminate HCV infection by 2030, which includes “a 90% reduction in new chronic HCV cases, a 65% reduction in HCV-related deaths, and treatment for 80% of eligible individuals with chronic HCV infection” (5).

HCV is an enveloped (E), single-stranded, positive-sense RNA virus belonging to the *Hepacivirus* genus of the *Flaviviridae* family (6). The HCV genome contains both highly conserved and highly variable regions. The 5' untranslated region, core, E1, and non-structural protein 5B regions are relatively well-conserved and are used for classification purposes. In contrast, the E2 glycoprotein region is the most variable part of the genome (7). HCV exhibits significant genetic diversity due to the high mutation rate of its viral polymerase and the high turnover of the virus (8). Based on phylogenetic and sequence analyses of the entire viral genome, seven genotypes (GTs) (1a+1b, 2, 3, 4, 5, 6, and 7) have been documented. HCV strains show extensive genetic diversity, with nucleotide regions differing by approximately 35%. Each GT is further subdivided into 67 confirmed and 21 provisional subtypes, with strains from the same family differing by less than 15% in nucleotide regions (9).

The distribution of HCV GTs varies across different geographical regions worldwide. GT1 is prevalent in North America, South America, Western and Northern Europe, accounting for 46% of all HCV cases. GT3 is common in South Asia, Australia, and parts of Western Europe, representing 30% of global HCV cases (10). GT2 is found predominantly in West Africa and South America, while GT4 is prevalent in Central and North Africa (10). GT5 is primarily located in the Middle East and North Africa but has also been reported in South Africa. GT6 is mostly distributed across Southern China and Southeast Asia (5). GT7 has been reported in Central Africa, having been isolated from patients in the Democratic Republic of Congo (9). In studies conducted on the general population in Türkiye, GT1 accounts for 76-93% of HCV cases, GT3 for 3.7-6.7%, GT2 for 1.5-2.2%, and GT4 for 1.1-9.8% (11). The global distribution of HCV genetic variations is likely influenced by increasing international travel, migration between countries, and historical events (7).

The dominant treatment for HCV infection previously consisted of pegylated interferon- α combined with the nucleotide analog ribavirin. Recently, the development of direct-acting antivirals (DAAs) has enabled near-complete eradication of HCV in infected individuals. However, the high cost of DAAs, the presence of undiagnosed patients, and the emergence and spread of resistant

mutants pose significant challenges to the elimination of HCV (6). Currently, the choice of DAA regimen, treatment duration, and sustained virological response remains dependent on the HCV GT and subtype (7). As the effects of pangenotypic treatments on different GTs are not yet fully understood, determining the HCV GT before treatment remains crucial.

This study aims to identify the dynamic GT distribution of HCV in cases of HCV infection presenting to Muğla Training and Research Hospital and to evaluate the relationship between HCV GT and factors such as age and gender.

Materials and Methods

This study included 230 HCV-RNA-positive patients, who underwent HCV GT testing in the Molecular Laboratory of the Muğla Training and Research Hospital between January 2019 and October 2024. Ethical approval was obtained from the Muğla Sıtkı Koçman University Medical Sciences Ethics Committee (approval number: 177, date: 23.12.2024).

Quantitative HCV-RNA Analysis

HCV-RNA in plasma samples was determined using quantitative real-time reverse transcription polymerase chain reaction (RT-PCR). Viral nucleic acid extraction was performed using the “QIA Symphony DSP Virus/Pathogen Midi Kit” (Qiagen, Catalog No: 937055, Hilden, Germany) with the QIA Symphony SP/AS device (Qiagen, Catalog No: 9001297, Hilden, Germany). Quantitative HCV-RNA PCR tests were conducted with the Arthus HCV QS-RGQ PCR Kit (Qiagen, Catalog No: 4518366, Hilden, Germany) using the Rotor-Gene Q real-time PCR system (Qiagen, Catalog No: 9001580, Hilden, Germany). The test's dynamic range was 50 IU/mL to 1×10^7 IU/mL, and the linear range was 1.77×10^6 IU/mL to 2.50×10^7 IU/mL.

