

Management Strategies of Fatal Liver Infection Due to Hepatitis C Virus (HCV)

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Abstract

Hepatitis is a liver inflammatory disease that can cause severe liver scarring. Hepatitis C is a blood-borne fatal disease of the liver that is caused by a virus called the hepatitis virus C (HCV), which lives in liver tissue and blood. It can be both an acute (short-term) illness (25-15%) and a chronic (long-term) infection (75-85%) that may gradually damage the liver. It is characterized by possible development of both liver and extra-hepatic disorders. The HCV infection is usually asymptomatic. Chronic infection with the HCV represents a major health problem worldwide that accounts for life-threatening liver disease, such as liver cirrhosis, hepatocellular carcinoma (HCC), liver failure, and ultimately needs liver transplantation, or to face unexpected premature death. Early treatment for hepatitis C is highly cost-effective and disease progression restricted, and can be avoided end-stage liver disease. The aim of this study is to identify the risk factors, transformation route, and complication of HCV for the management of the disease to save millions of lives.

Keywords: hepatitis virus C, genotype, cirrhosis, hepatocellular carcinoma

1. Introduction

Hepatitis C virus (HCV) is responsible for the major liver infection that damages the liver, and it may take 20-40 years to damage the liver. The HCV infection can cause either acute or chronic hepatitis, the severity of the disease ranges from mild to life-threatening. After an acute infection, about 15-45% clear spontaneously (without treatment), about 55-85% progress to chronic infection, and about 80% progress to chronic HCV infection due to viral replication occurrence in liver cell. Spontaneous clearance is more likely to happen within the first 12 months from initial infection (Aisyah et al., 2018). The HCV was most prevalent in the baby boomer generation (persons born between 1945 and 1965), which comprised about 75% population (Guadagnino et al., 1997). It is a blood-borne disease, and the most common ways of infection occur through unsafe injection practices, inadequate sterilization of medical equipment, blood transfusion and blood products without examination (Kim & Chang, 2013).

From 1990 to 2019, the incidence rates of HCV infection have remained stable. During this period, it is estimated that roughly 200 million people are infected globally by the HCV (Zeng et al., 2021). In 2018, about 143,000 people in the UK were living with chronic hepatitis C infection (NICE 2013). In 2017, there were about 115 million HCV infected people worldwide, of these 11.3 million (10%) resided in Eastern Europe and Central Asia (Maistat et al., 2017). In 2020, about 71 million people have chronic HCV infections around the globe. Therefore, it is a plague of humankind (WHO, 2021). The most affected regions are Central and East Asia and North Africa, and the top three countries with the highest disease burden are China (9.48 million), Pakistan (7.39 million) and India (6.13 million) (Dugan et al., 2021). About 530,000 cases (82%) of liver cancer per year worldwide are caused by viral hepatitis infection, with 118,000 cases associated with hepatitis C (Poynard et al., 2003). It is estimated that 4.1 million (1.6%) Americans have been infected with HCV, of whom 3.2 million are

chronically infected. At present about 160 million people worldwide are suffering from HCV infection, which is the leading cause of cirrhosis, hepatocellular carcinoma (HCC), and liver transplantation (Kutala et al., 2015).

At present about 325 million people worldwide have hepatitis B or C, and majority of them do not have access to life saving medications. There is no vaccine against HCV. Therefore, it is a major challenge worldwide for controlling the disease (Liang, 2013). In the absence of vaccination most exposed neonates and young children will be infected and become lifelong carriers (Gow & Mutimer, 2001). In 2020, HBV and HCV related disease led to 1.1 million deaths worldwide. Some patients progress quickly to liver cirrhosis and may develop HCC (Zeng et al., 2021). The burden of HCV is a global health concern as liver-related morbidity and mortality continue to rise due to people living with human immunodeficiency virus (HIV), hepatitis B, or both, and people who inject drugs. Antiviral medicines, such as pegylated interferon and ribavirin can be used to limit liver damage (Liang et al., 2000).

