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CRITICAL INSIGHT INTO THE GLOBAL EPIDEMIOLOGY OF VIRAL HEPATITIS ALONG WITH METHODS OF PREVENTION

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ABSTRACT: Even though viral hepatitis is a major public health concern around the world. It now has the attention and financial support of global health decision-makers. Every year, over 1.4 million individuals die due to viral hepatitis-related cirrhosis and liver cancer, with the majority of the population being unaware of their illness. This demographic has numerous challenges, including a profound ignorance, bias, inadequate access to health resources, and the implementation of innovative programs and policies. Even after implementing new strategies to manage the illness in recent years, the projected decline has not been evident. The study's major goal is to show current global illness frequency levels and investigate precautionary measures. The study's information and findings came from published scientific publications, online sources, and various search engines.

INTRODUCTION: The word hepatitis is derived from two words; the first is 'Hep' which is 'Hepar' in Greek for "liver" and 'itis', which means "inflammation". So Viral hepatitis is basically a liver inflammation caused by some hepatotropic viruses; this inflammation is nothing but swelling that occurs when tissues of the body get damaged or infected. Normally, hepatitis is referred as viral infection. It can damage organs (liver), which will affect various functions of that organ [1]. Hepatitis can be acute, a short-term infection that can be cured of its own, and chronic, a long-term infection that can progress to liver failure.

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It is a crucial worldwide health issue that affects the liver, and there are around a hundred million people affected by it. There are around five hepatotropic viruses that increase the global burden, and these are Hepatitis A Virus (HAV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Hepatitis D (delta) virus (HDV), and Hepatitis E Virus (HEV) [2]. Hepatitis can sometimes be caused by heavy alcohol use or through medico conditions and medication, but the disease is typical of viral origin. Hepatitis A virus infection is an acute and short-term disease whereas Hepatitis B, C and D are those types of hepatitis that are chronic and long term.

On the hand, the fifth type of hepatitis virus is hepatitis E virus; it is also acute but becomes a major problem in pregnant women. Chronic hepatitis B virus and chronic hepatitis C virus are the two major chronic viral hepatitis infections that causes 1.3 million deaths annually talking globally, the world health organization (WHO) estimates that

325 million people live with hepatitis B and C worldwide, and many of them testing and treatment is easily available. Within the United States, the most common hepatitis viruses are B, and C. Hepatitis B virus infection is widely spread in Asia-Pacific region and Sub-Saharan African region, whereas HCV infection spreads in all regions [3].

Etiology: Hepatitis viruses are the most common cause of hepatitis globally. But few other factors can also be a reason behind hepatitis. These factors are – drinking too much alcohol, medico conditions, or sometimes autoimmune diseases that can also cause a problem that will lead to hepatitis. If we talk about hepatitis A virus and hepatitis E virus, they share similarities. The transmission mode for both viruses is the fecal-oral route (from contaminated water, food, poor hygiene, and lack of sanitation). Whereas hepatitis B virus can be found in serum, vaginal mucus, semen, and tears even at very low levels, but is not found in the stool, urine, or sweat. The basic transmission route is parenteral, but it can also be transmitted through sexual contact with an infected person. It can also spread through infected blood or blood products or infected needles. Hepatitis C virus is transmitted through the parenteral route or through sexual contact.

The most common route is parenteral, and the other two routes are less common. Hepatitis D virus needs hepatitis B surface antigen as its capsid protein; however, the population infected with hepatitis d virus is definitely co-infected with hepatitis b virus. The accurate and precise etiology of autoimmune hepatitis is not known. But some factors such as environmental agents, drugs or hepatitis viruses, or Epstein - Barr virus may activate autoimmune response. Drugs such as Adalimumab, Nitrofurantoin, Minocycline, *etc.*, can activate autoimmune hepatitis. The accurate reason behind alcoholic hepatitis is unknown; many factors play a vital role in causing alcoholic hepatitis. These are the consumption of ethanol and its metabolites such as acetaldehyde; they destroy the hepatocyte cell membrane.

