

## Hepatitis G virus exposure in dialysis patients and blood donors in Isfahan-Iran

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### ABSTRACT

**Background:** Hepatitis G virus (HGV) is transmitted mainly by parenteral route and patients on maintenance hemodialysis (HD) are at risk for this infection. This study was conducted to estimate prevalence of infection through the presence of anti-HGV and to evaluate the clinical significance of HGV envelope protein E2 (anti-E2) in HD patients in compare with volunteer blood donors in Isfahan-Iran.

**Methods:** In a cross-sectional study, a total of 40 HD patients as cases and 40 healthy volunteer blood donors as negative controls were selected randomly in summer 2008. The epidemiological data were obtained in all subjects, and duration of HD was obtained in HD patients as well. All samples were tested for anti-E2 antibodies, hepatitis C virus (HCV)-antibody and hepatitis B virus surface antigen (HBs-Ag) by an enzyme-linked immunosorbent assay and a recombinant immunoblot assay was employed to confirm anti-HCV reactivity. Student's *t*-test, Chi-square test or Fisher exact test was used for data analysis and  $P < 0.05$  was considered as statistically significant.

**Results:** Ten of the 40 HD patients tested positive for anti-E2 (25%) and of 40 voluntary blood donors, 10 (5%) were positive for anti-E2 ( $P = 0.012$ ). Anti-HCV antibodies and HBs-Ag were found in 4 and 1 HD patients, respectively. In anti-E2-positive patients, co-infection with HCV or hepatitis B virus was not significant. Furthermore, the mean duration of hemodialysis in anti-E2 positive and anti-E2 negative patients did not have significant differences.

**Conclusions:** HD patients are at increased risk of HGV infection in Isfahan-Iran. Since hepatitis G is a good predictor for parenteral transmission, it is suggested to test all of the blood for transfusion for HGV infection.

**Keywords:** Hepatitis G, hemodialysis, Isfahan

### INTRODUCTION

Patients on maintenance hemodialysis (HD) have a high-risk of blood-borne viral infections. Some of the most common

viral infections are caused by hepatitis associated viruses such as hepatitis G virus (HGV).<sup>[1]</sup>

Hepatitis G virus is a positive-stranded RNA virus belonging to the *Flaviviridae* family. Controversial data exist concerning whether or not HGV replicates in the liver and the potential of HGV to cause hepatitis in humans is questionable.<sup>[2]</sup> However, the results of some studies suggest the possibility of a link between fulminant or acute hepatitis and HGV infection.<sup>[3]</sup>

Diagnostic method for determining an ongoing GB virus C (GBV-C)/HGV infection is to demonstrate a viremia by reverse transcriptase-polymerase chain reaction (PCR). However, an assay detecting antibodies to the envelope protein E2 (anti-E2) of HGV has been developed, and this serological marker is considered to be an indicator of the virus clearance. Thus, the presence of anti-E2 seems to testify to a past contact and is highly associated with protection from re-infection.<sup>[4]</sup>

As HGV is transmitted mainly by parenteral route, HGV is highly prevalent among population groups at risk of parenterally transmitted viral agents.

Thus, patients with chronic renal failure are at high-risk of acquiring this virus because they need frequent blood transfusions and undergo medical procedures that accompany bleeding.<sup>[5]</sup>

Time on HD, transfusion requirement, and renal transplantation are risk factors for HGV infection in patients on maintenance HD, with the prevalence ranging from 3% to 57% in transversal studies.<sup>[6]</sup>

For epidemiological reasons, the common HGV infection in humans, particularly in HD patients, is of interest for controlling parenterally transmitted viral infection in high-risk patients.<sup>[5]</sup>

The present data on the prevalence of HGV anti-E2 in HD patients is conflicting from 3% to 57% in the world.<sup>[4,7,8]</sup>

The aims of this study were to estimate prevalence of infection through the presence of anti-HGV and to evaluate the clinical significance of HGV envelope protein E2 (anti-E2) in HD patients in compare with volunteer blood donors in Isfahan-Iran. Also, we compared HGV exposure with age, sex, time on dialysis and co-infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) in HD patients.

## METHODS

In a cross-sectional study, a total of 40 patients from 2 HD units of Isfahan-Iran were selected randomly in summer 2008.

All patients underwent chronic HD treatment for end-stage renal disease during the study period.

Furthermore, 40 healthy volunteer blood donors who did not belong to any risk group for viral hepatitis served as negative controls. After being given a brief description of the purpose and procedure of the study, informed consent was obtained from all participants.

The epidemiological data including gender, age and history of HCV and HBV, were obtained in all subjects. Duration of HD was obtained in HD (HD) patients as well.

Blood samples were collected from all subjects (for patients, before HD). Serum samples were aliquoted and stored at  $-20^{\circ}\text{C}$  until processing.

Sera from the HD patients and the control group were tested for markers of HBV and HCV infections.

Hepatitis B virus surface antigen (HBs-Ag) was detected with commercially available enzyme-linked immunosorbent assays (ELISA, Diapro-Italy). Detection of anti-HCV antibody was measured using commercially available second-generation ELISA (ELISA, Diapro-Italy). A recombinant immunoblot assay (RIBA; Innogenetics, Ghent, Belgium) was employed to confirm anti-HCV reactivity.

In control group, everyone who was positive for HCV or HBs-Ag, excluded from the study and another blood donor was exchanged.

All samples were tested for anti-E2 antibodies by an enzyme-linked immunosorbent assay (Diagnostic, USA). Results were analyzed by optical density and were compared to the cutoff value with the help of kit-specific positive and negative controls, according to the manufacturer's instructions.

