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BRIEF ARTICLE

Hepatitis C virus genotypes in north eastern Algeria: A retrospective study

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Abstract

AIM: To determine the frequency of various hepatitis C virus (HCV) genotypes present in patients from north eastern Algeria.

METHODS: This is a retrospective cross-sectional study of 435 HCV infected patients from northeast Algeria, detected in the Sadelaoud laboratory and diagnosed between January 2010 and December 2012. The patients were diagnosed with HCV infection in their local hospitals and referred to be assessed for HCV genotype before the antiviral treatment. Demographic information (sex, age and address), genotype, subtype and viral load were retrieved from the patient medical records. The serum samples were tested by the type-specific genotyping assay.

RESULTS: The majority of the patients (82.5%) were from the central part of the examined region (P = 0.002). The mean age of the patients studied was 53.6 ± 11.5 years. HCV genotype 1 was the most frequent (88.7%), followed by genotypes 2 (8.5%), 4 (1.1%), 3 (0.9%) and 5 (0.2%). Genotype 6 was not detected in these patients. Mixed infection across the HCV subtypes was detected in twenty patients (4.6%). The genotype distribution was related to age and region. Genotype 1 was significantly less frequent in the ≥ 60 age group than in the younger age group (OR = 0.2; 95%CI: 0.1-0.5, P < 0.001). Furthermore, genotype 1 was more frequent in the central part of the examined region than elsewhere (P < 0.01).

CONCLUSION: The HCV genotype (type 1b was dominant) distribution in Algeria is different from those in other northern countries of Africa.

Key words: Hepatitis C virus; Prevalence; Genotype 1b; Viral load; Algeria

Core tip: Hepatitis C virus (HCV) infection is a common worldwide health problem; it is one of the major causes of chronic liver disease. HCV has at least six genotypes. The distribution of HCV genotypes varies greatly over the world. Genotype identification is clinically important to tailor the dosage and duration of treatment. The prevalence and HCV genotypes in Algeria are not known. In this study, we found that HCV genotype distribution in Algeria is different from the distribution detected in other northern countries of Africa.

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INTRODUCTION

Hepatitis C virus (HCV) infection is a major global public health issue. It is estimated that the global prevalence of HCV is approximately 2.8% (or 180 million people)[1] of the total population. HCV has a high viral heterogeneity. According to the nucleotide divergence, there are at least six genotypes, each of them containing a series of subtypes[2]. HCV genotypes have a striking geographical and epidemiological distribution and genotype identification is clinically important to tailor the dosage and duration of treatment because of different patterns of the treatment response and, consequently, distinct therapeutic approaches are required for each genotype[3]. In several areas of the world, HCV genotype 1 is reported as the most common infecting genotype among chronically infected patients. HCV genotypes 1, 2 and 3 appear to have a worldwide distribution and their relative prevalence varies from one geographical area to another[4]. HCV subtypes 1a and 1b are the most common genotypes in the United States[5] and Europe[6]. The predominant subtype reported from Japan is subtype 1b, responsible for up to 73% of cases of HCV infection[7,8]. HCV subtypes 2a and 2b are relatively common in North America, Europe and Japan and subtype 2c is found commonly in northern Italy[5,6]. HCV genotype 4 appears to be prevalent in north Africa and the Middle East[9,10] and genotypes 5 and 6 seem to be confined to South Africa and southeast Asia, respectively[11,12]. The north African data are based on information from only Egypt, Libya, Tunisia and Morocco. However, a published study on HCV genotype prevalence in Algeria[13-15] does not exist. Preliminary data by Benabdellah *et al*[16] reported that genotypes 2a/2c were predominant (47%) in 140 patients retrospectively evaluated between 2005 and 2011.

The aim of our study is to identify the prevalence of different HCV genotypes in north eastern Algeria and to assess the correlation between the HCV genotypes and demographic profile.

