ARTIGO ORIGINAL / ORIGINAL ARTICLE

HCV INFECTION IN NORTHEASTERN BRAZIL: unexpected high prevalence of genotype 3a and absence of African genotypes

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ABSTRACT *- The genomic diversity of HCV embraces 6 genotypes and at least 52 subtypes with clinical and epidemiological correlations. There is a paucity of studies assessing HCV genotypes and biomolecular epidemiology in Brazil. We studied genotype distribution and epidemiological aspects in 232 HCV carriers, 133 (57,9%) males and 99 (42,1%) females, followed in the liver disease referral unit in Salvador, BA, northeastern Brazil. All of them were anti-HCV positive by 3rd generation ELISA assay, and HCV-RNA positive by RT-PCR. Genotyping was performed by INNOLIPA. Assessment of risk factors for HCV infection showed that 93 (40%) had past blood transfusion, 14 (6%) intravenous drug use, 19 (8%) inhalation of cocaine, 28 (12%) tattooing, 15 (7%) were health care workers, 5 (2%) had reused disposable syringes, 5 (2%) had multiple risk factors and in 53 (23%) no risk factor was determined. Genotype 1a was observed in 75 (32%), 1b in 72 (31%), 3a in 61 (26%), 2ab in 14 (6%); 5 (2.5%) had mixed genotypes and 5 (2.5%) were undetermined. Patients with genotype 1 had a higher mean age ($P < 0.05$) and no particular risk factors were associated with a specific genotype. Genotype 1 largely predominates in northeast Brazil followed by genotype 3 which, in this population, does not seem to be related to intravenous drug abuse, in contrast to some European studies. Although 80% of the Salvador population comprises African-Brazilians, no African genotype was identified, which may mean that HCV was introduced into this region via European immigration. This study demonstrated some peculiarities of HCV epidemiology in Brazil and strongly suggests that HCV introduction to this region was probably related to European immigration.*

HEADINGS *- Hepatitis C-like viruses. Genotype. Hepatitis C, epidemiology.*

INTRODUCTION

The hepatitis C virus (HCV) is the major etiological agent of acute post-transfusional or community-acquired non-A non-B hepatitis[1]. Its genomic diversity has been well-documented and it is classified into 6 genotypes and 52 subtypes. Clinical and epidemiological correlations have been reported with the main genotype mostly in Europe and the USA[15].

In clinical evaluations, genotype 3a is associated with mild disease and a better response to antiviral therapy, while genotype 1, especially subtype 1b, is frequently associated with more severe disease; progression to cirrhosis or hepatocellular carcinoma, and high resistance to antiviral treatment[18].

In epidemiological analyses, genotype 1 largely predominates in the West, with genotype 3 usually found in association with intravenous drug abuse in Europe and the United States[7, 14]. In Africa and the Middle East and Asia other genotypes such as 4 , 5 and 6 have been observed; other than genotype 4, which is associated with low response to antiviral treatment[11, 16, 19], their responses to interferon are unknown.

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Brazil is a continental country which has received large immigration currents for the last two centuries. Immigrants of both European and African origin now have a heterogeneous distribution in the country. Understanding of viral introduction and dissemination routes therefore requires knowledge of the biomolecular epidemiology of HCV in the various regions.

Salvador is a city of 3 million inhabitants located in the northeastern part of the country. Its population is predominantly (80%) made up of African-Brazilians (negroes and mulattoes), descended from the slaves brought over from Guinee Bissal, Congo, Mozambique and Angola[2]. The major European immigration originated from Portugal and Spain.

This initial report indicates the genotypic distribution of HCV in a population drawn from a referral liver unit in Salvador in the State of Bahia, Brazil.

PATIENTS AND METHODS

From December 1994 until March 1998, 232 carriers of HCV who were candidates for antiviral therapy were evaluated in the liver unit. Most lived in the city of Salvador or its surrounding towns. Caucasoide phenotype were observed in 61% of the patients while 39% were mulattoes. Of the total, 133 (57.9%) were males with an average age of 45 (± 25) and 99 were females whose average age was 39 (± 18).

Forty one (17.6%) had persistently normal transaminase levels (ALT) while 192 (82.4%) showed fluctuating levels or persistent alterations. All patients were anti-HCV positive and HCV RNA positive on a standard RT-PCR procedure.

Risk factors for HCV contamination were as follows: 93/232 (40%) past blood transfusion, 14/232 (6%) intravenous drug abuse (IVDA), 19/232 (8%) associated with inhalation of cocaine, 28/232 (12%) tattooing, 15/232 (7%) occupation as health care worker, 5 (2%) reuse of disposable syringes, 5 (2%) multiple risks, while in 53/232 (23%) no risk factor could be determined (Figure 1).

The anti-HCV was performed in all patients using a third generation assay (Abbott, Chicago, ILL). The HCV-RNA was determined by a single step nested PCR using primers of the 5' NC region of the HCV genoma[10].

Genotyping was determined by INNOLIPA HCV II (Innogenetics, Belgium) which discriminates genotypes 1 to 6 using 5´ UR amplified fragments[8].

