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Factors Associated with Antibody Levels among Children Aged 15 to 59 Months Vaccinated against Hepatitis B during the Expanded Program on Immunization in Cameroon

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Abstract

Background: the hepatitis B virus infection remains a major public health problem worldwide. It can lead to a liver cirrhosis and/or hepatocellular carcinoma. The World Health Organisation (WHO) has recommended the implementation of generalised vaccination programs against hepatitis B. In Cameroon, this vaccine was introduced in the expanded program on immunization (EPI) in 2005, but few studies have assessed the immune response. Objective: the general objective of this study was to identify factors associated with antibody levels among children aged from 15 to 59 months vaccinated against hepatitis B during the EPI in Cameroon. Method: this was a cross-sectional study carried out from December 2021 to June 2022 in a paediatric centre of Yaoundé (Cameroon). We analysed the antibody level in children vaccinated against hepatitis B within the framework of the EPI. We enrolled children who had received a series of 3 intramuscular doses of hepatitis B vaccine at 6, 10 and 14 weeks after birth. Some children could receive a 4th booster dose between 12 months. The antibody level was assessed by measuring the anti-HBs in such children, aged 15 - 59 months. A good immunization was defined as a serum level of anti-HBs antibody level above 100 IU/mL; a poor immunization, for an anti-HBs antibody level between 10 and 100 IU/mL; and a non-immunization, for an anti-HBs antibody level < 10 IU/mL. Asso-

ciation between explored factors and poor or non-immunization was evaluated through the Chi square test. The significance threshold was defined at $p < 0.05$. Results: sixty subjects were included in the study with a slight female majority: 31 cases (52%). The average age was 38.5 ± 15.7 months (range 15 - 59 months). We found 32 (53%) cases of good immunization; 21 (35%) of poor immunization; and 7 children (12%) with a non-immunization. The only factor associated with poor or non-immunization was the age between 37 - 59 months ($p = 0.016$). Conclusion: Anti HBs Antibody levels in children vaccinated against hepatitis B virus were globally satisfactory in our series. Results show an association between low antibody levels with older age (over 36 months), suggesting a circulating antibodies levels decrease over time, yet deemed protecting until 59 months.

Keywords

Hepatitis B, Vaccination, Children, Antibody Levels, Immunization, Cameroon

1. Introduction

The hepatitis B virus (HBV) remains wildly expanded in the world. The prevalence in sub-Saharan Africa (SSA) is high, varying from 7% - 21% [1]. A chronic infection could lead to liver cirrhosis and/or liver cancer. The prevalence of HBV exposure is estimated at 60% among children between 0 and 5 years old [2]. Therefore, the World Health Organization (WHO) has recommended the implementation of generalized vaccination programs against the HBV into routine national infant immunization programs [3]. In Cameroon, this vaccine was introduced in the Expanded Program on Immunization (EPI) in 2005 [3]. This one is included in a pentavalent vaccine associated diphtheria-tetanus-pertussis (DTwP) and Haemophilus influenzae type b (Hib) [4] [5]. The three doses of the pentavalent vaccine are administrated according to the recommended schedule: first dose 6 weeks after birth and intervals between 2 injections of at least 30 days. For children born from a mother infected by the HBV, a first dose should be done at birth. For all children, another 4th booster dose at 12 months is recommended but not included on the EPI. And children born from a mother infected by HVB have also received a prior dose at the birth. The objective is to obtain an antibody titled anti-HBs ≥ 10 mUI/ml. Studies have shown that this serologic response is observed in almost 90% of cases. After a vaccination campaign, we observed a significant reduction in liver cirrhosis and hepatocellular carcinoma some years later in Taiwan [6]. Some factors may negatively affect the immunization and the child will risk an infection despite the vaccine administration. Among these factors, in literature we have: a hepatitis B infection in the mother [7], the poor nutritional status [8], an HIV infection of the child [9], the low number of doses [10], the poor type of vaccine [11], and the male sex of the

child [3]. In SSA, problems associated with conservation and cold chain of these vaccines could also affect their efficiency [3]. For this reason, the serologic response to the hepatitis B vaccine, and factors associated, have to be assessed in children in our area.

2. Objective

The general objective of this study was to identify factors associated with the antibody level among children aged from 15 to 59 months vaccinated against hepatitis B during the EPI in Cameroon.

