Indian J Med Res 136, July 2012, pp 3-6

Editorial

This is hepatitis - it is closer than you think

Viral hepatitis constitutes an enormous health burden, and is a major cause of morbidity and mortality globally. The magnitude of the problem can be highlighted by the fact that 1 in 12 people globally are living with chronic infections of either hepatitis B virus (HBV) or hepatitis C virus (HCV). Both HBV and HCV can cause chronic infection, imposing increased long-term health risk to the carriers themselves, and representing a significant reservoir of infection to non-infected persons. Unfortunately, awareness of these two diseases remains low even in endemic regions, and as a result, many persons at risk are not being tested, and those not infected do not have an effective strategy to avoid infection.

Hepatitis B virus

An estimated 2 billion people worldwide have been infected with the HBV, with an estimated 400 million people being chronically infected (*i.e.* 6% of the entire human population)[1]. Up to 40 per cent of those with chronic hepatitis B (CHB) will develop complications, including liver cirrhosis, decompensated liver disease, and hepatocellular carcinoma (HCC)[2]. This amounts to a high mortality rate of around 1 million people per year. HBV infection is highly endemic in many parts of the Asia-Pacific region, including China, where the prevalence rate ranges from 8 to 20 per cent. Other parts of Asia such as India have an intermediate endemicity, with a prevalence rate of 2 to 7 per cent. Since these two countries are the most populous in the world, this equates to the highest absolute numbers of HBV carriers observed, with approximately 100 million in China and 43 million in India[3,4].

In addition to the high prevalence of established infections, some 4.5 million new HBV infections occur each year worldwide. In areas where there is intermediate to high endemicity, the major routes of transmission are vertical maternal-foetal and early horizontal childhood transmission. Therefore, it seems only logical that the most effective method of preventing transmission of HBV is through the implementation of universal vaccination programmes directed at newborns and infants. As early as 1992, the World Health Organization (WHO) endorsed a recommendation that aimed for all countries to have universal childhood HBV vaccination by 1997. In fact, Taiwan had already launched a mass immunization programme back in 1984, resulting in a significant reduction of HCC in children and young adults more than a decade later[5,6]. Even though the vaccine has been available now for 3 decades, there are significant numbers of persons who have not been immunized. In a 2007 report by the WHO, 35 per cent of infants worldwide have not completed a course of HBV vaccine, with the lowest coverage rate occurring in South-East Asia[7]. There are many factors accounting for the low uptake of a mass vaccination programme. These include the lack of public education, poor public health infrastructure, and the huge economic burden. All these barriers must be overcome before universal vaccination against HBV can be implemented.

Even with universal vaccination, the expected decline in prevalence is delayed due to the high rate of existing chronic carriers. The majority of people with CHB are asymptomatic, therefore, these people are not aware of their carriage of infection. Although complete eradication of the HBV is not yet possible, there are many effective antiviral therapies which can effectively reduce inflammation, prevent disease progression, reverse liver fibrosis, and reduce the rate

This editorial is published on the occasion of World Hepatitis Day- July 28, 2012.

of HCC[8]. However, treatment is only effective if the people who are eligible for treatment are identified. Unfortunately, we are still seeing a significant number of people with CHB presenting with decompensated cirrhosis or HCC who have never known of their HBV carriage status. The importance of HBV screening should not be undermined, especially in areas of intermediate to high prevalence rates. Not only does screening identify persons who may be HBV carriers, but equally important is to identify non-carriers so that they may be vaccinated.

The Centers for Disease Control (CDC) updated guidelines in 2008 recommends routine HBV screening to all persons born in regions where HBV prevalence is intermediate (2-8%) or high (>8%)[9]. Screening for HBV infection can be initiated by testing for the presence of hepatitis B surface antigen (HBsAg). As with all screening programmes, counselling and referral for clinical evaluation should be available to all participants. If the person is found to be HBsAg positive, formal medical consultation is required to determine the activity of CHB disease and to assess the need for antiviral therapy, and to commence screening and surveillance for HCC. Family members of persons tested positive for HBsAg should also be screened for HBV infection. In HBsAg negative persons, the antibody to HBsAg (anti-HBs) should be tested to determine whether vaccination is required. Despite the availability of a screening programme, uptake is generally low. The barriers to screening are largely related to individuals, providers, and the healthcare system. The individual needs to be aware that they are at risk, that the disease can have serious long-term outcomes, and that effective treatments are available. Therefore, education and providing information to the public is of paramount importance. In fact, one of the key deficits is the lack of knowledge about transmission of HBV and its sequelae. Unfortunately, for those with low socio-economic and educational background where HBV prevalence is high, the rates of HBV screening are also the lowest. Other barriers include cultural beliefs, and the social stigma and costs associated with a positive test result. One must remember that the barriers created by the lack of knowledge is not only restricted to the at-risk individuals, but also to health care providers. They need to understand that screening is cost-effective and effective treatment is available.