HCV genotyping of the study population (GTs: 1a, 1b, 2a, 2b, 3a, 3b, 3k, 4a, 4d, 5a, 6, and 7a) was performed using the QIAGEN OneStep RT-PCR Kit (Qiagen, Catalog No: 210210 or 210212, Hilden, Germany) on the Qiagen PyroMark Q24 Pyrosequencing System (Qiagen, Hilden, Germany).

Statistical Analysis

Statistical analyses were performed using Statistical Package for Social Sciences version 22.0 (Armonk, NY, USA). The normality of variable distributions was assessed through visual methods (histograms and probability plots) and the Kolmogorov-Smirnov test. Quantitative variables were compared using the Mann-Whitney U test, while qualitative variables were analyzed using Pearson's chi-square test. Correlation coefficients and statistical significance between variables were calculated using Spearman's rank correlation coefficient test. Results with a p-value of less than 0.05 were considered statistically significant.

Results

This study included 220 chronic HCV patients whose HCV GTs were investigated using real-time PCR. The mean age of the 220 participants was 42.61 ± 17.09 years, with 30.45% being female and 9.1% being foreign nationals.

Among the 220 patients analyzed, GT1 was the most prevalent GT, observed in 66.4% of cases, followed by GT3 in 30.9%, GT4 in 1.8%, and GT2 in 0.9% (Figure 1). Among chronic HCV patients with GT1, subtype 1b was identified in 37.3%, and subtype 1a was identified in 29.1%. For GT2, only subtype 2a was detected in 0.9% of cases, with no other subtypes identified. Among GT3 patients, subtype 3a was present in 30.9% and subtype 3b in 0.5%. For GT4, only subtype 4a was detected in 1.8% of cases, with no other subtypes identified. GTs 5, 6, and 7 were not observed in the study population. Additionally, no mixed-GT infections were detected. The distribution of HCV GTs based on demographic and virological characteristics is presented in Table 1.

Of the patients tested for HCV GTs, 69.55% (153) were male, and 30.5% (67) were female. The proportion of males was statistically significant higher than that of females ($p=0.001$). The most common GTs in females were GT1b (58.2%) and GT1a (19.4%), whereas in males, GT3a (35.9%) and GT1a (33.3%) were more prevalent. The mean age of patients within the GT groups was highest in GT1b, with a mean of 52.74 ± 17.87 years. The median age for each GT group is shown in Table 1.

Among the patients tested, 90.9% (200) were Turkish nationals, while 9.1% (20) were foreign nationals. No statistically significant difference was found between Turkish and foreign patients ($p=0.068$). The most common GTs among Turkish patients were GT1b (34.0%) and GT3a (32.0%), while GT1b was predominant in foreign nationals (70.0%).

When evaluating GT distribution over the years, GT1b was found at the highest rates in 2021, 2022, 2023, and 2024, while GT1a was most common in 2019, and GT3a was most prevalent in 2020. No statistically significant difference in GT distribution across years was observed ($p=0.215$) (Table 1).

HCV GTs were most frequently observed in the 18-30 age group (30.9%, $n=68$), with the lowest occurrence in individuals under 18 years old (1 case). The most common GTs by age group were GT1b in 18-30 years, GT3a in 31-40 years, GT3a in 41-50 years, and GT1b in 51-60 years, and GT1b in individuals over 60 years. When comparing GT distributions among age groups, the prevalence in the 18-30 age group was statistically significantly higher than in other age groups ($p=0.001$) (Figure 2).

Discussion

HCV GTs exhibit varying prevalence across different regions of the world. The distribution of HCV GTs differs by geographic areas, populations, and even specific risk groups. Globally, GT1 accounts for 44% of HCV infections and 60% of infections in high- and middle-income countries. GT3 constitutes 25% of all HCV infections, GT4 accounts for 15%; while GTs 5, 7, and 8 represent less than 1% of global HCV infections (12). Effective control of HCV infections depends on determining GT distribution, as it is integral to predicting treatment response and selecting the appropriate DAA regimen and its duration. Changes in GT prevalence pose challenges in the development of vaccines and therapeutics (10).

