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Seropositivity of Hepatitis A in Children Aged 7–14 Years in Diyarbakir Province Center

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Background: Hepatitis A virus (HAV) is a common morbidity in society, and mortality is more common in older ages. It is important to identify the prevalence in the population, the development of primary protection methods, and vaccination policies. This study aimed to identify anti-HAV seropositivity in children in 3 different schools in Diyarbakır, Turkey, to evaluate the risk factors influencing prevalence, and thus to develop strategies to prevent infection.

Material/Methods: The study was a prospective investigation of 600 children with a mean age of 10.5 years (range, 7–14), including 291 males and 309 females.

Results: The seropositivity was 45.7% (41.2% in males and 49.8% females) with a statistically significant difference by sex (p=0.042). It was also significantly correlated with age. Factors significantly associated with seropositivity were educational level and income of parents, number of rooms in the house, type of toilet, number of siblings, and source of drinking water. Hence, older age, more siblings, crowded household, and low socioeconomic level are risk factors for seropositivity.

Conclusions: Protection strategies for the disease include improving socioeconomic level, increasing the level of education, disseminating appropriate drinking water, improving infrastructure and sewage disposal, and public health education on hygiene and the importance of vaccination. We also believe that active immunization against HAV in Turkey in general and in our province in particular can prevent infection in children and related complications in older people.

MeSH Keywords: Child • Hepatitis A Virus • Prevalence • Vaccination

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Background

Infection by hepatitis A virus (HAV) is a major public health concern worldwide, with a global disease incidence of about 1.5 million cases annually [1]. However, the rate of asymptomatic infection can be even higher. Infection in children <6 years of age is usually asymptomatic or mild, but in adolescents and adults it is more likely to be acute hepatitis, which may require hospital admission, and acute liver failure, but mortality is normally uncommon [2].

This has been a vaccine-preventable infection since 1992, but the vaccine is only recommended for areas with a high proportion of the population at risk of developing symptomatic infection [3].

The transmission of hepatitis A virus occurs mainly through the fecal-oral route or by close contact between individuals. The incidence rate and clinical course vary by age and are strongly associated with socioeconomic and hygiene conditions [4,5].

HAV infection shows geography-dependent patterns of age-related seroprevalence and incidence. That is to say, developing countries have high endemicity rates because of exposure to the virus during early childhood, while improvement in socioeconomic and hygienic conditions shifts the balance of infections from children to adults [5,6]. Although as mentioned earlier, the vaccination recommendation is based on the proportion of the population at high risk of infection, in 2006, the Centers for Disease Control and Prevention (CDC) issued a recommendation that all children 12–23 months of age should be vaccinated [7]. Since October 2012, the Ministry of Health in Turkey has ordered mandatory vaccination of children.

The rate of HAV infection depends on multiple factors. A study similar to the present study was conducted in Van City, in the eastern part of Turkey [8]. It is also important to have data on age-specific seroprevalence of HAV infection, which is helpful to determine susceptible populations, and reliable measures for vaccination have been recommended by the World Health Organization (WHO) [9]. The present study aimed to estimate the anti-HAV seroprevalence rate in children aged 7–14 years in 3 different schools in Diyarbakır, Turkey and to assess the association of seroprevalence with demographic characteristics, ages, socioeconomic status, and housing conditions. This is the first survey of hepatitis A seropositivity in south-eastern Turkey.

Material and Methods

Our study was proposed by the Diyarbakır Provincial Directorate of National Education and was carried out prospectively from 29.09.2011 to 04.10.2011 on 600 children ages 7–14 years who were studying in primary schools in different regions of Diyarbakır province. Subjects were selected to reflect the socioeconomic structure of the city. Children in the study were randomly selected and sampled according to their socioeconomic levels. Prior to deciding which primary schools to include, official permission was obtained from Diyarbakır Governorship, Diyarbakır Provincial Health Directorate, and Diyarbakır Provincial Directorate of National Education. From each school, 200 students were included. To ensure homogeneity in all classes, students were selected using a random number table, with 25 students from each branch (1st to 8th grades), totaling 200 students from 8 branches. The study was approved by the Local Ethics Committee of the Faculty of Medicine of Dicle University, dated 09.05.2011, number 126. According to the code of ethics, from September 19 to September 26, 2011, students' parents were asked for permission to enroll their children in the study. Approval for 600 students was obtained from their parents. A one-page approval form was prepared, addressing to the parents, about the aim and the content of the research and asking them to decide whether to allow their children to participate in the survey. In this form, places were assigned for the name and surname of the child and the investigator, and for the signatures of the parent and the investigator. A questionnaire was used by the parents who granted permission for their children to participate in the research. We used 600 student questionnaire forms and blood samples were taken for serological examination.

