

## Age-specific Prevalence of Antibodies to Hepatitis A in Children and Adolescents from Rio de Janeiro, Brazil, 1978 and 1995. Relationship of Prevalence to Environmental Factors

Claudia L Vitral/\*/+ , Clara FT Yoshida, Elba RS Lemos, Christiane S Teixeira\*, Ana MC Gaspar

Departamento de Virologia, Instituto Oswaldo Cruz, Av. Brasil 4365, 21045-900 Rio de Janeiro, RJ, Brasil  
\*Departamento de Microbiologia e Parasitologia, CCM/UFF, Rua Prof. Ernani Melo 101, 24210-130 Niterói, RJ, Brasil

*The age-specific prevalence of antibodies to hepatitis A virus (anti-HAV) was determined in two different population groups with low socio-economic status from Rio de Janeiro city, Brazil, whose serum samples were collected 17 years apart (Population 1, 1978; Population 2, 1995). In Population 2, analysis of the anti-HAV prevalence was also carried out with respect to environmental factors. Population 1 was composed of 520 stored sera collected from the umbilical cord of term neonates and children aged 1 month to 6 years. In population 2, 720 serum samples were collected from children and adolescents with ages ranging from 1 to 23 years. The overall prevalence rate of anti-HAV in Population 1 and Population 2 was 65.6% and 32.1%, respectively. In Population 1, the anti-HAV prevalence reached 88% at the age of 3, while in Population 2, it increased from 4.5% in children under the age of 3 to 66% in the group of adolescents over the age of 14. The low exposure to HAV infection in younger children from Population 2 could be a result of improved environmental hygiene and sanitation, as demonstrated by the presence of piped water, waste and sewage disposal systems in most houses from this population group. These findings indicate a possible change in the prevalence of hepatitis A in Rio de Janeiro.*

Key words: hepatitis A - seroepidemiology - anti-HAV

Hepatitis A virus (HAV) is an extremely stable virus which is spread primarily by the faecal-oral route, either directly from person to person or by contaminated food or water. The prevalence of HAV infection closely correlates with the degree of environmental sanitation and the prevailing socioeconomic and hygienic conditions. In developed countries, the incidence of HAV infection is low while in developing regions of the world, inadequate sanitation results in continuous transmission of HAV, especially to children and young individuals. However, the epidemiology of hepatitis A is in a state of flux. Improved sanitary conditions, particularly in the adequacy of water supply and the sewerage systems has been responsible for the decrease in the level of endemicity of hepatitis A in several countries (Chin et al. 1991, Poovorawan et al. 1993, Wu et al. 1993, Yap & Guan 1993, Perez-Trallero et al. 1994, Son & Kew 1994, Bolumar et al. 1995, Koff 1995).

In Brazil, hepatitis A is an endemic disease, accounting for 55% of acute hepatitis cases followed by the National Reference Center for Viral Hepatitis (Oswaldo Cruz Institute, Rio de Janeiro) (Gaspar et al. 1996). However, its prevalence is not well known throughout the country. Former seroprevalence studies conducted in some states have indicated a high prevalence of anti-HAV antibodies since the early childhood (Pannuti et al. 1985, Abuzwaida et al. 1987, Bensabath et al. 1987, Queiroz et al. 1995). The present study was undertaken with the aim to investigate the impact of sanitary condition improvements in the prevalence of hepatitis A in the city of Rio de Janeiro. The prevalence of HAV infection was investigated in children and adolescents from two population groups with low socioeconomic status and from distinct geographic areas, whose serum samples were collected 17 years apart (1978 and 1995).

### MATERIAL AND METHODS

#### *Study population*

*Population 1 (Rio de Janeiro, 1978) - Sampling consisted of 520 stored sera which had been col-*

+Corresponding author. Fax: +55-21-270.6397  
Received 17 November 1996  
Accepted 22 August 1997

lected in 1978 for a congenital and perinatal viral infection prevalence study (Nogueira et al. 1986). The population was composed by 50 cord sera from at term neonates of mother with ages ranging between 16 and 30 and 470 sera collected from children aged 1 month to 6 years. Serum samples were obtained from subjects who attended the Instituto Fernandes Figueira or seek the health unit of the Escola Nacional de Saúde Pública (Fundação Oswaldo Cruz, Rio de Janeiro) for immunization procedures, and at public institutions for the care of orphans and neglected children. Subjects were stratified into 10 age groups (cord sera, 1-3, 4-6, 7-9 and 10-12 months, 2, 3, 4, 5 and 6 years). The seroepidemiologic data was shown by age specific prevalence curve.

