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Correlation Between Timing of Hepatitis B Immunoglobulin to The Effectiveness of Mother to Child Transmission Prevention Program

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Abstract **-The Prevention Program for Hepatitis B from Mother to Child Transmission (PMTCT) was carried out in Pangkalpinang City, Bangka Belitung Province since 2016. Pregnant women detected HBsAg positive were recorded so their newborn could get Hepatitis B Immunoglobulin (HBIg). The aim of study to analyze the correlation between the timing of Hepatitis B Immunoglobulin (HBIg) to the effectiveness of Hepatitis B PMTCT program in Pangkalpinang City.This study using cross sectional approach. Number of research samples was 59 children born to HBsAg positive mothers, who were taken using consecutively sampling from HBIg recipient data of Pangkalpinang Health Office. Independent variables are the timing of HBIg, and completeness of the Hepatitis B immunization, that were known from the MCH books and interviews with mothers using questionnaires. Dependent variable is effectiveness of the Hepatitis B PMTCT program, that measured from HBsAg and AntiHBs testing of children using the Rapid Diagnostic Test (RDT). Data analysis using chi-square test. The results showed that 1 (1.7%) children with HBsAg were positive, and 29 (49.2%) children with Anti-HBs were positive. Based on the results of the chi-square test there is a significant correlation between the timing of HBIg administration (p-value = 0.007) and the completeness status of Hepatitis B immunization (p-value = 0.026) on the success of the Hepatitis B PMTCT program in Pangkalpinang City.The timing of HBIg is effective in preventing transmission of Hepatitis B from HBsAg positive mothers to their newborn. Recommendation for health workers to cause immunity or antibodies on child, the HBIg is given immediately or less than 12 hours after birth, and is supplemented with a completeness of Hepatitis B vaccine.**

Keywords: Hepatitis B, immunoglobulin, HBsAg, immunization, PMTCT

I. INTRODUCTION

Maternal and Child Health (MCH) is still a global development priority (SDGs), with a focus on promotive and preventive efforts such as the Prevention of Mother To Child Transsmission (PMTCT) program (United Nations, 2018).

World Health Organization (WHO) estimates that 257 million people in the world live with the chronic hepatitis B virus. Around 1.34 million mortality due to chronic hepatitis, cirrhosis and liver cancer. It is even expected to continue to increase, because vertical transmission from mother to baby has the potential to become cirrhosis of the liver and death (WHO, 2017). Indonesia is a country with a high prevalence. This is shown from the results of the 2018 riskesdas which showed that the prevalence of Hepatitis B was 0.39% (Riskesdas, 2018).

The prevalence of pregnant women infected with hepatitis B is currently 2.5%. With the risk of transmission from mother to child more than 90%. For this reason, the government in this case the Ministry of Health of the Republic of Indonesia undertakes preventive promotive efforts to eliminate infectious diseases in the context of Preventing Mother-to-Child Transmission (PPIA). Early detection in pregnant women is done to find out the presence of the HIV virus, syphilis and hepatitis B, this program is called triple elimination (Permenkes 52, 2017).

Vertical transmission of Hepatitis B from mothers with positive HBsAg in their infants has a 90% risk of becoming chronic and carrier. Specific prevention against hepatitis B infection is by immunization, which is divided into passive and

active Hepatitis B immunization. Passive immunization is by giving Hepatitis B immunoglobulin (HBIg) in a short time to immediately provide protection even if only for a short period (3-6 months). HBIg is only given in post-exposure conditions (needle stick injury, sexual contact, infants of Hepatitis B mothers, blood splattered to the mucosa or eyes).

HBIg should be given with the Hepatitis B vaccine so that the protection lasts longer. Whereas Active Immunization is to implement a universal immunization program for newborns by providing a recombinant Hepatitis B vaccine available. This vaccine consists of three series and if given as recommended will lead to the formation of a protective response which will ultimately succeed in reducing the prevalence of Hepatitis B virus infection (Permenkes 53, 2015).

Immunizations or vaccinations are given from birth to early children. Basic immunizations that must be given before a child is 1 year old include are : Hepatitis B (HB_0), BCG, $Polio_1$, DPT/HB_1, $Polio_2$, DPT/HB_2, $Polio_3$, DPT/HB_3, $Polio_4$, and Campak. After 1 year of age the child also receives additional immunization (booster) at the age of 18 months, namely DPT / HB4, Polio5 and when the child enters school age (Permenkes 12, 2017).

