

Prevalence and seroprotection level of hepatitis B virus among children in Dakar, Senegal

Babacar Ndiaye¹✉, Abdou Diop¹, Mam Coumba Diouf¹, Omar Gueye², Malick Ndao², Thierno Abdoulaye Diallo¹, Chantal Mahou¹, Abdoulaye Seck^{1,3}

¹Medical biology laboratory, Pasteur Institute of Dakar

²Public Health National Laboratory, Thies

³Bacteriology-Virology Laboratory, Cheikh Anta DIOP University, Dakar

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✉ Corresponding Author: nbabacar9@gmail.com

Abstract

Hepatitis B virus (HBV) infection is a major public health problem in sub-Saharan Africa. Since 2004, Senegal had introduced HBV vaccine in its expanded program of immunization, and in 2016, vaccination at birth was introduced. The aim of this study was to investigate the prevalence of HBV and the immunity of children. This was a retrospective study conducted at medical biology laboratory of Pasteur Institute in Dakar covering data from 2016 to 2020. We measured serological markers (HBsAg, anti-HBc, anti-HBsAb) by ARCHITECT® automated immunoassay platform (Abbott Diagnostics, Wiesbaden, Germany). Data entry was performed by Excel 2016 (Microsoft, USA), and statistical analysis by STATA 14.0 software (Stata Corp, USA). Bivariate analyses were performed using the chi-square test and a statistically significant difference was retained if $p < 0.05$. A total of 428 children were included with a mean age of 7.57 years, ranging from 6 months to 15 years. The prevalence of HBV was 0.47% (0.0-1.2). HBsAb were found in 372 children or 86.9% (95% CI = 83.9-90.2). The vaccination coverage rate was 82.48% and 4.44% had post-contact immunity. The immunization rate was 62.08% and seroprotection was better in boys (64.01%, $p=0.542$). The level of seroprotection decreased progressively with age ($p=0.001$). Hepatitis B is a real public health problem and prevention through vaccination is one of the most effective means of combating the disease. Strengthened strategies are needed to achieve the WHO's 2030 targets.

Keywords: Hepatitis B, Children, Immunization, Serological markers, HBV vaccine

Introduction

Hepatitis B is a major public health problem, representing a potentially fatal liver infection. Indeed, global estimates suggest that more than 2 billion people have been infected with hepatitis B virus (HBV) and that 257 million of these people are chronically infected (defined as HBs antigen (HBsAg) positive for at least 6 months) (Niang et al., 2017). In addition, 15-25% of people with chronic HBV infection die of cirrhosis or liver cancer (Nelson et al., 2016).

In children, approximately 70-90% of infants infected before the age of 1 year will develop chronic HBV infection,

compared to 20-50% of those infected between the ages of 1 and 5 years, and 5-10% of those infected after 5 years (WHO, 2009).

Thus, hepatitis B is the subject of a vaccination program that responds to a public health problem insofar as its complications can be serious (death by hepatic cirrhosis, hepatocellular carcinoma, or fulminant hepatitis) (Schütze et al., 2014).

However, most of these deaths occur in resource-poor countries in Asia and Africa. This is because, about 100 million persons in the World Health Organization (WHO)

African Region have chronic hepatitis B virus (HBV) infection, and all countries in the Region have an intermediate (2%–7%) or high ($\geq 8\%$) population prevalence of chronic HBV infection (Breakwell et al., 2017).

In the absence of effective preventive and therapeutic interventions, chronic hepatitis B infection (CHB) will result in an estimated 11.8 million deaths by 2030, mainly due to cirrhosis and hepatocellular carcinoma (HCC) (WHO, 2016). Nevertheless, the incidence of liver cancer has decreased after several decades since the start of hepatitis B vaccination due to the protection conferred (Pol, 2015; Chiang et al., 2013; Qu et al., 2014).

In 2015, global coverage with three doses of hepatitis B vaccine in early childhood reached 84%. This has significantly reduced HBV transmission in the first five years of life, as evidenced by the reduction in HBV prevalence among children to 1.3% (Rapport, 2017).

In Senegal, HBV vaccination has been introduced since 2004 in the Expanded Programme on Immunization (EPI), but it was only in 2016 that vaccination at birth was adopted. Following the implementation of measures to significantly reduce the spread of HBV infection in the population, it is necessary to assess their impact. It is in this context that we undertook this study to assess the following in children:

- HBV prevalence
- Vaccination coverage rate
- Level of protection against HBV

Methodology

Type, population and study period

This was a retrospective study conducted at medical biology laboratory of Pasteur Institute in Dakar covering data from 2016 to 2020.

