Hepatitis B in Senegal: A Successful Infant Vaccination Program but Urgent Need to Scale Up Screening and Treatment (ANRS 12356 AmBASS survey)

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Senegal introduced the infant hepatitis B virus (HBV) vaccination in 2004 and recently committed to eliminating hepatitis B by 2030. Updated epidemiological data are needed to provide information on the progress being made and to develop new interventions. We estimated the prevalence of hepatitis B surface antigen (HBsAg) in children and adults living in rural Senegal and assessed hepatitis B treatment eligibility. A cross-sectional population-based serosurvey of HBsAg was conducted in 2018-2019 in a large sample (n = 3,118) of residents living in the Niakhar area (Fatick region, Senegal). Individuals positive for HBsAg subsequently underwent clinical and biological assessments. Data were weighted for age and sex and calibrated to be representative of the area's population. Among the 3,118 participants, 206 were HBsAg positive (prevalence, 6.9%; 95% confidence interval [CI], 5.6-8.1). Prevalence varied markedly according to age group in individuals aged 0-4, 5-14, 15-34, and ≥35 years as follows: 0.0% (95% CI, 0.00-0.01); 1.5% (95% CI, 0.0-2.3); 12.4% (95% CI, 9.1-15.6); and 8.8% (95% CI, 6.1-11.5), respectively. Of those subsequently assessed, 50.9% (95% CI, 41.8-60.0) had active HBV infection; 4 (2.9%; 95% CI, 0.9-9.4) were eligible for hepatitis B treatment. *Conclusion:* In this first population-based serosurvey targeting children and adults in rural Senegal, HBsAg prevalence was very low in the former, meeting the World Health Organization's (WHO) < 1% HBsAg 2020 target; however, it was high in young adults (15-34 years old) born before the HBV vaccine was introduced in 2004. To reach national and WHO hepatitis elimination goals, general population testing (particularly for adolescents and young adults), care, and treatment scale-up need to be implemented. (*Hepatology Communications* 2022;6:1005-1015).

Hepatitis B surface antigen (HBsAg) prevalence in Africa is high (6.1%; 95% confidence interval [CI], 4.6-8.5), and an estimated 60 million individuals have chronic hepatitis B virus (HBV) infection.[1] West and Central Africa are the most affected subregions, with approximately 10% of the population chronically infected.[2]

In sub-Saharan Africa, HBV exposure predominantly occurs during early childhood, mostly through horizontal and mother-to-child transmission.[3] Following exposure, individuals either clear the virus or develop chronic infection. The risk of the latter is inversely related to age at infection, occurring in up to 90% of those infected perinatally but falling to less

Abbreviations: ALT, alanine aminotransferase; ANRS, French Agency for Research on AIDS and Viral Hepatitis; AST, aspartate aminotransferase; CI, confidence interval; DBS, dried blood spot; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDSS, Health and Demographic Surveillance System; HDV, hepatitis D virus; HIV, human immunodeficiency virus; ULN, upper limit of normal; WHO, World Health Organization.

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The data underlying this article cannot be shared publicly for the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

than 5% in individuals infected during adulthood.[4,5] The natural history of chronic HBV infection is complex; some individuals may remain asymptomatic and the infection may even resolve. For others, disease progression leads to chronic liver disease and the risk of cirrhosis or hepatocellular carcinoma.[6] In 2016, the World Health Organization (WHO) estimated that HBV infection caused 107,000 deaths in Africa.[7]

Hepatitis B is endemic in Senegal. A modeling study estimated HBsAg prevalence in the general population at 8.1% (95% CI, 7.5-9.0) in 2016.[2] However, prevalence estimates over the past 20 years have mostly relied on studies conducted in the capital Dakar in specific adult populations, including pregnant women,[8,9] persons coinfected with human immunodeficiency virus (HIV),[10,11] and blood donors.[12-14] Although two studies targeted children, both were conducted before 2016 in health care facilities in Dakar.[15,16]

To fight the HBV epidemic, Senegal has implemented several control measures. The three-dose hepatitis B vaccine, administered as a combined vaccine to infants 6, 10, and 14 weeks after birth, was introduced in the Expanded Program on Immunization in 2004; the monovalent birth-dose vaccine was added in 2016. The targets of the 2019-2023 Senegalese Strategic Plan to Fight Against Viral Hepatitis[17] reflect the aims of the WHO Global Health Sector Strategy, namely a 90% reduction in chronic HBV infection incidence, a 65% reduction in HBV mortality, and 80% treatment coverage among those eligible for treatment by 2030.[18] Key interventions to achieve this include decentralizing screening and treatment services at the health care system's regional and district levels.[17]

In order to design public health interventions that are adapted to the decentralization of HBV care in rural Senegal, up-to-date epidemiological data on HBV infection in adults and in children born after the vaccination program's introduction are needed. We aimed to document the prevalence of HBsAg in the general population in a rural area of Senegal and to estimate the proportion of individuals infected with HBV who are eligible for antiviral therapy, using national and WHO guidelines.

