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Seroprevalence of hepatitis A in children and adolescents

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Abstract

Objectives: To determine the seroprevalence of hepatitis A (HAV) in children and adolescents aged 1 to 14 years, and to identify factors associated with a history of infection.

Methods: This was a cross-sectional epidemiological study, conducted form February to August 2006 in the city of Curitiba, Paraná, Brazil, and the surrounding municipalities (Greater Curitiba). Laboratory analysis comprised qualitative assay for total HAV antibodies in whole blood samples.

Results: A total of 901 children and adolescents were recruited for the study. Age distribution was as follows: 1 to 4 years, n = 237 (26.3%); 5 to 9 years, n = 313 (34.7%); and 10 to 14 years, n = 351 (39%). The global rate of seroprevalence was 19.8%, and seroprevalence rates by age group were 3%, 21.1% and 29.9% respectively ($p < 0.01$). Multivariate analysis demonstrated that the following factors, in combination, had a positive association with the prevalence rate of antibodies against HAV in the study population: age groups 5 to 9 and 10 to 14 years, living in a household with more than one inhabitant per room, shared eating area and low per capita income.

Conclusions: The results show a low prevalence of antibodies against HAV, which justifies the use of prophylactic measures, including early vaccination.

J Pediatr (Rio J). 2011;87(5):419-24: Hepatitis A, seroepidemiological study, child, adolescent.

Introduction

The hepatitis A virus (HAV) is the most common cause of acute viral hepatitis in children[1] and is also responsible for 75% of all cases of viral hepatitis in the world. The disease has global distribution and is more common in areas with low levels of socioeconomic development. Incidence is elevated in developing countries and the majority of these populations will become infected before the age of ten.[2] The seroprevalence of HAV is low in developed countries and the greater part of those populations will remain susceptible to infection even at advanced ages.[3,4]

Over recent years, the improvements in sanitary conditions and in socioeconomic conditions that have taken place in some developing countries have changed the epidemiology of certain diseases, including hepatitis A.[5-9]

Hygiene and sanitation are primarily improved for populations from more privileged social classes.[10] These social inequalities mean that in a single geographical location an underprivileged population will still be being infected before the age of ten, while in higher social classes adolescents and adults remain susceptible. If these people

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do become infected later in life, they suffer greater HAV-related morbidity and mortality.[11]

The objective of this study was to determine the seroprevalence of hepatitis A among children and adolescents aged 1 to 14 years from Greater Curitiba, in Paraná, Brazil, and to identify factors associated with prior infections.

Materials and methods

This cross-sectional epidemiological study was undertaken with children and adolescents from Greater Curitiba between January 19 2006 and September 4 2006. The region contains 26 municipalities, covers a total area of 15,416.9 km^2 and had a population of 3,186,099 inhabitants in 2005, according to data from the Brazilian Institute of Geography and Statistics (IBGE - Instituto Brasileiro de Geografia e Estatística), making it the 118th largest urban conurbation in the world.

Sample size was calculated using initial estimates of the seroprevalence of HAV antibodies by age group, originally published by Foccacia et al.[12]: 1 to 4 years (12.1%), 5 to 9 years (28.1%), and 10 to 14 years (35.8%), and on the basis of population data from IBGE for these age groups within the study population, which contains 707,425 children and adolescents.[12] The sample size was calculated to a 95% confidence level (α error of 0.05) and a critical value $Z\alpha/2$ of 1.96. The final sample size required was therefore 901 children and adolescents distributed as follows: 237 (26.3%) aged 1 to 4 years; 313 (34.7%) aged 5 to 9 years and 351 (39%) aged 10 to 14 years.

The study recruited children and adolescents of both sexes aged 1 to 14 years after their legal guardians had signed free and informed consent forms. Children and adolescents were excluded if they had a prior history of hepatitis A vaccination , coagulopathies or immunodeficiencies or if they had used immunosuppressors or been given blood products during the previous 6 months. Children and adolescents whose tutors or legal guardians did not provide free and informed consent or who met any of the exclusion criteria did not take part in any stage of the study.

