

Epidemiological Factors Affecting Hepatitis A Seroprevalence in Childhood in a Developing Country

Gelişmekte Olan Bir Ülkede Çocukluk Çağında Hepatit A Seroprevalansını Etkileyen Epidemiyolojik Faktörler

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Abstract

Objective: The aim of this study was to determine the prevalence rate of hepatitis A virus (HAV) and the socio-epidemiological factors affecting HAV among children aged 0-18 years in Eastern Turkey.

Materials and Methods: The study sample consisted of 226 children aged 0-18 years who were registered at the Pediatrics Department of Atatürk University Medical Faculty for any reason except jaundice between January and May 2002. The presence of anti-HAV immunoglobulin G (IgG) in the children was determined by ELISA.

Results: The percentage of HAV IgG seropositivity among the 226 children was 59.7%. We detected an increase of HAV prevalence with age. The prevalence of HAV did not differ significantly in relation to gender. HAV prevalence was higher in children of rural areas than in children of urban and suburban areas ($P<0.001$). Only two of the 226 children had received the HAV vaccine. The percentage of HAV IgG seropositivity of unvaccinated children was 59.3%. HAV seroprevalence was higher in subjects who had a history of jaundice (84.6%) than in those who did not (58.2%). An increase in HAV prevalence was observed with a decrease in socio-economic status ($P<0.001$).

Conclusion: HAV prevalence was markedly high, but HAV vaccination of children was very low in Erzurum. The socio-demographic factors of age, settlement area, and socio-economic status of family were significantly associated with HAV prevalence.

Keywords: Hepatitis A, Children, Seroepidemiology

Özet

Giriş: Bu çalışmanın amacı, Türkiye' nin doğusundaki 0-18 yaş grubu çocuklar arasındaki Hepatit A prevalansını etkileyen sosyo-epidemiyolojik faktörler ve Hepatit A prevalansını saptamaktır

Gereç ve Yöntem: Çalışmadaki örnekler Ocak-Mayıs 2006 tarihleri arasında Atatürk Üniversitesi Tıp Fakültesi Pediatri Servisine sarılık dışında herhangi bir nedenle başvuran 0-18 yaş arası 226 çocuktan oluşmaktaydı. Bu çalışmada anti-HAV immunglobulin G (Ig G) varlığı ELISA yöntemi ile araştırıldı.

Bulgular: 226 çocuğun HAV IgG seropozitifliği % 59.7 idi. HAV prevalansının yaşla birlikte arttığı saptandı, ancak cins ile ilgili değildi. HAV prevalansı kırsal bölgede yaşayan çocuklarda şehirmerkezinde veya şehirlerin çevresinde yaşayanlardan daha yüksek bulundu ($P<0,001$). Çocukların yalnızca ikisi Hepatit A aşısı ile aşılanmıştı. Aşısız çocukların HAV IgG pozitifliği % 59.3 idi. HAV seroprevalansı sarılık öyküsü olanlarda (% 84.6) olmayanlardan (% 58.2) daha yüksek idi. Sosyoekonomik durumda azalma ile birlikte HAV prevalansında artış gözlemlendi ($P<0,001$).

Sonuç: Erzurum' da HAV prevalansı belirgin olarak yüksek bulundu. Fakat hepatit A ya karşı aşılama son derece düşük idi. Sosyo-demografik faktörler yaş, yerleşim yeri, ailenin sosyoekonomik düzeyi HAV prevalansı ile ilişkili olarak saptandı.

Anahtar Kelimeler: Hepatit A, Çocuk, Seroepidemioloji

Introduction

Hepatitis A virus (HAV) infection is endemic worldwide, but epidemics also occur. The number of infections is influenced by the degree of sanitation; in areas with extreme crowding and poor sanitation, the entire adult population will be seropositive. The clinical consequences of infection are age related. In young children the disease is largely asymptomatic. In older children, 40-50% develop jaundice, and this proportion rises to 70-80% in adults [1,2].

HAV is a classic enterically transmitted disease whose prevalence worldwide is closely tied to the level of economic development. In developing countries, subclinical, anicteric, asymptomatic children are the main source of the disease. In developed countries the prevalence of the disease in children and young adults is low because of the high level of sanitary conditions [3,4]. The estimated 73% of subjects in Turkey who are HAV positive are those who travel to hyperendemic regions or people who live together in places such as schools, armies, hospitals or institutions [5].

