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Original Article

Research of hepatitis a virus antibodies in children 0-18 aged in the province of Erzurum, Turkey

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Abstract

Aim: The aim of the study was to compare the anti-HAV IgG and Anti-HAV IgM seropositivity in children aged 0-18 in Erzurum with studies in our country and other countries, and also to evaluate the effect of seasons on hepatitis A infection.

Material and Methods: The study was conducted on the serum samples of 5086 patients aged 0-18 years, who were considered to have Hepatitis A or who applied with different complaints as a result of the examination of family physicians in Erzurum between 2015 and 2018. The results of these patients, obtained from Anti-HAV IgM and Anti-HAV IgG analysis by ELISA method in the Public Health Microbiology Laboratory, were evaluated retrospectively. Pearson chi-square test was used to analyze the categorical data such as gender, age and seasonal differences in anti-HAV IgM and Anti-HAV IgG positivity rates and $p < 0.05$ was considered significant.

Results: Anti-HAV IgG seropositivity was 69.0% (3510/5086) and Anti-HAV IgM positivity was 0.7% (33/5063). Anti-HAV IgM was positive in 1.1% of girls and 0.1% of boys. Anti-HAV IgG positivity was 89.9%, 83.3%, 62.5% 61.9% and 74.5% in the 0-3 age group, 4-7 age group, 8-11 age group, 12-15 age group and 16-18 age groups, respectively. Anti-HAV IgM positivity was 0, 0.2%, 0.2%, 1.0%, 0.9% in the 0-3 age group, 4-7 age group, 8-11 age group, 12-15 age group and 16-18 age groups, respectively. The highest anti-HAV IgM positivity was found in November (1.7%).

Conclusion: Total anti-HAV IgG seropositivity rate in our province showed many similarities with studies in Turkey and developing countries. The prevalence of anti-HAV IgM was the highest in November.

Keywords: Anti-HAV IgG; anti-HAV IgM; children; Hepatitis A; seroprevalence

INTRODUCTION

Hepatitis A Virus (HAV), which is in the family Picornaviridae, is a non-enveloped virus with linear positive polarity and with a single helical RNA, approximately 27 nm in diameter (1,2). HAV transmits through the consumption of contaminated water or food or through fecal-oral means as a result of contact with infected individuals, and infects millions of people worldwide every year (3-5). HAV is reported as the most common cause of acute viral hepatitis in developing countries (6,7). In Turkey, however, HAV has been reported as a factor responsible for up to 87.9% childhood acute viral hepatitis (8). While most patients have mild or asymptomatic HAV infection, a small number of patients develop severe life-threatening hepatitis (9). The clinic manifestation is closely related to the age of the patient. While HAV infection is asymptomatic or subclinical in children under 6 years of age, older children and adults often have a symptomatic disease manifestation (10). The age of contact with HAV varies according to the level of socioeconomic development of the region lived in. The majority of people infected in underdeveloped and developing countries are in the childhood, whereas in developed countries the infection occurs at a later age (11).

The evaluation and diagnosis of acute Hepatitis A require both laboratory data and clinical expertise (12). However, it is difficult to clinically distinguish Hepatitis A cases from other types of acute viral hepatitis. A specific diagnosis is made by the detection of HAV-specific Immunoglobulin M (IgM) antibodies in the serum. As an additional test, reverse transcriptase polymerase chain reaction (RT-PCR) can be utilized to detect HAV RNA (13).

Our study aims to compare HAV-specific Immunoglobulin G (anti-HAV IgG) and anti-HAV IgM seropositivity in children in the 0-18 age group, who admitted to family physicians under the suspicion of Hepatitis A or other

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complaints in Erzurum, with other studies in Turkey and other countries, and also to evaluate the effect of seasons on Hepatitis A infection.

MATERIAL and METHODS

Our study was carried out with children in 0-18 age group, who were considered to have acute Hepatitis A by family physicians or whose anti-HAV IgG and anti-HAV IgM serology was tested in three central districts of the province of Erzurum, between January 1st, 2015 and December 31st, 2018. The anti-HAV IgM and anti-HAV IgG results of 5086 patients, whose analyses were made by the ELISA method via Architect i2000SR instrument using the Architect HAVAb IgM and Architect HAVAb IgG kits in Public Health Microbiology Laboratory, were evaluated retrospectively.

In the evaluation of the findings, the results over 1.21 S/CO were considered positive for anti-HAV IgM, and the results equal to or greater than 1.00 S/CO were considered positive for anti-HAV IgG. To compare the HAV seropositivity differences, the present values were divided into five different age groups: 0-3, 4-7, 8-11, 12-15 and 16-18. Data were entered into the statistical package program and analyzed. Pearson chi-square test was used to compare categorical data such as gender, age and seasonal differences in anti-HAV IgG and anti-HAV IgM positivity rates, and the $p<0.05$ was considered statistically significant. Since this research is a retrospective study, contact with animals, travel and vaccination status could not be determined.