The patients who were recruited for this study had appointments for tests or consultations at the Universidade Federal do Paraná (UFPR) Hospital de Clínicas, and so this was a sample of convenience selected from patients treated by the Brazilian National Health Service (SUS - Sistema Único de Saúde).

Patients and their tutors responded to a socioeconomic questionnaire administered by trained interviewers. The questionnaire covered: type of residence; number of inhabitants at home; location of toilets and method of waste disposal; the type of water supply used at home; contact with hepatitis cases; attendance at educational institution or daycare; parents' educational level and occupation and family income.

A sample of approximately 1 mL of blood was taken from each patient, centrifuged and stored at -20 °C in a freezer. At the end of the study period all samples underwent qualitative assays for antibodies against the hepatitis A virus (anti-HAV).

The hospital's clinical analysis laboratory conducted all tests using microparticle enzyme immunoassay (MEIA, AxSym System, Abbott Laboratories). Samples with an S/CO ratio (sample/cohort) between 0.000 and 1.000 were classified as positive, and samples with S/CO from 1.001 to 3.000 were classified as negative.

Statistical analysis

Data were analyzed with descriptive statistics and patients were subdivided into three age groups, in common with the study undertaken by Foccacia et al.:[12] 1 to 4 years, 5 to 9 years and 10 to 14 years. Univariate and multivariate analyses were performed with logistic regression. The logistic regression analysis was conducted using the forward selection method and variables were chosen for the initial model on the basis of a p value of < 0.10 in the univariate analysis. Odds ratios (OR) were calculated to a 95% confidence interval. Analyses were run using Minitab® version 14.2.

In a further descriptive step, the population of the state capital (the city of Curitiba) was compared to the population of the surrounding area.

This study was approved by the Research Ethics Committee at the UFPR Hospital de Clínicas.

Results

One hundred and seventy-eight (178) of the 901 eligible samples (19.8%) were positive for total anti-HAV. Fifty point two percent (50.2%) of the samples were from males and the majority of the patients (51.1%) were from the city of Curitiba. The mean age of study participants was 7.6±4 years.

Two hundred and thirty-seven of the children and adolescents enrolled on the study were aged 1 to 4 years, 313 were 5 to 9 and 351 were 10 to 14 years old. The proportions of each age group positive for total anti-HAV were 3%, 21.1% and 29.9%, respectively.

Univariate analysis detected statistically significant associations between positive total anti-HAV results and the following variables: age group; number of children in household; location of residence; number of rooms; number of inhabitants per room; shared eating area; method of disposal of excreta; attendance at school or daycare; contact with hepatitis cases; total and per capita monthly income; and mother's and father's educational levels (Table 1). No statistically significant association was observed between total anti-HAV antibodies and the following variables: sex,

Table 1 - Univariate analysis of hepatitis A seroprevalence in Greater Curitiba, Paraná, Brazil, 2006

