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A Review on Hepatitis and It's Treatment Options

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ABSTRACT

There are five basic forms of hepatitis, which is defined as inflammation of the liver mostly caused by viral infections A, B, C, D and E. The importance of chronic hepatitis B and C is highlighted in this report's analysis of the prevalence, clinical implications and modes of transmission of this illness worldwide. The World Health Organisation estimates that 354 million people worldwide suffer from chronic hepatitis B and C, which can cause significant health issues like cirrhosis and liver cancer. The paper describes the modes of transmission, emphasizing that body fluids and blood are the main means of transmission for hepatitis B, C and D, whereas contaminated food and water are the main means of transmission for hepatitis A and E. Risk factors that contribute to the spread of include the use of intravenous drugs, risky sexual behaviour and immunization exemption. These viruses reducing incidence rates requires preventive efforts, especially the availability of A and D vaccinations. The therapy of hepatitis C has changed dramatically as a result of advancements in antiviral therapies, which have high cure rates and greatly improved patient outcomes. In summary, the hepatitis epidemic must be stopped by implementing efficient public health measures, such as raising awareness, vaccinating the public and facilitating treatment access. To address the issues raised by this global health concern and move closer to the objective of eradicating the threat that hepatitis poses to public health, more research and surveillance are required.

Keywords: Hepatitis, Clinical implications, Immunization exemption, Global health and Surveillance.

INTRODUCTION

Hepatitis

Hepatitis is the term for liver inflammation. An injury or infection to the body's tissues results in inflammation. As a result, the liver cannot function correctly. Acute (short-term) or chronic (long term) hepatitis infections are both possible. Only certain forms of hepatitis can produce acute infections, but other types of infections can cause both acute and chronic illnesses. There are various forms of hepatitis, each with its own etiology. Viral hepatitis is the most prevalent kind and is caused by one of several viruses. These are A, B, C, D, and E hepatitis viruses. Where A, B, and C are the most prevalent (**MedlinePlus *et al.*, 2016**). Specifically, types B and C cause chronic illness in hundreds of millions of people and, when combined, are the most common cause of cancer and liver

cirrhosis. Most cases of hepatitis A and E are brought on by consuming tainted food or water. Parenteral contact with contaminated bodily fluids typically results in the development of hepatitis B, C, and D. Acute infections might cause little or no symptoms, or they can cause severe exhaustion, dark urine, nausea, vomiting, and stomach pain in addition to jaundice (yellowing of the skin and eyes) **(WHO. *et al.*, 2016)**.

Signs and symptoms of Hepatitis: Frequent symptoms of hepatitis include fever, dark urine, jaundice, whiteness of eyes, joint pain, vomiting, fatigue, abdominal pain, nausea.

- **Types of Hepatitis**

Hepatitis A

Positive-strand RNA hepatitis A virus (HAV) can persist in the environment and spread through the fecal-oral pathway because it is stable at low pH and moderate temperature **(Martin *et al.*, 2006)**. Hepatitis A virus (HAV) is still a major cause of acute viral hepatitis globally, despite the development of a highly safe and effective vaccination against the disease in the early 1990s **(Tong *et al.*, 1995).**

Epidemiology: HAV infections are seen around the globe, with greater prevalence in developing countries and low-income regions **(Jacobsen *et al.*, 2018).** In South Asia and sub-Saharan Africa, where early childhood exposure is common, HAV is hyperendemic and there are almost no at-risk adults. Latin America, the Middle East, North Africa, Eastern Europe, and middle-class Asian regions are home to intermediate endemicity **(Jacobsen *et al., 2005*).** If two persons are in close proximity to one another, HAV can be spread through sexual contact **(Lemon *et al.,1985).*** Child to parent transmission is a regular occurrence, which is why daycare facilities are frequently linked to the development of HAV **(Klevens *et at.*, 2010).** The most common cause of HAV from contaminated food and water is a food service employee who neglected to properly wash and sanitize their hands after handling excrement (**Schwarz *et al.*, 2008).** 11,200 people died from acute hepatitis A in 2015 **(GBD *et al.*, 2016).** The amount of hepatovirus A in circulation is lower in developed nations than it is in underdeveloped nations. Since the majority of adults and adolescents in poor nations have already experienced the illness, they are immune. Adults in middle-income nations may be exposed to or at risk for certain diseases **(Jacobsen *et al.*, 2010*).***

Diagnosis of Hepatitis A: HAV is eliminated in the feces at the conclusion of the incubation period, but the identification of HAV-specific IgM antibodies in the blood allows for a precise diagnosis. The blood only contains IgM antibodies after an acute hepatitis A infection. It appears 1-2 weeks following the original illness and lasts for up to 14 weeks. IgG antibodies in the blood indicate that the sickness has progressed past its acute phase and that the patient is no longer susceptible to infection. After vaccination, IgG antibodies to HAV are also detected in the blood, and the detection of these antibodies serves as the basis for testing for viral immunity **(Stapleton *et al.*, 1995).**

Prevention of Hepatitis A: Sanitation, hygiene, and vaccination can all help to prevent hepatitis A **(Rayan *et al.*, 2004)**, **(NHS *et al.*, 2009)**. Both offer proactive defense against upcoming infections. For almost 25 years, the vaccine offers protection against HAV in over 95% of instances **(Nothdurft *et al.*, 2008).** Injectable vaccinations are administered. Two to four weeks after vaccination, the first dosage offers protection for a year; six to twelve

months later, the second booster dose offers protection for more than twenty years **(CDC *et al.*, 2007).** In the US, vaccinations are advised for children between the ages of one and two **(Matheny *et al., 2014).*** This vaccination is advised for people who have never been immunized before and who have travelled and may travel in the future ***(*Matheny *et al.*, 2014**). The CDC advises men who have intercourse with other men to get vaccinated against illness **(CDC *et al.*, 2017).**

