Original Article

Risk Factors and Genotypes of Hepatitis C Virus Infection in Libyan Patients

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ABSTRACT

Background: The prevalence and incidence of HCV infection varies geographically due to exposure to different risk factors. Identification of HCV genotype is important to defining the epidemiology of the disease. The objective of this study was to describe genotype distribution and its relation to risk factors among HCV infected patients attending virology clinic of the Department of Infectious Diseases at the Tripoli Medical Centre. **Methods**: The medical records of 891 Libyan chronic HCV infected patients registered and followed up from January 2003 to January 2007 were reviewed. Data gathered includes patient's age, gender, risk factors and family history of HCV infection. Statistical analysis was performed using *t*, x^2 and contingency coefficient tests. **Results**: The mean age was 40.22±13.09 years. Two thirds of patients were males. Normal alanine aminotransferase (ALT) at diagnosis was found in 62% of the patients. HCV RNA < 2 million copies at diagnosis was found among 54% of patients. HCV genotype 1 (G1) was the most frequent (30.9%), followed by G4 (29.2%). Genotype 2 affected 19.3% and G3 13.6%. No classification of HCV genotype was available for 2% of the patients. Many subtypes of HCV were detected with different frequencies (G1a and b, G2a, b, c and a/c, G3a and G4a and c/d). All genotypes of HCV were more common among males (P<0.001). Genotype 3 was the most frequent among male patients (88.6%). Regarding the risk factors, 33% of patients had a history of hospitalization and/or surgical procedures, and 22.7% had a history of blood transfusion. A past history of intravenous drug abuse (IVDA) was reported by 15% of the patients, and 15.9% reported a history of dental procedures. The relationship between the genotype of HCV and risk factors was statistically significant (P<0.001). No history of risky exposure was found among 10.8% of patients. **Conclusion:** Genotypes 1 and 4 were more predominant among HCV infected patients. Males were affected more than females and they presented themselves to the clinic at a younger age. The results of this study strongly suggest the need for implementing strict infection control measures in hospitals and dental clinics to reduce the nosocomial transmission of HCV, as well as measures to control the problem of intravenous drug users in the community.

INTRODUCTION

Hepatitis C Virus is the most frequent cause of chronic viral hepatitis in the world [1]. The prevalence and incidence of HCV infection varies geographically due to the evolution of risk factors [2]. Up to 80% of patients with acute viral hepatitis C develop chronic viral hepatitis [2]. In Libya, HCV infection has become a public health problem. A national sero-epidemiological survey showed that the prevalence of HCV antibodies in the general population was 1.2% [3].

HCV has marked genetic heterogeneity with nucleotide variability between different isolates [4,5]. Phylogenetic analysis indicates that there are at least 6 different genotypes of HCV and more than 90 subtypes [5,6]. HCV genotypes 1, 2 and 3 are distributed worldwide, whereas genotypes 4, 5 and 6 are found mainly in certain areas [6,7]. For example, genotype 4 is highly prevalent in Egypt and many central African countries [7-11]. Data on the genotype of HCV infections in Libya are scarce. One recent study from Benghazi showed that G4 was the most prevalent HCV genotype in the eastern part of the country [12].

Some studies showed that there is little difference in the severity of disease or in the outcome of patients infected with different genotypes [13]. However, the genotype of HCV does affect recommendations and counseling regarding interferon treatment [14-16]. Moreover, when using combination therapy, the recommended dose and duration of treatment depend on the genotype of the virus [17,18]. Some studies showed that patients with genotypes 2 and 3 are more likely to respond to interferon-based therapy [17,18]. On the other hand, genotyping of HCV infection is helpful in defining the epidemiology of the disease because it does not change during the course of infection [1,2].

Genotype distribution of HCV has not been described before in Tripoli. The objective of this study was to analyze the genotype distribution and its relation to risk factors among chronic HCV infected patients attending the virology clinic of the Department of Infectious Diseases at the Tripoli Medical Centre.

METHODS

This study was carried out at the Tripoli Medical Centre. The medical records of 1279 Libyan chronic HCV infected patients were reviewed. These patients had been registered and followed up at the virology clinic of the Department of Infectious Diseases, Tripoli Medical Centre, from January 2003 to January 2007. Genotyping was done only for 891 of these patients (69.7%).

Patient's age, gender and, in the initial screening, nationality were recorded. Non-Libyan patients were excluded from the study. Patients who had a history of hemodialysis were also excluded from the study. Data gathered included risk factors for HCV infection (history of blood transfusion with or without blood disease, intravenous drug abuse "IVDA", hospital admission with or without surgical intervention, dental intervention, unsafe sexual activity and/or promiscuity). Ethical approval from the Department of Infectious Diseases at the Tripoli Medical Centre was obtained.

