ORIGINAL ARTICLE

A PROSPECTIVE CROSS-SECTIONAL STUDY ON THE PREVALENCE AND FACTORS ASSOCIATED WITH SEROPROTECTION AFTER PRIMARY SERIES OF HEPATITIS B VACCINATION

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The authors declare that the data presented are original material and has not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all authors, and all authors have met the requirements for authorship.

ABSTRACT

OBJECTIVES: To determine the prevalence and factors associated with seroprotection among children 3 months to 18 years old with primary Hepatitis B vaccination series.

METHODOLOGY: This is a prospective cross-sectional study done among children 3 months to 18 years old with complete primary series of Hepatitis B vaccination. Demographic, social and clinical data were correlated with reactivity to antibody to Hepatitis B surface antigen (anti-HBs) ($\geq$10 IU/L), total antibody to Hepatitis B core antigen (total anti-HBc) and Hepatitis B surface antigen (HBsAg) serologic tests.

RESULTS: Among 110 subjects from different age groups, 52% had seroprotective anti-HBs levels, with the highest noted among infants (3 months-2 years) at 82%, followed by 41% from the childhood group (3-9 years) and 26% from adolescent group (10-18 years). Seventy-four percent of subjects with <5 years interval from vaccination were seroprotected, 26% in subjects after 5-10 years, and 38% at more than 10 years after vaccination with significant difference on multi-logistic regression (p value 0.000/0.020). None of the other factors including gender, geographic area, age at first dose, vaccination schedule, type and place of vaccination were significantly associated with seroprotection.

CONCLUSION: Fifty-two percent of patients among different age groups were seroprotected. Seroprotection was significantly associated with the interval year after vaccination demonstrated at < 50% 5 years and beyond post-vaccination.

KEYWORDS: *Hepatitis B seroprotection, Hepatitis B immunization, anti- HBs*

INTRODUCTION

The burden of Hepatitis B infection cannot be underestimated. The disease accounts for 30% of liver cirrhosis and 53% of hepatocellular carcinoma (HCC) cases worldwide. In young children, most Hepatitis B infections are asymptomatic and unrecognized until complications develop after decades. This disease though is a vaccine-preventable one since the introduction of the hepatitis B vaccine.

Information on the prevalence of seroprotection among children who completed Hepatitis B vaccine in the country is still limited. Factors affecting such response to Hepatitis B vaccine have been shown in some studies [1]. Furthermore, among those who initially responded to a primary three-dose vaccination series, around 15–50% demonstrate low or undetectable antibody to Hepatitis B surface antigen (anti-HBs) levels 5–10 years after primary vaccination [2]. Since the infection and its sequelae are not essentially an issue for childhood survival, Hepatitis B immunization primarily targeting young children remains to be under prioritized [3].

While the universal infant Hepatitis B vaccination was introduced into the National Immunization Program in 1992, because of insufficient funds, the program was never fully implemented in our country until January 2007[4]. And despite an 88% estimated coverage with three doses of Hepatitis B-containing vaccine after a birth dose, we know that seroprotection is more important as this translates to prevention of the disease rather than immunization coverage.

This paper aims to determine the prevalence of seroprotection among children given primary series of Hepatitis B vaccine and look onto the factors that may affect response. Data on these can help identify certain areas that need improvement in our national immunization program including vaccination schedule recommendation to fully combat the scourge of Hepatitis B infection and address factors that affect seroprotection after primary immunization with hepatitis B vaccine.

MATERIALS AND METHODS

This prospective cross-sectional study was done among children ages 3 months to 18 years old seen at outpatient department with records showing complete immunization of primary series of Hepatitis B vaccine with details on the vaccination schedule used, number of doses, place of vaccination, type of vaccine and the site of injection. Children without any record or with incomplete record of immunization history, in immunocompromised state, those who received the last dose of vaccine within four weeks from the time of conduct of the study and those who received booster doses of hepatitis B vaccine were excluded.