Parameter	n total	n (%) anti-HAV +	OR	p	95%CI
Age group					
1 to 4 years	237	7 (3)	1		
5 to 9 years	313	66 (21.1)	8.8	< 0,001	4.0-19.5
10 to 14 years	351	105 (29.9)	14	< 0,001	6.4-30.8
Number of inhabitants (children)					
≤ 2	652	101 (15.5)	1		
> 2	249	77 (30.9)	2.44	< 0.001	1.73-3.44
Location of residence					
Urban	848	160 (18.9)	1		
Rural	53	18 (34)	2.21	0.009	1.22-4.01
Number of rooms in residence					
> 5	425	68 (16)	1		
≤ 5	476	110 (23.1)	1.58	0.008	1.13-2.21
Number of inhabitants per room					
< 1	568	87 (15.3)	1		
≥ 1	333	91 (27.3)	2.08	< 0.001	1.49-2.90
Type of bathroom					
Internal	832	165 (19.8)	1		
External	69	13 (18.8)	0.94	0.843	0.50-1.76
Shared eating area					
No	363	46 (12.7)	1		
Yes	538	132 (24.5)	2.24	< 0.001	1.55-3.23
Water supply					
Mains supply	833	163 (19.6)	1		
Well/pump	68	15 (22.1)	1.16	0.620	0.64-2.12
Disposal of excreta					
Sewer	638	114 (17.9)	1		
Septic tank/other	263	64 (24.3)	1.48	0.027	1.04-2.09
Schools					
Does not attend.	167	5 (3)	1		
Daycare/kindergarten	173	18 (10.4)	3.76	0.011	1.36-10.4
Elementary school	561	155 (27.6)	12.4	< 0.001	4.98-30.7
Contact with hepatitis					
No	734	135 (18.4)	1		
Yes	126	33 (26.2)	1.57	0.043	1.02-2.44
Mother works away from home					
No	419	73 (17.4)	1		
Yes	480	105 (21.9)	1.33	0.095	0.95-1.85
Father works away from home					
Yes	760	144 (18.9)	1		
No	77	20 (26)	1.50	0.141	0.87-2.58
Number of workers in household					
> 2	79	10 (12.7)	1		
≤ 2	822	168 (20.4)	1.77	0.101	0.89-3.51
Total monthly income					
≥ 3 x minimum wage	265	32 (12.1)	1		
< 3 x minimum wage	630	145 (23)	2.18	< 0.001	1.44-3.29
Per capita income					
≥ 1 x minimum wage	163	15 (9.2)	1		
< 1 x minimum wage	732	162 (22.1)	2.80	< 0.001	1.60-4.90
Mother's education					
High school/higher education	390	48 (12.3)	1		
Illiterate/elementary school	506	129 (25.5)	2.44	< 0.001	1.70-3.50
Father's education					
High school/higher education	331	37 (11.2)	1		
Illiterate/elementary school	490	123 (25.1)	2.66	< 0.001	1.79-3.97

95%CI = 95% confidence interval; anti-HAV = hepatitis A antibodies; OR = odds ratio.

number of adult inhabitants, type of bathroom and type of water supply.

Only the following factors continued to have an association with positive total anti-HAV result after multivariate analysis: age groups 5 to 9 and 10 to 14, living in a household with more than one inhabitant per room, shared eating area and per capita income below the minimum wage (Table 2).

Table 2 - Multivariate logistic regression analysis of hepatitis A seroprevalence in Greater Curitiba, Paraná, Brazil, 2006

Parameter	adjusted OR	p	95%CI
Age group (years)			
1 to 4	1		
5 to 9	9.36	< 0.001	3.91-22.40
10 to 14	18.49	< 0.001	7.85-43.58
Number of inhabitants per room			
< 1	1		
≥ 1	2.18	< 0.001	1.51-3.14
Shared eating area			
No	1		
Yes	1.65	0.014	1.11-2.46
Per capita income			
≥ 1 x minimum wage	1		
< 1 x minimum wage	2.69	0.001	1.50-4.84

95%CI = 95% confidence interval; OR = odds ratio.

The next stage of the study, also descriptive, involved subdividing the study population into residents of the city of Curitiba and residents of the surrounding areas. The 901 children and adolescents enrolled on the study broke down to 460 from the capital and 451 from other municipalities in Greater Curitiba.

It was found that although 100% of the residences in the capital had running water, the inhabitants of approximately 4% of them also used some other type of water supply. In the other subset, approximately 4% of residences did not have running water while 88.7% only used this type of water supply.

