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Hepatitis G Viruses (HGV): A Study on Prevalence, Transmission, and Co-Infection

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Abstract

Hepatitis virus infection is an increasing severe life-threating complication that gradually damages the liver. Hepatitis G is identified as a blood-borne pathogen that can cause various problems in human body. The hepatitis G virus (HGV) is also known as GB virus C (GBV-C) that is a newly described human virus of member of the Flaviviridae family and is similar genome organization as hepatitis C virus (HCV), and may be a cause of chronic liver disease. Some investigations have demanded that it is not associated with any known disease, but may be a cause of co-infection with HBV, HCV and HIV infection. The HGV is widespread around the world that has been ascertained to influence course and prognosis in the HIV-infected patient. It has been detected in patients with idiopathic fulminant hepatic failure (FHF) and hepatocellular carcinoma. It can be transmitted by blood transfusion, volunteer blood donors, and other parenteral processes. At present very little information is available about hepatitis G virus (HGV) infection and pathogenesis. This study tries to discuss the virology, symptoms, transmission, and co-infection of the HGV.

Keywords: GBV-C, fulminant hepatic failure, blood donor, co-infection

1. Introduction

Hepatitis G is a viral infection that is caused by hepatitis G virus (HGV), which is first isolated from the serum of hepatitis patients in 1995. The GBV-C genome is similar to hepatitis C virus (HCV) RNA in its organization (Linnen et al., 1996). Some studies suggested that GBV-C is a major cause of life-threatening liver diseases, such as acute hepatic failure, chronic hepatitis, liver cirrhosis, hepatocellular carcinoma (HCC) and relatively rare fatal fulminant hepatitis. The ALT levels may be increased in GBV-C infected persons (Mulrooney-Cousins & Michalak, 2024). There is also controversy about the role of HGV infection in the pathogenesis of chronic liver disease. Some clinical studies suggest that HGV does not cause chronic liver disease in human (Linnen et al., 1996).

In the mid-1960s, German microbiologist and virologist Friedrich W. Deinhardt (1926-1992) and his colleagues were the first to demonstrate the transmission of human viral hepatitis in non-human primates (Deinhardt et al., 1967). The GBV-C was discovered through the study of cases of hepatitis non-A, non-B, non-E by two independent groups of investigators at Abbott Laboratories and GeneLabs of the USA (Simons et al., 1995). The GBV-C is named after a 34-year-old surgeon, Frederick George Barker (GB), who fell ill in 1966 with a non-A non-B, non-C hepatitis which at the time was thought to have been caused by a new infectious hepatic virus (Reshetnyak et al., 2008). Later, the putative agent contained in this inoculum has been referred to as the ‘GB agent’ (Zuckerman, 1995).

The GBV-C is isolated in 1996 that causes acute and chronic infection, and often infects persons already infected with hepatitis C virus (HCV). As it infects human beings, it was renamed as human pegivirus type 1 (HPgV-1)

(Xiang et al., 2004). There are three types of GB viruses, GBV-A, GBV-B, and GBV-C. The first two forms: GBV-A and, GBV-B belonging to closely-related viruses of the Flaviviridae family are considered as tamarin agents that can be spread to animals, and only GBV-B caused hepatitis. The third virus GBV-C is the most likely viral hepatitis candidate in humans (Simons et al., 1995). Approximately 2% of blood donors and 15-20% of injection drug users in the USA have detectable GBV-C RNA (Barusruk & Urwijitaroon, 2006). GBV-C infection is common among HIV-positive people, and several studies have found that HIV-positive individuals co-infected with GBV-C survive significantly for longer periods of time than HIV infected people without GBV-C (Polgreen et al., 2003).

2. Literature Review

The literature review is an introductory section of a scholarly research that tries to designate the contributions of other scholars in the same research field (Polit & Hungler, 2013). It helps the new researchers to appreciate the subject matter, and also it serves as an indicator of the subject that has been carried out before (Creswell, 2007). Patricia M. Mulrooney-Cousins and Tomasz I. Michalak have overviewed the current molecular methods of detection and quantification of hepatitis virus genomes, with special emphasis on the assays commercially available and applicable for clinical use (Mulrooney-Cousins & Michalak, 2024). Juan Carlos Saiz and his coworkers have studied the RNA sequences of the recently identified HGV to detect idiopathic fulminant hepatic failure (FHF) in patients but the role of this agent in the disease remains controversial (Sáiz, 1997).

