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Original Article

Post Vaccination Immunity Status Against Hepatitis B Virus Infection-An Analytical Study

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Abstract:

Introduction: Hepatitis B vaccine has shown to be highly efficacious in preventing hepatitis B virus (HBV infection). Immunization with this vaccine reduces the subsequent development of chronic hepatitis B in young children from perinatal or early childhood exposure to HBV.[8,9] However, the duration of satisfactory protection level conferred by hepatitis B vaccination is not well understood.[10,11] Previous thinking was that this vaccination would provide effective coverage for five to seven years.[12,13] But subsequently it has been proved that it offers long-term immunity.

Methods: This is a cross sectional observational study. All the patients were collected among the admitted patients of Paediatric ward, Dhaka National Medical College (DNMC) from January to December, 2019.

Result: This study reveals 49.12% children have developed adequate immunity i.e. Anti-HBs antibody level >100 mIU /ml, and 38.60% showed poor response (10-100 mIU /ml). Only 12.28 % are nonresponsive. Poor responders also having satisfactory immunity, may be for a shorter period. Difference of immunity level developed between two groups, 1 yr. - 6yrs and > 6 yrs. -12 yrs. is obvious. The reason is not very clear. More elaborate studies are required to probe on these facts.

Conclusion: Acquisition of acceptable immunity level following our vaccination schedule is satisfactory (87.72%). Larger study should be conducted to develop a consensus of opinion.

Key words: Hepatitis B Vaccination, Immunity, HBV.

Introduction:

American physician Baruch Blumberg discovered what he called the "Australia Antigen" (now called HBsAg) in the serum of an Australian Aboriginal person in 1963.[1] In 1968, this protein was proved to be a part of the virus that causes "serum hepatitis" (hepatitis B) by virologist Alfred Prince.[2]

Hepatitis B vaccine was first approved by United States in 1981.[3] One recombinant version has become available in the market since 1986.[4] It is included in the World Health Organization's Essential Medicines list. These two versions were developed by Maurice Hilleman and his team.[5,6,7]

Hepatitis B vaccine (both plasma derived and recombinant) has been demonstrated to be highly effective in preventing hepatitis B virus (HBV) infection. Immunization with this vaccine if begins at birth has subsequently dramatically reduce the development of chronic hepatitis B in children of perinatal or early childhood exposure to HBV.[8,9] However, the duration of protection conferred by hepatitis B vaccination is not well understood.[10,11] It was previously suggested that the vaccination would only provide effective coverage for five to seven years.[12,13] But subsequently it has been appreciated that long-term immunity derives from immunological memory and hence subsequent testing and administration of booster dose is unnecessary in successfully vaccinated immune-competent individuals.[14]

Following the primary course of three vaccinations, a blood test may be taken after an interval of 1–4 months to measure the response level.[15] World Health Organization (WHO) has recommended Hepatitis B vaccination along with DPT and Oral Polio vaccine[16] offered schedule for hepatitis B immunization of children consists of a dose within 24 hours of birth followed by a second and third dose of hepatitis B containing vaccines at intervals of at least 4 weeks[17]

Bangladesh included Hepatitis B vaccination since 2005 and pentavalent vaccination (DPT + Hepatitis B + Hib) since 2009 in national EPI schedule. The recommended schedule is at the age of 6, 10 and 14 weeks.[18]

This is a study of 57 children, those have been vaccinated as per national EPI schedule. We have undertaken the study to see the level of immunity against Hepatitis B virus among children in our perspective conferred by this immunization schedule.

Materials & Method:

This is a cross sectional observational study. All the patients were collected from the Paediatric in-patient department of Dhaka National Medical College (DNMC) during the year 2019, who had been admitted with different diseases. Total 57 children were included in this study by purposive random selection technique, those had been vaccinated for Hepatitis B virus infection as per national immunization schedule during first year of life. All of them received full 03 courses of vaccine.