The aim of this study was to determine the prevalence rate of detectable antibodies against HAV among children aged 0-18 years and to detect the socio-epidemiological factors affecting its prevalence in Erzurum, a cosmopolitan city in Eastern Turkey.

Materials and Methods

The study sample consisted of 226 children aged 0-18 years who were registered at the Pediatrics Department of Atatürk University Medical Faculty for any reason except jaundice between January and May 2002. A composite index was used to determine the socio-economic levels of the families [6]. According to these levels, the families were classified into three groups: high, moderate and low socio-economic levels. A questionnaire about several socio-demographic characteristics of the subjects was used to obtain data on HAV epidemiology. Socio-demographic characteristics including age, gender, settlement area, family size, the presence of a toilet and running water inside the house, educational levels of parents and socio-economic status were obtained from all parents of the children, and a pediatrician examined the subjects. Following the interviews and with parental approval, blood samples were taken from subjects who needed blood tests for their current complaints. IgG antibodies against HAV were measured using Dode-Behring micro-ELISA kits [7].

Percentages of subjects who were seropositive in terms of IgG antibodies against HAV were tabulated with their 95% confidence intervals (CIs) according to age, gender, settlement area, family size, educational levels of parents, socio-economic status, whether there was a toilet and running water inside the house, previous jaundice history and HAV vaccination. The association between the socio-demographic variables and the prevalence of IgG antibodies against HAV was analyzed by calculation of the odds ratio (OR) and the corresponding 95% CIs [8].

Results

A total of 226 children aged 0-18 years participated in the study. The prevalence rate of the children with respect to age is shown in Figure 1. HAV prevalence with respect to different variables, such as age, gender, settlement area, family size, toilet, running water, parents' education, socio-economic status, HAV vaccine and jaundice is shown in Table 1.

The overall HAV seroprevalence rate among these subjects was 59.7%. Of subjects included in the study, 51.3% were male and 48.7% were female. There was no difference between male (60.3%) and female (59.0%) subjects in terms of HAV IgG seropositivity. Among the 226 children, only two had received the HAV vaccine. The HAV IgG positivity percentage of unvaccinated children was 59.3%.

Discussion

HAV infection is the most common form of hepatitis in the pediatric age group in underdeveloped and developing countries and sometimes has a fulminating course. It is endemic in Turkey and one of the major health problems of the country. The consumption of contaminated food or water is implicated in its transmission. No carrier state is known, and transmission is person-to-person during the preicteric stage of the disease. The household attack rate is approximately 10 to 20%. Epidemics occur when there is fecal contamination of water or food [9].

In developing countries with inadequate hygiene and sanitation, HAV infection is endemic and most children are infected in the first years of life. In developed countries, infection early in life is uncommon and serologic evidence of infection gradually increases with age. Overall incidence rates have been decreasing as socio-economic conditions improve. There are approximately 30,000 reported cases of HAV infection in the United States of America each year, but this figure is believed to be an underestimate of its true incidence as many of the infections are subclinical. Approximately 80,000 cases and 134,000 infections occurred in

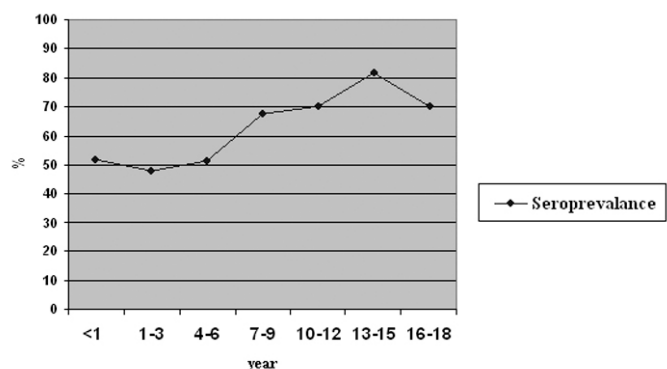


Fig. 1 — The prevalence rate of HAV in the children with respect to age.

1994, according to Centers for Disease Control (CDC) estimates. About 10% of these cases occur in daycare centers that care for children who are not toilet trained. Rates vary among racial/ethnic and geographic groups, probably because of socio-economic differences and the degree of crowding in living conditions. The incidence of HAV infection in Americans who travel to endemic areas is not known [10]. The ratio of anicteric to clinical cases in children is 12:1, whereas this ratio in adults is reversed and is 1:3.

