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Prevalence of hepatitis A in the capitals of the States of North, Southeast and South regions of Brazil: decrease in prevalence and some consequences

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ABSTRACT

Hepatitis A virus (HAV) infection has been considered one of the leading causes of acute hepatitis. The aim of the present study was to estimate the prevalence of HAV among children and adolescents in a population-based study in the capitals of the States of the North, Southeast and South of Brazil and identify predictive factors for the infection. A multi-stage sampling was used to select subjects aged between 5-9 and 10-19 years. Individual and household levels aside from the level of variables in the areas were collected. The outcome was the total IgG antibodies to HAV levels detected using a commercial Enzyme Immuno Assay (EIA). The associations between HAV and the independent variables were assessed using the odds ratio. A multilevel analysis was performed by GLLAMM using the Stata software. The prevalence of HAV infection in the 5-9 and 10-19 age groups was 28.7% and 67.5%, respectively for the North, 20.6% and 37.7%, for the Southeast and 18.9% and 34.5% for the South Region. The prevalence of HAV increased according to age in all sites. Variables related to education at the individual level (North and South), family and area level (South and Southeast) and family income level (Southeast and South) were independently associated with HAV infection. This emphasizes the need for individualized strategies to prevent the infection.

KEYWORDS: Hepatitis A infection. Risk factors. Brazil. Multilevel analysis.

INTRODUCTION

Hepatitis A (HA) has been considered one of the leading causes of acute hepatitis worldwide; it is primarily transmitted through contaminated food or water, and can also occur in high-risk groups, such as injecting drug users, men who have sex with men (MSM), people travelling to high endemicity areas and in isolated populations[1-3].

The prevalence of HA varies according to geographical regions. In developing countries with poor sanitary conditions, people tend to be infected during childhood and are usually asymptomatic or have few symptoms. On the contrary, in developed countries with good sanitary conditions, the incidence of HA in adults can result more frequently in severe hepatitis. Fulminant and fatal HA can occur, particularly in older individuals[4-9].

In Brazil, some reports demonstrated that the epidemiology of HAV has undergone considerable changes[10-13]. The result of this household survey in the Northeast,

Midwest and Federal District had been previous published and showed an overall prevalence of 47.7%, classifying these regions as intermediate endemicity regions for HAV[14].

The aim of the present study was to estimate the prevalence of HAV among children and adolescents in a population-based study in the capital of the States of the North, Southeast and South of Brazil. A secondary objective was to identify predictive factors for HAV infection.

MATERIALS AND METHODS

A population-based household survey was conducted in every capital of the States in the North, Southeast and South regions from 2005 to 2009. The methodology used was described in a previous publication[15]. A multi-stage cluster sampling scheme was applied based on the Brazilian population as determined by the year 2000 census[16]. The target population consisted of individuals aged from 5-9 and 10 -19 years, residents of private households in the North, South and Southeast Brazilian regions. Further details of the sampling strategy and of the parameters used to estimate the sample size were published elsewhere[15]. As these parameters were related to each of the regions as a whole, the results that might be obtained for each of the capitals individually would lack precision. This sample was considered to be representative of the population aged 5-9 and 10-19 years in the ensemble of State capitals of each macro-region.

The North region includes seven States and their respective capitals (in parenthesis): Roraima (Boa Vista), Amapa (Macapa), Para (Belem), Amazonas (Manaus), Rondonia (Porto Velho), Acre (Rio Branco), Tocantins (Palmas). The total population of these capital cities for the 5-9 and 10-19-year age groups were 414,281 and 860,922, respectively. The Southeast region includes four States: Espirito Santo (Vitoria), Rio de Janeiro (Rio de Janeiro), Minas Gerais (Belo Horizonte) and Sao Paulo (Sao Paulo). The total population for the 5-9 and 10-19-year age groups were 1,458,833 and 3,295,110, respectively. The South region includes three States: Parana (Curitiba), Santa Catarina (Florianopolis) and Rio Grande do Sul (Porto Alegre). The total population for the 5-9 and 10-19-year age groups were 259,621 and 586,270, respectively[16].

