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**ORIGINAL ARTICLE**

# Prevalence and risk factors of the hepatitis G (HGV) infection in hemodialysis patients

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## ABSTRACT

**Background**: GBV-C and HGV are different isolates of the same virus which were identified by two independent research groups. HGV is a blood-borne virus and a member of flaviviridae. This virus is present in the volunteer blood donors. The aim of this study was to assess the prevalence of HGV-RNA by PCR and investigation of risk factors for viral transmission.

**Materials and methods**: In all patients (n=269), HGV-RNA were detected by RT-PCR. Liver function tests performed by colorimetric method and epidemiologic data were obtained to evaluate risk factors for HGV in hemodialysis patients.

**Results**: Viremia was seen in %12.6 of patients. It was found that blood transfusion increased the risk of HGV infection significantly (P<0.05). There was no association between HGV infection and duration of hemodialysis or age of the patients.

**Conclusion**: Prevalence of HGV in hemodialysis patients is high and among the investigated risk factors, only the number of transfusion of blood or blood products increases the risk of new infection during hemodialysis.

**Keywords**: *GBV-C, Hemodialysis, Hepatitis G, Prevalence, Risk factor*.
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## INTRODUCTION

GB virus C (GBV-C) and hepatitis G virus (HGV) are different isolates of the same virus which were identified by two independent research groups (simon et al. 1995, Linnen et al. 1996) (1,2).

GBV-C/HGV is an enveloped positive-stranded RNA virus with a genome of about 9.4 kb belongs to Flaviviridae family (2,3).

GBV-C/HGV is a blood-borne virus (4,5). Infection with HGV is common (5) and the virus is present in the volunteer blood donor population (6,7,8,9,10). There is a weak association between transmission of HGV and the onset of acute hepatitis, and also, there is no convincing evidence in favor of fulminant hepatic failure due to acute HGV infection.

Although HGV is able to persist in humans, so far a chronic hepatitis due to HGV infection has not been reported (4,7,11,12).

GBV-C/HGV is transmitted mainly by parenteral route (5,9,13). Thus, patients with

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chronic renal failure are at high risk of acquiring this virus because they need frequent blood transfusions and undergo medical procedures that accompany bleeding (2,3,7).

For epidemiological reasons, the common HGV infection in humans, particularly in hemodialysis patients, is of interest for controlling parenterally transmitted viral infection in high risk patients.

The aim of the present study was to determine the prevalence of GBV-C/HGV RNA (viremia) by PCR method in hemodialysis patients in Tehran. Furthermore, risk factors for viral transmission were also investigated.

## PATIENTS and METHODS

The study was performed in 40 hemodialysis units of Tehran, Iran in 2005 and 2006. A total of 269 patients were selected randomly from these units. All patients underwent chronic hemodialysis treatment for end-stage renal disease during the study period. The number of patients in each hemodialysis unit varied from 2 to 10. The following epidemiological data were obtained in all patients: (I) Gender and age. (II) Duration of hemodialysis (III) Number of blood transfusions (none, 1-5, 6-15, >15); (IV) Known chronic liver disease (V) Liver function tests (AST, ALT, ALP).

Blood samples were collected from all patients before hemodialysis. The blood was centrifuged immediately at the unit, and plasma was separated and stored at -20°C. All Samples subsequently were tested for liver function tests by a colorimetric method.

HGV-RNA was extracted from 100µL plasma samples using the guanidine isothiocyanate-phenol-chloroform method and reverse transcribed using random primer and Moloney murine leukemia Virus (MMLV) reverse transcriptase (Fermentas). The oligonucleotide primers for amplification of c-DNA by PCR were designed on highly conserved domains of the 5′ non-coding regions. The nucleotide sequences of the primers were 5′-CACTATAGGTGGGTCTTAAG-3′ (150-169nt), (numbers were based on the HGV genome published by Leary et al.) (26) and 5′-GCCTATTGGTCAAGAGAGAC-3′ (352-333nt) for the first PCR; and 5′-GCGCACGGTCCACAGGTGTT-3′ (207-226nt) and 5′-GGGCGACGTGGACCGTACGT-3′ (326-307nt) for the second PCR. Polymerase Chain reaction amplification was performed for 30 cycles (94°C for 30s; 55°C for 90s; 72°C for 90s) in the first PCR and 35 cycles with the same time-temperature conditions in the second PCR. Amplified products were separated with agarose gel (2%) electrophoresis and visualized by ethidium bromide staining.

