Original Article

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Shifting Epidemiology of Hepatitis A Infection and Vaccination Status of Children Aged 6 Months-12 Years: Time for Mass Vaccination

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Abstract

Objective: This study was designed to determine the current age-related hepatitis A virus (HAV) seroprevalance, vaccination status of children and to evaluate the epidemiological shift in HAV serostatus living in Tekirdağ, which is located in Thrace region, the European part of Turkey.

Methods: Children 6 months-12 years of age with simple health problems were included. Blood samples were studied for HAV IgM and IgG collectively. A questionnaire addressing several characteristics of subjects was administered to obtain basic descriptive data on HAV epidemiology. Vaccination status of the children was recorded according to the immunization cards.

Findings: The overall anti-HAV IgM and anti-HAV IgG prevalance in children aged 6 months – 12 years was 3.3% and 25.4% respectively. Maximum hepatitis A IgM positivity was in the 7-12 years age group 4.8% (n= 12; *P*<0.001) and maximum hepatitis A IgG positivity in the same age group was 34% (n=85; *P*<0.001). HAV vaccination rate among patients aged more than 2 years was 11.03%. HAV IgG seroprevalance was higher in children of low monthly income families (36.1%, n=78; *P*<0.001) than in the intermediate (17%, n=31) and high income families (11.1%, n=6).

Conclusion: These results indicate a shift in Hepatitis A seroprevalance when compared with the previous studies. As HAV infection in childhood is decreasing, the pool of susceptible adolescents and young adults is increasing. Introduction of hepatitis A vaccination into the national immunization schedule of Turkey should be considered.

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Key Words: Hepatitis; Hepatitis A Virus; Vaccination; Immunization

Introduction

Acute viral hepatitis A is a common and worldwide infectious disease caused by hepatitis A virus (HAV), seen most commonly in developing countries. Most HAV infections occur through fecal–oral transmission, either by direct contact with an infected person or by ingestion of contaminated food or water[1]. Seroprevalance rates are highly correlated with socioeconomic conditions and access to clean water and sanitation[2,3]. With the improving hygienic and socioeconomic conditions, the incidence of HAV infection has decreased. However, this decrease in the incidence is usually accompanied by a shift in the age of the first contact with HAV infection

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towards older age groups. This shift is likely to produce an increase in morbidity, perhaps mortality, and a higher propensity for outbreaks of hepatitis A[4]. Therefore, it is important to detect such shifts, leading to greater disease burden. Although HAV vaccine is available in pharmacies, it is not included in 'Expanded Program on Immunization' and it is not funded by the Turkish government. However, the discussions about who should routinely be vaccinated still continue[5]. To our knowledge, there have been no studies indicating both the shift in HAV serostatus and vaccination status of children in Turkey. This study was designed to determine the current age-related HAV seroprevalance, vaccination status of children and to evaluate the epidemiological shift in HAV serostatus living in Tekirdağ, which is located in Thrace region, the European part of Turkey.

Subjects and Methods

Tekirdağ is located at the Marmara region, which is the socioeconomically most developed among the provinces of Turkey[6]. Tekirdağ, has a population of approximately 800.000. The 6 months - 12 years old age group consists of 27% of the total population. The study was conducted in Namık Kemal University hospital, which is the only referral health center in the city. This hospital is a tertiary health care center which provides health care to all of the city.

Children 6 months-12 years of age who attended the pediatric outpatient clinic during March-November 2010 with simple health problems (for example, upper respiratory tract infection) not suggesting hepatitis, or who attended healthy child examination were enrolled in this prospective and cross-sectional study. Exclusion criteria included: Immunodeficiency or history of chronic disease, and incomplete questionnaires. Children with nausea, vomiting and jaundice were also excluded. The children were divided into three age groups: group 1, 6 months-1 year of age; group 2, 2-6 years of age; group 3, 7-12 years of age. The minimum sample size to determine HAV infection prevalance was calculated as 180 using the formula $[n=(t_1-a)^2.(pq)/s^2]$. We surpassed this minimum sample size by having 452 subjects in our study.

Parents or legal guardians gave informed consent. Blood samples were studied for HAV IgM and IgG collectively with enzyme-linked immunosorbent assay using Vitros ECI Q J&J Company Ortho Clinical Diagnostic Operator.

