A Voice to a Silent Disease - Hepatitis

Dr. Awantika Singh[1], Dr. Deepak Bhargaya[2]

P.G. Student[1], Professor & HOD[2], Department of Oral Pathology & Microbiology, School of Dental Sciences Sharda University,Greater Noida[1,2]

Abstract

Hepatitis is a viral disease of liver that result from various causes. There are various types of hepatitis like A, B, C, D, E and G. Among all of them hepatitis B and C are more dangerous. Infectious hepatitis presents with 4 phases- viral replication phase, prodormal phase, icteric phase and convalescent phase. Dental professionals are said to be at high risk as there are certain conditions like lichen planus, sjogren's syndrome, sialedinitis and HIV are also associated with hepatitis. Routine blood tests, serologic tests, PCR and nucleic acid based tests are available as diagnostic aids that helps in diagnosis and treatment.

Keywords : Hepatitis , hepatitis virus, diagnosis, prophylaxis and dental professionals

Introduction

Hepatitis, is an inflammation of the liver that may result from various causes, both infectious organisms and noninfectious factors (eg, alcohol, drugs, autoimmune diseases, and metabolic diseases). Other hepatotropic viruses that causes hepatitis include hepatitis D virus (HDV) and hepatitis E virus (HEV).[1]. The common types of hepatitis are hepatitis A, B, C, D, E, and G. Hepatitis B and C can lead to permanent liver damage and in many cases death [2]. Dental professionals are said to be at a high risk of infections caused by various microorganisms like Mycobacterium tuberculosis, hepatitis B and hepatitis C viruses (HBV and HCV respectively), streptococci, staphylococci, HIV, mumps, herpes simplex virus type 1, influenza, and rubella [3]

Types of Hepatitis Virus

Infectious hepatitis (hepatitis A) is transmitted via oro-faecal route and is caused by the hepatitis A virus (HAV), an RNA picornavirus .The disease is typically mild and self-limiting, and is characterized by the sudden onset of nonspecific symptoms[19] with short incubation period of 50 days and occur primarily in children and young adults, sporadically and in epidemics.[4]

Serum hepatitis (hepatitis B) is parenterally transmitted, with an incubation period of 50–100 days and transmitted through sexual contact, contact with contaminated blood, and from mother to child. It do not spread through food, water, or casual contact, occurs sporadically in any age group, but older individuals are also affected.[5] It has been calculated that 1.53% of all patients reporting to the dental clinic are HBV carriers. An important consideration among dental professionals is the risk of percutaneous transmission through punctures or cuts and transmission through saliva as a result of absorption from mucosal surfaces. [19]

HCV as reported as the causative agent of 95% of cases of non-A and non-B hepatitis in 1989. It is the main cause of chronic liver disease and mainly transmitted via the parenteral route from infected blood. [19]The incubation period range from 3 to 20 weeks, with a mean of 7 weeks. Most infected individuals have 10 folds elevated transient alanine amino transferase (ALT) level before the symptoms develop. [9] The prevalence of the infection among dental professionals is similar to that found of HBV.

Hepatitis D virus (HDV) is an RNA defective virus that requires HBV for it's replication and spread through same sources and modes as HBV.[4]

Hepatitis E virus (HEV) is an RNA virus. It is excreted in the stools and spreads by the fecal-oral route. Clinically it resembles acute Hepatitis A virus (HAV) infection that recovers.[4]

Hepatitis G virus (HGV) is an RNA virus. It rarely occurs as a solitary infection, it appears as a co-infection with hepatitis A, B, or C. It is known to be transmitted through the blood transfusions.[6]

Autoimmune hepatitis is a multisystem disorder that can occur in both males and females of all ages. This condition can co-exist with other liver diseases and also triggered by certain viral infections and chemicals (eg, minocycline).[10]

Epidemiology

It is estimated that more than 350 million individuals suffer from chronic HBV infection and Hepatitis C virus is the leading cause of liver-related morbidity and mortality with more than 150 million individuals are chronically infected with HCV worldwide. [24] The worldwide HBV infection rate is higher in dentists than in the general population: 6 times higher in the USA, 4 times higher in Germany and 2.5 times higher in Japan. The incidence of HBV infection among dentists is 10.8% in Brazil , 9% in the USA and 7% in Germany [11]. In UK HBV affects less than 0.1% of the population and HBC affects 0.5 to 1 %. [3] Similar to chronic HBV infection, the burden of chronic HCV is likely to be several times higher. The prevalence in Western European countries, as well as Australia, is 1.25%; similar to those in the US [24] The estimated prevalence of HCV in Africa is 5.3%. [7] Egypt has the highest worldwide prevalence (17.5%)[27] .Since the beginning of 2017, 14 countries, i.e. Austria, the Czech Republic, Denmark, Finland, France, Germany, Ireland, Latvia, Lithuania, the Netherlands, Poland, Portugal, Slovenia and Spain reported 5 983 cases of hepatitis A , which was higher than the average annual number of cases reported between 2007 and 2016 (2 506 cases).[26]

