Scientific Research Publishing

Open Journal of Pediatrics, 2022, 12, 203-212
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Completeness and Timeliness of Hepatitis B Vaccination in Preschool Children: Determinants for Good and Timely Uptake in Libreville, Gabon

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How to cite this paper: Minto'o, S., Bignoumba, E.I., Loembe, F., Mekame, A., Abang, L., Zoua, D. and Ategbo, S. (2022) Completeness and Timeliness of Hepatitis B Vaccination in Preschool Children: Determinants for Good and Timely Uptake in Libreville, Gabon. *Open Journal of Pediatrics*, **12**, 203-212.
https://doi.org/10.4236/ojped.2022.121022

Received: December 2, 2021
Accepted: March 18, 2022
Published: March 21, 2022

Abstract

Background: Gabon is endemic for hepatitis B, but they have still not reached the WHO goal for Hepatitis B vaccination coverage. We aimed to determine the rate of completeness and timeliness of hepatitis B vaccination among children under 15 years of age in Libreville. **Methods:** Cross-sectional study conducted over 9 months, including children randomly selected from vaccination centres, nurseries and kindergartens. We collected data on the child, socio-economic characteristics of the families, and dates of administration of hepatitis B vaccines. We determined the compliance of the vaccination dates according to the vaccination start pattern. **Results:** We included 453 children, of whom 236 were girls, for a sex ratio of 0.92. A total of 87% (95% CI [83.9% - 90.1%]) of children had started and completed their 3 doses of vaccine before the 12th month of age. 149 subjects had received their 3 doses on time according to the original vaccination schedule, *i.e.* 32.9% (95% CI [28.6% - 37.2%]). Factors significantly associated with completeness were vaccination in a public centre OR = 114 [47.2 - 347] $p < 0.0001$, young age at 1st dose OR = 3 [1.6 - 5.5] $p < 0.001$. Age at first dose was the predictor of timeliness aOR = 1.3 (95% CI [1.2 - 1.5] $p < 0.001$). **Conclusion:** The respect for the vaccination deadlines is insufficient in our context, solutions exist to improve this situation.

Keywords

Hepatitis B, Vaccination, Timeliness, Completeness, Children, Gabon

1. Introduction

Hepatitis B virus (or HBV) infection is a global public health problem affecting about 500 million people worldwide, and responsible for nearly one million deaths in 2017 [1]. The prevalence of chronic HBV infection is estimated at 6.1% in Africa and 7.4% in Gabon [1] [2].

Vaccination is the best means of preventing hepatitis B because it provides safe and effective protection in over 95% of cases [3]. The efficacy of immunization induced by vaccination depends on the timeliness of dose administration [4] [5].

Universal vaccination against hepatitis B for infants under 12 months of age has been in place in Gabon since 2004. This vaccination is administered in combination with the diphtheria-tetanus-pertussis-Haemophilus influenza b (Penta) vaccines at 6, 10 and 14 weeks in the vaccination centres of the Expanded Program of Immunization (EPI) in Gabon [6]. However, this vaccination schedule does not include a birth dose as recommended by the WHO and is widely practised in South East Asia [4] [7]. It should also be noted that vaccination against hepatitis B can be done by isolated or combined dose (Penta or Hexa) in private practice. Hepatitis B vaccination coverage among infants was estimated to be 71.3% in 2010 [8] [9].

Our impression in the field was that there were a proportion of children who started hepatitis B vaccination but did not complete their schedule and that families' compliance with the schedule was not accurate. We conducted a survey with the primary aim of assessing the completeness and timeliness of hepatitis B vaccination among children before the age of 12 months in Libreville. The secondary objective was to identify factors related to non-completeness or delay of vaccination.

2. Material and Method

Type and setting of the study: This is a cross-sectional, multicenter study conducted over 9 months from April 1 to December 31, 2019. It took place in Libreville, in the vaccination and outpatient departments of 2 hospitals and 3 health centres selected at random.