Maria Teresa Maidana and her coauthors have found an interesting interaction pattern between HIV-1 and GBV-C/HGV that results protection against progression to AIDS (Maidana et al., 2005). Lubna Qureshi and her coauthors have observed that the prevalence of HGV was 3.6% in liver disease and more prone in male with younger ages, and it was also correlated with HCV and HDV (Qureshi et al., 2020). Vasiliy Ivanovich Reshetnyak and his coworkers have shown that GBV-C has been ascertained to influence course and prognosis in the HIV-infected patient. They have observed that the frequent presence of GBV-C in co-infections, hematological diseases, and biliary pathology gives no grounds to determine it as an “accidental tourist” that is of no significance (Reshetnyak et al., 2008).

Viroj Wiwanitkit has tried to inform that GBV-C is transmitted through the blood and blood products, sexually, and vertically from infected mothers to children. He has also studied the prevalence of HGV infection among the voluntary blood donors in the previous reports (Wiwanitkit, 2005). Angelo Pavesi has studied the origin and evolution of GBV-C using a set of fully sequenced strains of worldwide origin (Pavesi, 2001). Sharon E. Frey and her coauthors have studied a cross-sectional epidemiology to evaluate the role of sexual activity and sexually transmitted diseases (STDs) in the transmission of HGV and other hepatitis virus infections (Frey et al., 2002). Amitis Ramezani and her coworkers have wanted to determine the frequency of HGV exposure in Iranian blood donors as well as co-infection with HBV and HCV, and also the co-existence of HGV RNA and anti-HGV (Ramezani et al., 2008).

3. Research Methodology of the Study

Research is an essential and influential tool to the academicians to lead the academic atmosphere. It tries to remove existing mistakes and misconceptions, and adds new knowledge with the present stock of knowledge (Pandey & Pandey, 2015). Methodology is an organized and meaningful procedural works that tries to describe the types of research and the types of data (Somekh & Lewin, 2005). It relates to nature and power to science, truth, and epistemology (Ramazanoglu & Holland, 2002). Research methodology is the procedure to perform research in a systematic and process-oriented way that provides a guideline to the researchers to investigate a problem (Abbasi, 2015). To rationalize the selection of a research methodology, a researcher must understand its philosophical origins and unique characteristics (Rieger, 2019).

To prepare this article, I have consulted secondary data sources related to hepatitis viruses (Mohajan, 2024a-k). I have prepared this paper by consulting the books of famous authors, journals, handbooks, theses, and also by taking the help from the internet, websites, etc. (Mohajan, 2017, 2018, 2020; Mohajan & Mohajan, 2023a-d).

4. Objective of the Study

Main objective of this article is to discuss the aspects of global HGV infection. The blood donors are in high risk of the HGV infection through blood transfusion. The HGV is a new member of hepatotropic virus belonging to the family of Flavivirldae (Wang et al., 2019). Other minor objectives of the study are as follows:

1) to focus on virology of HGV,

2) to highlight on symptoms, diagnosis, and treatment of HGV, and

3) to discuss the transmission of HGV.

5. Virology of HGV

The HGV is a single-stranded, spherical enveloped, positive-sense RNA virus of the Flaviviridae family and a member of the genus Pegivirus and about 50nm in diameter (Alter, 1996). Genome of it is about 9.3kb in length with encoding a single polyprotein of about 3,000 amino acids and contains a single long open reading frame (ORF) encoding two structural proteins, such as E1 and E2, and five non-structural proteins, such as NS2, NS3, NS4, NS5A, and NS5B with molecular weights of 20, 70, 28, 55, and 57kDa, respectively, by cellular signal peptidases and two viral proteases (Pilot-Matias et al., 1996; Stapleton et al., 2010). The HGV is a lymphotropic virus that does not cause hepatitis (Theodore & Lemon, 1997). The large ORF is preceded by an apparent 5′ non-translated region (NTR) of about 450 nucleotides and is followed by a 3′ NTR of about 300 nucleotides. The virus replicates in cells of the hematopoietic system (George et al., 2012). If HIV-positive persons are co-infected with GBV-C, a positive effect is seen (Polgreen et al., 2003).