Participants and Methods

STUDY DESIGN

The French Agency for Research on AIDS and Viral Hepatitis(ANRS) 12356 AmBASS (AMpleur et conséquences de l'infection chronique par le virus de l'hépatite B en Afrique Sub-Saharienne [burden and impacts of chronic HBV infection in sub-Saharan

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Africa]) cross-sectional survey was conducted between October 2018 and May 2019 in a large sample of residents living in the area covered by the Niakhar Health and Demographic Surveillance System (HDSS) in the region of Fatick. In 2018, Fatick was selected as Senegal's pilot region for the decentralization of HBV care. The HDSS is located 135 km east of Dakar and covers 203 km^2, with a population of 44,854 individuals in 30 villages.[19] It has four primary health care posts managed by nurses (study area map in Fig. 1).[20] Two health care centers managed by physicians (reference facilities at the district level) and the regional hospital are located close to the HDSS area.

Survey Sampling Strategy

The survey methodology is extensively described elsewhere.[20] Household sampling was performed using a two-stage stratified design with simple random sampling at both stages. We first selected 11 villages according to their levels of infrastructure (three semiurban, eight rural) and then 401 households among these villages. The sample size (n = 3,200 individuals) was determined so as to have a precision of ±1.2% for the prevalence of HBsAg positivity in the general population (assuming a 10%-17% prevalence of HBsAg, based on previous studies in Senegal) and ±3.0% in each of the following age groups: ≤14, 15-34, and ≥35 years old.[20]

Study Population

Participants aged 0-14 years were considered as children and those ≥15 years old as adults. Among selected households, all residents ≥6 months old were invited to participate in the survey, except adults unable to sign informed consent and children whose