Inclusion criteria

We included all patients from 6 months to 15 years old received for the determination of the following biological parameters: HBs antigen (HBsAg), HBs antibodies (HBsAb), and HBc antibodies (HBcAb).

A sample of 3 milliliters of blood was taken from each child by venipuncture in vacuum tubes. After centrifugation, sera are stored locally at -20°C and subsequently sent and analyzed in the laboratory.

Data collection

The data collected were: general characteristics (Age, Gender) and serological data (HBsAg, HBsAb, HBcAb).

Determination of serological markers

HBsAg, HBsAb, and HBcAb were tested using ARCHITECT® automated immunoassay platform (Abbott Diagnostics, Wiesbaden, Germany). ARCHITECT® analyzer provides HBsAb levels measured in international units per liter (IU/L) with a linear range of 2.50 to 1000 IU/L.

Definition of hepatitis B seroprotection

Patients with anti-HBsAb levels ≥ 10 IU/L were considered seroprotected against HBV and a good seroprotection level was defined as an HBsAb level ≥ 100 IU/L (Komatsu, 2014). In contrast, patients with an HBsAb level < 10 IU/L were considered non-seroprotected.

Data analysis

Data entry was performed by Excel 2016 (Microsoft, USA) and statistical analysis by STATA 14.0 software (StataCorp, USA). Bivariate analyses were performed using the chi-square test and a statistically significant difference was retained if $p < 0.05$.

Table 1. Characteristics of the study population

	Number	% (95% CI)
Gender		
Women	154	35.98 (31.3-40.7)
Men	274	64.02 (59.3-68.7)
Gender ratio M/F	1,78	
Mean age (Extremes)	7,57 years [7,12– 8,01] [6 months – 15 years]	
Age group		
<5	140	32.71 (28.5-37.4)
[5-10]	150	35.05 (30.4-39.7)
>10	138	32.24 (30.4-36.7)
Total	428	100.0 (100.0-100.0)

Ethical aspects

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Results

Characteristics of study population

A total of 428 children were included with a mean age of 7.57 years (7.12-8.01) ranging from 6 months to 15 years. The sex ratio was 1.78 with a male predominance (274/428, 64.02%). The distribution of the population according to age group was fairly homogeneous between the different classes (Table 1).

HBV serological markers

Marker of infection (HBsAg): prevalence and distribution by age and sex

The prevalence of HBsAg was very low, found in only 2 children/428 or 0.47% (0.0-1.2) (Table 2). These were

children aged over 10 years and were male. There was no statistically significant difference either for age group (p=0.121) or for sex (p=0.288).

Table 2. Seroprevalence of HBs antigen (HBsAg)

HBsAg	N	% (95% CI)
Negative	426	99,53 (98.8-100.0)
Positive	2	0,47 (0.0-1.2)
Total	428	100

Contact (HBcAb) and seroprotection (HBsAb) markers against HBV

Among the children, 22 showed contact marker (HBcAb) or 5.14% (95% CI = 3.3-7.2). HBsAb were found in 372 children or 86.9% (95% CI = 83.9-90.2). The vaccination coverage rate [HBsAb (+) and HBcAb (-)] was 82.48% and 19 children or 4.44% had post-contact immunity [HBsAb (+) and HBcAb (+)] (Table 3).

Table 3. Seroprotection and contact with virus

Antibodies	HBsAb (-)	HBsAb (+)	Total	p-value
	N (%)	N (%)	N (%)	
HBcAb (-) N (%)	53(12.38)	353 (82.48)	406 (47.15)	p = 0.937
HBcAb (+) N (%)	3 (0.70)	19 (4.44)	22 (52.85)	
Total N (%)	56 (13.08)	372 (86.92)	428 (100)	

Level of seroprotection of the population

Immunization against HBV defined by an antibody level higher than 10 IU/L was found in 270 patients i.e., 63.08%.

Male children were better protected (64.02%) than female children (35.98%) without any statistically significant difference (p=0.542) (Table 4).