2.1. Conduct of the Study

- **Calculation of the number of subjects needed**

We calculated the sample size using Statcalc in Epi info7.2 software. We entered 170,000 as the size of the target population (children aged 0 - 6 years https://www.populationpyramid.net/fr/gabon/2017). The acceptable margin of error was 5%, taking as reference the estimated prevalence of hepatitis B vaccination coverage at 1 year of age of 71% [8] [9] in Gabon. The attenuation factor of our survey model was 1.3, the confidence interval was 95%, the number of clusters was 5, and the total number of subjects needed was 420, or 84 per cluster.

- **Sampling**

The study population consisted of children aged 4 months to 6 years, who

came for consultation, weighing or vaccination, or were hospitalized. They were selected by random selection.

We did not include children without a booklet or with a blank booklet; children with no dose of hepatitis B vaccine; any child brought by a third person who is not the child's parent or guardian; any child under 4 months of age or over 6 years of age; any child whose parent refused to participate. The data collected included the child's age and sex; place of recruitment; age at first dose (in days) of hepatitis B vaccine; type of vaccine at first dose; dates of the child's other hepatitis B vaccinations; and the parents' socioeconomic data at birth and in the first six months after birth.

2.2. Case Definition

We considered two types of schedule: the EPI schedule (combined dose administered at 6, 10 and 14 weeks; and the WHO schedule (1st isolated dose at birth). Vaccination at birth was considered as such when it occurred within the first 72 hours of life. For children vaccinated in EPI centres, the interval between each dose of vaccine was 28 days, with a tolerance of 5 days to take into account certain adjustments in the field. We counted as:

- "Complete" means any child who has started a hepatitis B vaccination, and who had received his 3rd dose before the age of 12 months.
- "Non-complete" means any child who has started a hepatitis B vaccination, and who had not received 3 doses before the age of 12 months, or who had received their 3rd dose after the age of 12 months.
- "Up to date" means any "complete" child who had received each of his or her doses within the time frame prescribed by the immunization schedule followed: the EPI schedule or the WHO schedule.
- "Late" means all children in "full" who had at least one dose out of time, with a tolerance of a 5-day mark-up.

2.3. Statistical Analysis

Data were collected on Epi Info 7.2.2. We performed a descriptive analysis to determine the characteristics of the sample and to estimate the prevalence of immunization coverage. Quantitative data were expressed as a median for children, mean for parents' age. We compared medians with the Wilcoxon-Mann-Whitney test and means with the Student's t-test. The categorical data were expressed as frequencies, to compare them we used the Chi-square test of independence, and when the number of children did not allow it we used the Fisher's correction. Completeness, non-completeness, delay and up-to-date vaccination rates were expressed with a 95% confidence interval. We created univariate and multivariate logistic regression analyses (adjusted odd ratio—aOR) to measure the relationship between parent and child parameters and completeness or timeliness of the vaccination schedule. The dependent variables in the univariate model were: age and sex of the child, sibling rank, age of both parents at the

child's birth, the income-earning activity of both parents at birth, age at 1st dose, time between doses, and completeness of schedule only at EPI centre. The variables were chosen for the multivariate model based on statistical significance in the univariate models and relevance based on the literature. The threshold for statistical significance was set at $p < 0.05$ for a two-tailed test. Confidence intervals were calculated using the Miettinen method. The analysis was performed using Epi Info 7.2.2 from the CDC, the verification of our results on MS Excel software, the multivariate analysis was performed using the online statistical analysis software Pvalue (https://www.pvalue.io/fr/).

2.4. Ethical Considerations

This survey was approved by the EPI Directorate of Gabon, the directors of the university hospitals and health centres participating in the study before its deployment in the field. Following the instructions of these directors, we did not collect information on the religion or ethnicity of the children's parents. The parents' agreement was obtained by signing an informed consent form.

3. Results

We included 453 children, 394 of whom had started and completed their vaccination schedule before the 12th month, *i.e.* 87% (95% CI [83.9% - 90.1%]) of children were complete for their hepatitis B vaccination.

Analysis of the characteristics of children in general, and according to whether they had completed their hepatitis B vaccination schedule, showed that there was no significant difference by gender, with children who had received a single first dose completing their schedule less than those who had received a combined first dose in the EPI. There was no difference in general for the place where children were recruited, but children recruited in the CHUL had a significant ($p = 0.02$) higher vaccination coverage than other groups. Children who started their first dose with an isolated injection of hepatitis B vaccine had a significant lower vaccination coverage than children who started in an EPI centre with a combined dose ($p < 0.001$) Also children who completed their programme only in EPI centres had a higher vaccination coverage than those who mixed their program ($p < 0.001$) (**Table 1**).

