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Article Review - Recent Advances in Hepatitis C Virus: Therapy and Diagnosis

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ABSTRACT

Hepatitis C virus (HCV) is one of the major causes of chronic liver disease worldwide. Significant progress has been made in both diagnosis and treatment over recent years. Modern serological and molecular tests now enable early detection of the virus, allowing timely and effective treatment. Direct-acting antivirals (DAAs) have revolutionized therapy, achieving cure rates exceeding 95% with minimal side effects. This paper reviews the etiology, epidemiology, pathophysiology, clinical stages, diagnostic advancements, treatment options, preventive strategies, and future directions in the fight against Hepatitis C.

Keywords- Hepatitis C, HCV, Direct-Acting Antivirals (DAAs), Liver Cirrhosis, Diagnosis, Prevention, Antiviral Therapy.

I. INTRODUCTION

Hepatitis C virus (HCV) is one of the most destructive viral diseases, primarily affecting the liver, and can lead to liver cirrhosis and liver cancer if left untreated. Despite the health challenges posed by this virus, recent advancements in diagnostics and treatment have made significant progress, enhancing the chances of controlling the disease.

In the field of diagnostics, modern and advanced techniques are now being used to detect the virus with greater accuracy, enabling early detection and the initiation of treatment before the disease progresses to advanced stages. (1)

As for treatment, there has been a tremendous shift with the introduction of direct-acting antivirals (DAAs) for HCV. These medications have shown great effectiveness in eradicating the virus with fewer side effects compared to traditional treatments like interferon. These new treatments have significantly improved cure rates, with studies showing cure rates exceeding 95% in many patients. Additionally, these medications have helped reduce the long-term cost of treatment. According to the World Health Organization (WHO) report in 2023, early diagnosis is crucial in reducing the global spread of the virus, as 42% of cases are still undiagnosed, highlighting the need for enhanced global screening strategies with the goal of eliminating the virus by 2030 (2).

The advancements in diagnostics and treatment suggest that the fight against HCV has become more effective in recent years, opening new possibilities to reduce the impact of this virus on public health in the near future.

II. VIRAL HEPATITIS

Hepatitis is a term used to refer to a group of diseases that affect the liver due to a viral infection, leading to inflammation and damage to liver cells. The types of hepatitis viruses vary from one virus to another. Some of the most prominent types include:

Hepatitis A:

Cause: It is caused by the Hepatitis A virus (HAV), which is primarily transmitted through the consumption of contaminated food or water from the feces of an infected person (2).

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Prevention: Hepatitis A can be prevented by improving personal hygiene practices, ensuring water safety, and vaccination with the Hepatitis A vaccine (2).

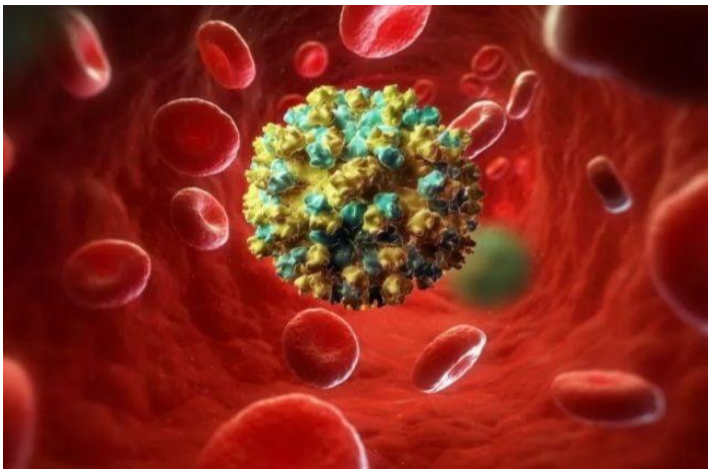
Hepatitis B:

Cause: It is caused by the Hepatitis B virus (HBV), which is transmitted through contact with blood or other bodily fluids from an infected person. Modes of transmission include sexual contact, sharing needles, and transmission from mother to child during birth. (2)

Prevention: A safe and effective vaccine is available for the prevention of Hepatitis B. It is also recommended to avoid behaviors that increase the risk of exposure to the virus, such as sharing needles or engaging in unsafe sex.