Statistical analysis

Dichotomous variables were analysed by using χ^2 analysis or Fisher's exact test when necessary. Student's *t*-test were used to analyse continous variables.

Alpha level of .05 was taken in consideration for statistical tests.

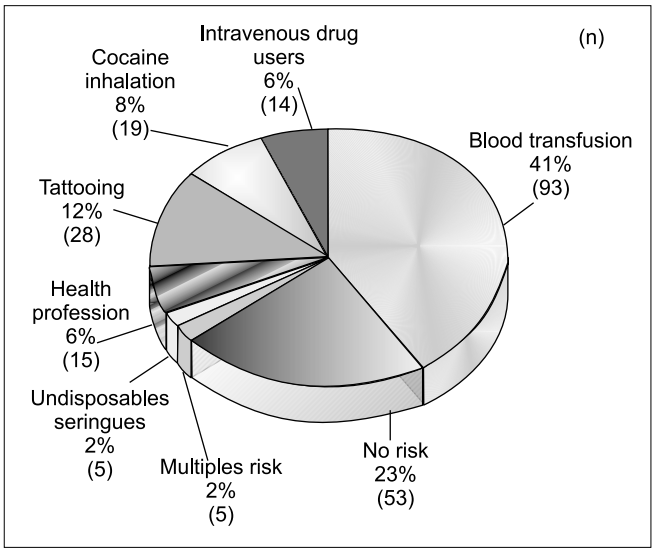

Figure 1 – Risk factor for HCV transmission

RESULTS

Prevalence of HCV genotypes

Genotype 1a was observed in 75 (33%) of the patients, 1b in 72 (31%), 3a in 61 (26%), 2ab in 14 (6%), and 5 (2%) had mixed genotypes , while in 5 (2%) no genotype determination was achieved (Figure 1).

Patients with genotype 1 had an average age of 55 (± 23) compared with 38(± 18) for genotype 3 (P <0.05). The ALT pattern (fluctuating, persistently elevated or normal) was similar for all genotypes (Table 1).

Table 1 – Mean age and ALT levels among patients with different HCV genotypes

Genotype	Mean Age	Mean ALT (N.V. 36)
1 a b	55 (±/- 23)	123 (± 55)
3 a	38 (± 18)*	108 (± 41)
2 a b	44 (± 21)	112 (± 39)

N.V. = Normal value

* P <0.05

Assessment of risk factor for HCV showed that 93 (41%) had past blood transfusion, 14 (6%) intravevous drug use, 19 (8%) inhalation of cocaine, 28 (12%) tattooing, 15 (7%) were health care workers, 5 (2%) had reused disposable seringes, 5 (2%) had multiples risk factors and in 53 (23%) no risk factor was identified (Fig. 2).

No particular risk factor was associated with any specific genotype; in particular, the distribution of intravenous drug abusers was similar among patients with genotype 3 and patients carrying other genotypes (Table 2).

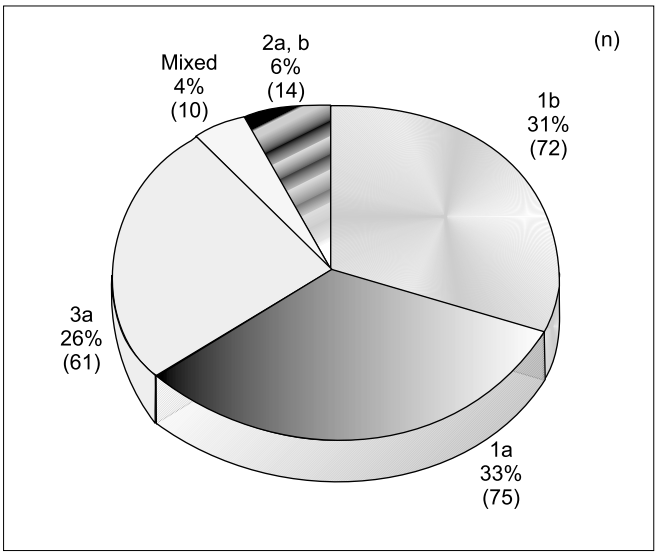

Figure 2 – Genotype distribution

Table 2 – Risk factors in patients with HCV. Comparison of genotypes 3 and 1

Type	n	BT%	IVDU	CI	Tat	HW	DS	MR	NR
1	147	57 (39)	10 (7)	14 (10)	18 (12)	8 (5)	2 (1)	2 (1)	36 (24)
3	61	26 (43)	2 (3)	4 (6)	7 (11)	5 (8)	1 (2)	1 (2)	15 (24)
***P* <0.05**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**	**NS**

BT: Blood transfusion, **IVDU**: Intravenous drug use, **CI**: Cocaine inhalation, **Tat**: Tattooing, **HW**: Health care workers

DS: Reuse of disposable syringes, **MR**: Multiple risks, **NR**: No risk, **NS**: Not significant.

DISCUSSION

The continental dimensions of Brazil as well as the different ethnic groups which make up its population make it of special interest in the understanding of HCV epidemiology and particularly dissemination routes of the virus. Because of its ethnic composition, Salvador appears an ideal region for the study of the biomolecular epidemiology of HCV.