With regard to means of excreta disposal, the great majority of the residences in the capital (94.1%) were connected to the public sewer system, while in the surrounding areas only 63.3% had this service. Septic tanks as the only method of disposal was more common outside of the capital (34.7%) than in the city of Curitiba (4.3%). When the two subsets were compared in terms of income, it was observed that both mean income and per capita income were higher in the capital.

Taking all age groups together, the prevalence of total anti-HAV antibodies was greater in the surrounding areas than in the capital, at 22% and 17% respectively (p = 0.07). The difference in positive results was primarily concentrated in the 10-to-14 age group, in which the difference was statistically significant (p = 0.02, 95%CI 1.1-2.8), as illustrated in Figure 1.

Discussion

There are enormous socioeconomic differences in Latin America, both between countries and within them. In Brazil, which is a very large country, these differences are even more marked because of the great variability in standards of hygiene and sanitation. These regional differences can be illustrated by analyzing the availability of drinking water and public sewers. Taking the country as a whole, the majority of households do have access to these services, but analyzing the country's administrative regions separately, sewers, for example, exist in 81.7% of municipalities in the Southeast region, but just 5.8% of those in the North.[9,13]

The overall prevalence of antibodies against hepatitis A observed in this study was lower than the rates observed in other studies conducted in Brazil[2,14-17] and other developing countries,[1,18,19] and is more similar to reports from developed countries, such as England, the United States, Spain and Israel.[3,5,20,21]

When seroprevalence was analyzed by age group, there was a very low prevalence of antibodies in the 1 to 4 age group (3%), which is comparable to figures from developed countries.[9,20,22,23] There was a slower rate of increase in seroprevalence with increasing age, in comparison with other studies conducted in Brazil,[2,13,14] and the rate is similar to figures from other developing countries that have enjoyed socioeconomic improvement over recent years, such as Lebanon, for example, where positivity in the 6 to 10 age group was 27.7%,[7] and Saudi Arabia, with 30% positivity in the 12 to 15 age group.[6] A multicenter study conducted

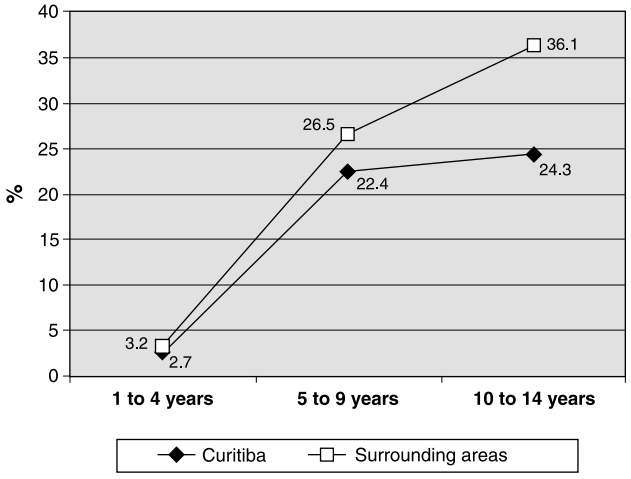

Figure 1 - Seroprevalence of hepatitis A virus antibodies by age group and broken down by location of residence: city of Curitiba or other towns in Greater Curitiba

in four of Brazil's five regions found prevalence rates of antibodies against hepatitis A of 35.1%, 53.9% and 60.7% in children aged 1 to 5 years, 6 to 10 years and 11 to 15 years, respectively. The same study also observed a significantly higher total anti-HAV seroprevalence in the subset with the lowest social and economic status and seroprevalence that varied depending on region, with the highest rates in the North and Northeast of the country.[24] Another recent publication, describing the seroprevalence of antibodies against HAV among children and adolescents in three regions of Brazil, reported prevalence rates of 41.5% and 57.4%, in 5-to-9-year-olds and 10-to-19-year-olds respectively, in the Northeast region, 32.3% and 56%, respectively, in the Mid West and 3.8 and 65.1%, respectively, in the Distrito Federal.[25]

It is probable that the results of the univariate analysis indicating positive associations with inadequate excreta disposal methods with mother's educational level were affected by confounding factors which were then eliminated in the multivariate analysis.

