Ege Tip Dergisi 46(1) : 1 - 6, 2007

# THE EPIDEMIOLOGY OF HEPATITIS A INFECTION IN THE POPULATION OF BORNOVA, IZMIR, TURKEY

IZMIR'DE HEPATIT A ENFEKSIYONU EPIDEMIYOLOJISI

Ferda ÖZKINAY<sup>1</sup> Tijen ÖZACAR<sup>2</sup> Cumhur GÜNDÜZ<sup>2</sup> Zafer KURUGÖL<sup>1</sup> İmre ALTUĞLU<sup>2</sup> Cihangir ÖZKİNAY<sup>1</sup> Güldane KOTUROĞLU<sup>1</sup> Fadıl VARDAR<sup>1</sup>

Department of<sup>1,</sup> Pediatrics<sup>2</sup> Micrbiology,<sup>3</sup> Medical Biology, Faculty of Medicine, Ege University, İzmir, Turkey.

Key words : Epidemiology, prevalence, risk factors hepatitis A

Anahtar sözcükler : Epidemiyoloji, prevalans, hepatit A risk faktörleri

#### SUMMARY

Background: In this study we aimed to assess the age specific prevalence of hepatitis A in population living in Bornova, Izmir /TURKEY and to identify risk factors for the hepatitis A infection.

Methods: This study population was composed of 1124 healthy subjects aged 1 to 65 years old. Subjects were stratified into seven age groups. Antibodies to hepatitis A virus (HAV) were determined by enzyme immunoassay test kits. For each subject a questionnaire inquiring about socioeconomic factors was completed.

Results: Prevalence of anti-HAV significantly increased with age showing two peaks in the groups of 7-10 ages and 19-24 ages. The seropositivity was 5.9%, 12.7%, 33%, 32.8%, 43.2%, 71.4%, 91.7% in the age groups 1-2, 3-6, 7-10, 11-14, 15-18, 19-24, > 24. People living in rural area had a significantly higher prevalence of HAV infection than people living in urban area. Socioeconomic factors significantly affected the prevalence of HAV infection. Higher parents' education, use of tap water and higher income were protective.

Conclusion: This study showed that HAV infection is moderately endemic in İzmir. There is a significant difference in the prevalence of HAV antibodies between people and different socioeconomic levels. Vaccination against hepatitis A should be considered before primary school period because the infection shows a peak in this period.

## ÖZET

Bu çalışma ile İzmir ilinde hepatit A enfeksiyonunun farklı yaş gruplarında seroprevalansının ve buna etki eden sosyo-ekonomik faktörlerin saptanması amaçlanmıştır.

Çalışmaya yaşları 1-65 yaş arasında değişen 1124 kişi alınmıştır ve bu olgular yaşlarına göre 7 gruba ayrılmıştır. Hepatit A antikorları enzim immunoassay yöntemi ile test edimiştir. Çalışma grubundaki herkese sosyo-ekonomik koşulları içeren bir anket uygulanmıştır.

Anti-HAV prevalansı 7-10 ve 19-24 yaşlarında pik yapmakta idi. Yaş gruplarına özgün prevalanslar 1-2 yaş arasında % 5.9, 3-6 yaş arsında % 12.7, 7-10 yaş arasında % 33, 11-14 yaş arsında % 32.8, 15-18 yaş arasında % 43.2, 19-24 yaş arasında % 71.4 ve 24 yaş üstünde % 91.7 olarak bulunmuştur.

Yazışma adresi: Ferda ÖZKINAY, Ege University, Faculty of Medicine Department of Pediatrics, İZMİR

Makalenin geliş tarihi : 02.01.2006 ; kabul tarihi : 18.05.2006

Kırsal alanda yaşayanlarda prevalans kentlerde yaşayanlara göre daha yüksek bulunmuştur. Hepatit A enfeksiyonu prevalansı ile sosyo-ekonomik faktörler arasında anlamlı olarak ilişki saptanmıştır. Aile eğitiminin yüksek olması ve sosyo-ekonomik faktörlerin iyi olması hepatit A' dan koruyucu faktörlerdir.

