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Hepatitis: Types, Mode of Infection, Symptoms and Treatment

Anil Kumar*

School of Biotechnology, Devi Ahilya University, India

Corresponding author: Anil Kumar, School of Biotechnology, Devi Ahilya University, India

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Abstract

Hepatitis is a dreaded viral disease which mainly affects the liver of humans. There are different types of hepatitis, each caused by a specific virus. Some viruses are RNA virus whereas others are DNA virus. In this mini-review, different types of hepatitis viz. hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E, hepatitis F and hepatitis G have been briefly described. For each type, mode of infection, symptoms and available treatments have been briefly described.

Keywords: Hepatitis A; Hepatitis B; Hepatitis C; Hepatitis D; Hepatitis E; Hepatitis F; Hepatitis G; Virus; Tenofovir

Introduction

Hepatitis is a fatal viral disease which affects the liver of the person. If proper diagnosis and treatment is not carried out, the patient may even collapse. In hepatitis, there is inflammation of the liver. The liver is very important body organ which is fully involved in the metabolism of biomolecules and protects the body against infections. Upon inflammation, its functions are disturbed. It has been found that excess alcohol consumption, certain toxins, medicines may cause hepatitis. The hepatitis is a viral disease and now it is known that there are different types of hepatitis depending upon the type of hepatitis virus infects the human body.

Various Types of Hepatitis

There are following types of hepatitis known

Hepatitis A

The hepatitis A is also called acute epidemic hepatitis or infective hepatitis or short incubation hepatitis. It has been found that hepatitis A virus generally enters in the body through mouth and buccal cavity with food and/or water like polio virus. This virus is also found in faecal matter and therefore, more chances are there to get infection of this virus in the body from the places having contamination of faecal matter. The places like school, mental hospital, places where many people do meetings together for a longer time are considered to be the main contaminated sites for hepatitis A virus. The virus may also enter in the body through blood if contaminated needle is used or contaminated blood transfusion is carried out. It enters the liver cells and infects them. When the virus enters in the body through mouth and reaches in the stomach, it is not killed by the acid present in the stomach. From stomach, it enters into the small intestine and then in the mucosal epithelial cells. It multiplies in these mucosal epithelial cells and reaches to nearby cells. After multiplication, it reaches to hepatocyte cells through blood stream. When there is attack of the virus on the liver, initially person's hunger gets decreased and person feels tired. After some time, person feels uneasiness in the belly and gets fever. Further, person gets jaundice and liver gets hardened. When person suffers from jaundice, initially sometimes person feels a little better. Jaundice is not considered to be much fatal disease and it persists for nearly one to three weeks and person may recover after two to six weeks.

The hepatitis A virus, also called as HAV is an icosohedral shaped virus and belongs to the family, picornaviridae. The virus has single stranded RNA genome and its capsid is not enveloped. The capsid has subunits called as capsomeres. It is shown that each capsomere is consisted of five protomers, and each protomer is consisted of three proteins called as VP1, VP2 and VP3. These proteins help the virus to enter inside the cell. The diameter of the virus is nearly 27 nanometers. The virus has some similarity with picornavirus. It also attacks chimpanzees and marmosets. For vaccine development, this virus is propagated using tissue culture techniques. Classically, diagnosis of Hepatitis A is done in the faeces of the suspect using immune-electron microscopy. Besides, blood is also tested for the presence of hepatitis A virus. Now a days, presence of the virus is also tested using molecular

biology tools like polymerase chain reaction (PCR) amplification with specific primers. The PCR is also used for checking viral load. If virus of hepatitis A is present in the body, specific antibodies for the virus are produced in the body as a defence mechanism. In the market, active vaccine of hepatitis A is not available, however, passive antibodies are used as a defence mechanism. This virus can also be detected using radioimmunoassay and/ or enzyme linked immunosorbent assay.

Hepatitis B

This disease is also called as serum hepatitis or homologous serum jaundice or long incubation hepatitis or cancer of the liver. The virus responsible for this disease is called as hepatitis B virus. Contrary to hepatitis A virus, this virus has diameter of nearly 42 nanometers and contains double stranded DNA. The virus is characterized by the presence of a specific protein called as hepatitis B surface antigen (HBSAG) or Australian antigen on its outer surface of the protein coat. This virus enters in humans through blood stream. If a person gets infected through blood transfusion having hepatitis B virus (of course by mistake), the virus gets propagated inside the body. This virus may also enter in the body through contaminated syringe, needle, sexual contact, spit (saliva) etc. If a pregnant woman gets infection of this virus by any mean, virus may also enter in the body of the infant through placenta. After entering in the body, through blood stream, virus enters in the liver cells and causes jaundice. Jaundice is generally diagnosed by an increased amount of bilirubin in the blood.