Pathology: Hepatitis is mainly caused by the hepatitis virus. How these viruses infect the liver cell? - So basically what happens is that these viruses enter inside the human body by any means of transmission, and when they reach the liver through the circulation of the body, and once inside the liver, these cells inoculate and become hepatocytes which are the cells of the liver (liver is made up of a large number of hepatocytes which are arranged in clusters called lobules). After getting inside the liver cells these viruses start to multiplying there (because it is a very favorable environment for the growth and multiplication of these viruses). But the growth and multiplication of these viruses do not lead to liver cell damage. These viruses will change the structure of the antigen present on the surface of the hepatocyte. Because of this change, the body recognizes these hepatocytes as foreign material and starts to destroy those hepatocytes by the mechanism of "self-medicated immune damage".

The body tries to destroy a maximum number of infected hepatocytes by the mechanism of apoptosis. It's fine in case of an acute infection (hepatitis A, E). Because they don't have any chronic action potential. But it really becomes a problem in the case of hepatitis C and B. because these viruses live dormant inside the hepatocytes, which ultimately reactivate after many years and start to infect new hepatocytes. Again the self-medicated immune damage activates and leads to the destruction of a large number of hepatocytes in the liver. And after the long run this will lead to severe liver cell damage, fibrosis, and destruction of liver architecture.

Mechanism: To begin with, let's discuss viruses. The five types of hepatitis viruses are further divided from each other on the basis of their genome. In that case, hepatitis A virus, hepatitis C virus, hepatitis D virus and hepatitis E virus have single-stranded RNA, whereas the other virus that is hepatitis B virus – it has double-stranded DNA, which is specifically partially double-stranded DNA. So firstly we discuss the pathogenesis of HAV, HCV, HDV and HEV. These viruses get inside the cell through the endocytosis mechanism and then they shed off their outer coating so they shed off their envelope, shed off their capsomere, and then release inside the cell as single-stranded RNA. Then this single-stranded RNA goes to the host ribosome and uses the host ribosome to synthesize proteins (as we know ribosome is the cell's protein factory).

And it will synthesize proteins such as capsomere, antigens, RNA polymerase, and DNA polymerase. Then these proteins send into the endoplasmic reticulum or golgi apparatus, where they get synthesized and make small vesicles containing all these proteins. However, on the other hand, the other single stranded RNA will also enter the cell. With the help of RNA polymerase (specifically RNA-dependent RNA polymerase), they will synthesize and make more copies of RNA. Because of this, the levels of RNA in the body will increase. So now, there are more RNA and proteins present; they will combine and form more viruses. And after the completion of the process, these viruses will come out of the cell to infect other cells or even a complete organ such as the liver. Now, in the case of hepatitis B virus, which has partially double-stranded DNA. This virus will also enter the cell through the endocytosis mechanism.

It will also shed off its outer coating and enters as partially double-stranded DNA. Unlike the other four types of hepatitis viruses, its target will be the nucleus. So the PDS DNA will enter inside the nucleus where there are DNA repairing enzymes are already present, which will repair that partial double-stranded DNA and make it complete double-stranded DNA(it has an ability of self-replication). This double-stranded DNA either with the help of RNA polymerase, performs transcription and makes viral mRNA which will go to the ribosome where it will make proteins such as capsomere, antigen, RNA polymerase, DNA polymerase and perform the same mechanism and will make protein vesicles.

Another thing that can happen is that they can make a specific type of RNA called pre-genomic RNA. And hepatitis B virus is a retro type of virus that means reverse transcriptase enzyme is present inside it. This will reverse the transcriptase process, take RNA, and make DNA from it. This DNA will eventually convert into partially double-stranded DNA. And then, this PDS DNA will combine with vesicles and form other copies of the virus, which will release out of the cell and infect other cells. When the process takes place inside the cell, and when the virus actively accumulates in the cell, they lead to lysis of the hepatocyte, which will lead to cell death, and that's how hepatocytes get damaged.