In each of the locations where the survey was carried out, the same standard protocol was used. Data were collected by an interview using a structured questionnaire during the household visits. Blood samples were collected after the interviews. Both procedures were performed by trained health personnel.

The inclusion criteria were subjects aged between 5-9 and 10 -19 years. All participants or guardians (in the case of children under the age of 13 years) were interviewed. Thus individual and household levels data were collected during the household visits and the following variables levels in each area were retrieved from a subset of census data: level of education of the head of the household (average years of schooling), literacy of the head of the household (%), household headed by a woman (%), head of the household being an illiterate woman (%), individuals in the households who are at the same time literate and aged 15-19 years old (%), water supply coverage (%) and solid waste collection coverage (%).

During the household visit, blood samples were collected, transported and stored according to standard procedures. Total IgG antibodies to HAV virus were detected using a commercial enzyme immunoassay kit (HAVAB EIA, Abbott Laboratories, Abbot Park, IL, USA) in central public health laboratories. Laboratory tests were validated and the quality control was monitored. Seropositive results were interpreted as current or past HA infection (ever infected). Borderline results (0.15%) and inadequate samples were excluded from the analysis.

The sample size was calculated based on an expected prevalence of HAV-infection of 30% and α <0.05. Within each region and age stratum, the sample was proportional with respect to different capital cities.

The overall prevalence of seropositivity and 95% CI were calculated for each study locations (North, Southeast and South) by age-group, corrected for the design effect[17]. The association between HA infection and independent variables was assessed using the Odds ratio (OR) and their respective 95% CI; a P-value less than 5% was considered statistically significant. The OR was corrected by a random design effect due to the study design. The weighting was also applied because different sampling fractions were adopted for the two age groups. Firstly, a univariate analysis was performed separately for each age group. As the identified risk factors were similar in the two populations, they were combined to increase the statistical power of the study. Individual household and area level of variables associated with the outcome in the univariate analysis (P<0.10) were successively included in a multilevel model. Generalized Linear and Latent Mixed Models (GLLAMM) were used to perform the multilevel analysis using the Stata software, version 9.2 (StataCorp, College Station, TX, USA)[18].

Written consent was obtained from all participants and, in the case of minors, from their legal guardians. The project was submitted to the National Research Ethics Committee (CONEP) of the Brazilian National Health Council and to the local research ethics committees in each location

RESULTS

Table 1 presents the total number of patients included in the study in each region according to their demographic characteristics, households and areas. There is a balance between age groups and sex at individual level in different regions. There are major differences in socio-economic conditions of household variable levels directly associated with the transmission of hepatitis A, such as water supply, regular water supply and sewage disposal.

Table 2 presents the estimated and the achieved sample size (number of individuals included in the study), for the ensemble of capitals of each Brazilian region in the age groups considered, and their distribution by State capital.

The prevalence of hepatitis A infection (anti-HAV-IgG) for each age group in the North, Southeast and South regions are presented in Table 3. The North region had higher rates in relation to the South and Southeast. In addition, the results of HAV prevalences by State capital are shown exploratory only; wide confidence intervals were observed.

Table 4 shows the main characteristic of individual variables. Increased age was a risk factor for HAV in all regions. Literacy had a protective effect in the Southeast and South regions. Schooling had a protective effect in the North and Southeast regions.

The association among being the head of a family, household level variables and HAV infection are shown in Tables 5 and 6. It was observed that in the North region the income of the head of the household was not associated with HAV infection, while in the two other regions there was an inverse association. Literacy and a higher level of education of the head of the household had a protective effect in the South and Southeast regions.

