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High prevalence of hepatitis B virus and low vaccine response in children and adolescents in Northeastern Brazil

Rogério Soares Castro[1], **Bárbara Silva Cordeiro**[1], **Marco Aurélio Ferreira Rolim**[1], **Alessandra Porto de Macedo Costa**[1], **Max Diego Cruz Santos**[1], **Marcos Antonio Custódio Neto da Silva**[2], **Ingrid de Campos Albuquerque**[3], **Lena Maria Barros Fonseca**[3], **João Renato Rebello Pinho**[4], **Michelle Soares Gomes Gouvêa**[4], **Antônio Augusto Moura da Silva**[5], **Adalgisa de Souza Paiva Ferreira**[1,6]

ABSTRACT

Children have an increased likelihood of becoming carriers of the chronic hepatitis B virus. A total of 1,381 children and adolescents were assessed in five municipalities of Maranhao State, Brazil, for detection of anti-HBc, HBsAg and anti-HBs serologic markers and sociodemographic and behavioral features. Among those who were HBsAg negative and anti-HBc negative, the proportion of anti-HBs positives was calculated after the individuals had completed the vaccination schedule. The robust variance of the Poisson's regression model was used in order to have adjusted tables and calculate the prevalence ratio. Multivariate analysis was performed to identify the factors associated with the prevalence of anti-HBc with or without HBsAg and the vaccine response. It was observed that 163 children were anti-HBc positive and nine individuals were HBsAg positive. The factors associated with the infection were: municipality of residence (residing in Morros municipality or Humberto de Campos municipality), residence in a rural area, aged between 13 and 15 years old, and illicit drug use. The percentage of individuals who were anti-HBc negative and received all three doses of the vaccine was 48.5%. Among these, only 276 (38.9%) had antibodies at protective concentrations. In an adjusted analysis, Morros municipality presented an increased positivity of vaccine response ($p < 0.001$), and the age ranging between 6 and 10 years old presented a reduced frequency of response. This study reveals a high prevalence of current and past HBV infection within the targeted age group which, in addition to the low vaccination coverage and serological responses, raises concerns about the management of prevention measures, especially the quality of vaccination in these locations.

KEYWORDS: Prevalence. Hepatitis B. Vaccine response. Children.

INTRODUCTION

Hepatitis B virus (HBV) has a worldwide distribution and is a major public health problem. An estimated 350 million people worldwide live with the virus, which resulted in 887,000 deaths in 2015[1]. HBV infection may lead to severe acute fulminant disease or chronic complications such as liver cirrhosis and hepatocarcinoma. In Brazil, approximately 17,000 new cases are diagnosed and reported per year[2].

In a population-based prevalence survey of hepatitis A, B, and C virus infections in Brazilian capitals conducted in 2010, it was found that 7.4% of all Brazilian

[1]Universidade Federal do Maranhão, Hospital Universitário, Empresa Brasileira de Serviços Hospitalares, São Luís, Maranhão, Brazil

[2]Universidade Federal do Maranhão, Centro de Ciências de Imperatriz, Curso de Medicina, Imperatriz, Maranhão, Brazil

[3]Universidade Federal do Maranhão, Departamento de Enfermagem, São Luís, Maranhão, Brazil

[4]Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Laboratório de Gastroenterologia e Hepatologia Tropical (LIM-07), São Paulo, São Paulo, Brazil

[5]Universidade Federal do Maranhão, Departamento de Saúde Pública, São Luís, Maranhão, Brazil

[6]Universidade Federal do Maranhão, Departamento de Medicina I, São Luís, Maranhão, Brazil

Correspondence to: Adalgisa de Souza Paiva Ferreira
Universidade Federal do Maranhão, Departamento de Medicina I, Praça Gonçalves Dias, CEP 65020-240, Centro, São Luís, MA, Brazil

E-mail: adalgisa.ferreira@ufma.br

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capitals displayed HBV (anti-HBc) exposure markers. Among the group, with ages ranging from 10 to 19 years old, this rate was 1.1%; as for the group aged 20 to 69 years old it was 11.6%. HBsAg was positive in 0.37% of the entire population, 0.05% for the group aged 10 to 19 years old and 0.6% for the group aged 20 to 69 years old[3], qualifying Brazil as a low-endemicity country.