Hepatitis A Virus: Hepatitis A virus belongs to the 'picornaviridae' family and has the hepatovirus genus. It is sometimes called infectious hepatitis. It is not chronic and hence does not cause any damage to the liver. It is a small virus around 27-32 nm in diameter, having a naked capsid structure and a single-stranded RNA genome [4]. The average incubation period for the hepatitis A virus is 30 days. Once the virus is ingested, it enters the bloodstream through the oropharynx and travels to the liver. After replicating in the liver cells, the virus is eliminated through the bile or the stool. Even a large amount of the virus is excreting out through the stool around ten days before symptoms appear. Hepatitis A virus infection is less common in all high-income countries and more common in developing countries where sanitation is poor, and access to clean water is limited.

It's more common in parts of Africa, Central and South America, Eastern Europe, and a few Asia regions. It is primarily transmitted through the oral fecal route (through contaminated water and food) and has an incubation period of around one month. After that, the icteric symptoms start unexpectedly in the form of jaundice (yellowing of the skin and whites of the eyes). The hepatitis A virus is found in the blood or the stool of the infected person and is spread even if someone mistakenly ingests a very small amount of the virus. The disease can be spread from close contact with the infected person and is so contagious that people can spread it before they feel sick. Hepatitis A viral infection is more common in children of 5-14.

Children have very little or no clinical symptoms, but it is the opposite in the case of adults where 80% of the adults (infected) are symptomatic. And the symptoms associated with hepatitis A is loss of appetite, diarrhea, fever, nausea(sickness), malaise(general discomfort), and jaundice (yellow skin); after 15 - 40 days, these symptoms intensify for 4 to 6 days before the jaundice phase starts. Around 70 – 80 % of the adults experience jaundice, while just 10% of children do. And the percentage of recovery cases is 99%.

The detection makes the diagnosis of antibodies in the blood. But because of the long incubation time, it becomes difficult to identify the source of infection. The recovery time for hepatitis A is

around 6 weeks. The HAV vaccine is introduced in 1995 and from that time cases has decreased by 95% [5].

Hepatitis B Virus: Hepatitis B virus is a partially double-stranded DNA virus. It belongs to 'hepadnaviridae' family. It is 42 nm in diameter and contains a lipid coat that includes hepatitis B surface antigen that covers the inner nucleocapsid, which comprises hepatitis B core antigen. The incubation time for the hepatitis B virus is around 90 days. Hepatitis B virus infection is a universal life-threatening disease that causes liver damage and has high morbidity and mortality rate. In the late 40s, Frederick Mac Callum gave the term serum hepatitis. And the virus was first discovered in 1965 by Dr. Baruch Blumberg. It is received during birth or from person to person [6].

Hepatitis B virus infection can be acute or chronic; if it is an acute hepatitis B virus infection, it will last 6 months after someone comes in contact with the hepatitis B virus. This can lead to fatigue, fever, nausea, abdominal pain and jaundice, and pain in muscles, stomach, and joints. If it is a chronic hepatitis B virus infection, it will be a long-term problem that can only happen when the hepatitis B virus remains inside the person's body. Most people suffering from chronic hepatitis B virus don't feel any symptoms, but it is much more severe and can cause liver damage (cirrhosis), liver cancer, and death. People who are chronically infected can spread this virus to others as they don't feel any symptoms.

Adults can fight against this virus, but it turns chronic in the case of children and infants because they cannot fight against the virus, so they are at a high risk of getting chronic hepatitis B virus infection. Today, HBV has the highest prevalence in the western pacific and African region. Due to the massive uptake in vaccination, HBV is seen less in North America. In 2015, a study showed that around 257 million people are affected by chronic hepatitis B virus infection, out of which 900 thousand people die each other. In 2016, it was estimated that out of ten people, one person is infected from hepatitis B infection globally, and out of each six, only one is receiving treatment[7]. A small subset of individuals with acute hepatitis can also develop acute liver failure, leading to death. In some people, it can cause chronic liver failure, leading to cirrhosis and liver cancer. Treatment of chronic hepatitis B virus infection may include Antiviral medications as these antiviral agents don't have any cross action with human cells and are harmless so the main focus is on their development [8].

