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Seroprevalence and Genotype Distribution of Hepatitis C Virus in Mogadishu, Somalia: A Comprehensive Study

Mogadişu, Somali'de Hepatit C Virusu Seroprevalansı ve Genotip Dağılımı: Kapsamlı Bir Çalışma

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Abstract

Liver cancer is the second-most common form of cancer among men in Somalia. However, data on the epidemiology of hepatitis C virus (HCV) infections are limited. This study aimed to examine the basic epidemiological characteristics of HCV infections, in Mogadishu, Somalia. In this study, anti-HCV seropositivity was investigated in participants who applied to a tertiary care hospital in Mogadishu between 2015 and 2019 using an Architect anti-HCV immunoassay. HCV genotype determinations were performed in two different accredited external laboratories located in Turkey. A total of 115,659 tests were included the study reported for 102,601 different individuals and anti-HCV seropositivity were found for 1,447 different patients (1.41%). Seropositivity was found as 0.26% among healthy individuals (20/7,789), which is a subgroup of the study population. Furthermore, seropositivity was found in 0.26% (55/20,784) of individuals under the age of 20 years and 6.2% (424/6,837) of aged >70 years. Finally, seropositivity was significantly more prevalent among men than among women (1.64% and 1.15%, respectively; p<0.0001). Seventy-three HCV genotypes were determined in 71 patients, including Genotype 1a (5.48%), Genotype 1b (10.96%), Genotype 3 (31.5%),

Genotype 4 (49.3%), and Genotype 5 (2.74%). Mixed genotypes (Genotypes 3 and 4) were detected in two patients. This study is the most comprehensive epidemiological study carried out in Somalia since the discovery of HCV, and also it is the first study to investigate HCV genotypes among Somali residents. We believe that the data presented herein will contribute to the development of preventive health policies.

Keywords: Anti-HCV, Architect, Seroprevalence, Liver cancer.

Özet

Karaciğer kanseri, Somali'de erkekler arasında en yaygın ikinci kanser türüdür. Ancak, hepatit C virusu (HCV) enfeksiyonlarının epidemiyolojisine ilişkin veriler sınırlıdır. Bu çalışma, Somali Mogadişu'da HCV enfeksiyonlarının temel epidemiyolojik özelliklerini incelemeyi amaçlamıştır. Bu çalışmada 2015-2019 yılları arasında Mogadişu'da üçüncü basamak bir hastaneye başvuran katılımcılarda Architect anti-HCV immunoassay ile anti-HCV seropozitifliği araştırılmıştır. HCV genotip tayinleri Türkiye'de bulunan iki ayrı akredite dış laboratuvarda gerçekleştirilmiştir. Çalışmaya 102.601 farklı birey için rapor edilen toplam 115.659 test dahil edilmiş ve 1.447 farklı hastada (%1.41) anti-HCV seropozitifliği bulunmuştur. Çalışma popülasyonunun bir alt grubu olan sağlıklı bireylerde seropozitiflik %0.26 (20/7.789) olarak bulundu. Seropozitiflik ayrıca 20 yaş altı bireylerde %0.26 (55/20.784) ve 70 yaş üstü bireylerde %6.2 (424/6.837) olarak saptandı. Son olarak, seropozitiflik erkeklerde kadınlara göre anlamlı derecede daha yüksekti (sırasıyla %1.64 ve %1.15; p<0.0001). Genotip 1a (%5.48), Genotip 1b (%10.96), Genotip 3 (%31.5), Genotip 4 (%49.3) ve Genotip 5 (%2.74) olmak üzere 71 hastada 73 HCV genotipi belirlendi. İki hastada çoklu genotip (Genotip 3 ve 4) varlığı tespit edildi. Bu çalışma, HCV'nin keşfinden bu yana Somali'de yürütülen en kapsamlı epidemiyolojik çalışma olup, Somali'de yerleşik halk arasında HCV genotiplerini araştıran ilk çalışmadır. Burada sunulan verilerin koruyucu sağlık politikalarının geliştirilmesine katkı sağlayacağına inanıyoruz.

Anahtar Kelimeler: Anti-HCV, Architect, Seroprevalans, Karaciğer kanseri.