Hepatitis C:

Hepatitis C is a liver infection caused by the hepatitis C virus (HCV). The infection spreads when blood contaminated with the virus enters the bloodstream of a healthy person. It can lead to acute or chronic liver inflammation, with severity ranging from a mild illness lasting a few weeks to a serious, lifelong condition.



Hepatitis D:

Cause: It is caused by the Hepatitis D virus (HDV), an incomplete virus that requires the presence of the Hepatitis B virus (HBV) to replicate. Prevention: There is no specific vaccine for Hepatitis D, but vaccination against Hepatitis B helps prevent infection. (2)

Hepatitis E:

Cause: It is caused by the Hepatitis E virus (HEV). It is primarily transmitted through the consumption of water or food contaminated with the feces of an infected person, especially in areas with poor sanitation systems.

Prevention: Prevention measures include improving personal hygiene practices and ensuring the safety of water and food. A vaccine for Hepatitis E is available in some countries, but it is not widely accessible. (2)

III. ETIOLOGY & EPIDEMIOLOGY

Etiology:

Hepatitis C virus (HCV) is an RNA virus belonging to the Flaviviridae family and is considered one of the viruses responsible for chronic liver inflammation. This virus is characterized by different genotypes that vary between individuals based on geographical regions. Hepatitis C virus (HCV) is transmitted by percutaneous or permucosa exposure to infectious blood or blood-derived body fluids. Based on the results of cohort and acute case control studies, risk factors associated with acquiring HCV infection in the United States have included transfusion of blood and blood products and transplantation of solid organs from infected donors (4).

Intravenous drug use (IVDU) has been the second major rout of transmission, initially in the industrialized countries from the 1960s, but now affecting many countries in the world, in urban as well as in rural areas where DU has recently emerged, especially in the USA (5).

The risk of mother-to-infant transmission has been estimated around 6% from HCV mono infected mothers and twice higher from HCV-HIV co- infected mothers (6).

Sexual Transmission:

The transmission of the virus through unprotected sexual intercourse is a potential cause of infection, especially if there are cuts or sores in the genital area. However, this mode of transmission is less common compared to other routes.

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Epidemiology:

Hepatitis C infection remains a major global health challenge, affecting millions of people worldwide. According to the World Health

Organization, it is estimated that more than 70 million people globally are living with chronic Hepatitis C infection (2).

1. Geographic Distribution: Hepatitis C is found worldwide, but the rates of infection vary by region. High infection rates are found in Southeast Asia, Africa, parts of Eastern Europe, and Latin America. However, infection rates can differ significantly between countries depending on the availability of prevention and treatment programs (7).
2. Factors Affecting Transmission: Contaminated Needles: Drug injection is one of the primary causes of transmission of the virus (2). Untested Blood Products: Transmission through untested blood transfusions or surgical procedures using unsterilized instruments (7) Occupational Exposure: Healthcare workers who are frequently exposed to blood are at increased risk (2) Sexual Transmission: Although the virus is not easily transmitted through sexual contact, some cases occur among individuals engaging in unprotected sexual activities (7).
3. At-Risk Populations: People who inject drugs are among the highest-risk groups for infection (2). Healthcare workers who are routinely exposed to blood or other bodily fluids (7). Patients receiving blood or blood products from untested sources

IV. PATHOPHYSIOLOGY

1. Virus Entry into Hepatocytes:

Upon infection with Hepatitis C virus, the virus attaches to receptors on the surface of hepatocytes (such as CD81 and SR-B1), facilitating its entry into the cells. After entering, the virus disassembles inside the cell, and replication begins. (8)

2. Interaction with the Immune System:

Hepatitis C virus evades the human immune system by constantly changing its genetic structure, preventing immune cells from effectively recognizing it. It also contributes to immune suppression by reducing T- cell activity. (9)