Hepatitis C Virus: Hepatitis C virus belongs to the 'flaviviridae' family. It is a non-enveloped single-stranded RNA virus. The incubation period for the hepatitis C virus is approximately around 40 days. This virus has a single-stranded (positive-sense) RNA genome. It is around 55-65nm in diameter. This virus has an outer membrane made up of lipids that also contain two types of viral glycoproteins; E1 and E2 (these two are the subunits of the envelope glycoprotein). The main function of E1 is to get attached to the membrane surface of the targeted cell, and E2 helps in host-receptor binding. There are 6 different genotypes of the hepatitis C virus. Genotype 1 infection is the most prevalent as it accounts for around 70% of cases, whereas in the United States, genotype 1a and genotype 1b is more prevalent. But globally, genotype 1a is less prevalent. Genotype 3 is the second most prevalent hepatitis C virus genotype as it accounts for 30% of cases globally. Genotype 4 is mostly found in the Middle East and Africa, accounting for more than 80% of cases. It can lead to both acute and chronic infection. Viral hepatitis is becoming the 7th leading cause of death worldwide and out of which half of the population is passed due to HCV infection, which is also a reason for liver fibrosis, cirrhosis, and carcinoma [9].

The hepatitis C virus infects around 130-150 million people (worldwide), and a significant number of chronically infected will develop liver cirrhosis and liver cancer. It has become the leading cause of liver transplants. Around 350,000 -500,000 people die each year from hepatitis C-related liver diseases. Egypt accounts for the highest frequency of HCV globally, where the frequency of this virus increases steadily in every age group [10]. The most effective mode of transmission of HCV is through direct contact with infected blood or percutaneous exposure to blood (for example, transfusion or transplantation from an infected donor). It is most commonly spread through cross-contamination, reused needles and

syringes *etc.* [10]. It cannot be spread through kissing, coughing or sharing eating utensils as it is not found in food and water. Newly infected individuals may not require any treatment because in some cases, the immune system will clear the infection, but if it turns chronic with time, treatment must be given. WHO approves therapy with pan-genotypic direct-acting antiviral (DAAs) in the case of a population above 12 years. Outcomes from the treatment with pan-genotypic DAAs are very efficient, and the duration of the treatment is short (around 12 – 24 weeks). Medication like glecaprevir and pibrentesvir has strong antiviral activity and is effective against all HCV genotypes. Countries like Canada, United States, and Europe have approved the regimens for sofosbuvir/velpatasvir/voxilaprevir to treat HCV patients suffering from HCV [11].

Hepatitis D Virus: In the mid-1970s; Mario Rizzetto (an Italian virologist) first reported hepatitis D virus as a nuclear antigen in patients infected with HBV who had severe liver disease. This virus belongs to the 'kolmioviridae' family, and it is spherical in shape and around 36nm in diameter. Its envelope contains phospholipids and three proteins taken from the hepatitis B virus. These proteins are small, large, and medium hepatitis B surface antigens. They are arranged like a cover surrounding the ribonucleoprotein that contains the genome. This type of hepatitis is also known as 'delta hepatitis'. HDV is a Satellite RNA virus that can only multiply along with the presence of HBV. Hepatitis D virus worsens the symptoms of hepatitis B virus. And the symptoms may include nausea, vomiting, abdominal pain, jaundice, joint pain, loss of appetite, and dark-colored urine.

