ISSN 2089 - 2136

Tropical Medicine Journal

Volume 03, No. 2, 2013

TMJ	Volume 03	Number 02	Page 95 - 195	ISSN 2089 - 2136

Center for Tropical Medicine, Faculty of Medicine, Universitas Gadjah Mada
in collaboration with Indonesian Society of Tropical Medicine and Infectious Disease (PETRI)

Address : Tropical Medicine Journal, PAU Building, Jalan Teknika Utara Barek, Yogyakarta
Universitas Gadjah Mada, Yogyakarta 55281, Phone : +62-274-588483, E-mail: tropmedjournal@gmail.com

TROPICAL MEDICINE JOURNAL

ISSN : 2089-2136
Center for Tropical Medicine, Faculty of Medicine, Universitas Gadjah Mada in collaboration with Indonesian Society of Tropical Medicine and Infectious Disease (PETRI)

Volume 03, Number 02

CONTENTS

Immune Response against Hepatitis B Virus after Vaccination among Low Birth Weight and Preterm Newborns: A Retrospective Cohort Study in Magelang District Central Java

Muhardison[1*], Hari Kusnanto[2], Nenny Sri Mulyani[3]
[1]Postgraduate Program of Public Health, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia; [2]Department of Public Health, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia; [3]Department of Pediatric, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia.

Corresponding author: sutan_adrin@yahoo.com

ABSTRACT

Introduction: Hepatitis B virus (HBV) infection is a major cause of morbidity and mortality in the world. Over 2 billion people are infected with HBV and 378 million are carriers. The mortality rate is approximately 1-2 million and over 4 millions acute clinical cases are documented each year. The prevalence of HBV infection in Indonesia is 3-20%. Vertical and horizontal transmission in newborn and children occurs in 25-45%. Near 25-50% of children are infected before 5 years. The most effective approach to reduce the burden of HBV infection is mass vaccination of newborns and children.

Objectives: To determine immune response against HBV after HBV vaccine among low birth weight (LBW) and preterm newborns after HBV vaccination, and factors related to the immune response i.e. gender and weight gain in the first 6 months of life.

Methods: During May-July 2012, 106 infants aged 13-15 months were recruited after HBV vaccination. They were completed 4 doses of HBV basic vaccination in 0, 2, 3, and 4 months of life. Sera were examined for anti-HBs antibody titers using ELISA.

Results: A total of 98 subjects (92.5%) completed the study. Immune response of LBW subjects were positive in 89.7%, newborns were 95.9%. The Relative Risk (RR) were 2.5 CI (0.50 to 12.2) p=0.2178. Gender was not related to immune response RR 0.6 CI (0.15 to 2.69) p=0.6996. Gestational age associated with immune response RR 8 CI (1.05 to 63.9) p=0.0399. The first 6 months weight was not related to immune response RR 3.6 CI (0.73 to 17.7) p=0.1178. Logistic regression analysis showed LBW was not correlated with the immune response OR 1 CI (0.16 to 7.17) p=0.929. Gestational age correlated with immune response OR 9 CI (1.05 to 79.3) p=0.044 and the first 6 months of weight was not correlated with immune response OR 3.7 CI (0.65 to 21.1) p=0.138.

Conclusion: Immune response against HBV after vaccination was similar between LBW and NBW. Immune response was correlated with gestational age.

Keywords: Hepatitis B vaccine, immune response, LBW and preterm.

INTISARI

Pendahuluan: Infeksi Virus Hepatitis B (HBV) adalah salah satu peyebab utama mobiditas dan mortalitas di duna. Lebih dari 2 miliar orang terinfeksi oleh HBV dan 378 juta adalah karier. Angka mortalitas berkisar 1-2 juta dan lebih dari 4 juta kasus akut terjadi setiap tahunnya. Prevalensi infeksi HBV di Indonesia adalah 3-20%. Penularan vertikal dan horizontal pada bayi baru lahir dan anak-anak terjadi 25-45%. Hampir 25-50% anak-anak terinfeksi HBV sebelum usia 5 tahun. Pendekatan paling efektif untuk mengurangi infeksi HBV adalah dengan melakukan vaksinasi masal pada bayi baru lahir dan anak-anak.