3. Hepatitis and Liver Fibrosis:

Chronic hepatitis resulting from HCV infection leads to ongoing inflammatory reactions. Over time, this inflammation causes destruction of liver tissue and stimulates the process of fibrosis (scarring) in the liver. Fibrosis can progress to cirrhosis and liver failure in some cases. (10)

4. Virus Effect on Hepatocytes:

The virus causes damage to hepatocytes through multiple mechanisms, such as oxidative stress, cytokine production, and direct effects on the DNA of liver cells. (11)

5. Progression to Liver Cancer:

It is well known that chronic hepatitis resulting from Hepatitis C virus is a major risk factor for the development of hepatocellular carcinoma (HCC). The virus promotes tumor growth through its effect on DNA repair mechanisms and increasing liver inflammation (12).

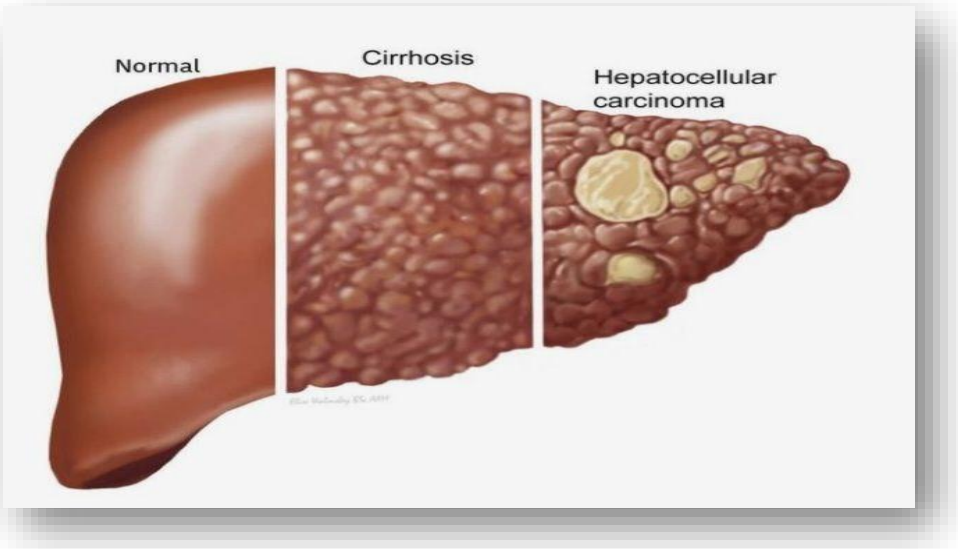

Figure (1) illustrates the stages of the virus's impact on the liver.

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V. SYMPTOMS & STAGES

Initially, many people infected with the hepatitis C virus (HCV) show no clear symptoms, making it difficult to detect the infection in its early stages. Some patients may experience mild symptoms, while others may show no symptoms at all. However, in other cases, symptoms may appear after a period of infection, which could include the following:

1. Yellowing of the skin and eyes (jaundice)
2. Dark-colored urine
3. Pale or clay-colored stool
4. Loss of appetite
5. Extreme fatigue
6. Nausea and vomiting
7. Abdominal pain

Stages:

Hepatitis C infection can progress through several stages before leading to cirrhosis or liver cancer. The infection can persist for years without showing. Symptoms, making diagnosis challenging. The main stages of hepatitis C infection include:

1. Acute Infection:

In this stage, the virus first enters the body after exposure, and some patients. may experience mild to moderate symptoms like fatigue or jaundice, but many may not show any symptoms at all. In some cases, acute infection may resolve spontaneously without treatment, but in most cases, the infection becomes chronic (2).

2. Chronic Infection:

If the virus is not cleared during the acute phase, it remains in the body and can lead to chronic infection that lasts for many years. At this stage, no symptoms may be evident for several years, but the virus continues to cause gradual damage to the liver, leading to cirrhosis or even liver cancer in advanced cases (13).