Hepatitis B

Hepatitis B is a form of viral hepatitis that damages the liver and is an infectious disease brought on by the Hepatitis B virus (HBV) **(WHO *et al*., 2022) (Logan *et al*., 1987).** Both acute and chronic infections may result from it **(WHO *et al.*, 2022).** Exposure to contaminated blood or bodily fluids spreads the infection **(WHO *et al.*, 2014).** Holding hands, sharing cutlery, kissing, hugging, coughing, sneezing, or nursing cannot transfer the hepatitis B virus **(CDC *et al.*, 2011)**. After exposure, the infection might be identified 30 to 60 days later **(WHO *et al.*, 2014).**

Epidemiology: As of 2019, there were at least 296 million cases of chronic HBV infection worldwide, or 3.8% of the total population. That year, there were an additional 1.5 million instances of acute HBV infection **(WHO *et al.*, 2022).** Globally, regional prevalence's vary from approximately 7.5% in Africa to 0.5% in the America **(WHO *et al.*, 2022).** Where there is a 2–7% chronic infection rate in places with moderate incidence, the disease primarily spreads horizontally, frequently among youngsters, although it can also spread vertically **(Alter *et al.*, 2003).** As of 2018, the estimated proportion of people living with HBV infection in the US was 0.26% **(Roberts *et al.*, 2022).**

Diagnosis of Hepatitis A: Assays, or tests for the identification of hepatitis B virus infection, are performed on serum or blood samples to identify the presence of either host-generated antibodies or viral antigens, which are the virus's manufactured proteins. These assays require complicated interpretation **(Bonino *et al*., 1987)**. The most common test for this illness is the hepatitis B surface antigen (HBsAg). It is the initial detectable antigen produced by the virus following infection. But this antigen might not be present in the early stages of an infection, and it might not be noticeable in the latter stages when the host is eliminating it. An internal "core particle" that encloses the viral genome is present in the infectious virion. The 180 or 240 copies of the core protein, also referred to as the hepatitis B core antigen, or HBcAg, make up the icosahedral core particle. IgM antibodies specific to the hepatitis B core antigen (*anti-HBc IgM*) may be the only serological evidence of disease. Therefore, most hepatitis B diagnostic panels contain HBsAg and total anti-HBc (both IgM and IgG) **(Karayiannis *et al.*, 2009).**

Prevention of Hepatitis B: Since 1991, the United States has routinely recommended vaccinations for babies to prevent hepatitis B. The first dose of the vaccine is typically advised within a day of birth. The hepatitis B vaccine was the first to be capable of preventing cancer, specifically liver cancer **(Schillie *et al.*, 2017)**.

Hepatitis C

The hepatitis C virus (HCV) is the infectious agent that causes hepatitis C, an illness that mostly affects the liver **(Ryan *et al.,* 2004)**. During the initial infection period, patients frequently have minimal or no symptoms. Early signs can include fever, black urine, abdominal pain, and yellow colored skin **(Q&A *et al.,* 2020)**.

Epidemiology: In a 2021 report, the World Health Organization predicted that, as of 2019, 58 million people worldwide have chronic hepatitis C **(WHO *et al.,* 2022)**. An estimated 1.5 million people contract hepatitis C year, and 290,000 people pass away from conditions connected to the virus, primarily cirrhosis and liver cancer **(WHO *et al.,* 2022)**. The 20th century saw a significant rise in the prevalence of hepatitis C infection as a result of both the reuse of improperly sanitized medical equipment and intravenous drug misuse **(Alter *et al.,* 2007)**. In 2015, the number of HCV cases grew overall, with around 950,000 new infections and 1.7 million treatment cases. 2015 saw an increase in the overall number of HCV cases with around 950,000 new infections and 1.7 million treatment cases **(Lombardi *et al.,* 2019)**.

Diagnosis of Hepatitis C: Hepatitis C can be diagnosed using a variety of methods, such as the quantitative HCV RNA polymerase chain reaction (PCR), recombinant immunoblot assay, and HCV antibody enzyme immunoassay (ELISA) **(Wilkins *et al.,* 2013)**. One to two weeks after infection, HCV RNA can be found by PCR, but it can take much longer for antibodies to develop and become visible **(Ozaras *et al.,* 2009)**. Patients with acute illnesses typically appear with mild, nonspecific flu-like symptoms, making diagnosis difficult **(Westbrook *et al.,* 2014)**. Most chronic infections don't show any symptoms for the first few decades **(Kanwal *et al.,* 2011)**. They are consequently most frequently found after looking into higher liver enzyme levels or while screening high-risk patients on a regular basis. The difference between acute and chronic infections cannot be determined by testing **(Alter *et al.,* 2007)**. Infant diagnosis is challenging since mother antibodies might last up to 18 months **(Robinson *et al.,* 2008)**.

