

Low hepatitis B vaccination coverage among hepatitis B virus carriers communicants in an eastern Brazilian Amazon city

Candida Maria Abrahão Oliveira (✉ candidaoliveira@iec.gov.br)

Instituto Evandro Chagas

Alex Junior Souza de Souza

Instituto Evandro Chagas

Maria de Jesus de Souza Brasil

Instituto Evandro Chagas

Manoel do Carmo Pereira Soares

Instituto Evandro Chagas

Heloisa Marceliano Nunes

Instituto Evandro Chagas

Márcio Roberto Teixeira Nunes

Instituto Evandro Chagas

Research note

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Abstract

Objective Hepatitis B virus (HBV), even though it is an immunopreventable disease, represents a serious worldwide public health problem. This study evaluated hepatitis B vaccination coverage and the frequency of infection in HBV carrier communicants 20 years after vaccine implementation in the city of Belém, located in the eastern Brazilian Amazon.

Results The study, developed between 2015 to 2018, included 288 (n = 288) communicants of HBV carriers. The analyzed population was 53.5% male, with a mean age of 9.4 years (ranging 4 months to 19 years old and a median age of 10 years). Among the examined samples, no HBV carriers (HBsAg positive) were detected; total isolated anti-HBc was detected in 2.1%; 4.2% were anti-HBc total/anti-HBs and 42% anti-HBs isolated, attributed to vaccination; 41.7% received a complete vaccination schedule (three/four doses) and 58.3% were susceptible to HBV. Although the research did not detect HBV in the studied population, there was presence of infection and a significant number of susceptible individuals.

Introduction

Hepatitis B virus (HBV) has primary tropism by hepatocytes and can produce both acute and chronic infection in humans [1, 2]. The HBV can be transmitted by parenteral, sexual and vertical transmission [3]. A significant number of HBV infections occur during adolescence and in young adults, due to unprotected sexual relations, multiple partners, abusive use of alcohol and injectable drugs, tattoos and piercings, normal characteristics of their psychosocial development, assuming behaviors of risk without current or future concerns [4].

The present study aimed to evaluate coverage of the hepatitis B vaccination and the frequency of infection in communicants with HBV carriers, 20 years after the vaccine was implanted in the municipality of Belém, located in the eastern Brazilian Amazon. Specifically, the study sought to evaluate the seroepidemiological situation through serological and molecular surveys, detect prevalence and incidence among communicants of HBV carriers and, if necessary, refer for treatment and evaluate the immune response to the hepatitis B vaccine by referring those susceptible to vaccination.

Materials And Methods

The cross-sectional study was developed among HBV carrier communicants in Belém city. The project execution was approved by the Research Ethics Committee involving Human Beings, Approval Opinion No. 1.436.84828. A period of 19 years was considered, prior to the introduction of the hepatitis B vaccine in the city of Belém. To calculate the sample size “n” of the research, we considered the average number of ≈ 4 individuals among the families in northern Brazil [5] and an average of 12 people per year, resulting in the estimated minimum sample of 271 participants. A final number of 288 (n = 288) individuals participated in the study. The research excludes HBV carriers and people over the age of 20 at the time of the investigation. Parents (both or just one of them) were usually excluded.

The study was conducted by a research institute of the eastern Brazilian Amazon between July 2015 and July 2018. The identification of hepatitis B cases was carried out by searching the database of the Hepatology Section (SAHEP) of Evandro Chagas Institute (IEC), Health Surveillance Secretary (SVS) and Ministry of Health (MS) from 1998 to 2006 and SINAN from 2007 to 2017. After signing a Free and Informed Consent Form (signed by legal representatives for individuals under 18 years old), a questionnaire was applied to obtain demographic and epidemiological data.

Approximately 8 mL of blood was collected from each research participant. The serum samples obtained by centrifugation were tested by immunoenzymatic technique (ELISA) for the research HBsAg, total anti-HBc, and anti-HBs markers, using commercial kits from laboratories Biomérieux® and/or Biolisa® (Lyon, France), Dia.Pro® (Milan, Italy) and SYM - Symbiosys® (São Paulo, Brazil), respectively. The anti-HBc isolated reagent or inconclusive samples were tested for HBV molecular detection.

Isolated anti-HBc reactive or inconclusive samples were routed for molecular detection using the QIAamp MinElute Virus Spin kit (Qiagen) according to the manufacturer's instructions and subjected to amplification (by Nested-PCR) of a 734 bp fragment of the genes encoding the viral polymerase and HBsAg [6, 7].

The results were stored in the SAHEP/IEC database and the statistical analyses were conducted using EPIINFO 2007 software, version 7.1.0.6. Data analysis was performed using the BioEstat 5.0 program. To measure the central tendency, we used the time elapsed between the third / fourth dose of the vaccine and blood collection was done by calculating the average. For statistical inference, the chi-square test was used to analyze the association between the variables: gender, vaccine dose and isolated anti-HBc + serological marker, all using a statistical significance level of 5% ($p \leq 0.05$) [8].

