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Original Article

# Influence of Hepatitis B immunization to prevent vertical transmission of Hep-B virus in infants born from Hep-B positive mother

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## Abstract

***Background*** Hepatitis B is one of the most common infectious diseases worldwide. Indonesia has moderate-high endemicity for hepatitis B infection. Perinatal transmission increases the risk for chronic hepatitis B. Infants from HBsAg-positive mothers should receive hepatitis B immunoglobulin (HBIG) and vaccination within 12 hours of birth, but this practice is not routinely done in Indonesia due to financial constraints.

***Objectives*** To determine the influence of Hep-B immunization on preventing Hepatitis B vertical transmission.

***Methods*** A descriptive cohort study was conducted from May 2009 – January 2010. Subjects were term infants born from HBsAg-positive mothers with no history of HBIG administration. They had received complete hepatitis B immunization and 1 month after the last dose were evaluated for HBsAg and anti-HBs. Cord blood was also taken during labor to measure HBsAg.

***Results*** There were 22 infants born from HBsAg-positive mother who met the inclusion criteria. HBsAg was positive in 6 of 22 cord blood specimens. There were 15 infants who completed this study. One of 15 infants had positive HBsAg after completed hepatitis B immunization and 12 of 15 infants had protective level of anti-HBs. Effectiveness of hepatitis B immunization to prevent vertical transmission in this study was 70-90%.

***Conclusion*** Hepatitis B immunization can prevent vertical transmission of hepatitis B in infants born to mothers who are HBsAg-positive even without administration of HBIG. **[Paediatr Indones. 2010;50:321-5]**.

***Keywords:*** *vertical transmission, HBsAg-positive mother, hepatitis B immunization*

Hepatitis B (Hep-B) is one of the most common infectious diseases worldwide.[1-3] Most of infant and children are usually infected during perinatal period or through vertical transmission from infected mother and remaining closed contact with infected households.[4-6] Vertical transmission is very important in infants because the infection is mostly asymptomatic but had greater risk of having chronic liver disease compared to those infected in adolescence or adulthood.[1-6] Newborns from HBsAg-positive mothers should receive HBIG within 12 hours after birth, together with Hep-B immunization (birth-dose).[4,7,8] Birth-dose Hep-B could prevent perinatal transmission as high as 80-95%.[9-15] The main purpose of giving the first Hep-B immunization soon after birth is to prevent Hep-B infection in exposure babies and considered as a prophylaxis therapy after exposure. Efficacy of Hep-B immunization in preventing perinatal transmission will decrease if interval of the birth dose is extended, so

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WHO recommend the first dose to be given within 24 hours after birth.[7,15]

In most developing countries like Indonesia, screening test for Hep-B in pregnant women is not routinely done and the price of HBIG that is unaffordable for many people makes it difficult to provide in high risk babies. This study was conducted to determine the incidence of HBsAg positivity after completed Hep-B immunization in infants who were born from HBsAg-positive mothers without administration of HBIG and the proportion of those infants with protective level of anti-HBs.

## Methods

A descriptive cohort study was conducted from May 2009 to January 2010 as part of a larger study on the prevalence of HBsAg-positive pregnant women in Jakarta after 12 years of hepatitis B immunization policy implementation. Subjects were infants born from HBsAg-positive mothers recruited consecutively, with inclusion criteria of birth weight ≥2000 grams, positive maternal serum HBsAg and obtained parental consent. Cord blood samples were also taken during labor and later measured for HBsAg if maternal serum was HBsAg positive. If the parents can afford to pay for HBIG, then it will be administered and the infants will considered as control. Due to financial constraint, none of the infants in this study received HBIG. All but one subject received a birth dose of hepatitis B vaccine. Subjects were vaccinated with 3 doses of recombinant vaccine DTP-HB® every 4-6 weeks, started from the age of 2 month. One month after the third dose of DTP-HB®, serum HBsAg and anti-HBs in infants were evaluated. Those with non-protective anti-HBs levels received 3 more doses of hepatitis B vaccine in every 2 months using Unjiect®. Serum HBsAg was checked by *enzyme-linked immunosorbent assay* (ELISA) methods using Elecsys HBsAg® (catalog number 11820532122) and PreciControl HBsAg® as control (catalog number 11876309122). Subject with positive serum HBsAg was referred to the Gastrohepatology Division for further evaluation. Data was analyzed using SPSS for Windows version 17.0. Ethical clearance was obtained from the Medical Research Ethics Committee of the Medical School University of Indonesia.