Prevention of Hepatitis C: There isn't a vaccination that can prevent hepatitis C as of 2022 **(CDC *et al*., 2023)**. When injectable drug users combine harm reduction tactics, such giving them fresh needles and syringes and treating their substance abuse, their chance of contracting hepatitis C is reduced by approximately 75% **(Hagan *et al.,* 2011)**. Both blood donor screening and following standard operating procedures in medical facilities are critical on a nationwide scale **(Ray *et al.,* 2009)**. When possible, medicine should be administered orally rather than by injection in nations with limited access to sterilized syringes (Alter et al., 2007). Recent research also suggests that treating people with active infection, thereby reducing the potential for transmission, may be an effective preventive measure **(Zelenev *et al.,* 2018)**. Hepatitis C vaccine phase 1 clinical trials are set to begin in the summer of 2023 **(Biden *et al*., 2023)**.

Hepatitis D

It is a viral hepatitis which is generally caused by the Hepatitis Delta Virus (HDV) **(NIDDK *et al*., 2020) (Farci *et al*., 2003) (Magnius *et al*., 2018)**. HDV can spread through co-infection (concurrent HBV infection) or superinfection (superimposition of HDV on chronic HBV-positive or HBV-carrying individuals). Because of the

severity of its effects, HDV infection infected individuals with chronic hepatitis B (superinfection) are regarded as having the most dangerous form of viral hepatitis **(WHO *et al.*, 2020)**.

Epidemiology: Globally, HDV is widely distributed. Hepatitis B vaccine campaigns, however, are helping to lower the prevalence in many higher income nations (though rates are still high in particular populations, such as drug injectors and immigrants from HDV-endemic regions) **(Asselah *et al.*, 2023)**. Wherever there is high HBV incidence, low-income areas are plagued by a significant medical problem due to HDV infection **(Rizzetto *et al.*, 2015)**. Due to concurrently high rates of HBV, the Amazon basin and low-income areas of Asia and Africa currently have high rates of HDV. Hepatitis D is co-infected with HIV in 12.5% of cases, and it affects 5% of patients with chronic hepatitis B infection worldwide **(WHO *et al.*, 2023)**.

Diagnosis of Hepatitis D: Testing for anti-HDV antibodies, which show previous viral exposure or active infection, is necessary for hepatitis D screening. Hepatitis D RNA levels are used to demonstrate active HDV infection in the presence of anti-HDV antibodies. As HDV requires a hepatitis B virus infection to infect humans, testing for HDV is only recommended in individuals who are positive for the hepatitis B surface antigen (i.e., those who have had or are currently infected with hepatitis B. Non-invasive liver imaging techniques like transient elastography, commonly referred to as the Fibro Scan, or biomarker-based Fibro Test have not been proven to be reliable quantitative indicators of liver fibrosis in people with long-term hepatitis D infection. A liver biopsy is typically required in patients with suspected liver cirrhosis or fibrosis **(Asselah *et al.*, 2023)**.

Prevention of Hepatitis D: Since hepatitis D needs an active hepatitis B virus to infect and multiply in humans, vaccination against hepatitis B protects against hepatitis D viral infection **(Brian *et al.*, 2010)**. The World Health Organization advises that everyone have a hepatitis B immunization. To prevent viral infections of hepatitis B and D, the hepatitis B vaccine is usually administered within 24 hours of birth **(WHO *et al.*, 2024)**. In order to avoid hepatitis B and D spreading through bodily fluids, people getting tattoos or body piercings should use sterile equipment. In addition, contaminated needles can spread the disease, so people who inject drugs should seek help to cease using drugs, use sterile needles, and refrain from sharing needles with others **(ALF *et al.*, 2022)**.

Hepatitis E

Hepatitis E is an infection with the hepatitis E virus (HEV) that results in liver inflammation **(Medscape, Kamar *et al.*, 2019, 2014)**. Similar to hepatitis A, hepatitis E typically has an acute and self-limiting course of illness (the illness is transient and the person recovers), with low death rates in areas with abundant resources; on the other hand, it can be more severe in individuals who are pregnant or have compromised immune systems, with significantly higher death rates. The condition is more common in pregnant women, especially in the third trimester, and is linked to fulminant liver failure, a clinical state that has a 20% fatality rate **(WHO et al., 2019) (Patra et al., 2007) (CDC *et al.*, 2018)**.

Epidemiology: Every year, the hepatitis E virus infects about 20 million people. In 2015, these caused almost three million acute illnesses and 44,000 fatalities **(CDC *et al.*, 2019)**. HEV infection can cause issues for pregnant women, who can develop an acute form of the disease that is deadly in at least 30% of cases. In the underdeveloped world, HEV is a leading source of disease and mortality, and it accounts for a disproportionate

share of deaths among expectant mothers. Although there have been outbreaks in the Middle East and Central America, hepatitis E is prevalent in Central Asia **(Teshale *et al.*, 2017) (Navaneethan *et al.*, 2008)**. Hepatitis E is becoming more common in affluent countries; in England and Wales alone, there were 848 instances of hepatitis E virus infection in 2015 **(Public Health England et al., 2019)**.

Diagnosis of Hepatitis E: Only a laboratory blood test that verifies the existence of HEV RNA or IgM antibodies to HEV may be relied upon for the diagnosis of hepatitis E **(CDC *et al.*, 2018)**. The Food and Drug Administration has never approved any serologic tests in the US for the diagnosis of HEV infection **(CDC *et al.*, 2018)**. To detect and quantify HEV RNA, the World Health Organization has created an international standard strain **(Baylis *et al.*, 2013)**. Three weeks following the onset of symptoms, the viremic window for HEV RNA detection in acute infection closes **(Webb *et al.*, 2019)**.

