

Seroprevalence of Hepatitis A Infection in the Turkish Republic of Northern Cyprus

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Aims: This study was conducted to determine the seroprevalence of hepatitis A virus (HAV) infection in the Turkish Republic of Northern Cyprus.

Materials and Methods: A total of 660 unvaccinated persons 1 to 30 years old were selected for the study with cluster sampling. Information on sociodemographic characteristics was gathered for each participant and, in 641 of them, anti-HAV antibodies were assayed using an enzyme immune assay.

Results: Anti-HAV prevalence in the Turkish population under the age of 30 in Northern Cyprus was 23.9%. For the age groups 1-5, 6-10 and 11-15 years, seroprevalence rates were relatively low (11.4, 9.4 and 12%, respectively). For age groups 16 years and over, HAV seroprevalence gradually increased with age, rising to 30.4% in 16 to 20 years and to 52.5% in 21 to 30 years of age. In addition to age, other variables significantly associated with HAV seroprevalence included low family income, family size, waste water sewage, and the education level of parents.

Conclusions: Anti-HAV seroprevalence in the Turkish Republic of Northern Cyprus shows an intermediate prevalence. As well as expanding health education and improving sanitation, a hepatitis A universal mass vaccination program would be logical for the population.

Key Words: Hepatitis A, seroprevalence, Turkish Republic of Northern Cyprus

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Kuzey Kıbrıs Türk Cumhuriyeti'nde Hepatit A Seroprevalansı

Amaç: Kuzey Kıbrıs Türk Cumhuriyeti'nde (KKTC) Hepatit A virus (HAV) enfeksiyonu seroprevalansını saptamak

Materyel ve Metod: 1-30 yaş arası toplam 660 kişi çalışmaya alındı. Çalışmaya alınan kişilerle ilgili sosyodemografik özellikler kaydedildikten sonra bunların 641'inde anti-HAV antikörleri enzim immünoassay yöntemi ile çalışıldı.

Bulgular: KKTC'de 30 yaş altında anti-HAV seroprevalansı % 23.9 olarak saptandı. Anti-HAV prevalansı, 1-5, 6-10, 11-15 yaş gruplarında sırasıyla % 11.4, %9.4 ve % 12 idi; 16 yaş üzerindeki popülasyonda HAV ı giderek artış göstererek 16-20 yaş grubunda HAV ı % 30.4, 21-30 yaş grubunda ise % 52.5'e yükseldi. Yaşın yanında anti-HAV seroprevalansını etkileyen diğer değişkenler ailenin düşük geliri olması, ailede yaşayan birey sayısı ve ebeveynin eğitim düzeyi idi.

Sonuç: KKTC HAV açısından orta endemisine göstermektedir. HAV enfeksiyonunu önlemek için toplum bazında sağlık eğitimi ve hijyen koşullarının iyileştirilmesi yanında ulusal aşı programına HAV aşısının eklenmesi akılcı bir yaklaşım olarak görülmektedir.

Anahtar Sözcükler: Hepatit A, seroprevalans, Kuzey Kıbrıs Türk Cumhuriyeti

Received: February 05, 2008
Accepted: August 28, 2008

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Introduction

Hepatitis A virus (HAV) infection is an important public health problem throughout the world. Approximately 1.5 million new HAV infections are estimated to occur worldwide each year (1). In order to take appropriate preventive health care measures against hepatitis A and develop vaccination protocols in a region, it is very important to know the incidence of the disease. The true incidence of HAV infection is not reflected in the number of reported cases of acute hepatitis A, since most infections are subclinical, particularly in children, and many cases are not reported (2). Determination of the anti-HAV antibodies in a population provides more reliable estimates of HAV infection prevalence.

According to serological studies, the age-specific prevalence of infection with HAV shows three epidemiologic patterns (low, intermediate, and high) (3). Industrialized Mediterranean countries such as France, Italy, Spain, Portugal and Greece are low endemicity areas for HAV infection (4-8), whereas other Mediterranean countries such as Turkey and Lebanon are considered to be intermediate endemicity areas (9,10). A seroepidemiologic study that looked into the anti-HAV prevalence in the Larnaca area of Southern Cyprus revealed a low prevalence (1.6%) in the Greek population in the age group 6-18 years (11). However, the epidemiology of HAV infection in the Turkish Republic of Northern Cyprus is not known, as no seroprevalence data are currently available. We therefore conducted this study to determine the seroprevalence of HAV infection in the 1 to 30- year-old Turkish population in Northern Cyprus and to identify the relationship between HAV seroprevalence and several characteristics of the study subjects.