Table 4. Level of protection by age group and gender

Level of protection					
Characteristics	<10	[10-100]	[101-1000]	Total	p-value
	N (%)	N (%)	N (%)		
Gender					
F	62 (40.25)	45 (29.22)	47 (30.51)	154 (35.98)	p=0.542
M	96 (35.03)	84 (30.65)	94 (34.30)	274 (64.01)	
Age group					
<5	27 (19.28)	46 (32.85)	67 (47.85)	140 (32.71)	p=0.001
[5-10]	65 (43.33)	44 (29.33)	41 (27.33)	150 (35.04)	
>10	66 (47.82)	39 (28.26)	33 (23.91)	138 (32.24)	
Total	158 (36.92)	129 (30.14)	141 (32.94)	428 (100)	

The seroprotection level decreased remarkably with age with high immunisation rates (>100 IU/L) observed in children under 5 years of age (47.85%) followed by those in the age group [5-10 years] with 27.33% and finally 23.91% in

children older than 10 years (Table 4). There was a statistically significant difference between immunisation rate and age group ($p=0.001$) (Fig 1).

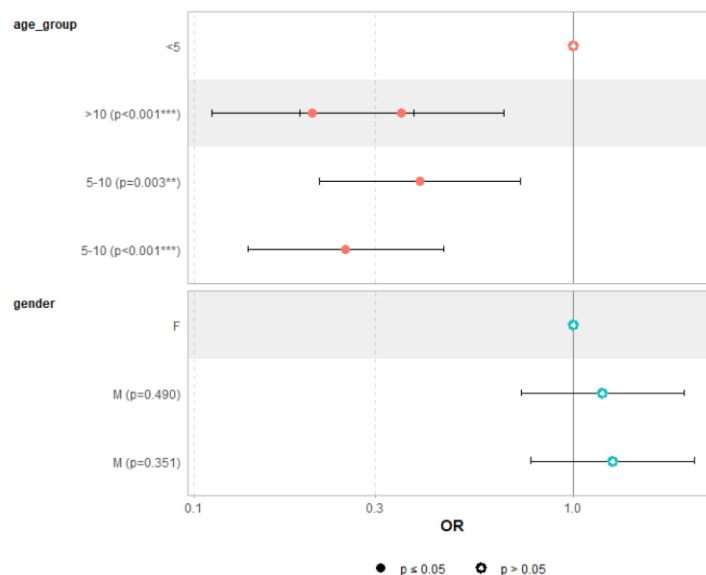


Fig. 1 Modelling the level of immunization rate of children

Discussion

Hepatitis B virus (HBV) infection is one of the major causes of acute and chronic liver disease in the world (Coppola et al., 2015). HBV vaccination has been a major advance in the fight against infection. The aim of our study was to determine the prevalence and to assess seroprotection against HBV in children aged 6 months to 15 years. We found a seroprevalence of HBV of 0.47%. In Senegal, before the introduction of vaccination, the prevalence of HBV in children was > 2% in 1993 (Excler et al., 1995). Years later, in a multicenter study conducted in 2010 in children aged 3 months to 6 years, Bekondi and colleagues reported prevalences of 0.2% and 0.7% in Senegal and Cameroon respectively (Bekondi et al., 2015). Another study conducted in 2016 reported a prevalence of 1.1% (Lô et al., 2019).

This is a very low prevalence which is part of a regression dynamic, thus proving the considerable impact of the introduction of vaccine in EPI in Senegal since 2004. In Gambia, surveys conducted between 1990 and 2008, most of which were associated with the Gambia Hepatitis Intervention Study (GHIS) an initiative that progressively introduced HepB into the Gambian routine immunization program during 1986–1990, showed that HBsAg prevalence decreased from 8% to 14.6% among 6 month–9-year-old children to < 2% among 1–5-year-old children post-HepB introduction (Chotard et al., 1992; Peto et al., 2014).

This trend has also been reported by other authors, notably in China, where HBV prevalence among the population aged 1 to 29 years fell from 10.1% in 1992 to 2.6% in 2014 (Cui et al., 2017).

On the other hand, progress in the prevention of mother-to-child transmission has played a major role in the decline in prevalence among children. Indeed, in areas of intermediate or high endemicity, the majority of chronic HBV infections in the population are attributable to mother-to-child (perinatal) and early childhood transmission (Mondiale et al., 2016). Therefore, systematic screening and initiation of treatment in case of high viral load are the key strategies put in place to prevent this vertical transmission (Niang et al., 2017).