2. Literature Review

In any research, the literature review is a section where research works of previous researchers are introduced briefly to make familiar with the new researchers in the research arena (Polit & Hungler, 2013). It is a hard-working search, scholarly inquiry, and investigation that aim for the discovery of new facts and findings (Adams et al., 2007). It helps the researchers to understand the subject, and it serves as an indicator of the subject that has been carried out previously (Creswell, 2007). Yasir Waheed and his coworkers have found that the prevalence, genotypes, and factors associated with HCV infection in the Pakistani population. They have observed that the most prevalent genotype of HCV is 3a and the prevalence is moderate in the general population but very high in injecting drug users and multi-transfused populations (Waheed et al., 2009).

Amal Ahmed Mohamed and his coauthors have found that about 130-175 million HCV patients are chronically infected, and over 350,000 die each. They have realized that chronic HCV is the primary cause of cirrhosis, HCC, and end-stage liver disease. They have stressed on the management and prevention of chronic HCV through the reduction of the risk of HCC and treating extra hepatic complications (Mohamed et al., 2015). Blaise K. Kutala and his coauthors have realized the beneficial effect of achieving a sustained virological response (SVR) after antiviral treatment against HCV. But they are in confusion whether unsuccessful treatment (non-SVR) also improves patient survival, especially in patients with advanced liver fibrosis. They have evaluated the incidence of death or liver transplantation in the 427 naive patients with a Child-Pugh score of A and advanced fibrosis (Kutala et al., 2015).

Francesco Negro has provided a thorough review on the extent of the HCV epidemic across Europe, with a discussion of the most important subgroups affected, and of the risk factors of infection, both traditional and new (Negro, 2014). Ellen Dugan and her coworkers have aimed to estimate the global prevalence of viremic HCV in 2019 among women of childbearing age through the literature search, modeling work, and extrapolation. They have applied test-and-treat strategies to reduce vertical transmission and total disease burden (Dugan et al., 2021). Roberta D'Ambrosio and Alessio Aghemo have studied antiviral treatment of chronic HCV for the persistent eradication of the virus through the sustained virological response (SVR) (D'Ambrosio & Aghemo, 2012).

T. Jake Liang has shown that despite major advances in the understanding and treatment of hepatitis C, a preventive vaccine has not been discovered yet. Therefore, the ultimate path to a successful preventive vaccine requires comprehensive evaluations of all aspects of protective immunity, innovative application of state-of-the-art vaccine technology and properly designed vaccine trials that can affirm definitive endpoints of efficacy (Liang, 2013). Mario U. Mondelli and his coauthors have shown that prevention with an effective vaccine is the best option to eradicate dangerous human pathogens. Since at present there is no vaccine of HCV, prevention of chronic liver disease is regarded as a more realistic and equally important goal to fight the deleterious effects of chronic HCV infection (Mondelli et al., 2005).

3. Research Methodology of the Study

To lead in the academic world an academician takes the research as an essential and influential work of his/her way of life (Pandey & Pandey, 2015). Methodology is a proper guideline of any valuable research that is considered as an organized procedure and follows scientific methods appropriately (Kothari, 2008). It provides the research design and analysis procedures to perform good research (Hallberg, 2006). Therefore, research methodology is a strategy for planning, arranging, designing, and conducting a meaningful and valuable research that tries to develop logic to generate theory within which the research is conducted (Remenyi et al., 1998).

This study is an exploratory and descriptive procedure that deals with a qualitative research approach (Mohajan, 2017, 2018, 2020). I have studied research papers, books and handbooks of renowned authors, and have collected materials from internet, websites, etc. to enrich this paper (Mohajan, 2024a-g).

4. Objective of the Study

Main objective of this article is to discuss the basic concept of acute and chronic HCV infection. Hepatitis C is an infection of the liver that may gradually damage the liver. The most people who are infected cannot able to clear the virus and develop a lifelong chronic infection. At present it is the leading cause for liver transplants in the USA (Franciscus, 2017). Other minor objectives of the study are as follows:

- 1) to focus on symptoms and transmission of HCV,
- 2) to highlight on virology and risk factors of HCV, and
- 3) to discuss diagnosis and treatment of HCV.

5. Virology of HCV

HCV is a small and single-stranded RNA Flaviviridae family and the genus Hepacivirus, encoding for a capsid protein, two envelope proteins, and some non-structural proteins. There are no direct morphological markers of the virus. The virus replicates in the hepatocyte and in other cells, such as lymphocytes, and macrophages that cause acute or chronic hepatitis, cirrhosis, and HCC (Waheed et al., 2009). The HCV contains dual layered wrapped nucleocapsid with lipid bilayer (Hakim et al., 2008).