Studies of HAV seroprevalence are rare in Turkey. In one study, seroprevalence was determined to be 67.1% in 549 children and adults in Istanbul. The HAV positivity in different age groups in this study was: 0-5 years (39.7%), 6-15 years (58%) and >25 years (75.6%) [11]. In children under 15 years of age in Kayseri (another big city in the middle of Anatolia), HAV positivity was 87.5%. In adults and youths older than 16 years, it was 97.1% [12]. In Erzurum, the HAV positivity in different age groups was: 3-6 years (33.3%), 7-10 years (78.6%) and 11-14 years (73.5%) in 1994 [13]. In our study, HAV prevalence was 59.7% in the 0-18 year age group. The high HAV seroprevalence in subjects <1 year of age (71.4%) was attributed to the presence of maternal antibodies. The fact that the seroprevalence rate decreased to 35.3% in the 1-2 year age group despite contact with HAV suggests that the high level of HAV seroprevalence in children under one year of age is caused by maternal antibodies. In Turkey, there have been three studies investigating the age of the disappearance of maternal antibodies [14-18]. According to the results of these studies, the age of disappearance of maternal antibodies is approximately 12 months. Chadha et al. [19] determined that the minimum value of anti-HAV IgG positivity was detected at 11.7 months of life.

In our study, HAV prevalence increased with age, with subjects above 8 years showing a very high HAV prevalence of 75.9-76.5%. In developing countries, most of the children exposed to HAV are under the age of 10 years. In related studies, it was shown that the age of being in contact with HAV infection is less than 3 years in India and 5 years in Pakistan [18,19]. In a study performed in another Eastern city of Turkey, it was determined that positivity was 72.5% at 6 years of age and 100% at >14 years [20]. HAV positivity in the 7-10-year age group was 78.6% in the study of Taşyaran et al. [13] in Erzurum in 1994. The similarity of our results to those of these previous studies indicates that nothing has changed in terms of hygienic and environmental conditions in our city. The HAV-IgG positivity in the 6-15 year age group was 58% in the study performed in Istanbul. HAV prevalence was markedly higher in Eastern Turkey than in Western Turkey. The difference in HAV prevalence between the western and eastern regions of Turkey can be attributed to the difference in socio-economic levels rather than a geographical difference. HAV seroprevalence showed no gender difference in our study. Similar results were observed between the studies of Turkey and foreign countries [13-15]. Socio-demographic factors such as settlement area, family size, education levels of parents, and socio-economic status of family were significantly related to HAV prevalence [13,16-22]. In our study, subjects living in rural areas showed higher HAV prevalence (82.1%) than subjects living in suburban (62.8%) and urban (18.2%) areas. An increase in HAV prevalence was observed with an increase in family size.

Table 1. HAV seroprevalence by several sociodemographic characteristics

| | HAV-IgG (+) n | % | OR (95% CI) | 95% CI | P |
|------------------------------|------------------|-------|-------------------|------------|-------|
| Age | | | | | |
| < 1 | 16 | 51.6 | 1.30 (1.11-1.53) | 27.1-76.1 | 0.042 |
| 1-3 | 24 | 48.0 | | 28.0-68.0 | |
| 4-6 | 24 | 51.1 | | 31.1-71.1 | |
| 7-9 | 21 | 67.7 | | 47.7-87.7 | |
| 10-12 | 21 | 70.0 | | 50.0-89.6 | |
| 13-15 | 22 | 81.5 | | 65.3-97.7 | |
| 16-18 | 7 | 70.0 | | 36.1-100.0 | |
| Gender | | | | | |
| Male | 70 | 60.3 | 1.05 (0.62-1.79) | 48.8-71.8 | 0.848 |
| Female | 65 | 59.0 | | 47.0-71.0 | |
| Settlement area | | | | | |
| Urban | 12 | 18.2 | 1.08 (0.58-2.02) | 0.00-40.0 | 0.000 |
| Suburban | 27 | 62.8 | | 44.6-81.0 | |
| Rural | 96 | 82.1 | | 81.8-82.4 | |
| Family size | | | | | |
| ≤5 | 46 | 41.5 | 0.86 (0.33-2.24) | 27.3-55.7 | 0.000 |
| >5 | 89 | 77.3 | | 68.6-86.0 | |
| Mother's education | | | | | |
| University | 6 | 23.1 | 1.42 (1.02-1.99) | 0.00-56.8 | 0.000 |
| High school | 7 | 21.2 | | 0.00-57.0 | |
| Secondary school | 4 | 26.7 | | 0.00-70.1 | |
| Primary school | 55 | 67.1 | | 54.7-79.5 | |
| Literate | 28 | 87.5 | | 75.3-99.7 | |
| No literacy | 35 | 92.1 | | 83.2-100 | |
| Father's education | | | | | |
| University | 21 | 31.8 | 1.78 (1.17-2.71) | 11.9-51.7 | 0.000 |
| High school | 24 | 46.2 | | 26.3-66.1 | |
| Secondary school | 15 | 71.4 | | 48.5-94.3 | |
| Primary school | 50 | 87.7 | | 78.6-96.8 | |
| Literate | 13 | 76.5 | | 53.5-99.5 | |
| No literacy | 12 | 92.3 | | 77.2-100 | |
| Socio-economic status | | | | | |
| High | 10 | 40.0 | 1.01 (0.63-1.61) | 9.6-70.4 | 0.000 |
| Middle | 12 | 32.4 | | 5.9-58.9 | |
| Bad | 31 | 60.8 | | 43.6-78.0 | |
| Worst | 82 | 72.6 | | 63.0-82.3 | |
| Toilet | | | | | |
| Indoor | 9 | 12.3 | 4.73 (0.49-45.72) | 0.00-33.8 | 0.000 |
| Outdoor | 126 | 82.4 | | 75.8-89.0 | |
| Tap water | | | | | |
| Yes | 9 | 14.8 | 0.42 (0.05-3.94) | 0.00-38.0 | 0.000 |
| No | 126 | 79.4 | | 72.3-86.5 | |
| Juandice | | | | | |
| No | 124 | 58.2 | 7.32 (1.43-37.56) | 49.5-66.9 | 0.039 |
| Yes | 11 | 84.6 | | 62.3-100 | |
| HAV vaccine | | | | | |
| Yes | 2 | 100.0 | 0.01 (0.00-1.01) | - | 0.218 |
| No | 133 | 59.3 | | 51.0-67.6 | |

