

A Mini Review on Viral Hepatitis Focusing Pakistani Population

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Abstract

Viral hepatitis causes several mortalities globally every year. The occurrence of this infection differs due to different geographic distribution and settings; this infection can exist throughout the year. Pakistan and Egypt endure 80% of the burden of this disease in the region. This infection is known as 'silent killer' due to unawareness of patients as they stay undiagnosed and untreated for several years before contracting disease complications. Very limited community based research on Hepatitis viral infections has been conducted in Pakistan; the data proposes such infections as endemic with prevalence in general population, blood donors and pregnant females. In Pakistan, viral hepatitis A and E cause maximum morbidity and hepatitis B, C and D cause maximum mortality. About 90% children in Pakistan suffer from hepatitis A in before 10 years of age due to poor sanitation and hygienic conditions; the disease can be silent in both children and adults. In Pakistan, acute viral hepatitis is mainly due to HEV especially in adults belonging to low socioeconomic groups. During summers, floods and rains, Hepatitis E mostly occurs as outbreaks and sporadic cases due to poor sanitation and lifestyle. The main mode of transmitting blood borne pathogens i.e. HBV, HCV and HIV in the developing countries is improper sterilization of invasive medical devices and therapeutic injections from reused needles and syringes. Approximately 1/3rd HBV-infected persons in Pakistan were co-infected with hepatitis D virus leading to chronic liver disease.

It has been observed that HCV replaced HBV in ensuing years and has appeared as the most common cause of liver disease. The delta viral infection may endure causing a major disease burden in Pakistan due to its substantial pool of positive cases. Precise information about hepatitis frequency in Pakistan is a requisite along with information about the major risk and infection factors to target it specifically. It is essential to institute regional laboratories with economical technologies for testing viral hepatitis all over the country to exactly estimate hepatitis burden. Basic facilities like safe water supply and improved sanitation should be made available. A central registry for hepatitis and liver diseases and proper surveillance system is highly desirable in the country.

Introduction

Viral hepatitis is a grave health issue standing as the 8th main cause of mortality worldwide. The increasing burden of blood borne or water/food borne hepatotropic virus is alarming for Asian countries. Presently, 6 discrete kinds of hepatitis virus have been recognized namely hepatitis A, B, C, D, E and G viruses [1,2]. The hepatitis viral infections are acute (when it lasts <6 months) in nature but hepatitis B, C and D may be chronic too (when it lasts >6 months). The fecal-oral route is the major transmission mode for Hepatitis A virus (HAV) and Hepatitis E virus (HEV). The blood borne viruses are Hepatitis B virus (HBV), Hepatitis C virus (HCV), and Hepatitis D virus (HDV) that are principally communicated via breach in the skin or mucosa [3-5]. The infection can exist all through the year; although spring and summer peaks have been indicated. The climatic and behavioral factors like summer travel to endemic area, poor hygiene and environmental cleanliness, swimming in hot months, tattoo, increase in sexual contact, and food practices are important for diseases' seasonal appearance [6-8].

Pakistan and Egypt endure 80% of disease burden within the region, and nearly 12 million people suffer from hepatitis B or C within Pakistan [9]; the incidence rate is of about 150 000 cases every year. Majority people are unaware of catching this disease in health care settings. This infection is known as 'silent killer' since a lot of patients stay undiagnosed and untreated for several years before they contract complications and die. Pakistan Medical Research Council studied hepatitis prevalence from 2007-08 in all the provinces of Pakistan and found that about 13 million Pakistanis suffered from hepatitis B and C [10]. Reuse of syringes was identified as the main reason of infection in Pakistan even though other factors of infection were present [11]. Very limited community based research on Hepatitis viral infections have been done in Pakistan; mostly these are hospital or clinics based published studies that display a variation in the testified prevalence. In general, data proposes that these infections are endemic in Pakistan reporting prevalence statistics in general population, among pregnant women and blood donors [1].

To combat viral hepatitis prevalence and treat the sufferers, certain effective tools are available for which continuous research is essential in order to establish priorities in accomplishing eradication goals. The World Health Organization (WHO) has intended to attain universal abolition of both HBV and HCV infections by 2030. Yet, elimination infers consolidation of current tools i.e. well-organized screening strategies, extensive access to liver infection care and management, and antiviral therapy to eventually terminate the virus [12].