Materials and Methods

A prospective seroepidemiologic study of HAV infection was carried out in all areas of the Turkish Republic of Northern Cyprus in March 2006. The population of Turkish Cypriots was estimated to be 148,000 in 2003 by the United Nations. Of this population, about 72,000 (48%) were between 1 and 30 years. The study was approved by the Ethical Committee of the Ege University Medical Faculty.

The study population included healthy subjects aged 1-30 years who were born in Northern Cyprus. Subjects living in Northern Cyprus, but who had moved from Turkey, were excluded from the study. None of the subjects in the study group had been vaccinated with HAV vaccine.

The sampling method of 30 clusters recommended by the Expanded Programme on Immunization/World Health Organization (EPI/WHO) for field studies (12,13) was used for selecting subjects of a pre-determined number. The selection procedure was carried out by creating a cumulative list of community populations and selecting a systematic sample from a random start.

Although 600 subjects were sufficient to represent the studied population, a total of 660 subjects (22 for each cluster) were chosen for the study, taking into

consideration probable loss of the blood samples. A starting household was selected in each community by locating the ward's center, randomly selecting a house from a list of all houses falling along the line drawn from the ward center to the periphery in the chosen direction. The house was then examined to determine whether subjects of eligible age and sex were living there. Subsequently, the nearest household to the right was visited and the steps repeated until the desired number of persons were obtained. Only one individual for each family was selected for the study.

A questionnaire addressing several characteristics of the subjects was administered to obtain basic descriptive data on HAV epidemiology. The information was obtained from the parents of the children and from the adult-aged subjects themselves. The educational levels of those aged ≥ 16 years and of one of the parents (parent with the highest level) for those aged < 16 years, were classified as "group 1" (university level) or "group 2" (less than university level).

After written informed consent was obtained, blood samples were taken from each participant for seroprevalence analyses. Sera were stored at -20°C until tested and were further tested at the Microbiology Laboratory of Ege University Faculty of Medicine for total anti-HAV, using an enzyme-linked immunosorbent assay (RADIM S.p.a., Roma, Italy).

Statistical analyses were performed using SPSS for Windows version 13.0. A descriptive analysis was followed by bivariate analysis using a χ^2 test for comparison of the various sub-groups with a 5% statistical significance level. A multivariate logistic regression model was used to determine predictor variables associated with seroprevalence among the significant variables found by bivariate analysis.

Results

A total of 641 blood samples were examined (19 samples were excluded due to inadequate sample size or hemolysis). Anti-HAV antibodies were detected in 23.9% of 641 subjects under the age of 30 in the Turkish Republic of Northern Cyprus.

The distribution of HAV seroprevalences by age group is shown in Figure. For age groups 1-5, 6-10 and 11-15 years, seroprevalence rates were relatively low (11.4, 9.4

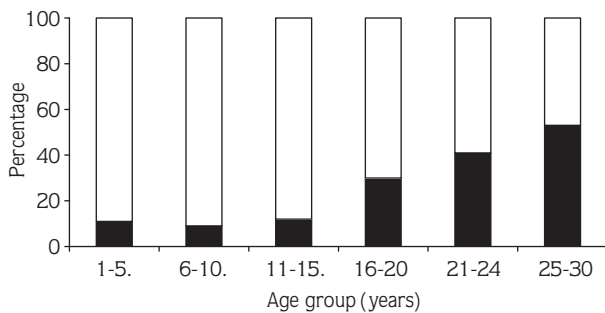


Figure. Seroprevalence of anti-HAV antibodies in the Turkish Republic of Northern Cyprus by age group. ■ Anti-HAV positive; □ Anti-HAV negative.

and 12%, respectively). For age groups 16 years and over, HAV seroprevalence gradually increased with age, rising to 30.4% in the 16 to 20 years of age group and to 52.5% in the 21 to 30 years of age group (Table). In addition to age, other variables significantly associated with HAV seroprevalence included low family income, family size, waste water sewage, and parental level of education. Seroprevalence was considerably higher in subjects with monthly family income ≤ 500 Euro than in those with monthly family income >501 Euro. Anti-HAV prevalence was also higher in large families with five and more members (35.5%) than in small families with four or fewer members (18.7%). The education level of parents was significantly correlated with HAV seroprevalence, with 4% prevalence in children with parents with a university education versus 12.9% in those with less education.