Contact with HAV seemed more likely in large families, which is not surprising if we accept that the higher number of family members is inversely correlated to the welfare level and socio-cultural development of the family. Decreasing levels of parent education are related to an increase in HAV prevalence. Subjects in a lower socio-economic class showed higher HAV prevalence than those in a higher socio-economic class. In a study by Szmuness et al. [23] in New York City, the level of HAV antibodies was shown to be higher by two- or three-fold in subjects with lower socio-economic status than in those with a higher level of welfare and living conditions. In a comparison study of provinces [14], seropositivity was significantly lower in Adana (56.7%), which has a high level of wealth, and Edirne (60.7%), which has a high level of education and socio-economic development, than in the poor provinces of Diyarbakır (91.9%). Seropositivity was generally lower in subjects living in houses with tap water and indoor toilets than in those without these facilities, suggesting that unplanned development without adequate sanitary infrastructures may be a risk factor for the disease [15]. Our study showed that the percentage of seropositivity was significantly high in populations living in houses without tap water and indoor toilets. The percentages of HAV IgG seropositivity in children who were living in houses with no indoor toilet or tap water were 82.4% and 79.4%, respectively.

Among subjects without a previous history of jaundice,

58.2% were positive for anti-HAV antibodies. This can be attributed to the infection being subclinical. HAV prevalence was higher in subjects with histories of jaundice than in subjects without. Our results are comparable to those in the literature [15,24]. In this study only two children ages 4 and 5 years were HAV vaccinated. Anti-HAV IgG positivity was detected in 133 (59.3%) of 224 subjects who were not vaccinated.

The results of our study showed that HAV seroprevalence is markedly high in children older than 8 years in Erzurum. Socio-demographic factors such as age, settlement area, family size, education levels of parents, socio-economic status of family, whether the houses have indoor toilets and tap water and

previous jaundice history were significantly associated with HAV prevalence. Unfortunately, the HAV vaccination rate of children is very low in Erzurum. Our results show that HAV is moderately endemic in Turkey, although seroprevalence differs from one region to another.

HAV vaccination is recommended in areas with high endemicity in some developed countries. The routine immunization schedule in the U.S. includes HAV vaccination [25]. When we consider that our region is endemic for HAV infection and that transmission of the disease occurs particularly in crowded environments with close contact, we recommend a routine vaccination program against HAV for all children of preschool age.

Conflict interest statement The authors declare that they have no conflict of interest to the publication of this article.

