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HCV genotypes among 1013 Saudi nationals: a multicenter study

Ibrahim Al Traif,[a] Mohammed A. Al Balwi,[b] Ibrahim Abdulkarim,[c] Fayaz A. Handoo,[a] Hamdan Saleh Alqhamdi,[a] Melfi Alotaibi,[d] Abdulrahman Aljumah,[a] Hamad Ibrahim Al Ashqar,[e] Khalid Bzeizi,[f] Mohammed Al Quaiz,[e] Abduljaleel Alalwan,[a] Waleed Al Hamoudi,[g] Khalid Alswat,[g] Faisal Sanai,[h] Ayman Abdo[g]

From the [a]King Saud bin Abdulaziz University for Health and Sciences; [b]Pathology and Laboratory Medicine, Molecular Pathology and Genetics, King Abdulaziz Medical City; [c]Medical, Biotechnology, King Abdulaziz Medical City; [d]Medicine Department, Riyadh Military Hospital; [e]Department of Medicine, King Faisal Specialist Hospital and Research Centre; [f]Gastroenterology and Hepatology Department, Riyadh Military Hospital;[g]Gastroentorogy and Hepatology, King Saud University College of Medicine; [h]Hepatobiliary Sciences and Liver Transplant, King Abdelaziz Medical City

Correspondence: Dr. Ibrahim Altraif · Hepatobiliary Sciences, National Guard Hospital Health Affairs, King Abdulaziz Medical City – National Guard Hospital Health Affairs, P.O. Box 22490 Riyadh 11426, Saudi Arabia · T: +966-1-801111, F: +966-1-8011111 · ibrahimtraif@yahoo.com

BACKGROUND AND OBJECTIVES: Hepatitis C virus (HCV) genotype (G) knowledge is essential for determining type, duration and rate of response to antiviral therapy, possible route of HCV transmission, and future vaccine development. Our aim was to study HCV genotypes and to provide precise data on genotype distribution in both genders and different age groups amongst Saudi patients.

DESIGN AND SETTING: Genotype data from molecular laboratories at four different tertiary care hospitals in Riyadh from January 2006 until December 2010 were collected and analyzed.

PATIENTS AND METHODS: Consecutive data on genotype, sex and age was collected from 1013 Saudi patients. Genotyping was done by selective hybridization of amplicons to HCV genotype-specific oligonucleotides.

RESULTS: We found G1 in 262 patients (25.9%), G2 in 44 (4.4 %), G3 in 29 (2.9 %), G4 in 608 (60%), and 3 patients (0.3%) each of G5 and G6. In addition, 64 (6.3%) patients had mixed genotypes, mostly G4 and G1. On subtyping in 191 G1 patients, 67 (35.1%) were G1a, and 124 (64.9 %) G1b. Age distribution showed that 18 (1.7%) were 0-20 years, 173 (17.1 %) 21-40 years, 521 (51.4%) 41-60 years and 301(29.7%) >60 years. There was no significant difference in frequency of G1, G3 and G4 among the two genders.

CONCLUSION: G1 and G4 are the predominant genotypes in Saudi patients infected with HCV (85.9%), with a similar distribution among the two sexes and no significant changes in genotype distribution over the past decade.

Hepatitis C virus (HCV) is classified into different genotypes based on nucleoside sequence variability according to Simmonds classification with six major genotypes and over 30 subtypes identified.[1] The knowledge of HCV genotype is important for determining the type, duration and rate of response to antiviral therapy, prognosis, possible route of transmission, and for HCV vaccine development in the future.[2,3]

Data on prevalence of HCV genotypes (G) in Saudi Arabia is limited and mostly based on small numbers of patients.[4-6] The aim of the present study was to analyze all consecutive HCV genotype data available from 2006 to 2010 from four tertiary care liver centers of Saudi Arabia, and to provide accurate data on HCV genotype distribution in different age groups and both sexes.

PATIENTS AND METHODS

Genotype data collected from molecular laboratories at four different tertiary care hospitals in Riyadh (King Abdulaziz Medical City, King Faisal Specialist Hospital and Research Centre, Riyadh Military Hospital and Liver Disease Research Center, King Saud University) from January 2006 until December 2010 were collected and analyzed. The study was approved by the institutional review boards of all participating centers.

Patients with positive HCV-RNA were routinely genotyped prior to antiviral therapy/ liver transplan-

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Table 1. Genotype and age distribution.

Genotype	0-20 years		21-40 years		41-60 years		>60 years		Total
	n	%	n	%	n	%	n	%	
G1	7	2.7	54	20.5	125	47.7	76	28.9	262
G2	3	6.8	2	4.5	23	52.3	16	36.4	44
G3	1	3.4	6	20.7	17	58.6	5	17.2	29
G4	7	1.2	104	17.1	319	52.5	178	29.3	608
G5	0	0.0	0	0.0	1	33.3	2	66.7	3
G6	0	0.0	0	0.0	3	100	0	0.0	3
Mixed	0	0.0	7	10.9	33	51.5	24	37.5	64

Table 2. Sex distribution and HCV subtype in 191 genotype 1 Saudi patients.