The students were brought to 2 prepared rooms, and ~3 to 4 cc venous blood was taken from the left antecubital region through the vena mediana cubiti in a Vacutainer- compatible biochemical tube in accordance with the rules of injection safety, without keeping the students waiting. The name, surname, class, and branch of the student are recorded in the biochemistry tubes. Blood samples were centrifuged on the same day to separate the sera, which were stored at –80°C. Blood collection took place between 29.9.2011 and 04.10.2011 during working hours. The analyses of samples were started in November 2011. Anti-HAV total antibodies (IgM + IgG) were analyzed by Electro Chemiluminescence immunoassay (ECLIA) using a Roche Cobas E 601 device within 2 h after samples were taken from the freezer and thawed to room temperature. A Cobas Elecsys Anti-HAV reagent kit was used for the analyses and the values were evaluated as IU/L. Values larger than 20 IU/L were classified as seropositive and those less than 20 UU/L were classified as seronegative.

Data analysis

Descriptive statistics of continuous variables are expressed as mean and standard deviation (SD) values. The cut-off variables were transformed into cross-tabulations and analyzed

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Table 1. The relationship between sex and total anti-HAV seropositivity.

	Anti-HAV				
	Negative, N (%)		Positive, N (%)		Total
Male	171	(58.8)	120	(41.2)	291
Female	155	(50.2)	154	(49.8)	309
Total	326	(54.3)	247	(45.7)	600

χ^2=92.391, p=0.000.

Table 2. Relationship between age and total anti-HAV seropositivity.

Age	Anti-HAV				Total
	Negative, N (%)		Positive, N (%)		
7	65	(86.7)	10	(13.3)	75
8	58	(76.3)	18	(23.7)	76
9	46	(63.0)	27	(37.0)	73
10	42	(56.0)	33	(46.0)	75
11	41	(53.2)	36	(46.8)	77
12	29	(39.7)	44	(60.3)	73
13	25	(33.3)	50	(66.7)	75
14	20	(26.3)	56	(73.7)	76
Total	**326**		**274**		**600**

χ^2=92.391, p=0.000

by the Yates-corrected chi-square test. The assumption of normal distribution of data was tested with the Kolmogorov-Smirnov test. The mean values of the variables were analyzed by t test. Hypotheses were bidirectional and statistically significant if $p \leq 0.05$. Statistical analyses were performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL).

Results

Of the 600 children who participated in the study, 291 (48.5%) were male, 309 (51.5%) were female, and their mean age was 10.5 years (range, 7–14 years). Total anti-HAV positivity was detected in 45.7% of the children participating in the study. Anti-HAV seropositivity in boys was 41.2% and 49.8% in girls, and the difference between the 2 groups was statistically significant (p=0.042) (Table 1).

Anti-HAV seropositivity was examined separately in each age group; 7 years, 8 years, 9 years, 10 years, 11 years, 12 years, 13 years, and 14 years. we found anti-HAV seropositivity increases with increasing age, and the difference was statistically significant (p<0.001) (Table 2).

According to the region of the settlement, 3 different schools were sampled. A total of 600 students, 200 from each school, were studied. Seropositivity was low in Kayapınar region and the difference was statistically significant (p<0.001) (Table 3).

Anti-HAV seropositivity was found in 67.4% of the children with non-illiterate mothers, 50.3% with mothers having a primary school degree, 25.0% with mothers having a secondary school degree, 34.7% with mothers holding a high school degree, and 24.3% with mothers who graduated from a university. As the educational level of the mothers increased, the seropositivity decreased significantly in the children (p<0.001) (Table 4). A similar trend was found between the education level of fathers and the anti-HAV seropositivity in their children, as shown in Table 4. A significant difference was also found in the levels of anti-HAV seropositivity in children with unemployed *vs.* employed parents (p<0.000) (Table 4).

Data show that anti-HAV seropositivity was significantly dependent on housing conditions, such as income, the number of family members and rooms in the house, heating system, drinking water sources, and type of toilets (Table 5). It was observed that ani-HAV seropositivity significantly decreased with increasing income of family members (p<0.001) (Table 5).

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Table 3. The relationship between the settlements and anti-HAV seropositivity.

Region	Anti-HAV				Total
	Negative, N (%)		Positive, N (%)		
Bağlar	61	(30.5)	139	(69.5)	200
Yenişehir	115	(57.5)	85	(42.5)	200
Kayapınar	150	(75.0)	50	(25.0)	200
Total	**326**		**274**		**600**

χ^2=81.022, p=0.000.

