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AGE-SPECIFIC SEROPREVALENCE OF HEPATITIS A AMONG SCHOOL CHILDREN IN CENTRAL TUNISIA

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Abstract. Hepatitis A virus (HAV) has different epidemiologic and clinical patterns, depending on the level of endemicity in a given geographic area. Tunisia is considered a region of high endemicity for hepatitis. Improvement of socioeconomic conditions in this country has made a determination of the seroprevalence of this disease advisable. We assessed the seroprevalence of HAV in Sousse in central Tunisia. A total of 2,400 school children 5–20 years of age (mean ± SD age = 11.7 ± 3.5 years) were selected by two-stage cluster sampling and tested serologically for IgG antibody to HAV by using an enzyme-linked immunosorbent assay. The overall seroprevalence among this population was 60% (44%, in children < 10 years old, 58% in those 10–15 years of age, and 83% in those > 15 years of age. Seroprevalence also varied according to area of residence. At the age of 10, 21.3% of school children living in the urban areas and 87.7% of those living in rural areas had antibodies to HAV. Other factors that increased seroprevalence included non-potable water, crowding, and a low education level of parents with odds ratios of 4.37, 2.96, and 2.62, respectively. This study has shown an increase of seroprevalence with age, suggesting that transmission among younger children has decreased, particularly in urban areas. Programs to prevent hepatitis A may need to be modified based upon the changing age distribution of the disease and mass vaccination program could be indicated if additional incidence and prevalence data confirm the intermediate endemicity of HAV.

INTRODUCTION

Hepatitis A virus (HAV) is transmitted via the orofecal route and has a global distribution. However, the true incidence of hepatitis A is often underestimated because of under-reporting as a result of its widely asymptomatic and milder forms of infection. Thus, the epidemiologic pattern of HAV in a given country is indicated primarily by its seroprevalence and only secondarily by disease incidence. The epidemiology of HAV is highly correlated with age and level of hygiene.[1–3] Three epidemiologic patterns of endemicity (low, intermediate, and high), are seen worldwide. Each pattern has a different rate of infection, prevailing age of infection, and transmission model. However, these three epidemiologic patterns can coexist in different groups of the total population in one country.

In industrialized countries, which are characterized by a low endemicity pattern, prevalence is low during childhood, but the non-immune adult population (seroprevalence ranges from 13% to 50% in adults)[2,4–6] is exposed to epidemics and severe forms of hepatitis A, mostly limited to risk groups. In regions of intermediate endemicity where hygiene conditions are variable, seroprevalence in adults varies from 60% to 97%. Young children are usually not infected and infection occurs at a later age in adolescents and young adults, which explains the higher incidence of symptomatic hepatitis.[2,5–7]

In developing countries, low economic status, high crowding, and inadequate water treatment contribute to a high endemicity pattern; more than 90% of the population has acquired natural immunity before 10 years of age and often shows asymptomatic forms. In those countries, overt forms of hepatitis A are relatively rare with exceptional severe forms.[1,6]

The epidemiologic pattern of hepatitis A infection is currently changing in many developing countries where socioeconomic conditions are improving. As a result, these countries no longer demonstrate the epidemiologic characteristics of countries with a high endemicity of hepatitis A and other infectious diseases transmitted via the orofecal route. Studies conducted in such emerging countries have reported epidemiologic changes over the last decades, indicating that hepatitis A affects the population at a later age,[3,7–9] drawing these countries closer to those with intermediate endemicity with an increased risk of symptomatic, potentially more severe disease forms that occur in older individuals.

In Tunisia, epidemiologic data on HAV are fragmentary and limited to studies on acute symptomatic hepatitis A infection. In the 1970s and 1980s, such studies showed a high endemicity of hepatitis A at a maximum age of 5–10 years, with a higher frequency pattern in fall.[10] Serologic diagnosis has recently been used more widely in this country, and an incidence rate of 11.9/100,000 inhabitants was reported in 1998, although this figure is most likely an underestimate.[11] No age-specific seroprevalence data are currently available in Tunisia. The aim of this study was to determine the age-specific seroprevalence of HAV in a young population according to socioeconomic status, and to detect a likely change in the epidemiology of infection.

SUBJECTS AND METHODS

Study design and population. This study was a descriptive, cross-sectional, sero-epidemiologic investigation of HAV among school children in the governorate of Sousse in April 2002. In 2000, the population of Sousse was 494,900 inhabitants, of whom 302,200 (61%) were 5–25 years old.[12] The study was reviewed and approved by the University Hospital Farhat Hached Ethical Committee.

The targeted population included children and those 5–23 years old in elementary and secondary schools of the private and public sectors in the governorate of Sousse during the

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school year of 2001–2002. This study population constituted a representative sample of school children.