Prevention of Hepatitis E: The most crucial step in preventing hepatitis E is sanitation, which includes better personal hygiene practices, hygienic food preparation, increased standards for public water supplies, and appropriate handling and disposal of human waste. As a result, the disease's prevention techniques are comparable to those of many other illnesses that afflict underdeveloped countries **(WHO *et al.*, 2019)**. The hepatitis E virus is killed by cooking meat at 71 °C (159.8 °F) for five minutes; however, other temperatures require varied amounts of time to inactivate the virus **(FSAI *et al.*, 2019)**.

- **Pathogenesis**

Pathogenesis of Hepatitis A Virus (HAV): A recent study found that whereas a nonenveloped, naked form of HAV is excreted through feces, a quasi-enveloped form of HAV (eHAV) is found in the serum and plasma of infected individuals **(Feng *et al.*, 2013)**. Released from hepatocytes, eHAV eventually loses its lipid envelope in the biliary canaliculus when it comes into contact with high bile salt concentrations **(Walker *et al.*, 2015) (Hirai-Yuki *et al.*, 2016)**. HAV can benefit from the unique properties of nonenveloped HAV and eHAV for effective viral transmission and immune evasion, respectively. The quasi-envelope of eHAV cloaks the capsid within infected hosts, protecting it from neutralizing antibodies that go after capsid proteins **(Feng *et al.*, 2013)**. Peaks in viremia and fecal virus shedding during acute hepatitis A are followed by hepatocellular damage, which is indicated by elevated liver enzymes in the serum, such as ALT **(Shin *et al.*, 2016a)**. Viral shedding in feces often lasts for two to three weeks after the initial rise in serum ALT levels, while sensitive reverse transcription polymerase chain reaction techniques may detect it for longer times **(Martin *et al.*, 2006).** Hepatitis C virus (HCV) RNA was found to be persistent in the liver of chimpanzees for months following the termination of fecal viral discharge **(Lanford *et al.*, 2011)**. HAV antigens have also been found in the crypt cells of the small intestine in owl monkeys (Aotus trivirgatus) that have received an oral HAV vaccination **(Asher *et al.*, 1995)**. There is no human confirmation of this. Furthermore, HAV has been found in saliva and tonsils soon after viremia, despite saliva having a relatively low viral titer **(Cohen *et al.*, 1989)**.

Pathogenesis of Hepatitis B Virus (HBV): A primary cause of Hepatocellular Carcinoma (HCC) is HBV. About 80% of newly diagnosed HCC in HBV endemic regions, like the Asia Pacific region, are linked to chronic HBV infection **(Zhu *et al.*, 2016)**. In persistent HBV patients, liver cirrhosis can dramatically raise the risk for HCC **(Rapti *et al.*, 2015)**. The risk for HCC can also be influenced by other variables like age, gender, serum alanine

aminotransferase (ALT) level, serum HBV DNA level (i.e., viral load), and HBeAg level **(Tseng *et al.*, 2012)**. For instance, the combination of a high ALT level, HBeAg positive, and a serum HBV DNA level of ≥10,000 copies/mL is thought to be a strong predictor for the development of HCC, regardless of the degree of liver cirrhosis **(Yang *et al.*, 2002) (Chen *et al.*, 2006).** Additionally, a high viral load by itself is predictive with postoperative HCC recurrence **(Wu *et al.*, 2009) (Hung *et al.*, 2008)**. Additionally, HCC shows a gender gap among HBV carriers, with a 5–7:1 male to female ratio **(Wang *et al.*, 2015)**. In HBV transgenic mice, the similar gender difference in HCC incidence was also noted **(Na *et al.*, 2011)**. At least some of this gender difference can be ascribed to the positive feedback loop between HBV and the androgen receptor (AR) **(Zheng *et al.*, 2007)**. Citation 249 states that HBx can bind to AR and increase its activity. Citation 340 states that AR can be activated by activating Src and glycogen synthase kinase-β (GSK3β) **(Yang *et al.*, 2009)**. Citation 109 and Citation 110 state that this process can then activate HBV gene expression through its AREs located in the HBV genome, enhancing HBV replication and ultimately leading to carcinogenesis **(Tian *et al.*, 2012) (Wang *et al.*, 2009)**.

Pathogenesis of Hepatitis C Virus (HCV): The HCV virus is not cytotoxic **(Irshad *et al.*, 2006)**. It enters the liver cell and replicates concurrently, leading to immune-mediated cytolysis and a host of additional phenomena like oxidative stress, insulin resistance, and hepatic steatosis. Furthermore, this causes necrosis of the cells. A major part of HCV pathogenesis and disease causation is played by the proteins and peptides encoded by various sub-genomic sections of the HCV genome and their quasispecies, which impact the aforementioned mechanism. The section that follows provides a brief overview of HCV etiology in light of these variables **(Haid *et al.*, 2013)**.

Pathogenesis of Hepatitis D Virus (HDV): Only in hepatocytes does HDV reproduce. Thus, liver damage is the primary organ affected by HDV infection-related cellular damage. It is believed that immune-mediated liver damage contributes to HDV infection **(Niro *et al.*, 2012)**. Acute HDV infection is thought to cause degenerative changes in infected hepatocytes, which

are associated with cytopathic hepatocellular damage. These changes include reduced eosinophilic cytoplasm and pyknotic nuclei, as well as a lack of inflammatory cells in the liver parenchyma. Additionally, these results are clear from in vitro (cell culture system) research **(Cole *et al.*, 1991)**. It has been observed that immune-mediated responses differ between acute and chronic HDV infection **(Casey *et al.*, 2006) (Fiedler *et al.*, 2006)**. It could account for HDV superinfection's chronicity and persistence. The primary means of virus clearance by cytotoxic T lymphocytes is the destruction of HDV-infected cells. Failure to eradicate the infection and the development of a chronic infection have been linked to a delayed and inadequate immune response with the capacity to identify a restricted number of viral epitopes. Fulminant hepatic failure has been reported in 5% of people superinfected with HDV and 1% of those co-infected with HBV and HDV. It is suggested that fulminant hepatic failure is caused by an overexaggerated immunological response, namely a cell-mediated one, which results in extensive hepatocyte necrosis and liver damage **(D'Ugo *et al.*, 2008) (Hansson *et al.*, 1991)**.

