



Distribution of Hepatitis C Virus Genotypes in Aydın Province

Aydın İlinde Hepatit C Virus Genotiplerinin Dağılımı

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ABSTRACT

Objectives: In this study, we evaluated the distribution and alteration of hepatitis C virus (HCV) genotypes throughout years which has a clinical importance in the treatment and follow-up.

Materials and Methods: Test results obtained from blood samples sent to the molecular microbiology laboratory at Aydın State Hospital for HCV genotype determination were analyzed retrospectively. A total of 182 samples collected between 2014 and 2018 were enrolled in the study. The determination of genotype and viral load of the samples were performed by real time polymerase chain reaction.

Results: 53.8% (98/182) of the samples were collected from male patients and 46.2% (84/182) from female patients. The mean age of the patients was 58.5±15.5 years. 69.2% of the samples were genotype 1b, 18.1% - genotype 1a, 2.2% - genotype 1 (those different from subtype 1a and 1b), 1.7% - genotype 2, 7.2% - genotype 3, and 1.7% of the samples were genotype 4.

Conclusion: In the present study, genotype 1 was the most common genotype (89.5%). Additionally, we have observed a decrease in the frequency of genotype 1b and a slightly increase in the frequency of other genotypes. Determination of HCV genotypes is important for treatment and prognosis of HCV infections.

Keywords: Hepatitis C virus, hepatitis C virus genotypes, epidemiology

ÖZ

Amaç: Çalışmamızda, hepatit C virüs (HCV) enfeksiyonunun tedavi ve takibinde önemli olan, HCV genotiplerinin dağılımı ve yıllar içindeki değişimi incelenmiştir.

Gereç ve Yöntemler: Aydın Devlet Hastanesi Moleküler Mikrobiyoloji Laboratuvarı'na 2014-2018 yılları arasında HCV genotip tayini için gönderilen kan örneklerinden elde edilen test sonuçları retrospektif olarak incelendi. Toplam 182 örneğin viral yükleri ve genotip tayini gerçek zamanlı polimeraz zincir reaksiyonu yöntemi ile belirlendi.

Bulgular: Örneklerin 98'i (%53,8) erkek, 84'ü (%46,2) kadın hastalara ait olup, yaş ortalaması 58,5±15,5 olarak hesaplanmıştır. Örneklerin %69,2'sinde genotip 1b, %18,1'inde genotip 1a, %2,2'sinde genotip 1 (1a, 1b dışı), %1,7'sinde genotip 2, %7,2'sinde genotip 3 ve %1,7'sinde genotip 4 saptanmıştır.

Sonuç: Çalışmamızda, en yüksek oranda genotip 1 (%89,5) rastlanmıştır. Genotip 1b oranında yıllar içinde azalma, diğer genotiplerde ise ılımlı bir artış saptanmıştır. HCV genotiplerinin takibi, tedavi ve prognoz açısından önemli olduğu gibi, epidemiyolojik açıdan da yol göstericidir.

Anahtar Kelimeler: Hepatit C virüs, hepatit C virüs genotipleri, epidemiyoloji

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Introduction

Hepatitis C virus (HCV) is an enveloped, single-stranded positive-sense RNA virus classified in the genus *Hepacivirus* of the family *Flaviviridae* (1). HCV infection is an important global public health problem (2). The virus is usually transmitted through blood transfusion, surgical and dental procedures, intravenous drug use and sexual intercourse (3,4,5). HCV infection becomes

chronic in approximately 75%-85% of cases. Cirrhosis develops in approximately 20-30% of patients over 20 years of HCV infection. Among these patients, hepatocellular carcinoma develops at a rate of 1%-4% (6). According to the World Health Organization, globally, an estimated 71 million people have chronic hepatitis C infection and approximately 399.000 people die each year from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma (7). In Turkey, it is estimated that around 1 million people are infected with HCV (8).