MATERIALS AND METHODS

We retrospectively evaluated 435 HCV infected patients examined between January 2010 and December 2012 in the Sadelaoud laboratory, a regional medical laboratory in the city of Batna and the only molecular biology laboratory in the eastern area of the country. The patients were diagnosed with the HCV infection in their local hospitals and referred to the Sadelaoud laboratory to be assessed for HCV genotype before antiviral treatment. We retrieved demographic information (sex, age and address), genotype, subtype and viral load from the patient medical records. The patients who were evaluated live in fifteen wilayas (provinces), the administrative regions which cover the eastern area of Algeria. These wilayas were classified into three regions for this study: the central part covering five wilayas (Batna, Khenchela, M'Sila, Oum El Bouaghi and Tebessa), the northern part (Annaba, Bordj Bouararidj, Constantine, Guelma, Jijel, Mila, Setif) and the southern part (Biskra, El Oued and Ouargla) (Figure 1).

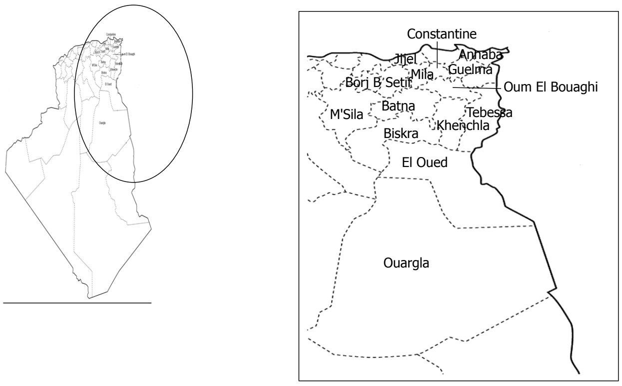

Figure 1 Hepatitis C virus genotype study coverage.

The HCV-RNA quantification was done by real time PCR (AmpliPrep/Cobas Taqman, Roche Molecular Systems, Branchburg, NJ, United States) with lower limit of detection of 15 IU/mL. Genotyping was done by INNO-LiPA HCV assay: Versant HCV genotype 2.0 assay (Siemens HealthCare Diagnostics, Tarrytown, NJ, United States). The genotype and HCV-RNA quantification were determined in a single laboratory, the Sadelaoud laboratory in Batna. The data about possible risk factors for HCV transmission were not available in the laboratory database.

Statistical analysis

Pearson's χ^2 and Fisher's exact tests were used to assess the differences in the patients' characteristics of the genotype, subtype, viral load, age, sex and region. Age was categorized into two groups: < 60 years and $\geqslant 60$ years and the genotype into two groups: "genotype 1" and "others" respectively. To assess the genotype distribution according to age and region, binomial logistic regression was performed with P: probability to be infected by genotype 1. The interaction of the covariate region on the association between the age and genotype was tested by the likelihood ratio test comparing the models with and without the interaction term. The interaction was significant if $P < 0.05$. The statistical analysis was done using the R version 2.15.1 statistical software.

RESULTS

Demographic features

The main demographic characteristics of the patients are shown in Table 1. The majority of the patients (82.5%, 359/435) were from the central part of the examined region ($P = 0.002$). The mean age of the patients studied was 53.6 ± 11.5 years (range 20 to 86 years) but over two thirds of the patients (70.6%, 307/435) were > 50 years old. There was a clear predominance of females (F/M ratio = 1.9). The female predominance was significant in all age groups ($P = 0.04$) except for the youngest in which we observed male predominance.

Table 1 Distribution of study population *n* (%)

Variables	Total	Sex		*P* value
		Male, 150 (34.5)	Female, 285 (65.5)	
Age (yr)	20-29	12 (8)	7 (2.5)	0.04
	30-39	13 (8.7)	20 (7)	
	40-49	28 (18.7)	48 (16.8)	
	50-59	50 (33.3)	128 (44.9)	
	60-69	33 (22)	63 (22.1)	
	> 70	14 (9.3)	19 (6.7)	
Region	Central	112 (74.66)	247 (86.66)	0.002
	North	31 (20.66)	26 (9.12)	
	South	7 (4.66)	12 (4.21)	