Introduction

Hepatitis C virus (HCV), which was identified as the main cause of non-A, non-B chronic hepatitis in 1989, is a flavivirus with a single-stranded positive-sense RNA genome [1,2]. This virus can lead to serious complications, such as cirrhosis and hepatocellular carcinoma (HCC), with a high rate of chronicity (55–85%); furthermore, this virus is the most common indication for chronic liver failure requiring transplantation (40–50%) [3,4]. Although the precise prevalence of chronic HCV infection is not yet known, it is estimated that more than 71 million people live with chronic hepatitis C worldwide, and this infection causes approximately 400,000 deaths each year [5,6]. The development and successful clinical use of direct-acting antiviral (DAA) drugs were milestones in the treatment of chronic hepatitis C infections [7,8]. An infection with any of the HCV genotypes can now be eliminated in more than 95% of infected people with short-term courses of well-tolerated drugs taken orally [9,10]. The idea that "HCV can be eradicated," which emerged due to the success of DAAs, was pioneered by the World Health Organization (WHO) in its mission to support health strategies with the aim of eliminating the virus globally by 2030 [5,11]. However, the reported number of new infection cases was higher than the number of treated cases in 2016 [12]. It is estimated that only 20% (14 million) of HCV cases are diagnosed worldwide; the infection will continue to spread through individuals who remain undiagnosed and may remain asymptomatic for years as well as marginalized groups who engage in risky behaviors and often have limited access to HCV screening and treatment [5,8]. In recent years, the diagnostic paradigm has changed in parallel with changing clinical needs [13]. Molecular diagnostic tests that can determine genotypes and provide quantitative results in the management of HCV infections (i.e., antiviral treatment planning and follow-up) have become critical [14]. However, the effects of these positive developments have remained minimal in Somalia. Developing countries, such as Somalia, face major challenges in achieving the diagnosis of infected people, widespread treatment access, and reduced treatment costs. The present study

aimed to produce epidemiological data that can be used to predict the prevalence of HCV infection in Somali society and contribute to the development of preventive public health policies. In addition, this study aimed to present field observations of the difficulties encountered in the diagnosis and treatment of HCV infections in Somalia.

Material and Method

This study was approved by the Ethics Committee of Somalia Turkey Recep Tayyip Erdogan Education and Research Hospital (reference numbers: MSTH/2724 for seroprevalence research and MSTH/3399 for genotype distribution research). Given the retrospective nature of this study (i.e., the data was obtained from medical records), the ethics committee's informed consent requirement was waived for the present study population.

This retrospective cross-sectional study included all patients who requested HCV tests between June 2015 and November 2019 at Mogadishu Somalia-Turkey Recep Tayyip Erdoğan Training and Research Hospital. Data regarding the frequency and distribution of HCV infections were recorded and stratified by age and gender. Age was stratified into groups of 1–20, 21–40, 41–60, 41–60, 61–70, and >70 years old for statistical analysis. Patients with duplicate test results or incomplete data related to the studied variables were excluded from the analysis.

Serological tests

Anti-HCV serological tests were performed using an Architect anti-HCV chemiluminescence microparticle immunoassay (Abbott Diagnostics, Germany) on the Architect I 2000 SR system (Abbott Diagnostics, USA). The results were interpreted as follows: S/Co ≥ 1.00, reactive; S/Co < 1.00, non-reactive [15]. Some cases were re-tested, and further controls were performed using Healgen HCV One-Step Rapid Test Kits (Zhejiang Orient Gene Biotech, China).

Real-time reverse transcriptase polymerase chain reactions (PCRs) and genotyping

Tests for HCV-RNA (quantitative real-time polymerase chain reactions, RT-PCRs) and genotyping were performed in two external laboratories (accredited by the Turkey Ministry of Health) located in Istanbul, Turkey. The quantitative PCRs were performed with Cobas AmpliPrep and Cobas Taqman 48 systems (Roche Diagnostics, Germany). For the genotyping, PCR products amplified by Montania 4896 (Anatolia Geneworks, Turkey) and Applied Biosystems thermal cyclers were resolved on an ABI 3130 Genetic Analyzer (Life Technologies, USA).

Statistical analysis

The data were compiled and analyzed using SPSS v. 22.0 (IBM SPSS Statistics Version 22.0, Armonk, NY: IBM Corp.). Chi-square tests and Fisher's exact probability tests were used to assess the associations of the age and gender groups with seropositivity for the anti-hepatitis C antibody and its genotypic distribution. Results were considered statistically significant when $p<0.05$ with a 95% confidence interval (CI).