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HCV has 7 different genotypes and more than 60 subtypes (9,10). HCV genotypes 1, 2 and 3 are the most prevalent globally whereas genotype 4 is common in North Africa and Middle East, genotype 5 in South Africa and genotype 6 is common in Southeast Asia (2,11). Genotype 1 is the most common (46.2%) HCV genotype in the world followed by genotype 3 (30.1%). Genotype 2, 4 and 6 account for 22.8% of cases and genotype 5 is found in less than 1% of cases (11). Determination of geographical distribution of HCV genotypes is critical in the development of rational therapy protocols (12).

In this study, we aimed to determine the distribution of HCV genotypes in a five-year period in our region.

Materials and Methods

The results of HCV genotyping performed between 2014 and 2018 in 182 HCV RNA-positive patients in Aydin State Hospital were retrospectively evaluated. Repeated results from the same patients were excluded. Ethics committee approval was not required due to the retrospective design of the study.

Viral nucleic acid extractions were performed by a Magnesia 16 automated analyzer (Anatolia Geneworks, Turkey) using "Magnesia viral nucleic acid extraction kit EP" (Anatolia Geneworks, Turkey). Quantitation of viral nucleic acids was performed by real time-polymerase chain reaction (RT-PCR) targeting 5' UTR region in a Montania 4896 analyzer (Anatolia Geneworks, Turkey) using "Bosphore HCV Quantification Kit V2" (Anatolia Geneworks, Turkey). This assay had an analytical sensitivity of 25 IU/mL and a linearity range of 10¹-10⁹ IU/mL. HCV genotyping [genotypes 1a, 1b, 1 (those different from subtype 1a and 1b), 2,3,4,5,6] was performed by RT-PCR targeting NS5B region in a Montania 4896 analyzer (Anatolia Geneworks, Turkey) using "Bosphore HCV Quantification Kit V3" (Anatolia Geneworks, Turkey). All assays were performed according to the manufacturer's instructions.

Results

53.8% (98/182) of the samples were collected from male patients (mean age: 55.8±15.9 years) and 46.2% (84/182) of the samples were collected from female patients (mean age: 61.7±14.4 years). The mean age of the study population was 58.5±15.5 years. HCV RNA levels ranged between 694 and 31.580.000 IU/mL. 69.2% (126/182) of the samples were genotype 1b, 18.1%

(33/182) 1a, 2.2% (4/182) - 1 (those different from subtype 1a and 1b), 1.7% (3/182) - genotype 2, 7.2% (13/182) - genotype 3 and 1.7% (3/182) were genotype 4 (Figure 1).

Distribution of HCV genotypes by years (2014-2018) is presented in Table 1. Gender and age distribution of HCV genotypes between 2014 and 2018 are presented in Table 2.

There were 11 foreign national patients in this study. The nationalities and HCV genotypes of these patients are summarized in Table 3. Genotype 1b (72.7%) was the predominant genotype in this group.

Discussion

Genotype 1b is the most common HCV genotype in Turkey. Recent studies revealed that there has been a decline in the prevalence of HCV genotype 1b infections while an increase in the prevalence of infections caused by other genotypes. This alteration may be due to immigrants, touristic activities and different risk factors for HCV infection, as well as increased safety procedures in medical practice. Table 4 shows the results of some of the HCV genotyping studies in Turkey (13,14,15,16,17,18,19,20,21,22,23,24, 25,26,27).

In this study, HCV genotype 1 (89.5%) was found the most common genotype in Aydin. However, we have observed a decrease in the frequency of genotype 1b infection throughout years while a slight increase in genotype 1a infection. Additionally, there has been an increase in the genotype diversity over years particularly in genotype 3 and genotype 4, respectively.

