HIGH RATE OF HEPATITIS B VIRUS MOTHER-TO-CHILD TRANSMISSION IN LAO PEOPLE'S DEMOCRATIC REPUBLIC

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Abstract. Hepatitis B virus infection is endemic in Lao People's Democratic Republic (PDR). Among 3,000 pregnant women attending an antenatal clinic at Mother and Child Hospital in Vientiane, Lao PDR, 5.8% were HBsAg positive by a rapid test. Among serum samples of 47 infants aged 9-12 months born to HBsAg-positive mothers, 38% were anti-HBs negative. Percent anti-HBs negative children is significantly higher in those born to HBeAg positive mothers than in those born to HBeAg negative mothers (60% *vs* 25%, $p < 0.05$). Out of 47 HBsAg-positive mothers, 10 had infants who were HBsAg positive. None of the infants born to HBeAg negative mothers became HBsAg positive but 10/19 (52.6%) of infants born to HBeAg positive mothers became HBsAg positive. This high rate of mother-to-child transmission of HBV in an endemic country is of concern and indicates that routine vaccination program for Lao infants needs strengthening.

Keywords: hepatitis B virus, HBsAg, pregnant woman, mother-to-child transmission, Lao PDR

INTRODUCTION

More than a third of the world's population have been infected with hepatitis B virus (HBV) at some point during their life and half of the estimated 350 million chronic carriers worldwide live in Asia-Pacific region. Up to 40% of these individuals will die of liver-related complications or progress to hepatocellular carcinoma (Lavanchy, 2004).

Mother-to-child transmission (MTCT) is estimated to account for half of chronic HBV infection worldwide (Thio *et al*, 2015). The main routes of MTCT are through intrauterine transmission, during breast-feeding or other early mother-infant contacts. Without preventative interventions, approximately 40% of infants born to hepatitis B surface anti-

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gen (HBsAg)-positive mothers become chronically infected with HBV. This risk increases to 70-90% in those born to HBsAg and hepatitis E antigen (HBeAg) double-positive mothers. Infants infected at birth have a 90% risk of developing chronic infection. This rate is reduced to 30% if infected between the ages of 1 and 5 years old and to 5-10% if infected after the age of 5 years old (Thio *et al*, 2015). The risk of infants to become chronically infected can be reduced by a combined early postnatal hepatitis B immunoglobulin (HBIg) treatment and HBV vaccination, but approximately 5-10% of these infants will still become chronically infected (Pan *et al*, 2012; Zhang *et al*, 2014). In many countries, an absence of widely available HBIg means that vaccination shortly after birth is the mainstay of HBV prevention and reduction in chronic disease.

HBV is endemic in Lao People's Democratic Republic (PDR) where approximately 50% of adults have been exposed to the virus, with a chronic infection rate of up to 10% (Jutavijittum *et al*, 2007; Black *et al*, 2014; Jutavijittum *et al*, 2014). MTCT is believed to be a major route of infection in the country, and, whenever possible, pregnant women are tested upon their first visit to the hospital. Infants receive HBV vaccine shortly after birth and at 6, 10 and 14 weeks of age. The aim of this study was to determine the rate of seroconversion and MTCT among infants born to HBsAg-positive mothers in Lao PDR.

MATERIALS AND METHODS

Study participants

During 2008 and 2009, 3,000 pregnant women attending the antenatal clinic, Mother and Child Hospital, Vientiane, Lao PDR were recruited. All participating mothers were informed of the aims of the study and signed consent forms prior to enrolment. The study was approved by the Lao National Ethics Committee (no. 179) and the Research Ethics Committee, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand (no. 324/2010).

Assays

Presence of serum HBsAg was tested initially using Onsite HBsAg Rapid Test (CTK Biotech, San Diego, CA) and retested employing both ELISA (EIA; BioChain Institute, Inc, Newark, CA) and automated ARCHITECT® HBsAg assay (Abbott Japan, Chiba, Japan). Infant serum HBsAg was tested using BioChain test kit. HBeAg and anti-HBe antibodies were determined using EIA kits (IMMUNIS HBeAg/Ab EIA, Institute of Immunology Co, Ltd, Tokyo, Japan).