Results

Over a four-year period, 116,721 anti-HCV requests were identified retrospectively for 103,116 individuals. However, 458 patients did not provide any samples, and 57 patients provided insufficient samples and did not agree to provide new samples. Moreover, 547 duplicate test results were excluded from the analysis.

A total of 115,659 anti-HCV test results for 102,601 patients (54,416 male and 48,185 female) were eligible for the present study. Single tests were reported for 94,590 individuals, and multiple tests (ranging from 2 to 19) with intervals longer than at least a week were reported for 8,011 individuals. The mean age of the participants was 36.34 ± 20 years, with a range of 0 to 109 years. Positive results were found for 1,447 patients (1.41%), and negative results were found for the remaining 101,154 patients. The rate of anti-HCV positivity was found to increase with age in both men and women.

A subgroup of study participants were healthy individuals (7,789) without any complaints. These healthy participants request HCV testing for different purposes including (i) candidate student screenings, (ii) job applications, and (iii) visa permit requirements; the majority of those in the last group were seeking visa permits for Saudi Arabia and Qatar.

Table 1. Anti-HCV seropositivity by age* groups and gender in 102,601 different individuals.

Age groups →	0-10		11-20		21-30		31-40		41-50		51-60		61-70		71-100+		Total	
Anti-HCV status	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
Seropositive individuals (n: 1,447)	6	16	18	15	51	50	38	54	61	76	115	126	140	257	125	299	554	893
Seropositivity %	0.24	0.41	0.28	0.19	0.35	0.29	0.51	0.74	1.04	1.44	2.41	2.57	3.77	6.15	4.4	7.48	1.15	1.64
	0.34		0.23		0.32		0.62		1.23		2.49		5.03		6.2		1.41	
	0.26				0.42				1.82				5.57					
Total tested (n: 102,601)	2,548	3,895	6,468	7,873	14,507	16,950	7,480	7,336	5,859	5,292	4,765	4,895	3,717	4,179	2,841	3,996	48,185	54,416

*In repeat tests of the same patient, the patient's age at the date of the first test was selected. F: female, M: male.

Table 2. Distribution of anti-HCV seropositivity in different groups by gender.

Anti-HCV status →	Seropositive			Seronegative			Total tested	Age distribution
	F	M	total (%)	F	M	total	n	
Patients referred from other hospitals	3	12	15 (7.01)	79	120	199	214	5-92 (mean: 36.99 ±17.6, median 30)
Patients from refugee camps	1	2	3 (0.64)	224	243	467	470	0-85 (mean: 30.43 ±23.5, median 26)
Healthy individuals (students and officers)	0	8	8 (0.24)	28	3246	3274	3282	14-64 (mean: 23.5 ±4.8, median 22)
Healthy individuals (those seeking international travel/work permits, including Hajj pilgrims)	5	7	12 (0.27)	2603	1892	4495	4507	0-76 (mean: 27.56 ±8.2, median 25)
All study groups	554	893	1,447 (1.41)	47,631	53,523	101,154	102,601	0-109 (mean: 36.34 ±20, median 30)

F: female, M: male.

Seropositivity was significantly more prevalent among men (893/54,416 ; 1.64%) than among women (554/48,185 ; 1.15%; p<0.0001). Seropositivity in healthy individuals was 0.26% (20/7,789), when two different healthy groups (Table 2) were pooled.

A total of 73 HCV genotypes were found in 71 patients (35 female and 36 male). Genotype 1a was found in 4 patients (5.48%), Genotype 1b was found in 8 (10.96%), Genotype 2 was not found, Genotype 3 was found in 23 (31.5%), Genotype 4 was found in 36 (49.3%), and Genotype 5 was found in 2 (2.7%). Mixed infections (Genotypes 3 and 4) were detected in two patients (one female and one male). The frequency of Genotype 1b was significantly higher among men (n=7) than among women (n=1; p=0.030). The frequency of Genotype 3 was higher among women (n=14) than among men (n=9), but this difference was not statistically significant (p=0.180).