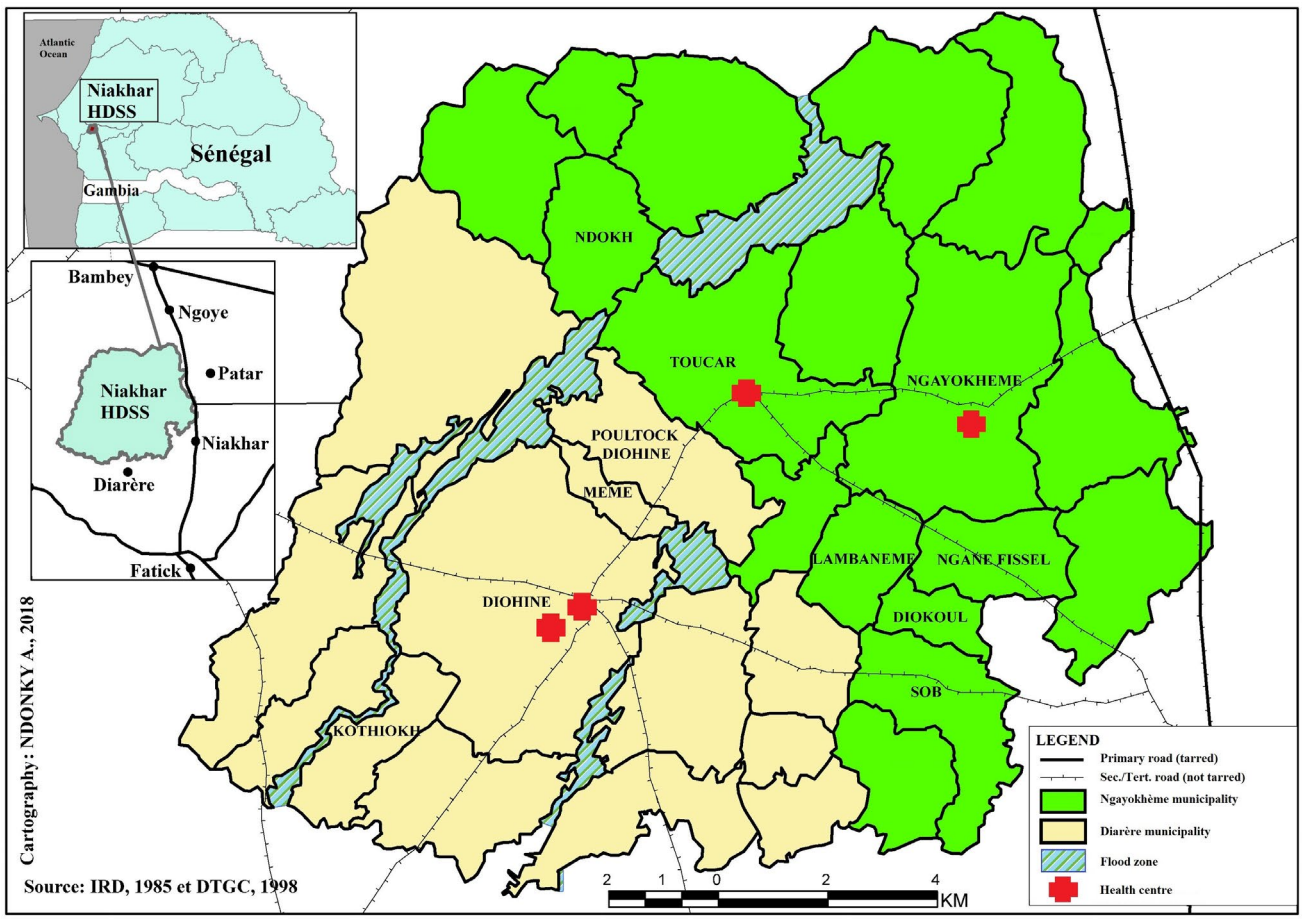

FIG. 1. Map of the area covered by the Niakhar HDSS with identification of the 11 villages and four health care posts participating in the ANRS 12356 AmBASS survey. (Source: IRD 1985 and DTGC 1998; Cartography: Ndonky A. 2018.). Reprinted with permission from Delaunay et al.[34]

parent or legal guardian was not present in the household at the time of the survey. Informed consent to participate was mandatory; parental consent was obtained for all participating minors.

Clinical and Biological Data Collection

Household members who agreed to participate received pretest counseling. Subsequently, dried blood spots (DBSs) (Whatman 903 Protein saver card) were collected by nurses using capillary whole blood to screen for HBV infection. Thanks to their high (>90%) diagnostic sensitivity and specificity compared with plasma or serum,[21] the WHO recommends DBS to detect HBsAg in areas where rapid diagnostic tests are unavailable or where there are no facilities or personnel to take venous blood samples. Using a standardized method,[22] DBSs were eluted to detect HBsAg by using a chemiluminescent microparticle immunoassay (ARCHITECT; Abbott, Sligo, Ireland). To determine optimal cut-off values for positivity and negativity using DBSs, we obtained paired capillary blood for DBSs and venous blood for serum samples from 39 individuals in the pilot study of AmBASS (see Supporting Table S1). Cut-off values were determined at 1.0 IU/mL (for negativity) and 1.5 IU/mL (for positivity). For HBsAg levels between 1.0 and 1.5 IU/mL using DBSs, we systematically performed a second HBsAg test using serum samples to confirm the status.

All participants received their HBsAg screening test results and posttest counseling. Additionally, individuals who were HBsAg positive underwent biological and clinical examinations in health care facilities to assess liver disease stage and treatment eligibility. Venous blood was collected for full blood count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), hepatitis B e antigen (HBeAg), HIV antibody (ARCHITECT; Abbott) and hepatitis D virus (HDV) antibody (enzyme linked immunosorbent assay; hepatitis delta; Virion\Sirion). Using DBSs, HBV DNA levels were quantified for all participants positive for HBsAg (reverse-transcription polymerase chain reaction; Gene Proof DNA; Biosynex; limit of detection, 26 IU/mL).[22]

All blood samples were transported to the Niakhar station laboratory where they were stored and transferred weekly for analysis to the Institute for Health Research, Epidemiological Surveillance and Training in Diamniadio.

Participants with ALT above the upper limit of normal (ULN) and HBV DNA > 2,000 IU/mL underwent transient elastography (FibroScan) in Dakar as they were potentially eligible for antiviral therapy according to Senegalese recommendations. All those identified eligible for antiviral therapy according to the national recommendations were then referred to the regional hospital of Fatick (20 km from the HDSS) where they were offered. The treatment was provided for free within the research project (for a 3-year period).