Children are more likely than adults to become chronic carriers of HBV. Among those infected in the first year of life or at birth, up to 90% become chronic carriers. This percentage decreases with age, being 30–50% for those aged 1 to 5 years old. In adulthood, at least 90% of individuals will recover in the first year of infection[1,4,5].

According to the World Health Organization (WHO), with the advent of vaccination, the prevalence of HBV infection around the world in children under the age of 5 years old in 2015 was 1.3%, compared with 4.7% before the vaccination programs[1].

In Brazil, the National Immunization Program (PNI) of the Ministry of Health has recommended the universal vaccination of children from birth since 1998. In 2016, through an Information Note[6], the Ministry of Health expanded the offer to the population regardless of age and/or vulnerability conditions. The goal of vaccination is seroconversion of anti-HBs with titers greater than 10 mIU/ml[7].

The complete vaccination schedule is capable of producing protective antibodies in more than 95% of neonates, children and young adults[1]. However, there are host factors (genetic or otherwise) that may influence the vaccine response, which is more effective in newborns, children and adolescents and less immunogenic among the elderly and immunocompromised individuals[8].

In addition to host-specific factors, situations that may affect the vaccine effectiveness may include those related to improper handling of the vaccine, such as loss of conservation, improper vaccination site, noncompliance with vials, maximum opening time, and other logistics-related factors[9].

Anti-HBs titers are known to decrease over time. It is estimated that 15 to 50% of children who have responded to the three-dose vaccination schedule will have low or undetectable titers after 5 to 15 years[10]. Despite this finding, it is already known that as long as there was an initial response, there is no need for booster doses because there is an anamnestic response[11,12].

This study was conducted to evaluate the factors associated with HBV infection and vaccine response in children and adolescents aged 1 to 15 years old, living in the municipalities of Axixa, Morros, Icatu, Humberto de Campos and Urbano Santos in Maranhao State, Northeastern Brazil, where the overall prevalence of HBV is 2.3%[13].

MATERIALS AND METHODS

Our study group for the hepatic diseases of Presidente Dutra University Hospital/Federal University of Maranhao (HUUFMA) noticed a large number of hepatitis B patients coming from certain cities in the Northeast of Maranhao State. This observation led to a population-based study for hepatitis B in the municipalities of Axixa, Morros, Icatu, Urbano Santos and Humberto de Campos between 2013 and 2014. The study included around 3,990 subjects who were over one year old[13].

The sample was prepared through cluster sampling in two stages: in the first, the census sectors were selected by drawing lots with probability proportional to the population, whereas in the second, individuals were drawn. Thirty census sectors were drawn among the five municipalities. In each census sector, blocks and streets were drawn, in addition to the corners of the blocks to decide on the starting point of data collection. The interviewers traveled clockwise from the starting point until the completion of the predicted samples. All households composed of residents or individuals authorized by their parents were included in the sample. Closed or absent households were visited twice before being replaced with another one.

All individuals, including parents or caregivers, underwent clinical, demographic and epidemiological questionnaires. After this stage, all individuals had their blood samples collected in duplicate and kept in a freezer at -70 °C for serological testing (HBsAg, anti-HBs, and anti-HBc).

The blood samples collected after the interview were submitted to enzyme-linked immunosorbent assay (ELISA) with commercial kits (Diasorin®, Italy) to detect HBsAg, anti-hepatitis B core antigen (anti-HBc) and anti-HBs.

An evaluation was carried out for the completion of this paper from a database of the survey with a sample population of 1,381 individuals aged 1 to 15 years old.