Hepatitis D virus has eight types of the genome with different geographic distributions. Genotype 1 is more prevalent in Europe. Whereas Genotype 2 and 4 are more prevalent in Asia. Genotype 3 in South Africa and genotype 5-8 cases are reported mostly in African regions. Globally, around 15-20 million people are affected by the HDV virus, and approximately around 5% of the population with HBV infection acquire HDV infection [12]. HDV and HBV can cause severe liver disease and this co-infection is considered the most severe form of hepatitis that can cause hepatocellular carcinoma.HDV is the smallest virus that has the capability of causing human disease [13]. The routes of HDV transmission occur through broken skin (injection, tattooing) or contact with infected blood or blood products. Transmission from mother to child is possible but rare [14]. Hepatitis D virus is most common in southern-eastern Europe, the Middle East, and west and central Africa. The old-age population is at high risk. The population has previous hepatitis history; however, tremendous progress has been made in treating chronic viral hepatitis over the past few years, but due to its unusual nature and seriousness of the disease, targeting HDV remains a big problem. Hepatitis D virus and Hepatitis B virus share the same surface glycoprotein, which means anti-hepatitis B virus vaccination can control hepatitis D virus infection [15].

Hepatitis E Virus: Hepatitis E virus is a small, non enveloped virus with a single-stranded, positive-sense RNA genome that is approximately 27-34 nm in size. This virus is spherical in shape and has four types of genotypes. Hepatitis E virus is classified in the genus 'orthohepevirus' of the 'Hepeviridae' family and is one of the most common causes of hepatitis worldwide. The incubation period of the hepatitis E virus is approximately around 2 to 9 weeks mostly around 50 days. Every year, an estimate of 20 million cases of HEV infection have been reported, out of which 3 million of the cases are symptomatic [16]. Recent studies showed that every year out of 10 pregnant women each 4 dies due to HEV infection. The women (pregnant) that are infected with HEV infection have higher risk of abortions and deaths.

Genotype 1 is more prevalent in tropical and subtropical regions such as Asia and Africa. Whereas genotype 2 is commonly reported in Mexico and Nigeria. Genotype 3 is reported in almost every region, including Asia, Europe, North and South America. Genotype 4 is limited to Asia and there are few cases in Europe. The virus is most prevalent in east and south Asia, Africa and Central America. The mode of transmission is the fecal and oral route (through contaminated food and water). Infections via mother to child or through parenteral pathways are less common [17]. Although HEV is presently known to exist in 2 manners; as exposed particles in the stools of

contaminated individuals and as wrapped virions in blood flow, the wrappers appear to shield the virions from deactivation by distributing specific antibodies [18]. Hepatitis E virus infection can be prevented by improving the quality of water, sanitation conditions and by making your surroundings hygienic and clean.

Strategy for the Search: Main search engines were EMBASE, google scholar, Medline, and CINAHL. Whereas international medical associations and public health organizations include the European association for the study of liver, the American Association for the study of liver disease, the Asia pacific association for the study of liver, and the gastroenterology society of Australia has been included. Many other websites were also explored, including WHO, USFDA, the European medicine agency, and the global health library.

Geographic Allocation of Viral Hepatitis:

African Continent: A considerable majority of the population in the highly endemic countries such as parts of Africa and Asia is immune to the hepatitis A virus. Because of that reason, hepatitis A epidemics are infrequent over there [19]. In sub-Saharan Africa, where virtually or almost all of the population acquires HAV immunity, the prevalence of HAV is highest over there. On the other hand, HBV also has a substantial disease burden in the sub-Saharan African population. HBV infection affects about 6.1 percent of the African population, while chronic HCV infection affects roughly around 18 million people [20, 21]. One of the most serious concerns linked with the high incidence of HAV is that individuals in affected areas are unaware of the disease and are under-educated about treatment and prevention [22].

Americans: Except for the high-income North-American regions, the frequency of hepatitis A is very high in the Americans. Whereas in the last few years, there has been a minor decrease in Central American regions. Infancy circulation is uncommon in middle endemic regions such as central and South America. The symptomatic illness affects adolescents and adults, and the epidemic is repeated [19]. By the age of 15, over half of those infected with HAV had gained immunity against the virus [22]. Anti-HCV-positive people make up about 7 to 9 million of the population in the Caribbean and Latin American countries.