In infants of mothers with Hepatitis B virus, HBIg should be given together with the Hepatitis B 0 vaccine on different sides of the body within 12 hours after birth. This policy has been proven effective (85-95%) in preventing hepatitis B virus infection and preventing chronicity (19-20%) whereas with the hepatitis B vaccine alone it has an effectiveness rate of 75%. If the mother's HBsAg is discovered a few days later, HBIg can be given if the baby is <7 days old. However, its effectiveness will decrease if given 3 days after exposure. Generally, HBIg is given with the Hepatitis B vaccine so that in addition to providing immediate protection, this combination also provides long-term protection (PPHI, 2006).

Therefore the purpose of this study was to analyze the correlation between the timing of HBIg and the effectiveness of the Prevention of Mother to Child Hepatitis B Transmission (PPIA) in Pangkalpinang City.

II. METHOD

Study Design

This research is observasional study using cross sectional design. Samples were children aged > 1 year who were born by Hepatitis B mothers and received HBIg. Sampling was done using consecutive sampling from HBIg recipient data from the City Health Office of Pangkalpinang.

III. DATA AND ANALYSIS

The dependent variable is the effectiveness of the PPIA Hepatitis B program, measured from children born to Hepatitis B mothers who are not infected with Hepatitis B virus (HBsAg negative) and children who have immunity or antibodies against Hepatitis B virus (positive Anti-HBs). Child HBsAg and Anti-HBs examination uses the Rapid Diagnostic Test (RDT) method.

The independent variable in this study was the timing of HBIg (time of injection) and the completeness status of Hepatitis B immunization on children. Data obtained from interviews with mothers using a questionnaire and checking the notes on the children's MCH handbook. Data analysis using the chi-square test, with $\alpha = 0.05$ and the confidence interval set was 95%.

IV. RESULTS

Characteristics of respondents

Based on the results of this study obtained a sample of 59 children (see Table 1). More male sex is 32 people (54.2%) than women. The most children blood type is blood type O Rh (+), which is 19 people (32.2%). More children who received HBIg injections in the <12 hour group were 45 people (76.3%) children, compared to children who got HBIg ≥ 12 hours. Likewise, the variable status of completeness of Hepatitis B immunization is more children with complete immunization status (84.7%) than children who are incomplete.

Next, for the status of transmission of Hepatitis B, it is known that there are 1 person (1.7%) children with HBsAg positive, while 58 children with HBsAg negative. As for the immunity or antibody known only 29 children (49.2%) who have positive Anti-HBs (Table 1).

This analysis shown the correlation between timing of HBIg with the effectiveness of Hepatitis B Mother to Child Transmission Prevention program (PPIA) obtained data for 27 (60.0%) of children who received HBIg <12 hours did not successfully contract Hepatitis B and had positive antibodies. Whereas in the group of children who received HBIg immunization ≥ 12 hours that succeeded in 2 (14.3%) children.

Table 1. Characteristic of Respondents

Variables	Frequencies	
	n	%
Age of child		
≥ 2 years	31	52.5
< 2 years	28	47.9
Sex		
Male	32	54.2
Female	27	45.8
Blood Type		
A Rh (+)	18	30.5
B Rh (+)	15	25.4
AB Rh (+)	7	11.9
O Rh (+)	19	32.2
Timing of HBIg		
≥ 12 hours	14	23.7
< 12 hours	45	76.3
Completeness of Hepatitis B Immunization		
No complete	9	15.3
Complete	50	84.7
HBsAg		
Positive	1	1.70
Negative	58	98.3
Anti-HBs		
Negative	30	50.8
Positive	29	49.2

Table 2. Results of bivariat analysis using chi-square test

Variables	Effectiveness PPIA				Total		*p-value*	PR 95% CI
	No		Yes					
	n	%	n	%	n	%		
Timing HBIg								
≥ 12 hours	12	85.7	2	14.3	14	100	0.007	9.00 (1.79-45.08)
< 12 hours	18	40.0	27	60.0	45	100		
Completeness of Hepatitis B Immunization								
No complete	8	88.9	1	11.1	9	100	0.026	10.18 (1.18-87.63)
Complete	22	44.0	28	56.0	50	100		

The analysis results obtained p-value <0.05 so it can be concluded that there is a statistically significant relationship between the time of HBIg immunization with the success of the PPIA program. Known OR value of 9,000 means children who receive HBIg <12 hours have 9 times the chance to succeed without contracting hepatitis B and have immunity (antibodies), compared with children who get HBIg ≥ 12 hours.