Lower maternal educational level was associated with a higher prevalence of antibodies. It is known that educational level is also related to family income and these two factors overlap. In one Brazilian study, children whose mothers had had between zero and three years of education had a prevalence of 32.55% compared with 13.57% among children whose mothers had had more than 11 years' education.[26] In our sample we also observed the positive association between lower mother's educational level and the presence of antibodies and also the same association with fathers' educational level. However, neither maternal nor fathers' educational level were retained in the final multivariate regression model. It is possible that the fact that few of the children's parents were illiterate and that this group was collapsed together with the primary education group may have affected the multivariate model.

The low prevalence of antibodies at young ages raises concerns about the risk of outbreaks or epidemics at daycare centers and schools and about the possibility of members of this population becoming infected at older ages when the effects of the disease can be more serious.[27]

The hepatitis A virus is transmitted by ingestion of contaminated food or water or by person-to-person contact. As regions develop and hygiene and sanitation are improved, contaminated food and water cease to be such frequent sources of transmission. No association whatsoever was detected between antibodies and type of household water supply. It is important to point out that the treated water supply has a coverage of almost 100% in the area and so it is possible that water does not constitute a risk factor for this population. In contrast, positive associations were detected with shared eating areas, low per capita income and intra-household fraternization, all factors that are directly related to cultural and socioeconomic conditions.

Inadequate excreta disposal methods have been identified as a risk factor for HAV transmission. When this variable was analyzed in isolation, we also observed a positive association with the presence of antibodies. However, the association was not confirmed by the multivariate analysis. Data provided by the city of Curitiba authorities show 75% coverage in terms of sewers and 70% in terms of sewage treatment, which are considered good when compared with other parts of Brazil.

Some authors have observed positive associations between lower mother's educational level and higher prevalence of HAV antibodies. The same effect was observed in our univariate analysis, but it was not confirmed by the multivariate analysis.[26]

This study also detected the existence of differences between towns that are very close to each other, as is the case of the municipalities that make up Greater Curitiba. As has been stated, the state capital had better conditions in terms of sewage and treated water than the surrounding areas. The literature shows that these services improve a location's hepatitis A epidemiological profile.

The two areas (Curitiba vs. other municipalities) were also compared in terms of the prevalence of antibodies and seropositivity was lower among children and adolescents from the capital than in the surrounding areas (17% vs. 22%), but this difference was not statistically significant. When the geographical subsets were further broken down by age, the regional difference was greatest in the 10-to-14 age group and this difference was statistically significant (24.3% vs. 36.1%, Figure 1).

Despite these differences, the municipalities in Greater Curitiba had lower seroprevalence rates than have been observed in the rest of Brazil. These results suggest that the improvements that have been achieved in the capital will also take place in the municipalities of the surrounding area in a few years' time.

Conclusions

The results reported here indicate the importance of preventative measures to avoid cases of hepatitis A infection among older people and to prevent epidemics becoming frequent. It is evident that it is necessary to invest in improving cultural and socioeconomic conditions, but it should be remembered that the improvements are slow to take effect and that it takes years for changes to occur.[27]

In contrast, vaccination against HAV has an impact in the short term, as has been observed in countries such as Israel, the United States, Spain and Canada.[11] In Argentina, which is one of Brazil's neighbors, a universal vaccination program against hepatitis was introduced for children aged 12 months in 2005. They observed an 88% drop in the incidence of the disease 2 years after initiating the program, with an impressive reduction in the number of cases of the

disease, not only in the age group vaccinated, but also among populations of children in other age groups, among adolescents and among adults and the elderly.[28] In this context, HAV vaccination programs for the young susceptible population should be considered, since they would avoid both morbidity and mortality, as has been shown in some other countries.[5,11,29,30]

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