



Acute Viral Hepatitis A (HAV) Frequency in Kırıkkale Province between 2006 and 2013 in the 0-18 Age Group

2006-2013 Yılları Arasında Kırıkkale İlinde 0-18 Yaş Grubunda Akut Hepatit A Enfeksiyonu Sıklığı

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ABSTRACT

Objectives: Hepatitis A is the most common type viral hepatitis in the world. We aimed to detect the incidence of acute hepatitis A (HAV) infection in Kırıkkale province in Turkey, which is placed among the developing countries.

Materials and Methods: IgM Anti-HAV test were studied in serum samples collected from 4.088 children aged 0-18 years, who received a pre-diagnosis of acute hepatitis between January 2006 and December 2013. The cases were divided into the three age groups as 0-5, 6-11, and 12-18 years.

Results: Out of 4.088 serologic examination samples, 299 (7.31%) were found to be positive for IgM anti-HAV. Seropositivity rate among the age groups were as follows: 7.69% in the 0-5 age group, 39.80% in the 6-11 age group, and 52.51% in the 12-18 age group.

Conclusion: Hepatitis A appears to predominantly infect adolescents and young adults in our country as in countries of intermediate hepatitis A endemicity. These kinds of studies will create a data source for studies evaluating vaccine efficacy throughout our country. (Viral Hepatitis Journal 2014; 20(3): 106-109)

Key words: Acute hepatitis A, hepatitis A virus, IgM anti-HAV, hepatitis A vaccine

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ÖZET

Amaç: Hepatit A enfeksiyonu dünyada en yaygın görülen viral hepatit enfeksiyonudur. Gelişmekte olan ülkeler arasında yer alan ülkemizde akut hepatit A (HAV) enfeksiyonunun Kırıkkale ilindeki sıklığını belirlemeyi amaçladık.

Gereç ve Yöntemler: Ocak 2006-Aralık 2013 tarihleri arasında akut hepatit ön tanısı ile başvuran 0-18 yaş arasındaki 4088 çocuktan alınan serum örneğinde anti-HAV IgM testi çalışılmıştır. Hastalara ait veriler hastane bilgi yönetim sisteminden retrospektif olarak toplanmıştır. Değerlendirmeye alınan olgular 0-5, 6-11, 12-18 olmak üzere üç yaş grubuna ayrılmıştır.

Bulgular: Ocak 2006-Aralık 2013 tarihleri arasında anti-HAV IgM testi çalışılan 4088 serum örneğinin 299'unda (%7,31) test sonucu pozitif bulunmuştur. Değerlendirmeye alınan yaş gruplarında seropozitiflik oranı; 0-5 yaş grubunda %7,69, 6-11 yaş grubunda %39,80 ve 12-18 yaş grubunda %52,51 olarak saptanmıştır.

Sonuç: Hepatit A için orta endemistide yer alan ülkelerde olduğu gibi ülkemizde de hepatit A hastalığı büyük çocukluk ve genç erişkinlerin hastalığı olarak karşımıza çıkmaktadır. Bu tip çalışmalar ülkemizdeki aşı etkinliğinin değerlendirilmesi çalışmaları için veri kaynağı oluşturacaktır. (Viral Hepatit Dergisi 2014; 20(3): 106-109)

Anahtar kelimeler: Akut hepatit A, hepatit A virüsü, anti-HAV IgM, hepatit A aşısı