The average age of both parents did not differ by completeness status, but children whose mothers were students had a lower completeness rate than the other categories (**Table 2**).

Regarding the punctuality of dose administration: among the children vaccinated according to the EPI, of the 280 who had their 1st dose on time, 37.9% (n = 106) had received their 2nd dose late, of the 174 who had received their 2nd dose on-time 24.7% (n = 43) had received their 3rd dose late. A total of 149 subjects had received their 3 doses on time according to the baseline vaccination schedule, *i.e.* 32.9% (95% CI [28.6% - 37.2%]) (**Figure 1**).

Factors associated with completeness of the vaccination coverage were: an age

Table 1. Characteristics of children in general and according to the completeness of hepatitis B vaccination coverage.

	TOTAL (N = 453)		COMPLETE (n = 393)		INCOMPLETE (n = 60)		*p*
	number	frequence	number	frequence	number	frequence	
Sex							
Female	236	52.1%	210	53.4%	26	43.3%	NS
Male	217	47.9%	183	46.6%	34	56.7%	
Recruitment location							
AWENDJE	96	21.2%	88	91.7%	8	8.3%	NS
NZENG-AYONG	86	19.0%	73	84.9%	13	15.1%	NS
OKALA	86	19.0%	73	84.9%	13	15.1%	NS
CHUL	95	21.0%	88	92.6%	7	7.4%	0.02
CHUME	90	19.8%	71	78.9%	19	21.1%	NS
Type 1st dose							
ISOLATED	71	15.7%	55	77.5%	16	22.5%	<0.001
PENTA PEV	382	84.5%	338	88.5%	44	11.5%	
EPI only							
YES	337	74.4%	336	85.5%	1	1.7%	<0.0001
NO	116	25.6%	57	49.1%	59	50.1%	
Rank							
Median	2		2		2		NS
Q1	1		1		1		NS
Q3	3		3		3		NS
Age at 1st dose (days)					(n = 60)		
Average	51.4 ± 10.6		47.6 ± 5.2		73.7 ± 54.7		<0.001
1st interval (days)					(n = 35)		
Average	32.7 ± 4.2		32.6 ± 4.1		34.7 ± 6.6		<0.0393
2an interval (days)							
Average	31.7 ± 3.2						

Table 2. Characteristics of the parents in general and according to the completeness or not of the hepatitis B vaccination.

	TOTAL (n = 453)	COMPLETE (n = 393)	INCOMPLETE (n = 60)	*p*
Mother's age at birth				
Average	27.1 ± 5.9	27.1 ± 5.8	27.1 ± 6.1	ns
Median	27	27	27	
Father's age at birth				
Average	33.4 ± 7.2	33.2 ±7.2	34.2 ± 7.3	ns

Continued

Median	33		33		34		
Mother's activity							
Pupil/Student	148	32.70%	125	31.80%	23	38.40%	**0.04**
Graduate student	56	12.40%	53	13.50%	3	5.00%	0.679
Unoccupied	112	24.70%	100	25.40%	12	20.00%	0.23
Liberal	43	9.60%	38	9.70%	5	8.30%	0.417
Employee	94	20.80%	77	19.60%	17	28.30%	0.053
Father's activity							
Pupil/Student	36	7.90%	32	8.10%	4	6.70%	0.479
Graduate student	26	5.70%	25	6.30%	1	1.70%	0.84
Unoccupied	18	4.00%	12	3.10%	5	8.30%	0.083
Liberal	123	27.20%	109	27.80%	14	23.30%	0.18
Employee	250	55.20%	215	54.70%	36	60.00%	0.28