Tujuan: Penelitian ini bertujuan untuk mengetahui respon imun terhadap HBV pasca vaksinasi diantara bayi berat lahir rendah (BBLR) dan bayi lahir kurang bulan. Serta untuk mengetahui faktor yang berhubungan dengan respon imun seperti jenis kelamin dan pertumbuhan berat badan pada enam bulan pertama.

Metode: Selama bulan Mei-Juli 2012 telah dilakukan penelitian pada 106 anak usia 13-15 bulan yang telah divaksinasi HBV empat kali pada usia 0, 2, 3, dan 4 bulan. Serum diambil dan dilakukan pengukuran titer anti-HBs antibody dengan metode ELISA.

Hasil: Sebanyak 98 subyek (92,5%) menyelesaikan studi. Respon imun BBLR (89,7%) bersama-sama dengan NBW (95,9%) RR 2,5 CI (0,50 12,2) p = 0,2178. Jenis kelamin tidak berhubungan dengan respon imun RR 0,6 CI (0,15 to 2,69) p=0,6996. Usia kehamilan berhubungan dengan respon imun RR 8 CI (1,05 to 63,9) p=0,0399. Berat bayi enam bulan pertama tidak berhubungan dengan respon imun RR 3,6 CI (0,73 - 17,7) p=0.1178. Analisis regresi logistic menunjukkan bahwa BBLR tidak berhubungan dengan respon imun OR 1 CI (0,16 - 7,17) p=0,929. Usia kehamilan berhubungan dengan respon imun OR 9 CI (1,05 - 79,3) p=0,044 ; dan berat bayi pada enam bulan pertama tidak berhubungan dengan respon imun OR 3,7 CI (0,65 - 21,1) p=0.138.

Simpulan: respon imun vaksin HBV setara antara BBLR dan bayi berat lahir cukup . Respon imun berhubungan dengan usia kehamilan.

Kata kunci: Vaksin HBV, respon imun, BBLR dan bayi lahir kurang bulan

INTRODUCTION

Hepatitis B Virus (HBV) infection was the main cause of morbidity and mortality. The transmissions of HBV have been become public health problem in the world. The vertical transmission from woman to infant was occurred at 24-45%, increasing the incidence of new infection of HBV in children.

The frequency of horizontal transmission was 79%. This was occurred amongst children, adolescent, adult. It was documented that 25-50% cases were new HBV infection involving children before their five year old. This condition become significant since the younger children get infection, the more probable to become chronic carrier[1,2].

It was proposed that HBV vaccination decreases the morbidity and mortality at two third in 2015. American Academy of Pediatrics (AAP) recommended the HBV vaccination for the new born and premature babies or Low Birth Weight ≥ 000gr. The vaccination schedule is similar with the normal infant without respect to the status of HBs Ag of the mother[3].

The incidence of LBW and premature babies has been increasing in the last 15 years. The newest advance of the caring for LBW and premature is important to be followed in order

to substantially increasing the survival[3]. The most effective approach to decrease the HBV infection and breaking the chain of transmission in their early life is by primary prevention through mass vaccination for the new born and children.

A national wide HBV vaccination programs was performed in Indonesia in 1997. One series of HBV vaccination able to gain optimal immune response at 95% in infant, children, adolescent and healthy adult[4]. Studies on immune response against HBV after vaccination was not conclusive reported that immune response against HBV was found lower in premature than the aterm infant[5].

Other studies[6,7] reported that, the premature and LBW infants have immune response that is comparable to the normal infants after hepatitis B vaccination with three doses in the different population.

Considering this inconclusive data, study to measure the immune response in LBW and normal infant and other factors that is influence the immune response is interesting.