Pakistan is determined to halt the growing infection rate through e.g. vaccination of high risk groups and newborns, use of blood screening for donation, auto-disposable syringes, public education and therapy of indigent patients free of cost; yet due to high infection rate and prevalence, more steps are required to be taken to end the emergent disease [11,13]. Nationally, prevention and treatment of Hepatitis is being executed in our country via provincial hepatitis prevention and control programs and in their absence, Pakistan Health Research Council working under Ministry of National Health Services, Regulation and Coordination, is managing hepatitis response through a 'Technical Advisory Group' at federal and provincial levels. Furthermore, the private segment is also contributing significantly in hepatitis management. A surveillance system of acute viral hepatitis has been established by a Field Epidemiology and Laboratory Testing Program in 5 tertiary-care, public hospitals located in Karachi, Lahore, Peshawar, Quetta, and Islamabad, generating the reports on quarterly basis. WHO and Centers for Disease Control and Prevention are also keenly involved to strengthen national response to hepatitis in Pakistan. On hepatitis C, the National guidelines were established in 2015-2016. Recently, a National Hepatitis Strategic Framework has been established in line with Global Health Sector Strategy for Viral Hepatitis (2016-2021) and WHO Regional Action Plan (2017-2021) with agreement of national and the provincial stakeholders [14].

Discussions

Viral hepatitis causes 1.4 million mortalities annually worldwide which are comparable to HIV, malaria and tuberculosis causing 1.5 million, 1.2 million, and 1.2 million mortalities respectively, every year. Nearly 250 and 130-150 million people get ill due to Hepatitis B and C, respectively [15,16]. Pakistan has a high burden of viral hepatitis; hepatitis A and E resulting in maximum morbidity and hepatitis B, C and D causing maximum mortality [1].

Food Borne Hepatitis A and E

There is a high risk of infection for the developing countries due to oro-fecal, food borne pathogens [2].

Hepatitis A

Poor sanitation and hygienic conditions cause hepatitis A in 90% children in Pakistan before 10 years of age [3-5,17-20]. Previously it was thought to be an acute infection that produced subclinical events in children but now it has been shown as a devastating condition since in a recent study of 2,735 confirmed HAV cases with hepatitis A related liver failure, 36.7% died [21]. Variations have been observed over the last few years in the disease pattern of hepatitis A [20]. Isolation of HAV in fresh vegetables due to irrigation of fields with polluted water has been identified as major source of infection [22]. The disease can be silent in both children and adults. The classical signs and symptoms of hepatitis A are vague abdominal indications, fever, and malaise that not necessarily go together with hepatomegaly or jaundice [23]. In a study of 233 chronic liver disease cases, Hamid *et al* found that 97.8% were exposed to HAV [24]. The variability in the presenting complaints, mainly jaundice absence, it is probable that the exposure rates of acute hepatitis A are reported considerably lower than existing rate [25].

In Pakistan, 50 - 60% acute viral hepatitis A cases are in pediatric population of Pakistan and up to 100% of children tested HAV IgG positive by 14 years of age, indicate the exposure of disease during childhood [26]. Also, 5.4 - 6.1% adults as compared to children have been found acute HAV positive [27]. HAV infection is infrequent in adults but those who are exposed, experience extended convalescence and illness. Hepatitis A virus is very stable that can live for 12 weeks - 10 months in water [1,28,29]. The virus is also quite resistant to chemical or heat inactivation. Due to this reason, there can be recurrent incidence of waterborne and shellfish-transmitted HAV outbreaks [30-32]. Two doses of hepatitis A vaccine are suggested which yield life- long immunity but its use is suggested during epidemics and natural disasters [33].

Hepatitis E

This disease is severe with mortality rate of 0.4 - 4.0% but in last trimester of pregnancy, the mortality rate may extend 20% during epidemics particularly [34]. This infection is endemic but goes into mini epidemics in grave conditions in developing countries [1].