Genotyping results of HCV were considered if they were performed by gene amplification by using the Cobas-Amplicor HCV test (Roche Diagnostics, Basel, Switzerland) [19].

Data were analyzed using SPSS version 11.5 to identify the demographic characteristics and risk factors associated with the different HCV genotypes.

The distribution of HCV genotypes, age, gender and risk factors of different groups were compared by using *t*, x^2 and contingency coefficient tests.

RESULTS

The patients' ages ranged from 16 to 76 years with a mean of 40.22±13.09 years. The mean age of the males was 38.89±12.70 years and of the females 42.88±13.45 years. The difference was statistically significant (P<0.001).

Alanine aminotransferase (ALT) at diagnosis was normal in 62% of patients. HCV RNA < 2 million copies at diagnosis (low viral load) was found among 54% of patients. A positive family history of HCV infection was found among 3.2% of patients.

Table 2 shows that genotype 1 was the most frequent genotype, occurring in 30.9% of the

Table 1: The demographic and clinical characteristics of Libyan HCV infected patients attending the virology clinic at the Tripoli Medical Centre.

Demographic and clinical characteristics		
1.	Mean age and SD in years	40.22±13.09
2.	Mean age and SD in years by gender	Males 38.89±12.70 Females 42.88±13.45 (P=0.000)
3.	Age range in years	(16-76)
4.	Normal ALT at diagnosis	62%
5.	HCV RNA < 2 million copies at diagnosis	54%
6.	Family history of HCV infection	3.2%

patients. Genotype 2 was found in 172 patients (19.3% of patients), while genotype 3 infected 166 (13.6% of patients), and genotype 4 was found in 260 (29.2% of patients). Genotypes 5 and 6 were not detected at all in those patients. No classification of HCV genotype was available for 2% of the patients.

Table 2: The distribution of HCV genotypes.

Genotype of HCV		No of patients	Percent
1.	Unclassified HCV	18	2
2.	Genotype 1	275	30.9
3.	Genotype 2	172	19.3
4.	Genotype 3	166	18.6
5.	Genotype 4	260	29.2

The four genotypes and several subtypes were observed with different frequencies (Table 3). One quarter of the patients had unclassified genotype 4. Subtypes G2b and G4c/d were uncommon. Some patients were infected by more than one subtype, e.g. 3% of patients had G2a/c and 0.9% had G4c/d.

Table (4) shows that two thirds of the patients were males. All HCV genotypes were more common among males and the difference from females was statistically significant (P<0.001). Genotype 3 was the most frequent among males (88.6%), followed by G1 (66.5%). Genotypes 2 and 3 were found among 59.9% and 56.9% of male patients, respectively. On the other hand, the most frequent HCV genotype among females was G4 (43.1%) and the least common was G3 (11.4%).

One third of the patients had a history of hospitalization and/or surgical procedures (Table 5). A history of blood transfusion was recorded among 22.7% of the patients. A history of dental procedures and IVDA was recorded amongst 15.9% and 15% of the patients, respectively. A minority of the patients (2.6%) had a history of sex with an HCV infected person and/or promiscuity. No history of any risky exposures was found among 10.8% of the patients. There was a significant relationship between the HCV genotype and risk factors for infection (P<0.001).

Table 3: The distribution of subtypes of different HCV genotypes.

Genotype/ subtype	No of patients	Percent
Unclassified HCV	18	2
G1a	72	8.1
G1b	107	12
G1 unclassified	96	10.8
G2a	22	2.5
G2b	7	0.8
G2c	18	2
G2a/c	27	3
G2 unclassified	98	11
G3a	19	2.1
G3 unclassified	147	16.4
G4a	25	2.8
G4c/d	8	0.9
G4 unclassified	227	25.5
Total	891	100

Genotypes 1 and 4 were detected more frequently among patients who had a history of blood transfusion, hospitalization, surgical procedures, sexual contact with an HCV infected person, or promiscuity. Genotype 2 was found in one third of those who had a history of dental procedures. Genotype 3 was detected among 60.4% of patients who had a history of IVDA. Genotypes G1 and G4 were predominant in patients who had a history of sex with an HCV infected person and/or promiscuity. Moreover, 35.7% of patients who had a history of hospitalization and/or surgical procedures were affected by G1 and 30.3% of them were affected by G4. Genotype 4 was detected in 39.6% of those who had no history of risky exposure.

Table 4: The distribution of HCV genotypes according to gender. For differences between males and females, X^2 = 50.367 and P<0.001.

Genotype of HCV	Males (%)	Females (%)	Total
Unclassified HCV	12 (66.7)	6 (33.3)	18
Genotype 1	183 (66.5)	92 (33.5)	275
Genotype 2	103 (59.9)	69 (40.1)	172
Genotype 3	147 (88.6)	19 (11.4)	166
Genotype 4	148 (56.9)	112 (43.1)	260
Total	593 (66.6)	298 (33.4)	891

Table 5: The distribution of HCV genotypes according to risk factors. For the relationship between the HCV genotype and risk factors for infection, the contingency coefficient = 0.465, P<0.001.

