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Research Report

PROPORTION OF HBsAg AND HBeAg POSITIVE IN MATERNAL PATIENTS AND THEIR HBsAg POSITIVES BABIES WITH IMMUNOPROPHYLAXIS OF HBV IMMUNIZATION IN Dr. SOETOMO GENERAL HOSPITAL, SURABAYA

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ABSTRACT

Hepatitis B Virus (HBV) can be transmitted vertically from mother to her baby. Mothers with HBsAg and HBeAg positives have more risk of transmitting HBV to her baby rather than HBsAg positives only. The aim of this study is to determine the proportion of maternal patient with HBsAg and HBeAg positives and their HBsAg positives babies with immunoprophylaxis of HBV immunization. This study was performed by analytical observation using medical records in 2013-2014 at Obstetric and Gyn ecology Department, Dr. Soetomo Hospital. The samples were all maternal patients (3796) during that period and also their babies from HBsAg positives mothers. Unfortunately, several original medical records were not available. Thirty two (0,85%) out of 3781 maternal patients were found to be HBsAg positives, and three (9,37%) of 32 patients with HBsAg positives were HBeAg positives. From 32 mothers who were positive HBsAg, 22 complete medical records of their babies were found and all of them (100%) had been given Hepatitis B Immunoglobulin (HBIG) and hepatitis B vaccine less than twelve hours after birth. In three cases of the babies from HBeAg positives mothers which had been given prophylaxis properly, two cases each of which was with caesarean and spontaneous delivery were HBsAg negatives. Interestingly, the other one which born with spontaneous delivery was found to be HBsAg positives. Further study in this HBsAg positives baby, especially in analyzing its HBV DNA is needed. The epidemiology of hepatitis B in maternal patients, especially that with complete and neat data needs further research.

Keywords: *HBsAg, HBeAg, hepatitis B, maternal patient, vertical transmission*

ABSTRAK

Virus Hepatitis B (VHB) dapat ditularkan secara vertikal dari ibu ke anak. Pada ibu dengan HBsAg dan HBeAg positif lebih beresiko menularkan VHB pada anaknya daripada hanya positif HBsAg. Penelitian ini bertujuan untuk mengetahui proporsi ibu bersalin dengan HBsAg dan HBeAg positif dan bayi dengan HBsAg positif yang telah diberi imunoprofilaksis terhadap HBV. Penelitian ini dilakukan dengan teknik observasional analitik menggunakan rekam medis pasien ibu bersalin periode tahun 2013-2014 yang dirawat di Departemen Obstetri dan Ginekologi RSU Dr. Soetomo. Sampel penelitian ini adalah semua ibu bersalin (3796) pada periode tersebut serta bayi dari ibu bersalin yang positif HBsAg. Sayangnya, ada beberapa data asli yang tidak tersedia. Dari 3781 pasien ibu sebanyak 32 (0,85%) pasien ibu positif HBsAg. Dari ibu positif HBsAg ditemukan tiga (9,37%) pasien HBeAg positif. Dari 32 pasien ibu positif HBsAg, dapat dikumpulkan 22 rekam medis bayi yang lengkap dan semuanya (100%) sudah diberi Imunoglobulin Hepatitis B dan vaksin HBV kurang dari 12 jam sejak lahir. Pada tiga kasus anak dari ibu positif HBeAg yang telah diberi profilaksis, ditemukan negatif

HBsAg pada dua kasus dengan tindakan persalinan Caesar dan spontan. Menariknya, satu kasus lainnya dengan tindakan persalinan spontan ditemukan positif HBsAg. Diperlukan penelitian lebih lanjut mengenai analisis DNA VHB pada bayi yang positif HBsAg ini. Perlu pula penelitian lebih lanjut mengenai epidemologi hepatitis B pada ibu bersalin dengan data yang jelas dan lengkap.