MATERIALS AND METHODS

Subjects:

This was retrospective cohort study. Two parallel groups were observed in August to October 2013. Sampling was performed by cluster sampling in three area of Public Health Center with high incidence of LBW in Magelang District.This study had been approved by Research Ethic Committee of Faculty of Medicine, Universitas Gadjah Mada (MHREC). The subjects were consisted of 53 LBW infants and 53 normal birth weight (NBW) infants who have complete 4 series of the HBV vaccination at 0, 2, 3, and 4 months of their ages. The mothers, who their children was selected as subject, were invited to Public Health Center and Integrated Service Post. Informed consents were obtained from the mothers. Data were collected from medical records and child health cards.

Anti-HBs antibody titer measurement

Children were donate 1.5-2 ìl of blood. Titer of anti-HBs antibody was measured by using ELISA method. The anti-HBs antibody titer was categorized as negative if their anti-HBs titer is less than 10 IU/L and positive if more than 10 IU/L.

Statistical analysis

the correlation between two variable were analyzed using fisher's exact test and multivariable analysis by using logistic regression, with significance level $p<0.05$, and confidence level at 95%.

RESULTS AND DISCUSSIONS

The study was performed at Salaman 1, Salaman 2 and Borobudur Primary Health Care. Table 1 summarized the variables which were studied among LBW and normal children.

Table1. The characteristic of subjects involved in the study

Variable	Observation results	n	%
Anti-HBs Titers	<10 IU/L	7	7.2
	≥10 IU/L	91	92.8
Sex	Male	53	54.1
	Female	45	45.9
Birth weight	LBW	49	50.0
	NBW	49	50.0
Gestational age	<37 weeks	42	43.0
	≥37 weeks	56	57.0
Firts 6 month weight	Weight Decreased	40	40.8
	Weight Increased	58	59.2

Table 2. Relationship between birth weight, sex, gestational age and Weight the First 6 month weight and anti-HBs titers

Variable		Anti-HBs Titers			RR	95% CI	*p*
		<10 IU/L	≥10 IU/L	Total			
Birth weight	LBW	5	44	49	2.5	0.50-12.27	0.2178
	NBW	2	47	49			
	Total	7	91	98			
Sex	Male	3	50	53	0.6	0.15-2.69	0.6996
	Female	4	41	45			
	Total	7	91	98			
Gestational age	<37 weeks	6	36	42	8.0	1.05-63.96	0.0399*
	≥37 weeks	1	55	56			
	Total	7	91	98			
Weight firts 6 months	Gain weight	5	44	49	3.6	0.73-17.76	0.1178
	Loss weight	2	47	49			
	Total	7	91	98			

*Note: *: p=<0,05*

Table 2 showed the association analysis between birth weight, sex, gestational age and the first 6 month weight with anti-HBs titers. There was significant association between gestational ages and immune response (p<0.05).

Table 3 showed the significant positive correlation between the gestational age with the immune response p=0.044, OR=9.1 and 95%CI (1.05-79.3).

It was recommended by American Academy of Pediatrics that vaccination of HBV in the newborn particularly the premature ≥ 2000 gram and LBW (with good clinical condition) with same vaccination schedule to the normal infant appropriate to the chronological age or vaccination schedule without respect to the status of HBsAg of the woman[3,10].

Table 3 showed the logistic regression indicated that LBW infant had immune response 89.8% comparable with the normal birth weight 95.9% immune response. It was statistically had no difference, OR=1, 95% CI (0.16-7.18), p value= 0.929.

It was reported that immune response against HBV between LBW infant <2500 gram normal birth weight infant e”2500 gram was comparable. The HBV vaccine showed effective and safe to prevent the newborn, children, and adult from the transmission of HBV[7,6].

HBV vaccination with three dosages resulted in 90-99% newborn, children, adolescent and adult develop optimal immune response. It showed by the titer of anti-HBs ≥10 IU/L, and only 5-10% of the infant, health children, and adult who were vaccinated did not form optimal immune response[11].