In relation to the characteristics of the household, the lack of adequate water supply, sewage disposal and solid waste disposal were associated with the infection in the South region; a similar association with sewage disposal was also observed in the Southeast. None of the characteristics of the household was associated with the infection in the North region (Table 6).

Association between the level of variables in the area and HAV infection are detailed in Table 7. In the Southeast region,

Table 1 - Characteristics of individual, household and area levels among children and adolescents living in the North, Southeast and South regions of Brazil.

Characteristics	North	Southeast	South
Total of individuals sampled	**231**	**2,177**	**2,053**
Individual level – n (%)			
Female	105 (45.4)	1,099 (50.5)	1,046 (50.9)
5-9 years old	98 (42.4)	1,083 (49.7)	845 (41.2)
10 -19 years	133 (57.6)	1,094 (50.2)	1,208 (58.8)
HAV vaccine reported	13 (5.6)	130 (6.0)	81 (3.9)
School attendance	205 (88.7)	1,970 (90.5)	1,814 (88.4)
Illiterates ≥ 7 anos	9 (4.5)	108 (6.0)	57 (3.2)
Household level – n (%)			
Home ownership	188 (87.0)	1,602 (73.6)	1,526 (74.3)
Water supply	181 (78.3)	2,115 (97.1)	2,003 (97.6)
Pipe water inside the house	209 (96.8)	2,153 (98.9)	2,006 (91.9)
Regular water supply	39 (18.1)	654 (30.4)	1,413 (68.8)
Sewage disposal	60 (27.8)	1,894 (87.0)	1,510 (73.5)
Solid waste disposal	206 (95.4)	2,024 (93.0)	1,966 (95.8)
Area level – median % (P_{25}; P_{75})			
Illiterate head of the household	8.1 (5.3; 12.8)	7.2 (3.1; 13.9)	4.9 (1.6; 8.0)
Illiterate female, head of the household	11.5 (7.5; 17.2)	10.0 (5.6; 18.2)	8.2 (3.3; 15.2)
Mean level of schooling of the head of the household (years)	6.6 ± 1.8	6.2 (5.1; 7.5)	7.1 (5.8; 9.2)
15-19 years literate individuals	98.6 (96.6; 99.2)	98.8 (97.1; 100.0)	99,1 (98.0; 100.0)
Female head of the household	33.6 (26.1; 38.4)	29.4 (24.3; 34.5)	28,5 (24.1; 35.0)
Households with water supply	90.0 (18; 98.6)	100.0 (99.2; 100.0)	99,5 (99.1; 100.0)
Households with solid waste collection	98.7 (89.5; 99.7)	100.0 (99.7; 100.0)	100 (99.6; 100.0)

Table 2 - Population of each region and of the State capitals in the age groups 5 - 9 and 10 - 19 years old and the estimated and achieved sample size.

Regions State capitals	Population[a]		Sample size Estimated/achieved	
	5-9	10- 19	5 - 9	10 - 19
North region	**397,865**	**837,126**	**112/98**	**108/133**
Rio Branco	25,348	51,817	7/12	7/7
Macapa	32,662	65,390	8/12	8/11
Manaus	154,115	370,935	40/32	40/43
Belem	118175	270049	37/28	37/36
Porto Velho	29,877	63,191	10/5	10/15
Boa Vista	23,547	44,807	6/6	6/16
Palmas	14,141	29,788	4/3	4/5
Southeast region	**1,389,394**	**2,794,712**	**1,203/1,083**	**1,203/1,094**
Belo Horizonte	175,127	411,970	143/128	143/151
Vitoria	22,464	56,673	19/18	19/31
Rio de janeiro	433,908	947,643	375/307	375/333
Sao Paulo	757,895	1,749,199	666/630	666/579
South region	**254,075**	**576,602**	**1,324/845**	**1,324/1,208**
Curitiba	130,531	289,482	639/510	639/555
Florianopolis	25,739	62,468	138/94	138/110
Porto Alegre	97,805	224,652	547/241	547/543

[a]Population living in the urban area of the State capital according to the Instituto Brasileiro de Geografia e Estatistica (IBGE)[16].