Discussion

Approximately 1% of the world's population is infected with HCV, and the highest prevalence (2.3%) of HCV infection was observed in the Eastern Mediterranean Region (EMR), which includes Somalia [5,6]. In a 2019 study, policy indicators for the elimination of viral hepatitis were examined in 66 countries and 11 regions with the heaviest infection burdens; Somalia received the lowest score for HBV, and Somalia, Sudan, and Yemen received the lowest scores for HCV (no policy indicator) [16]. It is difficult to determine the frequency of HCV infections and the burden of related diseases in Somalia due to the limited number of relevant studies in the literature, many of which involved small groups and were carried out 25–30 years ago [17]. The difficulties limiting the determination of HCV prevalence in this region led researchers to create meta-analysis models with the aim of investigating population subgroups to guide

research, policy, and programming priorities for HCV prevention, control, and treatment [18]. In an EMR report published by the WHO in November 2020, an anti-HCV seroprevalence of 0.9% was estimated for the general population of Somalia [19].

In a systematic review and meta-analysis conducted in 2018 [20], which covered 12 studies of HCV conducted in Somalia or with Somali immigrants, the overall combined prevalence of HCV was estimated to be 4.84% (95% CI: 3.02–7.67%). In this review [20], the sizes of the study groups examined for HCV varied between 76 and 2,012 individuals. The high estimates of this review may have been due to the fact that many Somali immigrants are patients. In this review, the prevalence rates of blood donors, risk groups, children, and patients with chronic liver disease were 0.87%, 2.43%, 1.37%, and 29.8%, respectively [20].

The present study was conducted in the community of Mogadishu—Somalia's most populous city—and included more individuals than all previous studies of HCV in this area combined. The study group included more than 100,000 people from different age groups and had a general anti-HCV seroprevalence of 1.41%. Considering that 6,443 individuals were screened (0.34% positivity), including the population under 10 years old, we can say that these data are valuable in understanding the prevalence of HCV infection in the general population. Although the vast majority of our study group consisted of people who applied to the hospital for the treatment of other diseases, this group was epidemiologically valuable because it included 7,789 healthy people as well as many people who were screened prior to medical procedures, including surgical procedures (Table 2). When the study group was examined in 20-year age intervals, we observed a regular increase in seropositivity from 0.26% to 0.42%, 1.82%, and finally 5.57% (Table 1). Anti-HCV test results indicating low positivity (close to the cut-off value) are common problems in routine diagnostic laboratories and are especially common in regions with low HCV seroprevalence (<3%) [21-24]. One recent (2019) study examined samples with low positivity to compare several widely used anti-HCV test platforms and arrived at an S/Co value of 3.13 (95% CI: 2.69–3.65) for the Architect anti-HCV test; the test repetitions were significantly reduced, achieving an absolute positivity rate of 97.35% [15]. The small number of low positive results in our study were re-tested and re-evaluated.

Another approach to understanding the epidemiology of infectious diseases in the Somali population is to consider data obtained from Somali immigrants who settled mainly in American and European countries. One study conducted in 2012 examined immigrant patients from Somalia (854 patients) and other countries (12,654 patients) who were living in Minnesota and treated for various diseases at Mayo Clinic [25]. The highest seropositivity rate in non-Somali immigrants was observed in those between the ages of 40 and 60 years, and a decline in seropositivity was observed in those over the age of 60; in contrast, Somali immigrants exhibited increased seropositivity with age (from 0.00% to 0.27%, 13.1%, and finally 30.9% in 20-year age intervals), as in the present study [25]. In a study conducted in 1994 [26], the rate of seropositivity among immigrants from Somalia in Italia under the age of 40 years was very low (2.2%), while that of individuals over the age of 40 years was significantly higher (15.4%). These findings may indicate that a factor related to HCV transmission in Somalia existed in the past and that its effect has decreased in recent years.

The WHO reported [19] that many countries in the EMR, including Somalia, face difficulties in the implementation of healthcare safety measures, including blood donation screenings, medical equipment sterilization, and single-use needles and syringes. This is a major risk factor for HCV transmission in these countries. It should be noted that our hospital meets all the standards for tertiary inpatient treatment centers in Turkey. The implementation of common traditional practices (e.g., traditional phlebotomy called hijama) and emergency blood transfusions in unfavorable conditions has also been associated with HCV transmission in the Somali population [17,27,28]. In a previous study, the anti-HCV seropositivity rate in Somalia was found to be 1.7% (4/236) in a group exhibiting risky

behaviors for sexually transmitted diseases, and it was concluded that sexual transmission of HCV is a low probability for Somalia [29]. Although there is evidence of intravenous drug use in Somalia, the ratio of intravenous drug users to the total population in Somalia is estimated to be the lowest among the EMR countries (0.02%) [19]. The use of khat (chat or khat; *Catha edulis* Forsskal)—an addictive stimulant plant—is common in Somalia, but intravenous drug use is rare [19,30,31]. Although the use of khat is more common among people with HCV infections [32], it is also common in the general population (especially among people who exhibit risky behaviors) and is not a strong risk factor like intravenous drug use.

