

## GB Virus C Overview: Insights into Clinical Implication

Amitis Ramezani, Mohammad Banifazl, Arezoo Aghakhani

Amitis Ramezani, Arezoo Aghakhani, Department of Clinical Research, Pasteur Institute of Iran, Tehran, 13164, Iran

Mohammad Banifazl, Iranian society for support of patients with infectious diseases, Tehran, 13164, Iran

Amitis Ramezani, Pediatric Infectious Disease Research Center, Tehran University of Medical sciences, Tehran, 13164, Iran

Correspondence to: Arezoo Aghakhani, Department of Clinical Research, Pasteur Institute of Iran, No 69, Pasteur Ave., Tehran, 13164, Iran. [araghakhani@hotmail.com](mailto:araghakhani@hotmail.com)

Telephone: +098 2166968852 Fax: +098 2166465147

Received: April 24, 2012 Revised: September 5, 2012

Accepted: September 8, 2012

Published online: January 21, 2013

### ABSTRACT

GB virus C (GBV-C) is a single stranded positive sense RNA virus, which is a member of the Flaviviridae, discovered in 1995 and it is the most closely related human virus to hepatitis C virus (HCV). Unlike HCV, GBV-C considered to be lymphotropic and related to the viral population infecting CD8 T cells and B cells. GBV-C infection has not been convincingly associated with any known human disease; however, several studies have found an association between persistent GBV-C infection and improved survival with slower disease progression in GBV-C/HIV co-infected patients. GBV-C infection is relatively common and has a worldwide distribution and 1-5% of healthy blood donors in developed countries have GBV-C RNA in their sera. In this review we discuss the GB virus C natural history, epidemiology and its prevalence in different population, focusing on the disease associations and interaction with HIV infection.

© 2013 Thomson research. All rights reserved.

**Key words:** GB virus C (GBV-C); Epidemiology; Disease association

Ramezani A, Banifazl M, Aghakhani A. GB virus C Overview: Insights into Clinical Implication. *Journal of Gastroenterology and Hepatology Research* 2013; 2(1): 343-349 Available from: URL: <http://www.ghrnet.org/index./joghr/>

### INTRODUCTION

The GB virus C (GBV-C) is an enveloped, single-stranded positive RNA virus belonging to the family Flaviviridae<sup>[1]</sup>, which contains a single open reading frame (ORF) encoding two structural (E1 and E2) and five non-structural proteins<sup>[2,3]</sup>. GBV-C has a close sequence homology and genomic organization to hepatitis C virus (HCV) with about 30% similarity<sup>[4]</sup>, but its genome lacks the core region and hypervariable region of E2 gene<sup>[5]</sup>.

Although this virus was initially identified as a possible etiological agent of viral hepatitis in humans, and despite its similarity with HCV<sup>[1]</sup>, no convincing association between the virus and any disease entity has been identified and it appears to be a nonpathogenic human virus<sup>[6,7]</sup>. It does not seem that GBV-C be a hepatotropic virus and replicates in hepatocytes<sup>[6,8,9]</sup>. In fact GBV-C is a lymphotropic virus and related to the viral population infecting CD8 T cells and B cells<sup>[10]</sup>.

This virus is only may be important because of its inhibitory effect on human immunodeficiency virus (HIV) replication and its ability to inhibit HIV *in vitro*<sup>[11]</sup>. Some studies<sup>[11,12,13]</sup> showed that the virus is associated with improved survival, a lower mortality rate, slower disease progression among GBV-C/HIV co-infected patients and leading to a lower HIV viral load and higher counts of CD4<sup>+</sup> cells in these patients, although some studies have failed to demonstrate these beneficial effects<sup>[14]</sup>.

In this review we discuss the GB virus C natural history, epidemiology and its prevalence in different population, focusing on the disease associations and interaction with HIV infection.

### THE GB VIRUS C TRANSMISSION

GBV-C can be transmitted parenterally through blood and its derivative<sup>[15,16,17]</sup> and blood transfusion considered as a main risk factor for GBV-C transmission<sup>[6]</sup>.

Specific populations appeared to be particularly at risk for acquiring GBV-C infection, like those with exposure to blood and blood products, hemodialysis patients and injection drug users (IDUs)<sup>[8,18]</sup>. Several other non parenteral routes of infection have been considered for GBV-C transmission such as sexual contact<sup>[19]</sup>, percutaneous contamination from saliva<sup>[20]</sup>, nosocomial infection through patient to patient<sup>[21]</sup> and intrafamilial transmission<sup>[18,22]</sup>.

Several studies have shown that the prevalence of GBV-C

infections is correlated with sexual activity, independently of risks for parenteral exposures, in both heterosexual and homosexual populations<sup>[23]</sup> and male to male sex has been described as an effective way of transmission<sup>[24]</sup>.

Vertical route may also mediate GBV-C transmission<sup>[25]</sup> and an observational study reported the possible transmission of maternal GBV-C during pregnancy and delivery<sup>[19,26]</sup>.

## NATURAL HISTORY OF GBV-C

GBV-C infection is found worldwide and can cause persistent human infection<sup>[27]</sup> without clinical symptoms or disease in either immunocompromised or healthy individuals<sup>[7]</sup>.

Similar to other lymphotropic viruses, GBV-C is transmitted by parenteral and non parenteral routes such as sexually and vertically. Therefore, it is highly frequent in populations with other blood borne infections and sexually transmitted diseases<sup>[28]</sup>.

GBV-C viremia may persist for years but it is eventually cleared in 50-75% of cases and antibodies against the GBV-C E2 envelope usually appear<sup>[29]</sup>. In most populations, the rate of anti-E2 is 2-6 times higher than the viremia prevalence, suggesting that the GBV-C clear spontaneously by the immune system in most times<sup>[30]</sup> and the majority of infected cases with GBV-C clear viremia within 2 years of infection<sup>[31]</sup>.

There is some evidences that HIV infected patients and children may clear GBV-C more slowly than those with intact immune systems<sup>[32,33]</sup> and GBV-C viremia is much more common among immunosuppressed individuals than among healthy blood donors<sup>[34]</sup>.

The presence of GBV-C RNA in serum is associated with active GBV-C infection whereas detection of anti-E2 indicates prior infection<sup>[28]</sup>. Therefore anti-E2 antibody is considered as a useful marker for diagnosing GBV-C infections recovery and can be detected after clearance of the virus<sup>[35]</sup>.

The simultaneous detection of anti- E2 antibody and viral RNA seems to be rare and occurs only for a limited time<sup>[27]</sup>. The coexistence of the GBV-C viremia and anti-E2 occurs just before clearance, probably in the form of an immunocomplex<sup>[36]</sup>. In a multicenter study on HIV infected cases, 1.8% of patients with GBV-C viremia had detectable anti-E2 whereas 75% of patients who were negative for GBV-C RNA had E2 antibodies<sup>[13]</sup>.