Gestational age was one of parameter that might be used for assess immune response in premature infant[3]. Table 2 described that gestational age <37 week contributed to 9 times

Table 3. Multivariable analysis for variables associated with Anti-HBs titers

Anti-HBs	Model s 1	Model s 2	Model s 1
	OR (95% CI) *p*	OR (95% CI) *p*	OR (95% CI) *p*
Birth weight	1.1 (0.16-7.18) 0.929		
Gestational age	8.3 (0.82-85.1) 0.072	8.7 (0.99-76.5) 0.051	9 (1.05-79.3) 0.044*
Weight first 6 months	3.6 (0.64-21.1) 0.142	3.7 (0.65-21.1) 0.138	

Note: * p = *<0,05*

greater risk to have negative immune response compared to the gestational age ≥37 week. OR= 9.1 and 95 CI 1.05-79.3; *p value*=0.044.

Previous study reported that premature infant had correlation to the decreasing of *immunogenicity* after the provision of 3 dosage of HBV vaccine and lower titer anti-HBs antibody compared to the aterm infant[10,5].

CONCLUSION

The immune response against HBV of HBV vaccinated LBW infant was comparable to the normal infant. Immune response was correlated with gestational age.

REFERENCES

1. Cardell K. *Studies on Hepatitis B Vaccination and Factors Associated with the Vaccine Response*. Sweden: Linkoping University, 2009.
2. Gunawan S. *Hepatitis B dan Pencegahannya melalui Imunisasi di Indonesia*. Cermin Dunia Kedokteran, 1991;68:5-7.
3. Ome F, Garcia-sicilia J, Boceta R, Garc P. *Hepatitis B Response of Premature Infants after Primary and Booster Immunisation with a Diphtheria-Tetanus-Acellular Influenzae Type B Vaccine*, 2010.
4. Saari TN. *American academy of pediatrics,* 2003;112(1):193-8.
5. Soares M, Mussi-pinhata MM, Moysés S, Fumiko C, Yoshida T, Barbosa C, Souza S De. *Immunogenicity of Hepatitis B vaccine in preterm and full term infants vaccinated within the first week of life,* 2002;20:1557-62.
6. Belloni C, Chirico G, Pistorio A, Orsolini P, Tinelli C, Rondini G. *HBV vaccine/ : Immunogenicity of Hepatitis B Vaccine in Term and Pretrm Infants*. Acta pediatrica, 1998(March):336-8.
7. Lumblganon P, Kowsuwan P, Lumbiganon P, Taksaphan S, Panamonta M, Assateerawatts A. *Comparison of Immunogenicity of Hepatitis B Vaccine Between Low and Normal Birth Weight Infants*, 1992;61-3.
8. IDAI. *Pedoman Imunisasi di Indonesia. 4th ed.* Rahun, G. Suyitno, H. Hadinegoro, S. Kartasasmita, C. Ismoedijanto S, editor. Ikatan Dokter Anak Indonesia, 2011.
9. Depkes RI. *Riset Kesehatan Dasar 2007*, 2007.
10. Gad A, Shah S. *Special Immunization Considerations of the Preterm Infant*, 2007 (December): 385-91.
11. Eldesoky A, Mosaad Y, Zakria Y, Hamdy S. *Protective immunity after hepatitis B vaccination.* Arab Journal of Gastroenterology. Arab Journal of Gastroenterology, 2009;10(2):68-71. Available from: URL: http://dx.doi.org/10.1016/j.ajg. 2009.05.002.

12. Golebiowska M, Sobanka KD, Sokol CD, Sabanty W. *Hepatitis B Vaccination In Preterm Infant*. Pediatric, 1999);158(September):293-7.
13. Supariasa NI, Bakri BFI. *Penilaian Status Gizi*. Ester M, editor. Jakarta: Penerbit Buku Kedokteran EGC, 2001.
14. Sriyono. *Pola Pertumbuhan Berat Badan Dalam 6 Bulan Pertama Pada BBLR*. Gadjah Mada, 1994.
15. Depkes RI. *Buku Acuan: Pelatihan Imunisasi Dasar Bagi Pelaksana Imunisasi di UPK Swasta*. Jakarta: Ditjen PP & PL Depkes RI, 2009.

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Scientific Journal

1. *Standard journal article*

   You CH, Lee KY, Chey RY, Menguy R. Electro-gastro-graphic study of patients with unexplained nausea, bloating and vomiting. Gastroenterology 1980; 79(2):311-14.