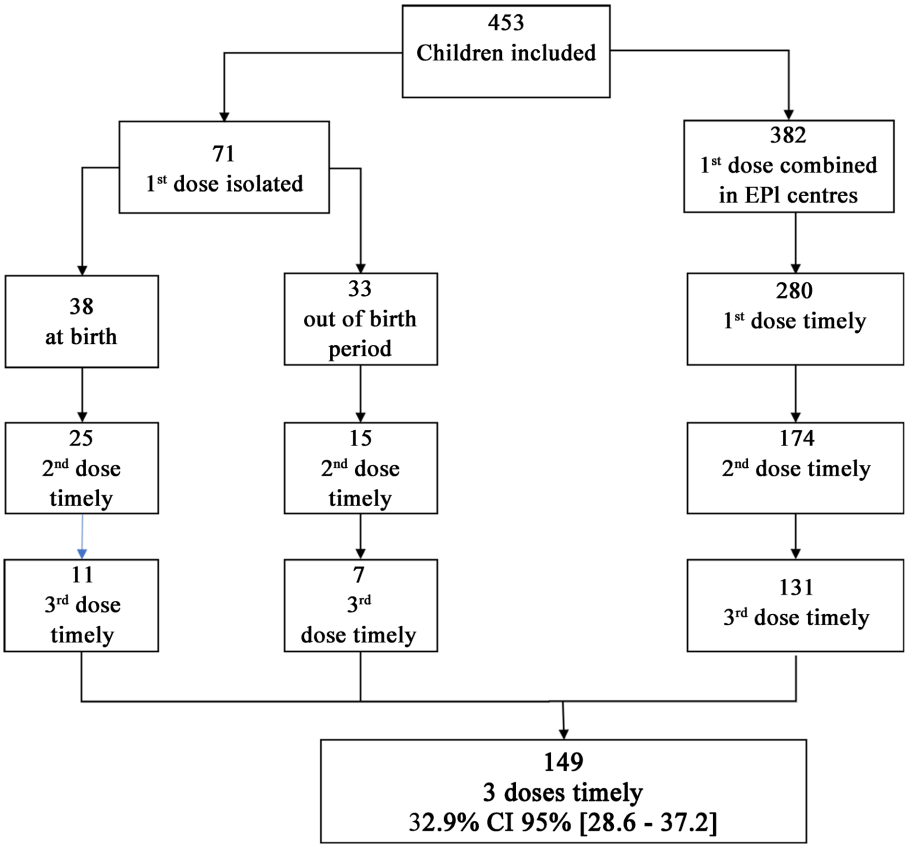

Figure 1. Flow chart of timely uptake of hepatitis B vaccination in preschool children in Libreville.

at first dose lower than the overall median age at first dose (OR = 3; $p < 0.001$); a schedule completed only in an EPI centre compared to schedule in mixed centres (OR = 114; $p < 0.001$); and a scheduled timely executed vs delayed schedule

(OR = 34.5; $p < 0.001$). Factors associated with timeliness of the administration of hepatitis B vaccine were: an age at first dose lower than the overall median age at first dose (OR = 6.8; $p < 0.0001$); a schedule completed only in an EPI centre compared to schedule in mixed centres (OR = 6.8; $p < 0.0001$); (Table 3). The first dose given in an EPI centre was the explanatory and predictive variable for completeness status aOR = 6.4 (95% CI [2.8 - 14.6]) $p < 0.001$. There was no explanatory variable for timeliness. Age at first dose was the predictor of timeliness aOR = 1.3 (95% CI [1.2 - 1.5], $p < 0.001$).

4. Discussion

For this study, we were able to gather a sample of participants representative of the children of Libreville. The general characteristics of the children and parents were similar to those of the last Demographic and Health Survey [10]. The distribution according to the site of inclusion did not show any significant difference either. Our sampling method and the characteristics of our sample allow us to extrapolate our results to the population of children in Libreville in the same age group. Libreville and its periphery represent 60% of the total population of Gabon [10].

In this study, we found that 87%, or nearly nine out of ten children who had started a hepatitis B vaccination had completed their schedule. This rate is close to 2011 WHO target of 90% hepatitis B vaccination coverage by 2020 [9]. While the WHO estimates hepatitis B vaccination coverage at 70%, this study reveals that the WHO vaccine targets are achievable. However, the national vaccination policy based on the EPI, although 87% followed, does not cover the first 6 weeks of the child's life as recommended by WHO. In fact, in the national vaccination scheme, the hepatitis B vaccine is introduced at the age of 6 weeks as part of the pentavalent vaccine, thus exposing children under 6 weeks of age to a risk of contamination against hepatitis B. A previous survey by Ategbo *et al.* showed a hepatitis B vaccination coverage rate of 71% [8].