Hepatitis E is endemic in Pakistan which is mostly occurring in summers, floods and rains [1,35]. In Pakistan, it occurred as outbreaks and sporadic cases in conditions that involved huge crowds of people in the areas with contaminated water supply due to poor sanitation and lifestyle [36,37]. There are several case reports describing water exposure as a probable risk factor for HEV infection acquisition [38,39]. In Pakistan, HEV is chief cause of acute viral hepatitis especially in grownups belonging to lower socioeconomic groups. The immunity of hepatitis E lasts for 8-10 years but afterwards the person is susceptible to re-infection. In Nepal, vaccine trial was carried out showing worthy results, but none is available commercially, hence hepatitis E infection prevention requires propagation [1,40]. Various studies have shown variability in reported prevalence of HEV; up to 20 to 22% of adults and 2.4% of children were found acutely infected. In a study, 14 to 26% of apparently healthy children were found to be exposed to hepatitis E (HEV IgG reactive) [41,42]. This infection has produced calamitous effects in pregnancy, causing 20 and 29.3% maternal deaths and perinatal death rate of up to 30.3 per 1,000 live births [43,44]. Once infected during epidemics in pregnancy, recovery is attained but 30% maternal or foetal loss is reported in late trimester [45]. HEV is also a substantial mortality cause in preexisting chronic liver disease patients [46]. There was a nosocomial outbreak of hepatitis E that was attributed to inappropriate sharing of intravenous administration sets between patients in a neurosurgery ward in Karachi; this led to an assumption that this infection may also be parenterally communicated but such similar reports in the literature are a very few [47].

It is vital to have accurate means of detection to facilitate early diagnosis and management for HEV infection due to substantial morbidity and mortality in Pakistan. Nevertheless, limited sensitivity of the serological assay available obstructs early diagnosis and treatment of this infection, specifically during outbreaks [48].

Hepatitis B, C, and D

Hepatitis B and Hepatitis C

Viral Hepatitis B and C infections spread via blood and secretions of body which enter human body via breach in mucosa, vein or skin. Both the viruses are the source of acute hepatitis which are cleared in 80% HBV cases and 20% HCV cases within 6 months. The virus may become chronic progressing to chronic

progressing to chronic liver disease in 20% HBV and 80% HCV cases. There is >90% risk for a new born becoming a long term HBV carrier after infection but the risk falls from in the first 6 months to about 25% by age of 5 years, and to 10% by age of 15 years. It is uncommon in adults (2%- 5%) to become chronic carriers who get infected later in life [1,49].

In the developed countries, primary mode of HCV and HBV infection transmission is injection drug use. The seroprevalence of infection among injection drug users on long term were 85.0% for HCV and 77.4% for HBV in USA and for 1 year or less, it was 64.7% for HCV and 49.8% for HBV [50]. An estimated 8 - 16 million HBV infections, 2-5 million HCV infections and 80,000-160,000 HIV infections worldwide are due to unsafe injection practices and their overuse [51]; Pakistan is found to have highest rate of intramuscular injections per individual per annum [52,53]. Khan *et al* found injections as the main risk factor for Hepatitis C infection in patients in a peri-urban community in Karachi in a cross sectional study [54]. Apart from intravenous drug use, the most common routes of HCV transmission include blood transfusions, haemodialysis, peri-natal infections, tattooing and needle-stick injuries in developed countries. Improper sterilization of invasive medical devices and therapeutic injections from reused syringes and needles is main mode of transmitting blood borne organisms which also includes hepatitis B virus (HBV), HCV and HIV in the developing countries [54].