Table 4. The relationship between anti-HAV seropositivity in children and the education level and employment status of their parents.

	Anti-HAV							
	Negative, N (%)				Positive, N (%)			
	Mother[m]		Father[f]		Mother[m]		Father[f]	
Education level								
Non-illiterate	62	(32.6)	12	(24.0)	128	(67.4)	38	(76.0)
Primary School Degree	73	(49.7)	66	(35.7)	74	(50.3)	119	(64.3)
Secondary School Degree	47	(65.3)	55	(57.3)	25	(34.7)	41	(42.7)
High School Degree	60	(75.0)	69	(66.3)	20	(25.0)	35	(33.7)
University Graduate	84	(75.7)	124	(75.2)	27	(24.3)	41	(24.8)
Employment								
Unemployed	237	(49.2)	17	(22.1)	245	(50.8)	60	(79.9)
Self-employed	9	(90.0)	187	(53.4)	1	(10.0)	163	(46.6)
State employee	80	(74.1)	122	(70.5)	28	(25.9)	173	(29.5)

[m] χ^2=74.982, p=0.000 (education); [f] χ^2=79.704, p=0.000 (education). [m] χ^2=27.268 p=0.000 (employment); [f] χ^2=50.671, p=0.000 (employment).

We also found that anti-HAV seropositivity significantly decreased with increasing number of family members in the house (p<0.001) (Table 5). A significant relationship was observed between the numbers of rooms in the children's house and anti-HAV seropositivity. Seropositivity was 66.0% for children living in houses with 2 or 3 rooms, and 28.2% and 27.3% for those living in houses with 4 and 5 rooms, respectively (p<0.001) (Table 5). Seropositivity was 67.1% in children living in houses heated with a stove compared with those (30.3%) living in houses heated with a central heating system, and the difference was statistically significant (p<0.001) (Table 5). Seropositivity was 49.0% in children drinking tap water, compared with 16.4% in those drinking bottled water, and the difference was statistically significant (p<0.001) (Table 5). The location of the toilet was stated to be in the house by all participants. Seropositivity was 58.6% in children using the squat type toilet (alaturka) and 29.4% in those using the closet type (sitting toilet). The rate in those using both types was 26.2%. The difference in anti-HAV seropositivity by type of toilet was statistically significant (p<0.001) (Table 5).

Of the children who participated in the study, 65 (9.2%) had a history of jaundice. Anti-HAV was positive in 93.8% of these children with jaundice history, whereas 39.8% of the remaining 535 of children without jaundice were anti-HAV positive. The difference between the 2 groups was statistically significant (p<0.001) (Table 6). Anti-HAV seropositivity was found to be 66.9% in 130 children with jaundice trait in their family, while it was 39.8% in children without jaundice trait. The difference between the 2 groups was statistically significant (p<0.001) (Table 6).

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Table 5. The relationship between the housing and income conditions and anti-HAV seropositivity.

	Anti-HAV				Total
	Negative N (%)		Positive N (%)		
Family members					
3	21	(100)	0	(0)	21
4	99	(73.9)	35	(26.1)	134
5	101	(66.0)	52	(34.0)	153
6	47	(48.0)	51	(52.0)	98
7	28	(35.0)	52	(65.0)	80
8	12	(24.5)	37	(75.5)	49
9	9	(31.0)	20	(69.0)	29
10	6	(40.0)	9	(60.0)	15
11	2	(14.3)	12	(85.7)	14
12	0	(0)	5	(100)	5
13	1	(50.0)	1	(50.0)	2
Number of rooms					
1	1	(33.3)	2	(66.7)	3
2	50	(34.0)	97	(64.0)	147
3	45	(34.1)	87	(65.9)	132
4	135	(71.8)	53	(28.2)	188
5	80	(72.7)	30	(27.3)	110
6	5	(50.0)	5	(50.0)	10
7	10	(100)	0	(0)	10
Heating system					
Stove	82	(32.9)	167	(67.1)	249
Central heating	239	(69.7)	104	(30.3)	343
Others	5	(62.5)	3	(37.5)	8
Drinking water resources					
Tap water	275	(51.0)	264	(49.1)	539
Bottled water	51	(83.6)	10	(16.4)	61
Type of toilet					
Closet (sitting)	77	(70.6)	32	(29.4)	109
Alaturka (squat)	145	(41.4)	205	(58.6)	350
Both	104	(73.8)	37	(26.2)	141
Income (TL)					
200–499 TL	9	(9.3)	88	(90.7)	97
500–999 TL	87	(51.5)	82	(48.5)	169
1000–1499 TL	40	(57.1)	30	(42.9)	70
1500–1999 TL	28	(62.2)	17	(37.8)	45
Above 2000 TL	162	(74.0)	57	(26.0)	219

χ^2=100.542, p=0.000 (family members); χ^2=93.412, p=0.000 (number of rooms); χ^2=78.735, p=0.000 (heating); χ^2=115.307, p=0.000 (water); χ^2=56.619, p=0.000 (toilet); χ^2=115.307, p=0.000 (income).

