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Short Communication

Genotyping of Hepatitis C virus (HCV) in infected patients from Saudi Arabia

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A molecular study was carried to investigate the prevalence of Hepatitis C virus (HCV) genotypes in HCV infected population of Saudi Arabia. A total of HCV-positive clinical specimens (serum, EDTA plasma) with viral loads above 2,000 IU/ml were collected for genotyping. Genotyping of 358 samples revealed four different genotypes including 1 (1a and 1b), 2a, 3 (3a) and 4. The most prevalent genotype was 4 with rate of 74.2% followed by genotype 3 (11.7%) and 1a (3.9%). The predominance of HCV genotype 4 in our population confirms the predominance of HCV genotype 4 in Saudi Arabia and most of the Arab countries in the Middle East.

Key words: Hepatitis C virus (HCV), genotypes, Saudi Arabia, Riyadh.

INTRODUCTION

Hepatitis C virus (HCV) infection is a global public health problem. World Health Organization (WHO) estimates up to 3% of the world's population to be infected with HCV and there are approximately 180 million individuals are thought to be infected. On average, 80% of acutely infected individuals develop a chronic infection (Lavanchy, 2009; Ghany, 2009). HCV has a positive-sense single-stranded RNA genome of flavivirus and about 9.6 kb containing one long open reading frame (ORF) with untranslated regions at both ends (Choo et al., 1989). So far, six major genotypes (HCV-1 to HCV-6) have been described, each containing multiple subtypes (for example, 1a, 1b, etc.) (Tokita et al., 1995). The genotype of the HCV strain appears to be an important determinant of the severity and aggressiveness of liver infection, as well as patient response to antiviral therapy (Zein, 2000). HCV genotypes display significant differences in their global distribution and prevalence, making genotyping a useful method for determining the source of HCV transmission in an infected localized population (Hnatyszyn, 2005).

HCV genotype 1, 2 and 3 are distributed worldwide and their relative prevalence varies from one geographic area to another, whereas genotype 4 is predominantly prevalent in the Middle East and Africa, genotype 5 in South Africa and genotype 6 in Southeast Asia (Zein, 2000; Gish and Lua, 1997). According to the recent studies, genotype 4 is predominant in Egypt, 4 and 1 in Kuwait and Syria, and genotype 1 in Lebanon, Iraq and Iran (Osaba, 2002; Pacsa et al., 2001; Zali et al., 2000) . Saudi Arabia shows an intermediate endemicity for HCV. Seroprevalence rates ranging from 0.9 to 5% have been reported among children and adults, respectively (Shobokshi et al., 1999). Some studies have indicated the predominance of genotype 4 in this region (Mellor et al., 1995; Al-Faleh et al., 1995). Hence HCV subtype distribution is needed to provide clues for studying epidemiology, the mode of transmission, and response to treatment. The objective of this study was to determine the distribution of HCV genotypes among the patients attending different hospitals and polyclinics in Riyadh, Saudi Arabia.

MATERIALS AND METHODS

This was a descriptive study conducted from January 2008 to December 2010 from different hospitals as well as polyclinics at Advanced Cell laboratory, Riyadh, Saudi Arabia. The latter is a reference laboratory serving a number of hospitals and polyclinics in Riyadh. Patients positive for anti-HCV antibodies were referred

Abbreviations: HCV, Hepatitis c virus; **WHO,** world health organization; **ORF,** open reading frame; **RNA**, ribonucleic acid; **PCR**, polymerase chain reaction; **EDTA,** ethylenediaminetetraacetic acid; **HCC,** hepatocellular carcinoma.

Table 1. Genotype distribution of 358 HCV positive patients.

Nationality	Total	HCV genotype						
		1	1a	1b	2a	3	3a	4
Saudi	208	-	6	7	5	8	-	182
Egyption	98	13	-	-	-	8	-	79
Pakistan	33	-	-	-	-	26	7	-
Others	17	-	8	5	-	-	-	4
Total (%)	358 (100)	13 (3.6)	14 (3.9)	12 (3.3)	5 (1.4)	42 (11.7)	7 (1.9)	265 (74.2)

Table 2. HCV Genotype among male and female.

