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Hepatitis B Virus (HBV) Infection in Patients at Pasteur Institute of Dakar in Senegal from 2016 to 2020: Prevalence and Seroprotection Level

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Abstract

Hepatitis B virus (HBV) infection is highly endemic in Senegal. Vaccination of all children against HBV was introduced in 1999 and included in Expanded Programme on Immunisation in 2005. The aim of this study was to assess the prevalence and immune status against HBV in patients received at Pasteur Institut in Dakar, Senegal. **Methods:** Between January 2016 and December 2020, patients aged between 1 and 96 years received laboratory were included in the study. Serum samples were analysed for HBV serology (HBs antigen: HBsAg, HBs antibody: HBsAb and HBc antibody: HBcAb) using ARCHITECT® analyser. Patients with anti-HBs antibody levels (HBsAb ≥ 10 IU/l) were considered seroprotected against HBV. **Results:** A total of 5629 patients were analysed with a mean age of 39 years and extremes from 1 to 96 years. The most represented age group was 31 - 45 years with 38.4%. HBsAg was present in 520 patients (9.2%) and was signed by sex and age group. Anti-HBc antibodies were found in 52.7% of patients and 1603 (28.48%) had isolated anti-HBs antibodies reflecting proportion of people vaccinated at the time of the study. However, 2143 patients (41.9%) had no seroprotection (HBsAb < 10 IU/L) and 640 (12.6%) had strong seroprotection defined as HBsAb > 1000 IU/L. **Conclusion:** Our results show a significant presence of virus in Senegalese population and low vaccination coverage, especially in adults. Evaluation of HBsAb levels and provision of HBV booster shots should be considered for children in Senegal.

Keywords

HBsAb, HBsAg, HBV, Seroprevalence, Seroprotection, Vaccination

1. Introduction

Hepatitis B virus (HBV) infection is a major public health problem and cause of morbidity and mortality worldwide, affecting an estimated 250 million people worldwide [1] and accounting for 650,000 deaths per year [2]. Most of these deaths occur in resource-poor countries in Asia and Africa. Without effective preventive and therapeutic interventions, chronic hepatitis B infection will result in an estimated 11.8 million deaths by 2030, mainly due to cirrhosis and hepatocellular carcinoma (HCC) [3]. The prevalence of hepatitis B surface antigen (HBsAg) carriage varies greatly by geographical area, and sub-Saharan Africa and the World Health Organisation (WHO) Western Pacific regions are areas of high prevalence, with 6.1% and 6.2% of the adult population infected respectively [4]. In Senegal, 85% of the general population have at least one HBV marker [5] and the prevalence of HBsAg assessed in several population groups of interest ranged from 7.35% in blood donors to 14% in prisoners. WHO has recently incorporated HBV elimination into its global health agenda and is planning 90% reduction in new HBV cases and a 65% reduction in HBV-related mortality by 2030. In order to achieve these ambitious goals, HBV transmission, especially in endemic countries, needs to be urgently improved. Since 2013, WHO has recommended vaccination against HBV within 24 hours for all children born to infected mothers. In Senegal the vaccine was introduced in Expanded Programme on Immunisation (EPI) in 2005. However, current coverage of three doses of HBV vaccine remains imperfect with an estimated coverage of less than 80% in 2015 in Africa. Recent findings have shown a low prevalence of HBsAg carriage in children in the country, due to vaccination [6], while a low immune response among vaccinated has been found in Dakar [7].

Following the 2016 call by WHO and the World Health Assembly to control and eliminate HBV worldwide, the objective of the following study was to assess the current HBV seroprevalence and vaccine profiles in Senegalese patients received at the medical biology laboratory of Pasteur Institute in Dakar.

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2. Material and Methods

2.1. 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.

2.2. Inclusion Criteria

We included all patients from 1 to 96 years old received for the determination of the following biological parameters: HBs antigen (HBsAg), anti-HBs antibodies (HBsAb) and HBc antibodies (HBcAb).