Anti-E2 is found more frequently than viremia among healthy blood donors<sup>[30,37]</sup> suggesting prior exposure and viral clearance. Although anti-E2 is a marker of past infection, detection may be lost by time<sup>[28]</sup> possibly more rapidly among HIV infected persons and thus it may be difficult to accurately estimate the true incidence of GBV-C infection<sup>[38]</sup>.

## EPIDEMIOLOGY AND DISEASE ASSOCIATION

GBV-C infection is relatively common and has a worldwide distribution<sup>[1]</sup>. In the general population the GBV-C infection is more prevalent than other blood-borne viruses such as hepatitis C and HIV in Western industrialized countries<sup>[38]</sup>. Between 1 and 5% of healthy blood donors in developed countries are viremic at the time of donation. The prevalence is higher in blood donors from developing countries<sup>[39]</sup> which up to 20% of blood donors were viremic in some studies<sup>[39,40]</sup>. Most people clear the virus and develop antibodies to the E2 envelope glycoprotein. Furthermore, infection is common in the normal population with up to 12.9% prevalence among paid blood donors in the United States of America<sup>[41]</sup>, 11% to 14% in West Africa or South Africa<sup>[15]</sup>, and as high as 37% among HIV-infected individuals<sup>[42]</sup>.

Some specific populations considered to be particularly at risk to GBV-C infection. For example, some high risk groups such as IDUs have evidence of past or active infection in up to 90% in some populations<sup>[30]</sup>. Amongst HCV infected patients, GBV-C incidence varies from 3.2 to 64.9%<sup>[18,43]</sup> and in HIV positive individuals it rates from 11.3% to 45%<sup>[24, 44]</sup>. Little work has been done on co-infection of GBV-C and HBV but no significant effect of this co-infection was reported<sup>[18]</sup>.

Several surveys designed to determine if GBV-C represented an etiological agent for acute or chronic hepatitis or not? Prospective and retrospective studies provided no evidence of epidemiological association between viremia and acute or chronic hepatitis<sup>[6,7]</sup> and further studies failed to demonstrate GBV-C replication in the livers of patients infected with hepatitis viruses<sup>[8]</sup>.

Numerous efforts were also made to link GBV-C with other disease, like hepatocellular carcinoma, lichen planus, cryoglobulinemia, Sjogrens' syndrome and malignant or non-malignant hematological illnesses, but all have failed to identify a specific association with these diseases and GBV-C infection<sup>[19]</sup>.

However, an association between this virus and improved clinical course in HIV infected patients has been suggested and inverse relationship between GBV-C and HIV plasma viral load was demonstrated in some studies<sup>[1,42]</sup>. GBV-C infection modulates T cell homeostasis in vivo through different mechanisms, such as alteration of cytokine and chemokine release and receptor expression; reduce T cell activation, proliferation and apoptosis, all of them have a role in improving HIV clinical outcomes. In vitro studies confirm these clinical data and show a beneficial effect of GBV-C on HIV infection<sup>[28]</sup>.

Some recent studies were carried out to identify the association between HCV and GBV-C infection<sup>[45,46,47]</sup>. Barbosa *et al.*<sup>[45]</sup> showed the lower degree of hepatic lesions in HCV/HIV/GBV-C infected patients, in comparison to HCV/HIV co-infected cases. Boodram *et al.*<sup>[46]</sup> reported an increased rate of GBV-C clearance in HIV negative IDUs with HCV infection. Another survey demonstrated that co-infection with GBV-C in patients with chronic HCV does not worsen the clinical course of chronic hepatitis C or diminish response of HCV to viral therapy<sup>[47]</sup>.

## GBV-C GENOTYPES

Currently, GBV-C has been classified into six genotypes and many subtypes based on their sequence diversity of either full genome length or a particular genomic range. Geographically, these genotypes and subtypes showed distinct distribution patterns. Genotype 1 is found mainly in Ghana, Zaire and West Africa<sup>[3]</sup> and is divided into five subtypes; genotype 2 (sub-classified as both 2a and 2b) in the United States and Europe<sup>[48]</sup>, Egypt, Nepal, Thailand, India, Turkey, Saudi Arabia, Pakistan, UAE and Myanmar<sup>[24]</sup>; genotype 3 in Asia<sup>[49,50,51]</sup>, including Japan, Philippines, China and Bolivia; genotype 4 in Southeast Asia like Myanmar, Cambodia, and Vietnam<sup>[52]</sup>; genotype 5 in South Africa<sup>[53]</sup> and genotype 6 which first detected from blood donors and hepatitis patients living in Indonesia<sup>[54,55]</sup>.

In South America, the genotypes 1, 2a, 2b and 3 have been reported. In Colombia, a high prevalence of GBV-C RNA and presence of genotype 3 were found among Colombian native Indians<sup>[18]</sup>.

In the Middle East like Iran, Turkey, Saudi Arabia and UAE, the prominent GBV-C was genotype 2, subtype 2a<sup>[24]</sup>.

## GBV-C PREVALENCE IN DIFFERENT POPULATION

Studies on the prevalence and correlation of GBV-C infection among different populations have identified many risk factors for GBV-C infection, such as injecting drug use (IDU)<sup>[27,51]</sup>, receipt of blood transfusion<sup>[56,57]</sup>, increased number of sexual partners<sup>[58]</sup>, having had sex with other men<sup>[24,27,44,57]</sup>, history of sexually transmitted infections (STIs)<sup>[56,58]</sup>, healthcare work<sup>[59]</sup>, incarceration<sup>[56]</sup>, hospitalization for performing medical procedures<sup>[27]</sup>, endoscopy<sup>[58]</sup>, snorting cocaine<sup>[56]</sup> and history of travel to Africa<sup>[27]</sup>.

GBV-C viremia is found in about 20% of high risk patients for parenteral exposure to blood borne pathogens, and past exposure was found in some HCV infected individuals without evidence of active GBV-C infection. For example, in some populations, the evidence of past or active infection was found in up to 90%<sup>[16]</sup>. Other high risk groups for GBV-C infection include hemophiliacs, hemodialysis patients, transfusion recipients and commercial sex workers, as well as HCV and HIV infected subjects<sup>[7]</sup>.

Due to shared transmission routes, co-infection with GBV-C is common among HIV infected patient with or without HCV. 10%-25% of chronic HCV infected patients and 14%-36% of HIV positive IDUs show the evidence of GBV-C co-infection<sup>[60,61]</sup>. Some recent studies have shown much higher GBV-C triple infection rate of 30%-36% among HIV/HCV co-infected individuals<sup>[62,63]</sup>.

