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Hepatitis A Virus (HAV) Infection: A Prevention Strategy Through Hygienic Maintenance and Vaccination

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Abstract

Hepatitis is considered as the inflammation of the liver. Hepatitis A is a highly contagious liver damageable, but vaccine-preventable disease that is caused by the hepatitis A virus (HAV). It is transmitted through food and water by oral-fecal contact that is contaminated with the undetectable microscopic stool (feces, poop) of an infected person with HAV that are too small to be seen. This virus can be spread through the household or sexual contact with an infected person. It can survive for extended periods in the environment. It is one of the widespread viruses that cause hepatitis all around the globe. Younger children are asymptomatic, but infection symptoms begin to clearer among the adults. The disease is self-limited. Hepatitis A vaccine is developed in 1995 in the USA that may protect against disease for as long as 20 to 30 years. This study aims to prevent and treat the hepatitis A viral infection for reducing morbidity and mortality through the hygiene practice and vaccination in due time.

Keywords: Hepatitis A, vaccine, immune globulin

1. Introduction

Hepatitis A virus (HAV) infection is the most common form of acute viral hepatitis in the world that can damage the liver (Ambrosch et al., 2004). HAV is tissue or cell specific and attacks only the liver. It is generally mild and self-limiting with a typical recovery in two weeks (Gerardi & Zimmerman, 2005). HAV infection accounted for about half of all acute onset icteric illness and acute liver failure cases, and is associated with significant morbidity and mortality (Sood et al., 2019). The HAV is found worldwide. It can survive very well in the environment. It can alive on hands for several hours and in food at room temperature for much longer. It also can survive in food even after freezing. Humans are considered to be the only important reservoir of HAV, and there are no insect or animal vectors (Wasley et al., 2010).

It is highly endemic in developing nations due to overcrowding and poor sanitation, and is spread through contaminated food and water, where infection occurs in children asymptomatically. It is usually spread from one person to another through unsafe food or water, or through sexual contact (Aggarwal & Goel, 2015). But the levels of hygiene and sanitation in middle income countries are improving gradually. Consequently, the HAV contamination is decreasing among these countries (WHO, 2016). Symptoms of HAV are fatigue, fever, headache, muscle ache, nausea, joint stiffness, diarrhea, lack of appetite, and vomiting (FDA, 2012).

The risk factors related to HAV infections are people who use illicit drugs, men having sex with men, people who inject drugs, homeless people, etc. (James et al., 2009). At present there are two types of vaccines to prevent HAV: i) can adsorb onto an aluminium hydroxide adjuvant, and ii) contains formalin-inactivated hepatitis A particles (Beck et al., 2004). In the absence of vaccination most exposed neonates and young children will be infected and become lifelong carriers (Gow & Mutimer, 2001). As per global estimates of mortality, HAV

infection ranked sixth amongst vaccine preventable infectious that causes of worldwide mortality (WHO, 2018).

From 1990 to 2019, the incidence rates of HAV infection have remained stable (Zeng et al., 2021). The World Health Organization (WHO) estimates that 1.5 million clinical cases of HAV are recorded per year with about 7,134 deaths in 2016. However, millions of HAV cases are recorded in underdeveloped countries (Savicka, 2022). During 2020, an estimated 19,900 people in the USA were infected with the HAV. Sometimes the life-threatening complications, such as fulminant hepatitis and hemolysis may develop with about 2% (Lednar et al., 1985). About 90% children have been infected with the HAV before the age of 10 years, most often without symptoms, and most of them live in low- and middle- income countries (Jacobsen & Wiersma, 2010).

2. Literature Review

The literature review is an introductory section of research that shows the works of previous researchers in the same field within the existing knowledge (Polit & Hungler, 2013). Emmet B. Keeffe and his coworkers have performed a study to compare the safety and immunogenicity of an inactivated hepatitis A vaccine in patients with chronic liver disease (CLD) with that in healthy subjects (Keeffe et al., 1998). F. Ambrosch and his coauthors have designed to assess the early antibody kinetics after a priming dose and the extent of the antibody increase after a booster dose of an inactivated virosomal HAV vaccine (Ambrosch et al., 2004).

Omid Gholizadeh and his coauthors want to examine the existing evidence for hepatitis A screening, diagnosis, and treatment. They have also discussed the structure of the HAV virus, the virus genome, how it is diagnosed, how it spreads, the importance of vaccination, and the factors derived from the HAV virus (Gholizadeh et al., 2023). Vikrant Sood and his coauthors have studied the HAV infection-related pediatric liver disease burden. They have observed that a significant proportion of subjects remain susceptible to HAV infection even after 10 years of age. They have suggested that population-based studies are required to further delineate the epidemiology of HAV infection in India for deciding introduction of HAV vaccine in the national immunization schedule (Sood et al., 2019).