Clinical Manifestation

Acute hepatitis

The incubation period of HBV ranges from 6 weeks to 6 months, and development of clinical manifestations is highly age dependent where infection produces typical illness in only 5 to 15% of children 1 to 5 years of age older children and adults are symptomatic in 33 to 50% of infections. Some patients may be entirely asymptomatic or only mildly symptomatic at presentation and others may present with rapid onset of fulminant hepatic failure (FHF) occurs in about 1 to 2% of persons with reported acute disease. [23]

Infectious hepatitis presents in 4 phases:

- **Phase 1 (viral replication phase)** – Patients are asymptomatic during this phase; serologic and enzyme markers are of help in hepatitis.
- **Phase 2 (prodromal phase)** – Anorexia, nausea, vomiting, alterations in taste, fatigue, arthralgias, malaise, urticaria, pruritus and some develop an aversion to cigarette smoke, patients are often diagnosed with gastroenteritis or a viral syndrome [7].
- **Phase 3 (icteric phase)** – Dark urine, followed by pale-colored stools, gastrointestinal (GI) symptoms and malaise are the symptoms, patients become icteric and may develop upper quadrant pain with hepatomegaly on right side.[8]
- **Phase 4 (convalescent phase)** – Symptoms and icterus resolve, and liver enzymes return to normal [8]

Chronic Hepatitis

Resolution of the acute infection occurs in only a few patients. At least 85% develop chronic infection.[9]. Chronic hepatitis is a diffuse inflammatory disorder of the liver with a duration of over 6 months in which the underlying cause can be infectious (mainly hepatitis C virus and, to a lesser extent, hepatitis B and D viruses), pharmacological or immunological [19] Persons with chronic HBV infection are at substantially increased risk of developing chronic liver diseases, including cirrhosis of the liver and primary hepatocellular carcinoma. [23]Cirrhosis develops in approximately 20% of hepatitis C virus patients and he median survival time from the onset of

the HCC is low: approximately five months [9]. Persons with chronic HBV infection are generally classified as having one of three histologic patterns on liver biopsy: chronic persistent hepatitis, chronic active hepatitis, and cirrhosis. [23] It is estimated that 30% of patients with chronic hepatitis C have at least one extrahepatic manifestation of the disease[9]

Conditions Associated With Hepatitis

Oral Lichen Planus

Lichen planus is a mucocutaneous disease that affects the oral mucosa. The disease represents a cell-mediated immune response. The prevalence of OLP and pitted keratolysis in the HBsAg carrier group has been found to be significantly high. HBsAg positivity may induce or cause proneness to OLP due to some mechanism that needs to be elucidated.[11] LP appears to be related to the pattern of immune dysregulation induced by HCV. The mechanism of HCV induced lichen planus is possibly related to the viral replication in lymphocytes.[12]

Salivary Gland Disorder

The salivary gland disorders that are associated with HCV infection like xerostomia, Sjögren's syndrome, and sialadenitis. Xerostomia increases patient susceptibility to caries and soft tissue disorders of oral cavity in combination with deficient hygiene and facilitate the development of candidiasis. Although bacteria are the main cause of sialadenitis, viruses such as HCV have been also implicated as causes of sialadenitis associated with xerostomia. Retroviral infections have previously been associated with sicca symptoms, but are not considered an etiologic agent of primary Sjogren's syndrome.[13]

HIV

Co-infection of Human immunodeficiency virus (HIV) with hepatitis B virus (HBV) is common, as they share routes of transmission. Human acquired immunodeficiency virus (HIV) attacks CD4+T cells, as critical cells in both cellular and humoral immunity. This leads to defective cell-mediated and humoral immune responses. [14] An estimated 25%–40% of HIV infected patients are thought to be infected with HCV, with the prevalence as high as 90% in some practices. HIV/HCV infected patients develop illness but have difficulty creating these same representations for HCV-related symptoms. [15]