Results

During the study period, 288 blood samples were collected after active search in homes of HBV carriers in the neighborhoods of Belém. The highest frequency of sample collection occurred in the neighborhoods of Benguí (11.8%, 34/288); Guamá (11.5%, 33/288), Val-de-Cães (8.7%, 25/288), Jurunas (8.3%, 24/288), Pedreira (6.9%, 20/288), Marco and Tapanã (5.9%, 17/288, respectively), Terra Firme (5.2%, 15/288) and Icoarací (3.5%, 10/288). The remaining 32.3% (93/288) were distributed in several other districts of Belém.

The sample consisted of 53.5% (154/288) males. The average age was nine years old (ranging from four months to 19 years) and a median age of 10 years. The highest frequency of individuals was found between 10 and 14 years old (29.2%; 84/288) and the lowest among < 1 year old (3.8%; 11/288).

Among the participants, 69% (199/288) were students and 56.3% (162/288) had incomplete/complete elementary school; 11.5% (33/288) had already undergone surgery; 1.7% (5/288) received blood transfusion; 3.8% (11/288) had piercings and 1.2% (3/288) tattoos; 7.3% (199/288) reported using condoms during sex; 2.8% (8/288) never used their own manicure kit; 0.3% (1/288) reported using

inhaled/injecting drugs and 3.5% (10/288) reported consuming alcohol. Also, 78.1% (225/288) reported lack of knowledge about hepatitis B vaccine; 5.6% (16/288) responded that the number of vaccine doses hampered the completion of the vaccination schedule; 54.9% (158/288) did not have a vaccination card; 1.4% (4/288) had difficulty finding the vaccine; 3.1% (9/288) were worried that the vaccine would be injectable and 9% (26/288) assumed a lack of interest about hepatitis B vaccine.

HBV serological analysis did not detect carriers of the HBV, characterized by the absence of HBsAg. Isolated anti-HBc was detected in 2.1% (6/288) reagent samples; 4.2% (12/288) of the samples examined were total anti-HBc/anti-HBs reagents and 42% (121/288) had isolated anti-HBs reagent, attributed to vaccination, where 73.3% were found in the 1 to 4 years old age group. Statistical significance was found for isolated anti-HBs by performing the chi-square adherence test for equal expected samples, with p (value) < 0.0001 (Table 1).

Table 1
Seroprevalence of HBV markers among communicants of HBV carriers, Belém, 2016–2018.

Age group (years)	N		anti-HBc+/anti-HBs+		isolated anti-HBc+		isolated anti-HBs+		P-value
	n (%)	CI 95%	n (%)	CI 95%	n (%)	CI 95%	n (%)	CI 95%	
< 1	11		4 (36.4)	(0.4–0.9)	–	(–)	7 (63.6)	(0.3–0.8)	
01–04	60		4 (6.7)	(0.92–4.2)	–	(–)	44 (73.3)	(0.9–4.2)	
05–09	70		1 (1.4)	(4.6–9.3)	–	(–)	21 (30.0)	(4.6–9.2)	< 0.0001*
10–14	84		1 (1.2)	(9.5–14.5)	4 (4.8)	(9.4–14.5)	22 (26.2)	(9.4–14.5)	
15–19	63		2 (3.2)	(14.8–19.3)	2 (3.2)	(14.6–19.6)	27 (42.9)	(14.6–19.6)	
Total	288		12 (4.2)	–	6 (2.1)	–	121 (42.0)	–	

Source: Research protocol; N = Population examined; Conventional sign used: – = numeric data equal to zero, not resulting from rounding; * HBV markers: HBsAg + = HBV carrier; total anti-HBc + / anti-HBs + = previous HBV infection profile; total + isolated anti-HBc = profile compatible with past or current HBV infection; anti-HBs + isolated = profile compatible with vaccine protection; * chi-square test for isolated anti-HBs variable.

Of the total participants examined, 41.6% (120/288) received complete (three/four dose) hepatitis B vaccine and 58.4% (168/288) were susceptible to HBV. Among those who received complete scheme, 51.8% (73/141) were under four years of age. This difference between the hepatitis B vaccine doses applied was statistically significant compared to the vaccine doses received because it was an immune response group, with p < 0.0001. The HBV-DNA was not detected in any of the 11 samples tested quantitative PCR.

Discussion

The study conducted by Souto showed that the distribution of HBV infection in Brazil showed the reduction of hepatitis B prevalence in the country, classifying the national territory as low endemicity to HBV [9]. The present study suggested a pattern of low endemicity, identified by the absence of the HBsAg serological marker [10].

During home visits, HBV patients were found living in places with difficult access and in precarious conditions, collaborating with the study of El Khouri, who linked hepatitis B infection to poor living conditions [11].

Study participants were considered at high risk for HBV infection according to behavioral issues, providing them with a sense of invulnerability, which was also perceived by Coutinho in his study on adolescents and hepatitis B vaccine [4]. In the current study, 9% of those examined pointed to lack of interest as the main reason for non-vaccination, although Carneiro et al., cited forgetfulness as the principal reason [12].