3. Cirrhosis:

If the infection persists for an extended period without treatment, it may progress to cirrhosis, where the liver begins to lose its normal functions due to Scarring and damage caused by continuous inflammation. Symptoms at this stage include abdominal swelling (ascites), frequent nosebleeds, and jaundice (7).

VI. ADVANCED DIAGNOSIS

Diagnosis of Hepatitis C: An Overview

Hepatitis C is a liver infection caused by the hepatitis C virus (HCV), primarily transmitted through blood-to-blood contact. Accurate diagnosis is crucial for effective management and treatment. The diagnostic process involves several steps, including initial screening and confirmatory testing.

1. Initial Screening: HCV Antibody Tests

The first step in diagnosing HCV infection is to detect the presence of antibodies against HCV (anti-HCV) in the blood. These antibodies indicate whether an individual has been exposed to the virus. The commonly used tests include:

- Enzyme Immunoassays (EIAs): Third-generation EIAs have a sensitivity and specificity of approximately 99%A (14)
- Rapid Diagnostic Tests (RDTs): These point-of-care tests provide results within 30 minutes. The OraQuickA® HCV Rapid Antibody Test, for instance, has a sensitivity of 94.1% and specificity of 99.5%A (14) A positive antibody test indicates exposure to HCV but does not confirm an active infection, as antibodies can persist even after the virus has been cleared.

2. Confirmatory Testing: HCV RNA Detection

To determine if the infection is active, nucleic acid testing (NAT) is performed to detect HCV RNA in the blood: Qualitative HCV RNA Tests: These tests confirm the presence or absence of the virus. (15) Quantitative HCV RNA Tests (Viral Load Tests): These measure the amount of virus in the blood, aiding in assessing the severity of infection and monitoring treatment response. (15)

HCV RNA can typically be detected within 2 weeks after exposure, making NAT essential for early diagnosis (15).

3. Additional Testing (HCV Genotyping):

Identifying the specific genotype of HCV is important for guiding treatment decisions:
HCV Genotype Test: This test determines the strain of HCV, as different genotypes may respond differently to antiviral therapies. [15]

4. Non-Invasive Assessment of Liver Fibrosis

Liver fibrosis assessment is essential in managing chronic HCV infection. The most commonly used non-invasive methods for assessing liver fibrosis include:

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1. FibroTest (or FibroSure): A blood test that combines several biomarkers to assess the degree of liver fibrosis.
2. Transient Elastography (FibroScan): An imaging technique that measures liver stiffness using vibration waves to determine the degree of fibrosis. (16)

5.Screening Recommendations

Routine HCV screening is recommended for:
All adults aged 18 years and older. At least once in their lifetime A [17]

- Pregnant women: During each pregnancy A
- Individuals with ongoing risk factors: Such as those who inject drugs. _Accurate diagnosis of hepatitis C involves a combination of serological and molecular tests to confirm active infection and guide treatment.

VII. ADVANCED TREATMENTS

Treatments and Recent Advances in Hepatitis C Management Hepatitis C treatment has undergone significant advancements in the past two decades, making it possible to achieve high cure rates with modern therapies, such as direct-acting antivirals (DAAs).

1-Traditional Treatments (Interferon-Based Therapies) Pegylated Interferon and Ribavirin (Peg-IFN + Ribavirin):

The traditional treatment involved a combination of interferon and ribavirin, where interferon was administered weekly via injections, and ribavirin was taken orally. However, this treatment had several drawbacks, including severe side effects such as fatigue, depression, and weight loss. Additionally, cure rates ranged from 40% to 80%, depending on the genotype and the severity of liver fibrosis.

Challenges and Side Effects:

Interferon treatment required constant monitoring of side effects, which included flu-like symptoms, depression, chronic fatigue, and other psychological and physical effects that made adherence to the treatment difficult for many patients. (18)

2. Direct-Acting Antiviral Medicines (DAAs)

For Hepatitis C Treatment Direct-acting antiviral (DAA) treatments, such as sofosbuvir and daclatasvir, have revolutionized the treatment of Hepatitis C. These medicines target the virus directly by preventing its replication, resulting in cure rates of up to 95%. The duration of treatment typically ranges from 12 to 24 weeks, depending on whether liver cirrhosis is present [19].