Pregnancy

Vertical transmission of HAV during the pregnancy is rare. [16]. HBV cannot infect the fetus because of it's size which does not allow to cross the placenta, unless there have been breaks in the maternal-fetal barrier, such as those that occur during amniocentesis. Infected women can transmit HBV to the infant during delivery. The newborn is at high risk to develop a chronic HBV infection, with its known long-term complications. [17] Only 25% of pregnant women report receiving blood products or using IV drugs when HCV infection is diagnosed. Concurrent alcoholism, IV drug use (38%), and coexisting infection with human immuno-deficiency virus (HIV) (33%) are major associated risk factors. [18]

Diagnosis

The disease can be diagnosed by testing HBV DNA, HBs Ag, and the antigen/antibody ratio using immuno-enzymatic assays. Different enzyme-linked immunosorbent assay and recombinant immunoblot assay techniques have also been used. The diagnostic gold standard is detection of the viral genome using real time-polymerase chain reaction (RT-PCR) technology. Liver biopsy is performed to check for amount of fibrosis and severity of the inflammation in long standing condition. These findings help the hepatologist to determine the treatment protocol and to establish wise treatment decisions. [19]

Diagnostic aids include

Routine blood tests that includes, albumin; alkaline phosphatase; ALT; AST; bilirubin; complete blood count, including platelets; prothrombin time [INR]

Serologic tests include immunoassays for antibodies and antigens. Targets are available to assess:

- Presence of infection
- Immune status
- Disease status
- Need for treatment

Nucleic acid-based tests, including real-time polymerase chain reaction (PCR) and transcription-mediated amplification (TMA) are used to:

- Detect viremia
- Measure viral load
- Genotyping tests

Laboratory Criteria for Diagnosis of Hepatitis

The clinical characteristics are almost same for all types of acute viral hepatitis, laboratory testing is needed to identify the specific viral cause of illness. The laboratory criteria for confirming each type of acute viral hepatitis are as follows: [1]

- ★ Acute hepatitis A - Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive
- ★ Acute hepatitis B - IgM antibody to hepatitis B core antigen (anti-HBc) positive or hepatitis B surface antigen (HBsAg) positive and - IgM anti-HAV negative (if performed)
- ★ Acute hepatitis C- Serum alanine aminotransferase levels higher than seven times the upper limit of normal, and - IgM anti-HAV negative, and --- IgM anti-HBc negative, or if not performed, HBsAg negative, and --- One of the following
- ★ Antibody to hepatitis C virus (anti-HCV) screening-test-positive, verified by an additional more specific assay (e.g., RIBA for anti-HCV or nucleic acid testing for HCV RNA) OR
- ★ Anti-HCV screening-test positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay (e.g., >3.8 for the enzyme immunoassays).

Dental Proffessional And Hepatitis

The hepatitis viruses of most concern to dentists are the bloodborne HBV, HCV and hepatitis D virus (HDV) since they are found in saliva. [25]To decrease the risk of hepatitis in dental health care workers, it is recommended that the dental professionals should be immunized against hepatitis virus and should always use individual protective equipments such as gloves, head caps, masks, etc and asking patient to rinse with antiseptic mouthwash, Since research had demonstrated that rinsing with an antiseptic mouthwash produced a 94.1% reduction in airborne contaminants, compared to the non-rinsed controls.[21]

Hepatitis leading to liver diseases is often associated with a decrease in plasma coagulation factor concentrations hence prior coagulation and hemostasis tests are required: complete blood count, bleeding time, prothrombin time / international normalized ratio (INR), thrombin time, thromboplastin time and liver biochemistry (GOT, GPT and GGT). Liver disease may also result in alterations in the metabolism of certain drugs. So high dosage should be avoided and possible complication to be ruled out. Patients with alcoholic cirrhosis show increased tolerance of anesthetics, sedatives and hypnotic agents; as a result, the anesthesia doses should be increased. Moreover preventive oral hygiene measures are indicated to lessen the need for dental surgical treatment[19]

In case there is an accidental exposure, these steps should be followed: Carefully wash the wound without rubbing, using soap and water or disinfectant of established efficacy against the virus (iodine solutions or chlorine formulations). Apply pressure beneath the level of the wound to induce bleeding to evacuate any possible infectious material. These measures reduces the number of viral units to below the threshold count required to cause infection (the infectious dose). Dilution with water may lower the viral count to below this threshold. A detailed medical and clinical history of the patient must be recorded .[21]

Prevention and Management

Patient Education:

Counselling of patients regarding the importance of follow-up to monitor for evidence of disease progression or development of complications. Instruct them not to share any articles with potential for contamination with blood, semen, or saliva, including needles, tooth brushes or razors. Instruct patients to restricting from using any hepatotoxins, including ethanol and acetaminophen. [20]

Work Practice Protocol:

- ✸ Use instruments to grasp needles, retract tissue, and load/unload needles and scalpels and discard used disposable syringes and

needles, scalpel blades, and other sharp items in appropriate puncture-resistant containers located as close as feasible to where the items were used.

