Distribution of hepatitis C virus genotypes in haemodialysis patients of Guilan, northern Islamic Republic of Iran

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ABSTRACT The incidence of hepatitis C virus (HCV) infection among patients undergoing haemodialysis is high. The aim of this study was to identify the HCV genotypes among chronic haemodialysis patients who were HCV positive in Guilan province, northern Islamic Republic of Iran. All patients on haemodialysis at Guilan haemodialysis centres were enrolled. Enzyme-linked immunosorbent assay and polymerase chain reaction testing were performed. Out of 514 enrolled patients, 11.9% were serologically HCV positive and 6.2% had positive HCV-RNA. HCV genotypes were determined with HCV genotype-specific primers. The most frequent genotypes were 1a (59.4%) and 3a (40.6%). There was no significant relationship between virus genotypes and sex or age. The HCV genotype pattern among haemodialysis patients in Guilan province was different from other countries of the Middle East and was more similar to North American and European countries where genotype 1 is predominant.

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Répartition des génotypes du virus de l’hépatite C chez des patients hémodiésé à Guilan (Nord de la République islamique d’Iran)

RÉSUMÉ L’incidence de l’infection par le virus de l’hépatite C chez les patients hémodialysés est élevée. La présente étude visait à identifier les génotypes du virus de l’hépatite C chez des patients hémodialysés infectés dans la province de Guilan (Nord de la République islamique d’Iran). Tous les patients hémodialysés dans les centres spécialisés de Guilan ont été recrutés. Un test immuno-enzymatique et une amplification en chaine par polymérase ont été réalisés. Sur 514 patients recrutés, 11,9 % étaient sérologiquement positifs au virus de l’hépatite C et 6,2 % étaient positifs à l’ARN-VHC. Les génotypes du virus de l’hépatite C ont été déterminés avec des amorces spécifiques de génotypes du virus. Les génotypes 1a (59,4 %) et 3a (40,6 %) étaient les plus fréquents. Aucune relation significative n’a été retrouvée entre les génotypes du virus et le sexe ou l’âge des patients. La répartition des génotypes du virus de l’hépatite C chez les patients hémodialysés dans la province de Guilan était différente de celle des autres pays du Moyen-Orient. Elle ressemblait davantage à la répartition observée en Amérique du Nord et dans les pays européens où le génotype 1 prédomine.

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Introduction

The incidence of hepatitis C virus (HCV) infection among patients undergoing haemodialysis is high. Patients with renal disease are at increased risk of acquiring HCV because of prolonged vascular access and the potential of exposure to infected patients and contaminated equipment. Hepatitis C is the most prevalent liver disease among haemodialysis patients. Meanwhile, liver disease itself is a significant cause of morbidity and mortality in patients with end-stage renal disease (ESRD) treated by dialysis or transplantation [1–3].

HCV is classified into 6 major genetic groups (designated genotypes 1 to 6), each comprising multiple subtypes (designated a, b, c, etc.). These genotypes have different geographical distributions. Genotype has been shown to be a predictor of the response to antiviral treatment. Furthermore, the genotyping of HCV is a useful tool in molecular studies carried out to establish the source of nosocomial infection outbreaks in haemodialysis centres [4,5].

HCV genotype prevalence varies in different parts of the world and is a considerable epidemiologic concern [6]. Although the relationship between virus genotype and disease severity is controversial, there is some evidence to suggest that patients with HCV subtype 1b have a poorer response to treatment with interferon alpha [6,7].

Previous studies from Islamic Republic of Iran have shown that genotypes 1a and 3a are the most common genotypes in our country [6,8–10]. This is different from the dominant genotypes of other countries in the Eastern Mediterranean region [6,11,12]. The aim of this study was to reveal the distribution of different HCV genotypes among haemodialysis patients in Guilan province which is located in the north of the Islamic Republic of Iran.

Methods

This cross-sectional survey was carried out at 11 haemodialysis units in Guilan from January to May 2008. A total of 514 patients with ESRD were under treatment of haemodialysis in Guilan within this period. They were asked to partake in this study and informed consent was obtained from all participants. The diagnosis of HCV was made on the basis of the presence of anti-HCV antibodies in sera detected by 3rd generation enzyme-linked immunosorbent assay (ELISA) kits (Diagnostic BiProbes srl), and positive HCV-RNA tested by polymerase chain reaction (PCR) amplification of 5’-UTR with nested primers (Artus Qiagen GmbH). Positive ELISA samples were frozen at –70 °C for PCR evaluation. HCV genotypes were determined with HCV genotype specific primers using HCV genotype kit (Biodiversity srl).

Statistical evaluations were performed using SPSS, version 14. Prevalences and 95% confidence intervals (CI) were calculated. The chi-squared test was used to analyse data and P value < 0.05 was considered statistically significant.

Results

The serological data collected showed that 61/514 (11.9%) patients had positive anti-HCV by ELISA. The prevalence of anti-HCV ranged from 0% to 25% in different areas of the province (data not shown). The test was confirmed by PCR in 32/514 (6.2%) patients.