The age range was from 01 year to 12 years, belongs to both sexes from urban and rural areas. Children below 01 year were non-cooperative and those above 12 years were excluded to maintain the harmonicas of age in the study group. We have tested them by EILISA method in the laboratory of Dhaka National Medical College (DNMC) for detection of Hepatitis B surface antibody (HBS antibody) in their serum. Children with any other chronic disease and severely malnourished were excluded from the study. Children, whose parent/s were non-cooperative, also not included.

Result:

Fifty-seven (57) children were include in the study, among them 29 were male and 28 were female.

Table-I: (n=57) Sex distribution.

Gender	Age (1 to 6 yrs.)	Age (>6 to 12 yrs.)	Total	Percentage
Male	13	16	29	50.88 %
Female	18	10	28	49.12 %
Total	**31**	**26**	**57**	**100%**

We have divided them into two groups to see the impact on immunity level if any.

Table-II: (n=57) Antibody status.

Serum level in our study population following pentavalent vaccination (DPT + Hepatitis B + Hib).

Gender	<10 mIU/ml	10-100 mIU/ml	100 mIU/ml
Male	04 (13.79%)	12 (41.37%)	13 (44.83%)
Female	03 (10.71%)	10 (35.71%)	15 (53.57%)
Total	**07 (12.28%)**	**22 (38.60%)**	**28 (49.12%)**

Immunity (HBS antibody) level according to age group

Table-III: (n=57) Immunity (Hbs Ab) level according to age group.

Age group	<10 mIU/ml	10-100 ml U/ml	>100 ml U/ml	P. value
(1 yr.- 6yrs)	05(16.13%)	12(38.71%)	14(45.16%)	0.595
(>6yrs.-12yrs.)	02(7.69%)	10 (38.46%)	14 (53.85%)	

Discussion:

The hepatitis B vaccine is a safe and effective and recommended for infants. This vaccine is also recommended for children, those have failed to be vaccinated during early infancy and for adults those are at higher risk for infection because of their job nature, lifestyle and living conditions.

All the children included in our study were vaccinated as per our national EPI schedule i.e.at the age of 6, 10 and 14 weeks. They were vaccinated in the National Medical College EPI center and also from neighboring Upo-Zilla Health Complexes.

Out of them 50.88% were male and 49.12 % were female.

The study reveals 49.12% children have developed adequate immunity level i.e. HBS antibody level is >100 mIU /ml, and 38.60% showing poor response (10-100 mIU /ml). The rest 12.28 % are non-responsive. Satisfactory immunity level should occurs in about 85–90% of vaccinated people. In our series 87.72% children have developed acceptable level of immunity. The children with poor response confer acceptable immunity level against Hep B virus infection but may require a booster dose to ensure long term immunity.

Following the course of three vaccinations, test should be done to establish if there is an **adequate response**, which is defined as anti-hepatitis B surface antigen (anti-Hbs) antibody level above 100 mIU/ml. Antibody level between 10 and 100 mIU/ml is considered as **poor response**, and these individuals although possessing sufficient immunity level should receive single booster dose vaccination, but do not require retesting.[19]

People who are non-responsive (anti-Hbs antibody level below 10 mIU/ml) should be checked for recent or past Hepatitis B infection. If so, give a repeat course of three vaccinations, followed by further testing 1–4 months

after finishing second course. Those who still do not respond to a second course of vaccination may respond to intradermal administration[20] or to a higher dose vaccine[21] or to a double dose of a combined hepatitis A and B vaccine.[22]

Poor responses are related with obesity, celiac disease, and mostly people who are suffering from immunosuppression.[23,24] One study suggests that hepatitis B vaccination is less effective in patients having HIV.[25] Hep B vaccine is sensitive to low temperatures and can be damaged by freezing. On the other hand, it is quite heat stable and use with a vaccine vial monitor (VVM) allows greater flexibility in transportation and storage. According to the WHO multi-dose vial policy (WHO/V&B/00.09), opened multi-dose vials of hepatitis B vaccine may be reused in subsequent immunization sessions for up to four weeks in fixed health facilities if all the following conditions are met:

1) The expiry date has not passed.
2) The vial has been stored under appropriate cold chain conditions (i.e. refrigerated between 2 °C and 8 °C).
3) The vaccine vial septum (where the needle is put in to withdraw doses) has not been submerged in water (to prevent this from happening, well-sealed ice packs should be used in vaccine carriers and water should not be allowed to accumulate where the vials are stored).
4) An aseptic technique has been used to withdraw all doses.
5) The vaccine vial monitor (VVM), if attached, has not reached the discard point.[26]

Vaccine those are not well maintained properly cannot conserve its efficacy and potency. This might be the crucial factor for immunization failure.

The Indian Academy of Pediatrics (IAP) Committee on Immunization has strongly recommended that the first dose of Hepatitis B vaccine should be given as early as possible after birth and preferably within 24 hours. The second dose may be given along with DPT at 6 weeks and third dose at 14 weeks.. But administering the vaccine earlier makes it easier and more ensured to achieve high immunization coverage. Hepatitis B vaccination at birth give protection to perinatal HBV infections. A variety of schedules have been advocated for hepatitis B immunization globally targeted, different age groups ,may be based on local epidemiological conditions and logistic supports There is no current evidence to support the idea that higher titers following vaccination with a particular schedule provide longer and higher protection from the disease.[27-32]

Newborn or infant vaccination aims to address the babies who would otherwise be affected perinatally or in early childhood, when the chance of becoming Chronic Hepatitis is highest, 90% among infants of HBsAg and hepatitis B antigen (HBAg)-positive mothers, infected during the first year after birth, develop chronic infection, compared to 30% of children infected in between 1st and 4th years of age and less than 5% of infected adults.[33]

The risk of HBV infection among infants born from HBsAg-positive mothers were found to be eight times higher when the first dose was administered 7 days after birth, compared to when it was administered within the first 72 hours after birth. Those countries where mothers usually deliver in a hospital or clinic, adequate first-dose HBV vaccine coverage can be achieved when the vaccine is given at birth, which facilitates potential of increased compliance for subsequent doses. Studies in the USA indicate that children who have received the first dose of hepatitis B vaccine during their first month of life (the birth dose) are more likely to complete the hepatitis B vaccination series as well as other immunizations.

In our series difference of immunity developed between two groups, 1 yr. - 6yrs and >6 yrs. -12 yrs. (Table-3) is obvious and p value is also close to be significant. The reason is not very clear. More elaborate studies are required to probe on these facts.

As cure is not possible with available therapy, the aim is long-term viral suppression. Emphasis should be put on health education of the general people, high-risk populations, and also health workers to increase knowledge on avoiding unsafe injection practices, high-risk sex, unnecessary blood transfusion and providing appropriate screening of blood products. These should be combined with screening and aggressive vaccination.[34]

Conclusion

This study was done among admitted patients in the Paediatric department of a single hospital. Acquisition of adequate immunity level following our vaccination schedule, found optimally satisfactory. Multicenter based larger studies should be conducted to develop a consensus of opinion.