Kata kunci: *HBsAg, HBeAg, hepatitis B, pasien bersalin, penularan vertikal*

INTRODUCTION

Hepatitis B Virus (HBV) infection was one of major global health problems because about two billion people in the world have been infected with HBV and more than 350 million people are chronic carriers.[1] In 2013, Indonesian Basic Health Research (Riskesdas) also found the highest cause of the prevalence of hepatitis in Indonesia is by HBV (21,8%).[1]

Hepatitis B virus can be transmitted parenterally, in contact with blood or other body fluids. In endemic area of chronic HBV infection, transmission mainly through vertical transmission, especially during perinatal and early childhood.[2] Approximately 3,9% of pregnant women in Indonesia in 2007 as a carrier of HBV infection.[3] Risk Factors of HBV infection can be divided based on agent, host, and environment. People who are susceptible to the infection of HBV are people who live in Asia, Africa, and other regions with high prevalence of HBV infection, has not been vaccinated, had sexual intercourse with someone who had HBV infection, living with a person infected with HBV, homosexuals, using parenteral drugs, undergoing hemodialysis, and someone who is undergoing chemotherapy or other immunosuppressive treatment.[4] In hemodialysis patients study, the most common HBV agent in East Java, especially in Surabaya had genotype B,[5] whereas the most common subtype in Java was adw.[6]

Hepatitis B virus infection can be diagnosed with a laboratory test. Screening of HBV infection commonly by Hepatitis B Surface Antigen (HBsAg) tests. Hepatitis B surface antigen appears in blood serum after 1-10 weeks of exposure to HBV. Hepatitis B surface Antigen test has a specificity of 99.7% and a sensitivity of 100%.[7] After discovering someone has positive HBsAg, further examination with HBeAg test is also recommended. Hepatitis B envelope Antigen is a test to determine whether there has been virus replication.[8]

Centers for Disease Control and Prevention (CDC) recommends that all pregnant women should be screened with HBsAg marker. If it is found only HBsAg positive, then the risk of perinatal transmission is 10%.[9] While newborns of an HBV carrier woman with HBsAg and HBeAg positive, have 90% risk of becoming infected and carrier.[10] It is because of the baby tolerance to virus antigen. If these babies are not treated properly, it can develop into Hepatocellular Carcinoma (HCC) and leads to death after decades. However, HBV infection can be prevented by providing effective vaccination. Hepatitis B Virus vaccine is effective to 90% adults and children if given in three doses (three injections with a period of 6 months). Injections with hepatitis B immunoglobulin (HBIG) and HBV vaccine may also be granted because HBIG can give immediate but temporary protection against the virus until HBV vaccine is effective.[11]

Infection of HBV is also very likely to transmit in medical personnel who assist the delivery. Prevalence in this group varies between 10%-20%.[9] Therefore, right education and techniques are needed for helping the delivery process in pregnant women and to care the infants who are at risk to be vertically infected by HBV. This study will analyze the proportion of maternal HBsAg and HBeAg positive and HBsAg positives babies with HBV immunoprophylaxis (HBIG and HBV vaccine) which was administrated to the babies of HBsAg positive maternal patients in Dr. Soetomo General Hospital during the period of 2013-2014. This information is expected to be useful as information to the public and government in order to develop the prevention to vertical transmission of HBV infection. This study was conducted in Dr. Soetomo General Hospital because: firstly, it has a lot of patients so that we can get a large number of samples. Secondly, it is a type A hospital in Indonesia which means it is supposed to have the best health care service in Indonesia. Therefore from knowing how is the result of prevention of vertical transmission of HBV in Dr. Soetomo General Hospital, this study will show how far Indonesia has been handling the prevention of HBV transmission.

MATERIAL AND METHOD

This study used a cross-sectional design. Materials used in this research were secondary data: medical records documents of maternal patients who were checked using HBsAg and HBeAg test, and her babies were born during the period of 2013-2014 in the Departement of Obstetric and Gynecology Dr. Soetomo General Hospital Surabaya. The samples of this study were chosen by total sampling technique.