While some patients may naturally clear the infection in acute cases without the need for treatment, chronic infection always requires treatment to prevent disease progression [19]. In addition to drug therapy, patients are advised to make lifestyle modifications, such as avoiding alcohol and maintaining a healthy weight to support the treatment [20].

3. World Health Organization Recommendations

The World Health Organization (WHO) recommends offering treatment to all adults, adolescents, and children aged 3 years and older with chronic Hepatitis C virus infection using direct-acting antivirals that target all genotypes of the virus. These treatments generally have few side effects and are effective in both acute and chronic cases [21].

4. Treatment in Advanced Cirrhosis Cases

In patients with decompensated cirrhosis due to Hepatitis C, studies have shown that treatment with direct-acting antivirals results in significant improvement in liver function scores, such as MELD and CTP [20]. Additionally, a multi-center Italian study demonstrated a significant increase in the rate of transition to CTP A, indicating a marked improvement in liver function [20].

5. Sofosbuvir/Velpatasvir Combination

Among the effective combination therapies, sofosbuvir and velpatasvir is a pan-genotypic treatment that targets all genotypes of the virus. This combination works by preventing the replication of the virus RNA, allowing the immune system to fight the virus and restore liver health [19]. However, patients are advised to consult with specialist physicians before starting treatment, especially in cases involving hypersensitivity to the drug components or co-infection with Hepatitis B. Such conditions require close monitoring to avoid complications [22].

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6. Overview of Key Medications

1. Sofosbuvir: Inhibits the RNA enzyme of the virus, preventing its replication within liver cells [19].
2. Daclatasvir: Inhibits the NS5A enzyme, which is crucial for the replication of the virus [19].
3. Ribavirin: A broad-spectrum antiviral drug that enhances the effectiveness of other treatments [19].
4. Velpatasvir: Used in combination with Sofosbuvir to target all genotypes of the virus [19].
5. Glecaprevir/Pibrentasvir: Effective in cases of liver cirrhosis or liver fibrosis [19].
6. Sofosbuvir/Ledipasvir: Commonly used for most genotypes of the virus [19].
7. Liver Transplantation

A liver transplant can be an option to treat severe liver damage caused by chronic Hepatitis C. The procedure involves replacing the damaged liver with a healthy one, usually from deceased donors, and sometimes from living donors who donate part of their liver.

However, a liver transplant alone does not cure Hepatitis C, as the infection can return. This requires additional treatment with antiviral drugs to prevent new liver damage. Recent studies have shown that these drugs can cure Hepatitis C after a transplant and sometimes even before it [22].

8. Vaccinations and Lifestyle Modifications

Vaccinations:

There is no vaccine for Hepatitis C, but doctors often recommend vaccines for Hepatitis A and B to prevent additional liver damage [22]. Lifestyle and Home Remedies:

1. Avoid alcohol: Speeds up liver damage.
2. Avoid liver-harming medications: Consult a doctor to review medications.
3. Prevent spreading the infection: Avoid sharing razors or toothbrushes; cover cuts; inform healthcare workers.
4. Sexual relationships: Inform your partner about your infection and use protection [22].

VIII. PREVENTION & FUTURE STRATEGIES

Hepatitis C virus (HCV) is an infectious disease that affects the liver and can lead to serious complications such as cirrhosis and liver cancer. Despite significant advances in understanding and treating this virus, prevention remains a key goal in controlling its spread.