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Table 6. Relationship between jaundice story and total anti-HAV seropositivity.

Jaundice history		Negative, N (%)		Positive, N (%)		Total
In children[a]	Yes	4	(6.2)	61	(93.8)	
	No	322	(60.2)	213	(39.8)	
In family[b]	Yes	43	(33.1)	87	(66.9)	
	No	283	(60.2)	187	(30.8)	

[a] χ^2=66.037 (p=0.000); [b] χ^2=29.137 (p=0.000).

Discussion

Studies carried out in different parts of Turkey indicate that hepatitis A prevalence varies by region, ranging from 7.8% to 88%, with lower seroprevalence generally noted in the western regions compared to the eastern [8,11–15]. The rate of 45.7% found in our study is a midpoint for a general picture of Turkey, but is significantly lower compared with the eastern cities, except for Malatya. For a comparison of these data with other countries, see references 9 and 10.

Our study demonstrates that HAV seropositivity rate increase with the age: 13.3% at age 7 years, 23.7% at 8 years, 37.0% at 9 years, 44.0% at 10 years, 46.8% at 11 years, 60.3% at 12 years, 66.7% at 13 years, and 73.7% at 14 years (Table 2). The rate is relatively consistent with the results obtained from different cities in Turkey [12–15]. Children under 6 years of age was excluded in this study. However, it is well-established that seropositivity occurs early in places such as nursery schools [16] and kindergartens.

Generally, studies indicate that there is no significant difference in the seroprevalence of HAV between females and males. However, we found that seropositivity was 41.2% in boys and 49.8% in girls (p=0.042). We cannot explain this significant difference.

It is generally accepted that that there exists a direct correlation between the neighborhood, namely the infrastructure, and anti-HAV seropositivity. Studies in Edirne [13] and Konya [14] in Turkey show that the settlements with poor infrastructure facilities had a higher rate of anti-HAV seropositivity. Similar outcomes were also observed in Spain [17] and Iran [18]. Seropositivity was evaluated according to the development of infrastructure in the settlements in all age groups in our study. The rate of seropositivity was 25.0% in Kayapınar, 42.5% in Yenişehir, and 69.5% in Bağlar. The development order of the regions studied is Kayapınar >Yenişehir >Bağlar. Data indicates that the regions with worse infrastructure had higher levels of anti-HAV seropositivity. Our results are quite consistent with the literature.

The other parameter that has a clear impact on the rate of anti-HAV seropositivity is the education level of parents [13,19,20]. Some studies specifically underline the importance of education level of mothers [15,21]. Higher education levels of the parents are associated with decreased seroprevalence of HAV infection by improving the quality of life of the children living in the family and the household by correcting the hygiene conditions of the children [22,23]. In fact, we have found similar results with the literature. Anti-HAV seropositivity was 67.4% for children with non-literate mothers, while this rate was only 24.3% for those with mothers who had graduated from universities (Table 4). The results were quite similar between the education level of fathers and anti-HAV seropositivity (Table 4). The difference is also significantly between ant-HAV seropositivity in children with employed *vs.* unemployed parents, and also varies by family income. Thus, it is clear that parents with better eduction and incomes have a greater opportunity to provide better conditions for their children, which could prevent the development and spread of HAV infection. These findings are also consistent with the literature.

Housing conditions are the main risk factors for transmission of infection. One of these is the number of people sharing a house. It is known that crowded living conditions accelerate the spread of hepatitis A. Diseases that are transmitted by person-to-person and fecal-oral routes spread rapidly, especially among people spending many hours together in institutions such as nursing homes, nurseries, and barracks [15]. Studies conducted in Turkey demonstrated that families living in crowded conditions have higher seropositivity [13,14,24,25]. For example, families with 6 members in a house had a seropositivity rate of 80.1%, while the rate was 66.7% in families with 5 members living together [25]. Similar findings were observed in other parts of the world [20,26]. In parallel with findings in the literature, we also found that the risk of the transmission of hepatitis A increases with increasing number of family members. Seropositivity was 0% in families with 3 members, 26.1% in those with 4 members, and 34% in those with 5 members. Seropositivity rates were 52.0%, 65.0%, 75.5% and 69.0% in families with 6, 7, 8, and 9 members living together, respectively (Table 5). A similar parameter affecting spread of infection within the family is the number of rooms in the house [13]. Our study shows significantly higher seropositivity with fewer rooms in the house (Table 5). Another parameter