According to WHO guidelines, pan-GT treatment regimens are preferred for individuals with chronic HCV. However, GT-specific treatments are recommended in countries where certain viral GTs

	Total (n)	Genotype 1a, n (%)	Genotype 1b, n (%)	Genotype 2a, n (%)	Genotype 3a, n (%)	Genotype 3b, n (%)	Genotype 4a, n (%)	p-value
Number	220	64 (29.1)	82 (37.3)	2 (0.9)	67 (30.5)	1 (0.5)	4 (1.8)	
Age, mean	42.61 ± 17.09	37.33 ± 15.40	52.74 ± 17.87	36.50 ± 17.68	35.54 ± 11.49	27 ± 0.0	44.75 ± 8.62	
Sex								
Female	67	13 (19.4)	39 (58.2)	1 (1.5)	12 (17.9)	0 (0.0)	2 (3.0)	
Male	153	51 (33.3)	43 (28.1)	1 (0.7)	55 (35.9)	1 (0.7)	2 (1.3)	0.001
Nationality								
Turkish	200	61 (30.5)	68 (34.0)	2 (1.0)	64 (32.0)	1 (0.5)	4 (2.0)	
Foreigner	20	3 (15.0)	14 (70.0)	0 (0.0)	3 (15.0)	0 (0.0)	0 (0.0)	0.068
Years								
2019	43	18 (41.9)	10 (23.3)	1 (2.3)	13 (30.2)	0 (0.0)	1 (2.3)	0.215
2020	42	13 (31.0)	10 (23.8)	0 (0.0)	17 (40.5)	0 (0.0)	2 (4.8)	
2021	41	7 (17.1)	20 (48.8)	0 (0.0)	13 (31.7)	0 (0.0)	1 (2.4)	
2022	29	9 (31.0)	12 (41.4)	0 (0.0)	8 (27.6)	0 (0.0)	0 (0.0)	
2023	29	11 (37.9)	13 (44.8)	0 (0.0)	5 (17.2)	0 (0.0)	0 (0.0)	
2024	36	6 (16.7)	17 (47.2)	1 (2.8)	11 (30.6)	1 (2.8)	0 (0.0)	

are more prevalent (13). GT1 is the most common globally and in developed countries. It responds well to second-generation DAAs, achieving viral eradication rates of over 90% (7).

Studies investigating GT distribution in chronic HCV patients worldwide show consistent regional variations. For instance, Pimenov et al. (13) reported GT1 dominance in Russia (53.6%), followed by GT3 (35.4%) and GT2 (7.8%). Similarly, Yang et al. (14) identified GT1 as the most prevalent in China (58.2%), with GT2 (18.4%) and GT3 (11.4%) being the second and third most common, respectively. In Brazil, Pereira et al. (15) found GT1 (46.98%), including subtypes 1a (14.1%) and 1b (15.7%), as the most frequent, followed by GT3a (13.0%), GT3 (7.1%), and GT2 (1.2%). Petruzzello et al. (16) reported that GT1b remained dominant across three study periods in Italy (51.8% in 2006-2008, 48.3% in 2009-2011, and 54.4% in 2012-2014). In Ethiopia, Hundie et al. (17) found GT4 to be the most prevalent (76.1%), followed by GT2 (13%) and GT1 (8.7%).

