

The Trend of Hepatitis A Epidemiology in Children, Based on Two Studies in the North of Iran

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Background: Epidemiology of hepatitis A virus (HAV) is changing over time. Giving awareness of this issue can be developed as a plan to prevent complications of the disease; it is especially very helpful in high risk children, such as those with chronic liver disease.

Objectives: The current study aimed to investigate the seroprevalence of anti-HAV antibodies in children with and without chronic liver diseases during two different periods.

Patients and Methods: Two studies were conducted on anti-HAV seroprevalence antibodies in children aged one to fifteen years who were referred to Amirkola Children's Hospital (Babol, North of Iran). The first study was conducted on 73 patients with chronic liver disease (CLD) in 2006, and the second study on 180 cases without it (NCLD) in 2011. Blood samples were collected from children and the sera were evaluated for anti-HAV antibodies via ELISA assay by Dia. Pro kit.

Results: Seroprevalence of HAV was 17.8% and 10% in the first and second study, respectively. There was no significant difference in age, sex, and place of residence between anti-HAV negative and positive subjects in the studies.

Conclusions: It appears that anti-HAV antibody seroprevalence has declined among children below 15 years with and without chronic liver disease, and it is likely that more children would be susceptible to HAV infection. Therefore, it is important to employ preventative strategies against HAV in chronic liver diseases.

Keywords: Hepatitis A Virus; Child; Chronic Liver Diseases

1. Background

Hepatitis A Virus is the most common form of acute viral hepatitis worldwide (1). Nearly 1.5 million clinical cases occur worldwide annually, but the rate is apparently ten folds higher (2). The prevalence of HAV is related to socio-economic and hygiene status, as well as living conditions (3-6). Several studies have shown that there is high prevalence rate of hepatitis A in Africa, central and South America, and South-East Asia (1-7). In countries with high incidence of HAV, nearly all children are infected with HAV, before the age of five with asymptomatic or mild pattern (1, 2, 8); due to the acquired protective anti-HAV antibody. Although acute hepatitis A is usually asymptomatic in children, acute liver failure, secondary to hepatitis A, may occur in patients with preexisting chronic liver disease (7-10). Available data documented that the risk of death due to HAV infection in patients with underlying chronic liver disease was 23 times more than those without chronic liver disease (11). On the other hand in recent years, a few

studies from developing countries reported a changing trend of HAV epidemiology with shift to intermediate or low endemicity, because of improved sanitary condition and hygiene practices (6, 12-15). Due to absence of HAV vaccination, Iran was previously considered a country with hyperendemic hepatitis A infection. The studies in Iran indicate that HAV infection is decreasing, especially in children (13, 16, 17). Based on the obtained information, mass immunization of all children could be suggested, but there are also barriers such as cost and feasibility; therefore, considering these problems, at least vaccination in high risk children, such as those with chronic liver diseases, can be recommended.

2. Objectives

Two studies were designed to evaluate the changes of anti-HAV antibody seroprevalence among children with and without chronic liver disease who were referred to a

large tertiary care pediatric hospital in North of Iran during two different periods. These data might influence the vaccination strategy against HAV in this region, at least for patients with chronic liver disease.

3. Patients and Methods

Two cross-sectional studies were conducted on children who were referred to Amirkola Children's Hospital in Babol city (Mazandaran Province), North of Iran. The first study was conducted on all known patients (73 cases) with chronic liver disease (CLD), aged one to fifteen years. The patients had no history of vaccination against hepatitis A virus; they were referred to gastroenterologist for periodic visits from winter 2005 to spring 2006 after diagnosis of their disease from 1999 to 2005. The chronic liver disease was confirmed by their clinical history, physical examination and laboratory tests data. The second study was conducted on 180 healthy and non-chronic liver disease (NCLD) children, aged one to fifteen years with no history of previous vaccination against hepatitis A virus referred to the laboratory of Amirkola Children Hospital in a period of two months in 2011. According to the results of the first study, the number of cases was doubled for second study. Before conducting the studies, written consent was obtained from all patients or their parents. Collected data included sex, age, place of residence, and 2-3 mL blood sample for measurement of total anti-HAV antibody (IgA, IgM). Anti-HAV antibody titer was assayed via ELISA assay by Dia. Pro kit. Data were analyzed by SPSS using t-test and chi square test, the seroprevalence HAV in the two studies were compared. $P < 0.05$ was defined as the level of significance.

4. Results

The demographic and seroprevalence data of the CLD patients in the first study are shown in Table 1. In the first study, 13 patients (17.8%) were seropositive for HAV infection and the mean age of subjects was 7.1 ± 4.9 years. CLD patients included those with hepatitis B and C, autoimmune hepatitis, cryptogenic cirrhosis, metabolic disease such as glycogen storage disease (GSD) and galactosemia, biliary atresia, byler syndrome, etc. Anti-HAV positive cases of the study included three chronic hepatitis B, two biliary atresia, one cryptogenic cirrhosis, and one case with byler syndrome. Seroprevalence and demographic inclusion criteria of CLD cases are shown in Table 1.

The second study included 116 (64.4%) male and 64 (35.6%) female children with the mean age of 7.85 ± 4.04 years. Eighteen patients (10%) were seropositive for HAV infection including 12 (10.3%) males and 6 (9.4%) females ($P = 0.836$), 8 (8%) urban and 10 (12.5%) rural ($P = 0.826$). Mean age of seropositive cases was 8.58 ± 5.08 years that 4.4%, 2.3% and 3.3% of them were in age groups 1 to < 5, 5 to < 10 and 10 to 15 years, respectively. There was no significant difference between the age of anti-HAV negative and positive subjects in this study ($P = 0.516$). Frequency of seropositive anti-HAV by sex and place of residence is shown in Table 2.