**Population 2 (Rio de Janeiro, 1995)** - The second population under study included 720 subjects attending public day-care centers, primary and secondary schools whose serum samples were collected in 1995. Individuals aged one to 23 and lived in Palmares neighborhood, located in Santa Cruz, a suburb of the western area of Rio de Janeiro. Subjects were stratified into 7 age groups (>3, 4-5, 6-7, 8-9, 10-11, 12-13 and >14 years). Before collecting the blood sample, epidemiological data were obtained in order to evaluate possible risk factors for HAV infection: age, place of residence, number of children and bedrooms in each home and sanitary conditions of housing (sewage disposal and water supply system and mode of waste collection).

**Laboratory test and statistical analysis** - All sera were stored at -20°C until tested. Anti-HAV antibodies were determined using a competitive "in-house" EIA (Vitral et al. 1991). Probability (p) was determined by chi-squared tests using Yates correction. Differences were regarded as significant when  $p \leq 0.05$ .

## RESULTS

**Population 1 (Rio de Janeiro, 1978)** - Anti-HAV was detected in 95.1% of cord sera and 90.2% of neonates aged 1 to 3 months, decreasing gradually from 55% in the 4-6 months age group to 4% in the 10-12 months age group (Fig. 1). From this time, the anti-HAV prevalence increased sharply to 23.2% at the age of 2 and to 88.1% at the age of 3, and then increased gradually to 98.1% by 6 years of age. The overall prevalence of anti-HAV in this population group was 65.6%.

**Population 2 (Rio de Janeiro, 1995)** - This population presented a low prevalence of anti-HAV in children under the age of 3 (4.5%) and at the 4-5 year age group (7.8%) (Fig. 2). From this time, the anti-HAV prevalence increased sharply to 19.7% in the 6-7 year age group, and then rose

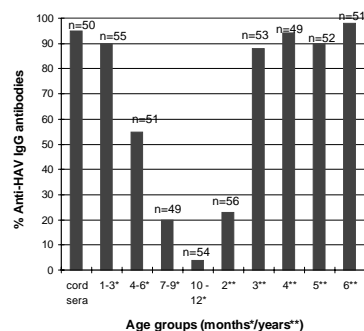


Fig. 1: age-specific prevalence of antibodies to hepatitis A virus among neonates and children, Rio de Janeiro, 1978 (Population 1), Brazil. Cord sera were collected from at term neonates of mothers with ages ranging between 16 and 30 years.

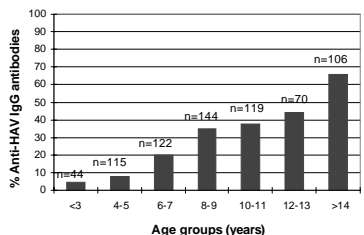


Fig. 2: age-specific prevalence of antibodies to hepatitis A virus among children and adolescents, Rio de Janeiro, 1995 (Population 2), Brazil.

gradually from 34.7% in the 8-9 year age group to 66% in the group of adolescents over the age of 14 (age 14 to 23). The overall prevalence was 32.1%.

In Table, it has been observed that most of subjects lived under adequate housing sanitary conditions, in view of the rate of presence of sewerage system (63.7%), piped water (88.5%) and a public service for waste collection (85.7%). When each one of these variants was correlated with the prevalence of anti-HAV, higher rates were observed when these facilities were absent. The anti-HAV prevalence was significantly lower among subjects who live in houses that had piped water ( $p=0.0003$ ) and a public service for waste collection ( $p=0.004$ ). However, there was no statistically significant difference in the anti-HAV prevalence when the presence of a sewage system was taken into consideration.