Sofia Persson and her coworkers describe development and evaluation of a reverse transcription droplet digital PCR and reverse transcription real-time PCR (RT-qPCR) assay for detection of HAV in food and clinical specimens (Persson et al., 2021). Tauseef Ahmad and his coworkers have analyzed a bibliometric analysis to build an all-inclusive view of the status of research on HAV for facilitating researchers, health professionals, and policymakers to understand the characteristics of research output in this particular domain (Ahmad et al., 2021).

3. Research Methodology of the Study

Research is an essential device to the academicians for the leading in academic area (Pandey & Pandey, 2015). Researchers often write a methodology section with details of the research analysis (Kothari, 2008). Methodology provides the research design and analysis procedures to perform a good research (Hallberg, 2006). Research methodology shows the ways to the novel researchers for organizing, planning, designing and conducting a good research (Legesse, 2014).

The valuable information of our research is collected from the published and unpublished data sources (Mohajan, 2024a-e). In this paper, we have depended on the secondary data sources of hepatitis A virus (HAV), such as journal articles, books of famous authors, conference papers, internet, websites, etc. (Mohajan, 2017, 2018, 2020).

4. Objective of the Study

Main objective of this article is to discuss the aspects of liver disease that is developed by hepatitis A virus. The HAV attacks only the human liver and there is no other virus vector. It is not fatal as like other hepatitis viruses and death occurs rarely (WHO, 2013). Other minor objectives of the study are as follows:

1) to highlight the etiology and virology of HAV,

2) to focus on clinical presentation, symptoms and risk sites of the disease, and

3) to show the prevention strategy of HAV through the vaccination.

5. Etiology of HAV

Hepatitis A virus (HAV) is a frequent type of viral hepatitis. It was first isolated in 1979. It is an ultramicroscopic infectious parasitic agent that is not considered as living organism and can only replicate within the cells of living host human (Venes & Taber, 2013). It is a hepatotropic virus of the family Picornaviridae, genus Hepatovirus, containing a positive sense, linear, single-stranded RNA virus (a 27nm picornavirus) surrounded by a protein capsid that replicates in the liver, secreted in the bile, blood, and shed in stool (Heymann, 2008). It is able to survive in the low pH of stomach acid exiting the host through the biliary tract (Martin & Lemon, 2006). The virus is hardy, surviving on human hands and fomites, and requiring temperatures higher than 185ºF (85ºC) for inactivation (Kemmer & Miskovsky, 2000).

The incubation period of HAV is from 15 to 50 days, with an average of 25 to 30 days (Franco et al., 2012). HAV is a hydrophobic virus, environmentally hardy, and difficult to eliminate from contaminated surfaces (FDA, 2012). It can survive outside the body for months, depending on the environmental conditions, such as freezing, heat, chemical treatment (e.g., detergents and acids), and desiccation due to the absence of an envelope, but it is inactivated by formalin and chlorine. It also survives for extended periods in seawater, fresh water, wastewater, and soil (CDC, 2018).

6. HAV Virology

HAV is a tiny enteric virus with diameter 27-32nm (nanometers) that is a small, non-enveloped, unusual hepatotropic virus classified in the genus Hepatovirus within the family Picornaviridae (Figure 1). It is a positive-strand RNA genome that infects only primates (Enkirch et al., 2019). The genome of it is relatively short; approximately 7,500 nucleotides long (Kulsuptrakul et al., 2021). The 5′ ends of the RNA are physically attached to a viral genome-linked protein (VPg) or 3B and also lack a normal cap configuration and a brief untranslated section at the 3′ ends of the genome, which ends in a poly (A) tail (Gholizadeh et al., 2023). The coding region consists of three functional regions: P1 has four structural proteins (VP1 to VP4), P2 has three non-structural poly-proteins (2A to 2C), and P3 has four non-structural poly-proteins (3A to 3D) (Kemmer & Miskovsky, 2000). Infectious viruses come in two types: naked and non-enveloped HAV virions, which are released into the stool (Yang et al., 2017).