In contrast, hepatitis B infects about 0.7 percent of the population except for Haiti; America has the lowest occurrence rate of HBV [22]. In recent decades, a high number of new cases of HBV have been brought into the United States due to people moving towards the country [23, 24]. Although HDV data is scarce in almost every part of the world, it has received widespread attention in North America. For the epidemiology of HEV little data is available. According to studies in Brazil, 3% of the population is infected with HEV, while another study indicated that 1.7 percent of the population is HEV positive [25, 26].

Eastern Mediterranean Region: In the last few years, the prevalence of HAV has reduced in North African and Middle Eastern countries, and it now has an intermediate prevalence [27]. According to the reports; around 3.3% of the population in this region are infected with HBV, and around 800,000 people are HCV positive. Surprisingly more than 14.5 million Egyptians have been diagnosed with HCV, with a million developing chronic HCV [28, 29]. Except for Somalia, Djibouti, and Sudan; which have greater incidence ratio; the eastern Mediterranean regions have a low prevalence, whereas HEV is mostly documented in Sudan, Pakistan, and Somalia, with the percentage of Yemen-12.7-18.5% ; Pakistan – 4.5% ; Sudan- 5-8.2% ; Somalia – 5.6- 21.3% [30].

European Continent: Hepatitis A virus infection incidents increase day by day from the west region towards the east. In Eastern Europe, juvenile transmission is less frequent, whereas adult transmission is more common [31]. Although the hepatitis A virus is still uncommon in Western Europe, community-wide outbreaks are commonly observed [19].

In 1996, the incidence of HAV was 15.1 per 100000 individuals, and by 2006, it had dropped to 3.9 per 100000 persons. Even after the diminishing prevalence of the hepatitis A virus in central and eastern Europe, it was taken as a severe public health hazard because of the epidemics occurring in the Czech Republic, Slovakia, and Latvia in 2008 [32].

The frequency of the hepatitis B virus is quite low in the European continent, but it becomes more frequent as you move towards east [33]. Chronic hepatitis B virus affects about 1.4 million of the population in Europe, while chronic hepatitis C virus affects approximately around 9 million people. Each year 36000 & 86000 people die due to hepatitis B virus and hepatitis C virus infections, respectively [34, 35].

Southeast Asia: Prevalence of Hepatitis A virus is high in almost every Southeast Asia, but new findings show that infection rates are dropping in other areas, such as India. For the last few years; in eastern regions hepatitis A virus has had a low frequency in the eastern areas. Around 5 million deaths are reported each year in the southeast region [35, 36]. A persistent hepatitis B virus infection affects around 100 million people. In this region, the frequency of chronic viral hepatitis is 30 times more than that of the human immunodeficiency virus (HIV) [37]. Unfortunately, around 65 percent of the patients infected with hepatitis B virus and 75 percent of patients infected with hepatitis C virus are ignorant towards the infection 38, 39. In this region, around 10 million people have hepatitis C [40]. At the same time, Hepatitis E virus infections are predicted to affect 12 million people each year [41-43]. This figure represents more than half of cases worldwide. Studies show that there are around 6.5 million symptomatic cases of hepatitis E and 400000 cases of hepatitis A cases are reported each year in this region. It's possible that genuine cases are significantly greater [44-47].

Western Pacific Region: This area of the earth is home to 28 percent of the world's population. In this corner of the globe, viral hepatitis kills more people than malaria, TB and HIV combined [34]. In highly developed regions like Australia and the Asia-Pacific, the frequency of Hepatitis A virus is low [48]. The cases of hepatitis A virus in the East Asian population is also decreasing as the region's socio-economic situation improves [49, 50]. 350 million people in this area are infected with the hepatitis B virus, accounting for 50% of all hepatitis b virus infections worldwide. This is also the region that accounts for 60 percent of all liver cancer cases globally [51]. In east-Asia, the prevalence of the hepatitis C virus ranges from 1 percent to 2 percent, with some nations in the region, such as Taiwan and Vietnam, having prevalence rates of 4.4 percent & 2.9 percent, respectively [52, 53]. Over 60 million people in the western pacific region are chronically infected with hepatitis C virus out of 150 million worldwide. Acute hepatitis B and E-related problems are believed to be responsible for 3% of the deaths in this region[53].