In this population, the prevalence of contact with HBV (anti-HBc positivity) was analyzed. Individuals who were anti-HBc negative (who had no contact with HBV) and possessed a vaccination card at the time of the interview were considered for evaluating the vaccine response, thus proving the complete vaccination for hepatitis B. An anti-HBs concentration equal to or greater than 10mUI/ml was considered as a positive response criterion. The defined age limit of 15 took into account that individuals in this age group had already been vaccinated for HBV (mandatory vaccination started in Brazil in 1998) , in the first year of the study.

Data analysis was performed using STATA version 12 and SPSS version 23.0 software, using the Poisson regression model with robust variance to build adjusted tables and calculate the prevalence ratio.

This study was submitted to the HUUFMA Scientific Committee for analysis by the HUUFMA Research Ethics Committee and received a Consubstantiated Opinion, approved under Nº 253/2011, and under No. 448,731, after the amendment (through Plataforma Brasil) that requested an extension of the length of the project, meeting the requirements of Resolution 466/12 of the National Health Council of the Ministry of Health.

RESULTS

Among 1,381 individuals included in the study, 53.8% were female. The mean age was 8.97 years old (standard deviation ± 3.91). Humberto de Campos municipality had 389 participants (28.17%), followed by Urbano Santos municipality with 311 (22.52%), Morros municipality with 310 (22.45%), Icatu municipality with 186 (13.47%) and Axixa municipality with 185 (13.40%) participants. A total of 64.9% of respondents lived in rural areas. Among these, 60.8% had a family income below an equivalent to one minimum wage. Approximately 75.6% were racially identified as mixed-race, 15.13% white and 9.27% black. The use of illicit drugs was reported by 11.2% of individuals; 5.9% reported current use, and 5.3% reported previous use. A total of 3.1% of the individuals stated that they had already started sexual activity (Table 1). In this population, the vaccination coverage with three recommended doses of the hepatitis B vaccine was present in 53.5% of children, while 40.9% had not received a single dose of the vaccine.

Exposure to the virus (anti-HBc +) was demonstrated in 163 individuals (11.8%). Active infection (HBsAg + and anti-HBc +) was observed in nine individuals (0.65%), who were 66% male and 66% over the age of 10.

The prevalence of exposure to the hepatitis B virus (positive for anti-HBc) reached 20.45% in the 13 to 15-year-old age group, 22.26% in Morros municipality and

Table 1 - Profile of demographic, socioeconomic and epidemiological variables of hepatitis B in individuals aged 1 to 15 years old; Maranhao State, Brazil, 2012–2016 (n = 1,381).

Variable	n	%
Municipality		
Axixa	185	13.4
Morros	310	22.4
Humberto de Campos	389	28.2
Icatu	186	13.5
Urbano Santos	311	22.5
Sex		
Male	638	46.2
Female	743	53.8
Ethnic group		
White	209	15.1
Black	128	9.3
Mixed ethnicity	1,044	75.6
Age		
1–3 years	142	10.3
4–6 years	240	17.4
7–9 years	345	25.0
10–12 years	341	24.7
13–15 years	313	22.6
Sector		
Urban	485	35.1
Rural	896	64.9
Education		
Illiterate	15	1.1
Up to 8 years of study	998	72.3
8 or more years of study	114	8.2
Ignored	254	18.4
Family income (minimum wage – Brazilian reais)		
More than R$724.00	477	34.6
Less than R$724.00	840	60.8
Ignored	64	4.6
Blood transfusion		
No	1,368	99.06
Yes	13	0.94
Alcohol consumption		
No	1,353	98.0
Yes	28	2.0
Illicit drugs		
Never used	914	66.2
Already used	73	5.3
Uses	82	5.9
Ignored	312	22.6
Piercing/sharp objects sharing		
No	889	64.4
Yes	492	35.6
Tattoo		
Do not have	1,378	99.8
Have	3	0.2
Sex life		
Not started	1,338	96.9
Started	43	3.1
Number of hepatitis B vaccine doses		
1 dose	25	1.8
2 doses	52	3.8
3 doses	739	59.1
No dose	565	40.9

14.51% with residents living in rural areas. There were no significant differences regarding ethnicity, family income or sex.

