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The epidemiology of hepatitis A in Rio de Janeiro: environmental and domestic risk factors

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SUMMARY

A serological study of hepatitis A was carried out in low-income areas scheduled for a major sanitation programme in Rio de Janeiro, Brazil. Blood spots were collected by finger puncture and transported on filter paper, and total antibodies to hepatitis A virus were detected by ELISA. Households were also interviewed to collect information on their environmental conditions and socio-economic status. A generalized linear model using a complementary log–log function was fitted to the data, using the logarithm of age as an explanatory variable to derive adjusted rate ratios (RR). The risk of infection was greater among households with 2–3 members per room (RR = 1·4; 95% CI = 1·04–1·8) or more than three per room (RR = 1·5; 95% CI = 1·2–2·0). People living on hilltops (RR = 1·5; 95% CI = 1·02–2·2), near to open sewers (RR = 1·2; 95% CI = 1·03–1·5) or lacking a kitchen (RR = 1·4; 95% CI = 1·08–1·9) were also at greater risk than others. The number of taps and water-using fittings in the house was associated with a protective effect (RR = 0·9 for each tap; 95% CI = 0·9–0·98). A significant protective association was found with maternal education but not with gender or household income. The results do not suggest a strong association with water quality. Ownership of a ceramic water filter was associated with a protective effect on the margin of significance, but the practice of boiling drinking-water was not, nor was the type of water source used. The results suggest that that the risk of infection with hepatitis A is determined by environmental variables in the domestic and public domains.

INTRODUCTION

Sero-epidemiological studies of hepatitis A have been carried out in various countries since the development of commercially available test kits in the 1970s [1–3]. These studies have found patterns of prevalence of antibodies to hepatitis A virus, which depend on the local environmental conditions and standard of living of the study population [4, 5]. These patterns fit broadly into three groups – of high, medium and low endemicity – which each have different implications for intervention strategies [6].

The low endemicity pattern, found in industrialized countries, shows a gradual increase in seroprevalence during the first two decades of life. Many are first infected in late youth or adulthood, so that the disease usually presents in a symptomatic and serious form. In the highly endemic pattern found in low-income developing countries, seroprevalence climbs steeply in the first decade of life and infection mainly takes subclinical forms [7]. Water-borne and food-borne epidemics are rare. Young children are the principal source of transmission of the virus. The intermediate pattern is typically found in middle income countries, where the above two patterns are present, but in different populations. Low endemicity is found in the relatively well-off areas of large cities where water

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supply and domestic hygiene have reached adequate levels, while high endemicity persists in the low-income urban periphery and rural areas. Studies from Latin America have usually found this mixed pattern [6].

In the first, low prevalence group, the main intervention strategy is immunization of specific groups or of the general population. Measures to ensure drinking-water quality and food hygiene can also help to prevent occasional epidemics [8]. In countries with a high prevalence of hepatitis A, the majority of the population has been naturally immunized from an early age, and vaccination is not a high priority. Transmission of the virus will gradually decline as a result of economic growth, bringing improvements in household income, urban services and domestic hygiene [9, 10]. The appropriate strategy for the intermediate case is less clear. Universal coverage with urban environmental services cannot be achieved overnight, but mass immunization may not be justified where most of the population is already immune; no clearly cost-effective intervention is evident.

The present study was conducted in an area where environmental conditions are still poor, and a major environmental sanitation project is under construction. The objective was to assess the current pattern of seroprevalence for hepatitis A antibodies, as well as to examine associations between seropositivity on the one hand, and socio-economic status and environmental conditions in the public and domestic domains on the other. It is planned to repeat the study after completion of the sanitation works.

MATERIAL AND METHODS

Study site

The site of the study was located in the county of Duque de Caxias in greater Rio de Janeiro, Brazil. The average household had 4·0 members, living in a house with 4·4 rooms, which generally included at least one bedroom and one bathroom. Piped water was supplied to 81·6 % of households, while a further 15·9 % used only well water. There was no formal sewerage system, but 48·1 % of households used septic tanks discharging to the rainwater drainage network. Only 43·6 % of households benefited from solid waste collection. The average household head had 5·3 years of schooling and a monthly income which at the time of the study would be equivalent to approximately US$294, or approximately two times the Brazilian minimum wage at the time. Among the 43 census tracts within that area, those 19 which were due to benefit most from the planned environmental interventions were selected for the study. In 1991, they encompassed a population of 29 729 living in 7565 households [11].