   Goate AM, Haynes AR, Owen MJ, Farral M, James LA, Lai LY, et al. Predisposing locus for Alzheimer's disease on chromosome 21. Lancet 1989;1:352-55.

2. *Organization as author*

   The Royal Marsden Hospital Bone-marrow Transplantation. Team. Failure of syngeneic bone-marrow graft without preconditioning in post-hepatitis marrow aplasia. Lancet 1977;2:742-44.

3. *No author given*

   Coffee drinking and cancer of the pancreas [editorial]. BMJ 1981;283-628.

4. *Article not in English*

   Massone L, Borghi S, Pestarino A, Piccini R, Gambini C. Localisations palmaires purpuriques de la dermatite herpetiforme. Ann Dermatol Venereol 1987;114:1545-47.

5. *Volume with supplement*

   Magni F, Rossoni G, Berti F, BN-52021 protects guinea-pig from heart anaphylaxis. Pharmacol Res Commun 1988;20 Suppl 5:75-78.

6. *Issue with supplement*

   Gardos G, Cole JO, Haskell D, Marby D, Paine SS, Moore P. The natural history of tardive dyskinesia. J Clin Psychopharmacol 1988;8(4 Suppl):31S-37S.

7. *Volume with part*

   Hanly C. Metaphysics and innateness: a psychoanalytic perspective.Int J Psychoanal 1988;69(Pt 3):389-99.

8. *Issue with part*

   Edwards L, Meyskens F, Levine N. Effect of oral isotretinoin on dysplastic nevi. J Am Acad Dermatol 1989;20(2 Pt 1):257-60.

9. *Issue with no volume*
   Baumeister AA. Origins and control of stereotyped movements. Monogr Am Assoc Ment Defic 1978; (3):353-84.
10. *No issue or volume*
    Danoek K. Skiing in and through the history of medicine. Nord Midicinhist Arsb 1982;86-100.
11. *Pagination in roman numerals*
    Ronne Y. Ansvarfall. Bloodtransfusion till fel patients. Vard-facket 1989;13:XXVI-XXVII.
12. *Type of article indicated as needed*
    Spargo PM, Manners JM, DDAVP and open heart surgery [letter]. Anaesthesia 1989;44: 363-64.
    Fuhrman SA, Joiner KA. Binding of the third component of complement C3 by Toxoplasma gondii [abstract]. Clin Res 1987; 35:475A.
13. *Article containing retraction*
    Shishido A. Retraction notice: Effect of platinum compounds on murine lymphocyte mitogenesis [Retraction of Alsabti EA, Ghalib ON, Salem MH. In: Jpn J Med Sci Biol 1979; 32:53-65). Jpn J Med Sci Biol 1980;33:235-37.
14. *Article retracted*
    Alsabti EA, Ghalib ON, Salem Mh. Effect of platinum compounds on murine lymphocyte mitogenesis [Retracted by Shishido A. In: Jpn J Med Sci Biol 1980;33:235-7]. Jpn J Med Sci Biol 1979;32:53-65.
15. *Article containing comment*
    Piccoli A, Bossatti A. Early steroid therapy in IgA neuropathy: still open question [comment]. Nephron 1989;51:289-91.
16. *Article in comment*
    Kobayashi Y, Fujii K, Hiki Y, Tateno S, Kurokawa A, Kamiyama M. Steroid therapy in IgA nephropathy: a retrospective study in heavy proteinuric cases [see comments]. Nephron 1988;48:12-7. Comment in: Nephron 1989;51:289-91.
17. *Article with published erratum*
    Schofield A. The CAGE questionnaire and psychological health [published erratum appears in Br J Addict 1989;84:701]. Br J Addict 1988;83:761-64.