3. Materials and Methods

We carried out a cross-sectional study from December 2021 to June 2022 at the Mother and Child Centre of the Chantal Biya Foundation (Yaoundé-Cameroon). It is a public health care centre specialized in children disease. We included all children aged from 15 to 59 months coming for any reason vaccinated before against the HVB during the EPI. The protocol recommends a series of 3 intramuscular doses of hepatitis B vaccine at 6, 10 and 14 weeks after birth. The programme has been adjusted to coincide with the oral poliomyelitis virus and diphteria-pertussis-tetanus vaccination schedule. Some children could receive a 4^{th} booster dose at 12 months. Children without a complete HBV vaccination attested by an immunization card were excluded.

Through a questionnaire, we collected sociodemographic data (age, sex, birth weight, HIV status and HBV status of the mother through the HBs Antigen), and we measured the weight of children. The weight-for-age Z-score (WAZ) was used to assess the nutritional status. The WAZ evaluation was using the Centres for Disease Control and Prevention 2000 child growth charts (CDC-2000). A poor nutritional status was defined when the WAZ ≤ -2. With the immunization card, we noted the time and the number of HVB vaccine dose.

Then we collected a 5 ml of venous blood sample at the elbow for analysis. All samples were tested for anti-HBs by VIDAS Anti-HBs Total II® with a specificity of 99% (95% confidence interval: [98.1% - 99.5%]) and a sensitivity of 99% (95% confidence interval: [98.2% - 99.5%]).

Anti-HBs antibodies were expressed in international units per milliliter (IU/mL). A good immunization was defined as a subject with an anti-HBs antibody level ≥ 100 IU/mL; a poor immunization was defined as an anti-HBs antibody level between 10 and 99 IU/mL; and a non-immunization was defined as an anti-HBs antibody level < 10 IU/mL.

Statistical analysis was carried out using Microsoft Excel and SPSS version 21 software. The association between factors and a poor or a non-immunization has been assessed through the Chi square test. The significance threshold was defined at $p < 0.05$. Parents of children gave their consent and the National Ethics Committee of the Faculty of Medicine and Biomedical sciences (University of Yaoundé 1/Cameroon) approved the study.

4. Results

A total of 77 children have been included. We excluded 17 due to the absence of an immunization card. Thus, we enrolled 60 children for the study with 29 males (48%). The mean age was 38.5 ± 15.7 months with a majority, 30 children (50%), aged between 37 - 59 months.

Most of children (56/60) had a birth weight ≥ 2500 grams. Looking at the WAZ, the nutritional status was good in 51/60 children (85%). One child over sixty have a mother infected by HIV and three others a mother infected by HBV. These children born from a mother infected by HBV received the first dose of HVB vaccine at the birth as recommended. All the 60 children received the three doses of vaccine at 6, 10 and 14 weeks after birth included in the EPI, and 12 children (20%) received a 4th booster dose at 12 months.

Regarding Anti-HBs levels, there were 32 (53%) cases of good immunization, 21 (35%) of poor immunization and 07 (12%) of non-immunization to hepatitis B virus (Figure 1).

The only factor associated wi poor or non-immunization was the age of 37-59 months ($p = 0.016$). The sex ($p = 0.809$), the weight birth < 2500 grams ($p = 0.106$), the poor nutritional status ($p = 0.384$), the 4th booster dose ($p = 0.301$), an HIV or HBV infection of the mother ($p = 0.970$) were not associated with the antibody level (Table 1).

5. Discussion

We approached 77 children but enrolled 60. We excluded 17 of them due to the absence of an immunization card to attest that the child received the injection. Some children came to the hospital for a care different from vaccination. For this reason, parents did not come with the immunization card. This document is useful to ensure the observation of the EPI schedule.

All the children have received the 3 doses of vaccine at 6, 10 and 14 weeks after birth. Children born from a mother infected by HVB have also received a prior dose at the birth [9]. This dose is a monovalent HVB vaccine, which is not

