Co-Infection of Hepatitis B and Hepatitis C Virus: An Epidemiological and Demographic Profile

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ABSTRACT

Hepatitis B and C are one of the major reasons of mortality among the patients of chronic liver disorders. According to WHO, >500 million people are infected worldwide with either hepatitis B virus (HBV) or hepatitis C virus (HCV), out of which, 1 million deaths occur every year. Due to a shared parenteral route of transmission, the HBV and HCV co-infection a common phenomenon. The association between HBV and HCV in coinfected individuals is multifaceted, and viral interference has been well described. It is generally observed that HBV replication is inhibited by HCV in the case of dual infection. The patients suffering from HBVHCV co-infection have more severe liver pathophysiology as compared to mono-infection of either of these viruses. These patients have higher chances of developing liver cirrhosis and hepatocellular carcinoma. Therefore, a thorough serological and virological examination is required before the onset of antiviral therapy. The age, gender and regional distribution of patients have a great impact on acquiring the disorder. Males have more chances of acquiring HBV and HCV infection than females. People residing in rural areas are more vulnerable to the infections than urban people. Both the infections have been found common among the patients of more than 40 years of age. Further, PWID (persons who inject drugs) are always at higher risk of HCV infections due to the usage of shared syringes. Current review focuses on the historical, epidemiological and demographic profile of HCV and HBV infections.

Keywords: Hepatitis B, hepatitis C, co-infection, drug abusers, epidemiology.

INTRODUCTION

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are the major reasons of chronic liver disorders. Both are responsible for approximately 96% of all hepatitis mortality. The World Health Organization (WHO) estimates that globally, 170 and 400 million people are infected with HCV and HBV globally [1]

HISTORICAL PERSPECTIVE

Hepatitis C was discovered in 1989 by utilizing molecular biology technique while observing the serum sample from experimentally infected animal and was identified to be an RNA virus of genus hepacivirus [2].

The HBV is a blood-borne virus that was discovered by Blumberg et al. in 1965, when they identified an unusual antigen in the blood sample of an Australian aborigine while working on the polymorphism of lipoprotein [3]. It was called as Australia antigen. After further research on Australia antigen (AuAg), they found in 1967 that it is responsible for causing hepatitis. In 1968, Alfred Prince at New York blood centre identified a serum antigen, which was related with post-transfusion hepatitis. He named it serum hepatitis antigen (SH antigen) and reported it to be identical to AuAg [4]. Almeida et al. [5] released the core particles

of previously discovered "Dane particles" [6] with the help of mild detergent, and demonstrated that hepatitis B patients formed antibodies against this core antigen (HBcAg), suggesting that the Dane particles were the causative viral agents of hepatitis B. HBV and HCV both are hepatotropic viruses that primary replicate within the liver cell. They share common route of transmission, especially in endemic areas, making coinfections a regular thing [7].

BURDEN OF DISEASE

HBV and HCV infections are unevenly distributed worldwide with a marked geographic variation. There is an estimation that the overall prevalence of HBsAg is reported to be 3.6% in which 248 million people are chronically infected with HBV all over the world by having highest prevalence in Asia, Sub-Saharan Africa and the Pacific Islands (19, 20).

Likewise, HCV is estimated with global prevalence of around 2.5% with 170 million chronic patients and ~4 million new cases each year [8]. The prevalence of HCV infection can be segregated into very low (0.01% to 0.1% prevalence; e.g. United Kingdom, Scandinavia); low *i.e.* 0.2% to 0.5% frequency (e.g. Western Europe, Australia, South Africa); intermediate (1-5% prevalence; e.g. Eastern Europe, Mediterranean, Middle East, and India); and high i.e. 17% to 26% frequency (e.g. Egypt) [9].

Epidemiology: The Indian Perspective

There is a lack of systematic and large population-based studies on the occurrence of hepatitis C. The estimated prevalence of HCV infections in India is about 0.09% – 2.02% [10]. The prevalence of HBV was measured as 0.71% in a large community based systematic study from West Bengal, India [11]. Further, a study conducted on 22,666 Indian Armed Forces trainees, evaluated the HCV seropositivity as 0.44% [12]. Bhaumik et al. concluded that the prevalence of HCV in India is highly variable [13].