A questionnaire addressing several characteristics of subjects was administered to obtain basic descriptive data on HAV epidemiology including age, sex, maternal education level and monthly income of the family. Vaccination status of the children was recorded according to the immunization cards. The information was obtained from the parents of the children. According to monthly income per family member in that family, the study population was divided into three groups. If the monthly income per family member was <287 Turkish Lira (TL), it was accepted as a low- income family; intermediate was between TL 287 and TL 825; and high income was >TL 825[7].

Statistical analysis was performed using SPSS version 15.0 (SPSS, Chicago, IL, USA). Demographics and environmental factors were evaluated using χ^2 test. A multiple logistic regression analysis that included mother's education level, family income and usage of toilet paper was performed to evaluate independent risk factors influencing anti-HAV IgG seropositivity. The results of the regression model are presented in terms of adjusted OR and 95% CI. $P<0.05$ was interpreted as statistically significant.

Findings

Four hundred and fifty-two children with suitable criteria were included in the study. The mean age was 6.9±2.2 years: 48% (n=217) were boys, 52% (n=235) were girls. The distribution of the children according to age group was as follows: group 1: 15.9% (n=72); group 2, 28.7% (n=130); and group 3, 55.4% (n=250). The overall HAV vaccination rate was 9.3% (n=42), however, HAV vaccination rate among patients aged more than 2 years was 11.03%. As per responses of the questionnaires, none of the children aged under 2 years had a history of vaccination.

Table 1: HAV seroprevalance and vaccination status of the patients according to age groups

Parameter	6 months – 1 year old n (%)	2-6 years old n (%)	7-12 years old n (%)	Total n (%)	*P*-value
HAV IgM (+)	-	3 (2.3)	12 (4.2)	15 (3.3)	<0.001
HAV IgG (+)	9 (12.5)	21 (16.1)	85 (34)	115 (25.4)	<0.001
HAV Vaccine (+)	-	32 (24.6)	10 (4)	42 (9.3)	<0.001

HAV: Hepatitis A virus

HAV vaccination rates according to the age are shown in Table 1. The overall anti-HAV IgM and anti-HAV IgG prevalance in children aged 6 months-12 years was 3.3% and 25.4% respectively. However, anti-HAV IgG seropositivity in patients with no vaccination was 16.1%. HAV IgM and IgG positivity according to age group is shown in Table 1. Maximum hepatitis A IgM positivity was in the 7-12 year age group 4.8% (n=12; *P*<0.001); maximum hepatitis A IgG positivity in the same age group was 34%, (n=85 *P*<0.001). HAV vaccination rate was significantly higher (24.6%) in 2-6 year old group (n=32; *P*<0.001) than in other age groups (Table 1).

Monthly income, education level and gender were not significantly different among age groups (*P*=0.6, 0.4, 0.7, respectively). Monthly income per family member was low in 47.7% (n=216), intermediate in 40.2% (n=182), and high in 11.9% (n=54), respectively. Factors associated with anti-HAV seropositivity is shown in Table 2. HAV IgG seroprevalance was higher in children of low monthly income families (36.1%, n=78; *P*<0.001) than in the intermediate income (17%, n=31) and high income families (11.1%, n=6) (Table 3). HAV vaccination rate was significantly lower in low income families (1.8%, n=4; *P*<0.001) than in the intermediate income (16.3%, n=30), and high income families (14.8%, n=8) (Table 4).

Discussion

As HAV infection is caused by an enterically transmitted virus, the great majority of the population in underdeveloped countries is infected in childhood or adolescence[8]. While the infection is mostly asymptomatic during childhood, the incidence of symptoms and complications increases in an advanced age. For this reason, age specific prevalance and its change with age are more important than the mean prevalance[9].

In recent years, a shift in prevalance of the disease has been reported in our country from several different regions[10-13]. In our study, we also detected a decrease in the rate of infection, when compared with above mentioned studies. To our knowledge, there is only one study on prevalance of hepatitis A infection in children from our region (Thrace), which was done in 2004 in Edirne, which is located next to our city. In that study, Erdogan et al found anti-HAV positivity of 29.3% among 0-19 year old children. None of the children was vaccinated[10]. However, in our study, we found an overall anti-HAV seropositivity of 16.1% in unvaccinated children. Also in our study, 9.3% of the children were vaccinated. This comparison indicates a shift in the average age of HAV infection from childhood to young adulthood. With this epidemiologic shift, the disease burden