Socioeconomic Data Collection

Fieldworkers administered a face-to-face socioeconomic questionnaire to participants to collect information on sociodemographic and socioeconomic characteristics, living conditions, knowledge about HBV infection, previous HBV diagnosis, and exposure to HBV infection risk factors (for children). Furthermore, another questionnaire, administered to the head of the household or household representative, gathered economic data on housing characteristics as well as durable goods and agricultural and farming resources at the household level. We used (i) vaccination cards (when available), (ii) biannual vaccination data from the HDSS database, and (iii) vaccination records in health care posts (where possible) to determine children's HBV vaccination status. Data were recorded electronically on tablets using Voxco Survey Software.

ETHICS APPROVAL

The ANRS 12356 AmBASS survey received ethical approval from the Senegalese National Ethical Committee for Research in Health (no.082MSAS/DPRS/CNERS) and authorization from the French Commission on Information Technology and Liberties (reference MMS/HG/OTB/AR181521). The survey conforms to the Declaration of Helsinki.

STATISTICAL ANALYSES

Data Weighting and Calibration

Data were weighted and calibrated to ensure that the survey sample was representative of the residents of the Niakhar HDSS aged ≥6 months in terms of sex and age (see Supporting Materials Box S1). All

analyses were performed using weighted and calibrated data.

Descriptive Analyses

The sociodemographic and economic characteristics of sampled households and individuals were described using percentages for categorical variables and means ± SD for continuous variables.

Prevalence Estimations

As per WHO recommendations for settings where HBsAg seroprevalence is above 0.4%, we considered that testing positive for HBsAg at a single assessment represented chronic HBV infection.[21] HBsAg positivity prevalence was first calculated for the total population, then for each group stratified by age and sex. A 95% CI was estimated using standard Wald confidence limits for proportions, except for children 0-4 years old, where the Agresti-Coull interval was used as no child in this age group was HBsAg positive.[23]

All analyses were performed using SAS, version 9.4, for Windows (SAS Institute Inc., Cary, NC) or Stata, version 14.2, for Windows (StataCorp, College Station, TX).

Hepatitis B Treatment Eligibility

Adults positive for HBsAg were assessed for treatment eligibility using both national and WHO guidelines.[24] Senegalese guidelines recommend treatment initiation if (i) ALT levels > 2 × ULN and HBV DNA > 20,000 IU/mL; or (ii) ALT > ULN and HBV DNA > 2,000 IU/mL and at least F2 liver fibrosis stage; or (iii) cirrhosis and detectable HBV DNA levels. The WHO recommends initiating antiviral treatment in the following situations: (i) clinical evidence of cirrhosis; or (ii) AST-to-platelet ratio index score above 2; or (iii) ≥30 years old with persistently abnormal ALT levels and HBV DNA > 20,000 IU/mL.[24] In our study, we applied the ALT value measured at a single time point.

The following ALT ULN values were used to determine treatment eligibility: i) 55 U/L (used by the laboratory Institute for Health Research, Epidemiological Surveillance and Training for national guidelines) and ii) 30 U/L for men and 19 U/L for women (WHO guidelines).[24]

Results

PARTICIPATION RATE AND CHARACTERISTICS OF STUDY PARTICIPANTS

The participation rate was 75.1% (301/401) among randomly selected households and 91.5% (3,118/3,409) among eligible residents of participating households.

A total of 1,530 adults and 1,588 children participated. Half (50.5%) the adults were male participants, mean age was 34.8 ± 16.7 years, 54.8% had at least primary education, and 56.5% were married (Table 1). Among children, 51.8% were boys, mean age was 7.6 ± 4.0 years (Table 2), and 87.8% of those aged ≥7 years (school initiation age in Senegal) attended school. Among children with available vaccination data (1,071/1,588; 68.4%), 90.1% of those 0-4 years old and 59.9% of those 5-14 years old had received three doses of pentavalent vaccine (71.9% overall). Furthermore, half (54.5%) the children born ≥2016 had received the birth-dose vaccine within 24 hours of birth.

PREVALENCE OF HBSAG POSITIVITY

Among the 3,118 survey participants, 206 tested HBsAg positive (189 adults, 17 children), corresponding to a prevalence of 6.9% (95% CI, 5.6-8.1). Prevalence was highest in those 15-34 years old (12.4%; 95% CI, 9.1-15.6) and those ≥35 years old (8.8%; 95% CI, 6.1-11.5). Prevalence was 12.5% (95% CI, 9.1-15.8) in adult men, 9.2% (95% CI, 7.0-11.4) in adult women, 0.0% (95% CI, 0.00-0.01) in children 0-4, and 1.5% (95% CI, 0.0-2.3) in children 5-14 years old (Table 3; Supporting Fig. S1).