Çıkar çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

Introduction

Hepatitis A, a self-limiting liver disease, is one of the common infectious diseases in the world. Classified under the Picornaviridae family, δ (HAV) is a small, unenveloped, and single-stranded RNA virus (1). Although it is known that an average of 1.5 million clinical hepatitis A cases occurs each year worldwide, the real figure is estimated to be ten times more than this (2). Transmitted through

the fecal-oral route, the virus can easily infect people via ingestion of contaminated food and water (1,3). Since the people in the areas of high endemicity are exposed to infection at early ages, the disease is rarely seen in this areas even though the susceptible population in the areas of low endemicity is in profusion, the contact with virus is low. Turkey is classified among the countries with intermediate hepatitis A endemicity, and the susceptibility in adolescents and young adults is high (4). While children under

the age of 6 commonly have the disease with no symptom or with cold-like symptoms, the advanced age group can develop the disease in a more serious way (5,6). Diagnosis of the disease is made by the detection of HAV-specific IgM antibodies in the blood (7). Hepatitis A vaccine has been included in the childhood vaccine schedule since October 2012 in our country as two doses applied at the end of 18th and 24th months (8). In this study, we aimed to determine the incidence of acute hepatitis A infection in the 0-18 age group in the Kirikkale Province within a period of 7 years and to create an epidemiological data source for our country.

Materials and Methods

We retrospectively evaluated 4018 patients in the 0-18 age group who were diagnosed with acute hepatitis A via anti-HAV immunoglobulin M (IgM anti-HAV) test between January 2006 and December 2013. The data were taken from the Hospital Information Management System (HIMS). 299 patients, whose IgM anti-HAV test results were positive, were detected in their files to be diagnosed with acute hepatitis A. Age and gender distribution of 299 patients with acute hepatitis diagnosis was evaluated. The method of IgM anti-HAV test was conducted via chemiluminescence microparticle immunoassay (Architect i 1000, Abbott, USA), chemiluminescence immunoassay (Vitros ECI Q, Ortho Clinical Diagnostics, USA, ADVIA Centaur Bayer-Siemens, Germany), and electrochemiluminescence immunoassay (Cobas 6000, Roche Diagnostic GmbH, Germany). The following IgM anti-HAV levels, as per the devices used, were considered positive: >1.2 S/CO for Architecti 1000, >1.2 S/CO for Vitros ECI Q, ≥ 1 COI, for Cobas 6000, and ≥ 1.2 S/CO for ADVIA Centaur. Each sample included in this study belonged to one person; recurrent negative values were not included in the study. In the results of each person who is found to be positive, one positive result was taken under review. SPSS 15 software package was run in the evaluations.

Results

IgM Anti-HAV tests were conducted on 4088 serum samples of 0-18 age group between January 2006 and December 2013 in the Kirikkale Province Hospitals Microbiology Laboratories. 299 (7.31%) serum samples were found to be positive. The number of males included in this study was 2.006 (50.54%) and the number of females was 2022 (49.46%). The distribution of the

seropositivity rate of 7.31% was 4.28% and 3.03% for males and females, respectively. The cases were divided into three age groups as 0-5, 6-11, and 12-18. The distribution of the positivity rate by the years and by the age groups is shown in Table 1 and Table 2. There was no significant difference between the male and female cases ($p>0.050$). In the comparison with the age groups, a significant difference in IgM anti-HAV seropositivity was detected. In the comparison with the age groups, the IgM anti-HAV seropositivity rate of 6-11 and 12-18 age groups was found to be significantly different from that of 0-5 age group.

Discussion

In parallel with the improvement of socio-economic status in the developed countries, the age span acquiring hepatitis A virus has been known to shift to adult ages. According to the statistics of the Ministry of Health in our country which is located on a region of intermediate endemicity, the number of acute hepatitis cases declined from 7063 in 2008 to 3894 in 2011 (2). Although the improvement in the hygiene practices and the social development caused the decline in the incidence of HAV infection in general, the determination of the disease prevalence is of high importance in that the measures should be taken against the disease due to the high mortality and morbidity associated with the disease in advanced ages. Considering that vaccination is of great importance in terms of the protective measures, the World Health Organization (WHO), taking into account of the economic condition and epidemiological data of the countries, proposes that the vaccination strategies should be determined (9). In line with the studies conducted in our country, from October 2012, hepatitis A vaccine has been included in the childhood vaccination schedule as two doses (8).

