

## Hepatology highlights

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### Hepatitis C virus infection in patients and family members attending two primary care clinics in Puebla, Mexico

**López-Colombo, *et al.*** Hepatitis C virus (HCV) transmission is mainly due to parenteral exposure. However, in absence of such risk factor, there are reports of intrafamilial spread of HCV and observational studies suggest an increased risk for households of infected subjects. This risk factor has been explored in the last two decades in different geographical areas around the world. However, there are contradictory results. Firstly, Ndong-Atome, *et al.*<sup>1</sup> found in a cross-sectional study was conducted in Dienga, in Gabon, involving 195 household members of 14 index cases of HCV infection. The investigators found an overall prevalence of antibody to HCV among household members of infected cases of 6.7%, with a significantly higher prevalence among sexual partners (35.7%) than non-sexual partners (7%). Furthermore, the HCV strains infecting different household contacts of index cases were concordant in only 40%, each of who was a sexual partner. This, and the discordance in HCV genotypes infecting the household members, indicate a limited role for intrafamilial transmission of HCV in this population. In another study Honda, *et al.*<sup>2</sup> evaluated the risk of hepatitis C virus transmission through household contact with chronic carriers using nucleotide sequence analysis. HCV patients (76 patients) were divided into two groups: familial transmission of HCV was studied in group A (53 patients); group B (23 patients) served as nonfamilial controls for group A. Of 88 family members of group

A patients, 18 (20%) had elevated serum ALT levels, 20 (23%) had antibodies against hepatitis C virus and 16 (18%) had hepatitis C virus RNA in serum. Nucleotide sequences of the region of the hepatitis C virus genome spanning the core and envelope genes were compared among the three groups. In group B, the average nucleotide sequence homology was  $91.0\% \pm 2.29\%$  (a pairwise comparison was made for each of the patients;  $n = 253$ ). Isolates from two family members were significantly more homologous to isolates from corresponding patients in group A than to isolates from group B patients. Of the two isolates from family members, one was from a child whose mother was a patient (97.7% homology) and one was from a spouse (98.1% homology). These results strongly suggest familial transmission of the same HCV strain.

In this issue **López-Colombo, *et al.*** determined the prevalence of HCV infection in patients and family members attending two primary care clinics. The investigators studied 10,214 subjects. They found 120 (1.17%) anti-HCV positive. Of the positive subjects, the HCV RNA was determined in 114 subjects and 36 were positive (31%). The more frequent risk factors were having a family history of cirrhosis (33.1%) and having a blood transfusion prior to 1995 (29%). The HCV genotypes found were 1a (29%), 1b (48.5%), 2/2b (12.8%), and 3a (6.5%). Also, the researches found an overall prevalence of antibody to HCV among household members of infected cases of 6.7%, with a significantly higher prevalence among sexual partners (35.7%) than non-sexual partners (7%).

This is one of the first studies carried out in Mexico on HCV infection in patients and family members. The sample size of the study as well as the design are good. However, the present study was carried out in one state in an urban area in two Clinics. It would be interesting to know the characteristics of both clinics as well as the medical attention provided and more information on the social and demographic characteristics of the population studied.

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### The role of *Interleukin 28B* gene polymorphism in Turkish patients with hepatocellular carcinoma

**Akkiz, et al.** It has been reported that genetic polymorphisms near the *interleukin-28B* (IL28B) gene might strongly associated with spontaneous and treatment-induced clearance of HCV.<sup>3</sup> Also IL28B has been associated with a poor treatment response rs12979860 T allele in patients with HCV infection and the liver fibrosis progression rate and the development of HCC.<sup>4</sup>

In this issue **Akkiz, et al.** investigated whether the rs12979860 polymorphism of IL28B gene affects the risk of HCC. Those investigators carried out a case-control study of 187 confirmed HCC patients and 208 healthy subjects (cancer and viral infection negative) and they found that the allele and genotype analysis showed no significant differences between the risk of HCC and IL28B gene rs12979860 polymorphism (OR = 1.10; 95% 0.59-2.08 P = 0.76 for genotype). However, in the HBV-related HCC subgroup, the TT genotype increased a 1.46-fold the risk of developing HCC, but not statistically significant (OR = 1.46; 95% 0.71-2.97 P = 0.30). The authors concluded that there is not significant association between IL28B rs12979860 genotypes with the risk of developing HCC in Turkish patients.

Two important criticisms on this study are the sample size and the main clinical characteristics of the patients are missing. In fact, the sample size is not good enough to find some differences and interestingly the HCV genotypes were not included. However, it added a little of information on this hot topic that but need to confirm in future studies in different populations.

One study from Italy by Fabris, et al.<sup>5</sup> those investigators studied 412 patients with cirrhosis due to hepatitis C (n = 199), hepatitis B (n = 75), alcohol (n = 110), and other causes (n = 28), of whom 256 underwent liver transplantation (OLT). HCC was demonstrated in the native liver of 85 OLT patients, 52 with viral cirrhosis, and 33 with non-viral

cirrhosis respectively. A group of 292 patients (235 HCV and 57 HBV positive) with mild chronic hepatitis and 344 healthy subjects served as controls. The investigators found a significant difference (p = 0.0005) was observed in IL-28B rs12979860 genotype frequencies between patients with viral cirrhosis (C/C = 99, C/T = 137, T/T = 38) and those with non-viral cirrhosis (C/C = 72, C/T = 58, T/T = 8). Patients with HCV related cirrhosis carried more frequently the T/T genotype in comparison to mild hepatitis C or HBV-related cirrhosis.

In more recent study Bochud, et al.<sup>6</sup> analyzed the association of IL28B polymorphisms with histological and follow-up features in 2335 chronically HCV-infected Caucasian patients. Assessable phenotypes before any antiviral treatment included necroinflammatory activity (n = 1,098), fibrosis (n = 1,527), fibrosis progression rate (n = 1,312), and HCC development (n = 1,915). The rare G allele at IL28B marker rs8099917 previously shown to be at risk of treatment failure was associated with lower activity (P = 0.04), lower fibrosis (P = 0.02) with a trend toward lower fibrosis progression rate (P = 0.06). When stratified according to HCV genotype, most significant associations were observed in patients infected with non-1 genotypes (P = 0.003 for activity, P = 0.001 for fibrosis, and P = 0.02 for fibrosis progression rate), where the odds ratio of having necroinflammation or rapid fibrosis progression for patients with IL28B genotypes TG or GG *vs.* TT were 0.48 (95% confidence intervals 0.30-0.78) and 0.56 (0.35-0.92), respectively. IL28B polymorphisms were not predictive of the development of HCC. Based on their results the investigators concluded that there is not association between IL28B polymorphisms and the occurrence of HCC among chronically HCV-infected patients, but the number of patients with HCC was likely insufficient to detect a significant effect, especially as the majority of patients with HCC were infected with HCV genotype 1 independent investigations are required to clarify the possible role of IL28B gene rs12979860 polymorphism on the risk of developing HCC in a larger series and also in patients of different ethnic origins.

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