CHARACTERISTICS OF PARTICIPANTS POSITIVE FOR HBSAG AND ANTI-HBV TREATMENT ELIGIBILITY

Mean ± SD age of the 206 participants positive for HBsAg was 30.3 ± 12.4 years in adults and 11.9 ± 2.5 years in children. HBV DNA was detected in 44.9% of these participants; 33.1% had HBV DNA

TABLE 1. CHARACTERISTICS OF PARTICIPATING ADULTS (I.E., ≥15 YEARS OLD) (N = 1,530), USING WEIGHTED AND CALIBRATED DATA (ANRS 12356 AMBASS SURVEY)

Characteristics (% of Missing Values)	% or Mean ± SD
Sociodemographic and socioeconomic characteristics	
Sex (0.0)	
Male	50.5
Female	49.5
Age group (years) (0.0)	
15-34	57.8
≥35	42.2
Age (years) (0.0)	34.8 ± 16.7
Matrimonial status (1.4)	
Single	39.5
Married (monogamous)	41.4
Married (polygamous)	15.1
Widowed or divorced	4.0
Having children (2.0)	58.3
No. of children	5.8 ± 4.1
Educational level (3.6)	
Never attended school	45.2
Primary or junior high school	35.4
High school or above	19.4
Economic activity (1.7)	
Agricultural activity	55.3
Nonagricultural activity	19.2
Studies/training	18.1
Inactive	7.4
Household index of life conditions (quartiles) (0.0)*	
First	17.3
Second	21.2
Third	24.5
Fourth	37.0
Number of months of presence in the household during the previous year (2.6)	9.7 ± 3.5
Health-related characteristics	
Physical impairment† (1.5)	1.6
Hospitalization during the previous year (1.6)	2.9
Health problems (illness or wound) during the previous 3 months (1.4)	18.6

*The household living conditions index was built using a multiple correspondence analysis of information on durable goods, agricultural and farming resources, and housing characteristics collected at the household level.
†Vision impairment (n = 11), lower limb disability (n = 10), upper limb disability (n = 4), asthma (n = 3), hearing impairment (n = 2), goiter (n = 1).

TABLE 2. CHARACTERISTICS OF PARTICIPATING CHILDREN (I.E., 0-14 YEARS OLD) (N = 1,588), USING WEIGHTED AND CALIBRATED DATA (ANRS 12356 AMBASS SURVEY)

Characteristics (% of Missing Values)	% or Mean ± SD
Sex (0.0)	
Male	51.8
Female	48.2
Age group (years) (0.0)	
0-4	31.4
5-9	36.7
10-14	31.9
Age (years) (0.0)	7.6 ± 4.0
Household index of life conditions (quartiles) (0.0)*	
First	17.6
Second	23.1
Third	24.3
Fourth	35.0
Enrolled in the Senegalese education system (only for those ≥7 years old), n = 862 (0.3)	
Yes	87.8
No	12.2
Regular school attendance during the 2017-2018 academic year (<5 days of absence), n = 758 (0.8)	98.0
Work activity in the previous year (persons ≥7 years old), n = 862	
Household agricultural or business activities (0.2)	52.6
Domestic activities (0.2)	66.1
Paid activities (0.3)	0.7
Disability or chronic health condition† (0.1)	1.7
Hospitalization in the previous year (0.0)	1.1
Illness or wound in the previous 3 months (0.8)	22.0
Three doses of pentavalent received (31.5)	71.9
Birth-dose vaccine received ≤24 hours after birth (born ≥2016, n = 272) (12.0)	54.5

*The household living conditions index was built using a multiple correspondence analysis of information on durable goods, agricultural and farming resources, and housing characteristics collected at the household level.
†Asthma (n = 24), sickle cell disease (n = 1), physical disability (n = 2), mute (n = 1), epilepsy (n = 1), vision impairment (n = 1).

levels of 2,000-19,999 IU/mL and the remaining 11.8% had levels ≥20,000 IU/mL.