## GBV-C PREVALENCE IN SPECIFIC GROUPS

### Blood donors

In European countries, the prevalence of anti-E2 which indicate resolved infection ranges from 10.5% to 24.2%<sup>[37,64,65,66]</sup>, in South Africa (20.3%) and Brazil (19.5%), even higher anti-E2 prevalence rates have been recorded<sup>[64]</sup>. Anti-E2 has been found in 7.3% of Canadian<sup>[67]</sup>, 10.5% of Norwegian<sup>[66]</sup> and 11.3% of Russian blood donors<sup>[68]</sup>.

In United States, GBV-C prevalence in blood donors was reported ranging from 0.8% to 12.9%<sup>[41,69]</sup>. In Egypt, El-Zayadi *et al.*<sup>[43]</sup> found the prevalence rate 12.2% for GBV-C infection among blood donors and they also showed that GBV-C co-infection rate in HBV and HCV infected patients were 7.6 and 64.9%, respectively<sup>[18]</sup>.

In Asian countries<sup>[64,70]</sup>, anti-E2 seropositivity has been found to be significantly lower (2.5-6.3%). In Iranian volunteer blood donors the prevalence of GBV-C was around 1%<sup>[35]</sup>. In Turkey the prevalence of GBV-C was 5% in blood donors<sup>[71]</sup> and in Thailand the GBV-C RNA positivity among blood donors was 4.8%<sup>[72]</sup>. Although in blood donors in Taiwan, a higher prevalence (10.2%) has been reported<sup>[73]</sup>. Besides, another study among northeastern Thai blood donors carrying HBsAg and anti-HCV revealed a higher frequency of GBV-C RNA (10% and 11%, respectively) in the coinfected cases when compared with the controls<sup>[74]</sup>.

### Hemodialysis patients

Patients with chronic renal failure are at high risk of acquiring the GBV-C because they require frequent blood transfusions and undergo medical procedures that accompany bleeding<sup>[75,76]</sup>.

The prevalence of anti-E2 in HD patients has been established in several studies, this rate is variable from 3.89% in Iran<sup>[75]</sup>, 7% in Japan<sup>[78]</sup>, 12.9–29% in Germany<sup>[77,79]</sup>, 14.2% in Belgium<sup>[80]</sup>, 15.6% in Taiwan<sup>[81]</sup> to 22% in Austria<sup>[82]</sup>.

In a study in Egyptian children, anti-E2 was positive in 41.2% of HD and 28.8% of predialysis children<sup>[83]</sup>.

GBV-C RNA prevalence rates in HD patients ranged from 11.5 to 27% in the USA<sup>[84,85]</sup>, 6-57.5% in Europe<sup>[86,87]</sup> and in Asia, from less than 2.2% in India<sup>[88]</sup> to 55% in Indonesia<sup>[89]</sup>.

In a study of hemodialysis patients in Germany, antibodies against

GBV-C were detected in 17.5% of patients and viremia in 19.6%. In addition, 3% of the patients were positive for both antibodies and GBV-C RNA<sup>[90]</sup>. In another study in Iran, 13.6% of HD patients had GBV-C RNA<sup>[91]</sup>. In a Chinese study, 16.42% of dialysis patients were GBV-C RNA positive and the positive rate of GBV-C RNA increased with the number of times of dialysis<sup>[9]</sup>. Ramos *et al.*<sup>[92]</sup> reported that 14.6% of dialysis patients were GBV-C RNA positive in Brazil.

In a study conducted by Hanci *et al.*<sup>[71]</sup> in Turkey the prevalence of GBV-C RNA in hemodialysis patients was 14% but in another study by Ozdarendeli *et al.*<sup>[93]</sup>, GBV-C RNA was detected in 10.2% of HD patients.

In a study in Egyptian children, GBV-C RNA was positive in 26.5% of HD and 13.6% of predialysis children<sup>[83]</sup>.

Few reports are available in patients on peritoneal dialysis treatment, but these report rates ranging from 0 by Campo *et al.* to 10.5% by Hyunjin and 20% by Fabrizi *et al.*<sup>[75]</sup>.

## HIV INFECTED INDIVIDUALS

Over the past several years there has been substantial controversy regarding the interactions between GBV-C and HIV. A number of studies have revealed improved survival among HIV coinfected patients, as compared with those only infected with HIV<sup>[11,13,27,42]</sup>. Other studies, however, have not shown such a survival advantage<sup>[58,94]</sup>.

GBV-C viremia is associated with improved initial response to antiretroviral regimens and sustained suppression of HIV viral loads for prolonged periods<sup>[19]</sup>. It is also associated with increased CD4<sup>+</sup> cell count, and delayed progression to AIDS in many studies<sup>[28]</sup>.

Two GBV-C proteins that specifically inhibit HIV replication are E2 and NS5A. The GBV-C NS5A mediates HIV inhibition by decreasing the surface expression of CXCR4, a major HIV co-receptor. The E2 protein inhibits HIV gp 41 which is necessary for membrane fusion and viral entry. GBV-C and HIV co-infection leads to reduced expression of the two major HIV co-receptors, CCR5 and CXCR4, on CD4<sup>+</sup> cells in terminal HIV infection, which cause delayed progression of HIV in GBV-C/HIV co-infected patients<sup>[1,62]</sup>. Besides GBV-C can elevate the levels of T helper 1 (Th1) cytokines, especially interleukine-2 which effectively control HIV viral load<sup>[19,62]</sup>.

GBV-C has worldwide distribution with a varying prevalence in subjects infected with HIV. The GBV-C RNA prevalence in patients with HIV range from 11.3%-15.5% in Iran, 13.5% in Argentina, 14%-22% in Spain, 16.7% in Ghana, 21% in Brazil, 26.2% in the Russian Federation, 16.8%-27% in Germany, 41% in Italy, and 24.2-45% in France<sup>[14,34,44,61,95,96]</sup>.

The study included 41 Japanese HIV-infected hemophilia patients, GBV-C viremia was detected in 26.8% of patients<sup>[97]</sup> and in an investigation in Danish cohort of HIV-infected men 24% of patients were positive for GBV-C<sup>[98]</sup>. In another study in three cohorts of pregnant women in Thailand, the prevalence of GBV-C infection was 33% among HIV infected women<sup>[99]</sup>.

## HCV INFECTED PATIENTS

GBV-C and HCV co-infection is common and GBV-C infection is related to HCV endemicity. GBV-C does not seem to have any negative impact on the course of HCV-related chronic liver disease. GBV-C also does not have any affect on the liver histology, transaminase levels or response to antiviral therapy; it was shown that GBV-C is sensitive to interferon-alpha with a relapse rate up to 53% comparable to HCV<sup>[100]</sup>.

Among newly diagnosed cases of blood-borne viral hepatitis in the

United States, GBV-C reported in 18% of cases, and 80% of them were also HCV co-infected<sup>[101]</sup>.

In a study in Germany on HCV infected patients, 17.5% showed GBV-C co-infection. The rate of co-infection varied significantly according to geographical area; 20.5% in European vs. 10.9% in Japan (except some at risk groups such as IDUs, hemodialysis patients, patients after liver transplantation). Additionally, co-infection occurred in 38% of IDUs<sup>[100]</sup>.