Gender	HCV genotype							Total (%)
	1	1a	1b	2a	3	3a	4	
Male	13	3	2	1	36	7	178	240 (67)
Female	0	11	10	4	6	0	87	118 (33)

to the reference laboratory for detection of HCV RNA level and for genotyping. The study was designed to include patient's demographics (age, sex and nationality) as well. Detection of HCV ribonucleic acid (RNA) was carried out on a 500 ul sample of each serum sample positive for anti-HCV antibodies, using a commercial polymerase chain reaction (PCR) -based test (Taqman amplicor, Roche, USA) and following manufacturer's instructions. Internal control supplied by the manufacturer was added to each specimen, as an extraction and amplification control. HCV positive clinical specimens (serum, ethylenediaminetetraacetic acid) (EDTA) plasma with viral loads >2,000 IU/ml were selected for genotyping using Versant HCV genotype assay (LiPA) 2.0 (Innogenetics, Siemens Healthcare Diagnostics, USA). This kit allows an improved and more accurate distinction between HCV genotype 1 and subtypes c to l of genotype 6 as well as between subtypes a and b of genotype 1. Data was analyzed using SPSS-14 version. A p Value of < 0.5 was considered significant for statistical analysis.

RESULTS

Genotype distribution in 358 HCV-positive patients is shown in Table 1. Overall, HCV genotype 4 was the most predominant genotype (74.2%) followed by genotype 3 (11.7%) and 1a (3.9%). Differences in genotype distribution were statistically significant ($p < 0.5$). HCV genotype distribution among HCV-positive Saudi patients is similar to that in Egyptian population in which genotype 4 predominates. However, genotypes 3 and 3a was the most common genotypes among Pakistani patients (Table1). Distribution of genotype 4 was similar among males (74.2%) and females (73.7%). However distribution of types 1a and 1b was higher among females while type 3 was more commonly seen among males ($p < 0.5$) (Table 2).

DISCUSSION

Understanding of the geographic distribution of common genotypes requires detailed knowledge about the routes of transmission, prevalence of HCV in general population and in the various high risk groups, and also phylogenic evolution of types and subtypes over a long period (Zali et al., 2000). Unfortunately, there is little information available on these topics, particularly from Middle East countries and more specifically from Saudi Arabia. Studies suggest that infections caused by different HCV subtypes may have different clinical outcome and that some subtypes are associated more frequently with advanced liver disease and hepatocellular carcinoma (HCC) (McHutchison et al., 1998). This is the first published study to report on the genotyping of HCV in different nationalities groups of HCV-positive patients in Saudi Arabia, representing close to a population-based sample.

The results show that HCV genotype 4 is the predominant genotype (74.2%) among Saudi patients followed by 3 (11.7%) and 1a (3.9%) . HCV genotype 4 is the predominant genotype among males and females. There is lack of comprehensive data on the distribution of HCV genotypes in Middle East countries, particularly in the Saudi Arabia; however there are few studies which have reported high prevalence of genotype 4 in these countries (Osaba, 2002; Bdour, 2002) . Genotype 4 is also predomi-nant in Egyptian patients as reported by Ray et al. (2000) as a most common genotype in Egypt.

The infection with genotypes 1a and 4 may be considered a risk factor for the induction of neu-oncoprotein over expression and subsequent development of hepatocellular carcinoma (Zekri et al., 2000). The predominance of HCV genotypes 3 in the Pakistani patients are in agreement with other report by Mujeeb on genotyping of HCV isolates in Pakistan (Mujeeb, 2002) . It is of interest to note that in contrast to Arab countries genotype 4 can hardly be detected in non-Arab Middle Eastern countries such as Pakistan (Idrees and Riazuddin, 2008). The presence of other genotypes such as 2a, and 1b among

Saudi Arabian patients can be attributed to many factors. These include the expatriates from different nationalities resided in Saudi Arabia for quite some time and participated in blood donation.

According to the World Health Organization, 180 million individuals in the world are infected with HCV and this is a growing global problem. The development of an effective vaccine remains the ideal way to combat HCV infection. In addition to the implications for clinical outcome of infection, and for treatment, genotyping of HCV also has major implications for HCV vaccine development. Recent data suggest that for a vaccine to be fully protective it should contain a range of deferent envelope proteins corresponding to the common genotypes in particular geographic regions. Vaccines for use in the Middle East should, therefore, not be based only on genotype 4 sequences; other genotypes such as 1a and 1b are also equally important. Finally, genotyping of HCV may be a useful epidemiological marker particularly in establishing suspected unconventional routes of HCV transmission such as vertical, intraspousal or interfamilial transmission (Alfaresi, 2011).

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