A majority (n = 163; 74.6%) of participants who tested HBsAg positive underwent additional clinical and biological examinations (Table 4). Of these, 6.6% of the adults but no child had a family history of hepatocellular carcinoma or cirrhosis in a first-degree relative and 3.0% had ongoing clinical signs suggestive of decompensated cirrhosis (edema, ascites, icterus), but this was not confirmed by laboratory tests (see Supporting Table S2). None of the 163 assessed had signs suggesting extrahepatic complications of chronic HBV infection (vasculitis, cryoglobulinemia, vascular purpura, arthromylagia, liver damage, livedo, or

TABLE 3. PREVALENCE OF HBSAG IN THE RURAL AREA OF NIAKHAR, SENEGAL, USING WEIGHTED AND CALIBRATED DATA (ANRS 12356 AMBASS SURVEY)

	Number of Individuals Positive for HBsAg (prevalence, 95% CI)		
	All	Male	Female
Age classes (years)			
0-4	0 (0.0%, 0.00-0.01)	0 (0.0%, 0.00-0.02)	0 (0.0%, 0.00-0.02)
5-14	17 (1.5%, 0.0-2.3)	9 (1.3%, 0.3-2.2)	8 (1.8%, 0.4-3.1)
15-34	115 (12.4%, 9.1-15.6)	59 (15.9%, 10.9-20.9)	56 (9.1%, 5.9-12.2)
≥35	74 (8.8%, 6.1-11.5)	34 (8.2%, 4.4-12.0)	40 (9.5%, 6.2-12.8)
Children*	17 (1.0%, 0.5-1.6)	9 (0.9%, 0.0-1.5)	8 (1.2%, 0.0-2.1)
Adults†	189 (10.9%, 8.8-12.9)	93 (12.5%, 9.1-15.8)	96 (9.2%, 7.0-11.4)
Total	206 (6.9%, 5.6-8.1)	102 (7.7%, 5.8-9.7)	104 (6.1%, 4.7-7.4)

*Children, <15 years old.
†Adults, ≥15 years old.

neuropathy). Furthermore, 13.1% were HBeAg positive, but none had HIV or HDV coinfection. Half the adults (51.2%) and a quarter (24.6%) of the children had HBeAg-negative chronic infection (formally known as inactive carrier state, i.e., HBeAg negative and anti-HBe positive and HBV DNA < 2,000 IU/mL and ALT < ULN).

Finally, only 2.9% (95% CI, 0.9-9.4) were eligible for treatment (4/163; 3 according to Senegalese recommendations and 1 according to WHO criteria). All 4 were men aged 16-39 years. The 3 participants eligible according to Senegalese criteria initiated treatment with tenofovir. Furthermore, a 14-year-old girl was potentially eligible according to Senegalese guidelines (i.e., ALT > ULN and HBV DNA > 2,000 IU/mL), but the FibroScan result was missing. Clinical and biological characteristics of these individuals are presented in Supporting Table S3.

Discussion

To the best of our knowledge, this is the first study to estimate chronic HBV infection prevalence in the general population in rural Senegal (including children born after the introduction of hepatitis B vaccination in the country's Expanded Program on Immunization in 2004) and to assess eligibility for hepatitis B treatment. We found a high prevalence of HBsAg positivity in the general population of the Niakhar HDSS (6.9%; 206/3,118), with large variations across different age groups. Specifically, while prevalence in children (0-14 years old) born after the HBV vaccination program started was close to 1% (17/1,588), it was above 10% (189/1,530) in those born beforehand. Half the individuals positive for HBsAg in our sample had active chronic HBV infection, but only 3% (4 men aged 16-39 years) were immediately eligible for treatment according to national or WHO guidelines.

HBsAg prevalence in our study was lower than that found for Senegal's general population in a systematic review based on published literature (11.06%; 95% CI, 10.72-11.40)[25] and slightly below but comparable to the prevalence estimated in a modeling study (8.1%; 95% CI, 7.5-9.0).[2] The high prevalence of HBsAg in adults is consistent with studies conducted in specific adult population groups in Dakar.[8-14] Interestingly, HBsAg prevalence was lower in those aged ≥35 years than in those 15-34 years. A decrease in prevalence with increasing age was also observed in The Gambia and could be explained by the spontaneous loss of HBsAg over time and by higher mortality rates in older adults who were HBsAg positive.[26]

The low prevalence of HBsAg in children (i.e., 0-14 years old) reflects findings for hospitalized children in Dakar born after 2004 (0.2% and 1.1%).[15,16] However, the prevalence in those aged 0-4 years was below that in those aged 5 years estimated in a modeling study (1.6%; 95% CI, 1.5-1.8).[2] Our data suggest that the WHO's target of achieving <1% prevalence of HBsAg in children under 5 years of age by 2020[18] was reached in the study area of Niakhar, probably thanks to the high coverage of the hepatitis B vaccination program in recent years. Specifically, another study using