Design and conduct of the study

Initially, a pilot study was conducted in two census tracts in the area, to ascertain age-specific seroprevalences of hepatitis A for use in the sample size calculations, to test the fieldwork questionnaires and also to validate the use of blood spots on filter paper from a finger prick as an alternative method for collection of blood samples [12].

The sample population was selected at random among the residents of the study area after conducting a census of all households. The sample was stratified in 13 age groups (1, 2, 3, 4, 5, 6, 7, 8, 9, 10–14, 15–19, 20–29 and 30 + years), and the number to be selected in each age group was calculated from the age-specific prevalence found in the pilot study. Figure 1 shows the prevalence of hepatitis A antibody by age group.

The fieldwork, beginning with the overall census, lasted from June to December 1997. Visits were made to the households of individuals selected for the sample, to collect blood samples for laboratory examination. The objectives of the study were explained and written consent was obtained from the subjects or, for minors, from their guardians. A finger prick was then made using an automatic lancet with a disposable point (Glucolet®–Bayer). Blood drops were spread on two 2·5 mm diameter circles marked on a filter-paper strip (Whatman® No. 1). Eluates were obtained from these filter papers and kept frozen at −20 °C. Total antibodies to hepatitis A virus (HAV) were assessed by using the competitive ELISA test (ETI-AB-HAVK-3, Sorin Biomedica Diagnostics S.p.A., Italy). No test was performed for anti-HAV IgM as the likelihood of detecting positive cases was very small.

The blood sample collection was followed by a household interview to collect information on the physical and sanitary conditions of the house and environs, and the socio-economic status of the family.

Data analysis

The age-specific seroprevalence of hepatitis A for the whole population has been published elsewhere [5],

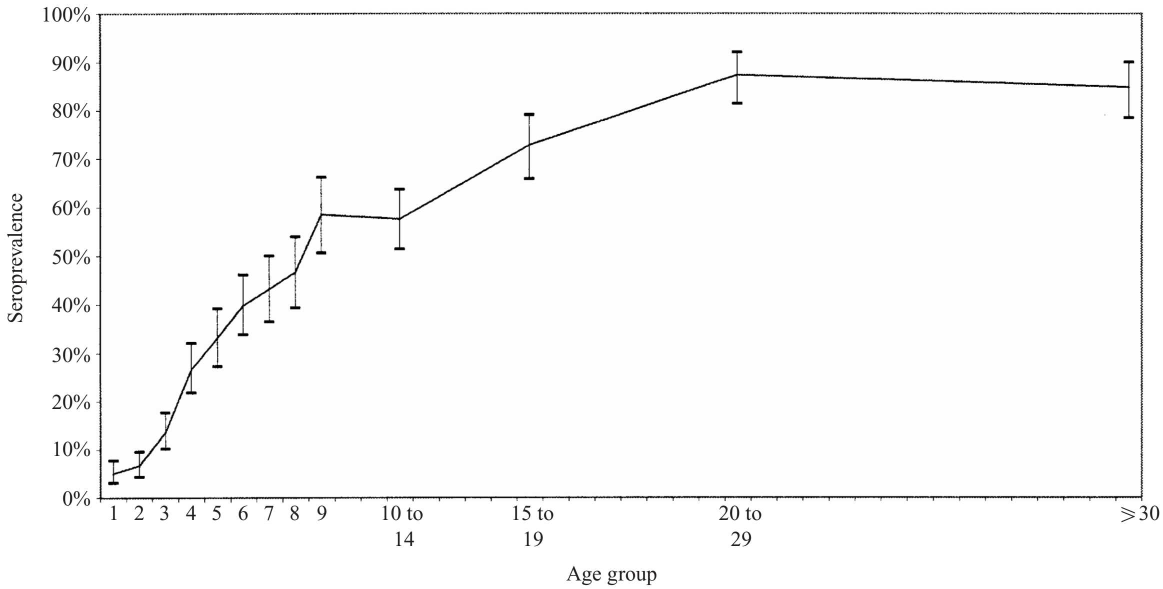

Fig. 1. Seroprevalence for hepatitis A (and 95% Cl) by age group in Duque de Caxias, Rio de Janeiro, Brazil ($n = 3271$).