Table 3 - Prevalence of hepatitis A infection (anti-HAV-IgG) for each age group, in the North, Southeast and South regions and in the State capitals.

Regions State capitals	Prevalence* (95%-CI) 5 – 9 years	Prevalence (95%-CI) 10 – 19 years	Prevalence** (95%-CI) 5 – 19 years
North Region	**28.7 (16.2 – 38.3)**	**67.5 (59.8 – 80.0)**	**58.3 (49.4 – 67.2)**
Rio Branco	25.0 (4.0 – 72.5)	57.1 (6.0 – 96.5)	42.7 (13.1 – 78.6)
Macapa	25,.0 (11.7 – 58.4)	45.5 (5.6 – 92.2)	38,.5 (14.8 – 69.2)
Manaus	25.0 (11.1 – 47.0)	84.6 (73.0 – 91.8)	69.4 (59.6 – 77.7)
Belem	25.0 (10.1 – 49.8)	55.6 (37.4 – 72.4)	47.3 (31.8 – 63.3)
Porto Velho	-	-	-
Boa Vista	83.3 (13,0 – 99,4)	80.0 (35.7 – 96.7)	80,.5 (46.0 – 95.3)
Palmas	66.7 (Not estimated)	100 (Not estimated)	92.6 (25.7 – 99.8)
Southeast Region	**20.6 (15.3 – 26.0)**	**37,.7 (33.2 – 42.1)**	**32.5 (28.6 – 36.3)**
Belo Horizonte	25.4 (15.9 – 38.0)	30.0 (20,.0 – 42.2)	28.7 (21.0 – 37.8)
Vitoria	22.2 (6.0 – 56.1)	48.4 (26.9 – 70.5)	43.0 (26.6 – 61.2)
Rio de janeiro	21.6 (12.4 – 34.7)	38.7 (29.9 – 48.3)	33.7 (26.3 – 42.0)
São Paulo	19.2 (12.8 – 27.6)	38.5 (32.7 – 44.7)	32.2 (27.0 – 37.9)
South Region	**18.9 (13.7 – 24.1)**	**34.5 (28.5 – 40.6)**	**30.8 (25.6 – 36.1)**
Curitiba	20.7 (13.9 – 30.0)	34.0 (25,.5 – 43.7)	30.2 (22.8 – 38.8)
Florianopolis	12.9 (7.0 – 22.5)	23.6 (13.2 – 38.5)	20.7 (12.3 – 32.7)
Porto Alegre	17.3 (11.1 – 25.8)	37.3 (28.3 – 47.3)	34.0 (26.1 – 42.9)

*Prevalence adjusted for random effect; **Prevalence adjusted for random effect and weighted by age group.

Table 4 - Association between individual variables and hepatitis A infection (anti-HAV-IgG), in the North, Southeast and South regions of Brazil.

Individual variables	North		Southeast		South	
	OR* (95% CI)	p	OR* (95% CI)	p	OR* (95% CI)	p
Gender						
Female	1.0		1.0		1.0	
Male	0.93 (0.47 – 1.84)	0.845	0.90 (0.70 – 1.14)	0.399	0.89 (0.73 – 1.09)	0.293
Age						
5-9	1.0		1,0		1,0	
10 -19	5.15 (2.69 – 9.87)	0.000	2.32 (1.69 – 3.18)	0.000	2.26 (1.65 – 3.11)	0.000
Literacy						
Yes	1.0		1.0		1.0	
No	2.11 (0.72 – 6.12)	0.170	0.51 (0,.34 – 0.77)	0.001	0.49 (0.32 – 0.76)	0.001
Schooling						
Illiterate	1.0		1.0		1.0	
≤ 8 years	0.56 (0.21 – 1.49)	0.247	0.71 (0.51 – 0.98)	0.038	1.50 (1.01 – 2.23)	0.044
9-11 years	0.07 (0.01 – 0.40)	0.002	0.41 (0.26 – 0.66)	0.000	1.71 (1.07 – 2.73)	0.024
College education	-	-	0.30 (0.12 – 0.71)	0.007	0.42 (0.15 – 1.15)	0.093

*Odds ratio corrected by random effect and weight sampling

Table 5 - Association between variables with the head of the family and hepatitis A infection (anti-HAV-IgG) in the North, Southeast and South regions of Brazil.