TABLE 4. CLINICAL AND BIOLOGICAL CHARACTERISTICS OF INDIVIDUALS POSITIVE FOR HBSAG WHO SUBSEQUENTLY UNDERWENT CLINICAL AND BIOLOGICAL EXAMINATION (N = 163), USING WEIGHTED AND CALIBRATED DATA (ANRS 12356 AMBASS SURVEY)

Characteristics (% of Missing Values)	Adults* %	Children† %
Body mass index (0.0)‡		
Underweight (<18.5)	54.2	56.5
Normal weight (18.5-24.9)	31.7	43.5
Overweight (25.0-29.9)	12.5	0.0
Obese (≥30.0)	1.7	0.0
Past medical history of chronic disease (0.0)	4.1§	0.0
Ongoing signs of cirrhosis (0.0)		
Edema (0.0)	0.9	0.0
Ascites (0.0)	0.4	0.0
Icterus (0.0)	1.2	0.0
Past history/symptoms (0.0)		
Previously diagnosed cirrhosis (0.0)	0.0	0.0
Gastrointestinal hemorrhage (0.0)	0.0	0.0
Encephalopathy (0.0)	0.0	0.0
Family history of hepatocellular carcinoma or cirrhosis in a first-degree relative (0.0)	6.6	0.0
HBV DNA (IU/mL) (0.0)		
Undetectable (<26)	50.0	59.7
26-1,999	28.2	0.0
2,000-19,999	9.7	11.2
≥20,000	12.1	29.1
Anti-HDV positive (2.7)	0.0	0.0
Anti-HIV positive (0.0)	0.0	0.0
HBeAg positive (0.0)	12.8	16.6
ALT‖ (0.0)		
<40	93.5	80.2
40-79	3.4	19.8
≥80	3.1	0.0
AST¶ (0.0)		
<34	93.3	75.5
34-67	5.5	19.8
≥68	1.3	4.7
APRI# (≥18 years old, n = 124) (12.7)		
<1.00	94.9	
1.00-1.99	5.1	Not applicable
≥2.00	0.0	
Inactive chronic HBV infection (0.0)		
HBeAg negative and anti-HBe positive and HBV DNA < 2,000 IU/mL and ALT < ULN‖	51.2	24.6
Eligible for antiviral treatment according to national recommendations (0.0)		
ALT > 2 × ULN‖ and HBV DNA > 20,000 IU/mL	0.5	0.0
ALT > ULN‖ and HBV DNA > 2,000 IU/mL, and FibroScan (at least F2 fibrosis)	2.1	14.7
Cirrhosis and HBV DNA	0.0	0.0
Eligible for antiviral treatment according to WHO guidelines (0.0)		
Clinical diagnosis of cirrhosis	0.0	0.0
APRI# score > 2.00	0.0	Not applicable
≥30 years old and persistently abnormal ALT levels (>30 U/L for men, >19 U/L for women) and HBV DNA > 20,000 IU/mL	0.5	Not applicable

*Adults, ≥15 years old (n = 147).
†Children, <15 years old (n = 17).
‡For individuals under 18 years old, body mass index for age curves were used.
§Asthma (n = 2), hypertension (n = 1), right hemiparesis (n = 1), paraplegia following cerebral tuberculomas (n = 1).
‖ULN for Senegalese recommendations, 55 U/L.
¶ULN threshold, 34 U/L.
#APRI = ([AST/ULN] ×100)/platelet count (10^9/L).
Abbreviation: APRI, aspartate aminotransferase-to-platelet-ratio-index.

data from the AmBASS survey in children born ≥2016 found that 90.1% of those 0-4 years old had received three doses of pentavalent vaccine and 66.8% of those born in 2017-2018 had received the birth dose within 24 hours of birth.[27] Key interventions to improve vaccination coverage include increasing outreach vaccination activities, encouraging caregivers to bring newborns born at home to health care facilities within 24 hours of birth, and finding innovative ways to remind caregivers of vaccination appointments.[27]

The low proportion of persons positive for HBsAg and eligible for hepatitis B treatment that we found (3%) is consistent with findings in studies conducted in The Gambia, where 3.7% (95% CI, 2.0-6.5) to 6.7% (95% CI, 5.1-8.3) of persons positive for HBsAg were eligible.[26,28] Interestingly, treatment eligibility in our study differed according to the guidelines used (WHO versus national recommendations). Specifically, 3 participants were eligible according to national recommendations and 1 according to WHO recommendations. This highlights the complexity of identifying eligible patients when different recommendations exist.[29] The 3 participants eligible according to the national recommendations have initiated treatment with tenofovir at the regional hospital of Fatick.