Of the HCV-RNA positive patients 24 (75.0%) were male and 8 (25.0%) were female and the most prevalent detected genotypes were genotypes 1a (59.4%, 95% CI: 42.4%–76.4%) and 3a (40.6%, 95% CI: 23.6%–57.7%). Among 24 males with HCV-RNA+ (positive PCR) 15 (62.5%) were genotype 1a and 9 (37.5%) were genotype 3a. Among females 50.0% were genotype 3a and 50.0% were 1a. There was no significant relationship between sex and HCV genotype (P > 0.05).

One interesting result was the high rate of genotype 3a to 1a (64.7% versus 35.3% respectively) among haemodialysis patients of Rasht, the capital city of the province, compared with other haemodialysis centres of Guilan (13.3% versus 86.7% respectively) (P = 0.005) (Table 1).

Patients were divided into 3 age groups (Table 1) but no significant relationship between HCV genotype and age group was detected (P > 0.05). The mean (SD) age of patients with genotype 1a was 49.3 (SD 15.6) years and with genotype 3a was 54.1 (SD 12.4) years (P = 0.37).

Discussion

This is the first study to investigate the seroprevalence and genotypes of HCV in haemodialysis patients in Guilan, Islamic Republic of Iran. The prevalence of anti-HCV positive ELISA test in our study was 11.9%, which is lower than the mean prevalence of anti-HCV among a haemodialysis population in Tehran (21.0%, range 2.9%–55.9%) [9]. In another study in a neighbouring province (Mazandaran), Taziki et al. reported a similar prevalence of 12% in 2006 [13]. In Saudi Arabia, Pakistan and Turkey the prevalences of HCV among haemodialysis patients were 84.6%, 68.0% and 19.1% respectively [14,15].

The predominant genotypes among our studied patients were 1a (59.4%) and 3a (40.6%). This is in accordance with Zali et al.’s study, the first study on prevalence of HCV genotyping from Iranian population, conducted on Tehran haemodialysis patients [8]. Later, Samimi-Rad et al., in a survey on Iranian anti-HCV positive patients from Tehran and 5 other cities of the country, showed that genotype 1a was predominant (47%) and genotypes 3a,
1b and 4 were detected in 36%, 8% and 7% of the patients respectively [10]. In another study at 45 haemodialysis centres of Tehran, Hosseini-Moghaddam et al. revealed that 3a (30.3%) and 1a (28.8%) were the most prevalent genotypes, and 1b, 3b and 4 accounted for 18.2%, 3.0%, and 16.7% respectively [9]. More recently, Somi et al. in East Azerbaijan reported 74.6%, 5.5% and 5.5% for genotypes 1a, 3a and 1b respectively [6]. Keyvani et al. also reported the same predominant genotypes in HCV-positive cases acquired from different sources [16]. Although genotype 4 is mainly reported from the Middle East and central Africa [17], only 2 studies in Islamic Republic of Iran reported genotype 4 among the top 4 common genotypes [9,10].

Similar to the previous studies on the genotype distribution in the Islamic Republic of Iran, none of our patients was infected by genotype 2. This finding is in contrast with the global HCV genotype distribution [9]. Generally, genotypes 1a and 3a are the most common genotypes in Islamic Republic of Iran and the current study confirmed this.

A noticeable point was the high prevalence of genotype 3a compared with 1a (almost twice as many) in Rasht haemodialysis centres. This is the reverse of other haemodialysis centres of the province, where genotype 1a was the most prevalent genotype. These differences in the predominant HCV genotype between the capital city and other cities in the province may reflect different sources of infection. This illustrates the value of genotyping in investigating HCV infection routes. More studies are needed to determine the sources of infection and where to focus infection control measures.
In comparison with other countries the pattern of our genotypes was different from other Middle East countries, where genotype 4 has been found to be the most prevalent subtype [4,18,19]. In fact the pattern was more similar to those reported from Brazil, France [20–22], England, Australia and Scotland [10]. In western neighbours of the Islamic Republic of Iran, such as Turkey, genotype 1b is prevalent. However, in eastern border countries such as Pakistan and India, genotype 3a (which is endemic in South-East Asia) is prevalent [8]. In North America and Northern Europe 1a is the most common subtype followed by 2b and 3a [18]. Worldwide the distribution of HCV genotypes and subtypes are shown in Table 2.

In our study, like the studies of Somi et al. [6] and Kabir et al. [22] there was no significant difference in genotype distribution in terms of age group and sex. This is different from reports in some countries such as Turkey and Korea, where genotype 1b was the prevalent genotype among older patients [23,24] and genotype 2 was the common HCV genotype among younger patients [25]. Only one study in the Islamic Republic of Iran has reported the relationship between age and HCV genotypes and showed that study 1b was the common genotype among older patients [16]. Generally, whenever the genotype of HCV is related to age, it is common to find genotype 1b in older patients.

## References

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### Conclusion

The HCV genotype pattern among haemodialysis patients in Guilan province was different from other countries of the Middle East and was more similar to North American and European countries where genotype 1 is predominant.

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