Prevalence rate was calculated. Fisher's exact test was used to evaluate the distribution of characteristics associated with GBV-C/HGV infection. Statistical significance was assessed at the 0.05 probability level in all analyses. Statistical evaluation was performed using SPSS (Version 13.0, SPSS Inc., USA) software.

## RESULTS

The Study Population (n=269) ranged in age from 20 to 83 years (average 50.7 years). 108 (40%) were males and 161 (60%) were females. The mean duration of hemodialysis treatment was 8.6 years. The range of transfusion of blood and blood products was from 0 to 48(mean=3). Hemodialysis was performed routinely 3 times a week in the patient population.

HGV-RNA by RT-PCR was detected in 34 out of 269 patients (12.6%) (Fig. 1). There was no association between GBV-C/HGV RNA and age, length of time on dialysis and liver function tests ($P>0.05$). In contrast a significant relation was seen between serum HGV-RNA positivity with the number of blood transfusion ($P<0.05$). Nine (3.3%) of the GBV-C/HGV RNA positive patients were co-infected with HCV (HCV RNA Positive). Thus,

combined viral replication of HCV and HGV is rare in the patients investigated.

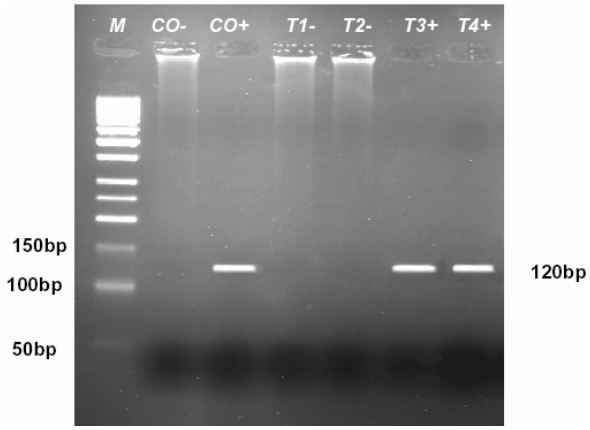


**Figure 1. Results of gel electrophoresis: marker (M), controls (Neg. and Pos.), negative tests (1 and 2) and positive tests (3 and 4)**

## DISCUSSION

The Present study represents the first investigation of GBV-C/HGV infection in patients with chronic renal failure in Tehran, Iran.

Regarding hemodialysis patients, GBV-C/HGV RNA prevalence rates range from 3.1% to 15% in Japan (14,15), 11.5% to 20% in the US(16,17), and 6% to 57.5% in Europe(18,19). It has also been reported a high rate (55%) in Indonesia (20). In South America, a prevalence of 17.5% was observed in Argentina (21). In addition, rates of 15% and 12.8% were detected in Rio de Janeiro, Brazil (22,23). Thus GBV-C/HGV infection prevalence in Tehran hemodialysis patients (12.6%) could be regarded as an intermediate level.

The majority of the published studies enrolled less than 200 patients and a few studies performed in more than 200 patients, have been published (3,5,12,27,28). Our data demonstrate that results obtained from less than 200 patients might under or overestimate the prevalence of HGV-RNA (3-58%). Thus the wide range could be explained by varying number of patients, in addition to geographic factors and the methods of detection of GBV-C/HGV RNA (especially the use of different primers). Since in the present study 269 patients were enrolled, the calculated prevalence data for hepatitis G in hemodialysis patients are reliable. However, in general, all results published showed that hepatitis G infection measured by HGV-RNA was common in hemodialysis patients, and this was also confirmed by our study. We found hepatitis G viremia in 12.6% of the hemodialysis patients.

Patients on maintenance hemodialysis treatment are at high risk for acquisition of parenterally transmitted viral infection (18,24). Hepatitis G is a good predictor for parenteral transmission, as the virus is mainly transmited by this rout and is common in our population. Nearly 2-6% of volunteer blood donors in Asia and up to >20% in South Africa are infected with HGV (3).

We showed that administration of blood and blood products, but not length of time on hemodialysis is a main risk factor for transmission of hepatitis G. Thus patient to patient transmission during hemodialysis is not common, and prevention of nosocomial transmission of HGV is effective in the evaluated Iranian hemodialysis patients.

Liver function tests were normal in the majority of hepatitis G patients, confirming that only small number of patients suffer from acute hepatitis (7). Co-infection with HCV is uncommon (3.3%), which confirms data of previous trials (25).

In conclusion, patients on maintenance hemodialysis treatment are at high risk for acquisition of parenterally transmitted viral infections. However, for the common HGV infection, no increased risk during hemodialysis was observed, except after administration of blood products. Thus prevention of nosocomial transmission of hepatitis viruses is effective in Iranian hemodialysis patients.

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