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Diyala University

College of Medicine

Department of Microbiology

Serological Study on Hepatitis G Virus among Patients and Risky Groups in Diyala Province.

A thesis

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Submitted By

Manal Ihsan Hassan

B.Sc.in Microbiology Science, Al-Mustansiriya

Supervised By

Prof. Dr.

Abdulrazak Shafiq Hasan

Ph.D. Med. Microbiology

College of Medicine

Diyala University

Prof. Dr.

Nadhim Ghazal Noaman

Ph. D. Comm. Med.

College of Medicine

Diyala University

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Chapter one

1.1. Introduction

Hepatitis G virus (HGV) or Human pegivirus (HPgV) is a positive sense enveloped RNA virus belong to the *Flaviviridae* family and a member of the *Pegivirus* genus (Stapleton et *al*., 2010). It was firstly identified in 1995 (Simons *et al*., 1995). It has been classified into seven genotypes and many subtypes with distinct geographical distributions (Singh and Blackard, 2017). HGV is phylogenetically related to hepatitis C virus (HCV), but replicates primarily in lymphocytes, monocytes and poorly, in hepatocytes (George and Stapleton, 2006). However, the commonly detected HGV in bone marrow supports that it may be a major replication site of this virus (Kisiel *et al*., 2013).

Hepatitis G virus is transmitted by contaminated blood and blood products, intravenous drug use, from mother to child, sexually, and possibly through close social contacts (Vasiliy *et al.*, 2008). HGV has been suggested to be a causative agent for non-A-non-E hepatitis. Although, several data suggest that HGV is not a major cause of liver disease despite recent data indicating that it may infect and replicate in hepatocytes, and more associated with chronic viral liver disease (Darwish et al., 1998; Halasz *et al*., 2001), or increased the severity of chronic liver disease, liver cirrhosis and risk of Hepatocellular carcinoma (HCC) and other hematological malignancies (Jain et *al*., 1999; Kaya *et al*., 2002; Yang *et al*., 2006).

Infection by HGV has been found worldwide and currently infects approximately one sixth of the world's population. High prevalence is observed among subjects with the risk of parenteral exposures including those with exposure to blood and blood products, those on hemodialysis, and intravenous drug users. Sexual contact and vertical transmission may also occur (Stapleton, 2003; Fallahian *et al*., 2010).

Because of shared modes of transmission, individuals infected with HIV are often co-infected with HGV; the prevalence of HGV viremia in HIV patients ranges from 14% to 43% and particularly high among HIV positive injecting blood users (Zhang *et al*., 2006; Jogeda *et al*., 2017). It has been found that HGV infection in HIV-positive people is associated with prolonged survival and *in vitro* coinfection of human lymphocytes with HGV and HIV lead to decreased HIV replication (Baggio-Zappia and Hernandes Granato, 2009). Whereas, to supporting that although parenteral route is the most effective way, other routes such as sexual contact and intra-familial contact may also play role in HGV transmission (Kaya *et al*., 2004).

HGV is detectable in all ethnic groups. Results of blood donors described in 30 reports revealed viral RNA in 4.8%, including Caucasians 4.5%, Asians 3.4%, and Africans 17.2%, suggesting blood screening due to the high risk of infection (Wiwanitkit, 2005; Dencs and Sebestyen, 2007). Keeping in the same issue, 4.3% of healthy blood donors in Saudi Arabia were positive for anti-HGV antibodies, compelling to recommend HGV screening for all blood donors (Alhetheel and El-Hazmi, 2014). Likewise, 5% of volunteer blood donors in Isfahan-Iran were positive for anti-E2 antibody of HGV (Salehi *et al*., 2014). The rate of HGV infection in healthy Kuwaiti and Jordanian blood donors was 24.6 and 9.8%, respectively, (Odeh *et al*., 2010). Based on PCR genotyping assay, HGV-RNA was detected in 4.1% among blood donors from in Eastern Anatolia, and the presence of G2 strains reveals the limited genetic diversity of the HGV circulating in Turkey (Kalkan *et al*., 2005). Furthermore, HGV-RNA, and anti-HGV E2 antibody was detected in 61% of the multi-transfused Egyptian children and 15% of the controls (Salama and Selim Oel, 2009). In India, HGV-RNA was detected in 17.7% multi-transfused patients and 23%, and 93.5% of HGV-positive patients were found to be co-infected with either HBV 38.7% or HCV 74.1% (Asim *et al*.,2008).

Previous data had demonstrated an occupational risk of HGV infection in dialysis patients and medical staff (Fallahian *et al*., 2010). In this regard, the prevalence of HGV infection as detected serologically by anti HGV E2 antibody was 0% in dialysis staff, 3.89% in hemodialysis patients, and 0% in continuous ambulatory peritoneal dialysis patients from Iran (Eslamifar *et al*., 2007). However, in another study from Isfahan, 25% of HD patients were positive for HGV anti-E2 antibody (Salehi *et al*., 2014). In Brazil, HGV RNA was detected by RT-PCR in 12.8% of patients with chronic renal failure undergoing hemodialysis (Watanabe *et al*., 2003). Furthermore, it has been reported that anti-HGV antibodies were positive in 62.5% and 36.1% of anti-HCV positive and anti-HCV negative HD patients respectively, and the HGV-RNA was detected in 63.6% of patients with positive anti-HGV antibodies (Kopec *et al*., 2010). In Egyptian children with HD for chronic renal failure, HGV RNA was positive in 26.5% of HD and 13.6% of pre-dialysis children, and the anti-E2 was positive in 41.2% of HD and 28.8% of pre-dialysis children (Hammad and Zaghloul, 2009).

Studies investigating the HGV infection rate among patients with congenital bleeding disorders had yielded discordant results. In Poland, there was negative positivity rate of HGV among patients with congenital bleeding disorders (hemophilia A, B, and other factor deficiencies) (Kucharska *et al*.; 2016). In another study, the HGV RNA was identified in 3.2%; 23.7% and in 0%, of blood donors, adult and children hemophilia patients respectively, and the HGV anti-E2 was found in 23.6%; 37% and 25% respectively (Grabarczyk *et al*., 2006). In Brazil, the HGV RNA was detected in 14.2 % of thalassemia patients, (Watanabe *et al*., 2003). Additionally, in Turkey, the prevalence of HGV-RNA among anti-HCV positive multi-transfused thalassemia patients was 12.5% (Gamberini *et al*., 2004).

Beside its high co-infection rate with HIV, multiple data had reported high co-infection rates with other hepatitis viruses too (Berzsenyi et al., 2005; Praharaj et al., 2006). In KSA for instance, 4.1%, and 3.8% of positive HGV antibodies were reported among patients with chronic HBV and HCV respectively (Alhetheel *et al*., 2014). Again in Thailand, HGV RNA was found 10% and 11% in HBV and HCV positive blood donors respectively (Barusruk and Urwijitaroon, 2006). Meanwhile, other reports low co-infection rates (Li *et al*., 2006; Kucharska *et al*., 2016).

1.2. Aims of the study

The absence of data on the prevalence of HGV in Diyala province was the main stimulus to carry out this study which comes out to achieve the following goals:

1. Serological determination of the HGV infection rate among acute and chronic icteric patients and to figure out the rate of co-infection with other hepatitis viruses.
2. Determination of the HGV infection rate among risk groups including renal dialysis, Thalassemia patients, patients with HBV and HCV chronic diseases, Healthcare workers as well as those under high risk practices and to explore the effect of certain risk factors.
3. Determination of the HGV infection rate among normal healthy population in Diyala province and to explore the effect of certain demographic factors.