2.3. Inclusion Criteria

The data collected were: general characteristics (Age, Gender) and serological

data (HBsAg, HBsAb, HBcAb).

2.4. Determination of Serological Markers

HBsAg, HBsAb and HBcAb were tested using ARCHITECT® automated immunoassay platform (Abbott Diagnostics, Wiesbaden, Germany). ARCHITECT® analyser provides HBsAb levels measured in international units per litre (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 level of seroprotection was defined as an HBsAb level ≥ 100 IU/L [8]. In contrast, patients with an HBsAb level < 10 IU/L were considered non-seroprotected.

2.5. 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 $p < 0.05$.

3. Results

3.1. Characteristics of Study Population

A total of 5629 patients were included with a mean age of 39 years (95% CI: 38.9 - 39.8) and women represented 61.4% (95% CI: 60.2 - 62.6). The most represented age group was [31 - 45 years] with 38.4% (95% CI: 37.1 - 39.7) (Table 1).

3.2. Serological Markers

3.2.1. HBsAg Positivity by Age and Sex

Of the 5629 patients analysed, 520 were HBsAg positive, giving an overall prevalence

Table 1. Characteristics of the study population.

	Number	% (95% CI)
Gender		
Women	3455	61.4 (60.2 - 62.6)
Men	2174	38.6 (37.4 - 39.8)
Gender ratio M/F	0.33	
Mean age (Extremes)	39 years (38.9 - 39.8) (1 – 96 years)	
Age group		
[1 - 15]	427	7.6 (6.9 - 8.3)
[16 - 30]	1164	20.7 (19.6 - 21.7)
[31 - 45]	2163	38.4 (37.1 - 39.7)
[46 - 60]	1262	22.4 (21.3 - 23.6)
[>60]	613	10.9 (10.1 - 11.7)
Total	5629	100

of 9.2% (95% CI: 8.5-10). This HBsAg positivity was significant by gender (4.76% in men) and by age group (4.62% in patients aged 31 - 45 years) (Table 2).

3.2.2. Contact with the Virus and Vaccination Coverage

HBcAb were found in 2975 (52.7%; 95% CI: 51.4 - 54) patients. The presence of HBcAb as an indication of previous contact with the virus correlated with the presence of HBsAb showed a statistically significant difference ($p < 0.0001$) (Table 3). Of the 5629 patients analysed, 1603 (28.48%) had isolated HBsAb reflecting the proportion of individuals vaccinated at the time of the study.

3.2.3. Level of Protection

Table 4 shows the level of protection and associated factors (Age, Sex) in 5109 HBsAg-negative patients of study. 28.48% of women were not seroprotected (HBsAb < 10 IU/ml) against 13.46% for men. However, 34.22% and 23.84% in women and men respectively had HBsAb level ≥ 10 IU/ml. There was a statistically significant difference between sexes ($p < 0.0001$). For patients with seroprotective levels of HBsAb (HBsAb-10 IU/L), the rate was significantly higher in patients aged 31 - 45 years (21.07%) than in patients aged 46 - 60 years (14.82%) and patients aged 16 - 30 years (9.43%), $p < 0.0001$.

Table 2. HBsAg positivity by age and sex

Characteristics	HBsAg (+)		HBsAg (−)		P-value
	N	%	N	%	
Gender					
Male	268	4.76	1906	33.86	p < 0.0001
Female	252	4.48	3203	56.90	
Age group					
[1 - 15]	2	0.04	425	7.55	
[16 - 30]	110	1.95	1054	18.72	
[31 - 45]	260	4.62	1903	33.81	p <0.0001
[46 60]	114	2.03	1148	20.39	
>60	34	0.60	579	10.29	
Total	520	9.24	5109	90.76	

Table 3. Seroprotection and contact with the virus.