Table 1. *Seroprevalence and 95% confidence intervals (95% CI) for hepatitis A seropositivity, Rio de Janeiro, Brazil*

Characteristic	No.	Seroprevalence (%)	95% CI
Age group (years completed)			
1	339	5·01	2·70–7·35
2	367	7·08	4·44–9·72
3	323	12·69	9·04–16·34
4	284	27·46	22·24–32·69
5	238	32·35	26·37–38·34
6	237	39·66	33·39–45·94
7	205	42·93	36·09–49·76
8	184	45·65	38·39–52·92
9	155	58·06	50·21–65·92
Mother's/carer's (years of schooling)			
0–3	513	32·55	28·48–36·62
4–7	1010	27·43	24·67–30·18
8–10	507	20·12	16·62–23·62
11+	280	13·57	9·53–17·61
Household income			
< 5 minimum wages	1762	26·79	24·72–28·86
> 5 minimum wages	394	17·01	13·28–20·73

and is shown in Figure 1. In order to study associations between seroprevalence and other variables, the dataset was restricted to children aged 1–9 years, for whom a household questionnaire had been completed ($n = 2332$).

The variables included in the analysis are shown in Tables 1 and 2. Education of the mother (or other woman responsible for the children of the household) was assessed in years of schooling and entered the models as an ordinal variable. Total income of the household was expressed as a function of the Brazilian regular minimum wage, and entered the models as a dichotomous variable (< 5 and > 5 minimum wages, equivalent to US$734 per month). 'Location of house' described its position in relation to the topography (hilltop *vs.* valley or slope of the hill). Crowding was defined as the number of persons living in the household per room, and was categorized at

Table 2. *Results of multivariate analysis. Adjusted Rate Ratios (RR) and 95% confidence intervals (95% CI) for hepatitis A seropositivity according to environmental and domestic characteristics, Rio de Janeiro, Brazil*

Characteristic	Age-adjusted RR*	95% CI	Fully-adjusted RR†	95% CI
Location of house‡				
Valley or hillside	1·0		1·0	
Hill top	1·54	1·08–2·22	1·51	1·02–2·23
Crowding (persons/room)‡				
< 2	1·0		1·0	
2–3	1·58	1·22–2·03	1·36	1·04–1·79
> 3	2·07	1·65–2·60	1·52	1·18–1·97
Open sewer in front of house‡				
No	1·0		1·0	
Yes	1·37	1·16–1·61	1·24	1·03–1·49
Rubbish collection				
No	1·0		1·0	
Yes	0·78	0·64–0·95	1·21	0·97–1·52
Sewerage system				
No	1·0		1·0	
Yes	0·76	0·64–0·89	0·99	0·82–1·20
Source of water				
Public system and well	1·0		1·0	
Well	1·39	1·04–1·66	1·09	0·80–1·49
Public system	1·31	1·04–1·84	1·01	0·79–1·31
Type of well				
Do not use, or use dug well	1·0		1·0	
Borehole	0·64	0·46–0·89	0·73	0·51–1·06
Number of water taps‡	0·85	0·82–0·89	0·93	0·88–0·98
Kitchen in the house‡				
Yes	1·0		1·0	
No	2·11	1·65–2·70	1·44	1·08–1·93
Water storage tank				
Substandard	1·0		1·0	
Standard	0·58	0·49–0·68	0·85	0·68–1·06
Water treatment-filter‡				
Yes	1·0		1·0	
No	1·52	1·29–1·79	1·23	1·02–1·48

* Adjusted for log[age].

† Adjusted for log[age], income, maternal education and the other variables in the table.