Other studies have reported the incidence of GBV-C co-infection with HCV, varying from 3.2% in Colombian blood donors to 64.9% in Egyptian HCV infected patients<sup>[18,43]</sup>.

In Europe the prevalence of GBV-C infection in HCV infected patients, ranges from 16-21% in France<sup>[102,103]</sup>, 16% in UK<sup>[104]</sup>, 19-21% in Spain<sup>[105,106]</sup> and 24.4% in Germany<sup>[17]</sup>. In United States, GBV-C prevalence in patients with chronic HCV was reported about 20%<sup>[6]</sup>. GBV-C/HCV co infection was seen more prevalent in Asian countries such as Saudi Arabia (31%)<sup>[107]</sup>, China (31.5%)<sup>[108]</sup> and Iran (43.6%)<sup>[109]</sup>. Only in Japan this co-infection is low as 11% in HCV infected cases.

Little work has been done on HBV and GBV-C co-infection but it has been shown that GBV-C has no effect on HBV-DNA levels or disease progression<sup>[24]</sup>.

## SUMMARY

The GBV-C is an enveloped, single-stranded positive RNA virus belonging to the family Flaviviridae and has a close sequence homology to HCV.

Overall findings indicate that GBV-C infections generally are asymptomatic, transient and self-limiting and have not been associated with any known human disease; however, several studies found an association between GBV-C infection and improved survival in GBV-C/HIV co-infected patients.

GBV-C can be transmitted parenterally through blood and blood products, hemodialysis, intravenous drug use, sexual and vertical routes.

GBV-C viremia may persist for years but it is cleared eventually in 50–75% of cases and antibodies against GBV-C E2 envelope usually appear. GBV-C infection is relatively common and has a worldwide distribution. 1-5% of healthy blood donors in developed countries have GBV-C RNA in their sera. The prevalence is higher in blood donors from developing countries, which up to 20% of blood donors were viremic in some studies. Currently, GBV-C has been classified into six genotypes and many subtypes based on their sequence diversity.

The advances studies on GBV-C, especially in the context of HIV co-infection, should be carried out to identify the essential mechanisms of HIV clearance for future anti-HIV research. Better understanding of this influence of GBV-C on HIV infection is important to identify novel approaches to HIV therapy to slow the progression of HIV infection, without treatment problems such as drug resistance and toxicity.

## REFERENCES

- 1 Giret MT, Kallas EG. GBV-C: state of the art and future prospects. *Curr HIV/AIDS Rep* 2012; **9**: 26-33
- 2 Fukushi S, Kurihara C, Ishiyama N, Okamura H, Hoshino FB, Oya A, Katayama K. Nucleotide sequence of the 5' non-coding region of hepatitis G virus isolated from Japanese patients: comparison with reported isolates. *Biochem Biophys Res Commun* 1996; **226**: 314-318
- 3 Muerhoff AS, Simons JN, Leary TP, Erker JC, Chalmers ML, Pilot-Matias TJ, Dawson GJ, Desai SM, Mushahwar IK. Se-

- quence heterogeneity within the 5'-terminal region of the hepatitis GB virus C genome and evidence for genotypes. *J Hepatol* 1996; **25**: 379-384
- 4 Reed KE, Gorbalenya AE, Rice CM. The NS5A/NS5 proteins of viruses from three genera of the family flaviviridae are phosphorylated by associated serine/threonine kinases. *J Virol* 1998; **72**: 6199-6206
- 5 Feng Y, Zhao W, Feng Y, Dai J, Li Z, Zhang X, Liu L, Bai J, Zhang H, Lu L, Xia X. A novel genotype of GB virus C: its identification and predominance among injecting drug users in Yunnan, China. *PLoS One* 2011; **6**: e21151
- 6 Alter HJ. G-pers creepers, where'd you get those papers? A reassessment of the literature on the hepatitis G virus. *Transfusion* 1997; **37**: 569-572
- 7 Stapleton JT. GB virus type C/Hepatitis G virus. *Semin Liver Dis* 2003; **23**: 137-148
- 8 Radkowski M, Wang LF, Vargas H, Rakela J, Laskus T. Lack of evidence for GB virus C/hepatitis G virus replication in peripheral blood mononuclear cells. *J Hepatol* 1998; **28**: 179-183
- 9 Zhu WF, Yin LM, Li P, Huang J, Zhuang H. Pathogenicity of GB virus C on virus hepatitis and hemodialysis patients. *World J Gastroenterol* 2003; **9**: 1739-1742
- 10 Ruiz V, Giordano M, Rivero CW, Minassian ML, Cuestas ML, Trinks J, Mathet VL, Oubiña JR. GB virus C quasispecies detected in plasma and lymphocyte subsets in a natural human infection. *J Gen Virol* 2010; **91**: 1687-1692
- 11 Xiang J, Wünschmann S, Diekema DJ, Klinzman D, Patrick KD, George SL, Stapleton JT. Effect of coinfection with GB virus C on survival among patients with HIV infection. *N Engl J Med* 2001; **345**: 707-714
- 12 Yeo AE, Matsumoto A, Hisada M, Shih JW, Alter HJ, Goedert JJ. Effect of hepatitis G virus infection on progression of HIV infection in patients with hemophilia. Multicenter Hemophilia Cohort Study. *Ann Intern Med* 2000; **132**: 959-963
- 13 Williams CF, Klinzman D, Yamashita TE, Xiang J, Polgreen PM, Rinaldo C, Liu C, Phair J, Margolick JB, Zdunek D, Hess G, Stapleton JT. Persistent GB virus C infection and survival in HIV-infected men. *N Engl J Med* 2004; **350**: 981-990
- 14 Alves-Sousa VK, Komninakis SC, Baggio-Zappia GL, Barbosa AJ, Mantovani NP, Diaz RS, Abrão P, Lanzara GA, Granato CF. Short communication: Evaluation of GB virus C/hepatitis G viral load among HIV type 1-coinfected patients in São Paulo, Brazil. *AIDS Res Hum Retroviruses* 2012; **28**: 1301-1304
- 15 Casteling A, Song E, Sim J, Blaauw D, Heyns A, Schweizer R, Margolick L, Kuun E, Field S, Schoub B, Vardas E. GB virus C prevalence in blood donors and high risk groups for parenterally transmitted agents from Gauteng, South Africa. *J Med Virol* 1998; **55**: 103-108
- 16 Thomas DL, Nakatsuji Y, Shih JW, Alter HJ, Nelson KE, As-temborski JA, Lyles CM, Vlahov D. Persistence and clinical significance of hepatitis G virus infections in injecting drug users. *J Infect Dis* 1997; **176**: 586-592
- 17 Feucht HH, Zollner B, Polywka S, Laufs R. Vertical transmission of hepatitis G. *Lancet* 1996; **347**: 615-616
- 18 Alvarado-Mora MV, Botelho L, Nishiya A, Neto RA, Gomes-Gouvêa MS, Gutierrez MF, Carrilho FJ, Pinho JR. Frequency and genotypic distribution of GB virus C (GBV-C) among Colombian population with Hepatitis B (HBV) or Hepatitis C (HCV) infection. *Virol J* 2011; **8**: 345
- 19 Shankar EM, Balakrishnan P, Vignesh R, Velu V, Jayakumar P, Solomon S. Current Views on the Pathophysiology of GB Virus C Coinfection with HIV-1 Infection. *Curr Infect Dis Rep* 2011; **13**: 47-52
- 20 Lyra AC, Pinho JR, Silva LK, Sousa L, Saraceni CP, Braga EL, Pereira JE, Zarife MA, Reis MG, Lyra LG, Silva LC, Carrilho FJ. HEV, TTV and GBV-C/HGV markers in patients with acute viral hepatitis. *Braz J Med Biol Res* 2005; **38**: 767-775
- 21 Liu HF, Cornu C, Jadoul M, Dahan K, Loute G, Goubau P. Molecular analysis of GB virus C isolates in Belgian hemo-