Table 3. Factors associated with the completeness and timeliness of hepatitis B vaccine uptake.

CHARACTERISTICS	COMPLETENESS			TIMELY		
	OR	95% CI	*p*	OR	95% CI	*p*
Age at 1st dose < median	3	[1.6 - 5.5]	<0.001	6.8	[4.3 - 10.8]	<0.0001
Mother's age < median	1.01	[0.6 - 1.8]	*NS*	0.7	[0.5 - 1.1]	NS
Father's age < median	1.07	[0.6 - 1.8]	*NS*	1.05	[0.6 - 1.8]	NS
Father employee vs. other	0.8	[0.5 - 1.4]	*NS*	0.6	[0.4 - 0.9]	NS
EPI only vs non EPI	(aOR) 114	[47.2 - 347]	<0.0001	3.3	[1.9 - 5.6]	<0.0001
1st dose EPI	2.2	[1.2 - 4.2]	=0.012	1.45	[0.8 - 2.6]	NS
CHUL vs other places	1.88	[0.98 - 4.8]	*NS*	0.5	[0.3 - 0.8]	NS
Timely	34.5	[4.5 - 234.6]	<0.001			

The factors associated with complete vaccination coverage were: age at the first dose lower than the median age of vaccination for the [first] dose; the fact of carrying out all the vaccinations in an EPI centre and the punctuality of vaccination sessions. In these factors, we can identify elements linked to the commitment of parents to vaccinate to protect their children: age of children at the first dose and punctuality of vaccination sessions; and an element linked to the State's vaccination policy: carrying out the vaccines in an EPI centre. A meta-analysis of 2020 shows that in 15 sub-Saharan African countries, parents' conviction to vaccinate their children is an essential element, and parents' beliefs influenced the decision [11]. In Vietnam, a survey conducted in the Mekong Delta region shows that government involvement in providing immunization to the population is critical to achieving the WHO targets for hepatitis B vaccination. In this study, parents reported the lack of hepatitis vaccination as being since it was not carried out by vaccinators in 53% of cases [12].

Adherence to vaccination dates ensures optimal immunization against the target disease [1]. In our series, 1 in 3 children (32.9%) had received their 3 doses of hepatitis B vaccine on time. This could imply that strictly speaking only 1 out of 3 children in our context have a solid immunity against HBV infection. The factors associated with timely vaccination are also related to the parent's decision to vaccinate (age at the date of the first vaccination), but also to the state's coverage of the vaccine (vaccination in an EPI centre). The age of the child at the time of the first vaccination is determined by both the parents and the vaccinators. Indeed, the latter indicates to the parents the dates of the forthcoming vaccinations, and the parents take the children to the centre according to these indications. An oversight or an error could therefore distort the completeness or the respect of the deadlines if the parents are not attentive. Age at first dose was predictive of timeliness. This finding was found in several studies conducted in developing countries, and the age of the child was mentioned in 17/62 studies pooled by a meta-analysis as a predictor of compliance [13]. It seems appropriate to explore solutions that would involve modern means of communication to remind people of the dates of vaccination, in addition to recording the dates in the vaccination booklet [14].

5. Conclusion

The completeness of the hepatitis B vaccination is close to the WHO objectives. Emphasis should be placed on the respect of vaccination deadlines. Analysis of the factors associated with timely immunization gives us insight into the solutions to be proposed. These solutions must involve vaccinators and motivate parents to have their children vaccinated. One of these solutions could be the use of sms or whatsapp reminder messages like experienced in Kenya. This solution is easily affordable in a country like Gabon where internet access covers more than 80% of the population.

Acknowledgements

The entire team acknowledges the directors and the staff of the following institutions: Gabon Expanded Program of Immunisation, Centre Hospitalier Universitaire de Libreville, Centre Hospitalier Universitaire Mère et Enfant de Libreville, Centre de Santé de Awendjé, Centre de Santé de Akébé

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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