References

1. Blumberg BS, Alter HJ, Visnich S. "A "New" Antigen In Leukemia Sera". JAMA 1965, 191 (7): 541–6. doi:10.1001/jama.1965.03080070025007. PMID 14239025.
2. Howard, Colin; Zuckerman, Arie J. (1979). Hepatitis viruses of man. Boston: Academic Press. pp. 16–18. ISBN 978-0-12-782150-4.
3. Moticka E (25 November 2015).A Historical Perspective on Evidence-Based Immunology. p. 336. ISBN 9780123983756.
4. World Health Organization . "Hepatitis B vaccines: WHO position paper – July 2017". Wkly. Epidemiol. Rec. 2017, 92 (27): 369–92. hdl:10665/255873. PMID 28685564. Lay summary (PDF).
5. Tulchinsky, Theodore H. (2018). "Maurice Hilleman: Creator of Vaccines That Changed the World". Case Studies in Public Health: 443–470. doi:10.1016/B978-0-12-804571-8.00003-2. ISBN 9780128045718. PMC 7150172.
6. Oransky, Ivan "Maurice R Hilleman". The Lancet. 2005,365 (9472): 1682. doi:10.1016/S0140-6736(05)66536-1. ISSN 0140-6736. PMID 15912596. S2CID 46630955.
7. Offit, Paul A. (2007). "Chapter 8: Blood". Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases (PDF). HarperCollins. pp. 115–126, 136–140.
8. MastEE, AlterMJ, MargolisHS. Strategies to prevent and control hepatitis B and C virus infections: a global perspective, Vaccine . 1999 Mar 26;17(13-14):1730-3. doi: 10.1016/s0264-410x(98) 00415-0. CrossrefPubMed
9. MastEE, MargolisHS, FioreAE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents, MMWR Recomm Rep . 2005 Dec 23;54(RR-16):1-31. PMID: 16371945
10. DentingerCM, McMahon BJ, ButlerJC, et al. Persistence of antibody to hepatitis B and protection from disease among Alaska natives immunized at birth, Pediatr Infect Dis J . 2005 Sep;24(9):786-92. doi: 10.1097/01.inf.0000176617. 63457.9f. Cross ref. PubMed
11. McMahon BJ, BrudenDL, PetersenKM, et al. Antibody levels and protection after hepatitis B vaccination: results of a 15-year follow-up, Ann Intern Med. 2005 Mar 1; 142(5):333-41. doi: 10.7326/0003-4819-142-5-200503010-00008. Cross ref. PubMed
12. Krugman S, Davidson M (1987). "Hepatitis B vaccine: prospects for duration of immunity". Yale J Biol Med. 1987 Jul-Aug; 60(4): 333–339. PMC 2590237. PMID 3660859.
13. Petersen KM, Bulkow LR, McMahon BJ, Zanis C, Getty M, Peters H, Parkinson AJ (July 2004). "Duration of hepatitis B immunity in low risk children receiving hepatitis B vaccinations from birth". Pediatr Infect Dis J . 2004 Jul;23(7):650-5. doi: 10.1097/01.inf.0000130952. 96259.fd PMID 15247604. Archived from the original on 5 June 2015.
14. Gabbuti A, Romanò L, Blanc P, Meacci F, Amendola A, Mele A, Mazzotta F, Zanetti AR, "Long-term immunogenicity of hepatitis B vaccination in a cohort of Italian healthy adolescents". Vaccine. 2007,25 (16): 3129–32. doi:10.1016/j.vaccine. 2007.01.045. PMID 17291637.
15. Joint Committee on Vaccination and Immunisation." Chapter 18: Hepatitis B". Immunisation Against Infectious Disease 2006 ("The Green Book") (3rd edition (Chapter 18 revised 10 October 2007) ed.). Edinburgh: Stationery Office. p. 468. ISBN 978-0-11-322528-6. Archived from the original(PDF) on 7 January 2013.
16. Dey SK, Nahar z, Chowdhury s, Shahidullah M, Rahman SA . Immune response to Hepatitis B Vaccine in Term and Preterm Babies Received as per EPI schedule., Bangladesh J Child Health, 2009 ; 33(1): 1-5.
17. WHO Immunization schedule for Children (web site)
18. Karim R, Rahman MS, Uddin MS, Immune response against Hepatitis B virus after Pentavalent Vaccination in Children . Mymensingh Med J. 2018 Apr; 27(2):294-297. PMID: 29769493
19. Joint Committee on Vaccination and Immunisation (2006). "Chapter 18: Hepatitis B". Immunisation Against Infectious Disease 2006 ("The Green Book") (3rd edition (Chapter 18 revised 10 October 2007) ed.). Edinburgh: Stationery Office. p. 468. ISBN 978-0-11-322528-6. Archived from the original (PDF) on 7 January 2013.