Sonuç olarak, İzmir ilinde hepatit A enfeksiyonu orta endemisite olarak tanımlanan düzeydedir bunda sosyoekonomik faktörler önemli rol oynamaktadır. Prevalansın okul çağında arttığı göz önünde bulundurulduğunda okula başlamadan önce aşı yapılmasının yararlı olacağı düşünülmektedir.

### INTRODUCTION

Hepatitis A virus (HAV) infection is one of the most important public health problems all over the world. Seroprevalence of HAV infection shows great differences not only between different countries but also between different regions in the same country. It is inversely related to the level of socioeconomic status, sanitation and personal hygiene. Recent studies show that there has been a shift from high to medium endemicity of HAV infection, concomitant with a shift in the peak age of infection from childhood to adulthood in developed and developing countries (1,2,3,4,5). Three different endemicity patterns of HAV infection are observed worldwide.

1. Areas of high endemicity: HAV infection rates are high at young ages in these areas. Asymptomatic infection is common because most people become seropositive at an early age and outbreaks are rarely seen. The countries having low life standards and poor hygienic conditions show high endemicity for HAV infection.

2. Areas of intermediate endemicity: The peak rates of infection occur in late childhood or adolescence. Outbreaks are common. Symptomatic infection rate is high during outbreaks in all age groups. Intermediate endemicity pattern for HAV is seen in developing countries which have a population from different socioeconomic levels.

3. Areas of low endemicity. HAV infection rates are low in all age groups. The peak of infection occurs in adolescents and young adults. Outbreaks can be seen. Most developed countries have a low endemicity pattern for HAV infection (6,7,8).

Turkey shows many characteristics of developing countries. Recently public health conditions have improved and epidemiological pattern of infectious diseases have changed. To determine the prevalence of HAV infection in different parts of Turkey several studies have been conducted in the last 15 years (9-12). In the early 1990s these studies revealed a high endemicity rate in most areas (9,10,13). Recently a nation wide study showed significant differences between the HAV seroprevalence of different provinces of Turkey (14).

Izmir is the third crowded city of Turkey with a population of 3 million and located in the western part. In the Bornova area of Izmir about 500 000 inhabitants from different socioeconomic levels live. This study was carried out mainly in Bornova considering that the population in Bornova can reflect the characteristics of people living in Izmir because of its heterogeneous structure. This study has been conducted to reveal out the recent age-specific pattern of the prevalence of HAV infection and to compare the proportion of susceptible people from different socioeconomic groups in the city of İzmir /Turkey. This is the largest study on HAV epidemiology conducted in this area to date.

#### MATERIAL AND METHODS

Study populations:The study population was composed of 1124 apparently healthy subjects (571 males and 553 females) aged 1 to 65 years old.

In order to form the children and adolescent population in the study 4 primary-secondary schools, 4 high schools and 3 day care centers for children were selected. Adult population was composed of the parents or teachers of those children and volunteers who live in Bornova/İzmir.

The study group was stratified into the 7 groups according to the age. Using a standard questionnaire of 19 questions information about socioeconomic status and demographic data were collected from the parents of children and from the adults themselves. The questions included housing condition, residence area, education and the profession of parents (for subjects younger than 18 years old) and HAV vaccination status. Among 1160 responders 36 subjects were vaccinated against HAV. Those vaccinated children were excluded from the study.

Sample collection: A team of 5 people consisting of 3 physicians and 2 nurses visited schools and kindergartens to apply the questionnaire and to take blood samples. After obtaining informed consent from the parents of the children under 18 years old and from adults themselves blood samples were drawn and stored at -20 until tested.

Serological analysis and statistics: All sera were tested for total anti-HAV using commercially available immunoenzyme assay kits (Hepanostika, organon Techniqua, Holland). Statistical analysis was performed using SPSS WIN 10.0. Demographic and enviromental characteristics were compared by use of chi-square test for categorical variables and Student's t-test for continous variables, to identify imbalances in possible risk factors that might contribute to the differences in prevalance. A p value of <0.05 was considered statistically significant. Possible risk factors for hepatitis A infection were examined by univariate logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated from the regression coefficients. The study was approved by the ethics committe of Ege University Faculty of Medicine.