- Use individual protective equipments such as gloves, head caps, masks, etc.[21]
- In case any invasive procedure is to be performed in these patients, prior coagulation and hemostasis tests are required, which include complete blood count, bleeding time, prothrombin time/international normalized ratio (INR), thrombin time, thromboplastin time, and liver biochemistry tests and the hematologist and hepatologist must also be consulted. .[21]

3 . Post Prophylaxis :

	Hepatitis A	Hepatitis B	Hepatitis C
Minimum age Booster dose(Efficacy)	At birth	At birth	At birth
	Children- 6 months	Children(0-19) 1-4 months	1 month
	Adults- 6 months	Adults (>20 yrs) 1-2 months	
Booster dose (accead)	Children – 12 months Adults – 12 months	Children- 6-18 months Adults- 4 months	6 months

4 .Medication (Antiviral Therpy) :

Lamivudine in combination with conventional IFNα appears to be more effective than either agent alone in increasing the rate of HBsAg seroconversion [22] Also combination therapy of PEG-IFN alfa and ribavirin was introduced for HCV. [9]

Current Concept in Treatment Therapy

At present, there are seven treatments that have been approved for use in chronic HBV infection: two formulations of interferon and five nucleos(t)ide agents. Interferon mainly has immunomodulatory effects and limited direct antiviral effects. The current nucleos(t)ide agents approved for use are lamivudine, telbivudine, entecavir (ETV), adefovir dipivoxil and tenofovir disoproxil fumarate (TDF).[24] When interferon as a monotherapy was introduced for the treatment of HCV in 1991, SVR rates (sustained virological response) less than 10% were achieved. In 2002, combination therapy with Peg-IFN and ribavirin was approved by the US Food and Drug Administration (FDA) which showed improvement greater than 50%. [9] The FDA had approved of DAAs has drastically changed the approach to the treatment of HCV. The benefits of DAAs like sofosbuvir, Simeprevir include daily dosing with an oral medication, a limited side-effect profile, a shorter treatment course than interferon therapy and cure rates exceeding 90% in many populations.[24] The pan-genotypic NS5B inhibitor sofosbuvir, in combination with NS5A inhibitors, was used in the treatment for HCV patients with advanced liver disease, with cure rates approaching those of patients without cirrhosis. An analysis from the TRIO network reported an overall SVR12 rate of 98% in patients with HIV/HCV co-infection treated with LDV/SOF for either 8, 12 or 24 weeks. [9]

Emerging Issues

HBV infection with mutated virus has been found in vaccinated persons in Italy, Singapore, The Gambia, and the United States and in liver transplant recipients that causes a change in one amino acid in the “a” determinant of the HBs protein, which is the proposed conformational epitope essential for recognition and neutralization by anti-HBs antibodies. Further studies and enhanced surveillance on the emergence of these variants remain high priorities in evaluating the effectiveness of current immunization strategies. [23]

Prognosis

HAV infection usually is mild and self-limited. Overall mortality is approximately 0.01%. [4] The risk of chronic HBV infection in infected older children and adults approaches 5-10%, the case-fatality rate in these patients is 80%. 50%-60% patients develop chronic infection due to hepatitis C and chronically infected patients are at risk for active hepatitis, cirrhosis, and HCC.[5]. Chronic co-infection with HBV and HDV often leads to rapidly progressive subacute or chronic hepatitis, with as many as 70-80% of these patients eventually developing cirrhosis. HEV infection usually is mild and self-limited. The case-fatality rate reaches 15-20% in pregnant women. [4]

Conclusion

Merely celebrating World Hepatitis Day on 28 July is not sufficient for increasing awareness in the community. It is an opportunity for the people and health policy makers globally for more knowledge sharing and finding better approaches for control of HBV and HCV infections in their communities.

Aware & Be Safe

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