Risk factor	Un-classified n (%)	G1 n (%)	G2 n (%)	G3 n (%)	G4 n (%)	Total n (%)
Blood transfusion	14 (6.9)	65 (32.2)	39 (19.3)	18 (8.9)	66 (32.7)	202 (22.7)
Dental procedures	0 (0)	36 (25.4)	47 (33.1)	17 (11.9)	42 (29.6)	142 (15.9)
IVDA	0 (0)	35 (26.2)	0 (0)	81 (60.4)	18 (13.4)	134 (15)
Sexual contact with HCV infected person and/or promiscuity	0 (0)	7 (30.4)	3 (13.1)	6 (26.1)	7 (30.4)	23 (2.6)
Hospitalization and/or surgical procedures	3 (1)	105 (35.7)	63 (21.4)	34 (1.6)	89 (30.3)	294 (33)
Unknown	1 (1.1)	27 (28.1)	20 (20.8)	10 (10.4)	38 (39.6)	96 (10.8)
Total	18	275	172	166	260	891

DISCUSSION

This study shows that HCV genotypes 1 and 4 are the more frequent genotypes among Libyan patients attending the virology clinic of the Department of Infectious Diseases at the Tripoli Medical Centre. A previous study conducted in Libya had shown that HCV infection with genotype 1 was more prevalent in the western region. A study in Tunisia (which borders the west of Libya) showed that genotype 1b was the most prevalent type of HCV infection (79%) [20]. The former study [12] also showed that genotype 4 was the most prevalent genotype in the eastern region of the country (63.6%), which resembles results reported from Saudi Arabia, where G4 were the most prevalent HCV among Saudi patients (62%), as well as among Egyptian patients living in Saudi Arabia [21].

Our study shows that Libyan male patients presented at the medical centre at a younger age than females. Moreover, nearly two thirds of the patients were males, and all HCV genotypes were more frequent among males, especially G3. G3 could be more common among males because 60% of subjects with a history of IVDA had type G3, and most likely IVDA in Libya is much more common among males.

Four genotypes and several subtypes were recognized with different frequencies, but genotypes 5 and 6 were not detected at all. Infection by more than one subtype occurred in a minority of cases. Importantly, we observed that the laboratory failed to classify the HCV genotype and subtype in many patients.

We observed a statistically significant relationship between the HCV genotype and the risk factor for infection. A history of hospitalization and/or surgical procedures was reported by one third of the patients. Previous hospitalization is a known risk factor for HCV infection in some countries [22,23]. Nosocomial transmission is likely if disinfection procedures are inadequate and contaminated equipment is shared between patients [24,25]. Other common histories associated with the infection reported by the patients in our study were blood transfusion, dental procedures and IVDA. Only a few patients (2.6%) gave a history of sexual contact with an infected HCV person and/or promiscuity.

Notably, 22.7% of the patients reported a history of blood transfusion. Worldwide, blood transfusion constitutes the most commonly recognized transmission mechanism of HCV [26].

A past history of IVDA was reported by 15% of the patients, but IVDA carries an extremely high risk of HCV infection. Data from the Centres for Disease Control (CDC, Atlanta, USA) showed that from 1986 to 1988, IVDA was responsible for 42% of cases of acute hepatitis C [27]. Some studies showed that anti-HCV antibodies are present among 70 to 90% of IVDA [26].

The results of this study showed that a history of hospitalization and/or surgical procedures were more frequent among patients who had G1. A study from France had shown that genotype 1 is associated more commonly with blood transfusion [28]. Genotype 2 was not recorded among patients who had a history of IVDA, while genotype 3 was the most frequent one among those patients. A study from southeast France showed some similar results, where it was found that G3 was associated with IVDA [29]. Genotypes 2 and 4 were also common in patients who had a history of hospitalization and/or surgical procedures and blood transfusion. A positive family history of HCV infection was found only among a minority of patients. HCV RNA < 2 million copies at diagnosis (low viral load) was found in approximately half of the patients. Nearly two thirds of the patients presented to the clinic initially with normal ALT.

CONCLUSION

Genotypes 1 and 4 are predominant among patients chronically infected with HCV and attending the virology clinic at the Tripoli Medical Centre. Twice as many males as females were infected with HCV and they presented themselves to the clinic at an earlier age. The most common risk factors were a past history of hospitalization and/or surgical procedures, blood transfusion, dental procedures, and intravenous drug abuse (IVDA). The results of this study constitute a strong indicator that strict infection control measures should be implemented in hospitals and dental clinics to reduce the nosocomial transmission of HCV, and that ways to reduce the number of intravenous drug users in the community should be sought.

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