The HGV can be classified into 7 genotypes (GTs) and many subtypes with distinct geographical distributions (Feng et al., 2011). The GT1 is prevalent in West Africa that has two subtypes: 1a and 1b. The GT2 is predominant in Europe and the USA, and two subtypes: 2a and 2b are identified (Nakatsuji et al., 1995). The GT3 is found in Asia and South America. The GT4 is seen in Southeast. The GT5 is present in Central and Southern Africa. The GT6 can be encountered in Southeast Asia. The GT7 has been reported in China (Singh et al., 2017).

5.1 Symptoms of HGV

The majority of immunocompetent individuals clear GBV-C viReMa, but in some individuals, infection persists for decades (Linnen et al., 1996). The incubation period of GBV-C is 2-4 weeks. The GBV-C causes mild disease with persistent viremia for months or years. About 60-70% of people infected with HGV cures automatically and develops antibodies, but the rest causes fulminant and chronic carriers lasting for several decades (Yoshiba, 1995). Shortly after its discovery, a number of studies attempted to link GBV-C to human diseases. The studies failed to demonstrate GBV-C replication in the livers of patients infected with acute or chronic hepatitis (Laskus et al., 1998).

5.2 Transmission of HGV

GBV-C is transmitted predominantly through parenteral routes, with a high seroprevalence among intravenous illicit drug users (Frey et al., 2002). Also blood-borne, and sexual and vertical transmissions of GBV-C have been identified. Children remain infected and asymptomatic for long periods (Brechot et al., 1998). The HGV also can be transmitted by injection drug use, hemodialysis, and homosexual and bisexual relationships, and organ transplantation (Stark et al., 1996).

About 14-43% individuals infected with human immunodeficiency virus (HIV) are often co-infected with GBV-C. Children born to HGV RNA positive women co-infected with HIV are also likely to be HGV infected (George et al., 2006). GBV-C infection has been found worldwide infecting about one-sixth of the global population (about 750 million people) (Yu et al., 2022). The blood dependent persons, such as haemophiliacs patients, hemodialysis patients, thalassemic, intravenous drug users, and liver transplanted patients are the highest prevalence and risk of transmission of HGV. Screening blood donors for blood-borne pathogens is very critical for these recipients' safety. Some researchers do not stress on blood screening (Belli et al., 1996).

5.3 Diagnosis and Treatment

HGV RNA can be measured in serum by reverse transcriptase polymerase chain reaction of the 5' non-coding region. The HGV can be detected by RT-PCR in the blood or liver tissue of patients with fulminant hepatic failure of chronic liver disease of unknown etiology (Lefrère, 2008). Only little is known about the treatment of a HGV infection. There is currently no recommended treatment for GBV-C. The patients are treated with Interferon-alpha (IFN-alpha). The HIV-infected patients develop GBV-C E2 antibodies and clear the virus, but this appears to occur at a significantly slower rate (Stapleton, 2003). In a study it is reported a significant delay in mortality among Japanese individuals co-infected with GBV-C/HIV, compared with those infected with HIV alone (Toyoda et al., 1998).

6. Conclusions

From this study, I have realized that GBV-C is a newly identified human RNA virus, belonging to the Flaviviridae family that can be transmitted through the blood donors and by other parenteral mechanisms. Many studies have tried to explore the transmission, prevalence, possible clinical disease process, and pathology of HGV. Most GBV-C infections are subclinical or mild, and do not cause significant liver disease and cannot worsen the current liver disease; and also, severe hepatitis with HGV is rare. Some studies have shown that GBV-C may cause chronic infection in human but the role of this agent in chronic liver disease is poorly understood. Some studies have suggested that GBV-C/HIV co-infection has confirmed an association with prolonged survival. However, evidence suggests that HGV do not cause hepatitis in humans.

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