Head of family (variables)	North		Southeast		South	
	OR* (95% CI)	p	OR* (95% CI)	p	OR* (95% CI)	p
Paid work in the previous week						
Yes	1.0		1.0		1.0	
No	1.05 (0.49 – 2.25)	0.881	1.23 (0.93 – 1.63)	0.131	1.31 (0.99 - 1.72)	0.053
Income (minimum wage)						
< 1	1.0		1.0		1.0	
1 - 2	0.83 (0.33 – 2.07)	0.698	0.92 (0.63 – 1.33)	0.666	0.93 (0.66 – 1.32)	0.709
2 - 3	1.15 (0.36 – 3.63)	0.807	0.55 (0.38 – 0.81)	0.003	0.67 (0.42 – 1.07)	0.102
3 - 5	0.56 (0.14 – 2.25)	0.418	0.34 (0,.19 – 0.59)	0.000	0.38 (0.24 – 0.59)	0.000
5 - 10	0.65 (0.13 – 3.08)	0.592	0,.34 (0.19 – 0.59)	0.000	0.22 (0.12 – 0.38)	0.000
> 10	0.47 (0,.07 – 3.02)	0.431	0,.67 (0.32 – 1.40)	0.289	0.18 (0.08 – 0.39)	0.000
Literacy						
Yes	1.0		1.0		1.0	
No	2.18 (0.53 – 8.89)	0.273	1.70 (0.07 – 2,.70)	0.023	4.54 (2.26 – 9.12)	0.000
Schooling						
Illiterate						
≤ 8 years	0.82 (0.17 - 3,85)	0.807	0.91 (0.66 – 1.26)	0.599	0.65 (0.35 – 1.17)	0.155
9-11 years	0.71 (0.17 - 3.02)	0.651	0.72 (0.49 – 1.05)	0.096	0.57 (0.34 – 0.95)	0.033
College education	0.59 (0,.14 - 2. 34)	0.454	0.47 (0.31 – 0.70)	0.000	0.24 (0.14 – 0.40)	0.000

*Odds ratio corrected by random effect and weight sampling

there was an inverse association between socioeconomic conditions expressed either as the level of education or as the provision of public service and HAV infection for all variables analyzed, while in the South, an association was observed with variables related to the education of the head of the household and solid waste collection coverage. In the

Table 6 - Association between variables and the household level and hepatitis A infection (anti-HAV-IgG) in the North, Southeast and South regions of Brazil.

Household level (variables)	North		Southeast		South	
	OR* (95% CI)	p	OR* (95% CI)	p	OR* (95% CI)	p
Home ownership						
Yes	1.0		1.0		1.0	
No	1.78 (0.69 – 4.60)	0.228	1,.05 (0.76 – 1.44)	0.744	0.80 (0.57 – 1.12)	0.208
Water supply						
Yes	1.0		1.0		1.0	
No	0.78 (0,.32 – 1.87)	0.579	1.27 (0.64 – 2.50)	0.487	0.38 (0.06 - 2.42)	0.307
Piped water at home						
Yes	1.0		1.0		1.0	
No	-		-		-	
Lack of water supply						
Never	1.0		1.0		1.0	
At least one per month	0,.89 (0,.31 – 2.58)	0.834	1.37 (0,.88 – 2.11)	0.154	2.36 (1.53 – 3.65)	0.000
Rarely	0,.60 (0,.22 – 1,.63)	0.320	0,.75 (0.56 – 1.01)	0,.059	1.99 (1.40 – 2.83)	0.000
Sewage disposal						
Public system	1.0		1.0		1.0	
Septic tank	0.83 (0.38 – 1.77)	0.628	1.24 (0,.78 – 1.99)	0.352	1.32 (0.84 – 2.07)	0.222
Other destination	1.55 (0.31 – 7.77)	0.593	1.55 (1.03 – 2.35)	0.035	3.78 (2,.35 – 6.07)	0.000
Solid waste disposal						
Collect by public service	1.0		1.0		1.0	
Other destination	4.19 (0.35 – 49,7)	0.256	1,.82 (0,.79 – 4.18)	0.154	2,.37 (1.12 – .95)	0.024