Over the past decade, antiviral therapy for HBV infection has improved dramatically, and agents such as tenofovir and entecavir are highly potent drugs with minimal risk of resistance. Unfortunately, the cost of therapy may be prohibitive for the vast majority living in low socio-economic regions, especially as most will require long-term therapy. The changes required to increase accessibility to treatment needs to be made at the level of policy makers, and it is important to incorporate these treatments as an essential component in their drug formulary.

Hepatitis C virus

HCV is a RNA virus that was first discovered in 1989. An estimated 170 million people worldwide have chronic HCV infection, affecting 2-3 per cent of the world population[10]. Despite the low prevalence rate of HCV infection in Asia, the sheer population of China and India means that China alone has more HCV infection than all of Europe or America, with an estimated 13 million carriers. India has an estimated 9.5 million carriers. Most countries have a prevalence rate of 1-2 per cent, although countries such as Taiwan and Pakistan appear to have a higher rate of 4-5 per cent[11]. There are also significant regional differences within each country, which reflect the underlying risk factor for HCV transmission.

Prior to the 1980s, the most common source of HCV transmission in developed countries was either through intravenous drug use or transfusions of contaminated blood products. The latter has virtually been eliminated by the introduction of routine testing on donated blood, although it remains problematic in developing countries where professional blood donation is still practiced. Intravenous drug use has now become the most common route of transmission in the developed world, and an increasing source in the developing nations. In developing regions, nosocomial transmission through the use of inadequately sterilized needles and syringes is also problematic, accounting for 2.3 to 4.7 million new infections each year[12,13]. This is exemplified by the high prevalence of HCV infection observed in Egypt which occurred as a result of the use of unsterilized needles and syringes during their mass programme for treating schistosomiasis[14]. In contrast to HBV, sexual transmission of HCV occurs infrequently, and the risk of perinatal transmission is low[15].

There is currently no effective vaccine available to prevent HCV transmission. Therefore, it is prudent to identify the risks associated with transmission and to modify these factors, as transmission is preventable. Reducing or preventing illicit intravenous drug usage, and increasing access to sterile injecting equipment will

decrease the greatest risk factor currently. In addition, at-risk groups should be screened for HCV carriage, which can be performed by testing for antibody to HCV (anti-HCV) and confirmed by determining whether HCV RNA is present.

Similar to HBV, HCV also leads to chronic infection, with the similar complications. An estimated 70 per cent of individuals exposed to HCV will become chronic carriers, of whom around 25 per cent will progress to the development of cirrhosis. Once cirrhosis is established, the annual rate of decompensation and HCC development is estimated to be about 4 per cent and 1.5-2.5 per cent, respectively[16]. HCV can effectively be cured with antiviral therapy, which currently consists of pegylated interferon α-2a/2b combined with ribavirin. Recently, new oral direct antiviral agents including boceprevir and telaprevir have been approved for HCV treatment, and in the near future, combination oral therapy without the need for IFN injection is likely to become a reality[17]. After completion of treatment, a sustained virological response (SVR) is defined as a negative HCV RNA after 6 months from cessation of therapy, which essentially means that the HCV is eradicated. The SVR rate ranges between 50-80 per cent depending on the viral genotype, which in turn is dependent on the geographic region[18]. Despite effective antiviral treatment being available, the uptake of treatment is low even in developed countries. The reasons for this are plentiful, including access to therapy, lack of public awareness, and the side-effects associated with anti-HCV therapy. The high cost of interferon-based therapy also means that treatment is unaffordable to the majority of people who reside in low and middle income countries. As the patents for interferon do not run out until at least 2015, generic compounds are currently not available.

Where we are

In 2012, at least 20 years after the discovery of HCV, and almost 40 years after the discovery of HBV, we have acquired insurmountable knowledge regarding these two infections, including the epidemiology, natural history, and treatment. We are also aware of the current endemic status of viral hepatitis, and the impact it has on both the individuals and collectively as a country. Therefore, it seems inexcusable, if not unforgiveable, that the path of inactivity is being taken. For many individuals, chronic hepatitis is a disease that affects other people, but the fact remains that everybody will know someone afflicted. And that is not even considering the notion that the majority have not been screened. The WHO guidelines on screening, published in 1968, remain relevant today for chronic viral hepatitis screening[19]. We have discussed previously the values and importance of screening and preventative strategies. However, for either to be successful, barriers must be overcome at three main levels – the at-risk individuals, the health care providers, and the infrastructure and government policies which make it possible. Increasing awareness and fostering education at these levels are essential, both at regional and global levels. At the World Health Assembly meeting in 2010, it was resolved that 28th July should be designated as World Hepatitis Day, a real opportunity to increase awareness and drive positive changes towards disease prevention and access to screening and treatment. Global organizations including the World Hepatitis Alliance (*http://www.worldhepatitisalliance.org*) and the Coalition to Eradicate Viral Hepatitis in Asian Pacific (CEVHAP *http://www.cevhap.org*) serves as important advocacy groups for people living with chronic viral hepatitis and as groups advocating for public policy reforms that strive to reduce the burden of viral hepatitis in the Asia-Pacific region. With all the knowledge we have accumulated, now is the time to make a difference.

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