TABLE  
Housing sanitary conditions in Population 2 (Rio de Janeiro, 1995) and its relationship with the prevalence of antibodies to hepatitis A virus

Housing sanitary conditions	n (%)	anti-HAV (%)	$\chi^2$	p-value
Sewage disposal system <sup>d</sup>				
Sewerage system	459 (63.7)	147 (32)	0.49	NS <sup>e</sup>
Cesspool	185 (25.7)	57 (30.8)		
None <sup>b</sup>	50 (6.9)	18 (36)		
Water supply system				
Piped water	637 (88.5)	190 (29.8)	16.50	0.0003
Artesian well	13 (1.8)	7 (53.8)		
None <sup>b</sup>	51 (7.1)	28 (54.9)		
Waste collection system				
Public service (Comlurb)	617 (85.7)	186 (30.1)	9.04	0.004
None <sup>b</sup>	89 (12.4)	41 (46.1)		

a: totals do not add up to 720 because of missing values; b: none, a system for sewage disposal, water supply or waste collection was not available at housing; c: NS, not significant p-values > 0.05.

The overcrowding factor and its relationship with the anti-HAV prevalence was assessed by taking into consideration the number of bedrooms and children in each household (Fig. 3). Anti-HAV prevalence was found to be positively related to the number of children living in the same home and inversely related to the number of bedrooms in the household.

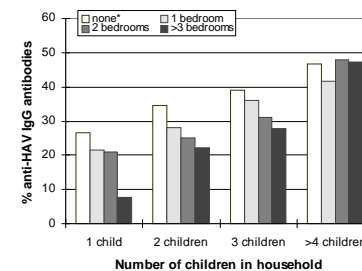


Fig. 3: anti-HAV prevalence according to the number of children and bedrooms in household. Subjects were from Population 2, Rio de Janeiro, 1995, Brazil. \*none, a separate room for sleeping was not available in the house.

## DISCUSSION

The full extent of the burden of hepatitis A in Brazil remains unknown, because the principal tools for studying morbidity involve passive surveillance systems that require physicians and other health care providers to report identified cases to local or state health departments. In spite of being

compulsory in Rio de Janeiro, reporting of viral hepatitis cases greatly underestimate the true incidence of infections because of underreporting and subclinical infections which are very common in younger individuals. Moreover, in most cases, there is no distinction between the causative hepatitis agents when cases are reported. An alternative and useful approach to understanding the frequency and defining the epidemiology of HAV infection is the measurement of IgG anti-HAV antibodies in serum samples representing the overall population or from specific population groups. These point-prevalence studies provide serologic and epidemiologic data, as the proportion of susceptible persons, useful in defining changing patterns in HAV epidemiology and risk factors associated with its transmission. To provide an insight in the epidemiological pattern of hepatitis A in Rio de Janeiro, a seroepidemiological study of health subjects was carried out in two population groups with low socioeconomic status from distinct geographic areas of the city, whose serum samples were collected 17 years apart (Population 1, 1978; Population 2, 1995).

Three main patterns of age-related exposure to HAV exist, depending on socioeconomic and hygienic conditions (Gust 1992). In developing countries with poor hygiene and sanitation, subclinical childhood infection is common, and most children become infected within the first few years of life, so that by the age of 10, most of the population is immune. In countries in which hygiene and sanitation have been steadily improving over the years, a declining incidence has been noted, with an increased proportion of infections occurring later in the adolescence or early adult life. The third pat-

tern is seen in developed countries with high standards of hygiene and sanitation, where HAV infection is uncommon in the young, being generally acquired during travel to endemic areas. In this present study, HAV infection was almost universal among individuals from Population 1, which presented an overall anti-HAV prevalence of 65.6%. Infection occurred very early in life, between 1 and 2 years of age, consistent with the epidemiological pattern seen in endemic areas. The only data provided from this population concerned the age and place of residence of the subjects. For this reason, the anti-HAV prevalence could not be correlated with environmental factors. However, most subjects lived either in slums or in public orphanages, places that generally present inadequate sanitary/hygienic conditions. By contrast, in Population 2 there was a low prevalence of anti-HAV in children under the age of 5 (11/159, 6.9%), and an increased proportion of infections being delayed until adolescence. The overall prevalence of anti-HAV was also lower (32.1%), in spite of this population being composed by older individuals. The low HAV exposure of younger children in this population may be a result of improved environmental hygiene and sanitation. As a matter of fact, most individuals in this population, in spite of their low socioeconomic status, lived under adequate sanitary conditions, having access to piped water and sewerage systems. These findings are in agreement with the results of several seroepidemiological studies which have been showing a marked change in the epidemiological pattern of hepatitis A in many parts of the world due to improvements in living standards (Chin et al. 1991, Poovorawan et al. 1993, Wu et al. 1993, Yap & Guan 1993, Perez-Trallero et al. 1994, Son & Kew 1994, Bolumar et al. 1995, Koff 1995).