The existence of HCV was first fully recognized in 1975 when the infection was not associated with hepatitis A virus (HAV) or hepatitis B virus (HBV) infections, and then defined the disease a non-A, non-B hepatitis (Feinstone et al., 1975). It cannot be clinically distinguished from other viral hepatitis with any reliability. Its only reservoir is human beings. Hepatitis C virus (HCV) is discovered in 1989 by three scientists Harvey J. Alter, Michael Houghton and Charles M. Rice as the major causative agent of “non-A, non-B hepatitis” (Choo et al., 1989). The HCV genome is found to consist of about 9,600 nucleotides in length, and it has a single open reading frame about that encodes a 3010 amino acid polyprotein that undergoes proteolytic processing to form structural and nonstructural viral protein. It is flanked at the termini by 5' and 3' untranslated regions critical for viral replication and translation (Gottwein & Bukh, 2008).

The HCV has 7 genotypes (GTs) and over 90 subtypes. The GTs 1, 2, and 3 are more common in the northern hemisphere (Smith et al., 2014). GT1 is the most common and is estimated to account for 83.4 million (46.2%), with wide geographical distribution in Northern and Western Europe, Asia, North and South America, and Australia (Messina et al., 2015). GT2 is mostly present in West and Central Africa that accounts for 16.5 million (9.1%). GT3 is the most common after GT1 that accounts for 54.3 million (30.1%) cases globally, about 75% of this number occur in south Asia (Lavanchy, 2011). GT4 is the most common in Egypt, GT5 is present only in South Africa, and GT6 is endemic in Hong Kong and Southern China. To date, only one GT7 infection has been reported that is isolated in Canada from a Central African immigrant (Murphy et al., 2007).

5.1 Symptoms of HCV

Most people (70-80%) have no symptoms when they are first infected with hepatitis C. Over time people with chronic HCV may develop various symptoms related to liver damage that is associated with a wide variety of related conditions (Franciscus, 2017). Sometimes the symptoms may develop within one to three months of infection. Chronic HCV infection is normally a slow progressive disease that may produce for many years after infection (Chuang et al., 2009). Some symptoms of it are jaundice, anorexia, vague abdominal discomfort, loss of appetite, nausea and vomiting, weight loss, fatigue, tiredness, abdominal pain, joint pain, fever, itching, abdominal swelling due to fluid, clay-colored or pale stools, and dark grayish urine (Purcell, 1997). Usually alanine aminotransferase (ALT) remains about seven times upper than the normal limit. Most HCV infected people carry the virus for the rest of their lives, and about 70% of them develop chronic liver disease (Maheshwari et al., 2008).

5.2 Risk Factors of HCV

People at the highest risk of infection are a person sexual relationship with a HCV infected person, and have a sexual partner with hepatitis C infection and are HIV positive (Mesquita et al., 1997). Some sensitive of HCV infection people are injecting or inhaling for drug users, have been in prison for a long time, persons born between 1945 and 1965, take medicine sharing needles, chronic hemodialysis patients, and was born in a country with a high prevalence of hepatitis C (NICE, 2013). Also, the people are in the risk of HCV infection; the recipients of clotting factor concentrate before 1987, recipients of blood transfusions before 1992, and have a practice of tattooing, acupuncture and skin piercing. Children born from HCV-positive mothers are also in the risk of HCV transformation. Homeless populations are at extremely high risk for infection with HCV (Manzini et al., 1995).

5.3 Transmission of HCV

The main route of HCV transmission is parenteral, and can be spread in human body through the contact with infected blood and blood products (horizontal transmission) without testing especially through the hemophiliacs, dialysis patients, and intravenous drug users (Tremolada et al., 1992). Transmission of HCV may also occur with

activities involving percutaneous exposure and the use of contaminated equipment (NICE, 2013). Other common modes of transmission are sexual, perinatal, and idiopathic. The HCV transmission (vertical transmission) from mother to infant during pregnancy or childbirth has been documented but the case is rare (less than 5%). If the mother is infected with both HCV and HIV, the probability of vertical transmission increases 4 to 5 folds (Rehermann & Nascimbeni, 2005).