An unadjusted analysis revealed associations between HBV exposure and the following variables: municipality of residence, age, area of residence, consumption of illicit drugs, initiation of sexual activity, number of vaccination doses for hepatitis B ($p < 0.001$), sharing sharp objects ($p = 0.024$) and alcohol consumption ($p = 0.003$) (Table 2).

These variables were subject to analysis adjusted by the Poisson's regression model and analyzed for the prevalence ratio with robust variance. An association with ages between 13 and 15 years old was confirmed (PR: 2.33, 95% CI: 1.22–4.46), along with being from the Morros municipality (PR: 6.11, 95% CI: 2, 61–14.34) or Humberto de Campos municipality (PR: 2.96, 95% CI: 1.25–7.01), residing in a rural area (PR: 1.85, 95% CI: 1.29–2,66) and consuming illicit drugs, either when the participant confirmed the use (PR: 2.56, 95% CI: 1.51–4.34) or when the individual refused to answer (PR: 1.48 CI 95%: 1.02–2.16) (Table 3).

Among the population studied, 1,218 individuals were aged less than or equal to 15 years old at the beginning of the study and had no active infection markers or were not in contact with the hepatitis B virus (HBsAg or anti-HBc). Among these, 729 (59.9%) were able to confirm their vaccination status with a vaccine card, and as for those, 671 (92.04%) received the complete schedule.

In order to assess the vaccine response, 671 individuals were evaluated (they had undergone the complete vaccination schedule and did not have a marker of previous contact with HBV); 54.25% were female, the mean age was 7.8 years old (standard deviation ± 3.6 years), 74.96% were mixed-race, 15.8% were white, and 9.24% were black. The rural area was represented by 64.53% of the children. Among these, only 261 children (38.9%) developed titers considered to be protective against the disease (anti-HBs ≥ 10 mIU/ml) (Table 4).

The unadjusted analysis identified an association between positive vaccine response, municipality of residence ($p < 0.001$) and age ($p = 0.02$) (Table 5). In an adjusted analysis, the Morros municipality showed a higher positivity of vaccine response, and the age group between 6 and 10 years old showed a lower frequency of response (PR: 0.72, 95% CI: 0.58–0.89) (Table 6).

DISCUSSION

This study, carried out with children and adolescents aged 1 to 15 years old in five municipalities in Maranhao State, identified a prevalence of 11.8% of HBV exposure, and among them, nine were active carriers of the virus (0.65%). The result of 11.8% prevalence is much higher than the national and Northeastern region averages for the group aged somewhere between 10 and 19 years old, estimated at 1.1% and 2.1%, respectively, and is comparable with the prevalence within the group aged 20 to 69 (11.6%) in the national average and in the Northeastern region (11.7%)[3,14]. Other cross-sectional studies indicate variations in the percentage of exposure to the virus or active infection in different populations across the state[15,16]. One study carried out in Buriticupu municipality found an even higher prevalence of HBV exposure, reaching 20.5% in individuals up to 20 years of age[15]. As there are no studies that evaluate the general population of the state or specifically the pediatric population, it is not possible to state or rule out whether this prevalence matches that in other municipalities, or whether this region in particular presents an especially worrying situation.

Compared with this study, those conducted in pediatric populations in other regions in Brazil revealed rates that are much lower in the Southern and Southeastern regions, ranging from 0.1% to 3.6% for anti-HBc and 0.02% to 1.8% positivity for HBsAg[17]; however, when examining the Northern region of the country (the region considered to be the most endemic for HBV in the country), prevalence rates of 23.1% for anti-HBc and 3.6% for HBsAg were found in children under age 15 in the Amazon region, even 19 years after the implementation of the universal vaccination program[18].