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that may indirectly influence transmission is the house heating system. Seropositivity was 67% of children living in houses heated with stoves, while this was 30.3% in children living in houses with central heating (Table 5). This may not be directly related to the spread of infection, but rather to the socioeconomic level, because people leaving in houses heated with stoves tend to have lower socioeconomic status. The other parameters that may influence the risk of hepatitis A infection in a household are the type of toilet and drinking water source. Our data indicates that these 2 parameters influence the level of anti-HAV seropositivity. We found that the relationship between the types of toilets and anti-HAV seropositivity was statistically significant and children using squat toilets had a significantly higher rate of anti-HAV seropositivity (Table 5). Similarly, anti-HAV seropositivity was significantly higher in children drinking tap water at home compared with those drinking bottled water (Table 5).

The prevalence of hepatitis A is mainly related to the socioeconomic situation [17–19,27–29], and HAV is especially endemic in countries with low socioeconomic status. The seroprevalence of anti-HAV decreases with increasing socioeconomic and education levels. The seroprevalence is also high within the populations with low socioeconomic conditions in Turkey [14,24,25]. Our study also indicated that higher family income is associated with lower anti-HAV seropositivity in children (Table 5).

Hepatitis A infection is often spread by contaminated food and beverages. Water and food contaminated with fecal material can lead to epidemics [30]. With developed infrastructure and clean drinking water supply in developed countries, HAV infection has shifted to early adulthood. Studies have shown that high drinking water quality is a protective factor against infection [31]. Studies in Turkey [14] and other countries [17,19] indicated that the seropositivity was directly related to the source and quality of water. Our study indicated that seropositivity was significantly higher in children drinking tap water (49.0%) compared with those drinking bottled water (16.4%).

Although hepatitis A infection is seen in children in different clinical forms, the disease is usually benign. It is mostly asymptomatic and diagnosed during screening. Most families do not give a history of jaundice. In a previous study conducted in Turkey in anti-HAV seropositive children, jaundice prevalence was 15.8–19% [24]. In our study, the rate was relatively high, at 22.2% (Table 6). This finding is consistent with the literature and it shows that hepatitis A infection is mostly asymptomatic in children.

It was found that anti-HAV seroprevalence is significantly higher in children living with some family members who have a history of jaundice, compared with those whose family members do not have a history of jaundice [24]. In our study, seropositivity was found to be 39.8% in children with family members without a history of jaundice, and 66.9% in children with family members with a history of jaundice (Table 6). The difference was statistically significant (p=0.000) and this is consistent with the literature. This means that one of the reasons for the spread of the infection is person-to-person transmission within the family.

In conclusion, the study indicated that prevalence of hepatitis A in children ages 7–14 years was 45.7%. This value is slightly higher than in some western provinces and lower than in some eastern ones [8,11–15]. Considering the 81% rate in Diyarbakır observed in a previous study, there appears to be a significant decline in seropositivity in recent years. It is understood that Diyarbakır has changed from a high endemic level to a medium endemic level [15]. Risk factors for the prevalence of hepatitis A are low socioeconomic level and housing conditions such as water resources, toilet types, and the number of people and rooms in the house. Improving socioeconomic level, increasing the level of education, disseminating appropriate drinking water, solving the infrastructure and sewage problems, and teaching necessary hygiene and the importance of vaccination will be protection strategies. We also believe that active immunization against HAV in Turkey in general and in our province in particular can prevent infection in younger people and related complications in older people.

Conclusions

1). Anti-HAV seropositivity was 45.7% in children participating in the study. Anti-HAV seropositivity was significantly different between males and females (p=0.042). 2). The anti-HAV seropositivity was found to increase with age, with a statistically significant difference (p=0.000). 3). Anti-HAV seropositivity was 69.5% in the region with low socioeconomic level and 25% in the region with high socioeconomic level, and the difference was statistically significant (p=0.000). 4). Educational levels and employment of parents had a significant effect on the level of anti-HAV seropositivity. 5). Housing conditions such as the number of persons and rooms, the heating system, the drinking water resources, and toilet types significantly influence the level of anti-HAV seropositivity. 6). Income and socioeconomic status were significant parameters in the reduction of infection; the other parameter related to these 2 factors was the neighborhood infrastructure, which could also be used to fight the spread of infection.

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Declaration of Interest

None.

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