20. Filippelli M, Lionetti E, Gennaro A, Lanzafame A, Arrigo T, Salpietro C, La Rosa M, Leonardi S (August 2014). "Hepatitis B vaccine by intradermal route in non responder patients: an update". World J. Gastroenterol. (Review). 20 (30): 10383–94. doi:10.3748/wjg.v20.i30.10383. PMC 4130845. PMID 25132754.

21. Levitz RE, Cooper BW, Regan HC (February 1995). "Immunization with high-dose intradermal recombinant hepatitis B vaccine in healthcare workers who failed to respond to intramuscular vaccination". Infection Control and Hospital Epidemiology. 16 (2): 88–91. doi:10.1086/647062. PMID 7759824.

22. Cardell K, Akerlind B, Sällberg M, Frydén A (August 2008). "Excellent response rate to a double dose of the combined hepatitis A and B vaccine in previous nonresponders to hepatitis B vaccine". The Journal of Infectious Diseases. 198 (3): 299–304. doi:10.1086/589722. PMID 18544037.

23. Filippelli M, Lionetti E, Gennaro A, Lanzafame A, Arrigo T, Salpietro C, La Rosa M, Leonardi S. "Hepatitis B vaccine by intradermal route in non responder patients: an update". World J. Gastroenterol. (Review). 2014, 20 (30): 10383–94. doi:10.3748/wjg.v20.i30.10383. PMC 4130845. PMID 25132754.

24. Roome AJ, Walsh SJ, Cartter ML, Hadler JL. "Hepatitis B vaccine responsiveness in Connecticut public safety personnel". JAMA. 1993, 270 (24): 2931–4. doi:10.1001/jama.270.24.2931. PMID 8254852.

25. Pasricha N, Datta U, Chawla Y, Singh S, Arora SK, Sud A, Minz RW, Saikia B, Singh H, James I, Sehgal S (March 2006). "Immune responses in patients with HIV infection after vaccination with recombinant Hepatitis B virus vaccine". BMC Infectious Diseases. 6: 65. doi:10.1186/1471-2334-6-65. PMC 1525180.

26. Hepatitis B,WHO/V&B/01.31, 2001,Page 22.

27. Gupta ML, Sharma U, Saxena S, Sharma ML, Pokharna DS. Vertical transmission of Hepatitis B surface antigen from asymptomatic carrier mothers. Indian Pediatr 1985; 22: 339-342.

28. Nayak NC, Panda SK, Zuckerman AJ, Bhan MK, Guha AK. Dynamics and impact of perinatal transmission of hepatitis B. J Med Virol 1987; 21:137-145.

29. Kulkarni ML, Reddy PV. Prevalence of HBsAg in asymptomatic carrier mothers and vertical transmission. Am J Dis Child 1988; 142: 124-125.

30. World Health Organization. Global Program for vaccines and immunization. Expanded program on immunization: Immunization policy, WHO GPV/GEN/95.03Rev.1, 1995.

31. Kumar TS, Abraham P, Raghuraman S, Cherian T. Immunogenicity of indigenous recombinant hepatitis B vaccine in infants following 0, 1, 2-month vaccination schedule. Indian Pediatr 2000; 37: 75-80.

32. Gomber S, Sharma R, Ramchandran VG, Talwar V, Sinha B. Immunogenicity of Hepatitis B vaccine incorporated into Expanded Program of Immunization Schedule. Indian Pediatr 2000; 37: 411-413.

33. WJ Edmunds, GF Medley, DJ Nokes, AJ Hall, HC WhittleThe influence of age on the development of the hepatitis B carrier state, Proc Biol Sci, 253 (1993), pp. 197-201 View Record in Scopus Google Scholar

34. World Health Organization, Practices to improve coverage of the hepatitis B birth dose vaccine, WHO (2013).

HYPERLINK "http://apps.who.int/iris/bitstream/10665/78616/1/WHO_IVB_12.11_eng.pdf" \t "_blank"Available