Table 2 Hepatitis C virus genotypes in eastern Algerian population

Genotype	*n* (%)	Subtype	*n* (%)
1	386 (88.7)	1a	6 (1.55)
		1a/1b	1 (0.26)
		1b	375 (97.2)
		Undefined subtypes	4 (1.0)
2	37 (8.5)	2a/2c	18 (48.6)
		2a	1 (2.7)
		2b	2 (5.4)
		Undefined subtypes	16 (43.2)
3	4 (0.9)	3a	4 (100)
4	5 (1.1)	4a	1 (20)
		4a/4c/4d	1 (20)
		Undefined subtypes	3 (60)
5	1 (0.2)	5a	1 (100)
Unclassified	2 (0.4)		2 (100)

Viral load

The viral load was assessed in all patients and the values were reported to the threshold of 600000 IU/mL: 276 patients (63.4%) had a viral load ≥ 600000 IU/mL and 159 (36.6%) had a viral load < 600000 UI/mL.

HCV genotypes

Five genotypes (1 to 5) and ten subtypes of HCV were identified in the studied population (Table 2). HCV genotype 1 was the most prevalent (88.7%), followed by genotypes 2 (8.5%), 4 (1.1%), 3 (0.9%) and 5 (0.2%). Genotype 6 was not detected in these patients. The most prevalent subtype was subtype 1b (86.2% out of the total). Twenty patients (4.6%) had mixed infection across the HCV subtypes: eighteen within subtype 2a/2c, one within subtype 1a/1b and one case with subtype 4a/4c/4d. There were no patients with mixed genotype infection. Genotypes 1 and 2 were found in the majority of wilayas (fourteen and ten respectively) (Figure 2). Genotypes 3 and 5 were found in the wilayas of Setif and Constantine respectively, and genotype 2 was found in the wilayas of Batna, Oum El Bouaghi and Setif.

Relationship between genotype and demographic profile

The genotype distribution is related to the age and region (Table 3). Genotype 1 was more frequent than the other genotypes in all age groups and regions. Genotype 1 was significantly less frequent in the ≥ 60 age group than in the younger age group (OR = 0.2; 95%CI: 0.1-0.5, *P* < 0.001) (Table 4). Furthermore, genotype 1 was more frequent in the central part than elsewhere (*P* < 0.01). We did not find a significant association between the HCV genotype and sex or viral load (Table 3).

Table 3 Hepatitis C virus genotypes according to age, sex, region and viral load *n* (%)

Risk factors	Genotype 1	Other genotypes	*P* value
Age (yr)			< 0.0001
< 60	284 (65.3)	22 (5.1)	
≥ 60	102 (23.4)	27 (6.2)	
Sex			0.8
Male	132 (30.3)	18 (4.1)	
Female	254 (58.4)	31 (7.1)	
Region			< 0.01
Central	327 (75.2)	32 (7.4)	
North	43 (9.9)	14 (3.2)	
South	16 (3.7)	3 (0.7)	
Viral load (IU/mL)			0.2
< 600000	144 (33.1)	15 (3.4)	
≥ 600000	241 (55.4)	33 (7.6)	

Table 4 Relationship between hepatitis C virus genotype and age

Age group (yr)	*n*	Genotype 1	Crude OR (95%CI)	Adjusted OR by region (95%CI)	Interaction Age × region
< 60	306	92.8%	0.30[b] (0.2-0.5)	0.20[b] (0.1-0.5)	No
≥ 60	129	79.1%			

[b] *P* < 0.001 *vs* genotype 1.

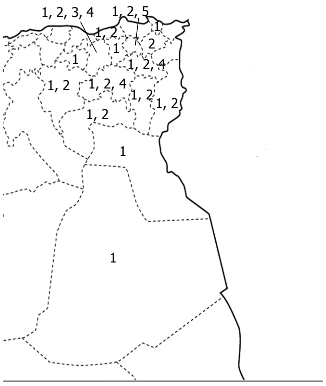

Figure 2 Hepatitis C virus genotype geographical pattern in eastern Algeria.