Sexual contact is less likely to transmit HCV but it depends on the type of sexual activity. Epidemiological studies show low rates of HCV infection in high promiscuity groups, such as prostitutes, homosexuals, and patients with sexually transmitted diseases (Tedder et al., 1991). The risk is higher with increased number of sexual partners, engaging in high-risk sexual practices, co-infection with sexually transmitted infections (STIs) and HIV, and engaging in sexual activities with those who are involved in high-risk behaviors. The HCV transmission is lowest with oral sex, higher with vaginal sex, and highest with anal sex (Mesquita et al., 1997).

The HCV can be transmitted through the ear and nose piercing, tattooing, acupuncture, reuse of syringes and needles in healthcare settings, use of injection drugs, blood transfusion, unsterilized dental equipment, surgical instruments, shaving and cosmetology instrument sharing, etc. (Raza, 2007). Other sources of HCV transmission are sharing drug injection; snorting or smoking equipment, such as needles, syringes, tourniquets, straws, pipes, cookers, wash and filters, etc.; household exposure through sharing of personal hygiene equipment, such as toothbrushes, razors, nail clippers, sex toys, etc.; practices using unsterilized objects, such as scarification, circumcision, etc. (Liou et al., 1992).

The HCV is not transmitted by casual contact like hugging or shaking hands, kissing on the cheek, coughing or sneezing, or sharing a bathroom. It also cannot spread through food, water, or in cross-contact, or sharing food and drinks, or sharing eating utensils and drinking glasses with the infected patients. The HCV has not been found in breast milk (Ogasawara et al., 1993).

5.4 Diagnosis of HCV

Diagnosis for HCV is recommended if a person is in one or more of the symptoms of HCV infection, such as fatigue, jaundice, nausea and vomiting, etc. The HCV is often remains undiagnosed for many years and usually diagnosed accidentally when patients present to physician with increased liver enzymes, or cryptogenic chronic liver disease. Infection with HCV can be diagnosed by specific antibody test using enzyme immunoassay (EIA), chemiluminescence immunoassays, and recombinant immunoblot assays (Ghany et al., 2009). Generally, HCV antibodies develop on 7-8 weeks after infection. Real-time polymerase chain reaction (RT-PCR) can be helpful in the detection of HCV in early onset of infection. It detects HCV RNA (Allain et al., 1991). The HCV viral load test estimates the number of viral particles per milliliter of blood that is useful in assessing prognosis and planning and monitoring treatment. It is often used to guide initial treatment decisions and to follow the progress of individuals undergoing treatment (Yuki et al., 1992).

5.5 Treatment of HCV Patient

There is no vaccine for hepatitis C, but several vaccines are currently under development (Strickland et al., 2008). The HCV vaccines will be difficult to develop due to the virus' different genotypes and its ability to change or mutate during infection (Franciscus, 2017). Treatment of the HCV is palliative and supportive. The effectiveness of the treatment varies according to many factors, such as the genotype, treatment regimen, and characteristics of the infected person. Response to treatment varies depending on the genotype (GT) with which the person is infected. Early detection and treatment can prevent serious liver damage and lead a long-term healthy life (Strickland et al., 2008). Identification of HCV genotype is useful in assessing prognosis and planning treatment. The treatment improves liver health by stopping liver damage caused by the HCV and even reversing some of the damages that have already occurred (Arcaini et al., 2016).

About 15-45% HCV infected patients cure automatically within six months without any treatment, and the rest may develop life-threatening chronic hepatitis that is the major cause of liver fibrosis, liver cirrhosis, HCC, and liver failure (Thomas & Zoulim, 2012). In 1996, only 9% has a chance of being cured of hepatitis C, but now treatments usually for 12-24 weeks, HCV has progressed to the point that more than 90% of the people who take the treatments can be cured (Franciscus, 2017).