Table 2. Distribution by age groups of IgM anti-Hepatitis A virus seropositivity in the 0-18 age group

Age Groups	Number of Patients (%)	Number of Positive Cases (%)
0-5	607 (14.85)	23 (7.69)
6-11	1554 (38.01)	119 (39.80)
12-18	1927 (47.14)	157 (52.51)
Total	4088 (100.00)	299 (100.00)

Table 1. Distribution by years of IgM anti-Hepatitis A virus positive test results in the 0-18 age group admitted to our hospital

Years	Total Number of Patients	Male Applicant (%)	Female Applicant (%)	Number of Positive Patients (%)	Positive Male	Positive Female
2006	466	258 (53.36)	208 (44.64)	41 (8.80)	23 (56.10)	18 (43.90)
2007	432	208 (48.15)	224 (51.85)	46 (10.65)	16 (34.78)	30 (65.22)
2008	515	250 (48.54)	265 (51.46)	33 (6.41)	14 (42.42)	19 (57.58)
2009	526	251 (47.72)	275 (52.28)	47 (8.94)	15 (31.91)	32 (68.09)
2010	546	300 (54.95)	246 (45.05)	43 (7.88)	23 (53.49)	20 (46.51)
2011	534	258 (48.31)	276 (51.69)	42 (7.87)	16 (38.10)	26 (61.90)
2012	521	276 (52.98)	245 (47.02)	23 (4.41)	8 (34.78)	15 (65.22)
2013	548	265 (48.36)	283 (51.64)	24 (4.38)	9 (37.50)	15 (62.50)
Total	4088	2066 (50.54)	2022 (49.46)	299 (7.31)	124 (41.47)	175 (58.53)

IgM anti-HAV seropositivity among children of the 0-18 age group was scanned and seropositivity of acute hepatitis A was found to be 7.31% in this study including 4.088 subjects. The seropositivity rate was witnessed to decline dramatically, especially between 2012 and 2013. The people participating in the study were divided into three age groups as 0-5, 6-11, and 12-18. The first age group included children under the age of 6, having hepatitis A infection with no symptom or with cold-like symptom (5,6). While IgM anti HAV seropositivity was 7.69% in this first age group, IgM anti HAV seropositivity rate was found to be 39.80% and 52.51% in the 6-11 and 12-18 age groups, respectively. A significant difference was observed in the seropositivity rates between the 0-5 age group and the 6-11 and 12-18 age groups. In the study conducted by Kaygusuz and his colleagues in our province in 2003, the age groups were divided into three groups as 0-4, 5-9, and 10-19 and the seropositivity rates were found to be 14.3%, 15.5% and 59.5%, respectively (10). When we made a comparison in terms of our region, in the course of the years, the seropositivity was observed to shift to the adolescents especially in the age group of 0-18 years.

The seropositivity rate in the 0-14 age group was found to be 68.02% in a study conducted in Hakkari and its vicinity in 2006. In a study conducted in Ankara, the seropositivity rates were found to be 18.4%, 25.1%, 25.5%, and 69% in the 0-4, 5-9, 10-14, and 15-20 age groups, respectively. Another study performed in İstanbul has reported seropositivity rates of 11.4%, 29%, and 49.7% in the 5-9, 10-14 and 15-19 age groups, respectively (11,12,13). While the seropositivity rate in Hatay, in 2007 was found to be 38.8% and 58.5% in the 0-9 and 10-19 age groups, respectively, it was 5.9%, 12.7%, 33%, 32.8% and 43.2% in the 1-2, 3-6, 7-10, 11-14, and 15-18 age groups, respectively in a study conducted in İzmir in the same year (14,15). In a study conducted by Okur et al. between 2007 and 2008 in Van province, the study group was divided into five age groups as 0-2, 3-5, 6-10, 11-15, and 16-18 and IgM anti-HAV seropositivity was found to be 8.2%, 26%, 16.2%, 8.7%, and 0.6%, respectively (16). Even though there are major variances among the provinces, when evaluation is made through the age groups, it could be said that the seropositivity is low in the provinces located in the Western Regions of our country.