# RESULTS

Prevalence of anti-HAV significantly increased with age showing two peaks in the groups of 7-10 ages and 19-24 ages. The overall prevalence was found to be 38.9% in the study group (Table 1). In the group of 928 subjects younger than 18 years of age the prevalence was 29.1% while it was 85.2% in the adult group.

Table 1. Age specific prevalence of anti-HAV

Age groups (years)	No. Positive/No tested	Anti-HAV seroprevalence (%)
1-2	3/51	5.9
3-6	21/166	12.7
7-10	75/227	33.0
11-14	120/366	32.8
15-18	51/118	43.2
19-24	45/63	71.4
≥ 25	122/133	91.7
Total	437/687	38.9

Prevalence of hepatitis A infection in relation to socioeconomic and demographic caracteristics of subjects is given Table 2. Statistical analysis showed that residence in rural area (OR, 1.5, 95% CI, 1.16-1.97), living in a crowded house (OR, 1.3, 95% CI, 1.23-1.40), consumption of non-hygienic water (OR. 4.19, 95% CI, 2.92-6.02) low family income (OR. 4.74, 95% CI, 3.65-6.15).19) are the risk factors for hepatitis A infection. No sex difference was observed regarding whole group.

Education levels of the parents were asked of the children and adolescents. Answers to this question were obtained from 751 subjects for the mother and 693 children for the father. The prevalence decreased significantly as the level of parents' education increased (p<0.05). Parents occupation significantly affected the prevalence. It was significantly low among children of officials and health care staff (Table3).

Table 2. Prevalence of HAV infection in relation to socioeconomic and demographic caracteristics of subjects

Characteristics	n (%)	HAV seroprevalance	<b>p</b> *	OR (95% CI)**	
Sex					
Male	571 (50.8)	38.0	p> 0.05	1.04 (0.92-1.17)	
Female	553 (49.2)	39.8			
Type of location					
Urban	943 (83.9)	36.1	P= 0.03	1.51 (1.16-1.97)	
Rural	181 (16.1)	48.2			
Family size					
<4	300 (26.7)	14.4	P< 0.001	1.31 (1.23-1.40)	
≥4	824 (73.3)	36.9			
Water supply					
Tap water	980 (87.2)	37.8	P< 0.001	4.19 (2.92-6.02)	
No tap water	144 (12.8)	75.5			
Family income					
Low income	249 (22.2)	75.3	P< 0.001	4.74 (3.65-6.15)	
Moderate-high income	875(77.8)	28.6			

\* Chi square test OR, odds ratio; CI, confidence interval; NS, not significant

\*\* Risk for hepatitis A infection

	Mother (n=751)	)	Father (n=693)	
	n (%) HAV s	eroprevalance	n (%) HAV seroprevalance	
Education*				
Uneducation	99 (13.2)	85.5	18 (2.6) 83.3	
Primary School	366 (48.7)	48.1	227 (32.8) 59.0	
Secondary School	251 (33.4)	11.5	190 (27.4) 21.6	
High School	35 (4.7)	10.9	258 (37.2) 13.2	
Occupation*				
Housewife	470 (62.6)	43.4	61 (8.8) 86.0	
Farmer	7 (1.0)	56.3	8 (1.2) 60.0	
Worker	56 (7.5)	45.8	342 (49.3) 46.8	
Official	184 (24.5)	13.2	260 (37.5) 21.1	
Health care staff	34 (4.4)	6.9	22 (3.2) 7.1	

Table 3. Anti-HAV seroprevalence of children and adolescent in relation to their parents education and occupation.

\* p<0.05

#### DISCUSSION

This study revealed that HAV infection shows intermediate endemicity pattern in the Bornova area of İzmir.

