Introduction

Hepatitis C is a disease with significant global impact. According to the World Health Organization there are 130 - 150 million people chronically infected with the hepatitis C virus (HCV), corresponding to 2 – 2.5% of the world's total population. There are considerable regional differences, in some countries, e.g., Egypt; the prevalence is > 10% **(WHO, 2013).** In Africa and the western Pacific the prevalence is significantly higher than in North America and Europe. It is estimated that there are 2 – 5 million HCV-positive persons in Europe. The prevalence of HCV antibodies in otherwise healthy blood donors is approximately 1.6 % in the United States, 1.15 % in Italy, 0.4 % in Germany, and 0.23 % in Scandinavia. The number of patients HCV RNA positive is estimated to be around 80 to 90 % of all HCV antibody-positive persons **(Hatzakis et al., 2011).**

The risk of chronic HCV infection is high. 75-100% of patients remain HCV RNA positive after acute hepatitis C. Most of these will have persistently elevated liver enzymes in further follow-up. By definition, hepatitis C is regarded to be chronic after persistence of more than six

months. Once chronic infection is established, there is a very low rate of spontaneous clearance (**Vogel et al., 2009).**

Hepatitis C virus infection has significant clinical hepatic and extrahepatic manifestations. Chronic HCV infection is associated with glucose and lipid metabolic derangements that induce a more rapid progression of the disease and significantly reduce the response rate to pegylated interferon plus ribavirin that is the standard of care **(Adinolfi et al., 2013).**

Hyperlipidemia means the quantity of cholesterol and / or triglyceride in plasma higher than the upper limit of normality. The level of lipid in plasma may be interfered by diseases, diets, environmental and lifestyle. The morbidity rate of fatty liver, atherosclerosis, myocardial infarction will decrease if hyperlipidemia can be diagnosed and treated timely. The liver is an important organ maintaining dynamic balance of the metabolism of cholesterol and triglyceride. Acute and chronic malfunction of the liver because of viral hepatitis, toxipathic hepatitis, liver cirrhosis and other diseases may induce hyperlipidemia. In China, the most common cause for hyperlipidemia in patients with liver diseases is viral hepatitis **(Shao-Ji, 2004).**

Patients with chronic hepatitis C infection also can have hyperlipidemia **(Alter & Mast, 1994)**. Glucose intolerance has been associated with HCV infection and this will also predispose them to dyslipidemia **(Antonelli et al., 2005), (Allison et al., 1994).** In United States, according to the results of an epidemiological study targeted the computerized data base of chronic hepatitis C patients of Stratton Veterans Affairs Medical center, the prevalence of hyperlipidemia in hepatitis C patients was 70.4 % **(Murthy et al., 2009).** Treating dyslipidemia is essential, especially if indications are compelling such as diabetes mellitus or arterial disease **(Fraser et al., 1996).** Providers may be concerned about treating dyslipidemia with drugs that may worsen transaminase levels. Untreated hyperlipidemia places them at risk for cardiovascular disease **(Grimbert et al., 1996), (Shintani et al., 2004).** There may be reluctance to treat hyperlipidemia in patients with hepatitis C, especially with statins (3-hydroxy-3-methylglutaryl coenzyme A inhibitors), for fear of worsening liver function. Studies have been published showing no increased statin-induced risk of hepatotoxicity in patients with elevated liver enzymes **(Chalasani et al., 2004), (Khorashadi et al., 2006).** There are also expert opinions regarding how to use statins in patients with

chronic liver disease **(Russo & Jacobson 2004)**. Liver expert panel's recommendation to The National Lipid Association Statin Safety Assessment Task Force on the use of statins in patients with chronic liver disease was that it was not a contraindication. Close monitoring of liver function while patients with hepatitis C are treated for hyperlipidemia can be done so that most of these patients can reap the benefits of lowering lipid levels **(Cohen et al., 2006).**

It is not clear what the prevalence of hyperlipidemia is and how often hyperlipidemia is treated in Egyptian patients with HCV. So, we will conduct this study to assess the prevalence of hyperlipidemia in Egyptian patients with HCV infection.

