1.0 Introduction
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1.1 History of hepatitis and hepatitis viruses

The term hepatitis denotes inflammation of the liver. Mankind knows hepatitis for many centuries. It was referred to as jaundice in the writings of the Babylonian Talmud (5th century BC), De Internis Affectionibus (460-375 BC) and ancient Chinese literature. The word jaundice in fact is derived from the French jaune meaning yellow and may be defined as yellowness of the integuments, conjunctivae, tissues and secretions caused by impregnation with bile pigments. Large epidemics of jaundice were recorded as early as the 17th century in military camps. Jaundice was viewed as obstructive in nature. Simultaneously, many clinicians suspected an infectious etiology (Weil 1886: 209-232). Cockayne (1912:1-28) believed that the disease reached the liver through blood and introduced the term infectious hepatitis to describe the epidemic form of the disease. Mc Donald (1908:208-229) postulated viral etiology as a cause of acute yellow atrophy of the liver. In 1923, Blumer described the pattern of illness found in 63 outbreaks of epidemic jaundice that was noted in the US between 1812 and 1922. The occurrence of epidemics continued through World War II during which time human volunteers confirmed viral etiology and uniqueness of hepatitis A (epidemic infectious jaundice) in comparison to hepatitis B (homologus serum jaundice) (Havens 1947:635-655, MacCallum et al. 1952:252-267; Krugman et al. 1967:365-373, Melnick and Boggs 1972:461-467). Transmission studies conducted in humans provided differentiation between A and B forms of the disease clinically and epidemiologically (Krugman et al. 1967). Studies conducted by other investigators also showed lack of cross immunity between the two types and established the efficacy of immunoglobulins in preventing infectious hepatitis (Krugman et al. 1960:823-830; Zuckerman 1983:3-32).

The term viral hepatitis is often thought to be synonymous with diseases caused by the known hepatotropic viruses, including hepatitis viruses A, B, C, D, and E. Infections with hepatitis viruses, have been also associated with a wide variety of extrahepatic manifestations.

HAV usually causes an acute infection which is self limited. HAV is the major public health problem worldwide. It is also known to cause persistent infection, fulminant hepatic failure (FHF), renal failure, late recovery and clinical relapse (Sjogren et al. 1987:221-226; Chio and Bakir 1992:413-416; Inoue et al. 1996:322-324; Bendre et al. 1999:1107-1112). HBV causes both acute and chronic infections. The chronic infection may lead an individual to the risk of chronic liver disease or primary hepatocellular carcinoma (Hoofnagle et al. 1978:219-244; Beasley et al. 1983:213-222). HCV produces persistent infection usually associated with subclinical disease, with only
approximately one quarter of acute cases resulting in jaundice (Dusheiko et al. 1993:283-302; Yoshiba et al. 1994:829-835). HDV is an "incomplete" virus and the only viroid known to infect man. Patients with HDV infection show super infection or coinfection with HBV (Popper et al. 1983:906-912; Purcell et al. 1987:79-89). HEV is the major cause of acute infection in almost all cases of enterically transmitted non A hepatitis in adults. It is not known to produce persistent infection but may lead to FHF, death and occasionally in renal failure (Khuroo et al. 1994:281-286; Verschuuren et al. 1997:799-801).

Serological exclusion of the known hepatitis viruses in clinically diagnosed viral hepatitis cases continues to point out the entities other than A, B, C, D, E. The cases of "non ABCDE" hepatitis, which appeared to be parenterally transmitted, have been reported to have association with HGV and TTV (Simons et al. 1995:564-569; Naoumov et al. 1998:195-197). Occurrence of outbreaks of enterically transmitted non-A, non-E hepatitis has also been reported (Arankalle et al. 1994:3428-3432; Luo et al. 1999: 59-64).

A number of other viruses associated with infections resulting occasionally into hepatitis include cytomegalovirus, Epstein-Barr virus, herpes simplex virus, yellow fever virus, rubella, parvovirus and viruses such as Lassa, Ebola and Marburg (Howard and Simpson 1983:139-158). However, within the defined objectives of this manuscript, the references and data in subsequent chapters would deal with hepatitis A, which is major public health problem in India.

Identification of virus particles by electron microscopy in stool samples from hepatitis A patients was a milestone in viral hepatitis research (Feinstone et al. 1973:1026-1028). Consequently, the epidemiology of HAV infection was defined using newly developed assays, which helped differentiation of acute and resolved infections (Duermeyer and vander Veen 1978:684-685; Safford et al. 1980:25-31). HAV grown in cell culture was found to be useful in development of hepatitis A vaccine (Provost and Hilleman 1979:213-221). The vaccine was subsequently shown to prevent hepatitis A effectively (Andre et al. 1992:s160-s168; CDC Report 1996:1-30). Although vaccine has been licensed in multiple countries, it has not been in wide use due to its cost. Improvements in public health sanitation and standards of living are leading to an increasing load of susceptible population and ultimately in disease burden (Martin & Lemon 2006:s164-s172).