EDITORIAL

Elimination of Hepatitis B: A Dream or Reality !

After its inception in medical knowledge in 1965, in the name of so called Australian antigen, Hepatitis B, during the last half century, plagued not only the Gastroenterologists or Hepatologists but also attained such a height of importance that, it became a matter of great concern for all medical professionals and general population because of its associated potentially relentless progressive nature which may lead to disabling morbidity and mortality[1].

This heralded an era of scientific endeavor for hepatitis B virus (HBV) research which successfully characterized this member of Hepandaviridae family and its multiple genotypes along with their geographic distribution throughout the globe. Researches also could uncover its different parenteral and mucosal routes of transmission and immunotolernt, immuo-reactive, low replicating stage and reactive phases of pathophysiology and their respective clinical significance. Tools for diagnosis and surveillance, medications, though not yet for cure but for suppression to non-injurious level (virtual cure) are available. Above all, effective vaccine against this virus is invented; even then, this infection could not be eliminated; nor even be reduced to a reasonably satisfactory level.

This is blamed to be due to widely variable global prevalence of Hepatitis B in countries, unequal economic and infrastructural facilities to address the problem; cost with variable effectively and availability and compliance of drugs are considered to be responsible. Ineffective and not totally scientific use of vaccination of WHO program [2, 3] are responsible for being unable to prevent acquisition of new infection both in adults and children.

Universal practice of antiseptic measures in all medical-surgical procedures, screening of blood and its products before transfusion, safe sexual practice especially with unknown partners and development of consciousness against practice of intravenous and other drug uses through different media have been proved effective in reducing horizontal transmission from 33% -10%[4].

During the last two decades, seven drugs: two formulations of interferon (IFN): conventional and pegylated (PegIFN) and five nucleos(t)ide analogues (NUCs): lamivudine, telbivudine, entecavir, adefovir, and tenofovir, have been approved for the treatment of hepatitis B. One year treatment with PegIFN in HBeAg-positive patients resulted in 29% to 32% HBeAg seroconversion and 3% to 7% HBsAg loss 24 weeks after completion of treatment[5]. Durable HBeAg loss in 81% of patients and 30% HBsAg loss was found after 3.5 years of completion of medications. Treatment with PegIFN in HBeAg-negative patients, also showed normalization of ALT level, reduction of HBV-DNA bellow <10,000IU/ml in 25% cases durng 1-year and HBsAg loss in 9% cases during 3 year follow up. These drugs are proven effective to suppress HBV replication, normalize aminotransferase (ALT) and also to reduce hepatic inflammation. Their use also have been reported to have reduced the extent of hepatic fibrosis and reversion of cirrhosis.

Orally administered anti-viral NUCs, though need to be continued almost for whole life, became the mainstay of treatment for Hepatitis B because of their potent antiviral activity, minimum side effects and strong barrier to resistance especially with the newer generations entacavir(1.2%) and tenofovir(0%)[5]. Continued treatment with entecavir or tenofovir for up to 5 years resulted in undetectable serum HBV DNA levels in 94% to 98% of patients, HBeAg seroconversion in 40% to 41%, and HBsAg loss in 3% to10% and in 74% cases fibrosis and cirrhosis were reported to have reversed [6,7].

The final goal of treatment of CHB is eradication of HBV to prevent further hepatic damage and regeneration of liver tissues. But because of persistence inhabitance of ccc-DNA of HBV in the hepatocytes after acquisition of chronic stage of infection, it enjoys a safe shelter from being attacked by all currently available anti-HBV drugs. So, presently eradication of DNA is not a realistic goal and HBsAg loss is considered 'functional cure' as it is associated with normal ALT, negative HBeAg and

DNA level <2000IU/ml. This is achieved only in a few percent of cases. A multi-prong approach with antiviral drugs targeting different steps of HBV replication cycle including eradication or silencing cccDNA combined with immunotherapy to restore immune responsiveness to HBV will be needed for patient to remain in a state of "functional cure".

Vaccination, like many other diseases, in susceptible individual against HBV is superior to treatment and interrupting the routes of transmission, as a strategy to fight HBV[8]. Because targeted populations at risk of HBV infection were not easy to access, the approach with universal vaccination to all newborns was considered cost-effective strategy [9–11], so the WHO recommended and adopted the Hepatitis B vaccine to incorporate into Expanded Program on Immunization (EPI) and as of 2012, 183 of the 193 of its member countries already have initiated it. In the face of heavy HBV burden, Taiwan launched a National Hepatitis B vaccination program in 1984. The 30-year experience of this program is an invaluable reference for the rest of the world [12]. Ninety percent reduction of HBsAg carriage among the vaccinated cohort, 32% diminution of fulminant hepatitis in infants, and almost none over one year child were notable observation, acute hepatitis due to HBV were also decreased [13]. Eighty percent HCC and >90% of its related death were declined among Taiwanese younger than 30 years of age [14]. Similar results were reported from Singapore, China, Thailand, Korea, Japan, and Alaska. It is to be noted that, in spite of universal HBV immunization, infants born to HBeAg positive carrier mothers with a viral loads of >7$\log_{10}$ and >9$\log_{10}$ may acquire HBV in 10% and 30% cases respectively.

A number of successful measures against Hepatitis B, including universal practice of antisepsis, development of effective drugs to treat chronic cases and incorporation of HBV vaccine in 94 percent countries have been taken, even then elimination of this virus is still in a critical juncture to the medic science and clinical practice. This is because, three-quarters of the affected people do not know they are infected[15]; screening uptake and diagnosis rates are low. Treatment uptake, compliance to drugs and follow up to monitor progress are low which result sub-optimal cure and burgeoning liver cancer[16]. So the challenge is to develop and implement actions plan to reduce this gap at every level in all countries.

Though most Hepatitis B infected individuals have indolent clinical character for many years, they have lifetime potentially to develop cirrhosis in 13-40 percent of cases with an annual rate of 1.2 percent. A good number of them progress to Hepatocellular carcinoma. So early diagnosis of this virally infected individual with appropriate tools of investigation, closed surveillance and put them on effective antiviral drugs with regular monitoring to see the response and complications of medicine have been strongly emphasized. In this regard, WHO have advocated developing a national plan with the involvement of people from all sectors of the community including representatives from affected groups, different media, NGOs and philanthropists; government and healthcare provider are to play role as stakeholders. Seventeen countries have already adopted this into action and are getting benefits as per[17]. Immunization through universal vaccinations will have to be more meticulous along with inclusion of a monovalent birth dose ([18]) and vaccination of vulnerable adults especially in HBV endemic countries.

With ensured all above mentioned groups and facilities to work together, a world free from Hepatitis B is not a dream but a practicability.

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