Study Procedure

Subject recruitment of children ages 3 months to 18 years old among patients at the pay and charity outpatient department with records of immunization of primary series of Hepatitis B vaccine was done. The principal investigator screened for potential subjects eligible for the study. Informed consent/assent was obtained, and history and physical examination were done. Laboratory requests were given to the parents for the child's serologic examination where ~ 5 ml of blood was obtained. Determination of Hepatitis B surface antigen (HBsAg), antibody to Hepatitis B surface antigen (anti-HBs) and total antibody to Hepatitis B core antigen (total anti-HBc) using enzyme-linked immunosorbent assay (ELISA) method were done in our medical center's laboratory. Parents/guardians were notified in person or via phone communication of the results of serologic tests and medical advice was given accordingly.

Based on statistics that children aged 1 to 5 years old with presenting symptoms of HBV infection would have probability of presenting with acute hepatitis at a rate of 5% to 15% [5], then, using the 5% rate of disease to develop with +/-5% margin

of error estimated at CI 95%, the sample size needed in this study was 100 cases as representative of patients in the general and adolescent pediatrics who have immunization records showing the status of hepatitis B vaccine during their infancy. The sample size was computed with projected dropout rate, the equation 100/(1-0.10) was used to arrive at a final sample size of 111 subjects.

Sample size [100] = {[1.96]^2 x [0.15] x [1-0.07]} / [0.07]^2

Ethics and IRB approval

This study adhered to the ethical principles set out in relevant guidelines, including the Declaration of Helsinki, WHO guidelines, International Conference on Harmonization-Good Clinical Practice, and National Ethics Guidelines for Health Research. This paper has been reviewed by the Institutional Review Board-Ethics Committee of the Philippine Children's Medical Center and was funded by the same institution, as well as by the Philippine Pediatric Society.

Operational Definition of Terms:

1. Seroprotection- the point in time when the amount of antibody in the blood is high enough to confer protection from the antigen that induced its production[6]. Seroprotection against HBV infection is having an anti-HBs level ≥10 IU/L when measured at least 1-3 months after having received a complete immunization schedule[7] using enzyme linked immunosorbent assay (ELISA) method.
2. Primary series of Hepatitis B vaccine-

a. Three-dose series of Hepatitis B vaccine using the schedule 0-1-2, 0-1-6, or other schedule, given at a minimum of 4-week interval, with or without a fourth dose (in cases when the third dose was given at < 24 weeks of age, or when the first dose was given to infants weighing < 2 kgs, OR

b. Three or four-dose Hepatitis B vaccine series as part of the National Immunization Program given by the Department of Health (0-6-10-14)

3. Booster – refers to a vaccination given some time after a primary vaccination series and with the aim of providing rapid protective immunity against a significant breakthrough infection[8]
4. HBsAg nonreactive, anti-HBs reactive, total anti-HBc nonreactive – there is seroprotection against Hepatitis B infection as a result of previous vaccine
5. HBsAg nonreactive, anti-HBs nonreactive, total anti-HBc nonreactive – low or no protective antibodies against Hepatitis B infection despite vaccination which may either be due to waning levels of antibody, or nonresponse to the vaccine
6. HBsAg reactive, anti-HBs nonreactive, total anti-HBc nonreactive – the patient is either in an early acute state of Hepatitis B infection, or in a carrier state with low or no protective antibody
7. HBsAg nonreactive, anti-HBs reactive, total anti-HBc reactive – there are protective antibodies as a result of natural infection with Hepatitis B
8. Place of vaccination – where vaccination was administered either from private clinic, local health center or both
9. Site of vaccination – part of the body where the vaccine was injected either in the thigh, deltoid, gluteal area, etc.
10. Type of vaccine - either monovalent vaccine alone was used or combination (two or more vaccines given as single shot) with or without monovalent dose
11. Age at the first dose of vaccine - vaccination given within 24 hours, > 24 hours-7 days, or > 7 days
12. Schedule of vaccine – schedule followed in giving of vaccine either 0-1-2, 0-1-6, 0-6-10-14, others
13. Interval years from last dose of vaccine to the conduct of this study – either 0-4 years, 5-10 years, > 10 years