*Odds ratio corrected by random effect and weight sampling

Table 7 - Association between variables and the area level and hepatitis A infection (anti-HAV-IgG) in the North, Southeast and South regions of Brazil.

Area level variables	North		Southeast		South	
	OR* (95% CI)	p	OR* (95% CI)	p	OR* (95% CI)	p
Illiterate head of the household (%)	1.05 (0.99 - 1.12)	0.117	1.06 (1.04 - 1.09)	0.000	1.14 (1.11 - 1.17)	0.000
Illiterate female, head of the household (%)	1.02 (0.98 - 1.07)	0.308	1.03 (1.01 - 1.05)	0.001	1.06 (1.04 - 1.08)	0.000
Schooling of the head of the household (mean years)	0.83 (0.68 - 1.02)	0.077	0.88 (0.80 - 0.97)	0.011	0.76 (0.69 - 0.83)	0.000
15-19 years literate individuals living in the household (%)	0.93 (0.81 - 1.06)	0.274	0.86 (0.79 - 0.93)	0.000	0.87 (0.75 - 1.01)	0.074
Female head of the household (%)	0.96 (0.92 - 1.00)	0.036	1.02 (1.00 - 1.03)	0.024	1.00 (0.98 - 1.02)	0.911
Water supply coverage (%)	1.00 (0,.99 - 1.01)	0.444	0.99 (0.98 - 0.99)	0.000	0.96 (0.91 - 1.03)	0.320
Solid waste collection coverage (%)	1,.00 (0.97 - 1.03)	0.857	0.98 (0.98 - 0.99)	0.000	0.93 (0.92 - 0.95)	0.000

*Odds ratio corrected by random effect and weight sampling.

North region, only the percentage of women that were head of the households was associated with the infection.

The multilevel model for individual, household and level of variables in the areas are presented in Table 8. Age was a risk factor for infection in all regions. Illiteracy (individual level) was independently associated with HAV infection in the North. In the Southeast, illiteracy of the head of the household (household level) and the percentage of females that were the head of households were risk factors for HAV. In the South, the variables independently associated with HAV infection were the lack of water supply and the type of sewage disposal at the household

Table 8 - Multilevel model for individual, household and area variables associated with hepatitis A infection.