RESULTS

The 3,000 mothers enrolled in the study were aged between 15-49 years old (mean 26.1 ± 4.9 years). Onsite HBsAg Rapid Test was positive in 174 (5.8%) women, mean age of 26.6 ± 4.8 years, and out of 172 available HBsAg-positive serum samples, one was negative when retested using EIA and ARCHITECT assays, indicating 0.5% false positive results of the rapid test. Of the 171 samples 73 (43%) and 86 (50%) were positive for HBeAg and anti-HBe antibodies, respectively.

Serum was available from 47 infants, 9-12 months of age born to HBsAg-positive mothers who returned to the hospital for measles vaccination. Ten (21%) infants were HBsAg-positive, all born to HBeAg-positive mothers [10/19 (53%)] (Table 1).Eighteen (38%) infants were anti-HBs negative, with percent born to HBeAg-positive mothers being higher than to HBeAg-negative mothers (58% (11/19) and 25.0% (7/28), respectively, $p < 0.05$).

Table 1
Seroprofile of infants aged 9-12 months born to HBsAg-positive mothers, Vientiane, Lao PDR, 2008-2009.

Infant seroprofile	HBeAg-positive mother	HBeAg-negative mother
	n (%)	*n* (%)
HBsAg+/anti-HBs-	10 (53)	0 (0)
HBsAg-/anti-HBs+	8 (42)	21 (75)
HBsAg-/anti-HBs-	1 (5)	7 (25)
Total	19 (100)	28 (100)

DISCUSSION

In this study, we found 5.8% of pregnant mothers attending an antenatal clinic in Vientiane, Lao PDR were positive for HBsAg, a prevalence similar to previous studies in female Lao blood donors and mothers (Jutavijittum *et al*, 2007; Black *et al*, 2014; Jutavijittum *et al*, 2014). The low percent anti-HBs antibodies in infants that we observe at a time where they should have had received 4 doses of HBV-containing vaccines, indicates that the infants had remained unprotected against HBV infection transmitted from their mother during infancy or by other routes later in life. Indeed, 21% were HBsAg-positive, all born to HBsAg- and HBeAg-positive mothers. This represents a MTCT rate of 53% in infants born to HBeAg positive mothers. This rate is substantially higher than the 16.9% of fully vaccinated infants born to HBeAg-positive mothers in a recent study in China, which showed that an additional administration of HBIg to infants reduces this rate to 7.9% (Zhang *et al*, 2014).

Although mothers who were HBeAg positive had high rates of MTCT, it is not known whether this was an independent risk factor or whether it reflected the high level of viremia, which is associated with HBeAg positivity (Xu *et al*, 2002; Zou *et al*, 2012). Another risk factor for MTCT includes vaginal delivery (Guo *et al*, 2013). These risk factors were not addressed in the current study.

It also remains unclear whether particular genotypes of HBV had higher propensities to result in MTCT. One study in Japan (Inui *et al*, 2007) and another in China (Ding *et al*, 2013) found an association between maternal infection with genotype C virus and MTCT, whilst other studies in China and Canada found no such association (Liu *et al*, 2009; Singh *et al*, 2011). In Lao PDR, C and B genotypes are most common, with a high proportion of mixed infections (Olinger *et al*, 2008; Andernach *et al*, 2012). The possibility of such profiles impacting on MTCT rate warrants further investigation.

The 3-dose HBV vaccine was introduced into Lao PDR national vaccination schedule in 2002 and was improved with the addition of a dose at birth in 2004. A target of 65% is set for the immunization coverage for HBV birth-dose and 80% for the third dose of HBV. However, vaccination coverage remains inadequate in Lao PDR, with only 28% receiving the birth-dose in 2011-2012 and only 78%

of children less than 1 year old received the DTP-HepB-Hib vaccinations in 2011 (MOH, 2011; *ibid*, 2012). HBIg is rarely available and thus vaccination remains the basic means of MTCT prevention.

A limitation to this study is that vaccination history was not recorded and we are therefore not sure whether the infants had been fully vaccinated against HBV. Nevertheless, the relatively high rate of MTCT of HBV identified in this study, even in a central hospital, is a major challenge to the fulfilment of WHO goal of reducing HBsAg prevalence in Lao PDR to 1% in children over the age of 5 years by the year 2017 (WHO WPRO, 2013).

ACKNOWLEDGEMENTS

The authors gratefully acknowledge financial support from the Faculty of Medicine, Chiang Mai University and the Faculty of Medicine, Kagawa University. We thank Ms Praijitr Tanan, Blood Bank of Maharaj Nakhon Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University for her excellent technical assistance, and Professor Claude Muller and Dr Antony Black for their comments and suggestions.

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