- dialysis patients. *J Med Virol* 1998; **55**: 118-122
- 22 Seifried C, Weber M, Bialleck H, Seifried E, Schrezenmeier H, Roth WK. High prevalence of GBV-C/HGV among relatives of GBV-C/HGV-positive blood donors in blood recipients and in patients with aplastic anemia. *Transfusion* 2004; **44**: 268-274
  - 23 Frey SE, Homan SM, Sokol-Anderson M, Cayco MT, Cortoreal P, Musial CE, Di Bisceglie A. Evidence for probable sexual transmission of the hepatitis g virus. *Clin Infect Dis* 2002; **34**: 1033-1038
  - 24 Berzsenyi MD, Bowden DS, Roberts SK. GB virus C: insights into co-infection. *J Clin Virol* 2005; **33**: 257-266
  - 25 Björkman P, Nauclér A, Winqvist N, Mushahwar I, Widell A. A case-control study of transmission routes for GB virus C/hepatitis G virus in Swedish blood donors lacking markers for hepatitis C virus infection. *Vox Sang* 2001; **81**: 148-153
  - 26 Posada D, Crandall KA. MODELTEST: testing the model of DNA substitution. *Bioinformatics* 1998; **14**: 817-818
  - 27 Lefrère JJ, Loiseau P, Maury J, Lasserre J, Mariotti M, Ravera N, Lerable J, Lefèvre G, Morand-Joubert L, Girot R. Natural history of GBV-C/hepatitis G virus infection through the follow-up of GBV-C/hepatitis G virus-infected blood donors and recipients studied by RNA polymerase chain reaction and anti-E2 serology. *Blood* 1997; **90**: 3776-3780
  - 28 Bhattarai N, Stapleton JT. GB virus C: the good boy virus? *Trends Microbiol* 2012; **20**: 124-130
  - 29 Kleinman S. Hepatitis G virus biology, epidemiology, and clinical manifestations: Implications for blood safety. *Transfus Med Rev* 2001; **15**: 201-212
  - 30 Thomas DL, Vlahov D, Alter HJ, Hunt JC, Marshall R, Astemborski J, Nelson KE. Association of antibody to GB virus C (hepatitis G virus) with viral clearance and protection from reinfection. *J Infect Dis* 1998; **177**: 539-542
  - 31 Tanaka E, Kiyosawa K, Shimoda K, Hino K, Tacke M, Schmolke S, Engel AM, Hess G. Evolution of hepatitis G virus infection and antibody response to envelope protein in patients with transfusion-associated non-A, non-B hepatitis. *J Viral Hepat* 1998; **5**: 153-159
  - 32 Chen HL, Chang MH, Lin HH, Ni YH, Hsu HY, Wang JT, Chen DS. Antibodies to E2 protein of hepatitis G virus in children: different responses according to age at infection. *J Pediatr* 1998; **133**: 382-385
  - 33 George SL, Wünschmann S, McCoy J, Xiang J, Stapleton JT. Interactions Between GB Virus Type C and HIV. *Curr Infect Dis Rep* 2002; **4**: 550-558
  - 34 Polgreen PM, Xiang J, Chang Q, Stapleton JT. GB virus type C/hepatitis G virus: a non-pathogenic flavivirus associated with prolonged survival in HIV-infected individuals. *Microbes Infect* 2003; **5**: 1255-1261
  - 35 Ramezani A, Gachkar L, Eslamifar A, Khoshbaten M, Jalilvand S, Adibi L, Salimi V, Hamkar R. Detection of hepatitis G virus envelope protein E2 antibody in blood donors. *Int J Infect Dis* 2008; **12**: 57-61
  - 36 Mushahwar IK, Zuckerman JN. Clinical implications of GB virus C. *J Med Virol* 1998; **56**: 1-3
  - 37 Tacke M, Schmolke S, Schlueter V, Sauleda S, Esteban JI, Tanaka E, Kiyosawa K, Alter HJ, Schmitt U, Hess G, Ofenloch-Haehnle B, Engel AM. Humoral immune response to the E2 protein of hepatitis G virus is associated with long-term recovery from infection and reveals a high frequency of hepatitis G virus exposure among healthy blood donors. *Hepatology* 1997; **26**: 1626-1633
  - 38 Bhanich Supapol W, Remis RS, Raboud J, Millson M, Tappero J, Kaul R, Kulkarni P, McConnell MS, Mock PA, McNicholl JM, Roongpisuthipong A, Chotpitayasunondh T, Shaffer N, Butera S. Prevalence and correlates of GB virus C infection in HIV-infected and HIV-uninfected pregnant women in Bangkok, Thailand. *J Med Virol* 2011; **83**: 33-44
  - 39 Mohr EL, Stapleton JT. GB virus type C interactions with HIV: the role of envelope glycoproteins. *J Viral Hepat* 2009; **16**: 757-768