Table 2: Factors associated with anti-HAV seropositivity

Parameter		n (%)	Anti-HAV Seroprevalance n (%)	Adjusted OR (95% CI)
Maternal Education	**>6 years**	258 (57.1)	42 (16.2)	Reference
	≤5 years	194 (42.9)	88 (45.3)	3.1 (1.2-5.3)
Family Income	**Intermediate or high**	236 (52.3)	39 (16.5)	Reference
	Low	216 (47.7)	91 (42.1)	3.3 (1.8-6.2)
Usage of Toilet Paper	**Yes**	381 (84.3)	81 (21.2)	Reference
	No	71 (15.7)	49 (69.0)	5.2 (2.2-10.3)

HAV: Hepatitis A virus; CI: Confidence Interval

Table 3: HAV seroprevalance according to the monthly income level

Monthly income level	HAV IgG (+) *		HAV IgM (+) n (%)
	Vaccine (-) n (%)	Vaccine (+) n (%)	
Low	78 (36.1)	4 (1.8)	11 (5)
Intermediate	31 (17)	30 (16.3)	3 (1.6)
High	6 (11.1)	8 (14.8)	1 (1.8)

*P. Value: <0.001 / HAV: Hepatitis A virus

associated with hepatitis A will increase as the infection in adulthood carries a substantial risk of morbidity and mortality. Furthermore, the seroprevalance of HAV in Turkey varies among geographical regions. Western and central regions of Turkey have intermediate endemicity; whereas eastern and southern regions are still the areas of high endemicity[14]. There is continuing immigration from the eastern and southeastern provinces to the central and western areas increasing the potential risk of HAV epidemics in our country.

Reduction in the prevalance of HAV infection has been reported recently in many studies[15-17]. Japan, Australia, New Zealand, Canada, the United States, and most of the European countries have low prevalance of anti-HAV. Altough anti-HAV rates still remain high in most Latin American, Asian, and Middle Eastern countries, and the average prevalance tends to decline. A number of countries have changed from high to moderate and from moderate to low endemicity, with a corresponding increase of the age of exposure from childhood to early adulthood[4,15-17]. There is strong evidence that these changes result from improvements in drinking water, sanitation facilities and hygiene practices, improvement of living standards and socioeconomic progress[4,13,15,18].

There are many studies relating HAV infection to the economic level. Two studies investigating the relationship between social factors and HAV infection indicated that anti-HAV seroprevalance rates in children increased with poor maternal education[19,20]. We also found that increased HAV seropositivity rate associated with less than 5 years duration of maternal education, low income level and not using toilet paper.

Safe and effective hepatitis A vaccines have been available since 1992, but are significantly underused[21]. The vaccines are highly immunogenic and provide long-term protection against hepatitis A[22,23]. In countries of intermediate endemicity, WHO recommends large-scale childhood vaccination to be considered as a supplement to health education and improved sanitaion[24]. The vaccine has been available in private practice in Turkey since 2000. However, to date, this vaccine has not been included in the national immunization program, because of its high cost. But the vaccine will be introduced to national immunization program in autumn 2012. In our study, we found a vaccination rate of 9.3%, and to our knowledge, this is the highest rate reported from our country. This can be explained as increasing awareness about the disease and low side effect profile of the vaccine. Also, our city is located in a region, which has a higher socio-economic status when compared with the other regions of the country. Differences in vaccination coverage rates between regions of the country are multifactorial and difficult to ascertain. However, since until recently the hepatitis A vaccine was not reimbursed among Turkish vaccines during the study, it is upheld that socioeconomic status, as well as the perceived magnitude of disease severity and necessity for hepatitis A vaccination may be essential elements contributing to the

Table 4: HAV vaccination status according to the family monthly income level

HAV Vaccine	Family monthly income level		
	Low n (%)	Intermediate n (%)	High n (%)
Positive	4 (1.8)	30 (16.3)	8 (14.8)
Negative	212 (98.2)	152 (83.7)	46 (85.2)

*P. Value: <0.001 / HAV: Hepatitis A virus

inter-territorial differences observed.

The present study was conducted in a university hospital, which is the only referral center in the city. Population based studies conducted in field (for example: schools or primary health care unit), instead of hospitals, and also multi-center studies instead of single center, may give more valuable data about seroprevalance rates of hepatitis A infection. This seems the limitation of the present study. But, there are similar studies well conducted in hospitals as in our study, so we believe our study reflects the current status of hepatitis A in our region.

Conclusion

The present study indicates that the pattern of endemicity of HAV infection is shifting in Turkey. To combat and control the infection, introduction of hepatitis A vaccination into the national immunization program seems to be rational for children aged >18 months. But there is still need for cost-effectiveness studies.

Conflict of Interest: None

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