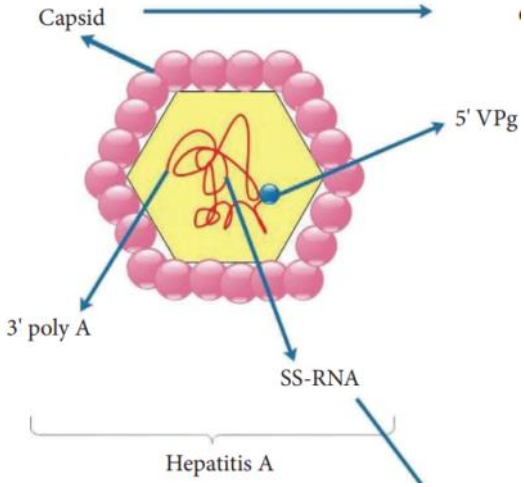

Figure 1. Genome structure of HAV

Source: Gholizadeh et al. (2023).

There are six HAV genotypes based on examining a 168-nucleotide fragment of the VP1-2A region. Only genotypes I, II and III infect humans and genotypes IV to VI cannot infect humans (Smith & Simmonds, 2018). Genotypes I, II, and III are further divided into subtypes A and B (Cella et al., 2018). HAV genotype I is the most common genotype found around the world: HAV genotype IA is prevalent more frequently than IB in South and North America, Europe, Asia and Africa (Ajmera et al., 2011); and HAV genotype IB is found among acute liver failure cases that is predominant in the Middle-East and South Africa (Robertson et al., 1992). HAV genotype II is not as common, and HAV genotype III is common around the world: HAV genotype IIIA circulates in Central Asia, Europe, Madagascar and the USA (Desbois et al., 2010).

7. Clinical Presentation

During the subsequent period, the jaundice disappears and in a majority of cases the disease retreats during 3-6 weeks, and the majority of patients become completely healthy with the physical and psychical activities return (Gluud & Gluud, 2009). Sometimes the patient still suffers from weakness, increased tiredness, arthralgia or dyspeptic disturbances for several months after the recovery from the disease due to posthepatitis syndrome. HAV never progresses into chronicity, but it can cause debilitating symptoms and acute liver failure, which is associated with high mortality (Squires et al., 2006).

There is no evidence of the disease transition to chronic hepatitis and is rarely fatal, and within six months the infected patient is cured completely without causing any longstanding chronic hepatitis (Little et al., 2018). Fulminant hepatitis A is rare but often results in death that occurs primarily in older individuals and in persons with underlying chronic liver disease (CLD) (Wagstaff et al., 1996). In this situation the patient occasionally

requires emergency liver transplantation (Yeung & Roberts, 2010).

It is a common disease with serologic evidence of infection by an enterovirus of the Picornaviridae family that causes acute hepatitis (Dentinger et al., 2001). It is typically a self-limiting disease and usually causes mild illness characterized by sudden onset of non-specific symptoms. In addition to the liver, HAV afflicts also other vital organs, such as heart, gastrointestinal tract, pancreas, and spleen (Koff, 1998).

8. Risk Site of HAV Infection

Anyone can be infected by HAV. However, higher risk of HAV infection are injection and non-injection illegal drug users, homeless people, people travel or live in HAV infected areas, persons who has sexual contact with HAV patient, persons with clotting factor disorders, men who have sexual encounters with other men, household members or caregivers of a person infected with HAV, people who may be exposed in a research laboratory setting and those with chronic liver disease, and people who is contacted with an infected person (Sfetcu et al., 2011; Gozlan et al., 2017). Persons who engage in anal pleasuring activities are at increased risk. Health-care personnel do not have an increased prevalence of HAV infections, and nosocomial HAV transmission is rare (WHO, 2016).

9. Transmission of HAV

The source of infection resides in contaminated food and the transmission takes place by the oral pathway through the “fecal-oral” system. When an individual eats or drinks food or water contaminated with HAV may be infected with this virus (Heymann, 2008). Transmission of HAV occurs almost exclusively through the contact of an infected person, traveling to an endemic region, and ingestion of contaminated food and water (enterically). It can spread through the sexual contact or from sharing needles with the infected person (Lemon et al., 2017). The risk of transmission of HAV from pregnant women to newborns seems to be low. If a person has direct contact with an infected person who has poor personal hygiene may be infected with HAV. Sharing of forks, spoons, knives, and other utensils that have virus on them can spread the HAV. The disease is not spread by kissing, sneezing or saliva (WHO, 2012).

Eating food or drinking water, such as fruits, vegetables, salad vegetables, ice, water, certain shellfish (e.g., mussels, oysters and clams), etc. that have been contaminated by feces and contain the virus can spread the HAV. It is spread world-wide and occurs in epidemies predominantly among children and young people who are often asymptomatic (about 70% of kids under six), but accurate figures are lacking. It affects more often organized collectives, such as kindergartens, schools, military units, etc. Breastfeeding is not a mode of transmission (WHO, 2019).