Antibodies	HBsAb (−) N (%)	HBsAb (+) N (%)	Total N (%)	P-value
HBcAb (−) N (%)	1051 (18.67)	1603 (28.48)	2654 (47.15)	
HBcAb (+) N (%)	517 (9.18)	2458 (43.67)	2975 (52.85)	p < 0.0001
Total N (%)	1568 (27.86)	4061 (72.14)	5629 (100)	

Table 4. Level of protection by age group and gender.

Characteristics	Level of protection				P-value
	<10 N (%)	[10-100] N (%)	[101-1000] N (%)	[>1000] N (%)	
Gender					
F	1455 (28.48)	660 (12.92)	660 (12.92)	428 (8.38)	p < 0.0001
M	688 (13.46)	507 (9.92)	499 (9.77)	212 (4.15)	
Age group					
[1 - 15]	156 (3.05)	129 (2.52)	110 (2.15)	30 (0.59)	p < 0.0001
[16 - 30]	572 (11.20)	178 (3.48)	161 (3.15)	143 (2.80)	
[31 - 45]	826 (16.17)	345 (6.75)	439 (8.59)	293 (5.73)	
[46 - 60]	391(7.65)	316 (6.19)	305 (5.97)	136 (2.66)	
>60	198 (3.88)	199 (3.90)	144 (2.82)	38 (0.74)	
Total	2143 (41.95)	1167 (22.84)	1159 (22.69)	640 (12.52)	

HBsAb level was significantly correlated with sex with higher rates for women than men.

Among the 5109 study patient in total, 2143 (41.95%; 95% CI: 40.6 - 43.4) were considered not seroprotected againt HBV (HBsAb < 10 IU/ml), 1167 (22.84; 95% CI: 21.7 - 24.0) with rates between 10 and 100 UI/ml, 1159 (22.69; 95% CI: 21.6 - 23.7) defined as the good level of protection. In contrast, 640 (12.5%; 95% CI: 11.6 - 13.4) had a high antibody level > 1000 IU/ml.

4. Discussion

The aim of this study was to evaluate seroprevalence of HBsAg in patients at Pasteur Institute in Dakar, Senegal, over a 5 years period and the level of HBV seroprotection. The mean age of our patients was 39 years (95% CI: 38.9 - 39.8) with extremes of 1 and 96 years. Women represented 61.4% (95% CI: 60.2 - 62.6) and the most represented age group was [31 - 45 years] with 38.4% (95% CI: 37.1 - 39.7).

The prevalence of HBsAg carriage among patients in our study was 9.2% (95% CI: 8.5 - 10). It is similar to that found in a previous study in Mali (8% and 12%) [9], higher than that of Kakisingi *et al.* in Democratic Republic of Congo (8.01%) [10] and lower than those reported by other African authors such as Buseri *et al.* [11] in Nigeria (18.6%), Kra *et al.* [12] in Abidjan (15.6%), Nagalo *et al.* [13] in Burkina Faso (13.4%) and Tounkara *et al.* [14] in Mali (14.9%). This high prevalence places Senegal, according to the WHO, in a zone of high endemicity for the hepatitis B virus (prevalence higher than 8%) [14] and could be explained by the fact that even if country has a national programme to combat hepatitis, the important place of perinatal transmission in our context of high endemicity favours chronic carriage of virus [15].

More than half of the carriers were at least 45 years old (6.61%) and were male dominated (4.76%). This finding is consistent with that reported by Bougoudogo *et al.* in Mali [16]. This young age could be related to early perinatal contamination with the hepatitis B virus [17].

In our study, HBsAg seroprevalence was more frequent in adults than children. This has been described in several studies which have shown that seroprevalence increases progressively with age [18]. The low prevalence of HBsAg carriage in children is probably explained by introduction of hepatitis B vaccine in Expanded Programme of Immunisation in Senegal since 2005 and absence of sexual transmission in this population.