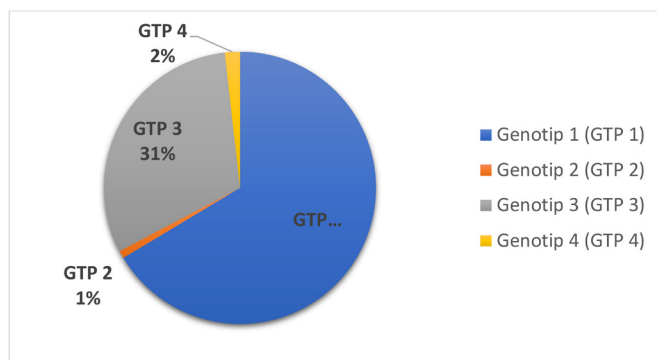


Figure 1. Distribution of hepatitis C virus genotypes in the study population

In Türkiye, GT1 has been reported as the leading cause of HCV infections, with prevalence ranging from 51.7% to 97.1% (7). Specific studies in Türkiye have demonstrated similar trends. For example, Cirt et al. (18) found GT1 to constitute 51.5% of infections in Gaziantep, followed by GT3 (21.4%) and GT4 (20%). Bulut et al. (19) reported GT1 as the most frequent in İstanbul (81.3%), followed by GT3 (8.8%) and GT2 (3.4%). Selek et al. (20) identified GT1b in 67.0% of cases, GT3 in 16.0%, GT1a in 14.2%, and GT2 in 2.8%. Kirdar et al. (21) observed GT1 as the most prevalent in Aydın (90.2%), followed by GT3 (5.9%), GT2 (2.1%), and GT4 (1.4%). Karabulut et al. (7) found GT1 to dominate (82.5%), followed by GT3 (10.7%), GT2 (4.6%), and GT4 (2.2%).

In line with other national studies, our study identified GT1 as the most common GT (66.4%), followed by GT3 (30.9%), GT4 (1.8%), and GT2 (0.9%). The prevalence of the most common subtype 1b, in Türkiye has been reported to range between 56.5% and 100% (7). In our study, among chronic HCV patients with GT1, subtype 1b was found in 37.3% and subtype 1a in 29.1%. For GT2, only subtype 2a was identified (0.9%). Among GT3 patients, subtype 3a was observed in 30.9% and subtype 3b was observed in 0.5%. For GT4, only subtype 4a was identified (1.8%).

Our findings reveal both similarities and notable differences compared to previous global and national studies on chronic HCV. GT1 remains the most commonly detected GT in Turkish patients, aligning with global studies, particularly in developed countries and Türkiye, where GT1 prevalence exceeds 50%.

Social events causing changes in society, such as war and migration, along with increased population mobility and various transmission routes, significantly influence the epidemiology of infections. In Europe, GT3 is the second most common GT, especially prevalent among intravenous drug users. The prevalence of GT3 in Türkiye varies substantially. In our study, GT3 ranked