‡ Variables which had a significant association after second adjustment (RR^2).

three levels (< 2, 2–3 and > 3 persons/room). The presence of visible sewage in front of the house, existence of a rubbish collection service, and the availability of a sewerage system entered the models as dichotomous variables (yes/no). The source of water was classified as being the piped public system, a well, or both. The type of well used in the house was dichotomized into use of a borehole *vs*. a dug well or none. The amount of water consumed by the household was assessed indirectly through the number of water taps in the house. We regarded the presence of a kitchen, a room specially reserved for preparing meals (yes/no), as an important indicator of hygiene. The way people stored water was classified as standard or substandard. The presence of a ceramic filter to treat the water (yes/no) was also recorded.

Data entry and analysis was carried out using Excel 97 (Microsoft) and Stata 5.0 software (Stata Corporation). A generalized linear model using a complementary log–log function was fitted to the data, using the logarithm of age (log[age]) as an explanatory variable. By applying this model, the rate ratios and 95% confidence intervals (95%CI) can be obtained [13].

The statistical analysis was carried out in three stages. In the first stage, each variable was tested, always including log[age] in the model. Then, the effects of those variables significantly associated with seropositivity for hepatitis A at the 10% level were evaluated in a model including log[age] and the two socio-economic variables (income and maternal education) as covariates. In the third stage, those variables that reached a significant association with hepatitis A at the 10% level were included in a final model, mutually adjusting for all of them.

RESULTS

Raw data

Table 1 shows the seroprevalence for hepatitis A according to age and socio-economic variables. As expected, the seroprevalence increased steadily with age, reaching around 60% at 9 years of age. Seroprevalence was negatively associated with socio-economic variables – the number of years of schooling of the mother/carer, and monthly household income.

Multivariate analysis

Table 2 shows the results of multivariate analysis of the environmental and domestic risk factors investigated in the study. Two sets of rate ratios for hepatitis A seropositivity are shown. The first (RR^1) is adjusted for log[age] alone, while the second (RR^2), is adjusted for log[age], socio-economic variables and for all other environmental and domestic variables. All of the risk factors included in the analysis were significantly associated with hepatitis A seropositivity after adjustment for log[age] alone. However, when socio-economic indicators (education and income) and all significant domestic and environmental variables were simultaneously included in the model, the associations of seropositivity only with house location, crowding, and the presence of a kitchen, of a water filter, and of number of taps, an open sewer in front of the house were significant.

After adjustment, the seroprevalence of hepatitis A was 51% higher among people living in houses situated on a hilltop when compared to those living in valleys or on a hillside. The adjusted rate for hepatitis A was also 36% and 52% higher among people living in houses with 2–3 and > 3 persons per room, respectively. Living in houses adjacent to sewage channels was associated with a 24% higher rate for hepatitis A.

Each additional water tap was associated with a decrease of 7% in the hepatitis A seroprevalence. The absence of a kitchen corresponded to an increase of 44%, while not using a ceramic water filter was associated with a 23% increase.

DISCUSSION

The slope of the age-seroprevalence graph (Fig. 1) suggests, at least in the first decade of life, a mean incidence of seroconversion of the order of 6% per year of age. This is greater than reported in other studies from Brazil [14], and is to be expected as the study population was selected from a low income community, whereas other studies have used representative samples of the population as a whole.

Of the various potential risk factors, crowding has a strong and significant association with seropositivity. Crowding has also been identified as a risk factor for hepatitis A in Italy [15]. There are several possible ways in which such an association could arise. First, it could arise from socio-economic confounding; but it remained positively associated even after controlling for socio-economic variables, such as education and income. Second, larger families have a greater number of members (particularly children) who can be exposed to pathogens externally and serve as index cases within the household. Third, the increased prevalence of seropositive children could be explained by greater promiscuity of contact and the difficulty of maintaining hygiene in an overcrowded household. In either case, the association with crowding suggests that transmission within the domestic domain, as opposed to the public domain [16], accounts for an important proportion of all cases.