Variables examined in this study were HBsAg and HBeAg positives status of maternal patients and immunization status (passive and active) of her babies from HBsAg positive mothers. Maternal patients that HBsAg positive, will be tested with HBeAg marker. At that time, the examination of HBsAg and HBeAg were done in Laboratory of Clinical Pathology at Dr. Soetomo General Hospital using ELISA technique. Data from the observation that had been collected, then it was processed and analyzed descriptively using simple statistics (percentages).

RESULT AND DISCUSSION

From the data in the period of January 2013-December 2014 that had been collected, 47 out of 3796 (1,24%) maternal patients were valid and found to be HBsAg positives, but unfortunately only 32 patients out of 3781 (0,85%) that were valid and met HBsAg and HBeAg data. This was because medical records are used for another research by another medical personnel.

This proportion of maternal patients who were HBsAg positives (0,85%) is smaller compared with the results in 2007 which prevalence of maternal patients with hepatitis B in Indonesia was 3,9%.[3] The result of this study does not represent the population because this study took samples from a refer center hospital. Therefore, only rare and complicated cases are handled here. Besides that, many cases of maternal patients with HBsAg positives can be handled in the local hospital.

The proportion of HBsAg negative was 99,15%. Out of 32 HBsAg positive maternal patients, there were 3 (9,37%) HBsAg and HBeAg positive maternal patients. From 32 positive HBsAg maternal patients, there were 22 medical records of the babies that successfully collected.

In Table 1, if the frequency of HBsAg positive maternal patients compared between 2013 and 2014, the higher proportion was in 2014 (0,97%) although there were the fewer number of maternal patients than in 2013.

In Table 2, from the maternal patients with complete HBsAg and HBeAg data, the highest frequency of HBsAg positive maternal patients in 2013 was in May, while in year the 2014 were in February, March, May, and October which had a same number of patients (two patients). Bhatt (2000) study showed that no seasonal distribution for HBV infection.[12] There was no incidence of HBV infection that had drastic increase in a particular season, only hepatitis A virus (HAV) which has a certain seasonal cycle. Its peaks in March and September.[13] Hepatitis A virus infection is an acute disease and can be cured and all of the transmission of HAV through the fecal-oral route.

Hepatitis B virus and hepatitis C virus (HCV) infection can develop to be a chronic disease so that the carrier of HBV and HCV infection always transmit the virus every year and month. According to Soemoharjo,[6] the transmission of HBV can pass through contact with the not intact body with blood, mucus of infected persons and also through sexual intercourse to infected persons. Therefore, this allows HBV infect anyone who had not infected and contact with blood on body fluid of HBV patients.

Based on delivery techniques in HBsAg positive maternal patients (Table 3), the most frequent technique used was Caesarean (62%). Based on Chang *et al* (2014) research, were found a decrease of HBV transmission in caesarean delivery technique,[14] because the doctors who helped childbirth process knew that there were higher risks for spontaneous delivery for increasing the transmission of HBV. Hepatitis B virus from amniotic fluid can enter the body through the wound in the baby's skin that happened because of entering the birth canal or accidentally swallowed if there was a contraction of the uterus (materno fetal micro infusion).[6] If there is no contraction during

Table 1. The frequency of positive HBsAg and HBeAg maternal patients in 2013 and 2014

Year	N		HBsAg Positives	%
	Incomplete Data	Complete Data		
2013	7	2541	20/2541	0.79%
2014	8	1240	12/1240	0.97%
Total	**15**	**3781**	**32/3781**	**0.85%**

Table 3. Delivery techniques in HBsAg positives maternal patients

Delivery Techniques	HBsAg Positives (%)	HBsAg and HBeAg Positives (%)
Spontan	11/29 (38%)	2/3 (67%)
Caesar	18/29 (62%)	1/3 (33%)
Total	**29 (100%)**	**3 (100%)**