## Results

Twenty two infants were enrolled this study. Seven subjects dropped out for many reason, 4 had moved out of Jakarta and 3 did not obtain parental consent (**Figure 1**). There were 13 boys and 9 girls, with 20 subjects born spontaneously and 2 subjects delivered by vacuum extraction. Birth-dose hepatitis B vaccination was given to 11/22 subjects within 24 hours of birth in keeping with WHO recommendations. Ten out of 22 subjects obtained it after 24 hours of birth and 1 never received birth-dose hepatitis B vaccination (**Table 1**). Median index of maternal serum HBsAg in this study was 897.8 (1.86 to 5.175). Cord blood samples were measured for HBsAg and were positive in 6/22 subjects. Median index of cord blood HBsAg was 0.5825 (0.19 to 667.4) (**Table 2**). None of the 5 subjects with HBsAg-positive cord blood were infected

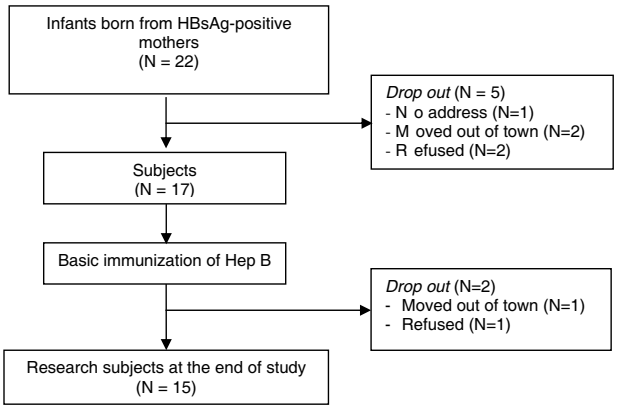


**Figure 1**. Research flow

**Table 1**. Characteristics of study subjects

| Characteristics | N = 22 |
|---|---|
| Sex | |
| Male | 13 |
| Female | 9 |
| Birth methods | |
| Spontaneous | 20 |
| Vacuum extraction | 2 |
| Timing of hepatitis B 1 injection | |
| Within first 24 hours of life | 11 |
| More than 24 hour | 10 |
| Unimmunized | 1 |
| Maternal HBsAg status before gave birth | |
| Positive | 3 |
| Negative | 6 |
| Unknown | 13 |

with hepatitis B at the end of this study, as shown by negative HBsAg (**Table 3**).

**Table 2.** HBsAg indexes of maternal blood, umbilical cord blood and subjects

| Subject | HBsAg index of maternal blood (initial) | HBsAg index of umbilical cord blood | HBsAg index of the subjects |
|---|---|---|---|
| 1 | 1.86 | 0.543 | 0.401 |
| 2 | 5.23 | 0.185 | 0.486 |
| 3 | 6.58 | 0.474 | *Drop out* |
| 4 | 12.25 | 0.605 | 0.485 |
| 5 | 13.89 | 0.444 | 0.518 |
| 6 | 16.26 | 0.565 | 0.458 |
| 7 | 38.92 | 0.435 | 0.529 |
| 8 | 188.10 | 0.462 | 0.449 |
| 9 | 214.30 | 0.422 | *Drop out* |
| 10 | 552.10 | 0.507 | *Drop out* |
| 11 | 609.60 | 667.4* | *Drop out* |
| 12 | 1186.00 | 0.954 | 0.583 |
| 13 | 1307.00 | 0.865 | 582.3* |
| 14 | 2038.00 | 0.926 | 0.479 |
| 15 | 2302.00 | 472.3* | 0.559 |
| 16 | 2450.00 | 105.9* | 0.381 |
| 17 | 3774.00 | 0.551 | *Drop out* |
| 18 | 3891.00 | 0.407 | *Drop out* |
| 19 | 4074.00 | 1.36* | 0.49 |
| 20 | 4672.00 | 0.600 | *Drop out* |
| 21 | 4765.00 | 1.84* | 0.525 |
| 22 | 5175.00 | 1.55* | 0.498 |

*positive if ≥1.

One out of 15 subjects had positive serum HBsAg even after received complete hepatitis B immunization. This female infant was born spontaneously at Mampang Prapatan community health center with birth weight of 3400 grams and received birth-dose hepatitis B less than 24 hours after birth. Maternal serum HBsAg at the beginning and end of this study were 1307 while cord blood HBsAg was negative. The infant's serum HBsAg was 582.3 and anti-HBs level was 1.5 IU/mL.

Two other subjects had non-protective anti-HBs levels with negative serum HBsAg. One subject was born spontaneously at a community health center and received birth-dose hepatitis B more than 24 hours after birth. The other subject was born spontaneously at Cipto Mangunkusumo Hospital and never received birth-dose hepatitis B. Both were later vaccinated at a community health center.

## Discussion

The high incidence of drop out due to the mobility of Jakarta's citizens and parents' refusal of performing blood test were considered to be the limitation of this study. Maternal HBeAg was also not evaluated thus transmission risk difference between sero-negative and positive mothers can not be assessed. There were 7 subjects who met drop out criteria due to moving out of Jakarta (3 subjects), moving to an unknown address (1 subject), and refuse blood sample procedure for further evaluation (3 subjects). Therefore, on final analysis there were only 15 out of 22 infants had complete data.