Since 80% of the population comprises African-Brazilians or mixed blood individuals (mulattoes), HCV genotypes prevalent in Africa were expected. The surprising observation that no patient was found to possess genotypes 4 or 5 raises questions about the theory that HCV was introduced into the Brazilian population via African immigration due to the slave trade.

Africa is considered a high endemicity area for HCV[12], and it is unlikely that HCV would have been absent in Africa during the time in which it is estimated that 2 millions slaves were traded with the state of Bahia during the last two centuries of Portuguese colonization. In addition, many characteristics of African culture and religions could contribute to the transmission of parenteral viruses.

Despite of predominating caucasoid fenotype among these patients, it does not seem to cause an overstimation of the European genotypes. In this state, most part of the population has mixed blood and there is no racial segregation or isolated African populations as observed in other countries.

In agreement with which that was found in other regions of Brazil, there exists a high prevalence of genotype 3a in the study population[3, 4, 9, 20]. The reason for this high prevalence is not clear, but it could be the result of recent introduction of HCV to Brazil via European immigration. However unlike the study population, the high prevalence of genotype 3a in Europe, mainly in some areas of the Iberic peninsula, seems to be associated with IVDA[5, 6, 13]. In Northeast Brazil, drug addition is more related to cocaine inhalation and the role of IVDU seems very limited in HCV transmission as demonstrated in this study.

On the other hand, intravenous vitamin injection, using non disposable seringes, was popular during the last two dacades, mainly among athletes and teenagers. This habit was stimulated in the belief that it increased the physical and sexual performance[13]. In our study, the patients who had genotype 3a were younger. This fact suggests that intravenous vitamins injection could have had an important role in HCV transmission in the last 30 years, as occurred with IVDU in Europe.

Many patients do not consider intravenous vitamins injection as a risk factor for acquiring HCV and omit this information. In addition, our epidemiologic HCV's protocol did not mentioned this risk factor because it was included in the context of IVDU.

As suggested by our group, HCV infection is an urban disease rather than a rural one[17]. Maybe many others urban habits could contribute to HCV transmission, specially parenteral transmission of genotype 3a in Brazil.

A follow up of this study with a larger number of patients is therefore warranted in order better to define the epidemiology of HCV strains in Brazil.

Paraná R, Vitvitski L, Berby F, Portugal M, Cotrim HP, Cavalcante A, Lyra L, Trepo C. Infecção pelo vírus da hepatite C no nordeste do Brasil: alta prevalência inesperada do genotipo 3a e ausência de genotipos africanos. Arq Gastroenterol 2000;37(4):213-216.

***RESUMO** - A organização e diversidade genômica do vírus da hepatite C define, pelo menos, 6 genotipos e 52 subtipos com peculiaridades clínicas e epidemiológicas. Há escassez de estudos referentes ao genotipo do vírus da hepatite C no Brasil, assim como sua epidemiologia biomolecular. Foram estudados a freqüência do genotipo e os aspectos epidemiológicos em 232 portadores do vírus da hepatite C, 133 (57,9%) homens e 99 (42,1%) mulheres, seguidos num centro de referência para doenças de fígado em Salvador, nordeste do Brasil. Todos os pacientes eram anti-HCV positivo por ELISA de terceira geração e HCV RNA positivo por RT PCR. O genotipo foi determinado por INNOLIPA. Os fatores de risco para o vírus da hepatite C verificados através de questionário padrão, demonstrou que 93 (40%) tinham história de transfusão, 14 (6%) eram usuários de droga venosa, 19 (18%) referiam inalação de cocaína, 28 (12%) tinham tatuagem, 15 (7%) eram trabalhadores da área da saúde, 5 (2%) referiram reutilização de seringas descartáveis, 5 (2%) tinham múltiplos fatores de risco e 53 (23%) não referiram nenhum fator de risco. O genotipo 1a foi observado em 75 (32%), 1b em 72 (31%), 3a em 61 (26%), 2a em 14 (6%), 5 (2,5%) tinham infecção por mais de um genotipo e 5 (2,5%) tiveram o genotipo indeterminado. Pacientes com genotipo 1 apresentavam média de idade mais alta (P <0,05) e nenhum fator de risco peculiar esteve associado a um genotipo específico. O genotipo 1 predominou amplamente no nordeste do Brasil, seguido pelo genotipo 3. Nesta população o genotipo 3 não parece estar relacionado ao uso de drogas venosas, em contraste ao que foi reportado nos estudos europeus. Embora 80% da população de Salvador seja composta por população negra ou miscigenada, nenhum genotipo africano foi identificado, o que pode significar que o vírus da hepatite C foi introduzido nesta região via imigração européia. Este estudo demonstra algumas peculiaridades da epidemiologia do vírus da hepatite C no Brasil e fortemente sugere que sua introdução nessa região esteve relacionada à imigração européia e não à africana.*

DESCRITORES - Vírus semelhantes ao da hepatite C. Genotipo. Hepatite C, epidemiologia.

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