Correlation between the completeness status of the hepatitis B immunization with the effectiveness of the PPIA Hepatitis B program obtained data that there were 28 (56.0%) children with complete hepatitis B immunization who did not successfully contract Hepatitis B and had immunity or antibodies. While in the group of children with incomplete immunizations, there were 1 (11.1%) children who successfully were not infected and had immunity. P-value = 0.026 or <0.05.

So it can be concluded that there is a significant correlation between the completeness of Hepatitis B immunization of children with the success of the PPIA Hepatitis B program. OR value of 10.182 can be interpreted that children who have complete hepatitis B immunization have a 10.182

times greater chance of successfully not contracting and having immunity against the hepatitis virus. B, compared to children whose Hepatitis B immunization status is incomplete.

V. DISCUSSION

Babies born to mothers with HBsAg positive, the administration of Hepatitis B vaccine (HB-0) and immunoglobulins should be done as soon as possible, preferably <24 hours (Ministry of Health, 2015). However, another theory in the technical guidelines for babies born to mothers with Hepatitis B, states that the action immediately after the baby is born <12 hours is the administration of a recombinant Hepatitis B vaccine and at the same time on the other side of the body is given immunoglobulin (HBIg) IM at a dose 0.5 ml (Pujiarto, et al, 2000).

The timing injection of HBIg is in accordance with the research of Evans, et al., In Haimen City China which obtained the results of HBIg and HB0 for 183 respondents in total <23 hours (Evans, et al, 2015). However, different results are shown by Ahmad N.'s research, in Magelang District, Central Java, only 42 of 61 respondents (68.85%) received HBIg <12 hours, while the remaining 19 respondents did not get HBIg at all because of the relatively high price and not knowing that their child must get HBIg immunization (Ahmad N., 2017).

Immunoglobulin is a passive immunization, so the child immediately gets antibodies or immunity against Hepatitis B. In contrast to the Hepatitis B vaccine which stimulates the child's body to release its own antibodies (active immunization). When the child goes through childbirth there is a risk of transmission from the mother, so the administration of HBIg after 12 hours has passed because it is feared that the virus from the mother has infected the child, before the child has antibodies.

Based on the results of this study it is known that all children born receive HBIg immunization but not all of them complete with Hepatitis B vaccine. There are 84.7% of children with complete hepatitis B immunization status, namely getting HB0, HB1, HB2 and HB3 vaccines before 1 year of age. While there are incomplete respondents who only receive HBIg and HB0 at birth, without being equipped with any other immunizations. There was even 1 respondent who only received HBIg without HB0 after birth, and this Anti-Hbs respondent was still negative. The results of this study show that there is a significant relationship between the completeness of the immunization status of children with the success of the PPIA program (p = 0.026).

Based on the Republic of Indonesia Minister of Health Regulation *(Permenkes)* number 53 of 2015 about the prevention of Hepatitis Virus it is stated that every baby born is given the Hepatitis B vaccine (HB-0) as soon as possible, but for babies born to mothers with positive HBsAg, the immunizations given are immunoglobulin (HBIg) and HB- 0 on different thighs, then proceed with the hepatitis B vaccine in accordance with the national immunization program, which is at the age of 2 months, 3 months and 4 months. Hepatitis B immunization can provide protection against hepatitis B infection for more than 20 years. The success of immunization is assessed from the detection of antibodies (anti-HBs) after giving full immunizations 3-4 times (Permenkes 53, 2015).

The result of this study similar with the results of the Beasley, et al. (1983), which states that the efficacy of HBIg alone is 71%, the efficacy of Hepatitis B vaccine alone is 75%, while the efficacy of Hepatitis B vaccine along with HBIg is 94%. However, different results were shown by Ahmad N, 2017 in Magelang District, where 61 respondents all received HB0 <12 hours, but only 68.85% received HBIg, and showed 0% transmission (Ahmad N., 2017).

VI. CONCLUSION AND RECOMMENDATION

Based on the results of this study there is a significant relationship between the time of HBIg administration (p = 0.007), and the status of completeness of Hepatitis B immunization (p = 0.026) with the success of the PPIA Hepatitis B program. The administration of HBIg immunization is effective in preventing transmission of Hepatitis B from mother to child, but to cause antibodies or immunity in children, HBIg alone is not enough so it must be supplemented with the entire Hepatitis B vaccine.

It is important to inform the health workers and family of Hepatitis B that the best time to give HBIg is <12 hours after the baby is born, and the baby must also get a complete Hepatitis B vaccine to prevent contracting Hepatitis B.

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