Plans for the Prevention of Viral Hepatitis: Multiple methods are required to prevent viral hepatitis, as mentioned below effectively;-BY Educating Citizens: Disease awareness education initiatives help to reduce disease spread [45, 53]. In impoverished nations, many chronic hepatitis patients are unaware of their illness. So it becomes critical to conduct community-wide education campaigns and to put in place local health measures[41]. These involve; educating local communities on how to execute blood transfusions safely and implementing effective screening processes for the use of donated blood. Health teachings and training should contain:-giving safe injections in hospitals and IV drug users and implement safer intimating practices. Moreover, health care employees should also receive safety training periods [54, 55, 56]. To prevent and reduce viral hepatitis risk, it is critical to effectively convey and emphasize the necessity of virus testing, routine checkups, and treatment[57, 58].

Improving Socio-Economic Conditions: The frequency of all types of viral hepatitis has been demonstrated to decrease if one's socio-economic position improves. Higher authorities should keep an eye on the global availability of safe drinking water, promote sanitary food handling and storage practices, and improves sanitization. In all the health care places, it is necessary to ensure that medical waste is safely disposed of [56-59].

Clinical Examination and Diagnosis: Clinical examination, early diagnosis, and routine follow-ups will stop the virus from spreading further and decrease morbidity and mortality rates [59, 60]. Giving proper medical support and initiating antiviral treatment, if available, should be initial steps. Unfortunately, in poorly developed nations, where health care is scarce, and medicines are sometimes prohibitively expensive, putting these measures in place can be difficult [61, 62].

Organizing Vaccination Campaigns: Organizing vaccination drives against hepatitis A virus, and hepatitis E virus infections is an important part of WHO's global hepatitis eliminating program [62, 64]. To ensure that its goal is carried out to the fullest extent as possible, WHO has given technical assistance and support to limit the disease spread. Many steps are taken; a few of them are ensuring safer blood transfusions, not using infected needles, and so many other measures. In low and moderately endemic regions, hepatitis A vaccination should be available for susceptible persons [62]. Even though the hepatitis B vaccine effectively prevents disease, only 27 percent of the babies in the globe receive birth dose [62]. Hepatitis B virus immunization at birth is essential to avoid vertical transmission since delay in vaccination does not completely clear the possibility of vertical transmission. It is necessary to establish a stable relationship between the mother's health and the vaccination process [51].

Nowadays, many therapies are available for the hepatitis B virus that can definitely improve the quality of life. But due to excessive costs, treatment is not available in many nations [63]. Each year, there are around 350000 people die as a result of hepatitis C virus infection [64, 65]. Because of the uniqueness, there is no treatment available to protect people from hepatitis C virus. It is an RNA virus that mutates quickly, which makes it difficult and challenging to develop a vaccine [66]. Old therapies based on the genotype of the virus are available. In contrast, safe blood transfusion procedures (similar to that of HBV) can be used to prevent the virus from spreading. Old interferon therapies have been demonstrated to be modestly effective in the long-term elimination of the viral genome [67].

On the other hand, pan-genotypic therapy for all the Hepatitis C virus genotypes has been a huge scientific accomplishment. New clinical trials of the once-daily combination therapy of sofosbuvir and velpatasvir have shown a persistent virological response rate of around 95 percent against all types of genotypes, regardless of prior therapies. The success rates of this new pan-genotypic combination therapy are far higher than the older one as it is safe and effective, but the high cost is a key drawback [59]. When the treatment is commonly available to all affected patients, the disease burden will reduce. The financial load on the health care system will be reduced, leading to a decrease in morbidity and mortality [60].