A systematic review of HBV prevalence studies in Brazil (conducted between 1999 and 2015) described that the virus is heterogeneously distributed in different regions of Brazil, ranging from less than 1% to 8%, with nonurban locations in the Northern, Northeastern and Central-Western regions having the highest rates[14], reinforcing that regions that are farther away from large centers and scarcely urbanized are more susceptible to HBV infection[19].

As for the risk factors related to the presence of anti-HBc, it was identified that living in the municipalities of Humberto de Campos and Morros was independently associated with higher rates than those associated with living in Axixa municipality. Although these are adjacent municipalities, according to the Brazilian Institute of Geography and Statistics (IBGE), Axixa municipality has a human development index (HDI) classified as medium, while the other four municipalities covered in the study are classified with low municipal HDI[20]. Some studies already indicate that lower socioeconomic indexes are linked to a higher prevalence of HBV infection[21], probably related to less adequate health services and conditions for the prevention of infectious diseases.

Likewise, residence in a rural area was shown to be associated with infection, probably also reflecting more

Table 2 - Unadjusted analysis of factors associated with Hepatitis B virus infection (anti-HBc positive) in individuals aged 1–15 years; Maranhao State, Brazil, 2012–2016 (n = 1,381).

Variable	N	PR	95% CI	p value
Municipality				< 0.001
Axixa	185	1	-	
Morros	310	6.86	3.03 – 15.4	
Humberto de Campos	389	4.12	1.80 – 9.42	
Icatu	186	2.48	0.98 – 6.27	
Urbano Santos	311	2.08	0.85 – 5.06	
Sex				0.777
Female	743	1	-	
Male	638	1.04	0.78 – 1.39	
Ethnic group				0.340
Black	128	1	-	
White	209	1.65	0.82 – 3.30	
Mixed ethnicity	1,044	1.54	0.83 – 2.86	
Age				< 0.001
1 to 3 years	142	1	-	
4 to 6 years	240	0.96	0.47 – 1.99	
7 to 9 years	345	0.89	0.45 – 1.78	
10 to 12 years	341	1.74	0.92 – 3.26	
13 to 15 years	313	2.63	1.43 – 4.85	
Sector				< 0.001
Urban	485	1	-	
Rural	896	2.13	1.47 – 3.07	
Family income (minimum wage – Brazilian reais)				0.061
More than R$724.00	477	1	-	
Less than R$724.00	840	1.42	1.02 – 1.97	
Ignored	64	0.82	0.34 – 2.00	
Alcohol consumption				0.003
No	1,353	1	-	
Yes	28	2.49	1.36 – 4.56	
Drugs				< 0.001
Never used	914	1	-	
Already used	73	1.16	0.58 – 2.30	
Uses	82	2.46	1.58 – 3.83	
Ignored	312	1.70	1.23 – 2.35	
Piercing/sharp objects sharing				0.024
No	889	1	-	
Yes	492	1.39	1.04 – 1.86	
Sex life				< 0.001
Not started	1,338	1	-	
Already started	43	2.69	1.67 – 4.35	
Number of hepatitis B vaccine doses				< 0.001
1 dose	25	1	-	
2 doses	52	1.04	0.44 – 2.41	
3 doses	739	0.38	0.18 – 0.79	
No dose	565	0.56	0.27 – 1.16	
Education				0.01
Illiterate	15	1		
< 8 years of study	998	1.86	0.27 – 12.4	
> 8 years of study	114	2.76	0.39 – 19.09	
Ignored	254	1.00	0.14 – 7.04	

Table 3 - Multivariate analysis of factors associated with hepatitis B virus infection (anti-HBc positive) in individuals aged 1 to 15 years old; Maranhao State, Brazil, 2012–2016 (n = 1,381).