Ethics Committee Approval:The ethics committee approval for our research was obtained from Atatürk University Clinical Research Committee with Decision No. 18 dated 13.02.2019.

RESULTS

Our study group consisted of 5086 patients in the 0-18 age group (mean 12.7±4 years), of which 3040 (59.8%) were female and 2046 (40.2%) were male children. Anti-HAV IgG was tested in 5086 patients, and anti-HAV IgM was tested in 5063 patients. Anti-HAV IgG seropositivity was 69.0% (3510/5086) and anti-HAV IgM positivity was found to be 0.7% (33/5063). Anti-HAV IgM was positive in 1.1% of female children and in 0.1% of male children. Anti-HAV IgG was positive by 70.9% in female children and 66.3% in male children ($p<0.05$). Anti-HAV IgG positivity was 89.9%, 83.3%, 62.5%, 61.9%, and 74.5% in the 0-3 age group, 4-7 age group, 8-11 age group, 12-15 age group and 16-18 age group, respectively ($p<0.05$). Anti-HAV IgM positivity was 0, 0.2%, 0.2%, 1.0%, 0.9% in the 0-3 age group, 4-7 age group, 8-11 age group, 12-15 age group and 16-18 age group, respectively. Differences between the groups were statistically significant ($p<0.05$) (Table 1).

On a seasonal basis, anti-HAV IgM positivity was detected in 31 (1.7%) samples in November, 1 (0.3%) sample in October in the autumn, and 1 (0.6%) sample in June in the summer ($p<0.05$) (Table 2).

Table 1. Distribution of Anti-HAV IgM and IgG serological results by gender and age groups

Characteristics	Number of Cases n (%)	HAV IgG(+) n (%)	p	Number of Cases n (%)	HAV IgG(+) n (%)	p
Gender						
Female	3040 (59.8)	2154 (70.9)	<0.001	3028 (59.8)	32 (1.1)	<0.001
Male	2046 (40.2)	1356 (66.3)		2035 (40.8)	1 (0.1)	
Total	5086 (100)	3510 (69.0)		5063 (100)	33 (0.7)	
Age Groups						
0-3	69 (1.4)	62 (89.9)	<0.001	69 (1.4)	0	0.04
4-7	568 (11.2)	473 (83.3)		563 (11.1)	1 (0.2)	
8-11	1329 (26.1)	831 (62.5)		1321 (26.1)	3 (0.2)	
12-15	1425 (28.0)	882 (61.9)		1416 (28.0)	14 (1.0)	
16-18	1695 (33.3)	1262 (74.5)		1694 (33.5)	15 (0.9)	
Total	5086 (100)	3510 (69.0)		5063 (100)	33 (0.7)	

Table 2. Distribution of anti-HAV IgM seropositive patients by months and seasons

Months	Number of tests made	Positive n (%)	Season	Positive n (%)	P value
March	263	0 (0)			
April	356	0 (0)	Spring	0 (0)	
May	275	0 (0)			
June	176	1 (0.6)			
July	239	0 (0)	Summer	1 (0.2)	
August	215	0 (0)			
September	361	0 (0)			<0.0001
October	380	1 (0.3)	Autumn	32 (1.3)	
November	1796	31 (1.7)			
December	632	0 (0)			
January	130	0 (0)	Winter	0 (0)	
February	240	0 (0)			
Total	5063	0 (0)		33 (0.7)	

DISCUSSION

There have been numerous studies on HAV seroprevalence in Turkey. In terms of HAV infection, Turkey is considered a moderate endemic region and the incidence of infection varies depending on socioeconomic differences between regions (14). In a study conducted by Tekay in Hakkari province, anti-HAV IgM antibody positivity was found as 5%, and anti-HAV IgG positivity was 63% in children in the 0-14 age group (15). In a study by Çiçek et al. (16) conducted in the province of Rize, anti-HAV IgM seropositivity was 2.5% and IgG positivity was 29.5%. In their study that investigates seroprevalence of Hepatitis A in children in the 0-18 age group in the province of Iğdır, Arvas et al. (17) found the anti-HAV IgM seropositivity as 18.1%. In Mexico, García-Juárez et al. (18) detected anti-HAV IgM antibody positivity as 13% and IgG antibody positivity as 51% in children. In a study of children aged 5-15 in India, anti-HAV IgG positivity was found as 54.5% (19). In Germany, Jablonka et al. (20) found a HAV total antibody positivity of 81.8% in refugees in the 0-17 age group. The anti-HAV IgG seropositivity was 0.7% and anti-HAV IgG seropositivity was 69% in the children in our study group. Although the results of our research are similar to the literature in terms of anti-HAV IgG, our anti-HAV IgM rates