Among the sanitary facilities evaluated in each household in Population 2, the absence of piped water was the one that presented the highest relationship with anti-HAV prevalence ( $p < 0,0005$ ). As a matter of fact, water is the major vehicle for the spread of HAV (Garin et al. 1996). Even in the presence of a sewage system, the possibility of HAV infection can not be discarded, in the view of the great stability of HAV and its continued presence in urban sewage even after treatment (Tsai et al. 1993). The anti-HAV prevalence also had a direct correlation with the number of children in each home and an upward trend as the number of bedrooms in the household decreased. However, this trend gradually decreased as the number of children in each home increased from 1 > 4. In fact, the presence of children less than 5 years old in a household represent one of the most commonly identified risk factors associated with hepatitis A

infection (Morales et al. 1992, Shapiro et al. 1992). This fact could be explained by the usually asymptomatic and often unrecognized clinical course of hepatitis A in young children, which enhances the chance for HAV dissemination.

This report shows a possible change in the epidemiological pattern of hepatitis A in a state of Brazil. Former seroepidemiological studies carried out in low socioeconomic level populations from different states detected a high percentage of hepatitis A immune individuals since early childhood. Queiroz et al. (1995), studying the age prevalence of HAV among street youths 7 to 21 years old from Goiânia city, Central Brazil, found values as high as 87.5% in the 7-10 year age group. A previous study conducted in Rio de Janeiro in two urban communities, Nova Iguaçú and Niterói, found an anti-HAV prevalence of 71.4% and 31.5%, respectively, in children under 5 years old (Abuzwaida et al. 1987). In São Paulo, the prevalence of anti-HAV in a population with low socioeconomic level was 75% in children aged 2 to 11 years and 100% in adults (Pannuti et al. 1985). In the county of Boca do Acre, located in the extreme southwestern corner of the Amazon Basin of Brazil, the anti-HAV prevalence was 45.8% in children aged 0-2 years, reaching 100% in children aged 10-14 years (Bensabath et al. 1987).

Improvements in general standards of sanitation have a paradoxical effect of considerably increasing the number of susceptible adults and creating the potential for large-scale epidemics. In this situation, prophylaxis against hepatitis A has become increasingly important. An inactivated HAV vaccine is already available throughout the world and proved to be effective in the prevention of HAV infection (Dentico et al. 1996, Nalin et al. 1996). However, strategies of vaccination should be based upon the epidemiology of the disease. Further hepatitis A seroprevalence studies in different geographical areas from Brazil would be crucial as an aid to assess the real extension of possible changes in the epidemiology of hepatitis A and its implication whether active immunization programs will be implemented in the future.

#### ACKNOWLEDGMENTS

To Márcia Bessa and all the employees from the Municipal Health Department of Palmares (Santa Cruz, Rio de Janeiro) involved in the collection of serum samples, and to Dr Lia Lewis for comments, suggestions and review of the manuscript.

#### REFERENCES

Abuzwaida ARN, Sidoni M, Yoshida CFT, Schatzmayr HG 1987. Seroepidemiology of hepatitis A and hepatitis B in two urban communities of Rio de Janeiro, Brazil. *Rev Inst Med Trop São Paulo* 24: 219-223.

