**Name of journal: World Journal of Hepatology**

**ESPS Manuscript NO: 2415**

**Columns: BRIEF ARTICLE**

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

**Rouabhia S *et al****.*Hepatitis C genotypes in Algeria

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**Received:** February 20, 2013 **Revised:** April 30, 2013

**Accepted:** June 1, 2013

**Published online:**

**Abstract**

**AIM:** To find out the frequency of various Hepatitis C virus (HCV) genotypes present in the patients from the northeast area of Algeria.

**METHODS:** This is a retrospective cross-sectional study of 435 HCV infected patients from the northeast area of Algeria detected in the Sadelaoud laboratory, diagnosed between January 2010 and December 2012. The patients were diagnosed with the HCV infection in their local hospitals and referred to be assessed for a 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. The HCV genotype 1 was the most frequent (88.7%) followed by the genotypes 2 (8.5%), 4 (1.1%), 3 (0.9%) and 5 (0.2%). The genotype 6 was not detected in these patients. The mixed infection across the HCV subtypes was detected in twenty patients (4.6%). The genotype distribution was related to the age and the region. The 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, the genotype 1 was more frequent in the central part of the examined region than in the others (*P* < 0.01).

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

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**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. The HCV has at least six genotypes. The distribution of the HCV genotypes varies greatly over the world. The genotype identification is clinically important to tailor the dosage and duration of the treatment. The prevalence and the HCV genotypes in Algeria are not known. In this study, we have found that the HCV genotypes distribution in Algeria is different from the distribution detected in other northern countries of Africa.

Rouabhia S, Sadelaoud M, Chaabna-Mokrane K, Toumi W, Abenavoli L. Hepatitis C virus genotypes in north eastern Algeria: A retrospective study.

Available from: URL:

DOI:

**INTRODUCTION**

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

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

**MATERIALS AND METHODS**

We have 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 laboratory of molecular biology 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 assess a HCV genotype before the antiviral treatment. From the patient medical records, we retrieved demographic information (sex, age and address), genotype, subtype and viral load. The patients were evaluated live in fifteen wilayas (provinces), the administrative regions which cover the eastern area of Algeria. These wilayas were classified in 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).

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 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 the HCV-RNA quantification were determined in a single laboratory, the Sadelaoud laboratory in Batna. The data about the possible risk factors for the HCV transmission were not available in the database of the laboratory.

***Statistical analysis***

The Pearson’s 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 in two groups: < 60 years and ≥ 60 years, and the genotype in two groups: “genotype 1” and “others” respectively. To assess the genotype distribution according to the age and region, the binomial logistic regression was performed with *P*: probability to be infected by the genotype 1. The interaction of the covariate region on the association between the age and the 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 more than two thirds of the patients (70.6%, 307/435) were > 50 years old. There was a clear predominance of the females (F/M ratio = 1.9). The female predominance was significant in all age groups (*P =* 0.04) except for the youngest ones in which we observed the male predominance.

***Viral load***

The viral load was assessed in all the 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). The HCV genotype 1 was the most prevalent (88.7%) followed by the genotypes 2 (8.5%), 4 (1.1%), 3 (0.9%) and 5 (0.2%). The genotype 6 was not detected in these patients. The most prevalent subtype was the subtype 1b (86.2% out of the total). Twenty patients (4.6%) had the mixed infection across the HCV subtypes: eighteen within the subtype 2a/2c, one within the subtype 1a/1b and one case with the subtype 4a/4c/4d. There were no patients with the mixed genotype infection. The genotypes 1 and 2 were found in the majority of wilayas (fourteen and ten respectively) (Figure 2). The genotypes 3 and 5 were found in the wilayas of Setif and Constantine respectively, and the 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). The genotype 1 was more frequent than the other genotypes in all age groups and regions. The 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, the genotype 1 was more frequent in the central part than in the others (*P* < 0.01). We did not find a significant association between the HCV genotype and the sex or viral load (Table 3).

