

THE SEROPREVALENCE OF HEPATITIS A IN ADULTS IN İZMİR: PRIOR TO INTRODUCING VACCINE INTO ROUTINE VACCINATION PROGRAM

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ABSTRACT

Objective: Hepatitis A virus (HAV) is an important public health problem in Turkey. This study was aimed to determine the population-based seroprevalence of HAV in İzmir.

Material and Method: In this cross-sectional study, a representative sample of the population, which was at the age of ≥ 15 years, was selected by using random stratification method. A total of 2156 healthy subjects participated in this present study. Blood specimens were collected for testing anti-HAV IgG, and were examined by using enzyme-linked immunosorbent assay (ELISA). A questionnaire was

also administered to obtain data regarding demographic characteristics and living conditions of the participants.

Results: Anti-HAV IgG positivity was 93.9%. It was found that anti-HAV IgG seropositivity was higher in the subjects with lower income levels, lower education status, at older age, whereas it was lower in younger and single subjects.

Conclusion: Improved water and food sanitation resulted in reduced seroprevalence of HAV at younger age groups in İzmir.

Key Words: Hepatitis A, population-based study, prevalence. *Nobel Med 2013; 9(3): 49-53*

İZMİR İLİNDE ERİŞKİNLERDE HEPATİT A VİRÜS SEROPREVALANSI: RUTİN AŞILAMA PROGRAMINA GİRİŞ ÖNCESİ DURUM

ÖZET

Amaç: Hepatit A halen ülkemizde önemli bir halk sağlığı sorunudur. Bu çalışmada İzmir'de toplum tabanlı Hepatit-A prevalansının belirlenmesi amaçlanmıştır.

Materyal ve Metod: Bu kesitsel çalışmada, İzmir ilini temsil edecek 15 yaş ve üzeri örneklem sayısı tabakalı örnekleme yöntemi kullanılarak hesaplanmıştır. Toplam 2156 sağlıklı kişi çalışmaya katılmıştır. Katılımcılardan anti-HAV IgG testi için kan örneği alınarak enzyme-linked immunosorbent assay (ELISA) yön-

temi ile çalışılmıştır. Katılımcıların demografik özellikleri ve yaşam koşullarına ilişkin verileri toplamaya yönelik bir anket uygulanmıştır.

Bulgular: Anti-HAV IgG pozitifliği %93,9 saptanmıştır. Anti-HAV IgG seropozitifliğinin gelir düzeyi düşük olanlarda, ileri yaşta ve ilköğretim mezunu ve daha az eğitimi olanlarda, daha fazla olduğu, genç ve bekarlarda ise daha düşük olduğu saptanmıştır.

Sonuç: İzmir'de su ve besin sanitasyonundaki iyileşme ile genç yaş grubunda HAV seropozitifliğinin oldukça düşük olduğu belirlenmiştir.

Anahtar Kelimeler: Hepatit A, toplum tabanlı çalışma, prevalans *Nobel Med 2013; 9(3): 49-53*

INTRODUCTION

Hepatitis A virus (HAV) is an important public health problem in the developing and underdeveloped countries. All over the world, it is estimated that at least 1.4 million new hepatitis A cases have been diagnosed annually.¹⁻³

While seroprevalence of HAV is correlated with age, socioeconomic status and level of development; it is also closely related to crowded environment, poor hygiene, unsafe and contaminated water use. The age of confrontation with virus depends on the socioeconomic status of the country, the region and the household.^{4,5} In many countries, improved socioeconomic status, living conditions, and better sanitation have reduced prevalence of HAV seropositivity in populations. However, outbreaks can sometimes be observed during travelling, immigration and natural disasters, like floods.⁶ Pattern changes in HAV epidemiology are commonly encountered in many developed countries. The infection patterns have been switched from hyperendemic to hypoendemic levels in many countries, particularly in the urban areas.⁷

As HAV belongs to a single serotype, individuals infected with the virus are immunized once, and their IgG antibodies are present during lifetime. Therefore, anti-HAV IgG is tested in the prevalence studies. The HAV seropositivity is an indicator of cumulative infection rate.⁶ It is important to identify epidemiological changes, and HAV seroprevalence in the country from the public health perspective.³ Moreover, identification of population-based prevalence guides us to take preventive measures against the disease. In parallel to the development level of the population, transmission rate increases with the increasing age. Thus, age-specific prevalences, and changes of them over time are more critical than the mean prevalence rate. In their meta-analysis study, Jacobsen and Wiersma reported that Turkey was at an intermediate level of endemic for HAV between years 1990 and 2005.⁸

This present study aimed to determine HAV seroprevalence in healthy subjects at and over 15 years of age, who represent a sample for the city of İzmir.