Aim of the Work

To assess the prevalence of the hyperlipidemia in Egyptian patients with chronic hepatitis C patients.

Hepatitis C Virus

History

Until 1975, only two hepatitis viruses had been identified, the "infectious hepatitis virus" (hepatitis A virus, HAV) and the "serum hepatitis virus" (hepatitis B virus, HBV). However, HAV and HBV were excluded from being the cause of approximately 65% of post-transfusion hepatitis. Therefore, these hepatitis cases were termed "non-A, non-B hepatitis" (NANBH) **(Feinstone et al., 1975)**. Inoculation of chimpanzees (Pan troglodytes) with blood products derived from humans with NANB hepatitis led to persistent increases of serum alanine aminotransferase (ALT) indicating that an infectious agent was the cause of the disease **(Alter et al., 1978), (Hollinger et al., 1978).** Subsequently, it was demonstrated that the NANBH agent could be inactivated by chloroform **(Feinstone et al., 1983).** Moreover, it was reported that the infectious agent was able to pass through 80 nm membrane filters **(Bradley et al., 1985).**

Taken together these findings suggested that the NANBH causing agent would be a small virus with a lipid envelope. However, the lack of a suitable cell culture

system for cultivation of the NANBH agent and the limited availability of chimpanzees prevented further characterization of the causative agent of NANBH for several years. In 1989, using a newly developed cloning strategy for nucleic acids derived from plasma of NANBH infected chimpanzees the genome of the major causative agent for NANBH was characterized **(Choo et al., 1989).** The corresponding infectious virus causing the majority of NANBH was subsequently termed hepatitis C virus (HCV) **(Bradley et al., 1985).**

Virology

HCV is a small-enveloped virus with one single-stranded positive-sense RNA molecule of approximately 9.6 kb. It is a member of the genus hepacivirus within the Flaviviridae family. This viral family contains four genera, flavivirus, pestivirus, hepacivirus, and the newly defined genus pegivirus **(Stapleton et al., 2011).**

Comparisons of HCV nucleotide sequences derived from individuals from different geographical regions revealed the presence of at least six major HCV genotypes with a large number of subtypes within each genotype **(Simmonds 2004) (Simmonds et al., 2005).** HCV strains

belonging to the major genotypes 1, 2, 4, and 5 are found in sub-Saharan Africa whereas genotypes 3 and 6 are detected with extremely high diversity in South East Asia. This suggests that these geographical areas could be the origin of the different HCV genotypes **(Ndjomou et al., 2003).** The emergence of different HCV genotypes in North America and Europe and other non-tropical countries appears to represent more recent epidemics introduced from the sites of the original HCV endemics **(Simmonds, 2001).**

In a very recent study more than 1300 (nearly) complete HCV coding region sequences were analysed in order to validate new genotype and subtype assignments and the study revealed the presence of at least 7 different HCV genotypes and 67 subtypes **(Smith et al., 2014).** However, the fast growing number of full-length HCV genome sequences will probably lead to even higher numbers of HCV genotypes. It has more recently been reported that inter-subtype as well as inter-genotype HCV recombinants occur. However, these recombination events appear to be rare **(Shi et al., 2012).**

Epidemiology

Hepatitis C infection is a disease with significant global impact. According to the World Health Organization there are 130 - 150 million people chronically infected with the hepatitis C virus (HCV), corresponding to 2-2.5% of the world's total population. There are considerable regional differences. In some countries, such as Egypt, the prevalence is >10% **(WHO, 2014).**

Hepatitis C virus is a major public health problem in Egypt specially genotype 4 **(Habib et al., 2001)**. Egypt has the highest prevalence of HCV in the world (overall prevalence of HCV antibody is 12% among the general population and reaches 40% in persons 40 years of age and above in rural areas whom at higher risk for coronary heart disease **(Medhat et al., 2002).**