Data Collection and Outcome

The following data were gathered from the subjects: age, gender, weight, length/height, weight-for-length / weight-for-height / BMI ; presence of jaundice, icteric sclera, organomegaly and other physical findings that may pertain to liver disease; parental educational attainment (elementary, high school, college, others); parents' occupation, vital status of each parent (alive or

deceased); socioeconomic status based on the income bracket, geographical area or the patient's place of residence based on the regions of the country where the child spent more than half of his lifetime. For analysis against seropositivity to HBsAg, the following data were also obtained: objective evidence of maternal HBsAg status (reactive, nonreactive, unknown) during prenatal check-up, history of transfusion of any blood product ≥ 1 week prior to conduct of study, mode of delivery (vaginal or caesarean section); history of sexual contact, and/or illicit drug use for subjects 10-18 years old. Patients' immunization records were evaluated and the following information were also collected to be analyzed against seroprotection: the site of vaccine injection, age at the first dose of vaccine, age at succeeding doses to identify the schedule used, interval in years from last dose of hepatitis B vaccine to the conduct of this study, place of vaccine administration and the type of vaccine given.

Seropositivity to anti-HBs, total anti-HBc and HBsAg, were the primary outcomes of interest in this study. Determination of patients' demographic profile and analysis of factors possibly affecting seropositivity were the secondary outcome measures. The association between the previously mentioned variables and the serologic results were statistically analyzed.

Data Processing and Data Analysis

Demographics, anti-HBs, total anti-HBc positivity results and HBsAg seropositivity were expressed in frequency and percentages. In testing associations among patients' profiles and anti-HBs, total anti-HBc or HBsAg seropositivity results, chi square test of independence with 2x2 Fischer Exact test adjustment were performed. Analysis in predicting seroprotection was done using multi-logistic regression modelling as well as estimating the odds ratio CI 95%. Any associated p-value less than 0.05 alpha was considered significant. STRATA ver.14 was the statistical software used in processing the data.

RESULTS

Among the 202 children screened with immunization records, only 163 subjects had complete primary series of Hepatitis B immunization. Upon exclusion using the criteria, 111 parents signed the informed consent, however, one parent refused blood re-extraction for validation of result hence was considered a drop out. A total of 110 subjects were left as study participants where fifty subjects (45%) were male and sixty subjects (55%) were female. The male to female ratio was 1:1.2. All subjects completed their vaccination within 1 year of age. Majority belonged to the age group 3-9 years old (42%) with a mean age in years of 5.23 +/- 4.34 SD. Eighty percent came from the National Capital Region (NCR) belonging to the lower middle income socioeconomic status (49%) but most parents were able to attain tertiary level of education (61%). Eighty-seven subjects (79%) had normal nutritional status (Table 1).

Among 110 subjects, 8 (7%) had nonreactive maternal HBsAg while only 1 (1%) had reactive results. The remaining 101 subjects (92%) had unknown maternal HBsAg status. Five percent had history of blood transfusion, while 93% of patients were delivered via normal spontaneous delivery. Among subjects 10-18 years old, none had history of sexual contact nor illicit drug use.

Table 1. Distribution of Subjects According to Sociodemographic Factors

SOCIODEMOGRAPHIC VARIABLES	TOTAL (n/%)
Age	
3 months-2 years old	41 (38%)
3-9 years old	46 (42%)
10-18 years old	23 (20%)
Mean +/- SD	5.23 +/- 4.34
Gender	
Male	50 (45%)
Female	60 (55%)
Geographic area	
Region I-V	22 (20%)
NCR	88 (80%)
Region VI-VIII	0 (0%)
Region IX-XIII	0 (0%)
Socioeconomic status	
Pay (Upper class)	20 (18%)
C1 (Upper middle class)	13 (12%)
C2 (Lower middle class)	54 (49%)
C3 (Upper lower class)	23 (21%)
Indigent (Lower class)	0 (0%)
Parents' Educational attainment	
Elementary	3 (3%)
High School	37 (33%)
College	67 (61%)
Others - Postgraduate	3 (3%)
Nutritional status	
Normal	87 (79%)
Overweight	13 (12%)
Obese	10 (9%)

Seropositivity to anti-HBs, total anti-HBc, HBsAg

Reactivity to anti-HBs (≥10 IU/L) was noted in 54% (59/110) of the study population (Figure 1). Among them, 52% (57/110) were seroprotected after Hepatitis B immunization having concomitant nonreactive results to total anti-HBc (Table 2) with nonreactive result to HBsAg. Three out of 110 participants (3%) were found to be reactive to total anti-HBc, while 1 subject (1%) had reactive results to HBsAg (Figure 1).