Table 1. Seroprevalence of HAV and Demographic Inclusion Criteria in Children with Chronic Liver Disease (the First Study)

	Number of Cases	Seropositive, No. (%)	P Value
Age interval, y			0.16
1 - <5	34	3 (8.8)	
5 - <10	17	6 (35.3)	
10 - 15	22	4 (18.2)	
Place of Residence			0.54
Rural	30	5 (16.7)	
Urban	43	8 (18.6)	
Gender			0.56
Male	38	7 (18.4)	
Female	35	6 (17.1)	

Table 2. Seroprevalence of HAV and Demographic Inclusion Criteria in Children with NCLD (the Second Study)

	Number of Cases	Seropositive No. (%)	P Value
Age interval, y			0.516
1 - <5	60	6 (10)	
5 - <10	60	3 (5)	
10 - 15	60	9 (15)	
Place of residence			0.826
Rural	80	10 (12.5)	
Urban	100	8 (8)	
Gender			0.836
Male	116	12 (10.3)	
Female	64	6 (9.4)	

5. Discussion

Two studies determined that less than 20% of the children with and without chronic liver disease in the region under study were HAV seropositive, thus the majority of CLD patients aged one to fifteen years will be at risk for HAV infection. Results of the two studies were compatible with those of the study in Azerbaijan (1.2-27.2%) and Tehran (21.1-26.6%) among healthy children younger than 15 years (13, 17). Other studies showed higher rate of HAV infection in Zanjan (42-45.4%) and Zabol (79.6-100%) among children lower than 15 years (18). Numerous studies stated the presence of anti-HAV antibody, due to economic status and place of residence (3, 19). Italy is a country with low incidence of HAV infection; a study in this country showed seroprevalence HAV were 2.3%, 3.9%, 10% and 9.7% in the age groups of 3-5, 6-7, 11-12, 14-16 years, respectively (20). In Japan anti-HAV seropositive was reported 12.2% in people lower than 20 years (3). Anti-HAV

antibody status in children with chronic liver disease is not evaluated in Iran yet. Although a study in Babol on patients with hepatitis B and C showed that 85.5% with B and 92.3% with C had IgG-anti-HAV, the seropositive rate in different age groups was 59.4% (10-19 years), 89.8% (20-29 years), and 97.5% (>29 years) (21). Another study on the adults more than 10 years old with chronic liver disease in East Azerbaijan, from 2005 to 2006 indicated that HAV seroprevalence IgG was 96.5% (8). In Korea, seropositive HAV infection in the patients with the mean age more than 40 years was 88.1% (22). They had been probably exposed to HAV infection in childhood or adolescence period. Moreover, the prevalence rate of HAV infection increases with age (3, 12). But the study by Acharya et al. from India reported that 97.6% of the patients with pre-existing chronic liver disease aged 4-18 years had anti-HAV antibody in their sera (8). Sanitary levels, geographic and socioeconomic conditions cause different seropositive rates of HAV infection. There are several reports of HAV seroprevalence from Mazandaran Province. The first study was conducted in 1997 among one to fifteen years old children in Sari in which the prevalence rate of HAV infection was 87%, and in the subgroups of 1-5, 5-10 and 12-15 years old it was 74.7%, 86.7% and 90.6%, respectively (13). The newest study in Mazandaran was carried out in 2011. In this study, HAV seroprevalence was 5.5%, 9%, 20.4% and 34/8% in the age groups 1-2.9, 3-6.9, 7-10.9 and 11-17.9 years, respectively. Saffar et al. found that anti-HAV antibody seropositive was 38/9% (among the 1-25 year old group), and the lowest prevalence was 5.2% in one to five years old children (13). Although the survey of less developed areas in Mazandaran Province such as Savadkuh city (13) showed declining HAV infection prevalence rate, the comparison of data in different years, showed a decreasing rate of HAV infection and the findings may indicate an epidemiological shifting in this province from higher to lower endemicity. Based on the two studies, most of the infected children were 5-10 (8.8%) years old in first study, and 10-15 (4.4%) years old in the second study; although World Health Organization (WHO) ranked Iran among the countries of high prevalence and with a rate more than 90% at 10 years of age, it seems that some parts of the country have lower endemicity (13, 17). Therefore, it is possible that the average age of the first infection with hepatitis A virus is changing from childhood to adolescence. Also some reports from Turkey, Italy, and India expressed similar results (23, 24). These differences indicate that the level of improved living conditions and hygiene status such as access to safe drinking water is not equal in different parts of the country. Therefore, to choose the right strategy about immunization against hepatitis A virus is important; especially for certain groups such as patients with chronic liver disease since they are at risk of higher fatality rate. In conclusion, according to the above findings, it is necessary to change preventative strategies in some areas of the country at least for patients with chronic liver disease.

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Authors' Contributions

Moslemi wrote manuscript; Esmailidooki designed the study and was responsible for the overall study management and patients diagnosis; Rezai and Safari Tirtashi collected data; Pornasrollah and Sharbatdaran conducted laboratory tests; Njafi and Karami for refer of some patients; Bijani conducted the statistical analysis.

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