In assessments made by Kalem et al. in the Konya Province between 2005 and 2009, the seropositivity rates were found to be 60%, 22%, 17%, 33%, and 49 % in the 0-2, 3-6, 7-10, 11-14 and 15-17 age groups, respectively. The researchers stated that the rate was high in the 0-2 age group due to the limited number of the patients in this group (17). A study conducted in Manisa-İzmir provinces and the vicinities in 2010, reported that the seropositivity rates were 34% in the 1-3 age group; 55% in the 5-9 age group; 52% in the 10-14 age group, and 62% in the 14-19 age group (18). In their study, Çetinkol et al. retrospectively evaluated the results of 728 patients admitted to Ünye State Hospital between 2009 and 2010 and reported that seropositivity rates were found to be 50%, 29.2%, 17.2%, and 37.5% in the in the age groups of 0-23 months, and 2-6, 7-10, and 11-20 years, respectively. In the 0-23 month age group, only 4 patients were assessed and 2 of them were found to be positive (19). In a study conducted by Alici et al. between 2011 and 2012 in İstanbul, the seropositivity rate was found to be 21% in the 0-10 age group, and 19% in the 11-20 age group (20).

The results of our study are similar to those of studies conducted in our country in the similar geographic regions with the socioeconomic status. In addition, when the data in all the studies are used as a base, we are of the opinion that it would not be wrong to state that a shift to adolescence period has been produced our country.

As for some studies conducted abroad between 2005 and 2006, in the evaluation of the 2.975 patients in terms of IgM anti-HAV, the positivity rate was found to be 41% for HAV in Iraq, which is of intermediate endemicity (21). As for Bangladesh, the IgM anti-HAV seropositivity between 2008 and 2009 was found to be 55.5% in the 0-15 age group (22).

In a study conducted on 400 samples in Tunisia between 2006 and 2008, the seropositivity was found to be 33.5% in children under the age of 6; 38.75% in the 6-15 age group. HAV RNA was also found to be positive in all the serum samples with IgM anti HAV positivity. The viral load was also determined to be higher within the period of September-March in comparison with the positivity in other months (23).

The data from the regions of intermediate endemicity, like our country, are comparable to the data obtained in our country. In a study conducted by Kurugöl et al. in the Turkish Republic of Northern Cyprus in 2009, the seropositivity was found to be 11.4% in the 1-5 age group; 9.4% in the 6-10 age group; and 12% in the 11-15 age group (24). IgM anti HAV test was found to be positive at a rate of 11.20% in a hepatitis A seroprevalence study in which 30.786 samples aged between 0 and 99 were evaluated between 2009 and 2010 in South Korea. The positivity rate was found to be 2.05% in the 0-10 age group; and 8.36% in the 11-20 age groups (25).

Of 666 patients taken into assessment in the Kashan Region of Iran, the seropositivity was found to be 4.2% in males and 3.7% in females (26). In our study, the seropositivity rate was found to be 7.31% in males and 4.28% in females; no significant difference was observed in the 0-18 age group between the studies conducted in our country as well as abroad (16,26).

The data obtained from the studies show that the disease emerges as a syndrome acquired in young adults and adolescents rather than in those in the early childhood (2). In addition, with the increase in the hygiene practices and regulation of environmental conditions arising from the positively changing socio-economic conditions, we encounter a population among adults susceptible to hepatitis A infection (27,28). Although the infection incidence is in decline, the importance of the infection is weakening due to the fact that adults have symptoms of disease more severe than children and the presence of a serious complication like fulminant hepatitis.

The most effective method to prevent the disease is vaccination. The vaccine has a preventive effect both in the development of clinical hepatitis and in the spread of the disease (29). Scientific evidences show that two doses of inactive hepatitis A vaccination can provide lifetime protection (27). Pharmacoeconomical studies also demonstrated that vaccination is cost effective (30). Hepatitis A is likely to be an eradicated infection disease due to vaccine and these features of vaccination (31). In a surveillance and vaccine evaluation study conducted in China within a period of about 20 years, it was reported that the incidence rate of hepatitis A was

observed to go into a decline of 90% (32). Hepatitis A vaccination, which had been made optionally in our country since 1995, has been introduced into the childhood vaccination schedule since October 2012 as two doses.