In Africa and the western Pacific the prevalence is significantly higher than in North America and Europe. It is estimated that there are 2 – 5 million HCV-positive persons in Europe **(Hatzakis et al., 2011)**. The prevalence of HCV antibodies in otherwise healthy blood donors is approximately 1.6% in the United States, 1.15% in Italy, 0.4% in Germany, and 0.23% in Scandinavia. The number of patients HCV RNA positive is estimated to be around 80

to 90% of all HCV antibody-positive persons **(WHO, 2014).** Certain groups are preferentially affected; the highest risk factor in most cases is injection drug use. But patients undergoing hemodialysis and persons who received blood transfusions before 1991 are at risk also. In Europe and the United States chronic hepatitis C is the most common chronic liver disease and the majority of liver transplants performed are for chronic HCV **(Rockstroh et al., 2012).**

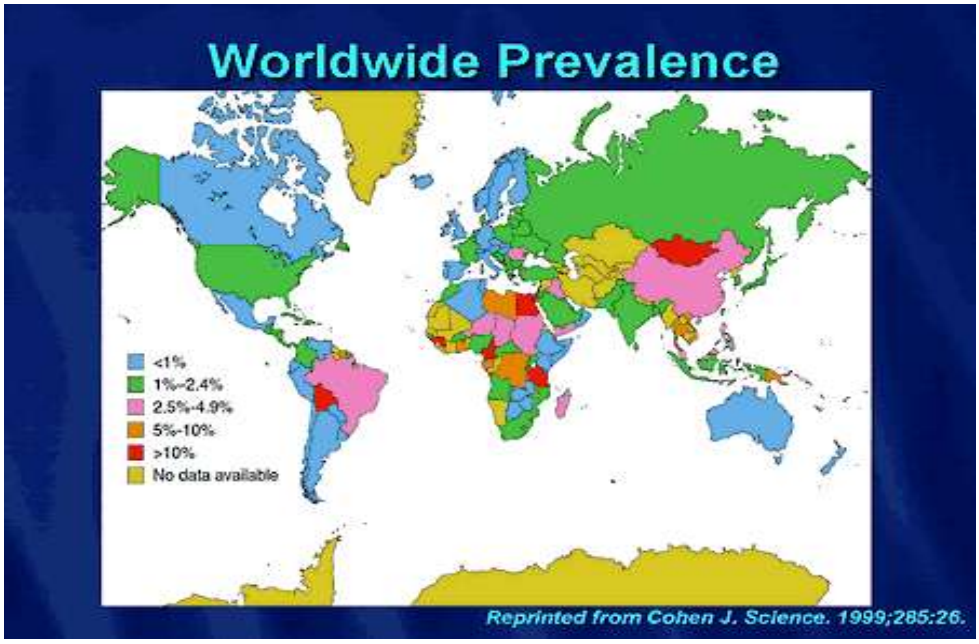

Figure (1): Map of hepatitis C prevalence worldwide.

It is difficult to determine the number of new HCV infections, as most acute cases are not noticed clinically. Fewer than 25% of acute cases of hepatitis C are clinically apparent **(Vogel et al., 2009).** In addition, the age of infection upon diagnosis is not possible to determine in most cases. Nevertheless, it is assumed that the number of new infections has considerably decreased over the past decades. In the US it is estimated that the number of new cases of acute HCV infection has fallen from approximately 230,000 per year in the 1980s to about 20,000 cases per year currently with an estimated 21,870 cases in 2012 **(Wasley et al., 2008)**. While this decrease is primarily associated with reduced infections in injection drug users, a probable consequence of changes in injection practices motivated by education about human immunodeficiency virus (HIV) transmission, it has remained steady, if notincreasing slightly, since the mid-2000s. Transfusion-associated hepatitis C has had little impact on this decline, as the number of cases has been reduced almost to zero. The only different trend is an increase in acute hepatitis C infections in HIV-positive men who have sex with men (MSM) globally over the last decade **(Boesecke et al., 2012).**