If diagnosis and treatment are not done in time to prevent multiplication of the virus, amount of virus load increases enormously and this virus in conjunction of hepato-cellular carcinoma cells may develop cancer of the liver. Persons infected with hepatitis B initially may not feel any specific symptoms. However, some people experience symptoms like yellow eyes and skin indicative of jaundice, dark urine, nausea, vomiting, abdominal pain, much tiredness, etc. In some cases when acute condition prevails, there may be liver failure (cirrhosis) and subsequently death.

It has been observed that cancer of the liver is lesser prevalent in developed countries including United States of America but is more prevalent in poor and developing countries like Africa, Republic of Mozambique, India etc. As per estimate, nearly 887,000 persons collapsed in 2015 who were suffering from cirrhosis and hepatocellular carcinoma (primary liver cancer). In 2018, it has been estimated that nearly 1.34 million deaths occurred due to hepatitis and 80% of these were due to liver cancer (either hepatitis B or hepatitis C). As per data of World Health Organization (WHO), in 2016, there were nearly 27 million people globally who were aware of that they are suffering from hepatitis B. This number is just nearly 10% of all persons with hepatitis B virus load. On the other hand, nearly 4.5 million persons were diagnosed for hepatitis B virus and were getting treatment. This number is nearly 16.7% of all the population with hepatitis B virus load. It has been found that male homosexuals and drugs addicts are more prone to hepatitis B virus infection [1].

It has been evidenced that nearly 1% patients with hepatitis B virus load also get infected with human immunodeficiency virus (HIV). On the other hand, it is shown that nearly 7.4% persons of total HIV infected have hepatitis B virus infection. That is the reason that as per recommendation of WHO in 2015, all the patients diagnosed for HIV infection must also be treated for hepatitis B virus (HBV) infection. The most popular medicine, Tenofovir used for treatment of HIV infection also works against HBV. The disease, hepatitis is so dangerous that WHO has decided to celebrate World Hepatitis Day on July 28 every year. The basic purpose of the day is to bring awareness and to unite Governments, non-government organizations (NGOs), medical doctors, pharmaceutical industries, general public to boost the global profile of viral hepatitis. Sometimes, patients who are treated for the disease, have virus in their body for years and may propagate again resulting in long duration disease called as chronic active hepatitis. For diagnosis, presence of HBV is detected using sensitive techniques like ELISA. The outer surface of viral particle has a protein, HBSAG which may be determined in blood serum and its presence is indicative of the presence of HBV. The levels of the enzymes, alanine amino transferase and aspartate amino transferase increase upon cirrhosis of the liver. Increased level of alpha fetoprotein has been shown to be the indication of liver cirrhosis (cancer) [2]. Arrieta et al. [3] showed that progressive elevation of alpha fetoprotein nearly 7 ng/ml/month in patients with liver cirrhosis is useful for the diagnosis of hepatocellular carcinoma in patients who do not reach alpha fetoprotein levels 200 ng/ml. Now a days, presence of HBV in the blood is detected using PCR which is a very powerful molecular biology tool. Specific primers are available commercially for the purpose. During treatment, viral load is also evaluated (whether decreasing by the treatment or not) using PCR. Author's laboratory earlier designed primers using X-antigen of HBV as a model and studied the effect of hairpin structure on PCR amplification efficiency [4]. An 8% nucleotide diversity has been found in the genomic sequences of different genotypes of HBV, and on that basis, HBV has been divided into 10 genotypes named as A to J. Chook et al. [5] designed six highly conserved, overlapping primer sets. They used 5154 HBV genomes of genotypes A to I present in GenBank nucleotide database.They successfully tested these primer sets on 126 plasma samples from Malaysia containing genotypes A to D and with viral loads ranging from 20 to 79,780,000 IU/ml. They also tested these primer sets using HBV reference panel of genotypes A to G and found 100% amplification and sequencing success.