Three different endemicity patterns of HAV infection are observed worldwide. Areas of high endemicity: HAV infection rates are high at young ages in these areas. Asymptomatic infection is common because most people become seropositive at an early age and outbreaks are rarely seen. The countries having low life standards and poor hygienic conditions show high endemicity for HAV infection. Areas of intermediate endemicity: The peak rates of infection occur in late childhood or adolescence. Outbreaks are common. Symptomatic infection rate is high during outbreaks in all age groups. Intermediate endemicity pattern for HAV is seen in developing countries which have a population from different socioeconomic levels. Areas of low endemicity. HAV infection rates are low in all age groups. The peak of infection occurs in adolescents and young adults. Outbreaks can be seen. Most developed countries have a low endemicity pattern for HAV infection (6,7,8).

According to the studies over the last 15 years India, some African countries such as Kenya, Ethiopia still have a high endemicity for HAV infection while most Asian and South American countries have shown a shift to intermediate endemicity (4, 15, 16, 17).

In India about 75% of children have become seropositive against HAV by the age of 3 years and virtually all of them by 10 years of age (15). The studies conducted in South Asia and China in the late 1970s and early 1980s

revealed about 90% of population were anti-HAV positive by age 10-15 years. In this area studies carried after 1990 showed significant decrease in the prevalence of hepatitis A in the same age group (4,18,19,20). Shifting HAV epidemiology has also been documented for Middle East countries such as Quatar, Saudi Arabia, Jordan (21).

In the early 1990s the high prevalence of HAV infection was observed in most areas of Turkey. In the study conducted by Baki A et al. in 1991 in Trabzon city (in northeastern Turkey) the prevalence of HAV infection among children between the ages of 13-18 was found to be 88.6% (10). In 1994 Taşyaran et al reported that the prevalence of HAV was 68.3 % in 180 children aged 3 to 14 years and living in Erzurum city (in eastern Turkey) (13). Aldeniz et al. reported that the prevalence of HAV is 12.2% in children aged 2 to 4 years while it was 63.3% in the age group of 10 to 15 years in the İstanbul area in 1998 (9). In a study conducted in İzmir City in 1996 the prevalence of HAV was reported to be 84% in the adolescents between the age of 16-18 (22). Comparing the results reported in our study, and the studies from other parts of Turkey, in our area the recent prevalence of HAV infection respectively low in young ages. There is also significant shift towards the older ages in most areas in Turkey.

In the study presented the rapid increase of the prevalence was observed in the age groups of 7-10 and 19-20 years as it is shown in Table 1. The similar result was also observed for İzmir area in Kanra et al's study

(14). Children in the age group 7-10 attend primary school in Turkey and almost all Turkish men do their obligatory military service at the age of 20. Therefore the risk of contact with infections is higher at those ages.

The previous studies comparing the prevalence of HAV infection in rural and urban areas revealed that there is significantly higher prevalence of HAV infection in rural areas (4,23,24). In Texas in children living in rural area the prevalence of HAV infection was found to be twice as high as that is found in children living in urban area (25). In our study similar to the other studies reported the higher prevalence of HAV infection was observed in children living in rural area (Table 2)

Education levels and occupation of the parents significantly affected the prevalence of HAV infection in children investigated in this study. A study conducted in Italy showed that as the education levels of parents increased the prevalence of HAV infection decreased as in our study (26).

In the study presented no additional occupational risk was detected for children of health care staff. Furthermore the lowest level of HAV prevalence was detected in children of officials and health care staff. This can be explained by better socioeconomically conditions of these groups. Vranchx et al. obtained similar result showing the lower prevalence of HAV infection among the health care professionals than in the general population in Belgium (27).

Living in crowded conditions is one of the most important factors for HAV transmission (28,29,30). Ochnio et al and Shotollini et al reported that as the number of people or siblings living in the same house increases the risk of acquiring HAV infection also increases (31,32). In our study it has also been observed that the number of people in the household significantly affected the prevalence of HAV infection.