Among foreign nationals (Azerbaijan, Russia, Syria, Ukraine, Romania, Mongolia) enrolled in this study, patients infected with genotype 3 were from Syria and Ukraine while those with

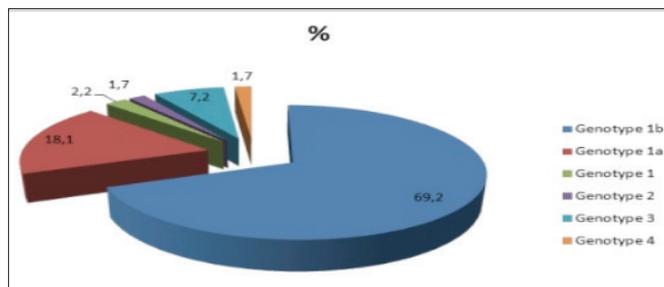


Figure 1. Distribution of hepatitis C virus genotypes

Table 1. Distribution of hepatitis C virus genotypes by years (2014-2018)

Year	HCV genotypes							
	Genotype 1 n (%)				Genotype 2 n (%)	Genotype 3 n (%)	Genotype 4 n (%)	Total n
	1a	1b	1	Genotype 1 Total				
2014	3 (42.9)	4 (57.1)	-	7 (100.0)	-	-	-	7
2015	4 (12.9)	25 (80.6)	-	29 (93.5)	1 (3.2)	1 (3.2)	-	31
2016	7 (19.4)	26 (72.2)	1 (2.8)	34 (94.4)	-	2 (5.6)	-	36
2017	14 (15.2)	61 (66.3)	3 (3.3)	78 (84.8)	2 (2.2)	9 (9.7)	3 (3.3)	92
2018	5 (31.3)	10 (62.5)	-	15 (93.8)	-	1 (6.2)	-	16
Total	33 (18.1)	126 (69.2)	4 (2.2)	163 (89.5)	3 (1.7)	13 (7.2)	3 (1.7)	182 (100.0)

HCV: Hepatitis C virus

genotype 4 were from Syria (Table 3). Touristic activities in the region and Syrian refugees may be the cause of increase in the diversity of HCV genotypes in Aydın province. Studies performed in various regions of Turkey including Mediterranean, Aegean and

southeast Anatolia regions shows that in the areas exposed to immigrant and touristic activities, genotype 1 was still responsible for the vast majority of cases, however, the prevalence of the other genotypes was higher than in the other regions of Turkey (Table 4).

Table 2. Gender and age distribution of hepatitis C virus genotypes between 2014 and 2018

	HCV genotypes n (%)					
	Genotype 1 (total) (n=163)			Genotype 2	Genotype 3	Genotype 4
	1a	1b	1			
Number (n=182)	33 (18.1)	126 (69.2)	4 (2.2)	3 (1.7)	13 (7.2)	3 (1.7)
Gender						
Male n=98 (53.8%)	22 (22.5)	60 (61.2)	3 (3.1)	2 (2.0)	9 (9.2)	2 (2.0)
Female n=84 (46.2%)	11 (13.1)	66 (78.5)	1 (1.2)	1 (1.2)	4 (4.8)	1 (1.2)
Age						
Median (min-max)	56.1 (18-92)	61.7 (24-82)	60.7 (48-72)	41.6 (27-51)	39.5 (17-61)	49.0 (44-54)

HCV: Hepatitis C virus, min: Minimum, max: Maximum

Table 3. Distribution of hepatitis C virus genotypes in foreign nationals

Country	Number	HCV genotypes n (%)			
		Genotype 1b	Genotype 2	Genotype 3	Genotype 4
Azerbaijan	4 (36.3)	4 (36.3)	-	-	-
Russia	2 (18.2)	2 (18.2)	-	-	-
Syria	2 (18.2)	-	-	1 (9.1)	1 (9.1)
Ukraine	1 (9.1)	-	-	1 (9.1)	-
Romania	1 (9.1)	1 (9.1)	-	-	-
Mongolia	1 (9.1)	1 (9.1)	-	-	-
Total	11 (100.0)	8 (72.7)	-	2 (18.2)	1 (9.1)