Pathogenesis of Hepatitis E Virus (HEV): Hepatitis E's pathophysiology is not well known. As HEV is thought to spread by the fecal-oral pathway, the method by which the virus enters the liver remains unknown. There can be a virus replication location outside of the liver. Before the virus reaches the liver, it may multiply in the gastrointestinal system. Pigs' colon, small intestine, lymph nodes, and liver have all been found to have negative strands of HEV RNA, which is indicative of extra-hepatic HEV replication **(Williams et al., 2001)**. Following

its replication in the hepatocyte cytoplasm, HEV is discharged into the blood and bile. Since HEV is not cytopathic, the liver damage caused by the infection may be immune-mediated by cytotoxic T lymphocytes and natural killer (NK) cells **(Emerson et al., 2013)**.

- **Treatment**

Treatment of Hepatitis A: Hepatitis A has no known specific treatment. After an infection, symptoms may take weeks or months to go away. The goal of therapy is to keep patients comfortable and on a balanced diet, replacing any fluids lost due to diarrhoea and vomiting **(WHO *et al*., 2014)**.

Treatment of Hepatitis B: Most persons with an acute hepatitis B infection recover on their own without medical intervention **(Hollinger *et al*., 2006) (CDC *et al*., 2017)**. Less than 1% of patients who have an extremely severe infection (fulminant hepatitis) or who are immunocompromised may need early antiviral therapy. On the other hand, in order to lower

the risk of liver cancer and cirrhosis, therapy for persistent infections could be required. Therapy candidates for chronic infection include those with levels of HBV DNA and alanine aminotransferase, a sign of liver damage, that are consistently increased in the serum **(Lai *et al*., 2007)**. Depending on the medicine and genotype, the course of treatment can span six months to a year **(Alberti *et al*., 2011)**. Depending on the medicine and genotype, the course of treatment can span six months to a year **(Terrault *et al*., 2016)**.

Treatment of Hepatitis C: It is recommended that people with chronic hepatitis C stay away from alcohol and liver-toxic drugs because, they have a higher risk of contracting hepatitis A and hepatitis B if they are also immunized against these diseases **(Wilkins *et al*., 2010)**. At lower dosages, acetaminophen use is usually regarded as safe. Because of the higher risk of bleeding, nonsteroidal anti-inflammatory medications (NSAIDs) are not advised for those with severe liver disease. Drinking coffee has been linked to a decreased incidence of liver damage in HCV patients **(Kim *et al*., 2016)**.

Treatment of Hepatitis D: The antiviral Hepcludex (bulevirtide) was authorized by the European Medicines Agency's Committee for Medicinal Products for Human Use in May 2020 to treat hepatitis D **(Hepcludex *et al*., 2020)**. Hepatitis D and B viruses cannot enter hepatocytes when bulevirtide binds to and inactivates the sodium/bile acid cotransporter **(Francisco *et al*., 2020) (MYR *et al*., 2020)**. Pegylated interferon alpha and bulevirtide may be administered together because of the theoretical synergistic impact that could result in higher therapeutic response rates **(Asselah *et al*., 2023)**.

Treatment of hepatitis E: For acute HEV infections, there is no suggested course of action. They typically self-limit and clear their HEVs on their own. In certain instances, immunocompetent patients with severe hepatitis have been recommended to take ribavirin **(Peron *et al*., 2011)**. Many studies have been conducted on ribavirin monotherapy for the treatment of chronic HEV infections in recipients of SOT **(Pischke** et al**., 2013)**.

RATIONALE, AIM AND OBJECTIVES BEHIND THE WORK

3.1 Rationale

Hepatitis is an inflammation of the liver that can be brought on by a number of things, such as autoimmune illnesses, alcoholism, toxins, viruses, and certain drugs. The rationale for studying hepatitis involves several key aspects such as Public Health Impact, Viral Types, Chronic Liver Disease, Vaccination and Treatment Advances.

3.2 Aim

The aim of the review is to explore the epidemiology, prevention and treatment of Hepatitis and to determine the risk factors and protective variables associated with Hepatitis transmission.

3.3 Objectives

- To look into how hepatitis affects mental health and quality of life.
- To comprehend the prevalence and epidemiology of hepatitis.
- To review existing preventative and treatment techniques for hepatitis.

MATERIAL AND METHODS

- **Materials**

I have read through numerous magazines, newsletters, papers, and scientific websites like Google Scholar, PubMed, and so forth. I have also read through in-depth reviews of "Hepatitis."

- **Methods**

I've read a number of articles about the many approaches taken to treating hepatitis. This study examines the various techniques and treatments. Vaccinations, Ayurvedic, Allopathic, and herbal remedies are among those few forms of treatment.

