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Original Article

Seroprevalence of hepatitis a and associated factors among 1-15 year old children in Eastern Turkey

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Abstract: Background: Hepatitis A is a common infectious disease during childhood worldwide. Recently, great deal of changes in the epidemiology has been reported. The seroepidemiologic studies of this infection are not sufficient in Eastern region of Turkey.Objective: To investigate the seroprevalence and association with socio-demographic variables of hepatitis A in 1-15 year old children in Van. Patients and Methods: This study was performed on 510 one to fifteen year old children from outpatient pediatric clinics in Yüzüncü Yıl University, Faculty of Medicine during last three months of 2009. Anti-HAV IgG was measured in sera by enzyme-linked immunosorbent assay. The information about subjects was recorded on standardized forms and a chart review survey was performed. Results: The overall ratio for seropositivity was 54.9%. Statistical significance was found between hepatitis A seroprevalence and age, collective use of domestic items, fresh water resources, localization and type of toilet and the number of households. Conclusion: This study provided the most recent data of seropositivity and revealed the preliminary indication of epidemiological shift in seroprevalence of Hepatitis A virus in a region with high endemicity.

Keywords: Hepatitis a antibodies, prevalence, seroepidemiologic studies, children

Introduction

Hepatitis A is one of the most common causes of acute viral hepatitis worldwide and caused by the hepatitis A virus (HAV), a nonenveloped RNA virus of the genus Hepatovirus in the family Picornaviridae [1, 2]. Generally, it is a self-limiting and asymptomatic disease in children that resolves spontaneously but approximately 70% of infected adolescents and adults present with an acute illness with distinct symptoms (jaundice, fever etc.) [2]. Although most patients recover within two months, it is a vaccine-preventable infectious disease that can be widely prevented by immunization strategies in childhood [1, 2].

Hepatitis A virus is mainly transmitted via the faecal-oral route or by close contact between persons (especially in households and homosexual men). The incidence rate and difference between age patterns of clinical courses are closely related to socioeconomic and also sanitation conditions such as ability to reach safe drinking water [3, 4]. The age-related seroprevalence and incidence of HAV infection differs geographically. Namely, in developing countries there is high endemicity rates due to exposure of pathogen during early childhood. On the other hand, improvement of socioeconomic status and sanitary conditions results in a shift of infections from pediatric ages to adulthood [2, 3, 5]. HAV infection rates can be reduced by improving livingconditions, and also an effective HAVvaccine has also been available since the licensure opened in 1995-1996 in USA (1). In 2006, the Centers for Disease Control and Prevention (CDC) have recommended that all children 12 to 23 months of age should be immunized [1]. Since October 2012 Ministry Of Health has put HAV vaccine in mandatory childhood vaccine schedule in Turkey.

The aim of this study was to evaluate the prevalence of anti-HAV IgG in children aged from 1 to 15 years old and to determine influencing factors, such as age, demographic characteristics, socio-economic status, and housing conditions

associated with the prevalence of this infection. This study also presents the unique data of seroepidemiological survey of Hepatitis A infection in Van region of Eastern Turkey.

Materials and methods

This study was conducted between October and December 2009 in Yüzüncü Yıl University, Faculty of Medicine. Our hospital is an important reference center located in Van with a population of 1.050.000 (in 2013). It is a frontier city which located at the Eastern region of Turkey. The neighbouring nation is Iran and our region is one of the worsest regions in Turkey according to socio-economical status.

