

RESEARCH NOTE

Hepatitis C Virus Genotypes among Blood Donors from Different Regions of Brazil

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Hepatitis C virus (HCV) is considered to be the major agent of viral hepatitis, resulting in chronic liver disease, cirrhosis, and hepatocellular carcinoma. Eleven HCV types, including at least 80 subtypes, have already been described and shown to have different geographical distribution (H Okamoto et al. 1997 *Viral Hep Rev* 3: 51-62). Several reports have suggested that HCV genotypes have distinct clinical outcomes with regard to disease severity and response to alfa-interferon (E Silini et al. 1995 *Hepatology* 21: 285-290, M Kobayashi et al. 1996 *Hepatology* 23: 695-699, NN Zein et al. 1996 *Ann Intern Med* 125: 634-639, U Hopf et al. 1996 *J Hepatol* 24: 67-73, P Simmonds et al. 1996 *J Hepatol* 24: 517-524). Differences in serological reactivity between HCV genotypes have also been reported (SK Dhaliwal et al. 1996 *J Med Virol* 48: 184-190, NN Zein et al. 1997 *J Clin Microbiol* 35: 311-312). In addition, vaccines against multiples HCV genotypes will be necessary and, therefore, mapping the distribution of viral genotypes is warranted. However, little is known about the genotypic analysis of HCV in Latin America. In Brazil, previous studies were carried out in Rio de Janeiro, São Paulo (southeastern region), and Porto Alegre (south region) (L Stuyver et al. 1993 *J Gen Virol* 74: 1093-1102,

L Bassit et al. 1994 *Transfusion* 34: S151, LP Krug et al. 1996 *Braz J Med Biol Res* 29: 1629-1632). Given the large size of the country, its mixture of cultures and races, the diversity in climatological regions and social conditions, and the limited amount of data concerning HCV genotypes in other Brazilian regions, we decided to investigate the distribution of HCV types and subtypes in blood donors from three different geographical regions of Brazil.

A total of 7,500 plasma samples from volunteer blood donors were tested for anti-HCV by ELISA (Innotest HCV Ab II, Innogenetics). These samples were obtained in state blood banks located in northeast (Rio Grande do Norte), southeast (Rio de Janeiro), and mid-west (Goiás) regions. This population ranged in age from 18 to 60 years. The large majority of the blood donors (95%) were men. Samples anti-HCV positive by ELISA were re-tested by line immunoassay (INNO-LIA HCV Ab II, Innogenetics). One hundred and thirteen positive samples were submitted to RNA extraction, reverse transcription, and nested PCR with primers complementary to the conserved areas of the 5' non-coding region. Seventy PCR-positive samples were genotyped by the line probe assay (INNO-LIPA HCV I, Innogenetics), which is based on the reverse hybridization of the amplified products with type-specific probes against HCV genotypes 1, 2, 3, 4 and their subtypes (Stuyver et al. *loc. cit.*).

Table shows the distribution of HCV genotypes. In the northeast area, subtypes 1b (35.3%) and 3a (35.3%) were the most frequent. In the mid-west, subtypes 1a (54.6%) and 3a (31.8%) had high prevalences, and in the southeast region, subtypes 1b (41.9%) and 1a (35.5%) were the most common. In all three regions, HCV genotype 1 was the most prevalent (70% of the total). Subtypes 1a (34.3%), 1b (30.0%), and 3a (25.7%) were frequently found in these Brazilian blood donors, while 2b was rare, and 2a was not detected. In four samples (5.7%) only the genotype was defined (type 1), and 1 (1.4%) mixed infection was found.

Studies on the genotype distribution in HCV positive samples have been conducted in several European countries, the US, and Japan, where genotype 1 accounted for the majority of these infections (Simmonds et al. *loc. cit.*, Zein et al. *loc. cit.*, JYN Lau et al. 1996 *Ann Intern Med* 124: 868-876, H Okamoto et al. 1996 *J Virol Methods* 57: 31-45). In our study, the proportions of blood donors with HCV types 1, 2, and 3 were 70.0%, 2.9%, and 25.7%, respectively. These data are similar to those previously found in the southeast and south regions of Brazil (Stuyver et al. *loc. cit.*, Bassit et al. *loc. cit.*, Krug et al. *loc. cit.*).

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TABLE
Hepatitis C Virus genotypes in blood donors from different regions of Brazil

	No.	No. (%) of blood donors with the following HCV genotypes						
		1a	1b	1	2a	2b	3a	Mixed
Northeast	17	1 (5.9)	6 (35.3)	2 (11.7)	0	1 (5.9)	6 (35.3)	1 (5.9)
Mid-west	22	12 (54.6)	2 (9.1)	0	0	1 (4.5)	7 (31.8)	0
Southeast	31	11 (35.5)	13 (41.9)	2 (6.5)	0	0	5 (16.1)	0
Total	70	24 (34.3)	21 (30.0)	4 (5.7)	0	2 (2.9)	18 (25.7)	1 (1.4)

Some variations were observed in the geographical distribution of HCV subtypes. In the northeast region of Brazil, subtypes 1b and 3a were more commonly found, while in the mid-west, subtype 1a was dominant. In the southeast region, subtypes 1b and 1a were more frequent. In addition, subtypes 2a and 2b were absent in blood donors from Rio de Janeiro, but they were previously detected in donors from São Paulo (Bassit et al. *loc. cit.*). Recently, we examined five samples of the northern region, where subtypes 1a (2 samples), 2b (2 samples), and 1b (1 sample) were found (data not shown). Although the number of samples studied was small, these findings indicate variation in genotype circulation in Brazil.

Recent data have shown a high prevalence of chronic hepatitis in viremic asymptomatic blood donors (GLA Bird et al. 1995 *J Viral Hep* 2: 261-

265, M Shindo et al. 1995 *Hepatology* 22: 418-425, D Prati et al. 1996 *Gastroenterology* 110: 178-183). Also, some reports suggest that genotype 1 (mainly subtype 1b) is associated with a higher rate of chronic active hepatitis or cirrhosis, and with a poorer response to treatment with alpha-interferon than with types 2 or 3 (Silini et al. *loc. cit.*, Kobayashi et al. *loc. cit.*, Zein et al. *loc. cit.*, Hopf et al. *loc. cit.*, Simmonds et al. *loc. cit.*). Among the asymptomatic blood donors in the present study, we found a high rate of subtypes 1a, 1b, and 3a. Further studies are necessary to evaluate the clinical course of these apparently healthy carriers.

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