- **Vaccines used for the Treatment of Hepatitis**

Vaccine for Hepatitis A: There are now two single-antigen hepatitis A vaccinations registered for use in the United States: VAQTA (Merck & Company, Inc., Whitehouse Station, New Jersey) and HAVRIX

(GlaxoSmithKline Biologicals, Rixensart, Belgium). Both are made from inactivated HAV and have similar immunogenicity and effectiveness **(Ashur *et al.*, 1999)**.

Table displays the dosages and administration regimens for various vaccinations.

Immunogenicity is not reduced by using one licensed vaccine to finish a series after beginning with another **(Bryan *et al.*, 2001) (Connor *et al.*, 2001)**.

Table 1.1 Displays the Dosages and Administration Regimens For Various Vaccinations

Vaccines	Age groups (Years)	Dose	Volume (ml)	No. of doses	Schedule (Months)
HAVRIX	1-18	720 ELISA units	0.5	2	0,6-12
	≥19	1,440 ELISA units	1.0	2	0,6-12
VAQTA	1-18	25 units	0.5	2	0,6-18
	≥19	50 units	1.0	2	0,6-18
TWINRIX	≥18	720 ELISA units/20 µg Hepatitis B vaccine	1.0	3	0,1,6

Vaccine for Hepatitis B Virus: The majority of hepatitis B vaccines on the market today are made using recombinant DNA technology, however the first approved hepatitis B vaccines were plasma-derived and contained pure HBsAg. Although hepatitis B vaccinations are normally administered in a three-dose series, vaccine formulations with two- and four-dose regimens have also been approved for use in certain age groups in the US **(ACIP *et al.*, 2005)**. For newborns fewer than six weeks of age, only the single-antigen hepatitis B vaccine is approved for administration at birth. At any age, single-antigen vaccinations can be given in addition to other vaccinations, and numerous combination shots that contain hepatitis B antigens have international and US licenses. Hepatitis B vaccinations are thought to be equally efficacious and immunogenic when administered to the right age range and at the dose advised by the manufacturer. As such, they can be used interchangeably **(Andre *et al.*, 1990)**.

Vaccine for Hepatitis E Virus: The possibility of a HEV vaccination has been raised by a number of lines of data. First, following spontaneously acquired and experimentally induced HEV infections in cynomolgus monkeys, serum antibodies to HEV are produced **(Tsarev *et al.*, 1994)**. Second, hepatitis E sero epidemiology indicates that those who have already contracted HEV are immune during outbreaks of the illness **(Bryan *et al.*, 1994)**. Ultimately, the achievement of passive immune prophylaxis in animals suggests that hepatitis E vaccine based on humoral immunity can be efficacious **(Quiroga *et al.*, 1996)**. The most promising subunit vaccine

candidate is the HEV ORF2-encoded protein because to its strong antigenicity. Prokaryotic cells have so far been shown to express the HEV ORF2 gene or its components **(Im *et al*., 2001) (Zhang *et al*., 1999)**.

- **Allopathic Drugs Used for the Treatment of Hepatitis**

For Hepatitis B

The chance of developing liver failure, cirrhosis, liver cancer, and hepatitis-related mortality is decreased with treatment for chronic HBV. At the moment, there are two forms of approved therapy for chronic HBV: Immune Modulator Drugs which strengthen the immune system and aid in the eradication of the hepatitis B virus. For around six months to a year, they are injected by medical personnel example Pegylated Interferon (Pegasys), Interferon Alpha (Intron A) and Antiviral Drugs which hinder or stop the virus from spreading example Tenofovir, Adefovir etc.

- **Current Treatment**

Since there has been a long-standing treatment for HBV, medical professionals are well-versed in its negative effects. Among these therapies are:

Nucleoside Analogues (NAs) or Oral Antivirals

Antivirals, often known as NAs, lessen the chance of liver damage by slowing down or eliminating the hepatitis B virus's ability to reproduce. A lower viral load results in less liver damage. NAs are taken orally as pills, and very few adverse effects are reported. First-line therapies, such entecavir and tenofovir disoproxil, are powerful and efficient at suppressing the virus, but their effects are only temporary. A patient might need to take these medications for the rest of their lives because stopping treatment causes the virus to recur. Adults' authorized HBV medications include first line drugs like as tenofovir Disoproxil, Tenofovir Alafenamide, Entecavir and second line drugs Telbivudine**,** Adefovir Dipivoxil**,** Lamivudine **(Alan *et al*., 2022)**.

For Hepatitis C

- **Direct Acting Antivirals (DAAs):** For hepatitis C, direct-acting antivirals (DAAs) are the most widely used medication. Usually, they are administered as pills. 97% percent of cases of hepatitis C can be cured with these drugs. They function by aiding in the prevention of HCV replication. For hepatitis C, three different kinds of DAAs are employed. They target nonstructural (NS) proteins or enzymes in an effort to impede the growth of HCV. These kinds consist of:
- **NS3/4 Protease Inhibitors:** Protease inhibitors work by preventing viruses from replicating, which can help halt infections from spreading throughout your body. Protease inhibitor grazoprevir treats genotypes 1 and 4 of hepatitis C. Elbasvir-grazoprevir is the name given to it and is exclusively accessible in conjunction with elbasvir. Zepatier is the brand name used to sell this combination of medications. Basically, they act by targeting the enzyme. Example includes Grazoprevir, Telaprevir, Paritaprevir, Boceprevir etc.
- **NS5A Inhibitors:** These medications' exact mode of action is unknown. They might function by preventing the virus from replicating itself. They might also aid in preventing drug resistance, which is the situation where a medicine loses its ability to treat a problem. These medications cover every HCV genotype. They can be taken either by alone or in conjunction with other drugs. Basically, they act by targeting the protein.