Variable	N	PR	95% CI	p value
Municipality				< 0.001
Axixa	185	1	-	
Morros	310	6.11	2.61 – 14.34	
Humberto de Campos	389	2.96	1.25 – 7.01	
Icatu	186	1.50	0.58 – 3.86	
Urbano Santos	311	1.51	0.58 – 3.92	
Sex				0.318
Female	743	1	-	
Male	638	1.15	0.87 – 1.51	
Ethnic group				0.173
Black	128	1	-	
White	209	1.58	0.82 – 3.07	
Mixed ethnicity	1,044	1.43	0.78 – 2.62	
Age				0.001
1 to 3 years	142	1	-	
4 to 6 years	240	1.15	0.57 – 2.31	
7 to 9 years	345	0.96	0.49 – 1.88	
10 to 12 years	341	1.61	0.83 – 3.10	
13 to 15 years	313	2.33	1.22 – 4.46	
Sector				< 0.001
Urban	485	1	-	
Rural	896	1.85	1.29 – 2.66	
Family income (minimum wage – Brazilian reais)				0.730
More than R$724.00	477	1	-	
Less than R$724.00	840	1.06	0.75 – 1.49	
Ignored	64	0.98	0.40 – 2.39	
Alcohol consumption				0.643
No	1,353	1	-	
Yes	28	1.14	0.64 – 2.03	
Illicit drugs				0.001
Never used	914	1	-	
Already used	73	1.55	0.74 – 3.25	
Uses	82	2.56	1.51 – 4.34	
Ignored	312	1.48	1.02 – 2.16	
Piercing/sharp objects sharing				0.630
No	889	1	-	
Yes	492	0.92	0.67 – 1.26	
Sex life				0.149
Not started	1,338	1	-	
Already started	43	1.43	0.87– 2.33	
Number of hepatitis B vaccine doses				0.290
3 doses	739	1	-	
2 doses	52	1.38	0.61 – 3.09	
1 dose	25	0.53	0.26 – 1.07	
No doses	565	0.70	0.34 – 1.40	

Table 4 - Profile of the hepatitis B vaccine response in individuals aged 1 to 15 years old; Maranhao State, Brazil, 2012–2016 (n = 671).

Variable	n	%
Municipality		
Morros	155	23.1
Axixa	117	17.4
Humberto de Campos	168	25.0
Icatu	73	10.9
Urbano Santos	158	23.6
Sex		
Male	307	45.7
Female	364	54.3
Age		
1–5 years	201	30.0
6–10 years	302	45.0
11–15 years	168	25.0
Sector		
Urban	238	35.5
Rural	433	64.5
Family income (minimum wage – Brazilian reais)		
Less than R$724.00	417	62.2
More than R$724.00	233	34.7
Ignored	21	3.1

precarious living conditions and failures in the health care system, which involves early diagnosis of the infection and health education[14,15]. These conditions make the regions that are more distant or isolated from large centers become endemic areas with an intermediate or high prevalence of HBV infection[14].

An elevated frequency of HBV contact markers was observed among individuals aged somewhere between 13 and 15 years old, a fact also observed in a study carried out in a *quilombola* community in the Northeast of Goias State (a population that is comparable to the one studied here), where a 7.4% prevalence of this marker was found in the group aged 0 to 10, rising to 16.6% in the group aged 11 to 20[22]. This result is probably related to the individual's insertion in classic risk behaviors, such as the initiation of sexual activity or the use of illicit drugs, observed through all studies conducted with this population of this age group[23].

In fact, the use of illicit drugs also proved to be an independent risk factor for infection, even when the individual refused to answer, suggesting that there may have been non-admission of illicit drug use by the interviewees. However, the majority of individuals in the region who have these habits used non-injecting drugs (mainly marijuana or crack), suggesting that it is an indirect risk factor for other mechanisms of virus transmission, such as unprotected sexual contact, in addition to functioning as a bridge for

Table 5 - Unadjusted analysis of factors associated with vaccine response (anti-HBs positive) in individuals aged 1 to 15 years old; Maranhao State, Brazil, 2012–2016 (n = 671).