Casual contact, such as in the usual workplace or school setting among people cannot spread the virus (WHO, 2013). If an individual is infected with HAV s/he may not infected further, since it causes lifetime immunity after first infection (Martin & Lemon, 2006). Outbreaks have been reported among men who have sex with men (MSM) and illicit drug users. Oral-anal-vaginal sexual contact with an infected person can spread HAV (WHO, 2016).

10. Symptoms of HAV

Sometimes an individual infected with HAV may have no symptoms or have very mild symptoms. Children younger than six years often have few or no symptoms, but they can still spread the infection. Infants and young children tend to have very mild symptoms than the adults (Wasley et al., 2006). Jaundice may occur in 70–80% of those infected as adults. There is no chronic persistent state and chronic liver damage does not occur. Symptoms of this disease usually appear within 3-4 weeks after swallowing the HAV (Linder & Malani, 2017). Some individuals may infect as quickly as 14 days. Sometimes the patients take as long as two months to be infected (Ciocca, 2000).

Some symptoms of it are fatigue, itching, poor appetite, loss of appetite, low-grade fever, dark urine, nausea, vomiting, anorexia, malaise, diarrhea, headache, febrility, pale or clay-colored stools, and jaundice (yellowing of eyes and skin) (Heymann, 2008). During HAV infection the aspartate aminotransferase (AST) serum level increases and reaches its maximal values. Urine contains serum bilirubin and urobilinogen, but does not increase significantly. The liver is moderately enlarged (Murphy et al., 2013).

11. Diagnosis of HAV

In the laboratory, clinical specimens, such as blood, feces, bile, liver biopsy, and total and direct bilirubin are utilized to detect HAV (Kozak et al., 2022). Detection of HAV is dependent on cell infection assays or molecular techniques for the presence of RNA or DNA (Gerardi & Zimmerman, 2005). Measurement of liver enzyme levels, such as alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGTP), and serum bilirubin (Koff, 1998); use of molecular virology methods, such as polymerase chain reaction (PCR) and nucleic acid hybridization assays to identify of antigens; specific

immunoglobulin M (IgM) antibodies to HAV (anti-HAV) and immunoglobulin G (IgG) antibodies are typically found in the earliest stage of disease by the use of enzyme-linked immunosorbent assay (Nainan et al., 2006).

In HAV infection the alanine transaminase (ALT) level is typically higher than the aspartate transaminase (AST) level, and the range for both is usually between 500 and 5,000 units per litre (Ribeiro et al., 2019). The IgM value ≥ 1 indicates a HAV infection positive result, and a value IgM ≤1 indicates a negative result. On the other hand, the IgG value ≥ 120 mIU/ml is considered to be positive HAV infection, and IgG value ≤ 120 mIU/ml indicates negative HAV infection (Pe´rez et al., 2003).

12. Treatment of HAV

No specific medication or antibiotic is available to treat a HAV patient. Treatment of the HAV is palliative and supportive care. Plenty of bed rest, eating healthy and well-balanced foods, drinking plenty of fluids, balanced nutrition, and avoid of drinking any alcohol, acetaminophen and other illegal drugs, may be prescribed especially during the acute phase (WHO, 2013).

Immunoglobulin M (IgM; where M for “macro”) is the largest of several isotypes of antibodies that are produced by vertebrates. It is the first antibody to appear in the response to initial exposure to an antigen (Capolunghi et al., 2013). On the other hand, immunoglobulin G (IgG; where G for “gamma”) is a type of antibody that represents about 75% of serum antibodies in human. It is the most common type of antibody found in blood circulation that is created and released by plasma B cells. Antibodies against the HAV belong to the IgM class, in later period to that of IgG (Cobb, 2019). These can prevent hepatitis A illness if they are given by injection within two weeks of exposure to the HAV (Winokur & Stapleton, 1992).

If a patient has chronic liver disease or a weakened immune system or is a carrier of the viruses and has impaired liver function, then dose modification and supportive care is necessary. About 30% of symptomatic patients require hospitalization for dehydration, severe prostration, coagulopathy, encephalopathy, or other evidence of hepatic decompensation (Brundage & Fitzpatrick, 2006).