Table 2. Frequency of maternal patients with HBsAg positive, and HBsAg, HBeAg positive

Month	2013		2014	
	HBsAg Positives	HBsAg Positives HBeAg Positives	HBsAg Positives	HBsAg Positives HBeAg Positives
Jan	3	1	1	0
Feb	0	0	2	0
Mar	1	0	2	0
Apr	1	0	0	0
May	5	0	2	0
Jun	1	1	0	0
Jul	0	1	1	0
Agt	0	0	1	0
Sept	0	0	1	0
Oct	1	0	2	0
Nov	1	0	0	0
Dec	4	0	0	0
Total	**17**	**3**	**12**	**0**

Table 4. Gestation age distribution in HBsAg positives and HBsAg, HBeAg positives patients

Gestation Age	HBsAg Positives (%)	HBsAg and HBeAg Positives (%)
Preterm	3/29 (10,34%)	0/3 (0%)
Aterm	26/29 (89,65%)	3/3 (100%)
Total	**29/29 (100%)**	**3/3 (100%)**

caesarean delivery then it will decrease the risk of HBV transmission.

In this study out of three maternal patients who had HBsAg and HBeAg positive, there were two patients who had spontaneous birth. It cannot be a reference because a small number of patients cannot represent the overall picture of delivery techniques that often used in HBeAg positive maternal patients.

In Table 4, both HBsAg positive and HBsAg, HBeAg positive maternal patients had the significant difference in the gestation age distribution, which term gestation had the higher frequency. Incidence of low birth weight and prematurity increased in women with acute hepatitis B.[15] Another study found that carrier HBsAg women had higher risk to become preterm labor.[16]

However, Wong et al research didn't find any association between HBV infection in maternal patients with preterm labor, same as this research results in Dr. Soetomo General Hospital.[17]

Based on the occupation as seen in figure 1, the most frequent occupation of maternal patients was housewife (13 patients), followed by private employees (10 patients). In 2014, a study in Nigeria at a University of Medicine, the highest number of jobs in the antenatal women who were HBsAg positive was unemployment (13 among 42 women).[18] The result study in Nigeria is similar to the result study in Dr. Soetomo.

General Hospital which is the most frequent occupation was housewife or unemployment. The previous result's study showed that low socioeconomic status that initiates multi-sexual partners, unprotected sexual intercourse was more susceptible to get Sexually Transmitted Disease.[18]

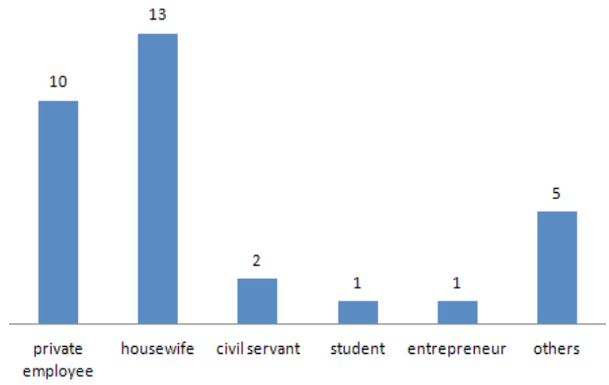

Figure 1. Bar Diagram of HBsAg positive maternal patiens based on Occupation distribution

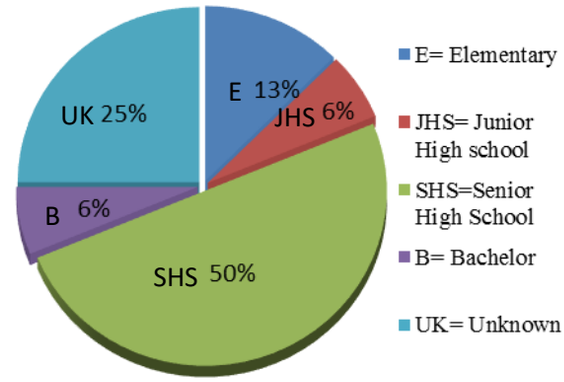

Figure 2. Circles Diagram of HBsAg positive maternal patients based on the education

Based on their education level, highest frequency in HBsAg positive maternal patients were Senior High School Graduate (50%) (Figure 2).