Thus, a continuation of the strategy should be encouraged with a view to achieving the WHO target of reducing HBsAg prevalence to 0.1% in children by 2030 (WHO, 2016).

We found a vaccination coverage rate of 82.48%. In 2016, vaccination coverage of 77.3% was reported by Lo. G and colleagues (Lô et al., 2019). Country-specific HepB3 coverage estimates for 2015 ranged from 16% in Equatorial Guinea to 98% in Rwanda, Seychelles, Swaziland, and the United Republic of Tanzania; 16 (34%) countries reported national HepB3 coverage of at least 90% (WHO, 2016).

This is an immunization coverage rate that has evolved in the country over the last 5 years. Indeed, the introduction of vaccination from birth since 2016 has played a major role in the increase of the vaccination coverage rate. Nevertheless, there is a certain margin in relation to the WHO's objective of reaching a vaccination coverage rate of 90% (Gara et al., 2015).

Countries have reported multiple barriers to HepB-BD introduction, including lack of financial support from Gavi, the vaccine alliance (10 countries), the need for evidence on the burden of chronic HBV infection and the risk of perinatal transmission in Africa (6 countries), insufficient cold chain storage (3 countries), lack of trained healthcare workers (HCWs) to attend births or conduct post-natal visits (2 countries), and a high proportion of home births (2 countries) (Pinto et al., 2017).

To achieve this goal, all potential decision makers and opinion leaders from a wide variety of organizations should be engaged, including Ministries of Health and Finance, professional societies, medical associations, donor agencies, non-governmental organizations, as well as community and religious leaders.

HBV immunization defined by an antibody level above 10 IU/L was found in 63.08% of children. In 2010, a seroprotection rate of 44% was reported (Bekondi et al., 2015) and in 2016, Lo G reported a seroprotection of 56.0% (Lô et al., 2019).

Between 2004 and 2016, vaccination against HBV was introduced into the EPI with the recommendation of injections at M1, M2 and M3. Vaccination at birth, introduced in 2016 in accordance with WHO recommendations, helps to ensure that children receive at least one dose of vaccine, thus simplifying the vaccination schedule. In African countries that have already introduced HepB-BD, several challenges, including timely administration of the HepB-BD, high prevalence of home births, the lack of services available to reach infants born at home and unreliable vaccine supply have limited HepB-BD implementation. In this section, we present those challenges and list some strategies that could help overcome them to improve HepB-BD coverage.

In developed countries high rates of seroprotection have been reported, notably in Italy where the seroprotection rate was 84.2% (Excler et al., 1995).

We found that male children were better protected (64.02%) than female children (35.98%) with no statistically significant difference. This was also reported by Lo et al. (Lô et al., 2019). The level of seroprotection decreased remarkably with age with a statistically significant difference. This age-dependent decrease in immunity was reported in Lo. G's study in 2016, also found a statistically significant difference (Lô et al., 2019). Some scholars still

considered that a decrease of anti-HBs titers below the seroprotective level (≥ 10 IU/l) or loss of anti-HBs requires the booster (Pinto et al., 2017).

The need for a booster dose is debatable among authors. There is evidence, confirmed that the protection induced by the recombinant HBV vaccine persists even when the anti-HBs titer declines below 10 IU/L (McMahon et al., 2005; Gara et al., 2015). Moreover, the cellular immune memories, regardless of anti-HBs titers, may maintain in subjects vaccinated during childhood for at least 32 years (Simons et al., 2016).

This study has certain limitations, in particular, the number of doses received by the children was not mentioned because the vaccination records were not available. In addition, potential factors that could influence the decline in immunity were not investigated. However, other studies with a broader approach could contribute to a better understanding of the results currently obtained.

Conclusion

Hepatitis B is a real public health problem and prevention through vaccination is one of the most effective means of combating the disease. Our study showed a low prevalence (0.47%) of HBV infection in children and a satisfactory vaccination coverage rate (82.48%), but the rate of seroprotection (63.08%) remains insufficient and immunity declining with age is a serious concern. Thus, the efforts deployed must be reinforced in order to achieve the WHO objectives in relation to the global health sector strategy against viral hepatitis.

Conflict of Interest

The author hereby declares no conflict of interest.

Consent for publication

The author declares that the work has consent for publication.

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