Recent numbers from Europe show an ongoing epidemic of acute HCV especially among intravenous drug users and MSM **(Rockstroh et al., 2012)**. CDC statistics, 2012 revealed that recent surgery and needle stick exposure represented >12% and >7% respectively in HCV transmission **(Mauss et al., 2015).**

Transmission

Parenteral exposure to the hepatitis C virus is the most efficient means of transmission. The majority of patients infected with HCV acquired the disease through intravenous drug use or blood transfusion **(Mauss et al., 2015).**

Injection drug use

Injection drug use has been the most commonly identified source of acute HCV infection. It is estimated that most newly acquired infections occur in individuals who have injected illicit drugs. The seroprevalence of anti-HCV antibodies in groups of intravenous drug users may be up to 70% with considerable variation depending on factors such as region, risk behavior, socioeconomic status, etc, underscoring the efficiency of transmission via direct blood contact **(Sutton et al., 2008).**

Blood transfusion

In the past, blood transfusion or use of other blood products was a major risk factor for transmission of HCV. In some historic cohorts 10% or more of patients who received blood transfusions were infected with hepatitis C. **(Alter et al., 1989).** However, blood donor screening for HCV since the early 1990s has nearly eliminated this transmission route. Blood donors are screened for anti-HCV antibodies at least in developed countries. The risk is now estimated to be between 1:500,000 and 1:1,000,000 units **(Pomper et al., 2003)**. In cohorts of multiply transfused patients such as hemophiliacs, over 90% of patients were infected with hepatitis C in the past. Since the use of routine inactivated virus procedures (e.g., heat inactivation or pasteurization) or recombinant clotting factors, new cases of hepatitis C infection have become uncommon in these patients **(Francois et al., 1993).**

Organ transplantation

Transplant recipients who receive organs from HCV-positive donors have a high risk of acquiring HCV infection. Transmission rates in different cohorts vary from 30 to 80% **(Pereira et al., 1991) (Roth et al., 1994)**. Therefore, most transplant organizations have developed

strategies for screening and selective utilization of organs from anti-HCV positive donors **(Mauss et al., 2015).**

Hemodialysis

Patients who participate in chronic hemodialysis programs are at increased risk for hepatitis C. The prevalence of HCV antibodies in such patients reaches 15%, although it has declined in recent years. A number of risk factors have been identified for HCV infection among dialysis patients. These include blood transfusions, duration of hemodialysis, prevalence of HCV infection in the dialysis unit, and type of dialysis. The risk is higher with in-hospital hemodialysis as opposed to peritoneal dialysis. The best strategy to prevent hemodialysis-associated HCV transmission is subject to debate **(Fissell et al., 2004).**

Needlestick injury

There is some risk of HCV transmission for healthcare workers after unintentional needlestick injury or exposure to other sharp objects. The incidence of seroconversion after exposure to an HCV-positive source is generally estimated to be less than 2 % **(MMWR [Morbidity and Mortality Weekly Report] 2001).** However, data are divergent and figures ranging from 0 to 10% can be found. Exposure of HCV to intact skin has not

been associated with HCV transmission **(Mitsui et al., 1992), (Sarrazin et al., 2010).**

Other rare transmission routes

Rare sources of percutaneous transmission of HCV are contaminated equipment used during medical procedures, procedures involved in traditional medicine (e.g., scarification, cupping), tattooing, and body piercing. All these routes bear the potential of transmitting HCV. However, in most instances it is not clear if the risk is due to the procedure itself, or whether there are possible contacts with persons involved who are HCV-positive. In addition, transmission via these routes is so rare that persons with exposure are not at increased risk for acquiring HCV **(Haley et al., 2001).**

Perinatal transmission

The risk of perinatal transmission of HCV in HCV RNA-positive mothers is estimated to be 5 % or less. In mothers coinfected with HIV this risk correlates with immunosuppression and has been described in up to 20 % **(Ohto et al., 1994).** Cesarean section has not been shown to reduce the transmission risk **(Pembrey et al., 2005).** There is no evidence that breastfeeding is a risk for infection among infants born to HCV-infected women.