The raw education data showed that the population with lower education status (Elementary, Junior High school, and Senior high school) were more prone to be infected with hepatitis B. It was because of lack of education in promotive prevention of the disease given in early grade school (Elementary, Junior High School, and Senior High School) (Figure 2).

This study found only 22 complete medical record documents of the babies from 32 HBsAg positive maternal patients (Table 5).

The remaining 10 files were not found in the medical records storage. All of 22 babies were given HBIG and HBV vaccine less than 12 hours after birth (100%). This result suggests that the prevention of transmission of HBV infection in Dr. Soetomo General Hospital had been done properly.

Table 5. Frequency of prophylactic administration of the baby from HBsAg positive maternal patients

Prophylaxis Action	Quantity (n=22)	Percentage
Hepatitis B vaccine	22	100%
HBIG	22	100%

Table 6. Data of babies from HBeAg positive maternal patients

	Delivery Technique	Gravida	Administration of Hepatitis B Vaccine and HBIG	Complete Vaccination (3 x)	HBsAg Status of the Child at This Time
Mother A	Spontaneous	Multigravida	yes	Complete	Positive
Mother B	Spontaneous	Multigravida	yes	Complete	Negative
Mother C	Caesarean	Multigravida	yes	Complete	Negative

As seen in Table 6, all children from HBeAg positive maternal patients had been given immunoprophylaxis (HBV vaccine and HBIG) less than 12 hours after birth and had undergone complete vaccination three times.

Two children from two maternal patients (one mother who delivered with caesarean and another mother with spontaneous delivery) were found to be negative HBsAg. But interestingly, the other child of the mother who had spontaneous delivery was HBsAg positive even though her child had been given phrophylaxis properly. This positive HBsAg of the child may be caused by the presence of escape mutant HBsAg in infants who had been given HBIG and HBV vaccination. Hepatitis B surface antigen (HBsAg) with arginine replacement for glycine at amino acid 145 is the most common escape mutant HBsAg found in several clinical samples.[19] All infants who fail to respond to immunophrophylaxis were born from HBeAg positive mothers who had HBV DNA levels ≥6 $\log_{10}$ copy/mL. The existence of HBV DNA in cord blood also reflects the failure to respond passive and active immunization.[20]

From the result in this study, there was no tendency of transmission of HBV through certain delivery technique, same as in Hu et al (2013) study which stated that if hepatitis B vaccine and HBIG were given immediately after birth, the choice of labor procedure didn't determine the tendency of HBV transmission.

CONCLUSION

The proportion of maternal patients who was HBsAg positive in Dr. Soetomo General Hospital in period of 2013-2014 was 0,85%. Some missing data should take into consideration. Out of 32 HBsAg positive maternal patients, there were three maternal patients who were positive HBeAg (9,37%). All of the children with complete medical record documents in this study (22 children) had been given HBIG and HBV vaccine properly (100%). A good management of the medical records is needed in every hospital so that the practitioner who used data for research will get correct and complete data, therefore the results will be more accurate.