Figure 1: Seropositivity to anti-HBs, total anti-HBc and HBsAg

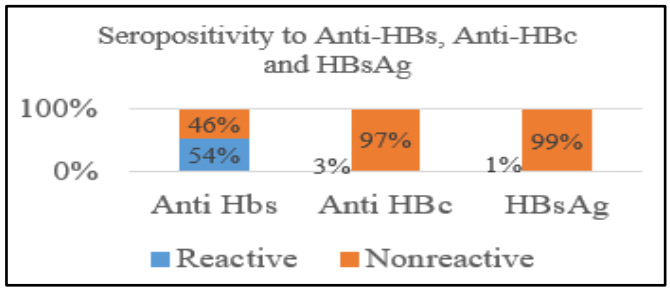

Table 2: Anti-HBs and total anti-HBc Results

	Anti-HBs	
	Reactive (≥ 10 IU/L)	Nonreactive (< 10 IU/L)
Total		
Anti HBc		
Reactive	2 (2%)	1 (1%)
Nonreactive	57 (52%)	50 (45%)

Factors affecting response after primary series of Hepatitis B Vaccine

Among the 57 seroprotected patients from hepatitis B vaccine, the highest seroprotection rate was noted at 82% (32/39) among the youngest age group of 3 months to 2 years, followed by 41% (19/46) among the 3 years to 9 years old group, and only 26% (6/23) from the adolescents 10-18 years old. Fourteen percent of the non-seroprotected subjects (7/51) were as young as 1-2 years old who all received vaccination from the local health center within NCR using combination vaccine with or without monovalent dose.

Majority from the seroprotected group at 56% (32/57) were female (Table 3). However, gender was not significantly associated with seroprotection (p 0.74).

Table 3. Factors Affecting Response to Primary Series of Hepatitis B Vaccine

VARIABLES	SEROPROTECTED (N/%) N= 57	NON-SEROPROTECTED (N/%) N=51	TOTAL N=108	P VALUE
Gender				
Male	25 (51%)	24 (49%)	49 (45%)	0.74
Female	32 (54%)	27 (46%)	59 (55%)	
Geographic Area				
Region I	1 (100%)	0 (0%)	1 (1%)	
Region II	0 (0%)	1 (100%)	1 (1%)	0.15
Region III	2 (29%)	5 (71%)	7 (6%)	
Region IV-A	10 (77%)	3 (23%)	13 (12%)	
NCR	44 (52%)	42 (48%)	86 (80%)	
Place of vaccine				
Private	8 (53%)	7 (47%)	15 (14%)	
Local health center	41 (50%)	41 (50%)	82 (76%)	0.37
Combination	8 (73%)	3 (27%)	11 (10%)	
Age at first dose of vaccine				
Within 24 hrs old	29 (55%)	24 (45%)	53 (49%)	0.79
>24 hours–7 days old	8 (57%)	6 (43%)	14 (13%)	
>7 days	20 (49%)	21 (51%)	41 (38%)	
Schedule of vaccine				
0-1-2	9 (32%)	19 (68%)	28 (26%)	
0-1-6	3 (100%)	0 (0%)	3 (3%)	
0-6w-10w-14w	15 (68%)	7 (32%)	22 (20%)	0.05
Others	30 (55%)	25 (45%)	55 (51%)	
Type of vaccine				
Monovalent alone	22 (41%)	32 (59%)	54 (50%)	
Combination with or without monovalent	35 (65%)	19 (35%)	54 (50%)	**0.01**
Interval years from the last dose of vaccine				
0-4 years	42 (74%)	15 (26%)	57 (53%)	
5-10years	10 (26%)	28 (74%)	38 (35%)	**0.0000**
>11 years	5 (38%)	8 (62%)	13 (12%)	