Variables	North		Southeast		South	
	OR* (95% CI)	p	OR* (95% CI)	p	OR* (95% CI)	p
Individual level						
Age	1,53 (1,29 – 1,82)	0,001	1,16 (1,12 – 1,20)	0,001	1,19 (1,14 – 1,24)	0,001
Schooling						
Illiterate and basic level	1,0				1,0	
Secondary level or more	0,10 (0,02 – 0,39)	0,001			0,61 (0,43 – 0,85)	0,004
Literacy						
Yes	1,0					
No	3,70 (1,04 – 13,2)	0,043				
Household level						
Lack of water supply						
Never			1,0		1,0	
At least one per month			0,89 (0,57 – 1,38)	0,606	1,79 (1,09 – 2,94)	0,020
Rarely			0,62 (0,47 – 0,83)	0,001	1,74 (1,18 – 2,56)	0,004
Sewage disposal						
Public system					1,0	
Septic tank					1,08 (0,73 – 1,59)	0,698
Other destination					1,98 (1,24 – 3,18)	0,004
Income oh head of household						
< 2			1,0		1,0	
2 or more			0,58 (0,45 – 0,75)	0,000	0,67 (0,52 – 0,87)	0,003
Schooling of head of household						
Illiterate						
≤ 8 years			0,80 (0,58 – 1,09)	0,162	0,85 (0,57 – 1,27)	0,436
9 years or more			0,64 (0,43 – 0,94)	0,023	0,57 (0,35 – 0,91)	0,021
Area level						
% Female head of household	0,94 (0,90 – 0,98)	0,007	1,02 (1,00 – 1,03)	0,009		
% Illiterate head of household			1,07 (1,03 – 1,10)	0,000	1,10 (1,06 – 1,14)	0,000
% Water supply covarage			0,98 (0,97 – 0,98)	0,000		

*Odds ratio corrected by random effect and weight sampling

level, and the percentage of illiteracy among the heads of households at the area level.

DISCUSSION

The present study shows an epidemiological shift of HAV infection from high to intermediate endemicity in the North and to low in endemicity in the Southeast and South regions when comparing the present results with the prevalences observed in the past[19]. The North was the region with the highest prevalence of HAV infection in children and adolescents, almost 70%, while the South and the Southeast had a prevalence of about 40%, reflecting better socio-economic status of their population. This shift was also observed in the Northeast and Midwest regions which became areas with intermediate endemicity[14] and placing Brazil as a country of intermediate and low endemicity for HAV.

HAV epidemiology is classically associated with socioeconomic conditions, mainly in less developed countries[3,13]. Our study showed, in a multilevel analysis, the association between socioeconomic conditions (factors measured at the individual, household and area levels) and HAV infection. However, there were differences in epidemiological profiles. In the North region, socioeconomic conditions were not related to an increased risk of HAV, probably because this area had poorer, though homogeneous conditions for all individuals, although, in the North, being

illiterate, at the individual level, was a risk factor for the infection. It is likely that this variable discriminates different degrees of poverty, being a marker of extreme poverty. Interestingly, in the Southeast, the income and schooling of the head of the households, sewage disposal and all variables related to the socioeconomic conditions at the area level were associated with the HAV infection, highlighting the relevance of a contextual effect. In the South, in addition to the variables related to schooling at the household and area levels, the lack of adequate water supply, sewage disposal and solid waste disposal were associated with the infection. Inadequate water supply, sewage disposal and solid waste disposal may be directly associated with the transmission of the disease but, in Brazil, they are also a marker of the socioeconomic conditions.

The interpretation of results of the North region must be done with caution; the lack of association with life conditions is probably due to the homogeneous low socio-economic conditions in this region.

All these findings point to the need to improve public services (water supply and sanitation) and show that broader interventions to raise the socioeconomic conditions of the population may have an important effect on the control of HAV virus transmission, in addition to improving the quality of life.

The present study has also demonstrated that some associations have a protective effect. Individual schooling was inversely associated with HAV infection in the North and in the South regions. Furthermore, higher incomes of the head of the household, as well as a higher level of schooling of the head of the household had a protective effect in Southeast and South regions. These results emphasize the importance of social determinants characteristics to improve the status of HAV, even in the most developed areas.

This study may not represent the current prevalence of HAV, given that in Brazil the vaccine has been introduced in the whole country for children from 12-23 months in 2014. Actually, in a previous study (2012), our group estimated that a universal childhood HA vaccination program would be associated to a significant impact on the epidemiology of the disease in all regions, resulting in a reduction in the number of cases of icteric hepatitis, of deaths for the disease and of life years lost, in a national perspective[20].