Variables	N	PR	95%CI	p value
Municipality				< 0.001
Morros	155	1	-	
Axixa	117	0.69	0.53 – 0.90	
Humberto de Campos	168	0.57	0.44 – 0.73	
Icatu	73	0.40	0.26 – 0.62	
Urbano Santos	158	0.58	0.45 – 0.75	
Sex				0.681
Male	364	1	-	
Female	307	1.04	0.86 – 1.25	
Age				0.002
1–5 years	201	1	-	
6–10 years	302	0.68	0.54 – 0.85	
11–15 years	168	0.92	0.73 – 1.16	
Sector				0.086
Urban	238	1	-	
Rural	433	1.19	0.97 – 1.47	
Family income (minimum wage – Brazilian reais)				0.309
Less than 1	417	1	-	
More than 1	233	0.87	0.71 – 1.08	
Ignored	21	0.69	0.35 – 1.38	

Table 6 - Multivariate analysis of factors associated with hepatitis B vaccine response (anti-HBs positive) in individuals aged 1 to 15 years old; Maranhao State, Brazil, 2012–2016 (n = 671).

Variable	N	PR	95% CI	p value
Municipality				
Morros	155	1	-	
Axixa	117	0.74	0.56 – 0.96	0.029
Humberto de Campos	168	0.59	0.46 – 0.76	0.000
Icatu	73	0.42	0.27 – 0.66	0.000
Urbano Santos	158	0.59	0.45 – 0.76	0.000
Sex				
Male	307	1	-	
Female	364	1.04	0.86 – 1.25	0.639
Age				
1–5 years	201	1	-	
6–10 years	302	0.72	0.58 – 0.89	0.003
11–15 years	168	0.94	0.75 – 1.18	0.640
Sector				
Urban	238	1	-	
Rural	433	1.16	0.93 – 1.44	0.186
Family income (minimum wage – Brazilian reais)				
Less than R$724.00	417	1	-	
More than R$724.00	233	0.88	0.70 – 1.11	0.309
Ignored	21	0.87	0.43 – 1.77	0.712

the later use of injectable drugs[24]. This issue reinforces the susceptibility of the drug user population as a risk group for infection[14,23], requiring specific approaches.

Active infection was present in 0.65% of those evaluated. That prevalence is higher than the national average of 0.055% for the 10 to 19 age group and comparable to the 0.6% rate found in the 20 to 69 age group[3]. When evaluating studies carried out abroad, where universal vaccination in children had already been implemented, the results found here were higher than the rates of 0.05%[25] found in children in Saudi Arabia, and those of 0.19% in Germany[26], but lower than the rates in China (1.6%)[27], Colombia (2%)[28] and Mexico (3.1%)[29], indicating the impact of these programs in reducing HBV infection.

The municipalities of Humberto de Campos and Morros were responsible for 77% of the total HBsAg carriers (active infection), suggesting that urgent measures should be prioritized in these locations, such as health education, strict prenatal care to prevent maternal-fetal transmission, and effective vaccination, which plays a fundamental role in controlling HBV infection. In addition to perinatal transmission, horizontal transmission (which occurs through household contact with family members) is more frequent within the pediatric age group[30]. Low socioeconomic, educational, and hygiene conditions and precarious and overcrowded households are characteristic of this population, which probably increase the spread of HBV infection in this population[31], mainly due to the increase in intra-household percutaneous contact. This reality further highlights the need for vaccination at birth to prevent this infection.