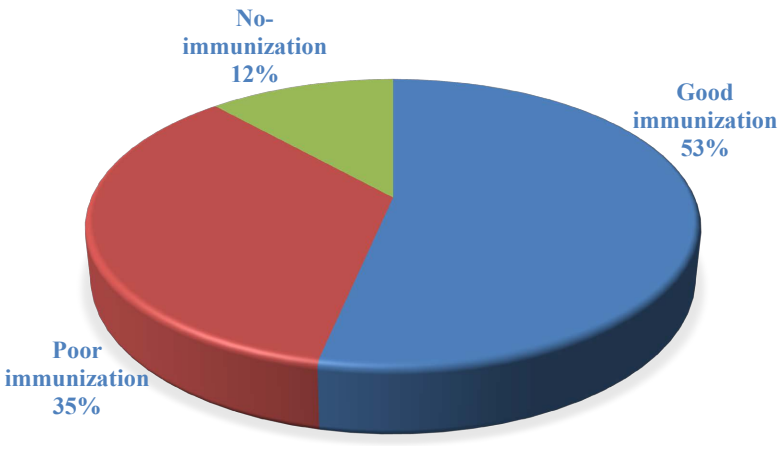

Figure 1. Classification of children according to the vaccine response.

Table 1. Factors associated with the immune response.

Factors	Number	Poor or non-immunization n = 28	p
Age (months)			
15 - 24	16	04	
25 - 36	13	04	**0.016**
37 - 59	31	**20**	
Sex			
Female	31	14	0.809
Male	29	14	
Vaccination protocol's			
03 doses of vaccine	48	24	0.301
03 dose of vaccine and a 4th booster dose at 12 months	12	04	
Nutritionnal status			
Good	51	25	0.384
Poor	09	3	
Mother infected by HIV or HBV			
Oui	04	02	0.970
Non	56	26	

yet included in the EPI schedule in Cameroon. Thus, parents have to pay by themselves to protect the baby. The cost could reduce the access to this prior dose of vaccine.

The nutritional status of children was quite good, despite the fact that we carried out the study in a developing country where malnutrition is common/prevalent. The explanation is the fact that our sample is coming from Yaoundé, the capital of the country. In urban area, parents have a better educational level and prevent malnutrition from their infants. Thus, the effect of the nutritional status on antibody levels was mild in our sample.

The antibody level in children vaccinated against the hepatitis B virus was globally satisfactory in our series with 88% of children with anti-HBs ≥ 10 UI/mL (53% of good immunization and 35% of poor immunization). On the other hand, 12% of children vaccinated are non-immunized. They remain exposed to an HVB infection. Identifying the cause of this poor response in some children is a challenge in improving immunization rate. In developed countries, the quality of vaccine should be discussed looking the storage conditions [3].

As concerned with associated factors, we did not find any association between the sex and the nutritional status with the serologic response to the vaccine as described in some other studies. We did not observe a difference between children born from a mother infected by HIV and other children. This result is probably due to methods of preventing mother-to-child transmission of HIV implemented in the country. It has been described in Botswana where they observed a high response to the HBV vaccine among children exposed to HIV but uninfected [8].

Concerning children from women infected by HVB, we did not observe a difference in anti-HBs levels with those with non-infected women. The vaccination at birth significantly reduces the transmission risk of the HBV to the baby [12] [13].

The factor associated with non or poor immunization was the age between 37 - 60 months. This result suggests the importance of serological monitoring of vaccination efficiency as age increases [3].

The limit of the study is the small size of the sample. We recommend carrying out an observational study about the vaccine against HBV efficacy in the general Cameroonian population, 17 years after its introduction in the EPI [14]. A study carried out in US shows that the antibody level remains satisfactory until the adolescence [15].

6. Conclusion

Antibody levels in children vaccinated against hepatitis B virus were globally satisfactory in our series. Results show an association between low antibody levels and increased age, over 36 months, suggesting circulating antibodies levels decrease over time but remain acceptable until 59 months.

Acknowledgements

We wish to assess the antibody level in children vaccinated against HVB during the EPI. In children with a poor immunization status, we want to identify factors leading to a poor antibody level. Thus, we can define a strategy to improve the protection against the HVB.

Ethical Approvals

Parents of children gave their consent and the National Ethics Committee of the Faculty of Medicine and Biomedical sciences (University of Yaoundé 1/Cameroon) approved the study. All children anti-HBs-negative were invited to return to receive an HBV vaccination.

Authors' Contributions

NDJITOYAP NDAM Antonin Wilson, principal investigator, conceptor, drafted the manuscript.

NDAM MEFIRE Alpha Hamed Béchir, investigator, data collection and analysis

BEKOLO Winnie, investigator.

NSENGA DJAPA Guy Roger, investigator.

NGO UM SAP Suzanne, interpretation of results.

KOKI NDOMBO Paul, materials tools, reviewer.

NDJITOYAP NDAM Elie Claude, the guarantor.

Conflicts of Interest

The authors declare no competing interests.

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