Since hepatitis A, caused by the hepatitis A virus, is the most common type of viral hepatitis, both in our country and in the world, the vaccination is an effective protection method for the development and spread of the infection. Vaccination of children living in the regions of intermediate endemicity is an application to prevent the disease from spreading in that it will make contribution to the provision of the public immunity (20). However, as well as the vaccination, the provision of the hygiene conditions, the elimination of infrastructure problems, and the creation of the improvement in public awareness will increase the protection effect incrementally which vaccine can make alone. Furthermore, our study and similar studies will create a data source for the studies on the evaluation of vaccine efficacy in our country.

References

- Cuthbert JA. Hepatitis A: old and new. *Clin Microbiol Rev.* 2001; 14: 38-58.
- Yoldaş Ö, Bulut A, Altındış M. Contemporary Approaches to Hepatitis A Infection. *Viral Hepatitis Journal.* 2012; 18(3): 81-86.
- Brundage SC, Fitzpatrick AN. Hepatitis A. *Am Fam Physician.* 2006; 73: 2162-2168.
- Bell BP. Global epidemiology of hepatitis A: implications for control strategies. 10th International Symposium on Viral Hepatitis and Liver Disease. International Medical Press. 2002: 13-18.
- Atkinson W. Hepatitis A. Epidemiology and prevention of vaccine-preventable diseases. 8th ed. Atlanta, Ga.: Centres for Disease Control and Prevention; 2005. p. 177-89, A11, A33-34.
- World Health Organization. Hepatitis A vaccine: WHO position paper. <http://www.who.int/docstore/wer/pdf/2000/wer7505.pdf>. Access Date :10.03.2014
- World Health Organization. Weekly epidemiological record. http://www.who.int/immunization/wer7505Hepatitis%20A_Feb00_position_paper.pdf. Access Date: 10.03.2014
- http://www.thsk.gov.tr/tr/dosya/bulasici-hastalıklar-db/asi/asi_takvimi_2013.pdf. Access Date: 10.03.2014
- <http://www.cdc.gov/vaccines/vpd-vac/hepA/Access> Date: 10.03.2014
- Kaygusuz S, Kılıç D, Ayaşlıoğlu E, Özlük Ö, Cerit L, Yıldırım A. HAV, HBV and HCV seropositivity results by gender and ages in Kırkkale. *Viral Hepatitis Journal.* 2003; 8(3): 160-165.
- Tekay F. The incidence of hepatitis A in children aged 0-14 admitted to Hakkari Public Hospital. *Dicle Med Journal.* 2006; (33)4: 245-247.
- Ağalar C, Kapuğası A, Demirdal T. Hepatitis A, B,C and E prevalence in Ankara between 0-20 ages and risk factors. *Calicut Medical Journal.* 2006; 4(2): 3.
- Koçdoğan FY. Prevalence of hepatitis in different age groups in Istanbul and its relationship with socioeconomic factors [Dissertation] Istanbul: The Ministry of Health, Haydarpaşa Numune Training and Research Hospital; Department of Infectious Diseases and Clinical Microbiology, 2006.
- Turhan E, Çetin M. Hepatitis A seroprevalence of patients admitted to Mustafa Kemal University, Faculty of Medicine, Training, Research and Practice hospital. *Viral Hepatitis Journal.* 2007; 12(1): 30-34.