**Table 3.** HBsAg status and anti-HBs of the subjects after completed hepatitis B basic immunization

| | Subjects' HBsAg (-), protective anti-HBs | Subjects' HBsAg (-), nonprotective anti-HBs | Subjects' HBsAg (+), protective anti-HBs | Subjects' HBsAg (+), nonprotective anti-HBs | N |
|---|---|---|---|---|---|
| Umbilical cord blood HBsAg | | | | | |
| Positive | 5 | 0 | 0 | 0 | 5 |
| Negative | 7 | 2 | 0 | 1 | 10 |
| Total | | | | | 15 |
| | | | | | |
| Birth-dose hepatitis B timing | | | | | |
| < 24 hour after birth | 4 | 0 | 0 | 1 | 5 |
| > 24 hour after birth | 8 | 1 | 0 | 0 | 8 |
| Not immunized | 0 | 1 | 0 | 0 | 1 |
| Total | 12 | 2 | 0 | 1 | 15 |

WHO recommend the first hepatitis B immunization (birth dose) should be given on the first 24 hours of life without knowing maternal HBsAg status.[15] In this study, 11 infants received their first immunization according to WHO recommendation, 10 infants had it more than 24 hour-old, and 1 infant did not receive birth dose immunization. This variation may be due to different policy advised by Ministry of Health Republic of Indonesia, that is giving the first Hepatitis B immunizaton on day 0-7 of life. Nevertheless, 14 of 15 infants in this study were not infected by HBV eventhough some of them received their first immunization more than 24 hours of age.

The lowest and highest HBsAg index values in maternal blood were 1.86 and 5,171 respectively. Six out of 22 cord blood sample were HBsAg positive. This study found that the higher HBsAg value in maternal blood, the more likely HBsAg was found positive in baby, although the index of both values was not related congruently. On the final assessment, no infants who had positive HBsAg in their cord blood were infected with hepatitis B virus (negative HBsAg after completed Hep-B immunization). This finding is accordance to studies by Wong et al[16,17] and Wiharta et al[18] who also found that transplacental transmission did not play a role in vertical transmission.

In this study there was one HBsAg-positive infant; therefore 14/15 infants from HBsAg-positive mothers who only obtained hepatitis B vaccination were not infected. These infants were at risk for being infected, since they were delivered by vaginal birth and did not obtain HBIG. The infant who was HBsAg-positive had also obtained hepatitis B immunization but was infected nevertheless, possibly due to the presence of HBeAg in the mother's serum, increasing the likelihood of vertical transmission.[1,12,13] The HBsAg-positive infant in this study was referred to the Gastrohepatology Clinic, Department of Child Health, Cipto Mangunkusumo Hospital. The infant was advised to undergo liver function tests and hepatobiliary ultrasound.

HBsAg-negative infants with non-protective anti-HBs levels (2 subjects) obtained additional doses of hepatitis B vaccine. Three doses of monovalent vaccine (Uniject®) were planned with 8-week intervals. Anti-HBs levels will be re-evaluated 1 month after the final dose. Presently both infants have had 2 doses of monovalent hepatitis B vaccine. Center for Disease Control and Prevention (CDC) has recommended 3 additional doses of hepatitis B immunization in infants of HBsAg-positive mothers when anti-HBs levels were non-protective after basic immunization.[4] A study by Roushan showed that revaccination with 2 doses in non-responder infants from HBsAg-positive mothers was also effective in achieving protective anti-HBs levels.[20]

Although it was not initially aimed by this study, the effectivity of hepatitis B immunization was calculated using the formula %E = [1-(rate of infection in vaccinated infants/rate of infection in unvaccinated infants)] x 100.[13] If the risk of hepatitis B infection in infants of HBsAg-positive mothers was 22-67%,[19] this study found that the rate of protection of hepatitis B immunization against vertical transmission in these infants was 70-90%.

Seven subjects who dropped out of the study had similar characteristics with the remaining 15 subjects regarding maternal age, gestational age, birth weight, and hepatitis B1-immunization. All drop-outs obtained hepatitis B1 immunization; 4 were vaccinated less than 24 hours and 3 were vaccinated more than 24 hours postnatally. Only 1 out of 7 subjects had positive cord blood HBsAg, and this subject was vaccinated less than 24 hours postnatally. Data regarding follow-up immunization and test results after completed basic hepatitis B immunization could not be obtained because all subjects could not or refused to be contacted. In conclusion, one of 15 infants had positive HBsAg after complete hepatitis B immunization and 12 of 15 infants had protective level of anti-HBs. Effectiveness of hepatitis B immunization to prevent vertical transmission in this study is 70-90%.

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