HEPATITIS– KNOW IT TO CONFRONT IT

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INTRODUCTION

Word liver derived from hepar- or hepat- which is a Greek word, a lifeline, indeed, relentlessly round the clock involved in from metabolism to digestion via aiding emulsification of lipid, synthesis of plasma protein to glycogen storage & also synthesis of bile & hormones to detoxification, to keep us hale and hearty. But, at times due to multiple factors like infection, drug, ischaemic, alcohol, drugs, metabolic etc, cause inflammation in liver, [hepat- (ἡπατ-) meaning liver, and suffix -itis, meaning "inflammation" (c. 1727)].¹ A group of viruses known as the hepatitis viruses cause most cases of hepatitis worldwide and the role, impact, epidemiology and prevention of this VIRUS induced HEPATITIS will be discussed in this article.

Generally, it’s divided in ACUTE & CHRONIC HEPATITIS (depending upon duration of the disease,< 6 month – ACUTE;>6 month- CHRONIC)

Acute Hepatitis

Ranging from subclinical disease to self-limited symptomatic disease to fulminant hepatic failure. Adults with acute hepatitis A or B are usually symptomatic. Persons with acute hepatitis C may be either symptomatic or asymptomatic (i.e., subclinical).

Typical symptoms of acute hepatitis are fatigue, anorexia, nausea, and vomiting. Very high amino transferase values (>1000 U/L) and hyperbilirubinemia are often observed. Severe cases of acute hepatitis may progress rapidly to acute liver failure, marked by poor hepatic synthetic function. This is often defined as a prothrombin time (PT) of 16 seconds or an international normalized ratio (INR) of 1.5 in the absence of previous liver disease.²

Acute viral hepatitis is more likely to be asymptomatic in younger people. Symptomatic individuals may present after convalescent stage of 7 to 10 days, with the total illness lasting 2 to 6 weeks.³

Chronic Hepatitis

Acute viral hepatitis may evolve into chronic hepatitis. Hepatitis A and hepatitis E never progress to chronic hepatitis, either clinically or histologically.

Histologic evolution to chronic hepatitis can be demonstrated in approximately 90-95% of cases of acute hepatitis B in neonates, 5% of cases of acute hepatitis B in adults, and as many as 85% of cases of acute hepatitis C. Some patients with chronic hepatitis remain asymptomatic for their entire lives. Other patients report fatigue (ranging from mild to severe) and dyspepsia.

Approximately 20% of patients with chronic hepatitis B or hepatitis C eventually develop cirrhosis, as evidenced by the histologic changes of severe fibrosis and nodular regeneration. Although some
patients with cirrhosis are asymptomatic, others develop life-threatening complications. The clinical illnesses of chronic hepatitis and cirrhosis may take months, years, or decades to evolve.\textsuperscript{[4]}

**Complications**

But, it leaves its stigmata too, more in cases of chronic hepatitis than in acute conditions, A small proportion of people with acute hepatitis progress to acute liver failure, in which the liver is unable to clear harmful substances from the circulation (leading to confusion and coma due to hepatic encephalopathy) and that known as FULMINANT HEPATITIS seen in 1\% of cases of acute hepatitis due to hepatitis A or B. Hepatitis E is a common cause in Asia and though resolves spontaneously in almost 50\% cases ,but requires liver transplantation in rest 50\% as lifesaving procedure.

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**Chronicity & CarrierState**

Among HEPATITIS viruses A & E present as ACUTE HEPATITIS mainly, but HEPATITIS B,C, and D results in chronicity, carrier state and cancer.\textsuperscript{[5]}

Characteristic of different subtypes differs significantly than each other ,HEP A & E chiefly transmitted by faeco-oral route ,whereas B,C,D via percutaneous, perinatal & sexual ,whereas the incubation period of A & E is 15-45 days & 14-60 days ,in case of B& C its 30-180 days & in HEP C its 15-160 days,cases of FULMINANT hepatitis chiefly seen in HEP D co infections whereas chronicity ,carrier state in cases of B,C,D \textsuperscript{[5][6]} HEP E associated with pregnancy state whereas HEP C is associated with transfusion related hepatitis cases[6]

**Epidemiology**

Worldwide, HAV is responsible for an estimated 1.4 million infections annually.\textsuperscript{[7]} HBV causes more than 4 million cases of acute hepatitis per year throughout the world, and it is estimated that approximately 350 million people are chronically infected with the virus.\textsuperscript{[8]} HBV leads to 1 million deaths annually as a result of viral hepatitis–induced liver disease.\textsuperscript{[8]}

The worldwide annual incidence of acute HCV infection is not easily estimated, because patients are often asymptomatic. An estimated 170 million people are chronically infected with HCV worldwide.\textsuperscript{[9]} China, the US, and Russia have the largest populations of anti-HCV positive IV drug users (IDUs). It is estimated that 6.4 million IDUs worldwide are positive for antibody to HBCAg (anti-HBc), and 1.2 million are HBsAg-positive.\textsuperscript{[9]}

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HAV infection is common in the less-developed nations of Africa, Asia, and Central and South America; the Middle East has a particularly high prevalence. Most patients in these regions are infected when they are young children.