  - 40 Stapleton JT, Fong S, Muerhoff AS, Bukh J, Simmonds P. The GB viruses: a review and proposed classification of GBV-A, GBV-C (HGV), and GBV-D in genus Pegivirus within the family Flaviviridae. *J Gen Virol* 2011; **92**: 233-246
  - 41 Dawson GJ, Schlauder GG, Pilot-Matias TJ, Thiele D, Leary TP, Murphy P, Rosenblatt JE, Simons JN, Martinson FE, Gutierrez RA, Lentino JR, Pachucki C, Muerhoff AS, Widell A, Tegtmeier G, Desai S, Mushahwar IK. Prevalence studies of GB virus-C infection using reverse transcriptase-polymerase chain reaction. *J Med Virol* 1996; **50**: 97-103
  - 42 Tillmann HL, Manns MP. GB virus-C infection in patients infected with the human immunodeficiency virus. *Antiviral Res* 2001; **52**: 83-90
  - 43 El-Zayadi AR, Abe K, Selim O, Naito H, Hess G, Ahdy A. Prevalence of GBV-C/hepatitis G virus viraemia among blood donors, health care personnel, chronic non-B non-C hepatitis, chronic hepatitis C and hemodialysis patients in Egypt. *J Virol Methods* 1999; **80**: 53-58
  - 44 Rey D, Vidinic-Moullard J, Meyer P, Schmitt C, Fritsch S, Lang JM, Stoll-Keller F. High prevalence of GB virus C/hepatitis G virus RNA and antibodies in patients infected with human immunodeficiency virus type 1. *Eur J Clin Microbiol Infect Dis* 2000; **19**: 721-724
  - 45 Barbosa Ade J, Baggio-Zappia GL, Dobo C, Alves-Sousa VK, Lanzara Gde A, Silva ID, Lanzoni VP, Granato CF. Analysis of GB virus C infection among HIV-HCV coinfecting patients. *Rev Soc Bras Med Trop* 2009; **42**: 591-593
  - 46 Boodram B, Hershow RC, Klinzman D, Stapleton JT. GB virus C infection among young, HIV-negative injection drug users with and without hepatitis C virus infection. *J Viral Hepat* 2011; **18**: e153-e159
  - 47 Hofer H, Aydin I, Neumueller-Guber S, Mueller C, Scherzer TM, Stauer K, Steindl-Munda P, Wrba F, Ferenci P. Prevalence and clinical significance of GB virus type C/hepatitis G virus coinfection in patients with chronic hepatitis C undergoing antiviral therapy. *J Viral Hepat* 2011; **18**: 513-517
  - 48 Muerhoff AS, Smith DB, Leary TP, Erker JC, Desai SM, Mushahwar IK. Identification of GB virus C variants by phylogenetic analysis of 5'-untranslated and coding region sequences. *J Virol* 1997; **71**: 6501-6508
  - 49 Okamoto H, Nakao H, Inoue T, Fukuda M, Kishimoto J, Iizuka H, Tsuda F, Miyakawa Y, Mayumi M. The entire nucleotide sequences of two GB virus C/hepatitis G virus isolates of distinct genotypes from Japan. *J Gen Virol* 1997; **78** ( Pt 4): 737-745
  - 50 Mukaide M, Mizokami M, Orito E, Ohba K, Nakano T, Ueda R, Hikiji K, Iino S, Shapiro S, Lahat N, Park YM, Kim BS, Oyunsuren T, Rezieg M, Al-Ahdal MN, Lau JY. Three different GB virus C/hepatitis G virus genotypes. Phylogenetic analysis and a genotyping assay based on restriction fragment length polymorphism. *FEBS Lett* 1997; **407**: 51-58
  - 51 Katayama K, Kageyama T, Fukushi S, Hoshino FB, Kurihara C, Ishiyama N, Okamura H, Oya A. Full-length GBV-C/HGV genomes from nine Japanese isolates: characterization by comparative analyses. *Arch Virol* 1998; **143**: 1063-1075
  - 52 Naito H, Win KM, Abe K. Identification of a novel genotype of hepatitis G virus in Southeast Asia. *J Clin Microbiol* 1999; **37**: 1217-1220
  - 53 Tucker TJ, Smuts H, Eickhaus P, Robson SC, Kirsch RE. Molecular characterization of the 5' non-coding region of South African GBV-C/HGV isolates: major deletion and evidence for a fourth genotype. *J Med Virol* 1999; **59**: 52-59
  - 54 Handajani R, Soetjipto MI, Suryohudoyo P, Adi P, Setiawan PB, Nidom CA, Soemarto R, Katayama Y, Fujii M, Hotta H. Prevalence of GB virus C/Hepatitis G virus infection among various populations in Surabaya, Indonesia, and identification of novel groups of sequence variants. *J Clin Microbiol* 2000; **38**: 662-668
  - 55 Muerhoff AS, Dawson GJ, Desai SM. A previously unrecog-