Strategies Implemented By WHO: Worldwide action plans and alliances can help to limit the viral hepatitis epidemics. For the treatment of viral hepatitis, various strategies have been implemented. WHO has an objective, and its aim is to remove viral hepatitis globally 60-65 completely. In this worldwide strategy, five major action plans have been considered. The specific areas are vaccination programs for hepatitis A, B, and E; mother-to-child transmission management; needles and transfusion products safety; harm minimization and therapy [68-70].

Model of Social Guidance: Patients who recovered from the disease effectively or safely can team up with a multidisciplinary medical team to provide complete viral hepatitis counseling, service, and therapy for others who face hurdles in healthcare delivery[61]. Important barriers that create problems in treatment; within hepatitis C virus-infected IV drug users should be tackled with solutions. Such spot therapy, an addiction management strategy, multidisciplinary teamwork, an advanced model of care is some of the options available [70-71]. A combination of therapeutic and behavioral therapies has been demonstrated to reduce hepatitis C virus infection among IV drug users [71, 73]. Hepatitis C virus infection is still common in IV drug users around the globe. Even after the accessibility of bearable and effective medication, morbidity and death rate due to hepatic diseases within the hepatitis C virus infection population continues to rise. A University of Sydney and an international organization have scheduled a professional discussion group to assess existing difficulties and establish future study goals for the care and treatment of hepatitis C virus in substance users. International experts in drug and alcohol abuse, infectious illness, and hepatology have gathered for the discussion to assess the latest scientific data, research challenges, and research objectives[70].

Support Therapy: In treating viral hepatitis, giving support therapy services is essential. For example, digital health services is an creative and

adaptable approach to treating chronic viral hepatitis patients. These are shown to be useful in providing health tests, commencing chronic illness management, and stepping in quickly when necessary. Digital health services have been a unique way to provide viral hepatitis treatment [66]. IV drug users, particularly those in prison, indigenous people, and those from different backgrounds, are at risk of contracting the hepatitis C virus. These are the folks who are cut off from standard healthcare practitioners and have low retention in the healthcare system. Providing service to these folks in the medical system and providing proper care is a novel action strategy required [66, 40]. The already stated digital health care services will be brought therapy to such individuals to make life simpler for them to receive medical care, especially for those who have mental drugs-related issues; this process will connect medical and society-based sectors while removing geographical, socio-economic, and structural barriers. Effective therapy of HCV infection reduces the risk of hepatic cancer and co-morbidities of the disease, improves the quality of life, and increases life expectancies [68, 69]. Delivering immediate treatment will enhance viral clearance and decrease risk factors. This process of digital services will help to minimize disease transmission[66].

Post-Exposure Prophylaxis: Contaminated needle injuries cause numerous episodes of viral hepatitis in medical professionals. The prevention of job-related incidents in healthcare systems should be addressed immediately. Once the virus infection is verified, an immediate IgG therapy plan should be easily accessible. This therapy might be able to prevent the illness from spreading. Individuals exposed to the virus should be treated in the same way. This quick response method could be a useful therapeutic tool for preventing illness and limiting outbreaks.

CONCLUSION: Even though there has been considerable success in implementing precautionary efforts worldwide, there are still numerous obstacles to be addressed if we want to decrease the burden of viral transmission. In 2017, the world health organization (WHO) released a documentation guide to formulate and evaluate nation viral hepatitis strategies. This advice might be useful in preventing viral hepatitis epidemics. Therefore, these steps must be taken to prevent epidemics and create a future free of viral hepatitis. Early immune system therapy is one of the most crucial things to managing an epidemic. The world health organization can incorporate post-exposure prophylaxis in their worldwide approach, which can be applied initially in the wealthy environment and then gradually accepted in emerging and poor nations. International bodies can hold meetings to discuss issues to fight against viral hepatitis on a global scale. Although no single strategy is sufficient to prevent viral hepatitis outbreaks, adopting a global perspective and applying different methods will reduce the worldwide morbidity and mortality rate.

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