Epidemics of HAV infection may be explained by person-to-person contact, such as occurs at institutions, or by exposure to a common source, such as consumption of contaminated water or food. As sanitation has improved, the overall prevalence of hepatitis A in the United States and in other parts of the developed world has decreased to less than 50%.

Out of the approximately 5% of the world’s population (i.e., 350 million people) that is chronically infected with HBV, about 20% will eventually develop HBV-related cirrhosis or HCC. According to the World Health Organization, HBV is the 10th leading cause of death worldwide.[10]

HCV is the most frequent cause of parenteral non-A, non-B (NANB) hepatitis worldwide. Hepatitis C is prevalent in 0.5-2% of populations in nations around the world. The highest rates of disease prevalence are found in patients with haemophilia and in IDUs.

In the 1980s, as many as 180,000 new cases of HCV infection were described each year in the United States; by 1995, there were only 28,000 new cases each year.[11] The decreasing incidence of HCV was explained by a decline in the number of cases of transfusion-associated hepatitis (because of improved screening of blood products) and by a decline in the number of cases associated with IV drug use. Screening of the US blood supply has dramatically reduced the incidence of transfusion-associated HCV infection.[12, 13] Before 1990, 37-58% of cases of acute HCV infection (then known as NANB) were attributed to the transfusion of contaminated blood products; today, only about 4% of acute cases are attributed to transfusion. HCV is estimated to contaminate 0.01-0.001% of units of transfused blood. Acute hepatitis C remains an important issue in dialysis units, where patients’ risk for HCV infection is about 0.15% per year.

HDV requires the presence of HBV to replicate; thus, HDV infection develops only in patients who are positive for HBsAg[14] and although hepatitis D is not a reportable disease, the CDC estimates that it results in 7500 infections each year. Approximately 4% of cases of acute hepatitis B are thought to involve coinfection with HDV. HDV is believed to infect approximately 5% of the world’s 350 million HBsAg carriers. The prevalence of HDV infection in South America and Africa is high HEV is the primary cause of enterally transmitted NANB hepatitis. It is transmitted via the fecal-oral route and appears to be endemic in some parts of the less-developed countries and associated with a high neonatal mortality.[15]

In one report, anti-HEV antibodies were found to be present in 29% of urban children and 24% of rural children in northern India.[16]

In last decade or so number of total viral hepatitis cases in India reduced from 153034 in 2000 to 94402 in 2011.[17][18]
Indian Perspective

It’s a major public health burden in India. Since 1955, several epidemics of hepatitis have been reported [19-26] and HEP E remain the major cause of sporadic infection among adults in India.

Table 1.

Major epidemics of hepatitis E virus (HEV) infection in India [19-26]

<table>
<thead>
<tr>
<th>Location (year)</th>
<th>Number affected</th>
<th>Incubation period (days)</th>
<th>Attack rate (%)</th>
<th>Mortality Overall n (%)</th>
<th>Pregnant women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delhi* (1955-56)</td>
<td>29 300</td>
<td>18–64</td>
<td>2.3</td>
<td>65 (0.22)</td>
<td>10.5</td>
</tr>
<tr>
<td>Kharagpur† (1960)</td>
<td>65</td>
<td>—</td>
<td>—</td>
<td>0 (0)</td>
<td>—</td>
</tr>
<tr>
<td>Aurangabad† (1961)</td>
<td>865</td>
<td>—</td>
<td>—</td>
<td>3 (0.34)</td>
<td>—</td>
</tr>
<tr>
<td>Siliguri† (1966)</td>
<td>4287</td>
<td>28–70</td>
<td>2–5.2</td>
<td>4 (0.09)</td>
<td>Na</td>
</tr>
<tr>
<td>Ahmedabad* (1975–76)</td>
<td>2572</td>
<td>—</td>
<td>—</td>
<td>62 (2.4)</td>
<td>—</td>
</tr>
<tr>
<td>Kashmir‡ (1978)</td>
<td>275</td>
<td>10–40</td>
<td>1.65</td>
<td>10 (3.6)</td>
<td>75</td>
</tr>
<tr>
<td>Azamgarh* (1979–80)</td>
<td>152</td>
<td>na</td>
<td>na</td>
<td>18 (12)</td>
<td>39</td>
</tr>
<tr>
<td>Kanpur* (1990–91)</td>
<td>79 091</td>
<td>14–56</td>
<td>3.76</td>
<td>48 (0.06)</td>
<td>Na</td>
</tr>
</tbody>
</table>

The first and the most well-studied epidemic of HEV affected 29 300 people in Delhi between December 1955 and January 1956 (Table 1). Most of the information on the epidemiological aspects of HEV has been derived from this epidemic HAV also spread by faeco-oral route, and prevalent in India, its prevalence is decreasing in adult [27], inference drawn from studies conducted in hospitals, but still most prevalent among children.