It has been shown that clean water and tap water at home are protective factors against HAV infection (25,33,34,35). Tap water is widely used in houses in our area but few houses have their own water sources or they supply water from the public taps outside the houses. Our study showed that the absence of tap water supply at home is a risk factor for HAV infection.

There have been many studies revealing that HAV infection is closely related to the economic level (6, 21, 23, 36). This study has also demonstrated that there is significant difference in the prevalence of HAV infection between the subjects from different economic levels in İzmir. While 92.6% of the children from low economic level become anti-HAV positive until the age of 18, only 27.2% of the children from the high economic level are anti-HAV positive at age of 18. After 18 years of age this difference is less significant. The reason for this could be that they attend schools where people from different socioeconomic level study or the males do their military service all together in their early twenties as mentioned above. In conclusion, HAV infection shows moderate endemicity rate in İzmir. However, there is still significant difference between people from different socioeconomic levels. Higher parents' education, use of tap water at home and higher income were protective. Increased number of people in house is a risk factor for HAV infection. The prevalence was significantly low among children of health care staff and officials. Comparison with the results from the other regions of Turkey showed that the lower levels of prevalence among the young ages were observed in Bornova/İzmir.

#### REFERENCES

- 1. Frösner GG, Papaevangelou G, Butler R. Antibody against hepatitis A in seven European countries. Am J Epidemiol 1979; 110:63-69.
- 2. Kunasol P, Cooksley G, Chan VF, et al. Hepatitis A virus: declining seroprevalance in children and adolescents in Southeast Asia. As J Trop Med Public Health 1998; 29:255-262.
- 3. Koff SR. Seroepidemiology of HepatitisA in The United States. J Infect Dis 1995; 171:19-23.
- 4. Barzaga BN: Hepatitis A shifting epidemiology in Southeast Asia an China. Vaccine 2000; 18:61-64.
- Abdool Karim SS, Coutsoudis A. Seroepidemiology of hepatitis A in Black South African Children. S Afr Med J 1993; 83:748-750.
- 6. Shapiro NC, Margolis HS. Worldwide epidemiology of hepatitis A virus infection. Journal of Hepatology 1993; 18:11-14.
- 7. Tanaka J. Hepatitis A shifting epidemiology in Latin America. Vaccine 2000; 18:57-60.
- 8. Forbes A, Willams R. Changing epidemiology and clinical aspects of hepatitis A. Br Med Bull 1990; 46: 303-318.
- Aldeniz C, Çavuşlu Ş, Altunay H, et al. İstanbul'da A ve E hepatitlerinin seroprevalansı. Viral Hepatit Dergisi (Turkish) 1998; 31-36.
- 10. Baki A, Aynacı M, Köksal I. Prevalance of antibody to hepatitis A virus among children in Trabzon, Turkey. Infection 1993; 21:132-133.