13. Prevention of HAV

Prevention strategy of HAV is not costly and difficult. Vaccination of vulnerable populations and children is the most important prevention practice. Postexposure prophylaxis should be offered to all unvaccinated persons who are in higher risk of HAV infection (Fiore, 2004). Physicians should instruct patients about thorough hand washing after defecation and diaper changing, and sanitary disposal of wastes. Ensuring careful food-handling practices, particularly of produce and shellfish, are public health focuses. Gown and gloves should be worn prior to disinfecting and cleaning affected areas (Halliday et al., 1991).

A person must wash hands carefully and thoroughly with soap and warm running water after using the toilet or changing diapers (Chen et al., 2010). S/he must do same process before preparing food and beverages, and before eating. An individual must drink pure water and use bottled water when s/he travels contaminated area (Atkinson, 2005). Everybody should take HAV vaccine to prevent the disease. Undercooked food should avoid and should not wash or prepare food using contaminated water. Raw or steamed shellfish should be avoided (Craig & Schaffner, 2004).

14. HAV Vaccine

The HAV vaccine is very safe and effective. It is made through the killing (inactivated) HAV by formaldehyde (Keeffe, 2006). Vaccine helps the immune system to recognize and fight bacteria and viruses that cause diseases. The HAV vaccine is introduced in 1995 in the USA by American microbiologist Maurice Ralph Hilleman (1919-2005) and his team that saves millions of lives every year (CDC, 2018). It is used to prevent infection caused by HAV. It is recommended for all children ages 12 to 23 months (Fiore et al., 2008).

At present four monovalent HAV vaccines are currently available in two classes of single-antigen inactivated viruses. These provide active immunization against HAV: i) three vaccines: Havrix® (GlaxoSmithKline), Avaxim® (Sanofi), and VAQTA® (Merck Sharp & Dohme (UK) Limited) are adsorbed onto an aluminium hydroxide adjuvant; and ii) the fourth Epaxal® (Berna Biotech Ltd, Bern, Switzerland), contains formalin-inactivated hepatitis A particles (Ambrosch et al., 2004). Epaxal can be injected intramuscularly, which is well tolerated and induces a rapid HAV neutralizing antibody response resulting in seroprotection (Loutan et al., 1994). These vaccines can be used interchangeably (Beck et al., 2004). Combined vaccine Twinrix® (GlaxoSmithKline) contains purified inactivated HAV adsorbed onto aluminium hydroxide that can be used for the protection against both HAV and HBV (Joines et al., 2001; Stoffel et al., 2003). Another combined vaccine Ambirix® (GlaxoSmithKline) contains purified recombinant HBV surface antigen adsorbed onto aluminium phosphate that also can be used for the protection against both HAV and HBV (Jarvis & Figgitt, 2003; Beran, 2007).

To produce each vaccine, cell culture adapted virus is propagated in human fibroblasts, purified from cell lysates,

inactivated with formalin, and adsorbed to an aluminum hydroxide adjuvant. A single dose of HAV vaccine provides protection for at least a year. A second dose is recommended to provide long lasting protection. Two doses of HAV vaccine at least six months apart are needed to be fully protected (Ott et al., 2012).

Most people have no side-effects of the vaccine, except mild soreness at the site of the injection. However, some less common side-effects (among about 5% people) are soreness at the site of injection, loss of appetite, tiredness, low-grade fever, drowsiness, dizziness, headache, etc. side effects are usually mild and only last a short-time (Bovier et al., 2002). Acetaminophen may be given for fever and soreness, but aspirin must not be given. If more severe life-threatening allergies or side-effects are seen, such as anaphylaxis (e.g., rashes or hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, etc.), the vaccination should be discontinued (Czeschinski et al., 2000).

Vaccines are sensitive to some extent to heat and cold, and should be stored in the original packaging at +2°C to +8°C, and should be protected from light. Heat speeds up the decline in potency of HAV and reduces the shelf life. Freezing causes increased reactogenicity and loss of potency of HAV (WHO, 2018).

15. Conclusions

From this study we have observed that hepatitis A is a viral infection of the liver that may cause a short-term sickness of the liver and usually does not cause complex liver problem. The disease is not last for a long-time. The clinical course of HAV is age-dependent and the infection tends to progress from infant in form to more severe forms in adults. The HAV usually spreads through the direct contact with an infected person. It is also transmitted through fecal contamination of food and water. HAV infection can result in a financial and social burden to students, teacher, workers, and other service holders. Recently, improvements in socioeconomic condition, personal hygiene, sanitation, and vaccination HAV infection rates have declined in both developed and low-income countries. Two vaccines of HAV are approved and available, and two doses at least six months apart remain active for life-long immunization.

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