The important policy implications highlighted by our study for hepatitis B elimination in Senegal can

be transferred to other West African countries. First, our results demonstrate the success of the Senegalese HBV vaccination program in reducing HBV infection prevalence below 1% in children and suggest that if current efforts continue, the country may achieve the WHO-desired 90% reduction in chronic HBV incidence by 2030 (i.e., 0.01% prevalence).[18]

Second, good acceptability of HBsAg screening (75.1% participation rate at the household level and 91.5% at the individual level) and good acceptability of HBV care (74.6% of those HBsAg positive underwent clinical and biological assessments) show that, as suggested elsewhere,[26] large-scale community-based screening seems feasible when provided for free, even in rural Senegal.

Third, our findings highlight important follow-up and future treatment needs. Specifically, at the population level, we estimate that 90 (95% CI, 28-290) of the 3,095 (95% CI, 2,512-3,633) persons positive for HBsAg living in the Niakhar HDSS are immediately eligible for treatment and that approximately 1,575 (95% CI, 1,293-1,857) have active chronic HBV infection; the latter run the risk of liver complications without timely treatment.[24] However, decentralized care for HBV in rural Senegal is hindered by high costs and unavailability of tests for both HBV monitoring and treatment eligibility assessment (e.g., FibroScan and viral load measurement). Patients living in the Fatick region must travel over 100 km to Dakar and pay FCFA 15,000 (US $26) for a FibroScan. Tenofovir is available at the regional hospital of Fatick, but a monthly fee of up to FCFA 5,000 (US $9) per month may be applied depending on health insurance coverage. The socioeconomic data we collected suggest that only an estimated 29% of the Niakhar HDDS population testing positive for HBV infection would have the means to pay for nationally recommended follow-up tests (i.e., two HBV DNA tests and two FibroScan per year for a total cost of FCFA 80,000 (US $138). Furthermore, only 28% of the Niakhar population would have the means to pay for both the nationally recommended tests and HBV treatment, which together can cost up to FCFA 140,000 per year (US $242). All the above findings highlight the need to develop alternative monitoring algorithms adapted to supply and demand constraints at the health system's decentralized level. For example, by measuring HBV DNA at the initial examination and then only when transaminases levels are abnormal, by using alternative methods to quantify HBV DNA levels,[30,31] or by adapting the frequency of follow-up (depending on whether HBV infection is active or inactive). Moreover, ensuring that people have access to HBV care and treatment according to their financial means is vital for the scaling up of care and treatment.

Our study has several limitations. First, it is not representative of the whole country. However, the Niakhar HDSS is quite representative of rural areas in Senegal in terms of demographic, socioeconomic, and health characteristics (see Supporting Table S4). Furthermore, the health services in the Niakhar HDSS are similar to those available in the rest of the country, and there are no specific interventions linked to hepatitis B that could impact the results of our study. Second, the prevalence of HBsAg may have been slightly underestimated by the use of DBSs. Depending on the distribution of HBsAg levels in the target population, the use of highly sensitive assays (e.g., limit of detection <0.1 IU/mL) may have identified more individuals infected with HBV.[32] However, this limitation is offset by the fact that people with low HBsAg levels are often inactive carriers and do not require antiviral therapy.[33] Furthermore, of the 32 tests falling within the range defined as undetermined using DBSs (i.e., between 1.0 and 1.5 IU/mL), only six tests were confirmed positive using blood samples, suggesting that we probably did not miss any individual positive for HBsAg. Finally, the measurement of ALT at a single time point to determine treatment eligibility and the absence of FibroScan in the region of the Niakahr HDSS may have missed some individuals in need of treatment.

To conclude, HBsAg prevalence was very low in children (<1%), highlighting the success of the Senegalese HBV vaccination program and suggesting that Senegal may be on a track to achieve the WHO target of a 90% reduction in chronic HBV infection incidence by 2030. Prevalence was highest in young adults, and those eligible for treatment were mostly young men. To reach hepatitis elimination goals in Senegal, general population testing (particularly for adolescents and young adults) and the scale-up of care and treatment are also needed.

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Appendix 1

THE ANRS 12356 AMBASS SURVEY STUDY GROUP

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