In Brazil, the National Immunization Program (PNI) has made vaccination for hepatitis B mandatory since 1998. Among the population studied, 1,218 individuals were aged less than or equal to 15 years old at the beginning of the study and had no infection markers active or contact with the hepatitis B virus (HBsAg or anti-HBc). Among these, 729 (59.9%) were able to confirm their vaccination status with a vaccine card, and as for those, 671 (92.04%) received the complete schedule. A rate of approximately 60% shows a low rate of vaccination coverage, which, in this population, should reach 100%.

Despite the PNI's recommendation for vaccination against the hepatitis B virus from birth, no records were found at the State Department of Health with data on vaccination coverage in the municipalities studied in 1998, suggesting a late implementation. The records show an average vaccination coverage from 1999 to 2012 of 70.82% in the region, with Humberto de Campos municipality having the highest average (84.76%), followed by Axixa

municipality (79.9%). The discrepancy shown here may also be related to the fact that some individuals may have been submitted to the vaccine but did not present their card for confirmation at the time of the study. The most alarming finding was that only 38.9% of children vaccinated with three doses had protective concentrations of the antibody.

The effectiveness of the HBV vaccine has been proven in many studies worldwide and in Brazilian studies within the pediatric population[12,32,33]. In another study carried out in Sao Paulo State, birth weight had an influence on the vaccine response; among those assessed who were born weighing more than 1,500 g, seroconversion was 100%, compared with 75% seroconversion for the group equal to or less than 1,500 g at birth[34].

It is known that failures in response (in healthy people) may be associated with genetic characteristics or the result of technical errors with the vaccine, such as administration or failure in packaging, both during transport and at the final destination[35-37].

In Brazil, Oliveira *et al.*[9] evaluated the quality of vaccinations for primary health care in 261 vaccination rooms in Minas Gerais State. They observed that the degree of conservation of the vaccines was not adequate in 59.3%, and 26.9% had a critical degree of quality, pointing to the need for training human resources, monitoring and evaluating the work process. Therefore, the low vaccine efficacy found in our study could be related to these factors, which could indirectly mirror the deficient socioeconomic indexes of the cities studied.

This speculation can be reinforced by the finding that the results were different among the municipalities studied, which may suggest that health promotion actions reflect the reality of each municipality, generating different results.

Another common situation, which could justify the result of low effectiveness found here, is the drop in anti-HBs titers that normally occurs with advancing age after vaccination[10,12,38]. A study of vaccinated children followed for 10 years found protective titers in 54.8% of the children[38]. To assess this possibility, analyses were performed comparing three age groups (1 to 5, 6 to 10 and 11 to 15 years old), and unexpectedly, the group aged between 6 and 10 was the one with the lowest rate of effective results, showing that it is unlikely that the low level of effectiveness identified is related to a progressive decline related to age.

It could be speculated that the lower response rate observed for the group aged between 6 and 10 years old is related to failures in health promotion policies in the state between 2004 and 2008, which could be reflected in these results and was already independent of the municipality studied.

Regarding the natural decline in antibodies with age, studies in other countries have shown conflicting results. A prospective cohort study conducted by Bruce *et al.*[32] in Alaska concluded that vaccine protection continues for more than 30 years, and that more than 94% of people in the study had evidence of protection. In contrast to this, in a study carried out in the USA[39], in which 420 adolescents were aged between 16 and 19 years old, 76% had anti-HBs < 10 mIU/ml. Nevertheless, there is already sufficient knowledge to determine that there is no need for booster doses of the vaccine for healthy individuals who had a satisfactory response after vaccination[40].

A prospective study evaluating these factors is being conducted by our group to identify whether they could be important in our population regarding the effectiveness of the HBV vaccine.

CONCLUSION

In conclusion, this study showed a high prevalence rate of active carriers and of previous contact with HBV in this age group in the region studied, and the effectiveness of the vaccine was lower than expected. These findings highlight the need to implement urgent measures to prevent infection among this population and are evidence that studies must be carried out to identify the real situation in the entire Maranhao State.

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