- Bensabath G, Hadler SC, Pereira Soares MC, Fields H, Maynard JE 1987. Características serológicas y epidemiológicas de la hepatitis vírica aguda en la cuenca amazónica del Brasil. *Bol Of Sanit Panam* 103: 351-362.
- Bolumar F, Giner-Duran K, Hernandez-Aguado I, Serradesfilis MA, Rebagliato M, Rodrigo JM 1995. Epidemiology of hepatitis A in Valencia, Spain: public health implications. *J Viral Hepatitis* 2: 145-149.
- Chin KP, Lok ASF, Wong LSK, Lai CL, Wu PC 1991. Current seroepidemiology of hepatitis A in Hong Kong. *J Med Virol* 34: 191-193.
- Dentico P, Volpe A, Buongiorno R, Chiriaco P, Poli C, Maracchione N 1996. Long-term immunogenicity of inactivated hepatitis A vaccine in healthy adults and children, p. 138-144. In Y Buisson, P Coursaget, M Kane (eds), *Enterically-transmitted Hepatitis Viruses*, La Sinarre, Tours, France.
- Garin D, Bizziagos E, Crance JM, Gantzer C, Lévêque F, Deloche R, Scharzbrod L 1996. Survival of infectious hepatitis A virus in mineral water and seawater, p. 48-49. In Y Buisson, P Coursaget, M Kane (eds), *Enterically-transmitted Hepatitis Viruses*, La Sinarre, Tours, France.
- Gaspar AMC, Oliveira JM, Silva MLP, Yoshida CFT 1996. Orally transmitted acute hepatitis in Rio de Janeiro, Brazil (1989-1995), p. 99-100. In Y Buisson, P Coursaget, M Kane (eds), *Enterically-transmitted Hepatitis Viruses*, La Sinarre, Tours, France.
- Gust ID 1992. Epidemiological patterns of hepatitis A in different parts of the world. *Vaccine* 10 (suppl 1): S56-S58.
- Koff RS 1995. Seroepidemiology of hepatitis A in the USA. *J Infect Dis* 171 (suppl 1): S19-S23.
- Morales JL, Huber L, Gallego S, Alvarez G, Diez-Delgado J, González A, Aguilar L, Dal-Ré R 1992. A seroepidemiologic study of hepatitis A in spanish children. Relationship of prevalence to age and socio-environmental factors. *Infection* 20: 194-196.
- Nalin DR, Brown L, Gress J, Hurmi W, Kuter BJ, Manns JR 1996. VAQTA<sup>®</sup>: Merck's hepatitis A vaccine, purified, inactivated, p. 124-129. In Y Buisson, P Coursaget, M Kane (eds), *Enterically-transmitted Hepatitis Viruses*, La Sinarre, Tours, France.
- Nogueira RMR, Schatzmayr HG, Assis CER, Pinhão AT 1986. Infecções pelo citomegalovirus e herpes simplex tipo 2. *Cln Ped* 10: 22-28.
- Pannuti CS, Mendonça JS, Carvalho MJM, Oselka GW, Amato Neto N 1985. Hepatitis A antibodies in two socio-economically distinct populations of São Paulo, Brazil. *Rev Inst Med Trop São Paulo* 27: 162-164.
- Perez-Trallero E, Cilla G, Urbietta M, Dorronsoro M, Otero F, Marimon JM 1994. Falling incidence and prevalence of hepatitis A in northern Spain. *Scand J Infect Dis* 26: 133-136.
- Poovorawan Y, Theamboonlers A, Chumdermpadetsuk S 1993. Changing seroepidemiology of HAV infection in Thailand. *Southeast Asian J Trop Med Public Health* 24: 250-254.
- Queiróz DAO, Cardoso DDP, Martelli CMT, Martins RMB, Porto SOB, Azevedo MSP, Borges AMT, Daher RR 1995. Seroepidemiologia da infecção pelo vírus da hepatite A em "meninos de/na rua" de Goiânia-Goiás. *Rev Soc Bras Med Trop* 28: 199-203.
- Shapiro CN, Coleman PJ, McQuillan GM, Alter MJ, Margolis HS 1992. Epidemiology of hepatitis A: seroepidemiology and risk groups in the USA. *Vaccine* 10 (suppl 1): S59-S62.
- Song E, Kew MC 1994. The seroepidemiology of HAV infection in South African chinese people. *J Viral Hepatitis* 1: 149-153.
- Tsai YL, Sobsey MD, Sangermano LR, Palmer CJ 1993. Simple method of concentrating enterovirus and hepatitis A virus from sewage and ocean water for rapid detection by reverse transcriptase-polymerase chain reaction. *Appl Environ Microbiol* 59: 3488-3491.
- Vital CL, Gaspar AMC, Yoshida CFT 1991. Two competitive enzyme immunoassays for the detection of IgG class antibodies of hepatitis A antigen. *Rev Soc Bras Med Trop* 24: 79-87.
- Wu J-S, Lu C-F, Wu L-Z, Wong C-K, Wu Y-C, Lu T-C, Chen K-L, Chen HY 1993. Changing seroepidemiology of HAV infection between two regions in Taiwan differing in socioeconomic status. *J Formos Med Assoc* 92: 812-815.
- Yap I, Guan R 1993. Hepatitis A sero-epidemiology in Singapore: a changing pattern. *Trans R Soc Trop Med Hyg* 87: 22-23.