MATERIAL and METHOD

Participants

In this cross-sectional population-based study conducted in İzmir, the total population of 3,739,353 subjects was included. Being a highly immigrated region, İzmir is a city where many individuals with different socioeconomic and cultural status live

together. The majority of the inhabitants live in the urban areas. The number of a representative sample of the İzmir population was estimated using EPI Info Statistical software (Centers for Disease Control and Prevention (2000): EpiInfo computer program. Centers for Disease Control and Prevention, Atlanta, Ga). Random stratification method was used. The number of subjects from each district was estimated in proportion to population of the district. In sample size calculation, 46.4% of seropositivity, which has been previously defined as the prevalence of city of İzmir, had been considered, and it was estimated that 1830 subjects should be interviewed for the confidence interval of 99%. List of subjects to be interviewed have been selected randomly in population registrations of family medicine centers by the Health Directorate of City of İzmir. In cases that some of the subjects could not be reached or they were reluctant to participate in the study, substitutes were selected in the same way with the randomized sampling method.

Procedures

Between dates January 2010 and March 2010, a total of 2156 healthy subjects, who were at and above 15 years of age, were reached from 29 districts of İzmir during this present study. The questionnaire was given to participants, and they were requested to fill up the questionnaire themselves. Each questionnaire took approximately 25 minutes answer. The questions were administered to obtain data regarding demographic characteristics and living conditions.

Blood samples, 8 cc from each, were drawn in to two gelatinated tubes (BD Vacutainer, Becton Dickinson, UK) from subjects who accepted to participate in the study. After all blood samples were centrifuged immediately, serum samples were stored at -80°C. After all serum samples were collected, they were studied for anti-HAV IgG test by ELISA method (Diasorin, Italy).

Ethical consideration

The study protocol was approved by the Ethics Committee of the İzmir Tepecik Training and Research Hospital (27.05.2009/4). The interviewers introduced themselves before applying the questionnaire, giving information on the subject and duration of the procedure. The subjects were informed that they were included in the study on voluntary basis. The participants were informed that they did not have to write their names on questionnaires; their information would be kept confidential and the information would be used only for research purposes. The written consents were obtained from the participants. →

Analysis

The statistical analysis was performed using SPSS 14.0 software. Chi-square test and percentages were used for analysis. P value of <0.05 was considered as the level of significance. The number of respondents to each question in the survey was different, non response were excluded from analysis for each question. Therefore, the total numbers of from variables were different.

RESULTS

The sociodemographic characteristics of the subjects and the prevalence of possible risk factors for HAV are shown in Table 1. The mean age was 44.05±16.83 (range: 15-94) years. The majority of the subjects were living in the urban areas. The majority of subjects were married, female, housewives with lower income levels and graduated from the primary school.

The prevalence of anti-HAV IgG positivity was 93.9% among 2156 participants. The confrontation with HAV was 94.1% in males, and 93.7% in females. There was no statistically significant difference between males and females in terms of anti-HAV IgG seropositivity. Significant relationships between anti-HAV IgG seropositivity and income level (Chi-square 11.211, p=0.004); education level (Chi-square: 109.07, p=0.000); marital status (Chi-square: 250.96, p=0.000); age (Chi-square: 324.30, p=0.000); and occupation (Chi-square: 277.36, p=0.000) were detected (Table 1). It was found that the anti-HAV IgG seropositivity was higher in the subjects with a lower income level and in those at older age, with primary education or uneducated subjects, those who lived collectively (in military post, dormitory, kindergarten) (Chi-square: 8.493, p=0.014), while it was lower in the younger and single subjects (Table 1).