### Statistical analysis

Data, expressed as the mean  $\pm$  standard deviation or percentage. To evaluate the distribution of characteristics associated with GBV-C/HGV infection, Student's *t*-test, Chi-square test or Fisher exact test was used. For comparisons between two independent groups, we used the Chi-squared or Fisher's exact test for categorical variables and the *t*-test for quantitative variables.

SPSS program (SPSS for Windows, release 18, SPSS Inc., Chicago, IL, USA) was used for data analysis and  $P < 0.05$  were considered as statistically significant.

## RESULTS

A total of 40 HD patients (19 male and 21 female) with mean age of  $49 \pm 18$  years and 40 male controls from voluntary blood donors with a mean age  $32 \pm 9$  years participated in the study.

Hemodialysis patients had been on dialysis for a mean of  $33.5 \pm 30$  months.

Ten of the 40 HD patients tested positive for anti-E2 (25%). The mean age of patients testing positive for anti-E2 was  $63 \pm 10$  years, and that of patients with negative anti-E2 was  $44 \pm 17$  years ( $P = 0.002$ ).

Anti-HCV antibodies and HBs-Ag were found in 4 and 1 HD patients, respectively. In anti-E2-positive patients, co-infection with HCV or HBV was not significant.

The mean duration of hemodialysis in anti-E2 positive and anti-E2 negative patients was  $37 \pm 26$  months and  $32 \pm 31$  months, respectively with no significant differences.

Of 40 voluntary blood donors, 2 (5%) were positive for anti-E2. The mean age of blood donors testing positive for anti-E2 was  $45 \pm 15$  years, and that of ones with negative anti-E2 was  $32 \pm 9$  years with no statistical differences.

Table 1 depicts the frequency of HGV infection in patients with HD and in voluntary blood donors.

## DISCUSSION

In our study, 25% of the HD patients and 5% of the voluntary blood donors tested positive for anti-E2, showing that HGV exposure was relatively high in the population of dialysis patients in Iran.

It is a fact that patients on maintenance HD represent a risk group for HGV infection, and the

**Table 1:** Comparison of HGV exposure in HD patients and voluntary blood donors

	HGV-Ab <sup>-</sup> (%)	HGV-Ab <sup>+</sup> (%)	P
HD patients	30 (75)	10 (25)	0.012
Voluntary blood donors	38 (95)	2 (5)	

HD=Hemodialysis, HGV-Ab=Hepatitis G virus antibody

prevalence of this infection is higher than in the general population. This fact has been attributed to blood transfusions and to nosocomial transmission in dialysis units.<sup>[1]</sup>

Hepatitis G virus and HCV belong to the same family of *Flaviviridae* and the clinical characteristics and risk factors of them may be similar. In our study, anti-HCV seropositivity was detected in four patients (10%), including one who were also infected with HGV. Thus, HD patients are at risk for both HGV and HCV infections, and blood transfusion may be the route of transmission of the two viruses in these patients. Hence, it seems to be necessary to test blood for transfusion for HGV infection as the same as for HCV. In our study, the prevalence of HGV infection (25%) was higher than anti-HCV seropositivity (10%), probably because blood for transfusion had been tested serologically for anti-HCV which is routinely tested since 1996 in Iran. We did not find any patient co-infected with HBV and HGV, probably because blood for transfusion had been examined for HBV, and HD patients were vaccinated against HBV. In this study we cannot ascertain whether HGV in association with HBV or HCV infection played any role in the severity of the HBV/HCV disease or whether disease manifestations would have been the same in the absence of HGV.

We had expected that the prevalence of HGV infection was significantly correlated with the duration of HD<sup>[9,10]</sup> but in the current study, there was no significant difference in the mean duration of hemodialysis in anti-E2 positive and anti-E2 negative patients. This may be due to small sample size in our study. Similar results were obtained by Ramos Filho *et al.*,<sup>[11]</sup> Huang *et al.*,<sup>[12]</sup> and Eslamifar *et al.*<sup>[4]</sup> who reported that there was no association between GBV-C/HGV infection and length of time on dialysis in HD patients.

However, as the length of time on HD was not a main risk factor for transmission of hepatitis G in our study, prevention of nosocomial transmission of HGV seems to be effective in Iranian HD patients.

In our study, HGV infection was associated with age that may be due to lower immunity in aged people.

The existing data on HGV prevalence in chronic dialysis patients is conflicting with a prevalence ranging from 3% to 57% in the world.<sup>[4]</sup>

In one preliminary study from Iran, the sera of patients on maintenance HD were reported

negative for GBV-C.<sup>[13]</sup>

In Two another studies, the prevalence of HGV in HD patients reported as 12.6% by PCR method<sup>[4]</sup> and 3.89% by serologic method in Tehran-Iran.<sup>[5]</sup>

It is reported that nearly 2–6% of volunteer blood donors in Asia are infected with HGV,<sup>[12]</sup> which is confirmed by our study. There is a requirement for comprehensive epidemiological studies in order to elucidate the prevalence of HGV in the general population and groups with high-risk sexual behavior in our country.<sup>[14]</sup>

## CONCLUSIONS

According to our results, HD patients are at increased risk of HGV infection in Isfahan-Iran.

Since hepatitis G is a good predictor for parenteral transmission, it is suggested to test all of the blood for transfusion for HGV infection.

Because of restricted samples we suggest that this study should be brought about with more samples.

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