Seventy seven percent (44/57) from the seroprotected group came from NCR (National Capital Region). All patients were injected in the thigh. Considering the place of vaccination, the number of seroprotected and nonseroprotected subjects were almost equally distributed among those from the private clinic and from the local health center. Although 72% (41/57) of the seroprotected group received their vaccines from local health center, this was not statistically significant (p 0.37), similar to geographic area when analyzed with seroprotection (p 0.15). Only 49% (53/110) of our study population received their

initial dose within 24 hours as recommended. Fifty one percent (29/57) of the seroprotected group received their first dose within 24 hours of birth, while 35% (20/57) were given beyond 1 week of age. Data also revealed that 53% of the seroprotected group (30/57) followed non-specific schedules with minimum of one-month interval between doses. None of these parameters (age at first dose and schedule followed) showed significant association with seroprotection, having p values of 0.79 and 0.05 respectively (Table 3).

The type of vaccine showed a significant difference when analyzed against seroprotection rate. Thirty-five patients (61%) from the seroprotected group were given combination vaccine, with a significant p value of 0.01. Among those who received monovalent type only, 59% (32/54) were nonseroprotected. Meanwhile, majority of those given combination vaccine were seroprotected at 65% (35/54). Protective anti-HBs levels were maintained in 74% (42/57) of subjects less than 5 years after vaccination, 26% (10/38) in cases after 5-10 years, and 38% in cases after 10 years from the last vaccine. This interval year from the last vaccination was analyzed and was also noted to have a significant p value of 0.0000.

Multilogistic regression analysis done on statistically significant variables (type of vaccine and interval years from last vaccination) revealed that only the interval time after vaccination was significant (Table 4). Children are 7 (1/0.13) times less likely to be seroprotected 5-10 years after the last vaccination and children are 4 (1/0.22) times less likely to be seroprotected more than 10 years after vaccination compared to children less than 5 years after vaccination.

Table 4. Multilogistic Regression Analysis of Interval Years as a Factor Affecting Seroprotection

	Odds Ratio	P>|z|	[95% Conf. Interval]	
Interval years from last vaccine dose				
0-4 years				
5-10 years	0.1275510	0.000	0.0502177	0.3239747
>10 years	0.2232143	0.020	0.0631043	0.7895593

Seropositivity to HBsAg and total anti-HBc

Out of 110 subjects, the only patient found to be reactive to HBsAg had concomitant reactive result to total anti-HBc and nonreactive result to anti-HBs (Table 2). The subject is a 6-year-old female, born to an HBsAg positive mother via normal spontaneous delivery (NSD), with no history of blood transfusion, and who received a birth dose of Hepatitis B vaccine together with Hepatitis B immunoglobulin within 12 hours of birth from a private hospital. Patient was asymptomatic at the time of serological survey.

Two of the study participants tested reactive to both total anti-HBc and anti-HBs, with nonreactive HBsAg. One was a 4-month-old male born to a mother with an unknown HBsAg status, delivered by NSD, received his first dose of vaccine at 1 week of life from the local health center. The other one was a 4-year-old female also born to a mother with an unknown HBsAg status, delivered by NSD, given the first dose of vaccine at 1 month of life from the local health center. Both were asymptomatic with no history of blood transfusion.

DISCUSSION

Hepatitis B immunization remains to be the mainstay in the prevention of Hepatitis B infection due to unavailability of specific treatment for the said virus. A complete series of Hepatitis B vaccine induces protective antibody levels in more than 95% of infants, children and young adults [9].

The prevalence rate of the anti-HBs among the pediatric Hepatitis B vaccinees after 5-11 years since primary immunization was determined to be 71.5% in 2007[10]. In an unpublished study in Cagayan de Oro in 2014, about 54% of children had anti-HBs seroprotective levels (>10mIU/ml) 5-6 years after three doses of Hepatitis B vaccine[11], while another unpublished study in Cebu City in 2015 found a seroprotection rate of 48% among children 3-6 years old[12]. In our study done among different age groups, 52% of the overall population were found to have seroprotective anti-HBs levels

after a complete Hepatitis B immunization. However, when grouped according to age, 82% were seroprotected among ages 3 months to 2 years old, 41% among 3-9 years old, and only 26% among 10-18 years old. Due to higher availability of immunization records among younger infants and children, majority of the study participants came from the said age groups and less from the adolescent group, which contributed to the non-homogenous distribution of subjects by age.