Moreover, the mean number of siblings was also higher in subjects with anti-HAV IgG positivity (t=9.15, p=0.000). No significant difference was found between the HAV seropositivity and residence regions as being rural or urban. Similarly, there was no statistically significant difference between the number of subjects living in the same house, and HAV seroprevalence. Jaundice history was detected in 10.7% of HAV positive subjects.

DISCUSSION

In this population-based study involving a representing sample of the city of İzmir, prevalence of anti-HAV IgG positivity defined as 93.9%. In the study conducted in 2008 in the city of İzmir, the authors reported anti-

Table 1: Distribution of the anti-HAV IgG seroprevalence in İzmir based on the sociodemographic and risk factors

	Total		Anti-HAV IgG (+)	
	N	(%)*	N	(%)**
Sex				
Female	1336	61.9	1239	93.7
Male	820	38.1	766	94.1
Age group				
15-19	135	6.4	92	68.1
20-24	144	6.8	106	73.6
25-29	197	9.3	175	88.8
30-34	201	9.6	191	94.6
35-39	222	10.5	216	97.3
40+	1208	57.4	1197	99.1
Education status				
Uneducated	243	11.4	238	97.9
Primary school	938	43.9	919	98.7
Secondary school	223	10.4	202	91.4
High school	436	20.3	378	87.9
College	301	14.0	254	85.5
Profession				
Housewife	874	41.7	847	96.9
Retired	357	17.0	355	99.4
Student	121	5.8	73	60.3
Civil servant	111	5.3	107	96.4
Employee	189	9.0	179	94.7
Other	445	21.2	409	91.9
Income level TL (per month)				
<1000	1297	64.2	1233	95.1
1000-2000	518	25.6	471	90.9
>2000	206	10.2	194	94.2
Marital status				
Married	1631	77.1	1596	97.9
Single	387	18.3	296	76.5
Divorced/Widow	97	4.6	94	96.9
Residence				
Rural	714	33.4	668	93.6
Urban	1424	66.6	1339	94.0
The number of households				
1-4	1654	78.5	1554	94.0
5-9	434	20.6	404	93.1
10+	19	0.9	19	100.0
History of living collectively or in communities				
1-4	925	52.3	882	95.4
5-9	845	47.7	779	92.1

*The percentage column, **The percentage row

HAV IgG seroprevalence as 46.4%.⁹ Prevalences from different regions of Turkey were reported ranging from 7.85 to 88% in different studies.² Remarkably, lower seroprevalences were reported in the Western regions when compared with the Eastern ones. This may be explained by lower socioeconomic and education levels of people living in the Eastern parts of Turkey as well as poor sanitation and increased number of the →

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household. Anti-HAV IgG was defined as 64.4% in the subjects, who were admitted to nine healthcare centers in Turkey.¹⁰ Kanra et al. reported that the prevalence was 71.3% in the subjects younger than 30 years of age in Turkey.¹¹ In a study conducting between 1998 and 2007 in Eskişehir, the authors reported the prevalence as 54% among 2418 individuals, who were admitted to the military hospital.¹² In another study performed in Erzurum in 1998, seropositivity rate was reported as 84.2% among 392 individuals younger than 30 years of age.¹³ In Erzurum, among 1142 individuals younger than 18 years of age were included in the study, and the prevalence rate was reported as 57.2%.¹⁴ In a study conducted in Konya, anti-HAV IgG positivity was defined as 67.8% in rural area, and 25.8% in urban area among 210 children under 6 years of age.¹⁵

In our study, increased seroprevalence with the increasing age was statistically significant. It was reported in several studies conducted in Turkey that the positivity rate was increased with the older age.^{9,13} This may be explained by poor food, water sanitation with poor infrastructure in the previous years. As it is observed all over the world, reaching clean drinking water and better living conditions have been achieved also in Turkey, so confrontation risk is decreased among children and adolescents. In a study conducted in 2008 in the city of İzmir, increasing seropositivity was observed with the increasing age; particularly over 95% of seropositivity in subjects older than 30 years of age. However, seropositivity in younger age groups were not consistent between two studies. This may be explained by increased immigration potential from the East of Turkey with resulting collective living concept, and lower income levels.