Six serotypes have been identified in hepatitis C [3-5,34,35,49] among which serotype 3 has been found as most easy to treat worldwide [55]. Serotype 3 is most common in Pakistan; several researches exhibited around 50-70% sustained viral response by interferon therapy when used for 6 months [56-58]. No vaccine is available for HCV prevention; this requires exercise of best clinical practices and standard operating procedures for sterilization and disposal of hospital waste along with regulation against hospitals and blood banks that are non-compliant [1]. World Health Organization compiled statistics that showed 2 to 5% of the Indian subcontinent being affected by hepatitis B while 4 - 5% of the Pakistani population was suffering from hepatitis C which is among the highest infection rates globally [59-61]. Nearly one-third HBV-infected cases in Pakistan were co-infected with hepatitis D virus which is a defective RNA virus that needs HBV for replication [62]. In apparently healthy persons, asymptomatic HBV and HCV can produce unbalanced Liver Function Tests [63]. Yet, in a study of healthy adult males undergoing medical assessment for employment; some had a normal ALT with HBV and HCV infection even in young age [64]. High occurrence of blood borne hepatitis infections were observed in patients upon pre- operative serological testing who went to see doctor for various conditions like cataract and plastic surgery. Therefore, routine screening of all preoperative patients for hepatitis should be done so as to control disease transmission [65,66]. Frequency of hepatitis infection is more common in rural than urban population and more in multiparas than primigravidas [67]. There is risk for pregnant females in Pakistan to contract blood borne infections as they usually develop severe anemia or postpartum hemorrhage, hence requiring blood transfusion, which might be unsafe [68]. The first national survey in Pakistan was conducted in 2007-2008 to assess hepatitis B and C prevalence [69] in which 47,043 individuals were tested; overall prevalence of hepatitis B and hepatitis C was found to be 2.4% and 4.8% respectively. Factors found to be linked with higher risk to attain hepatitis B and C were identified as exposure to therapeutic injections, history of surgeries, hospitalization, blood transfusion, increasing age, etc [69,70].

The patients' record treated for hepatitis B and C in 2 years via Prime Minister Program for the Prevention and Control of Hepatitis Viral Infection was assessed from 12 sites by Qureshi *et al.* [71]. It was revealed that just 3440 (45.4%) patients out of 7572, completed 6 months interferon therapy; available PCR reports of 1686 patients displayed success rate of 67% while non-responders were 33% [11]. The prevalence of viral hepatitis infection also differs due to geographic distribution and different settings. Among individuals who seek dental care, 32.7% were found to have HBV while 66% had HCV [72]. Reports from a tertiary care hospital, revealed around 4.4% spouses of hepatitis C patients with infection [73]. A study conducted in Jamshoro, Sindh showed a very high proportion of HCV affected by hepatitis B and C virus upon evaluation [74]. Various researches have shown difference in HCV infection prevalence among males and females [65,66,75]. This may be due the probability that the males receive health care more often than females in our society and that the males have the greater social freedom especially in rural areas than females [75].

It has been observed that HCV replaced HBV in ensuing years and appeared as the most common cause of liver disease [20,76]. The measures taken at the government level with the support of WHO, CDC etc. are hepatitis B vaccination, hepatitis B and C treatment by prime minister program for hepatitis control, and public awareness campaigns. FELTP (2009-2011) report is the only available surveillance data from our country [77].

Delta Virus

The presence of HBsAg is required by Delta virus for its transmission and existence; co infection ensuing high mortality due to fulminant hepatitis can be due to this virus [1]. In a previously known HBV carrier, super infection occurs due to delta virus exposure leading to chronic liver disease. It was reported that among 408 cases of chronic liver disease due to HBV infection, 44% had delta super infection and 1.4% had co infection [59]. At a public sector hospital in hepatology unit of Karachi, Riaz *et al* studied 531 cases of HDV; most of the cases (68%) were from Northern Sindh, then from Balochistan (17%) [78]. Chronic HBV patients were found with HDV antibody in 1444(16.6%) cases out of 8721cases showing HDV infected persons with some mild liver disease than the non-delta infected HBV persons [62]. The delta viral infection may endure causing a major disease burden in Pakistan due to its substantial pool of positive cases in certain areas of Sindh, Punjab and Baluchistan [59,78-82] and a small coverage of EPI for hepatitis B vaccine [83].

Conclusion

The precise information regarding hepatitis prevalence in our country is required along with the major risk and infection factors to target it specifically through effective healthcare services. Economical technology for testing viral hepatitis is also needed to be used in campaigns in key populace. It is essential to institute regional laboratories in all provinces linked with one central institute for exact estimation of hepatitis burden in our country. The burden of viral hepatitis cannot be reduced if basic amenities together with safe water supply and improved sanitation are not available. A central registry for hepatitis and liver diseases and proper surveillance system for viral hepatitis is highly needed.

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