DISCUSSION

This is the first study to establish HCV genotype prevalence carried out on a large number of patients covering the north eastern geographical region of Algeria. Genotype 1b was a significantly predominant (86.2%) type. The result differs from what was reported in north western Algeria where the genotype 2a/2c was predominant (47%)[16]. In our study, genotype was not determined in two patients (unclassified genotype). This could be due to the very low HCV viral load in those two patients. Also, 23 patients have an undefined subtype which may be due to the technical limits of our genotype determination tool.

The HCV genotype distribution is similar to those found in some neighboring countries; HCV genotype 1b is a dominant genotype in the studies conducted in Tunisia (84%) and Morocco (70.1%)[13,17-19]. However, the HCV genotype prevalence in our study differs from what has been reported in other countries of North Africa. In Libya, genotypes 1 and 4 are predominant among the patients chronically infected with HCV, 35.7% and 32.6% respectively[20,21], and in Egypt, genotype 4 is quasi-exclusive (91%) and genotype 1 never exceeds 10%[22,23]. Compared to our data, other Mediterranean countries, in particular France and Italy, report a lower prevalence of genotype 1 (57% and 62% respectively)[6].

We examined the distribution of HCV genotypes and the gender associated genotypes in this study. The results clearly show that there is no variation among HCV genotypes and gender as the different HCV genotypes were distributed with the same ratio in males and females. In contrast to our observation, HCV genotypes were not distributed with the same pattern detected in Algeria in males and females in Libya. In Libya, the prevalence of HCV genotype 1 was found to be significantly associated with males, while genotype 4 has frequently been found in females[18].

The distribution of HCV genotypes may vary due to the age of the population. In the United States and western European countries, HCV non-genotype 1 is increasingly prevalent in younger patients and this is attributed to risk exposure differences[6]. In our study, genotype 1 is associated with the age group younger than 60 years and is lower in the older age group. To the contrary, the HCV non-genotype 1 was higher among the patients over 60 years. This can be explained by the changing patterns of transmission of the infection related to the change of the health system in the country after its independence 50 years ago. Indeed, during colonization, the majority of the population lived in rural areas without hospitals; traditional medicine was widely used. After independence, the use of modern medicine and hospitalization was more frequent. The identified HCV genotypes showed regional differences in our study and the central part was significantly the most infected region by genotype 1. Also, there was no correlation between genotype distribution and viral load. The threshold of 600000 IU/mL was chosen because this threshold predicts sustained virological response in treated patients with genotype 1 HCV infection[24,25].

Our work is the first that evaluates the distribution of genotypes of HCV in north eastern Algeria. However, it has some limitations related to the retrospective design of the study and a selection bias is possible given the use of the data from a single laboratory, but in our case it is somewhat mitigated because the laboratory is the only one in the region.

In conclusion, we found that HCV 1b is a predominant genotype in eastern Algeria. Further studies are needed in different regions of the country to estimate the different epidemiology of the HCV genotypes.

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COMMENTS

Background

The hepatitis C virus (HCV) has at least six genotypes. Genotype identification is clinically important to tailor the dosage and duration of treatment. The distribution of HCV genotypes varies greatly over the world. However, there is no information from Algeria on this issue.

Research frontiers

The distribution of HCV genotypes varies greatly over the world. However, HCV genotype distribution in Algeria has not been known so far. As Algeria is close to African and European countries, the distribution of genotypes may be influenced by this geographical location.

Innovations and breakthroughs

This is a retrospective study to identify the prevalence of different HCV genotypes in Algeria and assess the correlation between the HCV genotype and demographic profile. It is the first study of its kind performed in the north eastern region of Algeria.

Applications

Genotype identification is clinically important to tailor the dosage and duration of treatment. The determination of HCV genotype distribution in Algeria can predict antiviral treatment needs and explain the possible risk factors for HCV transmission.

Peer review

The authors present very important information regarding the still open issue of HCV genotype distribution in Algeria. It is well written.

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