Preventing Mother-to-child Transmission of Hepatitis B Virus - A Success Story Which Can Be Enhanced

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In this issue of the Medical Journal of Malaysia, Ng et al report on the HBsAg prevalence rates of new students enrolled for undergraduate and postgraduate studies in the faculties of Medicine and Dentistry of University of Malaya, during the period from 2005 to 2011 [1]. On the whole, the HBsAg prevalence rate was 0.62% (18/ 2923 students) but the rate was lower at 0.20% (3/1533) for those born in or after 1989 (the year of implementation of hepatitis B universal immunization for newborns) compared to 1.08% (15/1390) for those born prior to 1989. The HBsAg prevalence rates also showed a declining trend from the beginning in 2005 till the end of study period.

As what the authors concluded, the hepatitis B virus (HBV) immunization programme is effective and after 22 years it is showing encouraging results. For this study cohort, our achievement is also in line with the WHO Western Pacific Region goal of achieving a seroprevalence of HBsAg of less than 2% by 2012 [2].

Worldwide, an estimated two billion people have been infected with HBV and there are an estimated 600,000 deaths annually from the complications of chronic hepatitis B (CHB)[3]. Although great strides had been made to treat CHB since its discovery in 1967, the fact remains that the chances for a cure of the disease is minimal in the majority of cases who acquired the infection perinatally.

Prevention from HBV infection is therefore of utmost importance in our battle against this infectious disease. Vaccine against the HBV has been available since 1982 and it is the first vaccine against a major human cancer, the hepatocellular carcinoma. HBV is a carcinogen partly due to the intergration of HBV DNA into human chromosome resulting in mutations, chromosomal instability and also the activation of the viral HBx regulatory protein[4]. Hepatocellular carcinoma is one of the top ten cancers afflicting Malaysians and in our experience the majority of them are related to HBV infection.

The current available evidence shows that HBV immunizations confer protection for at least two decades and a meta-analysis of 34 cohorts involving 9356 subjects found the cumulative incidence of HBV breakthrough infection after 5-20 years of primary vaccination was 0.7% with a range from 0 to 9.4% [5]. Similarly HBV vaccination has also been shown to decrease the occurrence of hepatocellular carcinoma [6].

Human beings are the reservoirs for the HBV and transmission is through cutaneous and mucosal exposure to infected blood and other body fluids, mainly semen and vaginal fluids. In our region perinatal or early childhood transmission is the most common mode of transmission [7]. The approach to eliminate HBV transmission has aptly started by universal HBV immunization of newborns to interrupt the most common mode of acquiring infection at the perinatal and during early childhood. Despite this, the interruption of HBV transmission is incomplete as shown in this study which reported a possible breakthrough HBV infection of 0.35% (6/1533) with at least half of these resulting in CHB as evident by the presence of HBsAg.

Failure in the HBV immunization for newborns can be due to various factors, some possible factors are mothers with HBsAg positivity, mothers with high viral loads or positive for HBeAg and failure of adherence to the vaccine schedules.

The third dose coverage of our Hepatitis B immunization has been good and in 2011 it was 97.14% [8]. Therefore to enhance vaccine responsiveness of the HBV immunization programme, other strategies focusing on the factors associated with high risk of perinatal transmission can be employed.

Adding passive immunization with hepatitis B immunoglobulin to the active immunization of newborns of HBsAg-positive mothers had been shown to reduce HBV occurrence. Compared with HBV vaccine alone, HBV vaccine plus hepatitis B immunoglobulin reduced hepatitis B occurrence (RR 0.54, 95% CI 0.41 to 0.73) [9].

Other studies have also shown that anti-viral therapy administered in late pregnancy may further reduce the risk of perinatal HBV infection from highly viremic mothers, as compared with passive and active immunization alone. In a meta-analysis on adding lamivudine to the passive-active HBV immunoprophylaxis, the lamivudine group had a 10.7–23.7% lower incidence of intrauterine infection, indicated by newborn HBsAg (OR=0.38, 95% CI 0.15–0.94, p=0.04) and HBV DNA (OR=0.22, 95% CI 0.12–0.40, P<0.001) seropositivity, and a 12.7–33.2% lower mother-to child

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transmission rate at 9–12 months, indicated by infant HBsAg (OR=0.31, 95% CI 0.15–0.63, P<0.01) and HBV DNA (OR=0.20, 95% CI 0.10–0.39, P<0.001) seropositivity[10]. Similarly a study using telbivudine on top of the passive-active HBV immunization, the incidence of perinatal transmission was lower in the infants born to the telbivudine-treated mothers than to the controls (0% vs. 8%; p=0.002)[11]. Data on the newest anti-viral agent, tenofovir also showed a decrease in mother-to child HBV transmission[12]. The Asia Pacific consensus statement on the management of chronic hepatitis B in 2012 recommended anti-viral therapy with telbivudine or tenofovir in the third trimester for the prevention of mother-to-child transmission in the setting of high maternal HBVDNA levels above 2 x 106 iu/ml[13].

A recent study from Taiwan on more than 2000 children born to HBsAg-positive mothers, it was found that children born to HBeAg-positive mothers to have a higher prevalence of HBsAg positivity compared to HBeAg-negative mothers (9.26% versus 0.23%, P< 0.001). To enhance the control of mother-to-infant transmission of HBV, the authors suggested using HBeAg in addition to HBsAg to screen mothers[14].

Another finding from this study is that 66.14% of the students have anti-HBs below 10 mIU/ml. Waning levels of anti-HBs in HBV immunized individuals have been reported as they enter adulthood. However, a study from Thailand showed that breakthrough HBV infection during the second decade post immunization, did not result in established CHB[15]. The 25th year survey on more than 3000 individuals less than 30 years old in Taiwan which adopted a nationwide HBV immunization for infants in 1984, showed efficacy in young adults[16]. At present booster vaccine dose is not recommended provided there were adequate sero-protection post immunization as these individuals are expected to mount an anamnestic response when exposed to HBV infection[7]. However it remains to be confirmed if the anamnestic response from HBV immunization will continue to protect against HBV infection beyond the first two and a half decades. On the other hand we do know HBV infection beyond the early childhood has better outcome and is associated with much lower risk of chronicity[7].

Will we ever eradicate Hepatitis B like small pox? Well the results from this study seem to suggest that this is possible. Enhancing the prevention of HBV transmission from maternal-to-child together with efforts to identify and treat existing CHB and prevention of transmission by other modes may make this goal achievable.

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