- nized sixth genotype of GB virus C revealed by analysis of 5'-untranslated region sequences. *J Med Virol* 2006; **78**: 105-111
- 56 Petrik J, Guella L, Wight DG, Pearson GM, Hinton J, Parker H, Allain JP, Alexander GJ. Hepatic histology in hepatitis C virus carriers coinfecting with hepatitis G virus. *Gut* 1998; **42**: 103-106
- 57 Hekmat S, Mohraz M, Vahabpour R, Jam S, Bahramali G, Banifazl M, Aghakhani A, Eslamifard A, Mahboudi F, Edalat R, Ramezani A. Frequency and genotype of GB virus C among Iranian patients infected with HIV. *J Med Virol* 2008; **80**: 1941-1946
- 58 Schwarze-Zander C, Blackard JT, Zheng H, Addo MM, Lin W, Robbins GK, Sherman KE, Zdunek D, Hess G, Chung RT. GB virus C (GBV-C) infection in hepatitis C virus (HCV)/HIV-coinfecting patients receiving HCV treatment: importance of the GBV-C genotype. *J Infect Dis* 2006; **194**: 410-419
- 59 Berzsenyi MD, Bowden DS, Kelly HA, Watson KM, Mijch AM, Hammond RA, Crowe SM, Roberts SK. Reduction in hepatitis C-related liver disease associated with GB virus C in human immunodeficiency virus coinfection. *Gastroenterology* 2007; **133**: 1821-1830
- 60 Tan D, Matsumoto A, Conry-Cantilena C, Melpolder JC, Shih JW, Leuther M, Hess G, Gibble JW, Ness PM, Alter HJ. Analysis of hepatitis G virus (HGV) RNA, antibody to HGV envelope protein, and risk factors for blood donors coinfecting with HGV and hepatitis C virus. *J Infect Dis* 1999; **179**: 1055-1061
- 61 Stark K, Doering CD, Bienzle U, Pauli G, Hamouda O, Engel AM, Schreiber E. Risk and clearance of GB virus C/hepatitis G virus infection in homosexual men: A longitudinal study. *J Med Virol* 1999; **59**: 303-306
- 62 Bjorkman P, Naucler A, Winqvist N, Mushahwar I, Widell A. A case-control study of transmission routes for GB virus C/hepatitis G virus in Swedish blood donors lacking markers for hepatitis C virus infection. *Vox Sang* 2001; **81**: 148-153
- 63 Christensen PB, Fisker N, Mygind LH, Krarup HB, Wedderkopp N, Varming K, Georgsen J. GB virus C epidemiology in Denmark: different routes of transmission in children and low- and high-risk adults. *J Med Virol* 2003; **70**: 156-162
- 64 Ross RS, Viazov S, Schmitt U, Schmolke S, Tacke M, Ofenloch-Haehnle B, Holtmann M, Müller N, Da Villa G, Yoshida CF, Oliveira JM, Szabo A, Paladi N, Kruppenbacher JP, Philipp T, Roggendorf M. Distinct prevalence of antibodies to the E2 protein of GB virus C/hepatitis G virus in different parts of the world. *J Med Virol* 1998; **54**: 103-106
- 65 Brojer E, Grabarczyk P, Kryczka W, Kucharski W, Kubicka J, Zupánska B. Analysis of hepatitis G virus infection markers in blood donors and patients with hepatitis. *J Viral Hepat* 1999; **6**: 471-475
- 66 Nordbø SA, Krokstad S, Winge P, Skjeldestad FE, Dalen AB. Prevalence of GB virus C (also called hepatitis G virus) markers in Norwegian blood donors. *J Clin Microbiol* 2000; **38**: 2584-2590
- 67 Giulivi A, Slinger R, Tepper M, Sher G, Scalia V, Kessler G, Gill P. Prevalence of GBV-C/hepatitis G virus viremia and anti-E2 in Canadian blood donors. *Vox Sang* 2000; **79**: 201-205
- 68 Novikov DV, Pimenov VK, Samokhvalov EI, Mokhonov VV, Kolobov AA, Kopnina EO, Matveeva EM, Kuzin SN, Shatalov AG, Prilipov AG, Selivanov NA, L'vov DK. Determination of hepatitis G virus markers in various risk groups. *Vopr Virusol* 2000; **45**: 20-22
- 69 Linnen J, Wages J, Zhang-Keck ZY, Fry KE, Krawczynski KZ, Alter H, Koonin E, Gallagher M, Alter M, Hadziyannis S, Karayiannis P, Fung K, Nakatsuji Y, Shih JW, Young L, Piatak M, Hoover C, Fernandez J, Chen S, Zou JC, Morris T, Hyams KC, Ismay S, Lifson JD, Hess G, Fong SK, Thomas H, Bradley D, Margolis H, Kim JP. Molecular cloning and disease association of hepatitis G virus: a transfusion-transmissible agent. *Science* 1996; **271**: 505-508
- 70 Saitoh H, Moriyama M, Matsumura H, Goto I, Tanaka N, Aarakawa Y. The clinical significance of GBV-C/HGV exposure in C-viral chronic liver disease and blood donors. *Hepatol Res* 2002; **22**: 288-296
- 71 Hanci SY, Cevahir N, Kaleli I, Hanci V. [Investigation of hepatitis G virus prevalence in hemodialysis patients and blood donors in Denizli, Turkey]. *Mikrobiyol Bul* 2008; **42**: 617-625
- 72 Wiwanitkit V. Hepatitis G, hepatitis SEN, hepatitis TT and hepatitis TT-like viruses: New emerging hepatitis viruses in pediatric patients. *J Ped Infect Dis* 2006; **1**: 83-88
- 73 Yang JF, Dai CY, Chuang WL, Lin WY, Lin ZY, Chen SC, Hsieh MY, Wang LY, Tsai JF, Chang WY, Yu ML. Prevalence and clinical significance of HGV/GBV-C infection in patients with chronic hepatitis B or C. *Jpn J Infect Dis* 2006; **59**: 25-30
- 74 Barusruk S, Urwijitaroon Y. High prevalence of HGV coinfection with HBV or HCV among northeastern Thai blood donors. *Southeast Asian J Trop Med Public Health* 2006; **37**: 289-293
- 75 Eslamifard A, Hamkar R, Ramezani A, Ahmadi F, Gachkar L, Jalilvand S, Adibi L, Atabak S, Khameneh A, Ghadimi R, Aghakhani A. Hepatitis G virus exposure in dialysis patients. *Int Urol Nephrol* 2007; **39**: 1257-1263
- 76 Eslamifard A, Hamkar R, Ramezani A, Ahmadi F, Gachkar L, Jalilvand S, Adibi L, Khameneh A, Atabak S, Ghadimi R, Aghakhani A. Hepatitis G virus exposure in dialysis staff. *Ther Apher Dial* 2007; **11**: 370-374
- 77 Schulte-Frohlinde E, Schmolke S, Reindl W, Schätzle G, Scherf J, Kopp KF, Classen M, Schlüter V. Significance of antibodies to the recombinant E2 protein of hepatitis G virus in haemodialysis patients. *J Viral Hepat* 1998; **5**: 341-344
- 78 Shibuya A, Takeuchi A, Kamata K, Saigenji K, Kobayashi N, Yoshida A. Prevalence of hepatitis G virus RNA and anti-E2 in a Japanese haemodialysis population. *Nephrol Dial Transplant* 1998; **13**: 2033-2036
- 79 Szabo A, Viazov S, Heemann U, Kribben A, Philipp T, Roggendorf M. GBV-C/HGV infection in renal dialysis and transplant patients. *Nephrol Dial Transplant* 1997; **12**: 2380-2384
- 80 Kallinowski B, Ahmadi R, Seipp S, Bommer J, Stremmel W. Clinical impact of GB-C virus in haemodialysis patients. *Nephrol Dial Transplant* 1998; **13**: 93-98
- 81 Huang JJ, Lee WC, Ruaan MK, Wang MC, Chang TT, Young KC. Incidence, transmission, and clinical significance of hepatitis G virus infection in hemodialysis patients. *Eur J Clin Microbiol Infect Dis* 2001; **20**: 374-379
- 82 Tribl B, Oesterreicher C, Pohanka E, Sunder-Plassmann G, Petermann D, Müller C. GBV-C/HGV in hemodialysis patients: anti-E2 antibodies and GBV-C/HGV-RNA in serum and peripheral blood mononuclear cells. *Kidney Int* 1998; **53**: 212-216
- 83 Hammad AM, Zaghoul MH. Hepatitis G virus infection in Egyptian children with chronic renal failure (single centre study). *Ann Clin Microbiol Antimicrob* 2009; **8**: 36
- 84 Bastani B, Frenche D, Gellens M, Di Bisceglie A. Infection with hepatitis G (HGV) and hepatitis C (HCV) in patients on chronic haemodialysis. *Am J Nephrol* 1996; **9**: 199A.
- 85 de Medina M, Ashby M, Schlüter V, Hill M, Leclercq B, Pennell JP, Jeffers LJ, Reddy KR, Schiff ER, Hess G, Perez GO. Prevalence of hepatitis C and G virus infection in chronic hemodialysis patients. *Am J Kidney Dis* 1998; **31**: 224-226
- 86 de Lamballerie X, Charrel RN, Dussol B. Hepatitis GB virus C in patients on hemodialysis. *N Engl J Med* 1996; **334**: 1549
- 87 Corun C, Jadoul M, Loute G, Goubau P. Hepatitis G virus infection in haemodialysis patients: epidemiology and clinical relevance. *Nephrol Dial Transplant* 1997; **12**: 1326-1329