Genotype	Sex	No. of patients (%)
1a	Male	42 (62.7)
	Female	25 (37.3)
1b	Male	59 (47.6)
	Female	65 (52.4)

Table 3. Genotype and gender distribution among 1013 Saudi patients.

HCV genotype	Sex		P
	Male	Female	
G1	145 (55.3%)	117 (44.7%)	.289
G2	21 (47.4%)	23 (52.6%)	.60
G3	20 (68.9%)	9 (31.1%)	.0002
G4	273 (44.9%)	335 (55.1%)	.307
G5	2 (66.7%)	1 (33.3%)	ND
G6	2 (66.7%)	1 (33.3%)	ND
Mixed	46 (71.9%)	18 (28.1%)	.0002

tation consideration. Viral RNA was extracted from patient plasma samples using an Abbott m2000sp (Abbott Molecular, Weisbaden, Germany). The resultant RNA reverse to cDNA was then amplified and detected using genotype specific fluorescent-labeled oligonucleotides probes. The assay was performed on Abbott m2000rt using the Abbott Real Time, INNO-LiPa HCV II, (Innogenetics, Ghent, Belgium). The assay was limited to HCV genotypes 1a, 1b, 2, 3, 4, 5, and 6. Demographic data on age and gender were collected to determine the exact prevalence of the different geno-

types among different age groups and both genders.

All variables were summarized and reported across the study cohorts using descriptive statistics. Categorical variables such as gender and genotype were summarized and are reported in terms of frequency distribution, whereas continuous variable (such as age) are reported in terms of mean and standard deviation. Genotype finding was measured nominally and compared between different genders using the chi square test. Results were declared significant at an α level <.05. Genotype was measured as a binomial variable (1= unmixed, 2=mixed) and compared across different age groups using the chi square test.

RESULTS

The sample under study consisted of 1013 patients, with mean (SD) age of 52.3 (13.3) and males accounting for 50.2%. HCV genotype distribution showed G1 in 262 patients (25.9%), G2 in 44 (4.4 %), G3 in 29 (2.9 %), G4 in 608 (60%), and 3 patients (0.3%) each of G5 and G6. In addition, 64 patients (6.3%) were of mixed genotyping, 75% of them were G1 and G4. Triple genotype was observed in two patients (3.1%). Age distribution showed that 18 (1.7%) were 0-20 years, 173 (17.1 %) 21-40 years, 521 (51.4%) 41-60 years and 301 (29.7%) >60 years (**Table 1**). Among the 191 G1 patients who had subtyping, 67 (35.1%) were G1a and 124 (64.9 %) were G1b, while the remaining 71 cases of G1 patients were not subtyped (**Table 2**).

Overall, there was no significant difference in genotype distribution in between the two sexes (P=.58). The frequency of the most common genotypes (G4 and G1) was not statistically significantly different in relation to gender, but there was a gender difference among G3 and mixed genotype, both being more common among males 68.9% vs. 31.1% for G3 and 71.9% vs. 28.1% for mixed (P=.0002, **Table 3**).

DISCUSSION

Our study is the largest multicentre genotyping data reported to date from Saudi Arabia. The G4 HCV infection remains the most prevalent in this country with a prevalence rate of 60% followed by G1 in 25.9%. This data indicates that there has not been a change in genotype distribution in the last ten years when compared with what was reported previously by Altraif, Shobokshi, and Fakeeh et al.[4-6] Shobokshi and Fakeeh et al[5,6] about a decade ago reported that there was no significant difference in HCV genotype epidemiology over the last decade in Saudi Arabia. However, the exposure to the disease seems to be limited to the young age group of 0-20 years, indicating that fewer individuals are being exposed to HCV infection nowadays since blood is routinely screened for HCV by all blood banks in Saudi Arabia.

There was no sex difference in genotype distribution among Saudi patients except for G3 and mixed genotype infection which was more frequent among males (P=.0002). There are reports that females tend to clear virus faster after infection than males and that may explain the difference among other unknown contributing factors.[7]

About 81% of our HCV patients were 41 years of age or older, indicating that HCV viremic disease is highest in this age group, which is consistent with other reports from the country.[4,5] The younger generation has a much lower exposure to HCV than the older generation mainly due to the introduction of mandatory blood donor screening over the last two decades. This decline parallels the improved health care standards in Saudi hospitals.

Mixed HCV genotype infection was seen in 6.3% of cases, occasionally with three different genotypes isolated from the same patient indicating possible multiple HCV exposure. Most (89%) of these patients were above 40 years of age. This could be the result of repeated HCV exposure due to multiple risk factors as they get older, which may be the result of repeated blood and blood products transfusion in the past and/or repeated iatrogenic nosocomial exposure or other risk factors.

Since our present study comes from four large national liver referral centers with three centers having liver transplantation facilities, we believe that this data is most representative of the current HCV genotype distribution in Saudi Arabia. On the other hand, the limitation of this study was the lack of clinical data on epidemiological risk factors accounting for HCV infections in our cohort.

In summary, the present study is the largest genotype data analysis reported from Saudi Arabia confirms that G4 and G1 are the predominant genotypes in Saudi patients infected with HCV and no significant change has occurred over the past decade in genotype distribution. However, the exposure to HCV infection seems to be limited in younger age group (<20 years), indicating that fewer young individuals are being exposed to HCV infection nowadays.

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