Table II.

Age-wise prevalence of hepatitis a virus antibody (anti-HAV) in schoolchildren in New Delhi

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>n</th>
<th>Anti-HAV positivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4–7</td>
<td>206</td>
<td>178 (86.4)</td>
</tr>
<tr>
<td>8–12</td>
<td>574</td>
<td>528 (91.2)</td>
</tr>
<tr>
<td>&gt; 12</td>
<td>644</td>
<td>622 (96.6)</td>
</tr>
</tbody>
</table>
The high risk groups reported from India include

i) Individuals with repeated parenteral exposure such as multitransfused patients with thalassemia/haemophilia, patients undergoing haemodialysis and professional sex workers,

ii) Professional blood donors,

iii) Healthcare workers with occupational exposure,

iv) Household contacts of individuals with chronic HBV infection, and

v) Individuals living in specific hyper endemic geographical areas.

In patients with thalassemia and haemophilia, HBsAg and anti-HBs positivity rates of 6%–60% and 29%–70%, respectively, have been reported. [30-39] HBsAg positivity among professional blood donors has been reported to be 15%–20% [40-41] However, among healthcare workers, HBsAg positivity has been reported to be 1.7%–40%. [42,43] Recently, 2 studies have shown that within India hyperendemic regions for HBV infection may exist—HBsAg positivity of 23.3% among the tribal population in the Andaman and Nicobar Islands, [44,45] and 5.2% among the Lambada.

Several published reports from India describe the relative frequency of various HCV in the northern and southern parts. In these studies, genotype 3 was found in 54%–90% of HCV-infected patients; overall, 60% of patients had genotype 3, 25% had genotype 1, 8% had genotype 2 and 2% had genotype 4 infection. HCV genotype 1 infection was more frequent in southern India than in the rest of the country [46,47,48,49, and 50]. Of patients with CLD, HCV is the aetiological agent in 14%–26% and 14%–20% of patients with hepatocellular cancer in India [51, 52]

HDV infection is common in Italy and Eastern Europe, South America, the Amazon basin and in the Mediterranean region; about 15 million persons are infected with HDV globally [53]. HDV superinfection and co-infection are rather infrequent in India. Initial studies from Chandigarh, Delhi, Mumbai and Kashmir reported a high prevalence of anti-HDV among patients with acute and chronic hepatitis, fulminant hepatitis and subacute liver failure. Recent studies have shown lower prevalence rates in healthy donors and in patients with severe liver disease.

Khuroo et al. reported in 1988 an epidemic of HDV from southern Kashmir, in which 35 of the 51 icteric patients were HBV carriers. Of the 24 HBV carriers who were tested for anti-HDV, 22 tested positive. The authors could not provide any explanation for the mode of spread of HDV in this epidemic.
Thus, both HDV superinfection and co-infection do occur in India though at a relatively low rate, and may be the cause of severe liver disease in a subset of patients [54-61].

Viral hepatitis is a major public health problem in India, which is hyperendemic for HAV and HEV. Seroprevalence studies reveal that 90%–100% of the population acquires anti-HAV antibody and becomes immune by adolescence. Many epidemics of HEV have been reported from India. HAV related liver disease is uncommon in India and occurs mainly in children. HEV is also the major cause of sporadic adult acute viral hepatitis and ALF. Pregnant women and patients with CLD constitute the high risk groups to contract HEV infection, and HEV-induced mortality among them is substantial, which underlines the need for preventive measures for such groups. Children with HAV and HEV co-infection are prone to develop ALF.

India has intermediate HBV endemicity, with a carrier frequency of 2%–4%. HBV is the major cause of CLD and HCC. Chronic HBV infection in India is acquired in childhood, presumably before 5 years of age, through horizontal transmission. Vertical transmission of HBV in India is considered to be infrequent. Inclusion of HBV vaccination in the expanded programme of immunization is essential to reduce the HBV carrier frequency and disease burden. HBV genotypes A and D are prevalent in India, which are similar to the HBV genotypes in the West. HCV infection in India has a population prevalence of around 1%, and occurs predominantly through transfusion and the use of unsterile glass syringes. HCV genotypes 3 and 2 are prevalent in 60%–80% of the population and they respond well to a combination of interferon and ribavirin. About 10%–15% of CLD and HCC are associated with HCV infection in India. HCV infection is also a major cause of post-transfusion hepatitis. HDV infection is infrequent in India and is present about 5%–10% of patients with HBV-related liver disease.