Mother's education is also significantly associated with a lower seroprevalence. There are a number of ways in which maternal education contributes to the protection of children from infection [17]. Educated mothers have greater power of decision and sense of self-efficacy, and are better informed.

There was a significant association between seropositivity and the presence of an open sewage channel running past the front of the house. This finding contradicts the judgement by Feachem *et al.* [18] that 'what happens to excreta – how they are transported, treated and re-used – is of less importance … than the transmission of infection in the home'. Studies of hepatitis A antibodies in municipal workers exposed to raw sewage have found differing results [19].

Skinhoj et al. [20] found a significantly higher prevalence than in a control group in Copenhagen, but De Serres et al. [21] found no such association in their study in Quebec, Canada. The difference in the present study is that it relates to children, who are not only immunologically naïve but also likely to have more intimate contact than adults with the waste-water, through play and other activity.

Since hepatitis A is transmitted by the faecal-oral route, it is to be expected that water supply would have some effect on it. The results of previous studies in Brazil suggest a protective association between water supply and the seroprevalence of hepatitis A [22]. Waterborne epidemics have been documented, but it has rarely been possible to distinguish the effects on endemic hepatitis A due to improved water quality (preventing water-borne transmission) from those of greater water quantity available for hygiene improvements (preventing so-called 'water-washed' transmission from person to person). In the present study, only two of the five indicators of water supply showed an association with seroprevalence, which was just significant.

The source of water, the type of well, and the type of water storage used in the household were not significantly associated with seropositivity after adjustment by multivariate analysis. This suggests that contamination of water sources is not the main mechanism for hepatitis A transmission in the study population.

The possession and use of a ceramic water filter was associated with a lower seroprevalence (suggestive of a water quality effect) though the association was on the margin of significance. Ceramic filters can remove enteric viruses [23], but there was no significant association of seroprevalence with the practice by some households of boiling their drinking-water. Moreover, there is another possible explanation for this association. Those owning filters are a self-selected group, so that concern with disease prevention may show itself in other ways, such as better hygiene, which help to prevent transmission.

A large number of water taps and fittings in the household was also associated with reduced prevalence. The number of taps is a good measure of water consumption [24]. Water consumption in a household is in turn an indicator of hygiene, as most water consumed in the house is for this purpose.

The connection with hygiene is supported by the association of seropositivity with a house location at the top of a hill. Households located in such places had a similar average income, and were no more or less likely to have an open sewer passing by the front door. On the other hand, residence on a hilltop was associated with irregularity of the piped water supply and the use of supplementary sources, particularly wells. While neither of the latter showed a significant association with hepatitis A seropositivity, it seems likely that hill top residence served as an indicator of constraints in the availability of piped water for hygiene.

It was hypothesized that the lack of a kitchen, a room specifically dedicated to food preparation, was also indicative of poor hygiene; the association of this variable with hepatitis A seropositivity further supports the hypothesis of hygiene-related transmission in the domestic domain.

To conclude, our data indicate a pattern of person-to-person transmission in the domestic domain, in which hygiene and the availability of water for hygiene plays an important role. A protective effect from improved water quality is also suggested, albeit more tentatively. The data indicate that additional transmission takes place in the public domain due to the presence of open sewer channels. The availability of a sewer network *per se*, and even of in-house excreta disposal is not itself protective of an individual household. Rather, by containing and removing the sewage of the community as a whole, the system protects households which would otherwise be exposed to it.

Our findings indicate that environmental measures have a role to play in the prevention of hepatitis A, apart from their role in preventing many other infections. However, their implementation to cover all low-income areas in Brazil will take many years yet. Meanwhile, children growing up in such communities are exposed to hepatitis A infection in the public domain, however much their families strive to achieve good domestic hygiene; vaccination offers them the possibility of protection in the short term.