Table 3. Some studies conducted on HAV IgG serology in Turkey

	Province	Years	Age group (years): IgG seropositivity rate (%)
Papatya et al (28)	Istanbul	2002	2-3:34.7%; 4-5:45.5%; 6-7:49.3%; 8-9:54.1%; 10-11:58.1%; 12-13: 62%; 14-15:88.3%
Isiklar et al (29)	Ankara	2004	1-4:19.1 %; 5-9:27.7%; 10-14:47.9 %
Ozen et al (30)	Malatya	2006	3-6:17.5%; 7-16:32.1%
Kalem et al (31)	Konya	2005-2009	0-2:60%; 3-6: 22%; 7-10: 17%; 11-14:33%; 15-17:49%
Turker et al (32)	Ankara	2011	0-4:33,3%; 5-9:20,9%; 10-14:29%; 15-19:43.9%
Halicioglu et al (33)	Izmir	2012	1-2: 21%; 3-5:15%; 6-8:20%; 9-11:33%; 12-14: 44%; 15-18: 52%
Yilmaz et al (27)	Kars	2012-2014	0-5:45.9%; 6-12:71.3%
Duran et al (23)	Bingol	2010-2016	<2:54.2%; 2-6:38.2%; 7-10:49.6%
Dogan et al (34)	Karabuk	2015-2016	2-6:66.7%; 7-18:11.5%
Kolancali et al (35)	Istanbul	2016	2-5: 59%; 6-16:19.6%
Calik et al (36)	Izmir	2015-2016	0-4:87.5%; 5-9:28%; 10-14:20.8%; 15-19:28.9%

were quite low compared to other studies. It is believed that the Hepatitis A vaccination performed at the 18th and 24th months in Turkey since 2012 has a partial effect on these results (21). The fact that the IgM seropositivity is zero, especially in the 0-3 age group, supports this idea. In addition, the low seropositivity of anti-HAV IgM in our province suggests that it is associated with our city's better infrastructure-sewerage system than other regions, and with more regular chlorination in our city's drinking water system. In addition, as seen from Table 3, while HAV IgG seropositivity ratios were low in child-age groups in the years of before 2012, when the vaccination program has been begun in Turkey, these ratios started to increase gradually after 2012. These findings presented in Table 3 strongly supports our assumption mentioned above related with positive impact of the vaccination program on IgG HAV seropositivity.

There are numerous studies investigating the effect of gender differences on seroprevalence. Arabacı et al. (22) reported that the rate of infection with Hepatitis A was 77% in female children and 81% in male children. Arvas et al. (17) reported a 19.6% anti-HAV IgM positivity in female children, and 17% in male children, and stated that the difference was not statistically significant. In their research, Duran et al. (23) identified acute Hepatitis A infection by 10.5% in female children, and 13.1% in male children, and stated that there was a statistically significant difference between the rates of anti-HAV IgM seropositivity in terms of gender. In China, Yan et al. (24) reported an 83.8% total anti-HAV positivity in males and 83.3% in females. In our study, anti-HAV IgM and IgG were found to be statistically higher in female children than that of male children.

In temperate regions, the autumn and winter months, characterized by more rain, are the most frequent periods of HAV infections (25). When we look at the studies conducted to investigate the relationship of anti-HAV IgM seropositivity with the seasons in Turkey, Duran et al. (23) investigated the distribution of anti-HAV IgM seropositive cases by months in their research conducted in the province of Bingöl. Anti-HAV IgM seropositivity was the highest in December (17.9%) and November (17.1%), and the lowest in May (4.6%) and June (5.2%). In a study by Parlak et al. (26) conducted in the province of Van, anti-HAV IgM positivity was found to have a seasonal variation, with the highest rates during the periods of increased rainfall in December (18.1%) and November (16.0%), and the lowest rates in April (2.5%) and May (2.5%), when the rainfall decreases. In a study by Yılmaz et al. (27) conducted in the province of Kars, anti-HAV IgM positivity was found to be the highest in September-November months (21%), and the lowest in December-February months (2.4%). In our study, anti-HAV IgM positivity was also higher in November (1.7%), October (0.3%) and June (0.6%), and no positive results were achieved in the other months. November and October are a period of intense autumn rains in our province and we believe that the contamination of drinking water sources leads to this increase.

CONCLUSION

Total anti-HAV IgG seropositivity rate in our province was showed many similarities with studies in Turkey and developing countries. The prevalence of anti-HAV IgM was the highest in November. For the prevention of hepatitis A infection, the individuals should be trained about the hygiene and their quality of life should be raised. In addition, the development of infrastructure systems in cities, improving the clean water facilities and strict monitoring of the chlorine levels of drinking-water, especially in October-November, where HAV infections increase significantly due to the rainfall, will reduce the incidence of HAV infection.

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