Previous studies demonstrated that anti-HBs titers decline over time[6,7]. Though according to a meta-analysis, protection provided by three or four doses of monovalent HB vaccine persists for at least two decades in the great majority of immunocompetent individuals[8], in some studies, antibodies have been demonstrated to become negative in 15-50% of the vaccine responders within 5-10 years[2, 13]A study in 2014 found that 88% seroprotection was seen in less than 5 years after vaccination, however, with less significant decrease to 78% between 5-10 years after vaccination, and 74% 10 years after vaccination[14]. It is quite alarming that, in our study, more than 50% of subjects are not seroprotected and assumed to be already at risk for Hepatitis B infection 5 years after their vaccination. Although a decreasing trend was observed, the higher seroprotection rate 11 years after vaccination compared with 5-10 years after vaccine may be due to recruitment bias that affected the distribution of subjects by age. Although Hepatitis B booster dose is not generally advised among immunocompetent persons due to vaccine-induced immune memory that persists for more than 20 years after immunization[9, 15], a three-dose booster series was recommended among nonseroprotected subjects in this study. Since nonseroprotected subjects in this study cannot be classified as to either being non-responders or secondary to waning levels of antibody because the serologic tests were done at various interval time post-vaccination, a three-dose Hepatitis B vaccination was recommended following a 0, 1, 6 months schedule. According to Su et al in 2013, 95% maintained protective anti-HBs level after a three-dose booster[16], unfortunately, repeat post vaccination testing was beyond the scope of our study.

Male gender is said to be associated with nonresponse to Hepatitis B vaccine, owing to the effect of the sex hormone testosterone that damages the production of the immunoglobulins[17]. Moreover, numerous immunological genes are also found in the X chromosome while only few ones are mapped in the Y chromosome[18]. However, similar to other findings[6, 7, 15] no gender difference was observed in this study.

Our center is a referral center in an urban setting thus most subjects came from National Capital Region with almost equal seroprotection and nonseroprotection rate based on geographical location. The youngest among the nonseroprotected group aged 1-2 years old came from NCR, specifically Quezon City. According to He et al in 2015, the possibility of a low level of or even a negative anti-HBs for children at or under age 3 should be a concern[19]. Circumstances surrounding administration of the vaccine should be investigated especially vaccine handling and storage. Unfortunately, this is beyond the scope of this study. The effectiveness of vaccine depends on the source of procurement and proper maintenance of cold chain, which is largely affected by the place where the vaccine was given. In a tropical country like ours, adherence to the recommended vaccine storage of refrigerator temperature between 2-8C remains a challenge among local health centers. In a study in 2011, 100% seroprotection was observed in children who received vaccine from a private source[20], in contrast with our findings of equal seroprotection and nonseroprotection rate among patients from both private and local health center. Although majority of the seroprotected group were patients who received vaccine from local health centers, this did not show any significant difference.

The WHO recommends that the first dose of vaccine be administered within 24 hours of birth to prevent mother to child transmission of infection[21]. Our data shows that only 48% (53/110) of the study population received their initial vaccine dose within 24 hours as recommended despite being covered by the Mandatory Infants and Children Health Immunization Act of 2011. Though some authors reported lower proportions of individuals with anti-HBs ≥ 10 mIU/mL if the first vaccine dose had been given directly after birth[22, 23], findings in this study are in accordance with other observations[24, 25] that this is not the case, hence, vaccination schedules starting at birth is supported in order to attain timely vaccination and higher vaccination rates.