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REFERENCES

1. Szmuness W, Dienstag JL, Purcell RH, et al. The prevalence of antibody to hepatitis A antigen in various parts of the world: a pilot study. Am J Epidemiol 1977; **106**: 392–8.
2. Kilpatrick ME, Escamilla J. Hepatitis A in Peru – the role of children. Am J Epidemiol 1986; **124**: 111–3.
3. Vranckx R. Hepatitis A virus infections in Belgian children. Infection 1993; **21**: 168–70.
4. Morales JL, Huber L, Gallego S, et al. A sero-epidemiologic study of hepatitis A in Spanish children. Relationship of prevalence to age and socio-environmental Factors. Infection 1992; **20**: 194–6.
5. Almeida LM, Costa MCE, Luiz RR, et al. Soroprevalência da hepatite A no município de Duque de Caxias, Rio de Janeiro, Brasil. Cadernos Saúde Coletiva 1988; **6** (Suppl. 1): 39–48.
6. Tapia-Conyer R, Santos JI, Cavalcanti AM, et al. Hepatitis A in Latin America; a changing epidemiologic pattern. Am J Trop Med Hyg 1999; **61**: 825–9.
7. Gust ID, Tilman AR. Hepatitis in the tropics. Med J Aust 1993; **129**: 691–5.
8. Gay NJ, Morgan-Capner P, Wright J, et al. Age-specific antibody prevalence to hepatitis A in England: implications for disease control. Epidemiol Infect 1994; **113**: 113–20.
9. Arankalle VA, Tsarek SA, Chadha MS, et al. Age-specific prevalence of antibodies to hepatitis A and E viruses in Pune, India 1982 and 1992. J Infect Dis 1995; **171**: 447–50.
10. Mäusezahl D, Cheng F, Zhang SQ, Tanner M. Hepatitis A in a Chinese urban population: the spectrum of social and behavioral risk factors. Int J Epidemiol 1996; **25**: 1271–9.
11. Fundação IBGE. Censo Brasileiro de 1991. Fundação Instituto Brasileiro de Geografia e Estatística 1991.
12. Almeida LM, Azevedo RS, Guimarães AAM, et al. Detection of antibodies against hepatitis A virus in eluates of blood spotted on filter-paper: a pilot study in Rio de Janeiro, Brazil. Trans Roy Soc Trop Med Hyg 1999; **93**: 401–4.
13. Martuzzi M, Elliott P. Estimating the incidence rate ratio in cross-sectional studies using a simple alternative to logistic regression. Ann Epidemiol 1998; **8**: 52–5.
14. Vitral CL, Yoshida CFT, Lemos ERS, et al. 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. Memórias do Instituto Oswaldo Cruz 1998; **93**: 1–5.
15. Catton MG, Locarnini SA. Hepatitis A virus epidemiology. In: Zuckerman AJ, Thomas HC, eds. Viral hepatitis. 2nd edn. London: Churchill-Livingstone, 1998.
16. Cairncross S, Blumenthal U, Kolsky P, Moraes L, Tayeh A. The public and domestic domains in the transmission of disease. Trop Med Int Health 1996; **1**: 27–34.
17. Caldwell JC. How is greater maternal education translated into lower child mortality? Health Transition Rev 1994; **4**: 111–25.
18. Feachem RG, Bradley DJ, Garelick, H, Mara DD. Sanitation and disease: health aspects of excreta and wastewater management. London: John Wiley, 1983; 37.
19. Cadilhac P, Roudot-Thoraval F. Seroprevalence of hepatits A virus infection among sewage workers in the Parisian area, France. Eur J Epidemiol 1996; **12**: 237–40.
20. Skinhoj P, Hollinger FB, Hovind-Hougen K, Louis P. Infectious liver diseases in three groups of Copenhagen workers: correlation of hepatitis A infection to sewage exposure. Arch Environl Hlth 1981; **36**: 139–43.
21. De Serres G, Levesque B, Higgins R, et al. The need for vaccination of sewer workers against leptospirosis and hepatitis A. Occ Environ Med 1995; **52**: 505–7.
22. Tanaka J. Hepatitis A; shifting epidemiology in Latin America. Vaccine 2000; **18**: S57–60.
23. Melnick JL, Gerba CP, Wallis C. Viruses in water. Bull WHO 1978; **56**: 499–503.
24. White GF, Bradley DJ, White AU. Drawers of water; domestic water use in East Africa. Chicago: Chicago University Press, 1972; 140.