The information about each one of 600 subjects who admitted to outpatient pediatrics clinics of our hospital were recorded on standardized forms and a chart review survey was performed. Patients with a story of jaundice or previously vaccined for HAV and who has been received blood or immunoglobulin preparations before study were excluded. Data analysis included age, gender, household size, main source of water in the household, number of members and rooms in home, socio-economic status according to monthly earnings, collective use of towels etc., localization and type of toilets. Subjects were divided into five main groups based on age (1-4 years, 5-8 years, 9-12 years and 13-15 years). Socio-economic status was assessed by using the data of Institute of Statistics, Turkey Government. Written and informed consent was obtained from parents or legal guardians. 3 mL of blood was withdrawn from each patient. Whole blood samples was centrifuged at 2000xG to obtain serum samples, which were then stored at -20°C until examination. Enzyme-linked immunosorbent assay (ELISA; Architect Systems and Abbot Diagnostics Division, USA) was used to determine anti-HAV IgG presence. The study was approved by the Ethics Committee of Yüzüncü Yıl University, Faculty of Medicine under the number.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, Chicago, IL) version 13.0. Data were reported as number and percents, descriptive statistics were used for continuous variables. Chi-square test or Fisher's exact test and multivariate regression analysis were used as appropriate to compare between the groups. A value of $P<0.05$ was accepted as significant.

Results

A total of 510 subjects aged 1-15 years were fullfilled the inclusion criterion, enrolled in study and tested for the presence of anti-HAV IgG. The majority of children were male (n=301, 59.1%) and groups according to age were as follows; 1-4 years (n=141), 5-8 years (n=151, 29.6%), 9-12 years (n=146) and 13-15 years (n=72) (**Table 1**). A statistically significant increase in anti-HAV IgG seropositivity was noted between lower to higher age groups (26.2%, 52.3%, 72.6% and 80.6% respectively, P<0.05, **Table 1**). The overall seroprevalence of anti-HAV IgG was 54.9% and there was no significant difference between genders (P=0.251).

Collective use of toothbrush and towels in household was significantly common in seropositive subjects (P=0.001). Seropositivity rate was higher among the subjects whose room count per a person in home was below 1, than those which the count equal to 1 or higher (P=0.001). The prevalence of anti-HAV IgG was significantly higher in children with intermediate and low socio-economic status (P=0.001, **Table 1**). Anti-HAV IgG positive individuals had significantly higher numbers of family members: 41.7% in who have below 5 members and 63.3% in who have 6 or higher members in home. Thus, family sizes were significantly different between the two groups (P<0.01).

Among subjects who reported as the main source of water in the household as licenced-wrapped water, city water and well water; seropositivity rates were 37.9%, 55.9% and 74.1%, respectively. The difference between the first and second or between second and third groups were statistically significant (P=0.001, **Table 1**). In 5-8 years age group, the seropositivity rate of individuals according to main source of water as follows; licenced-wrapped water, 33.3%; city water, 51.5%; well water 85% and the difference between this subgroups was significant (P<0.05, **Table 2**). On the other hand, this difference could not been found in other age groups. There was a significant difference between subjects who use only a squat toilet (Turkish-style) and who use flush toilet (European style) and squat toilet together (P=0.001, **Table 3**). The prevalence of anti-HAV

Table 1. Association between demographic features and the prevalance seropositivity among study population

Variables	N (total)	Anti-HAV IgG (+) n (%)	*P* value
Gender			
Female	209	120 (41)	x^2: 0.904, P=0.342
Male	301	160 (59)	
Age (years)			
1-4 years	141	37 (26.2)	
5-8 years	151	79 (52.3)	x^2: 84.799, P=0.001*
9-12 years	146	106 (72.6)	
13-15 years	72	58 (80.6)	
Number of household members			
<6 person	199	83 (41.7)	x^2: 22.942, P=0.001*
≥6 person	311	197 (63.3)	
Number of rooms per person			
<1	457	265 (58)	x^2: 16.902, P=0.001*
≥1	53	15 (28.3)	
Socioeconomic status			
Adequate (intermediate/high)	240	108 (45)	x^2: 17.952, P=0.001*
Inadequate (low)	270	172 (63.7)	
Water source			
Licenced-wrapped water	87	33 (37.9)	x^2: 18.932, P=0.001*
City water	365	204 (55.9)	
Well water	58	43 (74.1)	
Collective usage of personal belongings			
Towel	326	182 (55.8)	x^2: 21.833, P=0.001*
Towel + toothbrush	64	49 (76.6)	
None	120	49 (40.8)	
Type of toilet			
Squat toilet (Turkish-style)	408	240 (58.8)	x^2: 12.671, P=0.001*
Squat toilet + flush toilet (European style)	102	40 (39.2)	
Localization of toilet			
Indoor	425	219 (51.5)	x^2: 11.714, P=0.001*
Outdoor	85	61 (71.8)	

*P<0.05 was interpreted as statistically significant.