Two-stage cluster sampling was used for random selection of institutions and classes that was proportional to the number of school children in each institution. In the first stage, we sampled schools; in the second stage, we sampled classes from these schools. Sample size calculation was based on a 50% HAV seroprevalence estimation with a 2% precision rate and a 95% confidence level. The formula for sample size determination yielded a total of 2,400 school children. As regards urbanization level, Distribution of schools in various regions was taken into account during sampling. School children were allocated to three groups according to their school location: 1) urban area: children from schools in the city of Sousse, 2) sub-urban area: children from schools in municipal areas, and 3) rural area: children from school in non-municipal areas.

Collected data. Data collected included general information on school children (age, sex, educational level, and socioeconomic characteristics that included the number of siblings, type of residence, source of water supply, and waste water sewage) and their parents (origin, educational level, occupation, social insurance coverage). Participants were allocated to three age groups: 5–9 years, 10–15 years, and > 15 years. Housing was classified as modern in the case of a villa and old in the case of an apartment or traditional house. Based on educational level, parents were allocated into either group 1 (university level) or group 2 (other).

Data collection method. Epidemiologic data were collected from questionnaires and health files from school medical records. After informed consent was obtained from parents, blood samples were collected from school children for HAV serology. This study was conducted as part of collaboration between the Infectious Diseases, Epidemiology and Virology departments of the University Hospital Farhat Hached and the School Health Department. Four school physicians were involved with completion of questionnaires, and blood samples were obtained by four nurses, all with previous experience with a pediatric population. Serum samples were tested for IgG antibodies to HAV by a qualitative enzyme-linked immunosorbent assay (ETI-AB-HAVK-3; Diasorin, Stillwater, MN). Results were read on a multimode plate reader and results were compared with the optical densities of positive and negative controls.

Statistical analysis. Data were analyzed, using SPSS version 9.0 software (SPSS, Inc., Chicago, IL). A descriptive analysis was followed by bivariate analysis using a chi-square test for comparison of the various sub-groups with a 5% statistical significance level. A multivariate analysis with logistic regression was used to determine predictors variables associated with seroprevalence among the significant factors found by bivariate analysis. Odds ratios and 95% confidence intervals were calculated presented for these variables.

RESULTS

A total of 2,386 schoolchildren were enrolled in the study; 14 of the initial population of 2,400 were absent at the beginning of the study. The mean ± SD age of 2,352 school children was 11.7 ± 3.5 years with a range of 5.7 to 23 years. The sex ratio was 1.01 (1,199 males/1,187 females).

The overall prevalence of antibodies to HAV was 60% and was significantly correlated with the age and origin of participants. It was 44.2% in children < 10 years old and increased to 83% among those > 15 years old (Table 1). Antibodies to HAV were found in 89.9% of school children from rural areas, 69.1% from sub-urban areas, and 39.7% from the city of Sousse; their age distribution is shown in Table 2. In some schools in central Sousse, the seroprevalence of HAV ranged from 5.5% to 11% in children < 12 years old and from 30% to 50% in those > 15 years old. In rural areas, seroprevalence was 100% in those 10 years old in some schools. Besides age and origin, other variables significantly associated with HAV seroprevalence included source of drinking water, waste water sewage, number of people living in the same housing, type of housing, and education level of parents (Table 1). Multivariate analysis confirmed the specific effects of the residence of school children and source of drinking water. These two factors were independent of age, type of housing, and number of persons per household (Table 3).

TABLE 1

Seroprevalence of antibodies to hepatitis A virus (HAV) Tunisian school children according to known risk factors

Variable	Total, no. (%)	HAV + no. (%)	Odds ratio (95% CI)*
Sex			
Male	1,196 (50.3)	691 (57.7)	1
Female	1,180 (49.7)	734 (62.2)	1.2 (1.02–1.42)
Age group			
5–9	645 (27.4)	285 (44.2)	1
10–15	1,201 (51.1)	707 (58.9)	1.81 (1.48–2.20)
>15	506 (21.5)	420 (83)	6.17 (4.62–8.24)
Origin			
Urban	991 (41.5)	393 (39.7)	1
Suburban	1,034 (43.4)	714 (69.1)	3.40 (2.81–4.10)
Rural	361 (15.1)	324 (89.8)	13.32 (9.14–19.50)
Water supply			
Municipal	2,327 (97.5)	1,380 (59.3)	1
Other	59 (2.5)	51 (86.4)	4.37 (1.99–10.01)
Waste water sewage			
Yes	1,689 (70.8)	870 (51.5)	1
No	697 (29.2)	561 (80.5)	3.88 (3.13–4.82)
Housing			
Modern	293 (12.3)	102 (34.8)	1
Old	2,091 (87.7)	1,329 (63.6)	3.27 (2.51–4.26)
Parents education level			
University	620 (26.4)	263 (42.4)	1
Less	1,725 (73.6)	1,136 (65.9)	2.62 (2.16–3.17)
No. of persons/household			
2–5	1,028 (43.3)	467 (45.4)	1
>5	1,345 (56.7)	957 (71.2)	2.96 (2.49–3.53)

* CI = confidence interval; 1 = referent.