Cicalese [6], in his blog on Medscape showed that although test for determining level of alpha fetoprotein is cheaper, it can't be considered much reliable since it is only 40 to 64% sensitive. Many tumors even don't produce this protein at all, or some produce only at much advanced stage. The level of this protein also increases in chronic hepatitis C where level may reach up to 300 ng/ml. However, the level gets fluctuated and does not increase progressively [7]. In 1981, scientists were successful in developing vaccine for hepatitis B. The vaccine has highly purified hepatitis B antigen. In USA, the vaccine became commercially available in 1982. After a couple of years, researchers were able to produce vaccine by

recombinant DNA technology. The first license for the production of recombinant DNA expressed hepatitis B vaccine was granted in 1986. Researchers are engaged since long time to develop vaccines in plants using genetic engineering technique. Jafargholi Imani's group at the University of Giessen, Germany developed genetically modified carrot having vaccine for hepatitis B. They claimed that these genetically modified carrots can be grown on a mass scale within a fortnight or so. These plants will be able to provide eatable carrots [8]. Researchers are also successful in developing genetically modified potatoes with hepatitis B vaccine. In 2005, an edible vaccine of HBV was designed inside the potato which can be stored without a refrigerator. The authors transferred a gene of hepatitis B virus in the potato plant and plant was able to produce virus antigen. If this potato with HBV antigen is eaten, the antigen will show an immune response in the human body which will act as a booster dose against HBV [9,10]. Accordingly, to Hepatitis B Foundation, only seven antiviral drugs are approved for chronic hepatitis B virus infection. These drugs namely Tenofovir disoproxil, Tenofovir alafenamide, Entecavir, Telbivudine, Adefovir dipivoxil and Lamivudine are in the form of pills. Any one of these drugs is generally prescribed as one pill a day for about a year or so by the doctors. Besides, there are two immune modulators namely Pegylated interferon and Interferon alpha. The immune modulator is given as an injection. All these medicines have been found to exhibit some side effects [11].

Hepatitis C

This disease is caused by the virus called as hepatitis C virus. Like hepatitis A virus, this virus is also single stranded RNA virus. This virus could not be cultured in the laboratory easily. Marukian et al. [12] were able to culture hepatitis C virus. They showed that this virus multiplies mainly in the liver, however, its RNA has been found in B and T lymphocytes, monocytes and dendritic cells. However, in vitro replicated virus is unable to infect blood cells. Hepatitis C virus was discovered in 1989 by the scientists of Chiron Corporation, China after carrying intensive work for six years between 1982 and 1988 [13]. It was detected in a chimpanzee who was transfused blood of a person earlier suffering from Non-A and Non-B hepatitis. Before it, hepatitis which was considered to be present in a person without the presence of either hepatitis A virus or hepatitis B virus was being called Non-A and Non-B hepatitis. A single cDNA clone was isolated which was shown to be derived from a new flavi-like virus and that was called as hepatitis C virus (HCV). It was screened using antibodies derived from a diagnosed Non-A and Non-B hepatitis patient. This clone encoded an immunodominant epitope within HCV non-structural protein 4. As per data of WHO released on July 09, 2019, there are 71 million persons globally who have hepatitis C virus infection. This virus infects the liver and may cause both acute and chronic hepatitis which may be mild to severe and can last for a few weeks or sometimes very serious as a lifelong disease. Hepatitis C virus is the main cause of liver cancer. Hepatitis C virus also enters in the human body through blood stream. The chances are when a drug is injected using unsafe injection practices, unsafe health care, transfusion of infected blood. This virus may also get transferred through unsafe sexual practices. As per estimate of WHO, alone in 2016, nearly 399,000 persons died from hepatitis C due to liver cirrhosis or hepatocellular carcinoma [1]. It has been found that hepatitis C is curable and success rate is nearly 95%. Unfortunately, no effective vaccine is available against hepatitis C virus (HCV). Many researchers are engaged in developing vaccine for this virus. It has been found that generally persons with this virus don't exhibit any symptom. Persons with acute hepatitis C may experience fatigue, fever, nausea, vomiting, disturbed digestion, pain in abdomen, dark urine, green colored faeces, joint pain and even jaundice.

There are mainly two tests for diagnosis of HCV:

a) Testing for the presence of anti-HCV antibodies in the blood

b) Testing for the presence of RNA of HCV

It has been shown that many people with HCV spontaneously clear the virus without any medication due to strong immune response. Here, it is pertinent to mention that persons who have cleared HCV, will show positive test for anti-HCV antibodies. Persons with HCV are recommended to test for liver fibrosis and cirrhosis. The amount of liver damage is considered important for treatment decisions.