According to the presence of HBcAb, the data are stratified according to the presence or absence of HBcAb with HBsAb. HBcAb positive samples had significantly higher levels of HBsAb than HBsAb alone. In our study, we found that 28.48% of patients had HBsAb isolated without any contact with the virus, which is still a low vaccination coverage in general population, especially in adults. This coverage is similar to those reported in other studies worldwide [19] where it varied from 17% to 35%. In fact, vaccination coverage ranged from 50% to >90% [20] [21] in developed countries and 12% to 50% [22] in developing countries.

Vaccination is considered the most cost-effective way to control HBV infection, and early vaccination of newborns is essential to prevent perinatal HBV transmission. The successful introduction of the HBV vaccine into national hepatitis B control programme in Senegal has a significant impact on the prevalence of HBsAg among the population aged 1 - 15 years. According to WHO-UNICEF 2015 immunization report, HBV in 3 doses vaccination coverage has improved in Senegal and is estimated at 89% in Senegal [23].

According to level of protection 41.95% (95% CI: 40.6 - 43.4) were considered non-seroprotected against HBV as defined by HBsAb levels < 10 IU/ml and 12.5% (95% CI: 11.6 - 13.4) had a high antibody level > 1000 IU/ml. HBsAb levels above 10 IU/ml offer near total protection against HBV [24]. Typically, levels in 100 or 1000 IU/ml range are achieved after a series of three doses, and some authorities recommend a fourth dose if levels are between 10 and 100 IU/ml.

We also found that the seroprotection rate of HBsAb levels was higher in females than in males ($p < 0.0001$), suggesting gender-guided immune responses. Previous studies have reported better protective levels of HBsAb in vaccinated children and [25] [26] with higher levels in girls than in boys. Such a discrepancy could be attributed to differences in the primary immune response to vaccination, the type of vaccines used, the quality of vaccine storage (e.g. cold chain breakage), age groups, nutritional status and socio-economic or racial factors that were not investigated in our study [27]. Protective level of HBsAb increased with age ($p < 0.0001$).

Thus, vaccination in adulthood results in more effective HBV immunogenicity, most likely reflecting the progressive improvement of the immune system [28]. Indeed, the immune system in early childhood is characterised by impaired

T-cell function, weaker B-cell-T-cell interaction, a restricted immunoglobulin repertoire and a low affinity antibody response compared to adults 28. These factors, together with the presence of serum anti-HBs in some mothers [29], may affect the response to HBV vaccine in neonates and explain the lower immunogenicity of HBV vaccine when administered in infancy. These observations should prompt health authorities to reconsider their infant vaccination strategies for a more effective response.

Our study has a number of limitations: first, patients were not asked about the history of hepatitis B in the family. Secondly, we were not able to assess the number of doses of HBV vaccine administered. It has been shown previously that 3 doses is the best method to achieve effective protection against HBV. Thirdly, we did not collect the HIV, nutritional and clinical status of the children and were therefore unable to identify risk factors for poor seroprotection against the virus. Finally, our study was conducted in an urban centre where the HBV epidemic and vaccination coverage certainly differ from rural Senegal. This difference can be confirmed by the results of a larger study. The strengths of the study include the large sample size and the use of a test that has been shown to have high validity in other studies.

5. Conclusions

Viral hepatitis B remains a public health problem in Senegal, despite the fact that measures need to be taken to implement a national policy for fight against hepatitis in order to reduce prevalence rate of this infection and its complications. More than 15 years after the integration of the hepatitis B vaccine in their EPI, vaccination programmes must persist in improving vaccination coverage. The assessment of vaccination coverage based on vaccination records, maternal boosters or administrative data could be usefully reinforced by epidemiological data combined with immunological profiles. Serology based studies should be implemented regularly in African countries, as recommended by WHO. Among African populations studied, malnutrition, lack of maternal education and poverty are factors associated with non-adherence.

Country immunisation programmes need to actively address these issues.

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Authors' Contributions

All authors contributed to the drafting of the manuscript. All have read and approved the final version of the manuscript.

Conflicts of Interest

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

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