The HCV is successfully treated with pegylated interferon-alfa injections along with oral drugs, such as ribavirin has been effective (Jacobson, 2007). In 2013, the chronic HCV infection with the approval of second-generation direct-acting antivirals led the way for IFN-free combination regimens. About 30% of the infected patients are cured within six months and about 70% can develop chronic infection (D'Ambrosio & Aghemo, 2012). The combination of PegIFN-alfa and ribavirin for 24 or 48 weeks is the standard of care for treatment of HCV infection. First-generation NS3 protease inhibitors introduced in the market of HCV therapy since 2011 are telaprevir and boceprevir that are approved as a new standard line of therapy for GT1 (Aghemo et al., 2013). Recently, the combinations and newer treatments, such as polymerase inhibitors, protease inhibitors, and NS5A

inhibitors are recommended for HCV (Berg et al., 2006). GT1 patients are treated with a combination of HCV inhibitors and ribavirin for 8-24 weeks. GT2,3,4,5, and 6 people are treated with a combination of an HCV direct-acting antiviral (DAA) and ribavirin for 12-24 weeks and the cure rates are 80-100% (Franciscus, 2017).

Bed rest and fluids may be prescribed especially during the acute phase. Medicines can heal more than 90% of people with HCV that can be treated through the combination therapy with interferon and ribavirin. The ribavirin is not effective when used alone (Nahon et al., 2018). The recombinant immunoblot assay (RIBA) is a more specific test for anti-HCV antibody. HCV screening test of pregnant women is necessary to save the infants from hepatitis C (Naderi, 2014). Direct-acting antivirals (DAAs) treatment for chronic HCV infection may improve liver function and decrease the portal pressure of HCV patients with compensated cirrhosis (Berzigotti et al., 2015).

The HCV RNA appears in the blood within 1-2 weeks of infection in a majority of patients. About 30% of patients develop symptoms of acute HCV infection within 3-12 weeks after infection, with an average of 7 weeks (Carrat et al., 2019). It has a cytopathic effect and causes immune disorders. The infection can be very serious. The incubation period of this virus is 15 to 150 days. This virus may stay in the liver for years and it is not discovered until much damage is done in the liver (Hosry et al., 2016).

6. Nutrition Diet and Healthy Habits

A healthy, well-balanced diet is essential for a HCV infected patient. Such a diet is low in fat and sodium, high in complex carbohydrates, and has adequate protein. Consumption of processed foods, such as canned, frozen, and other preserved foods must be reduced, as these foods often contain chemical additives (Denniston et al., 2012). Non-dairy nutritious foods, such as soy, almond, cashew, coconut, hemp or rice milk must take properly. The patients should avoid high fat, salt, or sugar foods. Over-consumption of coffee, tea, and soda is harmful for HCV patients (Franciscus, 2017).

Heavy consumption of alcohol can severely accelerate HCV disease progression. Therefore, the people with HCV should avoid alcohol. They should avoid other recreational drugs and tobacco as usual (North et al., 2014). Moderate exercise, such as walking and swimming are generally recommended for all individuals who are not in an acute or end-stage phase of HCV. Exercise can reduce stress and is important for maintaining good health (Denniston et al., 2014).

7. Conclusions

From this study, I have observed that HCV can cause the liver disease hepatitis C that is a major health concern worldwide. At present more than 170 million people are infected with HCV worldwide. About 71 million people are chronically infected, and about 3-4 million people are newly infected every year, and from these about 700,000 people die each year worldwide from chronic HCV infection. The highest prevalence rates of HCV are seen in developing poor countries of Africa and Asia, with low prevalence rates are in developed countries of Europe and North America. Most patients with HCV infection are unaware about their infection for many years due to no symptoms. As a result, liver cirrhosis and HCC are developed before the identification of HCV infection. The high-cost HCV medications, regular outpatient visits, diagnostic, and routinely monitoring blood tests, etc. are common problems for patients and over burden to the family members. Successful treatment will stop the progression of liver disease, and maximum cases the patient will recover completely, and consequently, the numbers of HCV infected individuals will be reduced. To reduce the risk of further liver damage of a HCV patient needs to avoid alcohol if addicted, and should eat a healthy balanced diet, and undertake a regular physical exercise. At present the medical providers are much more knowledgeable about diagnosis, management and treatment of hepatitis C. More researches into several important areas of HCV infection must be increased through the development of more effective and better tolerated antiviral therapies and medications. Consumption of balanced diet and medications the patients must adopt lifestyle changes, such as good nutrition, exercise, and stress management to alleviate some side-effects to slow disease progression.

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