Of all the cancers seen in Somalia, HCC is the second-most common in men (10.5%) and the sixth-most common in women (4.8%) [31]; this may indicate that HCV infections are more common in Somali men than in Somali women. Compared to the worldwide (HCC is fifth and ninth most common cancer in men and women), HCC is more common among all cancers in Somalia; this may be related to limited treatment access in Somalia [33].

Determining the pre-treatment HCV genotype is one of the most important steps in HCV infection management, as it guides the determination of treatment duration and is accepted as the strongest indicator of a persistent viral response [14,34]. While the most common genotype in the world is Genotype 1, with a prevalence of 46.2%, data obtained from neighboring countries and studies of Somali immigrants have indicated that Genotypes 3 and 4 are more common in Somalia (Table 3) [25,30,34,35]. The present study was the first genotyping study performed in a population living in Somalia. The most common genotype in the present study was Genotype 4, and the second-most common was Genotype 3; this was consistent with the results of previous studies of Somali immigrants. Furthermore, the present study included the first data on the subtypes of Genotype 1 (Table 3). The frequency of Genotype 1b was significantly higher in men than in women (p=0.030).

Table 3. Genotype distribution in the present study and the results of other studies of Somali immigrants.

Genotypes	Genotype distribution	Genotype distribution in Somali immigrants				Worldwide
	Present study (Mogadishu)	A*	B*	C*	pooled (A+B+C)	D*
Genotype 1	12 (**16.4**%)	8 (22.2%)	18 (23.1%)	8 (15.1)	34 (**20.4**%)	**46.2**%
Genotype 2	0 (**0.0**%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (**0.0**%)	**9.1**%
Genotype 3	23 (**31.5**%)	10 (27.8%)	20 (25.6%)	12 (22.6%)	42 (**25.1**%)	**30.1**%
Genotype 4	36 (**49.3**%)	17 (47.2%)	38 (48.7%)	29 (54.7%)	84 (**50.3**%)	**8.3**%
Genotype 5	2 (**2.74**%)	1 (2.78%)	2 (2.56%)	3 (5.66%)	6 (**3.59**%)	**0.8**%
Genotype 6	0 (**0.0**%)	0 (0.0%)	Not studied	0 (0.0%)	0 (**0.0**%)	**5.4**%
Unknown	-	-	-	1 (1.89%)	1 (**0.6**%)	-
Total	**73**	**36**	**78**	**53**	**167**	~ 71 million

F: female, M: male. *References; A [25], B [35], C [30], D [34].

The use of HCV-RNA tests is becoming more widespread in the verification of suspicious positive serological test results; these tests are more sensitive than serological methods and enable more accurate evaluations of infected and immunocompromised individuals during the window period [21,13]. The determination of basal viral load with quantitative HCV-RNA tests, antiviral resistance monitoring, and HCV genotype determination have also become routine parts of HCV diagnosis, as these methods may serve to guide treatment decisions [14,21]. However, the use of molecular diagnostic tests is not common in Somalia, only applied for tuberculosis in WHO Tuberculosis Treatment Centers and for SARS-CoV-2 in a state laboratory. Some routine molecular diagnostic testing are carried out with great difficulty in external laboratories located in other countries (e.g., Turkey and Kenya), even for major infectious agents such as hepatitis B and C.

Conclusion

The present study reflected upon the distribution of HCV infection among several groups in the Somali population, including: different age, year, and gender groups; healthy students; a healthy group of official employees (the majority of which were young men); and a healthy group of individuals who applied for travel permits ranging widely in age (the majority of which were women). Furthermore, genotype distribution data was revealed for the first time for the settled Somali population. We believe that our comprehensive study results will contribute to the development of preventive policies and priorities for the reduction of HCV infections and the associated disease burden in Somalia.

Conflict of interest: The author(s) declare(s) that there is no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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