- 88 Desai MM, Pal RB, Banker DD. GB virus C/hepatitis G virus infection in Indian blood donors and high-risk groups. *Transfus Apher Sci* 2004; **30**: 111-117
- 89 Tsuda F, Hadiwandowo S, Sawada N, Fukuda M, Tanaka T, Okamoto H, Miyakawa Y, Mayumi M. Infection with GB virus C (GBV-C) in patients with chronic liver disease or on maintenance hemodialysis in Indonesia. *J Med Virol* 1996; **49**: 248-252
- 90 Hinrichsen H, Leimenstoll G, Stegen G, Schrader H, Fölsch UR, Schmidt WE. Prevalence of and risk factors for hepatitis G (HGV) infection in haemodialysis patients: a multicentre study. *Nephrol Dial Transplant* 2002; **17**: 271-275
- 91 Hosseini-Moghaddam SM, Keyvani H, Samadi M, Alavian SM, Mahdavi-mazdeh M, Daneshvar S, Razzaghi Z. GB virus type C infection in hemodialysis patients considering co-infection with hepatitis C virus. *J Med Virol* 2008; **80**: 1260-1263
- 92 Ramos Filho R, Carneiro MA, Teles SA, Dias MA, Cardoso DD, Lampe E, Yoshida CF, Martins RM. GB virus C/hepatitis G virus infection in dialysis patients and kidney transplant recipients in Central Brazil. *Mem Inst Oswaldo Cruz* 2004; **99**: 639-643
- 93 Ozdarendeli A, Toroman ZA, Kalkan A, Kilic SS, Ozden M, Doymaz MZ. Prevalence and genotypes of hepatitis G virus among hemodialysis patients in Eastern Anatolia, Turkey. *Med Princ Pract* 2005; **14**: 102-106
- 94 Birk M, Lindbäck S, Lidman C. No influence of GB virus C replication on the prognosis in a cohort of HIV-1-infected patients. *AIDS* 2002; **16**: 2482-2485
- 95 Haji Molla Hoseini M, Pourfathollah AA, Mohraz M, Soheili Z, Amini S, Aghaiepour M, Samiee S, Nikoogoftar M, Meshkani R. Evaluation of circulating natural type 1 interferon-producing cells in HIV/GBV-C and HIV/HCV coinfecting patients: a preliminary study. *Arch Med Res* 2007; **38**: 868-875
- 96 Massud I, Corti M, de Tezanos Pinto M, Pérez Bianco R, Picchio G, Baré P. Prevalence of hepatitis G virus infection in a cohort of hemophilic HIV positive patients. *Medicina (B Aires)* 2002; **62**: 173-175
- 97 Toyoda H, Fukuda Y, Hayakawa T, Takamatsu J, Saito H. Effect of GB virus C/hepatitis G virus coinfection on the course of HIV infection in hemophilia patients in Japan. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998; **17**: 209-213
- 98 Ryt-Hansen R, Katzenstein TL, Gerstoft J, Eugen-Olsen J. No influence of GB virus C on disease progression in a Danish cohort of HIV-infected men. *AIDS Res Hum Retroviruses* 2006; **22**: 496-498
- 99 Bhanich Supapol W, Remis RS, Raboud J, Millson M, Tappero J, Kaul R, Kulkarni P, McConnell MS, Mock PA, McNicholl JM, Roongpisuthipong A, Chotpitayasunondh T, Shaffer N, Butera S. Prevalence and correlates of GB virus C infection in HIV-infected and HIV-uninfected pregnant women in Bangkok, Thailand. *J Med Virol* 2011; **83**(1): 33-44
- 100 Rambusch EG, Wedemeyer H, Tillmann HL, Heringlake S, Manns MP. Significance of coinfection with hepatitis G virus for chronic hepatitis C--a review of the literature. *Z Gastroenterol* 1998; **36**: 41-53
- 101 Di Bisceglie AM. Hepatitis G virus infection: a work in progress. *Ann Intern Med* 1996; **125**: 772-773
- 102 Pawlowsky JM, Roudot-Thoraval F, Muerhoff AS, Pellerin M, Germanidis G, Desai SM, Bastie A, Darthuy F, Rémiré J, Zafrani ES, Soussy CJ, Mushahwar IK, Dhumeaux D. GB virus C (GBV-C) infection in patients with chronic hepatitis C. Influence on liver disease and on hepatitis virus behaviour: effect of interferon alfa therapy. *J Med Virol* 1998; **54**: 26-37
- 103 Martinot M, Marcellin P, Boyer N, Detmer J, Pouteau M, Castelnau C, Degott C, Aupérin A, Collins M, Kolberg J, Wilber J, Benhamou JP, Erlinger S. Influence of hepatitis G virus infection on the severity of liver disease and response to interferon-alpha in patients with chronic hepatitis C. *Ann Intern Med* 1997; **126**: 874-881
- 104 Hollingsworth RC, Minton EJ, Fraser-Moodie C, Metivier E, Rizzi PM, Irving WL, Jenkins D, Ryder SD. Hepatitis G infection: role in cryptogenic chronic liver disease and primary liver cell cancer in the UK. Trent Hepatitis C virus Study Group. *J Viral Hepat* 1998; **5**: 165-169
- 105 Quirós E, Piédrola G, Maroto MC. GBV-C RNA presence in several high-risk groups of Spain. *Eur J Epidemiol* 1998; **14**: 617-619
- 106 Sauleda S, Reesink HJ, Esteban JI, Hess G, Esteban R, Guardia J. Profiles of GBV-C/hepatitis G virus markers in patients coinfecting with hepatitis C virus. *J Med Virol* 1999; **59**: 45-51
- 107 Al-Knawy B, Okamoto H, Ahmed EL-Mekki A, Elbagir Khalafalla M, Al Wabel A, Qazi F, Khan A, Shatoor A. Distribution of hepatitis C genotype and co-infection rate with hepatitis G in Saudi Arabia. *Hepatol Res* 2002; **24**: 95
- 108 Yan J, Dennin RH. A high frequency of GBV-C/HGV coinfection in hepatitis C patients in Germany. *World J Gastroenterol* 2000; **6**: 833-841
- 109 Ghanbari R, Ravanshad M, Hosseini SY, Yaghoobi R, Shahzamani K. Genotyping and infection rate of GBV-C among Iranian HCV- infected patients. *Hepat Mon* 2010; **10**: 80-87
- 110 Kao JH, Chen PJ, Lai MY, Chen W, Chen DS. Effects of GB virus-C/hepatitis G virus on hepatitis B and C viremia in multiple hepatitis virus infections. *Arch Virol* 1998; **143**: 797-802
- Peer reviewer:** Natthawut Kaewpitoon, PhD, assistant professor, Head of Parasitic Disease Research Center, Institute of Medicine, Suranaree University of Technology, Nakhon Ratchasima, Thailand.