- 11. Doganci I, Haznedaroğlu T. Prevalence of hepatitis A, B, and C in Turkey. Eur J Clin Microbiol Infect Dis 1992; 11:661-662.
- 12. Ersoy B, Aydogan A, Dinçoguz A, Meral MS, Tugrul T. The seroprevlence of anti-HAV among 0-16 yearsolds referred to Pediatric Outpatient Clinics of a hospital. J Trop Pediatrics 1998; 44:55-56.
- 13. Taşyaran MA, Akdağ R, Akyüz M, et al. Erzurum yöresi çocuklarında fekal-oral bulaşan hepatit viruslarının seroprevalansı. Klinik Dergisi (Turkish) 1994; 7:74-78.
- 14. Kanra G, Tezcan S, Badur S and Turkish National Study Team. Hepatitis A seroprevalence in a random sample of the Turkish population by simultaneous EPI cluster and comparison with surveys in Turkey. Turk J Pediatr 2002; 44:204-210.
- 15. Arankalle VA, Tsarev SA, Chadha MS, et al. Age specifik prevalance of antibodies to hepatitis A and E viruses in Pune, India, 1982 and 1992. J Infect Dis 1995; 171:447-450.
- 16. Tsega E, Mengesha BG, Lindberg J, Nordenfelt E. hepatitis A, B and delta infection in Ethiopia: A serologic survey with demographic data. American Journal Epidemiology 1986; 123:344-351.
- 17. Wankya BM, Hansen DP, Ngindu AM, Feinstone SF, Purcell R. Seroepidemiology of hepatitis A and B in Kenya. A rural population survey in Machakos District. East African Medical Journal 1979; 56:134-138.
- Chin KP, Lok ASF, Wong LSK, Lai CHL, Wu PC. Current seroepidemiology of hepatitis A in Hong Kong. J Med Virol 1991; 34:191-193.
- 19. Aguilera GA, Romero YS, Regueiro BJ. Epidemiology and clinical manifestations of viral hepatitis. Enferm Infecc Microbiol Clin. 2006; 24:264-276.
- 20. Nelson KE. Global changes in the epidemiology of hepatitis A virus infections. Clin Infect Dis. 2006;42:1151-1152.
- 21. Tufenkeji H. Hepatitis A shifting epidemiology in the Middle East and Africa. Vaccine 2000; 18:65-67.
- Akbulut A: HAV enfeksiyonu. In: Kılıçturgay K Ed. Viral Hepatit (Turkish). Viral hepatitle savaşım Derneği, Bursa; 1998; 41-64.
- 23. Lopez H, Zitto T, Bare P, et al. Prevalance of anti-hepatitis A antibodies in an urban middle class area of Argentina: some asociated factors. Internal Journal Infectious Disease. nt-J-Infect-Dis. 2000; 4:34-37.
- 24. Garcia-Fulgueiras A, Rodriguez T, Tormo MJ, Perez-Flores D, Chirlaque D,
  - Navarro C. Prevalence of hepatitis A antibodies in southeastern Spain: a population-

based study. European Journal of Epidemiology 1997; 13:481-483.

- 25. Leach CT, Koo FC, Hilsenbeck SG, Jenson HB. The epidemiology of viral hepatitis in children in South Texas: increased prevalance of hepatitis A along the Texas-mexico border. The Journal of Infectious disease 1999; 180:509-513.
- Stroffolini T, Chiaramonte M, Franco E Rapicetta M, et al. Baseline seroepidemiology of hepatitis A virus infection among children and teenagers in Italy. Infection 1991; 19:97-100.
- 27. Vranckx R, Jacques P, Moens G. Prevalence of hepatitis A antibodies in a large sample of Belgian health care workers. Infection 1999; 27:256-258.
- 28. Ciocca M. Clinical course and consequences of hepatitis A infection. Vaccine 2000; 18:71-74.
- 29. Green MS, Zaaide Y. Sibship size as arisk factor for hepatitis A infection. Am J Epidemiol 1989; 129: 800-805.
- 30. Hadler SC, McFarland L. Hepatitis in day care centers: epidemiology and prevention. Rev Infect Dis 1986; 8:548-557.
- Ochnio JJ, Scheifele DW, Ho M. Hepatitis A virus infection in urban Children- Are preventive opportunities being missed?. The Journal of Infectious disease 1997; 176:1610-1613.
- 32. Stroffolini T, Pretolani S, Miglio F, et al. Population based survey of hepatitis A virus infection in the Republic of San Marino. European Journal of Epidemiology 1997; 13:687-689.
- 33. Melnick JL. History and epidemiology of hepatitis A virus. J Inf Dis 1995; 171:2-8.
- Shapiro CN, Coleman PJ, McQuillian GM, Alter MJ, Margolis HS: Epidemiology of hepatitis A : seroepidemiology and risk groups in the USA. Vaccine 1992; 10:59-62.
- Redlinger T, O'Rourke K, VanDerslice J: Hepatitis A among school children in a US-Mexico border community. Am J Pub Health 1997; 87:1715-1717.
- American Academy of Pediatrics: Hepatitis A. In:Peter G, ed. Red Book: Report of the Committee on Infectious Disease. 24th ed. Elk Grove Village, IL: American Academy of Pediatrics 1997; 237-246.