HBsAg is used as epidemiological marker to calculate the prevalence of hepatitis B infection [14]. Several studies have been carried out in India over the last two decades. According to WHO, in India hepatitis B is of intermediate endemicity (high endemicity >8%, intermediate endemicity 2-7%, low endemicity <2%), having about 4% inhabitants as chronic hepatitis B virus carrier *i.e.* approximately 5 crore individuals [15, 16]. Lodha *et al* published a systematic review of Hepatitis B in India analysing 128 papers and estimated the incidences of HBV infection in the range of 1–2%. Chowdhury *et al.* conducted a study on 7653 subjects and demonstrated that 2.97% population had HBsAg seropositivity; however, 90% of these infected individuals were found negative for Hepatitis B e antigen but seropositive for Hepatitis B e antibody [18].

Co-infection of HBV/HCV occurs frequently particularly in endemic regions and among individuals at increased risk of parenteral infections. The frequency of dual infection is not known at a precise level because of the lack of research on a large population. The frequency of HBV and HCV coinfection worldwide is estimated to be 5–20% in HBsAg positive and 2–10% in HCV-infected individuals (29). The pooled frequency of HCV-HBV coinfection in India is 1.89% (30). An investigation was conducted to evaluate the incidences

of HBV/HCV coinfection among patients with chronic liver disease in Chennai. The study comprised 251 patients who were tested for the presence of HBsAg, HBV-DNA and HCV-RNA by qualitative PCR evaluate HCV-HBV prevalence of about 5.9% [19].

DEMOGRAPHY

Gender wise distribution

Singh *et al* (2004) conduct a study enrolling 516 HCV patients and reported a high rural prevalence of infection (67.3%), with maximum cases from Ludhiana district (30.4%). 72.8% cases were of males, and the patients of the age group 41–60 years were most predominant comprising 44.8% of total patients [20]. Kundu *et al* (2015) also reported a higher incidence of HBsAg in males (27.03%) as compared to females (23.08%) [21]. Ahmed *et al.* demonstrated similar trends in gender wise distribution of HBV among cataract patients in Pakistan, reporting 72% incidences in males and 28% in females [22]. A study in Ethiopia also reported that males are more susceptible to HCV than females [23]. Similarly, Sood *et al* (2012) in Punjab reported a higher prevalence of HCV infection among (73%) in males than females (27%) [24].

Age-wise distribution

A study performed by Kundu *et al.* demonstrated that HBV majorly (38.46%) infects the individuals of age group 41-50; however, HCV affected the most among the people of age group 51-60 (42.86%). [21]. Also, Bhattacharya *et al.* demonstrated an 8.65% seroprevalence of HCV in 661 patients of 20-39 years of age group [25]. Devi *et al*. (2004) found highest seropositivity (46.6%) of HBV among the patients of age in the range of 30-40 years [26]. Singh *et al* (2014) in their study found the highest prevalence of HCV in 41-60 years (49.81%) age group followed by 21-40 years (30.04%) with a lowest prevalence in age group more than 80 (0.39%) and less than 20 (1.74%) in their study [20].

Residential factor urban/rural

Singh *et al.* demonstrated a predominant rural distribution (67.25%) of HCV infected over urban prevalence (32.75%) [20]. Kundu *et al.* showed higher anti HCV antibodies seropositivity among rural patients (18.92%) than urban one (15.38%) [21]. The poor hygienic and sanitation conditions along with lack of good medical services mainly contribute to the high prevalence of the infection among rural areas.

Iatrogenic factor

Malhotra *et al.* demonstrated the seroprevalence of HBV-HCV coinfection among haemodialysis patients. They examined 262 patients of all age group, out of which 88 (33.5%) were found to be positive for HBsAg and 2 (0.8%) were coinfected with HBV and HCV [27].

Drug abusers

India has a large PWID (persons who inject drugs) population. PWIDs possess an increased risk for HBV and HCV infections. The Centre for Disease Control (CDC) has estimate that about 2/3 of all community-acquired HCV infections belong to the administration of illicit drug injections [28]. The incidence of HCV among

PWID is near 65%, and can be up to 80% among long-term injectable drug abusers [29]. The rate of HBsAg positivity was reported earlier as 2.7–10.8% among intravenous drug users [30]. Chalana *et al* (2013) recruited 1318 patients admitted in psychiatric ward to determine the seroprevalence of HCV, HBV in substance dependent subjects. They found prevalence of HCV seropositive injection drug users (IVDUs) was 15.25%and 5.08% patients were found to be HBsAg positive [31]. Panda *et al (*2014) recruit a study on (intravenous drug users) IVDU‟s to determine the prevalence of HCV among the particular group and found the prevalence of HCV was 49% in their study [32].

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