Example include Elbasvir (a part of the combination medication Zepatier) and Ledipasvir (a part of the combination treatment of Harvoni).

- **NS5B Polymerase Inhibitors:** These medications function by inhibiting the NS5B enzyme. This enzyme is essential for HCV survival and self-replication. Example includes Sofosbuvir (Sovaldi) **(Ami *et al*., 2023)**.

For Hepatitis D

HDV currently has no known treatment. Pegylated interferon alfa is the medication that doctors administer most frequently until they find better alternatives. Not everyone gets the best results using Peg-IFNa. Numerous adverse consequences, including low energy, weight loss, flu-like symptoms, and mental health problems including depression, can also result from it. The ideal duration of HDV treatment is unknown to medical professionals. Peg-IFNa may need to be taken for a full year. Your doctor can advise you to continue taking PEG-IFNa for up to a year if a blood test reveals that you still have a particular level of the virus in your body. Example includes Interferon Alfa (peg-IFNa) **(Minesh *et al*., 2022)**.

For Hepatitis E

The following are the options for treating chronic HEV. Firstly, use of Ribavirin, second, pegylated IFN-α (pegIFN-α) administration and third, decrease of immunosuppression. **(H *et al*., 2012) (Y *et al*., 2016)**. First, it is necessary to assess if immunosuppressive medicine may be reduced **(H *et al*., 2012)**. The off-label usage of RBV, either alone or in conjunction with pegIFN-α, is the most often used HEV treatment. Numerous large-scale investigations have confirmed its effectiveness in lowering patients' viral loads for both acute and chronic illnesses **(N *et al*., 2010) (V *et al*., 2010) (S *et al*., 2013)**. Example includes Ribavirin, Pegylated IFN- alpha.

- **Ayurvedic Drugs used for the Treatment of Hepatitis**

Arogyavardhini Vati: Among the polyherbal-minerals listed in the Ayurvedic formula is Arogyavardhini Vati **(Santosh *et al*., 2016)**. Because it is safe and effective, it has been used for generations to treat liver problems, jaundice, and other skin conditions. Since "Vardhini" means to enrich and "Arogya" means good health, Arogyavardhini refers to something that enhances or enriches excellent health. This is recommended as a treatment for all three Dosha (humour) imbalances. In the context of Kustha vikaras, the formulation or yoga has been mentioned in Rasaratnasamucchaya **(Ambikadatta *et al*., 1994)**. Arogyavardhini was used to treat acute viral hepatitis, and the condition significantly improved while the drug had notable hepato-protective properties **(Antarkar *et al*., 1980)**. In a case study, a 53-year-old male patient complained of yellowish urine, decreased appetite, generalized weakness, nausea, and mild pain in the right hypochondriac region. The patient received six months of treatment with Herbo mineral preparations such as Phalatrikadi Kwath, Arogyavardhini Vati, Liv52 HB, and Rohitakarishta, among others, as described in traditional Ayurvedic texts. Before, during, and after the course of treatment, both subjective and objective assessments (pathological) were completed. After the course of treatment, notable alterations were noted in both subjective and objective indicators (as shown in figure 2.1) **(Ashish *et al*., 2019)**.

Figure 2.1 Arogyavardhini

Picorrhiza kurroa (Kutki): The other name of the Katuki is Picorrhiza kurroa. Greek words picrorhiza, which translate to "bitter" (picros) and "roots" (rhiza), are the source of the word. Within the Plantaginaceae family, the genus Picrorhiza has two species: Picrorhiza scrophulariiflora Pennell and Picrorhiza kurroa Royle ex Benth. The majority of species can be found in natural settings including mountainsides, cliffs, and cracks. The primary habitat of Picrorhiza kurroa Royle ex Benth is the Himalayan ranges of Nepal, Pakistan, and India, which are located between 3000 and 5000 meters above sea level **(Dutta *et al.*, 2007) (Chhetri *et al.*, 2005)**. Kutki has its biological activity and hepatoprotective activity. It has hypocholesterolaemic activity with reference to obesity **(Tiwari *et al.*, 1980)**. Subsequently, KHS-MRC researchers investigated P. kurroa-Kutki's involvement in NAFLD (Non-Alcoholic Fatty Liver Diseases), a rapidly developing serious health concern (as shown in figure 2.2) **(Harsh *et al.*, 2021)**.

Figure 2.2 Kutki (Picorrhiza Kurroa)

Bhui Amla: An annual plant, bhui amla grows best during the rainy season. The plant is known to grow to a considerable extent as a weed in various regions of the nation, including Bihar,

Uttar Pradesh, Tamil Nadu, Maharashtra, Punjab, and Sikkim. It can endure in tropical climates with lots of rains, allows for brief capture of water **(Vikas *et al*., 2014)**. Bhui amla has been utilized for ages as a significant hepatoprotective treatment. It has been documented that the phyllanthin and hypophyllanthin found in P. amurus have hepatoprotective properties. Its poor herbage, short availability time, and strict requirements cause it to be in scarce supply despite its great value as a hepatoprotective agent **(Thakur *et al*., 2011) (Sharma *et al*., 2011)**. Bhumi Amla belonging to the family Euphorbiaceae and having different Indian names like Bhuti, Bhum Amlak, Bhuamlaki, Bahupatri etc **(Verma** et al**., 2014).** According to reports, P. amarus aqueous extract has a hepatoprotective effect on rat liver damage brought on by ethanol **(Pramyothin *et al*.,** 2007**).** Another study found that bhui amla aqueous extract had a hepatoprotective effect against nime sulide-induced liver damage when administered at doses of 50 or 100 mg/kg body weight over a period of 7 days (as shown in figure 2.3) **(Chatterjee *et al*., 2006)**.