Several studies conducted in Turkey and in the world showed that the seroprevalences of HAV were similar between males and females. Similarly, in the study performed by Kanra et al., in which data from various cities of Turkey have been collected, HAV prevalences were 73% in females, and 69.3% in males.¹¹

In our study, the seroprevalence of HAV was higher in the subjects with lower socioeconomic levels. Erdogan et al. reported that HAV seroprevalence was significantly higher in subjects with lower (59.4%) and low to moderate economic levels (30.8%).¹⁶

The mean number of household was 3.8 in İzmir. In our study, numbers of household were also similar among HAV-negative and positive subjects. Crowded living environments cause easy transmission of hepatitis A.² Although this infection, which is transmitted between humans by fecal-oral route, can be rapidly transmitted in crowded environments with longer contact time

intervals, according to the results of our study there was no significant relationship between the numbers of households and the seropositivity.

Similar to previous studies, increased number of siblings and low income level were risk factors for HAV seropositivity.¹⁴ It has been previously reported that increased number of siblings affected HAV seropositivity markedly.^{11,16} In our study, we also observed that mean number of siblings was higher among HAV-infected subjects.

It has been reported previously in the publications that education level of subjects are related to hepatitis A infection, and as education level is increased prevalence is decreased.^{2,11} In another study conducted in US, the authors reported that HAV seropositivity decreased with increasing education level of the household.¹⁷ Similarly, in our study, HAV infection rate among subjects graduated from the primary school was significantly high when compared with the subjects in other groups.

In developed countries, HAV seropositivity is not widespread due to improved hygiene and sanitation standards. An age-specific prevalence is also present, producing a sigmoid curve.¹⁸ Improvements in reaching healthy and safe water, decreased intention for crowded living, increased income levels, and improvements in education levels caused decreased infection rate by 97% in Europe, 41% in the Middle East, and 57% in Asia, whereas no decrease was reported from Africa.¹⁹

The mean anti-HAV IgG prevalence was 32.4% in 2002 in US, while it was 65.3% in 2011 in Korea.^{17,20} Moreover, in Syria. Antaki et al. reported the seropositivity rate as 50% among the subjects 1-5 years of age, and 81% at the age of 6-10 years. In 2004 Mehr et al. reported the seropositivity rate from Iran as 22.3% among subjects at the age of 6 months and 15 years.^{21,22} In Hong Kong, the prevalence rate was reported as 71% in the overall population, reaching approximately 100% among subjects ≥ 50 years of age.²³

Vaccination against HAV is performed in several countries as a part of the national disease prevention program, whereas it is recommended only for subjects, who are at risk, like sewage workers, decontamination workers, people working in nursery homes, and people, who are scheduled for traveling to endemic areas.²⁴ In the countries where the HAV is highly endemic, improving sanitation services is recommended, while no vaccination is recommended in the countries where the HAV is mildly endemic. In moderately endemic areas, the vaccination is →

suggested to be effective.²⁵ HAV infection is included in the Reportable Disease List in Turkey. However, HAV vaccination is not included in the national vaccination program. The Turkish Ministry of Health, National Vaccination Advisory Committee has reported that the vaccine will be added up the routine schedule. This study can contribute valuable information for status of seroprevalence of HAV prior to introducing the vaccine into routine vaccination program.

CONCLUSION

It has been observed that hepatitis A susceptible population is composed of children and adolescents as it has been indicated in this present, population based study performed in the city of İzmir, and other previous studies from Turkey. Low income and lower education status were significant independent predictors of increased HAV infection rate.