Books and Other Monographs

18. *Personal author(s)*
    Colson JH, Armour WJ. Sports injuries and their treatment. 2nd rev. ed. London: S. Paul, 1986.
19. *Editor(s) as author*
    Diener HC, Wilkinson M, editors. Drug-induced headache. New York: Springer-Verlag, 1988.
20. *Organization(s) as author*
    Virginia Law Foundation. The medical and legal implications of AIDS. Charlottesville: The Foundation, 1987.
21. *Chapter in a book*
    Winstein L, Swartz MN. Pathologic properties of invading microorganisms. In: Sodeman WA Jr, Sodeman WA, editors. Pathologic Physiology, mechanisms of disease. Philadelphia: Saunders, 1974:457-72.
22. *Conference proceedings*
    Vivian VL, editor. Child abuse and neglect: a medical community response. Proceedings of the First AMA National Conference or Child Abuse and Neglect; 1984 Ma 30-31; Chicago. Chicago: American Medical Association, 1985.
23. *Conference paper*
    Harley NH. Comparing radon daughter dosimetric and risk models. In:Gammage RB, Kaye SV, editors. Indoor air and human health. Proceedings of the Seventh Life Sciences Symposium; 1984 Oct 29-31; Knoxville (TN). Chelsea (MI):Lewis, 1985:69-78
24. *Scientific or technical report*
    Akutsu T. Total heart replacement device. Bethesda (MD): National Institutes of Health. National Heart and Lung Institute; 1974 Apr. Report No.:NIH-NIHI-69-2185-4.
    Disertasi Youssef NM. School adjustment of children with congenital heart disease [dissertation]. Pittsburg (PA): Univ. of Pittsburg, 1988.

25. *Dissertation*
    Kay JG. Intracellular cytokine trafficking and phagocytosis in macrophages [Dissertation]. St Lucia, Qld: University of Queensland; 2007.
26. *Patent*
    Harred JF, Knight AR, McIntyre JS, inventors. Dow Chemical Company, assignee. Epoxidation process. US patent 3,654,317, 1972 Apr 4.

Other Published Material

27. *Newspaper article*
    Resberger B, Specter B. CFCs may be destroyed by natural process. The Washington Post 1989 Aug 7;Sect. A:2(col. 5).
28. *Audiovisual material*
    AIDS epidemic: the physician's role [videorecording]. Cleveland (OH): Academy of Medicine of Cleveland, 1987.
29. *Computer program*
    Renal system [computer program]. MS-DOS version. Edwardsville (KS): Medi-Sim, 1988.
30. *Legal material*
    Toxic Substances Control Act: Hearing on S. 776 Before the Subcomm. on the Environment of the Senate Comm. on Commerce, 94th Cong., 1st Sess. 343(1975).
31. *Map*
    Scotland [topographic map]. Washington: National Geographic Society (US), 1981.
32. Dictionary or Encyclopaedia
    Ectasia. Dorland's illustrated medical dictionary. 27th ed. Philadelphia: Saunders, 1988: 527.
33. *Classic material*
    The Winter's Tale: act 5, scene I, lines 13-16. The complete works of William Shakespeare. London: Rex, 1973.
34. *In press*
    Lillywhite HB, Donald JA. Pulmonary blood flow regulation in an aquatic snake. Science. In press.

Electronic Material

35. *Journal articel in the internet*
    Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1996 Jun 5];1(1):[24 screens]. Available from: URL: http://www.cdc.gov/ncidod/EID/eid.htm
36. *Monograph in electronic format*
    CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0 San Diego: CMEA; 1995.
37. Computer program
    Hemodynamics III: the ups and downs of hemodynamics [computer program]. Version 2.2. Orlando (FL): Computerized Educational System; 1993.

We thank to the reviewers of this edition:

dr. Abu Tholib, M.Sc., Ph.D., Sp.MK
dr. Ahmad Hamim Sadewa,Ph.D
dr. Arta Farmawati, Ph.D
dr. Elizabeth Henny Herningtyas, M.Si, Ph.D
Dr. Dra. Erna Kristin, Apt., M.Si.
dr. Hanggoro Tri Rinonce, Ph.D
dr. M. Lutfan Lazuardi, M.Kes., Ph.D
dr. Titik Nuryastuti, Ph.D, Sp.MK
dr. Tri Wibawa, Ph.D
Dra. Raden Ajeng Yayi Suryo Prabandari, M.Si., Ph.D