IgG was significantly higher in children whose toilet was located outside than who had an inside toilet in home (71.8% vs. 51.5%, P=0.001, **Table 1**).

Discussion

Hepatitis A virus infection is a major public health problem worldwide. It is estimated that nearly 1.4 million new cases occur worldwide each year and 11-22% of them have been required hospitalization [6]. Although great advance has been seen in health care and living conditions in world, a WHO report has shown that the number of cases increased from 177 million in 1990 to 212 million in 2005 and the death due to this infection from 30,282 to 35,245 [5]. These noteworthy data are evidence of the importance of HAV infections. There is an obvious decline in prevalance of hepatitis A infections during the previous decades in Europe and North America due to improvements in socioeconomic and hygienic conditions and also immunization programs [2]. Seropositivity rates of Anti-HAV IgG in pediatric age group in these regions are lower than

Table 2. Statistical analysis of characteristics among seropositive subjects according to age groups

Variables/Ages	1-4 years	5-8 years	9-12 years	13-15 years
Positivity of Anti-HAV IgG	n	n	n	n
Gender				
Female (Ref)	14	33	46	27
Male	23	46	60	31
P value	x^2: 0.947 P=0.004*	x^2: 1.559 P=0.212	x^2: 0.198 P=0.656	x^2: 3.215 P=0.200
Water source				
Licenced-wrapped water (Ref)	5	10	10	8
City water	26	52	83	43
Well water	6	17	13	7
P value	x^2: 3.215 P=0.200	x^2: 12.92 P=0.002*	x^2: 1.878 P=0.391	x^2: 0.054 P=0.817
Socioeconomic status				
Adequate (intermediate/high) (Ref)	15	29	35	29
Inadequate (low)	22	50	71	29
P value	x^2: 1.187 P=0.276	x^2: 13.528 P=0.001*	x^2: 8.779 P=0.003*	x^2: 0.001 P=1

*$P<0.05$ was interpreted as statistically significant. Ref: reference category in statistical analysis.

Table 3. Multivariate regression analysis for the model of Anti HAV IgG (+)

Variables	Anti HAV IgG (+)		
	Adj OR	95% CI	P
Water source			
Licensed wrapped water	0.86	0.66-2.01	0.47
City water	1.41	0.53-3.79	0.35
Well water	1.25	0.46-3.25	0.21
Socio-economic status			
Intermediate/high	0.64	0.25-1.38	0.09
Low	1.16	0.73-1.85	0.52
Number of rooms per person			
≥1	1.78	0.85-3.98	0.46
<1	0.62	0.25-1.42	0.26
Collective usage of personal belongings			
Towel	1.61	1.51-4.74	0.049
Towel + toothbrush	1.82	1.48-4.86	0.03
Localization of toilet			
Indoor	0.82	0.64-1.78	0.64
Outdoor	1.79	0.98-3.20	0.05
Type of toilet			
Squat toilet (turkish style)	1.34	0.71-2.53	0.36
Squat toilet + flush toilet (european style)	0.67	0.56-1.48	0.66

remaining countries, with a shift of exposure from childhood to early adulthood [2, 6, 7]. On the other hand, this epidemiological shift could lead an increase in morbidity, perhaps mortality, and a predisposition for local epidemics of HAV infection [4, 8]. In contrast, lower disease rates are seen in developing countries (e.g in Africa and Asia) so outbreaks are uncommon [6].

