

Hepatocellular Carcinoma in Pakistan: An Insight into Future

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Letter to the Editor

Hepatocellular Carcinoma (HCC) is one of the most prevalent type of cancer across the world and constitutes around 7% of all cancers. Approximately 750,000 new cases of liver cancer are reported per year globally [1,2]. The incidence of HCC increases with age and is highest in people aged around 70 years [2]. The distribution and onset of HCC varies significantly in different geographical regions of the world, might be due to causative factors and genetic makeup of the inhabitants. Among the risk factors for HCC, Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are well-known and their role is well established. Majority of HCC are viral borne and HBV/HCV are the main culprits behind 80% HCC globally [1]. Infection with HBV and HCV is one of the prominent source of chronic liver infections worldwide. It is estimated that approximately 350 million individuals are HBV and 200 million individuals are HCV carriers globally [3,4].

Although the knowledge about the molecular virology of these viruses is well established, the molecular mechanism from acute infection to HCC development are still not well known. The research data showed that HCC is a typical inflammation-related cancer but the exact mechanism is still not clear. Viral induced liver injury is mainly due to human immune response against viruses and there is no evidence that viral replication plays any role in liver injury directly [5]. T cells are recruited to liver during the acute stage of HBV and HCV infection. These cells are the key players in anti-viral immune response and help for resolution of infection as well as prevents development of chronic infection. However, there are studies supporting the role of these T cells in liver injury during HBV and HCV infection [6,7]. In liver injury the pathological process resulted into hostile environment which leads to survival of intrahepatic stem cells, also known as hepatic progenitor cells (in humans) rather than the regenerated hepatocytes. Abnormal dedifferentiation of hepatic progenitor cells during HBV/HCV infection under the influence of immune cells and certain cytokines, may lead to the tumorigenesis of human hepatocellular carcinoma [8,9].

Pakistan is a country with very high burden of viral hepatitis. Available data showed that there are around nine million HBV [10] and 11 million HCV carriers in Pakistan [11,12]. It is difficult to study the natural history of these diseases. The asymptomatic infection, difficulty to ascertain exact time of infection onset, data collection from general population, different risk groups and persons with multiple risk factors make it more difficult to generalize the natural history of the disease to whole country or whole population. However, it can be estimated that around 5% to 10% of chronic virally infected individuals develop HCC [13]. In recent years HBV infection goes down probably due to massive vaccination campaign by Government but the burden of HCV is on raise. Although the country is endemic for these infections but data regarding the prevalence of HBV and HCV in general population is very low [14]. The major transmission factors in Pakistan are unsafe blood transmission, injection drug usage, unsafe medical and dental procedures, treatment by quacks, barber's shops, unsafe sex practices and lack of education in general community [15-17]. Pakistan is a country with more than 200 million inhabitants. A recent review article summarized the previous data regarding the HCV epidemiology and concluded that there are only 32 studies analyzing the HCV prevalence

in Pakistan. In total only 111,926 individuals were examined in these 32 reports and mean prevalence of HCV was 5.7% (95% CI: 5.1-6.3) [18]. There is no proper estimation of HCC burden in the country due to unavailability of well managed surveillance system. However, the available data showed that prevalence of HCC in cirrhotic patients ranges from 3.7% to 16.7%. As already discussed that vaccine availability against HBV leads to reduce HBV infection, accordingly the prevalence of HBV in HCC patients is lower in recent era. Data published up to 1997 regarding the prevalence of HBV and HCV in HCC cases was 50% to 60% HBV and 10% to 25% HCV. Due to proper HBV vaccination of new born and adults a paradigm shift from HBV to HCV infection was noted after 1998. Studies published after 2000 from different regions of Pakistan showed that 50% to 80% HCC cases were HCV positive while only 20% to 30% HCC individuals were HBV positive [18]. A hospital based study in 2002 showed that 7% of hospital deaths were due to liver diseases like viral hepatitis, liver cancer and chronic liver disease [19]. Due to 50% to 85% chronicity ratio of HBV and HCV the number of chronic infection raises with time and leads to deaths ultimately. Accordingly, a study in 2008 consisting of nine-year data from a tertiary care hospital showed that 17% to 22% deaths were due to liver disease caused by HBV and HCV infections [20]. Studies needs to be done on each hospital of the country to have an idea about the actual danger caused by HBV and HCV infection.

There is need of a proper HBV and HCV surveillance system in Pakistan. By having a well-equipped management system, the hot spot of infections can be identified and it is easy for Government to design disease management policies. Prevention and treatment are the two basic ways of disease management. Prevention should be the priority; goals can be achieved by proper educating the health care providers and general population. All medical and dental procedures should follow the WHO guidelines. Treatment of the disease is costly and put a huge burden on the economy of the country. However, if the treatment is not given on time, the patient will develop HCC which has very poor prognosis, with only 12% survival at 5 years [21]. Liver transplant is the last option for HCC patients but for a country like Pakistan where per capita income is very low and no social medical insurance system; it is not feasible. The Government has taken certain initiatives regarding the treatment of HCV. Sofosbuvir is introduced in Pakistan on huge discount and it has shown a very good sustained virological response. The Government should take massive actions for the treatment of maximum patients. By providing the preventive measures and treating the infected individuals at acute or even chronic stage will be of great help to reduce the HCC burden in the future.

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