Opportunities for enhanced prevention and control of hepatitis C: An estimated 2.4 million people in the United States are living with hepatitis C virus (HCV) infection. In 2020, the Centers for Disease Control and Prevention updated hepatitis C screening recommendations to test adults aged ≥18 years at least once in a lifetime and pregnant persons during each pregnancy. For those with ongoing exposure to HCV, periodic testing is recommended. The recommended testing sequence is to obtain an HCV antibody test and, when positive, perform an HCV RNA test. Examination of HCV care cascades has found that incomplete HCV testing occurs when a separate visit is required to obtain the HCV RNA test. Hepatitis C core antigen testing has been shown to be a useful tool for diagnosing current HCV infection in some settings. Hepatitis C testing that is completed, accurate, and efficient is necessary to achieve hepatitis C elimination goals [23].

Prevention of Hepatitis C involves measures that prevent the transmission of the virus between individuals, as the virus is transmitted through blood. The main prevention strategies include:

- Health Education and Awareness: Increasing awareness about how the virus is transmitted and how to prevent it through educational campaigns, especially in areas where the infection rate is high (2).
- Use of Clean Needles: Encouraging needle exchange programs to reduce the risk of infection among people who inject drugs (13)
- Improved Blood Screening: Ensuring that all donated blood units are tested for the virus before being used in surgeries or medical treatments (2). Guidance regarding hepatitis C diagnostic testing after a known exposure in a

healthcare setting has been published [24]. Hepatitis C screening during each pregnancy allows identification of persons who could benefit from DAA medication during the postpartum period as well as infants who should undergo testing because of perinatal hepatitis C exposure.

Abbreviations: CKD, chronic kidney disease; HCV, hepatitis C virus; HIV, hurman immunodeficiency virus; PrEP, preexposure prophylaxis.

Hospital and Clinic Safety: Following strict medical protocols in hospitals and healthcare centers to ensure that medical equipment does not transmit the virus (7).

Future Strategies: Although modern treatments are effective in curing Hepatitis C, prevention still plays a critical role. Some future strategies that could have a significant impact on reducing the spread of the virus include:

Continuous Vaccine Development: Although there is currently no approved vaccine for Hepatitis C, ongoing research may lead to the development of an Effective vaccine (13). Vaccines represent a great hope for eliminating the virus globally.

Advances in Gene Therapies: With the advancement of genetic Science, gene therapies could become an effective treatment option for Hepatitis C, allowing for more personalized and effective treatments (7).

Global Strategies to Eliminate the Virus: Implementing global programs aimed at eliminating Hepatitis C by 2030, through providing effective treatments and expanding screening and treatment programs in developing countries (13).

IX. CONCLUSION

In conclusion, this research on recent advances in the diagnosis and therapy of Hepatitis C virus (HCV) highlights that HCV remains a global health threat, causing significant complications affecting the liver and other organs. A deeper understanding of the disease's pathophysiology and transmission mechanisms has greatly contributed to the improvement of diagnostic and therapeutic methods, significantly reducing the incidence of long-term consequences such as liver cirrhosis and liver cancer.

In recent years, we have witnessed remarkable advancements in diagnostic methods, ranging from advanced serological tests to genetic techniques that offer greater accuracy in detecting the virus and analyzing its mutations. These innovations have facilitated early detection, leading to more effective treatment outcomes. Regarding treatment, advancements in the development of direct-acting antiviral (DAA) drugs have provided safer and more effective therapeutic options. These treatments are characterized by higher cure rates and fewer side effects compared to previous therapies, offering hope to millions of patients.

In terms of prevention, the ability to reduce the spread of the virus has been enhanced through effective strategies, including improving preventive measures, increasing public awareness campaigns, and the potential development of vaccines in the near future. Despite these advances, the key remains ensuring the widespread availability of these treatments, especially in resource-limited regions. Looking to the future, continued medical advancements are expected to further enhance our ability to combat Hepatitis C. With the integration of modern technologies, we have the opportunity to achieve the eventual eradication of the disease in many regions, thus alleviating the global burden of this virus. In conclusion, focusing on improving diagnosis, treatment, and intensifying preventive strategies, along with collaboration between healthcare and research institutions, remains crucial in reducing the impact of Hepatitis C on public health in the years ahead.

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