HCC appears to be less common in India than would be expected from the prevalence rates of HBV and HCV.

The high disease burden of viral hepatitis and related CLD in India, calls for the setting up of a Hepatitis registry and formulation of government-supported prevention and control strategies

Prevention Strategies

Carefully planned strategies are chalked out to counter the menace
a) Strengthening prevention, screening and control of viral hepatitis and its related diseases;
b) Increasing hepatitis B vaccine coverage and integration into national immunization programmes; and
c) Coordinating a global response to hepatitis to increase access to treatment.

In rural India, defaecation in the open is common. This is the major cause of well water contamination, especially during the rainy season. Better sanitation, provision of clean drinking water, proper sewage disposal and public education are the mainstays for prevention of HEV infection. However, since these are difficult to achieve in developing countries with limited resources, the development of a vaccine may be a useful preventive strategy.

Recent studies have evaluated recombinant HEV ORF2 proteins as candidate vaccines. An ORF2-derived 62 kD recombinant protein prepared from the Burmese HEV strain and expressed in baculovirus has shown protection against biochemical or histological hepatitis in monkeys upon
challenge with a large dose of a heterologous HEV strain. However, the protection was short-lived. DNA vaccine administered through the gene gun has also been found to be immunogenic in animals [62, 63]

The preventive strategies for HAV infection are similar to those for HEV infection. However, unlike HEV, an effective, safe, immunogenic, live, attenuated HAV vaccine is commercially available in India and is being marketed aggressively. Among non-immune people, it provides seroconversion rates of >90% and nearly 100% after one and two doses (4–6 weeks apart), respectively. [64, 65]

The extremely high prevalence of anti-HAV antibody in the general population in India implies that a mass immunization programme against HAV would not be cost-effective. As the anti-HAV test is cheaper than the HAV vaccine, it may be cost-effective to do this test before administering the HAV vaccine.

HBV vaccination is a cost-effective method of preventing mortality due to such diseases. According to the Yaounde Declaration of WHO, to which India is a signatory, by 2000 all countries in the world would adopt universal HBV vaccination. Universal HBV vaccination has already been documented to decrease the carrier frequency and disease burden in Taiwan [66–69]

Quality control of donor screening in India is another area where more efforts are needed. In a study from New Delhi, 6% of HBsAg-negative units of blood from various blood banks in Delhi were found to be HBsAg positive on re-testing using a sensitive micro-ELISA technique.[70]

Awareness campaigns on the routes of community-acquired infection and on steps to prevent household and nosocomial spread of HBV infection need to be launched. All household contacts and medical/paramedical staff should be vaccinated against HBV. High risk groups need to be identified, screened for HBsAg and vaccinated against HBV.

For HEP C, Combination therapy with pegylated interferon α2b (1.5 mg/kg/week) or α2a (1.80 mg/week) with ribavirin (10.6 mg/kg/day) is recommended for patients with CH-C and compensated cirrhosis of the liver. [71]

Recognizing the tremendous burden caused by viral hepatitis, the World Health Assembly adopted resolution WHA63.18 in 2010, calling for a comprehensive approach to the prevention and control of viral hepatitis.

Following the resolution, WHO established the Global Hepatitis Programme with the following goals:

- To reduce the transmission of agents that cause viral hepatitis;
- To reduce the morbidity and mortality due to viral hepatitis through improving the care of patients with viral hepatitis; and
- To reduce the socio-economic impact of viral hepatitis at individual, community and population levels. [72]

Following the adoption of a viral hepatitis resolution during the 63rd World Health Assembly in May 2010, World Hepatitis Day was given global endorsement as the primary focus for national and international awareness-raising efforts and the date was changed to July 28 (in honour of Nobel
World Hepatitis Day was observed across the world on 28 July 2013. The theme for the year 2013 is “This is Hepatitis, Know it, Confront it” [74] - There is shift in the focus to move from awareness to commitment and action to address the “silent epidemic” of viral hepatitis. and decrease the morbidity, mortality and loss of quality of life spells from the disease and also to ease the burden it exert on health system across world ,by spreading awareness and strengthening preventive and therapeutic efforts across the globe.

REFERENCES
2. Extensive damage to and scarring of liver (i.e. cirrhosis) leads to weight loss, easy bruising and bleeding tendencies, peripheral edema (swelling of the legs) and accumulation of ascites (fluid in the peritoneal cavity). Eventually, cirrhosis may lead to various complications: esophageal varices (enlarged veins in the wall of the esophagus that can cause life-threatening bleeding) hepatic encephalopathy (confusion and coma) and hepatorenal syndrome (kidney dysfunction)
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