Table 4. Results of some of the hepatitis C virus genotyping studies in Turkey

Study (Reference)	Year	Province	Number (n)	Genotypes						
				Genotype 1 (total) n (%)	1a (%)	1b (%)	2 (%)	3 (%)	4 (%)	5 (%)
Abacioglu et al. (13)	1995	Izmir	89	84 (94.4)	(19.1)	(75.3)	3 (3.4)	-	2 (2.2)	-
Yarkin and Hafta (14)	2000	Adana/Mersin	62	60 (96.7)	(14.5)	(82.2)	2 (3.3)	-	-	-
Bozdayi et al. (15)	2004	Ankara	365	349 (95.0)	(11.0)	(84.0)	10 (3.0)	3 (1.0)	3 (1.0)	-
Altuglu et al. (16)	2008	Izmir	345	335 (97.1)	(9.9)	(87.2)	3 (0.9)	5 (1.4)	2 (0.6)	-
Gokahmetoglu et al. (17)	2011	Kayseri	146	90 (61.7)	(3.4)	(52.8)	4 (2.7)	-	52 (35.6)	-
Buruk et al. (18)	2013	Trabzon	304	282 (92.8)	(5.3)	(87.5)	5 (1.6)	15 (4.9)	2 (0.7)	-
Altuglu et al. (19)	2013	Izmir	535	499 (93.3)	(12.9)	(80.4)	8 (1.5)	20 (3.7)	8 (1.5)	-
Saglik et al. (20)	2014	Antalya	422	352 (83.4)	(14.7)	(63.3)	15 (3.5)	47 (11.1)	7 (1.6)	-
Kuscu et al. (21)	2014	Adana	369	289 (78.3)	-	-	23 (6.2)	54 (14.6)	3 (0.8)	-
Caliskan et al. (22)	2015	Kahramanmaraş	313	162 (51.7)	-	-	4 (1.3)	144 (46.0)	3 (1.0)	-
Kirdar et al. (23)	2015	Aydın	50	48 (96.0)	(18.0)	(72.0)	(2.0)	(2.0)	-	-
Kayman et al. (24)	2015	Kayseri	218	136 (62.4)	(2.3)	(60.1)	10 (4.6)	-	72 (33.0)	-
Duran et al. (25)	2016	Adana	119	85 (71.4)	(12.6)	(58.8)	9 (7.6)	20 (16.8)	4 (3.4)	1 (0.8)
Balin et al. (26)	2017	Elazığ	71	62 (87.3)	-	-	2 (2.8)	7 (9.9)	-	-
Harman et al. (27)	2017	Gaziantep	160	157 (98)	-	(98.0)	1 (0.75)	2 (1.25)	-	-
Presented study	2014-2018	Aydın	182	163 (89.5)	(18.1)	(69.2)	3 (1.7)	13 (7.2)	3 (1.7)	-

There are regional differences in the distribution of HCV genotypes in our country. The prevalence of HCV genotype 4 has been reported to be 35% in Kayseri (17,24) while there has been an obvious increase in infections caused by genotype 3 in the cities of southern parts of Turkey, such as Adana and Kahramanmaraş. In this patient population, intravenous drug abuse is relatively frequent (21,22,25). Genotype 5 infections are being reported in Syrian refugees (25).

Even though the frequency of genotype 1, which is associated with poor prognosis, is frequent in Turkey (85-90%), recent studies indicated a decrease in genotype 1 with an increase in other genotypes and regional increase in some genotypes.

Study Limitations

We conducted a retrospective study of the records. For these reason, there are some limitations. Some data, including possible transmission routes and risk factors, have not been obtained. Our data supports the dominance of genotype 1b infections in the area. However, there is an increase in the rate of infections caused by other genotypes.

Conclusion

As a result, data have to be updated periodically not only for epidemiological purposes but also and more importantly for prognosis and treatment.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.O.Ö., Concept: Y.T., Design: A.Ç.D. Data Collection or Processing: O.O.Ö., Analysis or Interpretation: A.Ç.D., Literature Search: Y.T., Writing: Y.T.

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