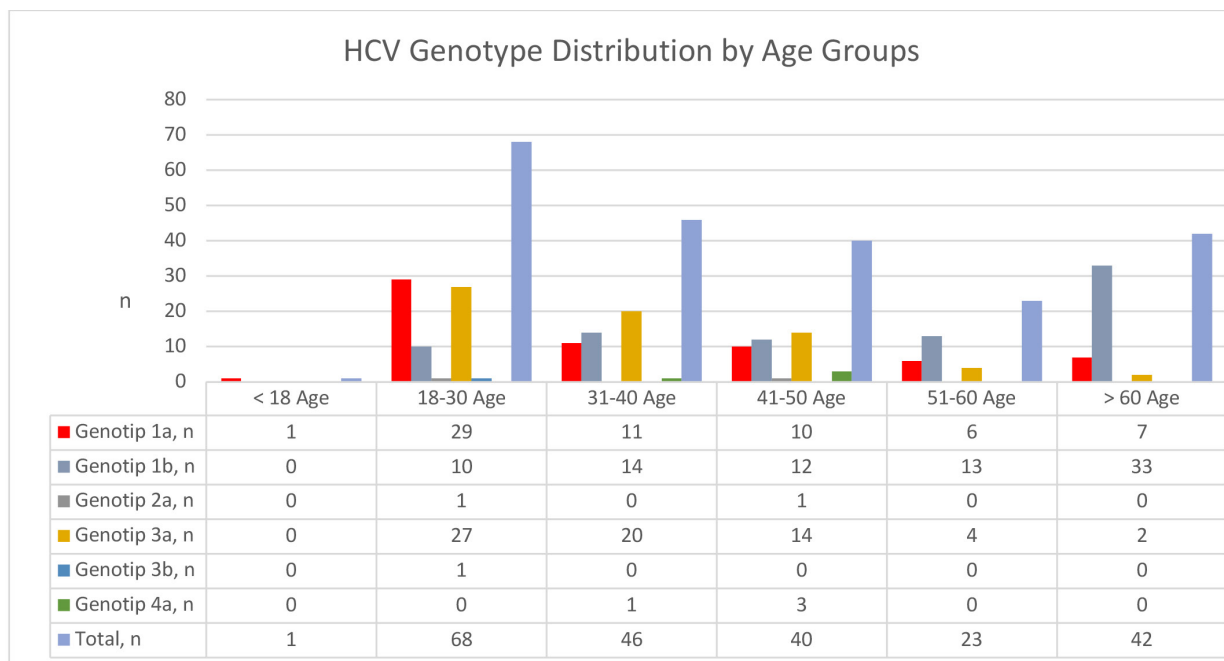


Figure 2. Distribution of hepatitis C virus genotype by age groups

second after GT1, accounting for 30.9% of cases. Muğla, a tourist city with intense tourism activity, experiences substantial human circulation and migration, which may explain the differences in HCV GTs observed in this region. In our study, subtype 1b was identified in 37.3% of cases, consistent with the high prevalence reported by Karabulut et al. (7). The predominance of subtype 1b among GT1 cases in Türkiye, compared to other countries, suggests that GT-specific treatment approaches, particularly for subtype 1b, may be effective given its favorable response to therapy.

This study revealed a significant association between GT distribution and patient sex. Among patients with identified HCV GTs, 69.5% were male, and 30.5% were female. The proportion of males was statistically significantly higher than females ($p=0.001$). Various epidemiological studies suggest that men may engage in higher-risk sexual behaviors, leading to a higher prevalence of HCV among men. Subtypes 1b and 1a were more common among women, whereas subtype 3a and subtype 1a were more common among men. Research by Pimenov et al. (13) in Russia showed that GT1 and GT3 were the most prevalent GTs among both men and women. Yang et al. (14) in China identified GT1 and GT2 as the most common GTs in both sexes. In Georgia, Baliashvili et al. (4) reported that GT3 and GT1b were predominant in men, while GT1b and GT2 were most common in women. Studies conducted in Türkiye also support these findings: Cirit et al. (18) in Gaziantep found that GT1 and GT4 were more prevalent among women, whereas GT1 and GT3 were more common among men. Bulut et al. (19) reported higher rates of subtype 1a and GT3 among men, with subtype 1b more prevalent among women. Karabulut et al. (7) found that GT1 and GT2 were more common in women, while GT3 and GT4 were more frequent in men. Variations in transmission routes, particularly sexual transmission and intravenous drug use, may influence the distribution of HCV GTs. Specific GTs may have distinct transmission tendencies, varying according to geographical and epidemiological factors. For example, men may exhibit more risk behaviors in certain regions, while women might have lower-risk transmission routes. Sexual transmission may account for the higher prevalence of certain GTs, such as GT1. Additionally, differences in intravenous drug use rates between men and women may lead to a higher prevalence of certain GTs among men. GT3a, for instance, is more frequently observed among intravenous drug users due to its association with the use of contaminated needles.

Among the patients whose HCV GT was investigated, 90.9% were Turkish citizens, while 9.1% were foreign nationals. No statistically significant difference was found between Turkish and foreign patients. The most common GTs among Turkish patients were GT1b (34.0%) and GT3a (32.0%), whereas GT1b was predominant among foreign patients (70.0%). This similarity may be attributed to the fact that foreign patients in Muğla are primarily long-term residents rather than transient visitors.

When evaluating GT distribution by year, GT1b was detected at the highest rates in 2021, 2022, 2023, and 2024, while GT1a was predominant in 2019, and GT3a was the most common in 2020. No statistically significant difference was observed in GT distribution across the years. The continued predominance of GT1b in recent years is consistent with previous studies indicating that GT1b remains the dominant strain in Türkiye and many other

regions. The transient increase in GT1a in 2019 and GT3a in 2020 may reflect localized outbreaks, demographic shifts in the tested patient population, or changes in injection drug use patterns, which are often associated with GT3a. However, the absence of a statistically significant difference over the years suggests that these fluctuations may result from random variation rather than a true epidemiological shift. Given that Muğla is a province in Türkiye with high levels of tourism, the continuous influx of people may contribute to ongoing changes in HCV GT distributions.