TABLE 2

Seroprevalence of antibody to hepatitis A virus by age and region among school children in central Tunisia

	5–9 years old No. (%)	10–15 years old No. (%)	>15 years old No. (%)	Global seroprevalence
Origin				
Rural	135 (87.7)	169 (90.9)	11 (100)	324 (89.9)
Suburban	88 (44)	332 (64.1)	287 (94.4)	714 (69.1)
Urban	62 (21.3)	206 (41.4)	122 (63.9)	393 (39.7)
Global seroprevalence	285 (44.2)	707 (58.9)	420 (83)	

TABLE 3

Multivariate analysis (logistic regression) of risk factors of prevalence of hepatitis A virus among school children in central Tunisia

Variable	Odds ratio (95% CI)	*P*
Origin	9.61 (6.56–14.07)	$<10^{-4}$
Water supply	4.76 (1.30–17.43)	0.01
Age	2.8 (2.41–3.25)	$< 10^{-4}$
Persons/household	2 (1.65–2.42)	$< 10^{-4}$
Type of house	0.46 (0.34–0.61)	$< 10^{-4}$

DISCUSSION

The results of this study have shown that the prevalence of hepatitis A may be lower in young Tunisians than it was in the 1970s. This indicates a changing pattern of HAV epidemiology in Tunisia. Only 44% of children < 10 years old and 83% of those > 15 years old are immune to HAV. In the 1970s and 1980s, the epidemiology of HAV in Tunisia was unclear. The few studies conducted at that time concluded that there was a high endemicity of HAV at an early age (5–10 years) regardless of the region.[10] The World Health Organization has ranked Tunisia among areas of high endemicity, with an estimated incidence of 150 cases/100,000 inhabitants/year and a seroprevalence $\geq$ 90% at 10 years of age.[2] This increase in HAV seroprevalence with age has also been found in India,[9] southern Taiwan,[8] and in Mexican adolescents who emigrated to the United States who showed an increase in HAV seroprevalence from 34% in five-year-old children to 81% in those > 14 years of age.[13] Improvement of hygiene and socioeconomic conditions has undoubtedly contributed to this epidemiologic shift. However, seroprevalence rates are still more elevated than those reported in European countries, where HAV seroprevalence rates do not exceed 25% in adolescents (Table 4).[14–16]

Regardless of age, seroprevalence rates for HAV were significantly lower in urban areas than in sub-urban and rural areas. Moreover, since we sampled areas according to school location, the seroprevalence in urban and suburban areas may have been overestimated for older school children who began primary school in rural areas. Seroprevalence rates were lowest within the urban area of Sousse, as low as 5% at 10 years of age in some schools. In contrast, in some rural areas, 100% of the school children of the same age were immune against HAV. Other predictive factors such as quality of drinking water, waste water sewage, crowding, and housing conditions, which reflect a the socioeconomic status and hygiene conditions of a population, were significantly associated with HAV seroprevalence rates. In an epidemiologic study conducted on HAV seroprevalence in Chile, in addition to the availability of a restroom and a refrigerator, the same risk factors were found.[17] Similarly, Dubois and others have shown that housing conditions and crowding are factors that are significantly associated with HAV seroprevalence.[1]

TABLE 4

Seroprevalence of hepatitis A virus (HAV) by age in several countries

Country	Year	Age group (years)	HAV + (%)
Spain[16]	1992–1993	5–12	11
		13–19	25
		20–29	54
Italy[17]	1989	3–5	2.3
		17–19	16.3
United-Kingdom[18]	1997	5–9	10.5
		10–14	13.9
		15–19	19.6
India[10]	1998	6–10	62.2
		11–15	68.5
		>16	80.8
This study	2002	5–9	44.2
		10–15	58.9
		>15	83

Significant sex differences, such as the slightly higher seroprevalence in females observed in our study, have not been reported by other investigators.[9,13,17,18] However, Hawkes and others reported a significantly higher HAV seroprevalence rate in boys 4–6 years of age.[19]

We have shown that the education level of parents was significantly correlated with HAV seroprevalence, reaching 42.4% in school children with parents with a university education versus 65.9% in those with less education. This finding was previously reported by Stroffolini and others.[15]

In conclusion, the results of this study suggest that HAV epidemiology has changed in Tunisia from a high to an intermediate endemicity pattern. Preventive activities should be adapted to this epidemiologic shift, which has left an increasing proportion of non-immune adults unprotected with a high risk of severe hepatitis A[20] with serious public health consequences. In addition to continued improvement of hygiene and socioeconomic conditions, mass vaccination as recommended by the World Health Organization[21] in areas of intermediate endemicity should be implemented in Tunisia.

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