Figure 2.3 Bhui Amla

Silybum marianum (Milk Thistle) The white streaks that run over the green leaves of this plant gave rise to its name. Should you tear or crush the leaves, a creamy white liquid will seep forth. It is also sometimes referred to as holy thistle or Mary thistle. These days, it grows all over the planet, including portions of North and South America, South Australia, and northern Africa. It is frequently referred to as silymarin and is a major constituent of the plant's seeds. Although they are not exactly the same substance, the terms silymarin and milk thistle are sometimes used interchangeably. Silymarin is regarded as an anti-inflammatory and antioxidant. It's one of the most often utilized herbal medicines for liver problems in the US. It is claimed that silymarin prevents poisons

from adhering to liver cells. Additionally, it controls free radicals. The processes that your body goes through produce these unstable chemicals. However, they can cause health problems and damage to healthy cells. Mixed outcomes have been found in medical study on milk thistle and liver health. According to studies, silymarin may aid in reducing inflammation and fostering cell repair. This could lessen the signs and symptoms of liver conditions such cirrhosis, fatty liver disease, liver cancer, and jaundice. Other research, on the other hand, has not demonstrated any efficacy against hepatitis C, a viral liver illness. Even at higher-than-normal doses of silymarin, persons with hepatitis C did not show any benefit, according to a significant study. When comparing the quality of life and viral levels of individuals taking milk thistle to those receiving a placebo, researchers discovered no differences (as shown in figure 2.4) **(Minesh *et al*., 2022)**.

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Figure 2.4 Milk Thistle (Silybum marianum)

Curcuma longa (Turmeric): Curcumin, a naturally occurring phenolic molecule, has been demonstrated to exhibit anti-inflammatory, anti-oxidant, and anti-proliferative properties on cells, significantly impacting their metabolism and capacity for proliferation **(B.B. *et al*., 2009) (B. *et al*., 2004)**. Depending on the virus, curcumin's mode of action varies and can include directly inhibiting the machinery used by the virus to replicate, like in the case of HIV **(C.J. *et al*., 1993)** or, as in the case of HCV, suppression of a cellular signalling pathway necessary for viral replication **(K. *et al*., 2010)**. Curcumin has the interesting ability to directly target cellular proteins and induce their breakdown, in addition to its ability to disrupt cell signalling at various levels and influence cellular enzymes (as shown in figure 2.5) **(P. *et al*., 2005)**.

Figure 2.5 Turmeric (Curcuma longa)

Zingiber Officinale (Ginger): Studies focus on plants that are traditionally used to treat liver disorders and support liver function. Antioxidant properties are well recognized to be present in ginger. Patients with liver illness have been using so-called complementary and alternative medicines at a significantly higher rate. Herbal therapy is the most widely used of these methods, despite their abundance **(Bass *et al*., 2002)**. The US FDA's "Generally Recognized as Safe" (GRAS) publication includes a list of ingredients that include ginger **(Langner *et al*., 1998)**. The polyphenolic chemicals gingerols, or 6-gingerol, 8-gingerol, and zingerone, were found to be the main active ingredients in the fresh ginger rhizome **(Zjicek *et al*., 1985)**. Furthermore, the most prevalent component in the gingerol family and the source of its distinctively strong flavour is gingerol [5-hydroxy-1-(4-hydroxy-3-methoxy phenyl) decan-3-one] (as shown in figure 2.6) **(Gruenwald *et al*., 2000)**.

Figure 2.6 Ginger (Zingiber officinale)

RESULT AND DISCUSSION

Hepatitis refers to inflammation of the liver, typically caused by viral infections (A, B, C, D and E), alcohol usage, toxins, or autoimmune illnesses. Symptoms may include weariness, jaundice, abdominal pain, and loss of appetite. There are two types of hepatitis: acute and chronic. A chronic infection increases the risk of malignancy or serious liver damage. Hepatitis A and B vaccinations are available, and antiviral medications can frequently be used to treat hepatitis C. Vaccination, healthy eating habits, and abstaining from unprotected sex and sharing needles are all examples of prevention. For those who put themselves at risk, routine medical examinations are crucial.

CONCLUSION

Conclusion may include public health importance, preventive measures and need for continued research. Hepatitis is a major worldwide health problem that affects millions of people and can cause serious liver problems. To improve results, early detection and treatment are essential. Reducing transmission largely depends on preventive measures like immunization and safe practices. In order to eliminate stigma and promote health, public awareness and education are crucial. For afflicted populations to live healthier futures, hepatitis must be managed and eventually eradicated through increased research and access to healthcare. The prognosis for people with viral hepatitis, especially hepatitis B and C, has significantly improved due to developments in diagnostic methods, antiviral medications, and immunizations. Global results are nevertheless impacted by disparities in timely intervention, awareness, and access to healthcare. Reducing the global hepatitis burden requires early discovery, suitable treatment, and preventative measures including vaccination. Controlling the disease's spread will require ongoing research into new treatments and vaccinations as well as public health campaigns centred on education and prevention. In the end, eradicating hepatitis as a significant public health concern requires a multifaceted strategy that includes increased access to healthcare, public education, and international cooperation.

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