HCV GTs were most commonly observed in the 18-30 age group (30.9%) and least common in individuals under 18 years old (one case). Comparisons of GT distribution across age groups revealed that the 18-30 age group exhibited statistically significant higher rates than other age groups. The most frequently observed GTs by age group were subtype 1b in the 18-30 age group, GT3a in the 31-40 and 41-50 age groups, and subtype 1b in the 51-60 and over-60 age groups. In Georgia, Baliashvili et al. (4) found that HCV GTs were most prevalent in the 40-49 age group, with GT3 being the most frequently identified GT. Hundie et al. (17) in Ethiopia observed the highest rates in the 31-40 age group, with GT4 being the most prevalent GT. Bulut et al. (19) reported the highest prevalence in the 61-70 age group, with subtype 1b as the dominant GT. Differences in GT distribution across age groups may be linked to transmission routes, immune system responses, treatment outcomes, and genetic factors. Transmission routes for HCV have evolved over time. During the 1980s and 1990s, transmission through blood transfusions and medical interventions played a significant role in HCV spread, with GT1 and GT2 being more common. However, since the late 1990s, younger populations have shown higher prevalence rates of GTs like 3a, associated with changes in transmission routes such as intravenous drug use and sexual transmission. In younger individuals, behaviors such as intravenous drug use and sexual transmission may increase the frequency of specific GTs, while older individuals may exhibit different GTs due to historical transmission routes and weakened immune systems. HCV GT distributions can vary among age groups, influenced by historical transmission patterns, risk behaviors, and advancements in healthcare services. GT1b has long remained the dominant strain in Türkiye and many other regions. Older individuals may have been infected during periods when GT1b was the most prevalent. Insufficient infection control measures may have facilitated the transmission of this GT due to past medical procedures, blood transfusions, and the absence of widespread screening and antiviral treatments. Before the implementation of stricter sterilization and blood safety regulations, hospital-acquired (nosocomial) infections played a significant role in HCV transmission. The association of GT1b with iatrogenic (medical intervention-related) transmission in healthcare settings may explain its higher prevalence among older individuals. Genotypic differences among age groups necessitate the individualization of treatment strategies. Older patients should be carefully managed due to fibrosis risk, comorbidities, and potential drug interactions. On the other hand, public health interventions are crucial for younger patients to prevent reinfection. Understanding these variations can contribute to the development of personalized treatment approaches, ultimately improving patient outcomes.

Study Limitations

The limitations of this study include its retrospective design, which prevented the evaluation of transmission routes and risk groups among the patients. Additionally, the GT distribution was based solely on patient data requested by clinicians, which may have influenced the proportional representation in our findings.

Conclusion

HCV infection remains a global public health concern. Achieving the WHO's plan to eliminate HCV as a public health threat by 2030 requires comprehensive characterization of HCV prevalence and GT distribution. In our study, among the patients whose HCV GTs were investigated, GT1 was the most common GT (66.4%), followed by GT3 (30.9%), GT4 (1.8%), and GT2 (0.9%). Differences in treatment responses may exist between HCV GTs. GT information is crucial for determining the most effective drug combinations to achieve optimal treatment outcomes. Understanding the distribution of HCV GTs can aid in epidemiological studies, in identifying transmission pathways, and in developing public health strategies. GT data remain a critical factor for the development of new treatment options and for exploring more effective therapies targeted at specific GTs.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Muğla Sıtkı Koçman University Medical Sciences Ethics Committee (approval number: 177, date: 23.12.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: M.K., A.A., Design: M.K., A.A., Data Collection or Processing: M.K., A.A., Analysis or Interpretation: M.K., Literature Search: M.K., Writing: M.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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