References

1. Fishman LN, Jonas MM, Lavine JE. Update on viral hepatitis in children. *Ped Clin North Am* 1996; 43: 57-71.
2. Koff RS. Hepatitis A. *Lancet* 1998; 351: 1643-9.
3. Koff RS. Seroepidemiology of hepatitis A in the United States. *J Inf Dis* 1995; 171: 19-23.
4. Shapiro CN, Coleman PJ, Me Quillon GM, et al. Epidemiology of hepatitis A: seroepidemiology and risk groups in the USA. *Vaccine* 1992; 10: 59-62.
5. Coşkun P, Keskin M, Senöz Z, et al: Hepatit A olguları çevresinde infeksiyon riski yayılım frekansı ve normal popülasyonda total anti-HAV prevalansı. *Viral Hepatit Derg* 1996; 2: 90.
6. Cohen L, Holliday M. *Statistics for Social Scientist*. London 1983; pp. 69-75.
7. Ochnio AJ, Scheifele DW, Ho M, Mitchell LA. New, ultrasensitive enzyme immunoassay for detecting vaccine and disease, induced hepatitis A virus-specific immunoglobulin G in saliva. *J Clin Microbiol* 1997; 35: 98-101.
8. Norusis NY. *SPSS advanced statistics*. Chicago: SPSS, 1988.
9. Snyder JD, Pickering LK. Viral Hepatitis. In: Behrman KJ, eds, *Nelson Textbook of Pediatrics* 16th ed. WB Saunders, Philadelphia, 2000; pp. 768-76.
10. Prevention of hepatitis A through active or passive immunization recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 1996; 45: 1-30.
11. Babacan F, Söyletir G, Eskitürk A. A tipi akut viral hepatitin yaşa ve mevsimlere göre dağılımı: Anti-HAV- IgG prevalansı. *Türk Mikrobiol Cem Derg* 1990; 20: 131.
12. Sakin Y, Yıldırım MS. HAV seroprevalansının yaş ve mevsimsel analizi. *Viral Hepatit Derg* 1996; 2: 70.
13. Taşyaran MA, Akdağ R, Akdüz M, et al. Erzurum bölgesi çocuklarında fekal-oral yolla hepatit virusunun seroprevalansı. *Klinik Derg* 1994, 7: 74.
14. Kanra G, Tercan S, Batur S and Turkish National Study Team. Hepatitis A seroprevalence in random sample of the Turkish population by simultaneous EPI cluster and comparison with surveys in Turkey. *Turk J Pediatr* 2002; 44: 204-10.
15. Chin KP, Lok AS, Wong LS, Lai CL, Wu PC. Current seroepidemiology of hepatitis A. *Hong Kong J Med Virol* 1991; 34: 191-3.
16. Alikışifoğlu M, Arvas A, Taştan Y, et al. Prevalence and persistence of hepatitis A antibody during the first year of life in Turkish infants. *Indian Pediatrics* 1999; 36: 1142-4.
17. Hacimustafaoğlu M, Sadıkoğlu G, Özakin C, et al. Maternal hepatit A antikorlarının çocuklardaki seyri. *Bursa Devlet Hastanesi Bül* 1999; 15: 143-6.
18. Öztürk C, Canatar T, Hallioğlu O, Kanik EA, Yılgör E. Okul öncesi çocuklarda anti-HAV seroprevalansı ve maternal hepatit A antikorlarının kaybolma yaşı. *Çocuk Derg* 2002; 2: 75-9.
19. Chadha MS, Chitomber SD, Shaikh NS, et al. Exposure of Indian children to hepatitis A virus vaccination age. *Indian J Med Res* 1999; 109: 11-5.
20. Arankelle VA, Tsarev SA, Chadha MS, et al. Age-specific prevalence of antibodies to hepatitis A ve E viruses in Pune, India, 1982-1992. *J Infect Dis* 1995; 171: 447-50.
21. Agbootwolla M, Isomura S, Miyake K, et al. Hepatitis A, B and C seroprevalence in Pakistan. *Indian J Pediatr* 1994; 61: 545-9.
22. Akbulut A, Kılıç SS, Felek S, Akbulut H. The prevalence of hepatitis A in the Elazığ Region. *Turk J Med Sci* 1996; 26: 375-8.
23. Szmunness W, Dienstag JL, Purcell RH, et al. Distribution of antibody to hepatitis A antigen in urban adult populations. *N Engl J Med* 1976; 295: 755-9.
24. Forbes A, Williams R. Changing epidemiology and clinical aspects of hepatitis A. *Br Med Bull* 1990; 46: 303-18.
25. Rosenthal P. Cost-effectiveness of hepatitis A vaccination in children, adolescents and adults. *Hepatology* 2003; 37: 44-51.