Dosing schedule is another important factor in the development of antibody response and titer level. There should be a minimum gap of 8 weeks between the 2nd and 3rd doses, and at least 16 weeks between the 1st and 3rd doses of Hepatitis B vaccination[26]. However, to minimize frequency of healthcare visits and not to miss patient's compliance, the dosing schedule in the EPI is at 6-10-14 weeks. The WHO has recommended 0-1-2 schedule for highly endemic countries like the Philippines however, in this study, 68% of those who followed this schedule were seronegative, similar to the findings of Mapandi of 43% seroprotection rate[27]. Yao et al in 2015 demonstrated a lower seropositive anti-HBs level with other schedules compared to 0-1-6 schedule[28], likewise our findings in this study showed 100% seroprotection among the 0-1-6 group. Although some studies have shown the 6-10-14 schedule to be effective, other studies demonstrated a low seroprotection rate of 68% compared to the 0-1-6 schedule[20]. Among those who followed this 0-6-10-14 schedule (subjects from the local health centers), this study found a 68% seroprotection rate, although overall, the vaccination schedule had no significant association with seroprotection.

Studies have compared combination and monovalent vaccines and have shown little difference between the two types in terms of immunogenicity after a dose of HBV at birth[29]. Combination vaccine is reported to have shown good immunogenicity and good long term anti-HBs persistence which could advantageously replace separate monovalent vaccines in areas of high Hepatitis B endemicity in terms of clinical, economic and strategic benefits[30]. In our study, majority from the seroprotected group were given combination vaccine although this did not show significant difference on multi-logistic regression. A higher seroprotection of 65% was also seen among those who were given combination vaccine with or without monovalent dose. Interestingly, 59% of those who only received monovalent vaccine were nonseroprotected. The variation in vaccine brands used may contribute to the difference in immunogenicity of the monovalent vaccine and could be a possible explanation for this finding. Vaccine brands that were used were not explored in this study as records from the patients mostly did not include this information.

In this study, 1% of the subject participant was positive to HBsAg that was a case of vertical transmission. This is closely similar to two separate local and unpublished studies in 2014 and 2015 reporting an HBsAg positivity rate of 0.3% and 0.6% among preschool and school aged children in Cebu City and Cagayan de Oro, respectively[11,12]. According to Wong et al in 2013, the Philippines is still highly endemic for Hepatitis B with a prevalence rate of 16.7%[31]. Since this is a single-center study in pediatrics with limited sample size, the finding of 1% Hepatitis B infection rate is not reflective of the true national HBsAg prevalence and cannot be used to conclude the effectiveness of our country's universal immunization program. However, with our findings of decreasing seroprotection rate at <50% 5 years and beyond after vaccination, there is a need to review our Hepatitis B immunization program, consider serologic anti-HBs level testing as early as 5 years post vaccination to monitor response, and probably

revisit the current recommendation regarding Hepatitis B booster administration.

The HBsAg reactive patient and her mother were advised further hepatitis serologic and liver function tests with follow up at subspecialty clinic. It is unfortunate that even if this patient was given the recommended Hepatitis B vaccine and hepatitis B immunoglobulin at birth as recommended to babies born to HBsAg reactive mothers, the patient still turned out HBsAg positive.

The two other study participants who tested reactive to total anti-HBc and were also reactive to anti-HBs but nonreactive to HBsAg, could be an indication of protective antibodies from natural infection. However, maternal transfer of antibody cannot be excluded in one patient who was 4 months of age. Both were advised specific testing of anti-HBc IgM and IgG and complete serologic viral hepatitis tests including maternal HBsAg work up.

CONCLUSION

In this study, 52% of patients among different age groups were found to have seroprotective anti-HBs levels after complete primary Hepatitis B vaccination. A decrease in seroprotection rate was demonstrated at < 50% 5 years and more post-vaccination with statistical significance. Gender, geographic area, age at first dose, place of vaccination, schedule and type of vaccine were among the other factors analyzed which, in this study, did not conclusively affect seroprotection rate.

RECOMMENDATION

There is a need to review the implementation of Hepatitis B immunization program in our country as well as the recommended hepatitis B vaccine schedule and booster recommendation. Further studies in the community, or among different hospital institutions should be carried out for larger study population to determine seroprotection rate and factors affecting it 1-2 months after vaccination. Subjects with hepatitis B booster can also be a good population to determine seroprotecton levels amongst them. Determination of anti-HBs levels 5 years or more post vaccination may be considered to detect the need for booster dose and prevent breakthrough Hepatitis B infection. Follow-up studies on the subjects who were not seroprotected should be done, with repeat anti-HBs testing post completion of booster doses to identify the true nonresponders.

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