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REFERENCES

- Curry MP, Chopra S: Acute Viral Hepatitis. Ed: Mandell GL, Bennett JE, Dolin R: Principles and Practice of Infectious Diseases. Sixth edition. Churchill Livingstone, Philadelphia 2005; 1426-1440.
- Franco E, Meleleo C, Serino L, Sorbara D, Zaratti L. Hepatitis A, epidemiology and prevention in developing countries. *World J Hepatol* 2012; 4: 68-73.
- Saha SK, Saha S, Shakur S, et al. Community-based cross-sectional seroprevalence study of hepatitis A in Bangladesh. *World J Gastroenterol* 2009; 15: 4932-4937.
- Xu ZY, Wang XY, Liu CQ, Li YT, Zhuang FC. Decline in the risk of hepatitis A virus infection in China, a country with booming economy and changing lifestyles. *J Viral Hepat* 2008; 15: 33-37.
- Ungan M, Yaman H, Taheri N. The prevalence of antibodies to hepatitis A among preschool children in an urban setting in Turkey. *J Trop Pediatr* 2002; 48: 180-182.
- Wang SM, Liu CC, Huang YS, Yang YJ, Lei HY. Change in Hepatitis A virus seroepidemiology in southern Taiwan: A Large Percentage of the Population Lack Protective Antibody. *J Med Virol* 2001; 64: 104-108.
- Kim YJ, Lee HS. Increasing incidence of hepatitis A in Korean adults. *Intervirology* 2010; 53: 10-14.
- Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. *Vaccine* 2010; 28: 6653-6657.
- Kurugol Z, Aslan A, Turkoglu E, Koturoglu G. Changing epidemiology of hepatitis A infection in İzmir, Turkey. *Vaccine* 2011; 29: 6259-6261.
- Ceyhan M, Yildirim I, Kurt N, et al. Differences in hepatitis A seroprevalence among geographical regions in Turkey: a need for regional vaccination recommendations. *J Viral Hepat* 2008; 15: 69-72.
- Kanra G, Tezcan S, Badur S, 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.
- Coşkun O, Erdem H, Gul HC, Eyigun CP. Changes in hepatitis A prevalence rates between 1998 and 2007 in Eskisehir, Turkey. *Int J Infect Dis* 2008; 12: 141.
- Vancelik S, Guraksin A, Alp H. Hepatitis A Seroepidemiology in Eastern Turkey. *East Afr Med J* 2006; 83: 86-90.
- Kaya D, Guler E, Ekerbicer HC, et al. Hepatitis A seroprevalence and its relationship with environmental factors in children of different age groups in Kahramanmaraş, Eastern Mediterranean region of Turkey. *J Viral Hepat* 2007; 14: 830-834.
- Atabek ME, Findik D, Gulyuz A, Erkul I. Prevalence of anti-HAV and anti-HEV antibodies in Konya, Turkey. *Health Policy* 2004; 67: 265-269.
- Erdogan MS, Oktun M, Tatman-Otkun M, Akata F, Ture M. The epidemiology of hepatitis A virus infection in children, in Edirne, Turkey. *Eur J Epidemiol* 2004; 19: 267-273.
- Fix AD, Martin OS, Gallicchio L, Vial PA, Lagos R. Age-specific prevalence of antibodies to hepatitis A in Santiago, Chile; risk factors and shift in age of infection among children and young adults. *Am J Trop Med Hyg* 2002; 66: 628-632.
- Lee HC, Ang LW, Chiew PK, James L, Goh KT. Changing epidemiological patterns of Hepatitis A infection in Singapore. *Ann Acad Med Singapore* 2011; 40: 439-447.
- Jacobsen KH, Koopman JS. The effects of socioeconomic development on worldwide hepatitis A virus seroprevalence patterns. *Int J Epidemiol* 2005; 34: 600-609.
- Yun SW, Lee WK, Cho SY. The seroprevalence rate, vaccination rate and seroconversion rate of hepatitis A in central region of Korea. *Korean J Gastroenterol* 2011; 57: 166-172.
- Antaki N, Kebbewar MK. Hepatitis A seroprevalence rate in Syria. *Trop Doct* 2000; 30: 99-101.
- Mehr AJ, Ardakani MJ, Hedayati M, et al. Age specific seroprevalence of hepatitis A infection among children visited in pediatric hospitals of Tehran, Iran. *Eur J Epidemiol* 2004; 19: 275-278.
- Wong KH, Liu YM, Ng PS, Young BW, Lee SS. Epidemiology of hepatitis A and hepatitis E infection and their determinants in adult Chinese community in Hong Kong. *J Med Virol* 2004; 72: 538-544.
- Mossong J, Putz L, Patiny S, Schneider F. Seroepidemiology of hepatitis A and hepatitis B virus in Luxembourg. *Epidemiol Infect* 2006; 134: 808-813.
- WHO. Hepatitis A vaccines. WHO position paper. *Weekly Epidemiol Rec* 2000; 75: 37-44.