**DISCUSSION**

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

The HCV genotype distribution is similar to those found in some neighboring countries. The 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, the genotypes 1 and 4 are predominant among the patients chronically infected with HCV, 35.7% and 32.6% respectively[20,21] and the data reported from Egypt, where the genotype 4 is quasi-exclusive (91%), and the genotype 1 never exceeds 10%[22,23]. Compared to our data, other Mediterranean countries, in particular France and Italy, report a lower prevalence of the genotype 1 (57% and 62% respectively)[6].

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

The distribution of the HCV genotypes may vary due to the age of the population. In the United States and the Western European countries, the HCV genotype non 1 is increasingly prevalent in the younger patients and it is attributed to the risk exposure differences[6]. In our study, the genotype 1 associated with the age group patients less than 60 years decreased in the older age group. To the contrary, the HCV genotype non 1 was higher among the elderly patients over 60 years. This can be explained by changing the patterns of the transmission of the infection related to the change of the health system in the country after its independence 50 years ago. Indeed, during the colonization the majority of the population lived in rural areas without hospitals; the traditional medicine was widely used then. After the independence, the use of modern medicine and hospitalization was more frequent. The identified HCV genotypes showed the regional differences in our study, and the central part was significantly the most infected region by the 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 virologic response in the treated patients with the genotype 1 HCV infection[24,25].

Our work is the first one that evaluates the distribution of the genotypes of HCV in north-eastern Algeria. However, it presents 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 have found that the 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.

**ACKNOWLEDGEMENTS**

The authors are grateful to Professor Hashem B [El-Serag](http://www.ncbi.nlm.nih.gov/pubmed?term=El-Serag%20HB%5BAuthor%5D&cauthor=true&cauthor_uid=23231980) (Baylor College of Medicine, Houston, Texas, United States) for his critical review of the manuscript and for his precious advices and to Miriam J Alter (University of Texas Medical Branch, Galveston, Texas, United States) for her updates on the hepatitis C prevalence in the world and to Professor Natasa Milic (Faculty of Medicine, University of Novi Sad, Serbia) for English revision and technical support.

**COMMENTS**

***Background***

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

***Research frontiers***

The distribution of the HCV genotypes varies greatly over the world. However, the HCV genotypes distribution in Algeria has not been known so far. As Algeria is close to African and European countries, the distribution of the 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 to assess the correlation between the HCV genotypes and the demographic profile. It is the first study of its kind performed in north eastern region of Algeria.

***Applications***

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

***Peer review***

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

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**P-Reviewers** HussainZ, Tandoi F, Sira MM  **S-Editor** Wen LL  **L-Editor**  **E-Editor**





**Figure 1 Hepatitis C virus genotypes study coverage.**



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

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

|  |  |  |
| --- | --- | --- |
|  | **Sex** | ***P*-value** |
|  |  | **Male**  | **Female**  |
|  | **Total** | **150 (34.5)** | **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 | Centre | 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*(%)** |
|  |  | 1a | 6(1.55) |
| 1 | 386(88.7) | 1a/1b | 1(0.26) |
|  |  | 1b | 375(97.2) |
|  |  | undefined subtypes | 4(1.0) |
|   |   | 2a/2c | 18(48.6) |
| 2 | 37(8.5) | 2a | 1(2.7) |
|  |  | 2b | 2(5.4) |
|   |   | undefined subtypes | 16(43.2) |
| 3 | 4(0.9) | 3a | 4(100) |
|   |   | 4a | 1(20) |
| 4 | 5(1.1) | 4a/4c/4d | 1(20) |
|   |   | undefined subtypes | 3(60) |
| 5 | 1(0.2) | 5a | 1(100) |
| Unclassified | 2(0.4) |   | 2(100) |

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

|  |  |  |  |
| --- | --- | --- | --- |
| **Risk** | **Genotype 1** | **Others** | ***P*-value** |
| **factors** |  | **genotypes *n***  |
| 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 |
| Centre | 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 x Region** |
| <60 | 306 | 92.8 | 0.30b(0.2; 0.5) | 0.20b(0.1; 0.5) | No |
| ≥60 | 129 | 79.1 |

b*P <* 0.001 *vs* **%** genotype 1.