The vaccination booklet was characterized as one of the difficulties during the research, considering that 54.9% of respondents did not have proof of vaccination. One of the ways to solve the problem of losses would be to implement an adequate computerized system with information about vaccines, which is compatible with a study by Santos and Oliveira, where they mentioned the lack of a personalized information system as one of the health system problems [13].

The absence of HBV carriers among the participants was in accordance with a prevalence study conducted in the state capitals and the Federal District of Brazil. However, it was expected to find in this study a higher percentage of reactive results, considering that the population was composed of individuals subjected to risk situations [14].

This research identified a rate of 42% (121/288) people with isolated anti-HBs attributed to vaccination, with the highest vaccination coverage of 36.4% in the age group of 1 to 4 years old. When analyzing the population from 0 to 9 years old, 59.6% of anti-HBs isolated reagent was found, inferior to the previous study that found a higher percentage than 70% of vaccinated children from 0 to 10 years old [9] and also inferior to the study conducted among children and adolescents from Egypt, with complete vaccination scheme that found 57.2% serological protection [15].

Vaccination coverage in the municipality of Belém was heterogeneous for the period analyzed, and below the national average. This was similar to what happened in a study in the city of Trindade, State of Goiás, which obtained unsatisfactory coverage in most years, considering the basis of hepatitis B prevention is the vaccine, which provides 90–95% protection to immunocompetent individuals, with an appropriate vaccination schedule [16, 17, 18].

The prevalence of 58.3% of non-vaccinated individuals found in the study conducted in Belém was higher than that found in two municipalities of Parauapebas Microregion, southeast of the state of Pará, where,

in the municipality of Canaã dos Carajás, the prevalence of 44.1% was detected, and in the municipality of Curionópolis, 36.4% were found susceptible to HBV [19].

Regarding the age group of children with vaccine delay, the highest prevalence was among children under one year old of age with 66.7%, higher than that found in Carneiro's study that identified 55% for children under the age of six months to one year [12].

Conclusion

The absence of HBV carriers among communicants under 20 years of age suggested that the municipality of Belém has low endemicity for this group.

The home visiting team found it difficult to collect material due to the fragility of the public safety system, frequent changes of address and factors associated with misinformation.

Among the survey participants, 58.3% had not completed the full vaccination schedule. They had negative results for the anti-HBs test and had never previously had the test performed. Thus, the research suggests the need for incremental continuing education programs in schools and intra-family control.

These results allowed us to infer the need for greater attention and control of communicants, adequate registration of vaccine doses, guidance to those responsible, strengthening immunization programs and increasing epidemiological surveillance, in addition to contributing information to the scientific community about the status of HBV carrier contacts.

Due to the prevalence rates in the Brazilian Amazon region, we suggest further studies on the prevalence of HBV in the age group of over 20 years old and the evaluation of the immune response in samples of the population, planning new studies on the behavior of the HBV and its natural history, and how to know the various factors contributing to the course of the infection.

Limitations

Limitations to the study include young people lacking information about HBV carrier status among the family members; worry about receiving the injectable vaccine; unfamiliarity about the importance of the vaccine, which can impact the response of vaccine coverage; blood collection, and incorrect answers during the interview from some young people because of shyness.

Abbreviations

HBV

Hepatitis B virus; HBsAg:Hepatitis B virus surface antigen; anti-HBc:Total antibodies to the hepatitis B virus core antigen; anti-HBs:Antibodies to hepatitis B virus surface antigen; SINAN:Notifiable Diseases Information System.

Declarations

Ethics approval and consent to participate

This study was carried out according to the guidelines established in the Declaration of Helsinki and was approved by the Research Ethics Committee involving Human Beings of the Evandro Chagas Institute, under approval Opinion No. 1,436,848. All participants / responsible provided in writing their free consent for the use of their data, scientific evaluation and publication.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study is included in this published article. Samples are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contribution

CMAO was responsible for all phases of the study, from conception to study design, data acquisition, analysis and interpretation of data, final writing and critical review of the manuscript. AJSS collaborated in the acquisition of data, analysis and interpretation of data, writing and critical review of the manuscript. MJSB and DCNB collaborated in the acquisition, analysis and interpretation of data and in the critical review. MCPS and HMN participated in the conception and design of the study, data acquisition, data analysis and interpretation, writing of the manuscript and critical review. Finally, MRTN participated in data acquisition, data analysis and interpretation, manuscript writing and critical review. All authors read and approved the final manuscript.

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Author details

¹Seção de Hepatologia, Instituto Evandro Chagas/ Secretaria de Vigilância em Saúde/Ministério da Saúde, Belém, Pará, Brasil

²Centro de Inovações Tecnológicas - CIT, Instituto Evandro Chagas/ Secretaria de Vigilância em Saúde/Ministério da Saúde, Ananindeua, Pará, Brasil

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