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REFERENCES

1. Riset Kesehatan Dasar [Internet]. Badan Penelitian Dan Pengembangan Kesehatan Kementerian Kesehatan RI. 2013. Available from: http://www.depkes.go.id/resources/download/general/Hasil Riskesdas 2013.pdf
2. DF de PM, T M, DJ T, RA VES, JL N-S, F ST, et al. Prevalence and factors associated with hepatitis B virus infection among senior citizens in a southern brazilian city. Hepat Mon. 2013;13(5).
3. Kusumawati L, Mulyani NS, Pramono D. Faktor-Faktor yang Berhubungan dengan Pemberian Imunisasi Hepatitis B 0-7 Hari. Ber Kedokt Masy. 2007;23(1):21–7.
4. Hepatitis B Are You at Risk? Vol. 21, DEPARTMENT OF HEALTH & HUMAN SERVICES Centers for Disease Control and Prevention. 2010.
5. Lusida MI, Sakugawa H, Nagano-fujii M, Handajani R, Setiawan PB, Nidom CA, et al. Genotype and Subtype Analyses of Hepatitis B Virus (HBV) and Possible Co-Infection of HBV and Hepatitis C Virus (HCV) or Hepatitis D Virus (HDV) in Blood Donors , Patients with Chronic Liver Disease and Patients on Hemodialysis in Surabaya , Indones. Microbiol Immunol. 2003;47(12):969–75.
6. Soemoharjo S. Hepatitis Virus B Edisi 2. Ed. 2 Cet. Jakarta: EGC; 2008.
7. Ashraf H, Alam NH, Rothermundt C, Brooks A, Bardhan P, Hossain L, et al. Prevalence and Risk Factors Of Hepatitis B and C Virus Infections in An Impoverished Urban Community in Dhaka, Bangladesh. BMC Infect Dis. 2010;10(208):1–8.
8. Indonesia DKR. Pedoman Pengendalian Hepatitis Virus. Jakarta: Kementrian Kesehatan RI; 2012.
9. Hepatitis B Epidemiology and Prevention of Vaccine-Preventable Diseases [Internet]. Centers for Disease Control and Prevention. 2012. Available from: https://www.cdc.gov/vaccines/pubs/pinkbook/hepb.html
10. Hepatitis B [Internet]. World Health Organization. 2002. Available from: http://www.who.int/csr/disease/hepatitis/HepatitisB_whocdscsrlyo2002_2.pdf
11. Horn T, Learned J. Hepatitis Virus dan HIV. AIDS Community Research Initiative of America (ACRIA); 2005.
12. Bhatt CP. Prevalence of viral Hepatitis B in BPKIHS Dharan, Nepal. J Nepal Med Assoc. 2000;39:281–3.
13. Memish ZA, Knawy B Al, El-Saed A. Incidence trends of viral hepatitis A, B, and C seropositivity over eight years of surveillance in Saudi Arabia. Int J Infect Dis. 2010;14(2):115–20.
14. MS C, S G, PC A, J M-B. Caesarean section to prevent transmission of hepatitis B: A meta-analysis. Can J Gastroenterol Hepatol. 2014;8(8):439–44.
15. MM J. Hepatitis B and Pregnancy: an underestimated issue. Liver Int. 2009;29(S1):133–9.
16. Aghamohammadi A, Nooritajer M. Maternal Hbsag Carrier and Pregnancy Outcome. Aust J Basic Appl Sci. 2011;5(3):607–10.
17. S W, LY C, V Y, Ho L. Hepatitis B carrier and perinatal outcome in singleton pregnancy. Am J Perinatol. 1999;16(9):485–8.
18. Ikeako L, Ezegwui H, Ajah L, Dim C, Okeke T. Seroprevalence of Human Immunodeficiency Virus, Hepatitis B, Hepatitis C, Syphilis and Co-infections among Antenatal Women in a Tertiary Institution in South-East Nigeria. Ann Med Health Sci Res. 2014;4(6):954–8.
19. Cooreman MP, Leroux-Roels G, Paulij WP. Vaccine- and Hepatitis B Immune Globulin-Induced Escape Mutations of Hepatitis B Virus Surface Antigen. J Biomed Sci. 2001;8(3):237–47.
20. Zou H, Chen Y, Duan Z, Zhang H, Pan C. Virologic factors associated with failure to passive–active immunoprophylaxis in infants born to HBsAg-positive mothers. J Viral Hepat. 2011;19(2):e18–25.