No population-based household survey was carried out ever since. However, one can estimate the prevalence chances through annual series cases assessed through the Brazilian Ministry of Health electronic site. The HA incidence was steady around 6,000 cases per year until 2014. Between 2014 and 2016, there was an 85.5% cumulative drop, independent of gender and geographical regions, after the introduction of the single-dose HAV vaccine program[21]. On the other hand, the results of this study reinforce the need of prevention for the population who are at increased risk of serious disease and were not impacted by the vaccine.

We emphasize that this new scenario poses several challenges, as there is an increase of susceptible individuals in adulthood, and the numbers are higher in low endemicity areas[5,7,8]. Another report of our group in which we presented the modeling of the HAV infection force for all Brazilian regions, showed that age at the midpoint of the population's susceptibility (age at which half of the population in that age group does not have anti-HA IgG antibodies) was 11.5 and 17 years old, respectively, for the intermediate and low HAV endemicity areas in that period[22].

Usually, HA infection is asymptomatic in children, but can be severe in adults, with symptoms occurring in most patients. Adults are also at risk of fulminant hepatic failure, that is associated to a high risk of death requiring emergency liver transplantation[23]. Furthermore, patients with preexisting liver damage such as those with non-alcoholic fatty liver disease (the most prevalent liver disease nowadays) are more prone to develop an acute liver failure associated with the chronic liver condition in cases of HAV infection[24].

The vaccine against HA is also a priority for the following situations: people with chronic liver diseases; chronic hepatitis B or C carriers; coagulation problems; people with genetic diseases; people with cystic fibrosis; candidates for organ transplantation; transplant recipients and donors of solid organ or bone marrow; people with blood disorders and patients with HIV. Recently, the need of vaccination in the group of men who have sex with men (MSM) has been emphasized given its importance in low endemic areas[25]. In the municipality of Sao Paulo, the largest population among all capitals, where the first outbreak was recorded in the country, there were almost one 1,400 cases between 2017 e 2018, and four deaths. In view of this occurrence, the municipality of Sao Paulo was the first city in Brazil to recommend the vaccination for people who have sexual practice including oral-anal contact, with priority for the MSM population[26]. In Rio de Janeiro, the number of cases rose again in 2017, increasing even more in 2018, reaching the same levels reported before the vaccination. Three other capitals from the South and the Southeast regions showed an upward trend in the number of cases among adult men, although less impressive numbers then the two previously mentioned. The large cities in the other three Brazilian regions showed a decrease or stabilization of cases without an increase among male adults. A change in the epidemiological pattern of HAV infection is emerging in the Southern and the South of Brazil[27,28].

Population-based surveys, such as this study, can obtain real prevalences, including asymptomatic cases, in addition to risk factors. However, due to its high cost and complexity, changes in the behavior of hepatitis A can be investigated through its temporal trend, according to age of incidence of symptomatic and fatal cases and outbreaks in MSM, providing some important information to estimate the disease burden, as recommended by WHO[29].

A strength of the study is that a robust methodology based on multilevel analyses was used to analyze variables at the individual, household and area levels that could be potentially associated with the HA infection, completing the publication of the other three regions of Brazil. Moreover, its baseline prevalence has also helped to explain the major outbreak that took place in the city of Sao Paulo among MSM, and the increment of cases in other cities in the South and Southeast regions among adult men. A limitation of the study is that the parameters used to estimate the sample size were adequate for the ensemble of capitals of each region. Therefore, the results shown for each State capital were presented only on exploratory basis, and are not accurate, as expressed by their wide confidence intervals.

CONCLUSION

In conclusion, the present study carried out in the capitals of the North, Southeast and South regions, demonstrated that Brazil has areas of intermediate and low endemicity of HA and a different profile of risk factors. This emphasizes the need for customized strategies to prevent the infection.

CONFLICT OF INTERESTS

All authors declare that they have no conflict of interests. In addition, all authors have read and approved the manuscript as submitted, are qualified for authorship, believe the submission represents honest work and take full responsibility for the reported findings.

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