Hepatitis D

This disease is caused by a virus called as hepatitis D virus (HDV). It is a mutant virus and is also called as Delta Agent or Delta virus. Generally, hepatitis D virus infection in the human body occurs along with hepatitis B virus. The HDV can be detected using ELISA or radioimmunoassay like HBV. HDV is a small circular RNA virus. It is shown that it is defective for multiplication, therefore, it is infected along with HBV. According to some researchers, hepatitis D is the most dreaded hepatitis disease and may lead to liver failure or liver cancer. Like HBV, this virus is also infected through blood stream and exhibits the same risk factors as with HBV. When there is infection of HDV along with HBV, it is called co-infection. Many times, when person suffers with chronic hepatitis B, HDV infection may occur at that stage too, and then it is called super infection. Mostly same medication is prescribed which is for HBV. According to some researchers, if amount of the medicine is increased, it is beneficial for lowering the viral load.

Hepatitis E

This disease is caused by a virus called as hepatitis E virus (HEV). Like hepatitis A virus, this virus also enters in the body through water and/or food. HEV is a non-enveloped and single stranded RNA containing virus. Its shape is icosahedral. This virus is multiplied only inside the living cells. It is active in other animals too. In fact, different genotypes of the virus are known. Genotypes 1 and 2 are found in humans only whereas Genotypes 3 and 4 are found in other animals like pigs, deer, wild boars etc. This virus remains active from 15 to 60 days. Like hepatitis B, in this disease also, patient suffers from jaundice and body ache as in flu. Generally,

when symptoms of HEV are visible in a person, these persist up to nearly two weeks. In most of the cases, disease is curable since virus remains active only up to 60 days. However, in some cases, this disease of HEV persists more and then there remain chances of liver failure (fulminant hepatitis) and person has to go for liver transplantation. Like hepatitis A, this disease of hepatitis E is more prominent in developing countries like Asian countries including India, African countries. It has been detected in central and middle America too. Mostly, this disease spreads as epidemic after rainy season especially when there is flood since at that time water has chances of contamination with faecal matter. The HEV can be detected using ELISA or radioimmunoassay like other types of hepatitis. According to report of WHO released in July 2019, there occurs nearly 20 million HEV infection cases annually at the global level and out of these, nearly 3.3 million cases exhibit symptoms. There were nearly 44,000 deaths due to HEV in 2015 globally [14]. Researchers in China have developed a vaccine for HEV infection and the same has been licensed. However, vaccine is not available anywhere else.

Hepatitis F

This disease is caused by hepatitis F virus (HFV). This virus is also called Toga virus. According to some researchers, this virus is only hypothetical and has not been proved. For the first time in 1994, a case of HFV infection was reported from India [15]. Thereafter, HFV infection have been detected in other countries too like England, France, Italy [16,17]. HFV is about 27 to 37 nanometers in diameter and has double stranded DNA. It has been found that basic symptoms of HFV infection are presence of HFV antigen and increase in the levels of transaminases enzymes in blood. These symptoms are visible nearly after 20 days when HFV enters in the body. At a later stage, there may be acute hepatitis in the liver. The HFV can be detected using ELISA or radioimmunoassay like other types of hepatitis.

Hepatitis G

This disease is caused by hepatitis G virus (HGV). This virus was discovered in 1995-1996 by two different independent research groups [18–20]. It is also called GBV-C based on the name of surgeon G. Baker who got sick in 1966 with a non-A, non-B hepatitis. At that time, it was considered to be a new infectious hepatitis virus [20]. The virus contains single stranded RNA of nearly 9.3 Kb. The genome is able to code two structural and five non-structural proteins. Many genotypes of HGV are known distributed diversely globally. It has been found that Genotypes 1 and 2 are dominant in Northern and Central Africa, and USA. Genotypes 3 and 4 are dominant in Asia. Genotype 5 has been detected in Central and Southern Africa whereas Genotype 6 has been reported in South East Asia. Genotype 7 has been shown in China. Sometimes, a person may have infection of multiple genotypes [21]. HGV infection has been found globally. It enters in the human body through blood stream. There are chances of infection if one uses unsafe blood transfusion, unsafe intravenous drug injection, parental exposure (subcutaneous, intramuscular or intravenous contact with blood or other body fluid). It also enters through sexual contact with an infected person. Therefore, it has been shown that HGV infected persons are generally HIV infected also.

Conclusion

Hepatitis is a dreaded disease which causes several deaths worldwide. There are different types of hepatitis. World Health Organization, Governments and other organizations are in efforts to control the disease effectively in order to reduce the number of deaths. There is need of more research in this field.

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