Turkey and especially Eastern region of country is located closely to Middle East where wars and great migrations of human have being occured with consequently low socio-economic status and large-scale educational matters. The overall prevalence rates of HAV among pediatric ages in Turkey during past years have been widely differed. Although the studies before 2008 revealed higher numbers that range between 29% and 63.8%, an obvious decrease has been reported in 2010-2012 (13%-29.5%) period in different provinces [6-10]. The overall seropositivity rate in our study was 54.9%. Comparing this data with previous reports, it seems that Van region is one of the areas with the highest prevalence of HAV in Turkey. A few studies conducted in Van have revealed similar results as following; 59.5% among 6-10 years in 2004 [11], 69.9% under 18 years of age in 2008 [12]. The prevalance has not been significantly changed during nearly a decade in Van.

In 2010, a study conducted in Tekirdağ which is located in socioeconomically most developed provinces of Turkey, revealed Anti-HAV prevalance under 12 years old chidren as 25.4%

[13]. In addition, Ceran et al. reported 40% seropositivity under 25 years old in 2011 from Istanbul which is the most populous city in Turkey [9]. The prevalence of anti-HAV IgG in present study was still high thus, it can be said that shift in the epidemiological pattern did not occur completely in our region. Previous data has revealed geographically differences of seropositivity of HAV in Turkey. Namely, Western and central regions had intermediate rates, while as our region (Van and other Eastern regions) showed high rates of seroprevalance [10].

There was a significant increase in seropositivity from lower to higher ages in our study which demonstrated a rise in age of primary exposure to the virus. This finding is consistent to several studies and is a evidence of improvement in sanitary conditions by time [2, 6, 9, 11, 12].

The number, type and localization of toilets in home are indicators of hygiene conditions. As reported before, there was a statistically significant difference between seropositivity and these variables [7]. These data presents importance of hygiene status, especially clean-up of hands, which is contibuting fecal-oral transmission route of HAV. Higher seropositivity rate among subjects who slept in crowded rooms (with more than one person) was determined as an important risk factor associated with hepatitis A. Because close indoor contact and existence of many susceptible subjects may result in person-to-person transmission [4]. Also several reports have shown such association [7, 9, 14]. Crowded family with low income might be a cause of collective usage of personal belongings such as toothbrush and towels in home. This collective usage was a statistically significant variable in our study similarly to previous data [7].

Hepatitis A infection is also a waterborne disease. The main source of water used by subjects was a significant variable in our study. In their extensive epidemiological survey, Jacobsen and Koopman reported that water coverage is a significant independent predictor of HAV infection rate, especially in developing countries [15]. The increased quantity of water source results in good washing and cleaning of both hands and kitchenware as well as decreased need for water storage that facilitates transmission of virus. On the other hand, increased quality of water causes diminished ingestion of the pathogen via oral route [15].

Safe and effective vaccines against hepatitis A are avaible since late 1990s, and vaccination usually used in control of outbreaks or prevention of travellers who went to regions with an increased incidence of infection [10]. Although vaccines had high efficacy, they have not been widely used in national immunization programs in many countries to date [16]. It has been reported that the incidence in regions with increased risk may be reduced through vaccination, specially in developed populations and there is a confusion of usage the vaccine in developing countries with high seropositivity in early ages [16, 17]. In addition, determination of cost-benefit issues has shown that targeted vaccination of more susceptible subjects (e.g homosexual men, travellers) is more rational than public vaccination, especially in developing countries [17].

Our study had some limitations. One of them was the heterogeneity of the subjects. The study included children from urban or suburban areas, with different custom and usage properties, and who lived in various socio-economic conditions. Other limitation was that national immunization program against HAV has not begun yet when the study conducted and so there was a lack of data that involves the effects of vaccination.

Conclusion

Our study provided the most recent data of seropositivity of HAV and perhaps confirms the start of epidemiological shift in seroprevalence from high endemicity region of Eastern Turkey. Further studies of seroprevalance are necessary to show the effects of national immunization program in our country.

Disclosure of conflict of interest

None.

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