- Özkinay F, Kurugöl Z, Koturoğlu G, Özacar T, Altuğlu I, Vardar F, Gündüz C, Özkinay C. The epidemiology of hepatitis A infection in the population of Bornova, İzmir, Turkey. *Ege Med Journal* 2007; 46(1): 1-6.
- Okur M, Erbey F, Acar MN, Güven A, Kaya A. Hepatitis A seropositivity in children between the ages of 0-18 in Van province and surrounding. *Duzce Medical Journal.* 2011; 13(2): 6-9.
- Kalem F, Erayman B, Yüksekaya Ş, Kara F. Hepatitis A seroepidemiology in Konya province. *Viral Hepatitis Journal.* 2013; 19(1): 19-22.
- Tosun S. Comparative status evaluation with hepatitis A in children and adults. X. National Congress of viral hepatitis, 1-4 April 2010.
- Çetinkol Y, Yıldırım AY. The Seroprevalence of Viral Hepatitis A in Patients Who Had Been Consulted at Ünye State Hospital. *The Medical Journal of Kocatepe,* 2011; 12(1): 18-22.
- Alıcı Ö, Ağalar C, Yazıcılar HA. Seroprevalence of Hepatitis A in Patients admitted to a Training and Research Hospital in Istanbul. *Viral Hepatitis Journal.* 2013; 19(3): 110-114.
- Turky MA, Akram W, Al-Naaimi SA, Omer AR, Al-Rawi JR. Analysis of Acute Viral Hepatitis (A and E) in Iraq. *Global Journal of Health Science.* 2011; 3(1): 70-76.
- Mahmud S, Karim B, Alam J, Saha SK, Ahmed SS, Begum J, et al. Age-specific prevalence of antibodies to Hepatitis A virus among Bangladeshi children. *DS (Child) H J.* 2012; 28 (1): 31-34.
- Gharbi-Khelifi H, Abid NB, Beji A, Bhiri L, Harrath R, Sdiri K, Billaud S, Ferre V, Aouni M. Seroprevalence and Molecular Characterisation of Human Hepatitis A virus in Serum Samples of Tunisian Patients with Clinical Symptoms of Viral Hepatitis. *Indian J Virol.* 2012; 23(1): 29-35.
- Kurugöl Z, Koturoğlu G, Akşit S, Özacar T. Seroprevalence of Hepatitis A Infection in the Turkish Republic of Northern Cyprus. *Turk J Med Sci.* 2009; 39(1): 109-113.
- Cho SE, Kim Y. Seroepidemiology of Hepatitis A in South Korea: A Nationwide Study by the Eone Reference Laboratory. *J Epidemiol.* 2013; 23(4): 270-274.
- Ardakani AT, Soltani B, Sehat M, Namjoo S, Rezaei MH. Seroprevalence of Anti-Hepatitis A Antibody Among 1-15 Year Old Children in Kashan-Iran. *Hepat Mon.* 2013; 13(5): 10553.
- WHO. Hepatitis A. Department of Communicable Disease Surveillance and Response. WHO/CDS/CSR/EDC/2000.7. <http://www.who.int/wer>Erişimtarihi: 10.03.2014
- Mistik R. Epidemiology of hepatitis A virus infection In: Tabak F, Tosun S. *Viral hepatitis 2013.* 1. Issue, Istanbul, Viral Hepatitis Prevention Society publication, 2013: 13-23.
- Brundage SC, Fitzpatrick AN. Hepatitis A. *Am Fam Physician.* 2006; 3(12): 2162-2168.
- Rein DB, Hicks KA, Wirth KE, Billah K, Finelli L, Fiore AE, Hoerger TJ, Bell BP, Armstrong GL. Cost-Effectiveness of Routine Childhood Vaccination for Hepatitis A in the United States. *Pediatrics.* 2007; 119: 12-21.
- Franco E, Meleleo C, Serino L, Sorbara D, Zaratti L. Hepatitis A: Epidemiology and prevention in developing countries. *World J Hepatol.* 2012; 4(3): 68-73.
- Koçdoğan FY. Prevalence of hepatitis in different age groups in Istanbul and its relationship with socioeconomic factors [Dissertation] Istanbul: Haydarpaşa Numune Training and Research Hospital 2006. PMID:19561383.