Anti-HAV prevalence was similar in different regions of Northern Cyprus (Table). There was no difference in seroprevalence rate between rural and urban areas. No significant association was found between seroprevalence and gender.

Discussion

To our knowledge, this is the first study in which the prevalence of anti-HAV was assessed in the Turkish Republic of Northern Cyprus. This study, which was conducted using the 30 cluster sampling method in all parts of Northern Cyprus, including both rural and urban areas, provides a representative data for the Turkish Republic of Northern Cyprus.

In our study, HAV seroprevalence in the Turkish population under the age of 30 in Northern Cyprus was

found as 23.9%. Because no participants reported active or passive immunization against HAV, we may assume that the seroprevalence mainly reflects prior exposure to HAV. Anti-HAV prevalence in Northern Cyprus is markedly lower than that reported from Turkey (14-16). In a recent seroprevalence study, HAV seroprevalence was found as 71.3% in the sera of 4462 subjects under the age of 30 in Turkey (10). According to the study results reported by Kanra et al. (10), HAV seroprevalence in children aged 10 years was 50% in Turkey, whereas the seroprevalence in the same age group of children was found as only 9.4% in Northern Cyprus.

Anti-HAV seroprevalence rates may generally vary by ethnic origin, socioeconomic status, urbanization level, and general hygiene conditions (17-20). When subjects were considered according to their area of residence, seropositivity rates were comparable in rural and urban areas in Northern Cyprus. The main reason for this is that general hygiene conditions such as toilet facilities and clean water supplies are similar among rural and urban areas of Northern Cyprus. However, HAV seroprevalence in the Turkish Republic of Northern Cyprus is still higher than seroprevalences reported in the Larnaca area of Southern Cyprus, where HAV seroprevalence was 1.6% in the Greek population in the age group of 6 to 18 years (11). This can be explained by the high level of socioeconomic and health conditions in the Greek population in Cyprus. In fact, as reported previously, our study shows clearly that indicators of low socioeconomic status (i.e. low family income, crowding, absence of waste water sewage, and lower education level of parents) were significantly associated with higher anti-HAV prevalence (7,19-23).

Several studies in the literature have reported that HAV seroprevalence rates were similar in females and males (14,16,17,23-26). However, some studies have reported a slightly higher HAV prevalence rate in females (10,21,27). In the present study, HAV prevalence in females was slightly higher than in males, but the difference was not statistically significant.

The results of our study show that Northern Cyprus is an intermediate endemicity area for HAV infection. Exposure to HAV occurs generally in young adults or those older. Improvements in sanitary conditions and hygiene standards will reduce childhood exposure and hence increase the proportion of susceptible adolescents and young adults, in whom symptomatic disease is more

Table. Seroprevalence of anti-HAV by sociodemographic variables in the Turkish Republic of Northern Cyprus (n=641).

	Number	Seroprevalence (%)	Odds ratio (95% CI)
Age			
1-5	123	11.4	Reference
6-10	126	09.4	0.82 (0.35-1.88)
11-15	132	12.0	1.06 (0.49-2.24)
16-20	125	30.4	3.40 (1.71-6.74)
21-30	135	52.5	8.57 (4.50-16.34)
Gender			
Male	304	20.7	Reference
Female	337	26.7	1.39 (0.96-2.01)
Region of residence			
Lefkoşa	169	21.4	Reference
Girne	136	25.2	1.22 (0.59-2.51)
Magosa	134	32.8	1.51 (0.72-3.17)
Güzelyurt	120	20.1	1.89 (0.86-3.54)
İskele	82	18.2	1.14 (0.53-2.41)
Location			
Rural	273	22.6	Reference
Urban	368	26.1	1.21 (0.84-1.76)
Family size			
≤ 4	444	18.7	Reference
≥ 4	197	35.5	2.39 (1.64-3.49)
Family income (monthly)			
> 501 Euro	578	18.9	Reference
≤ 500 Euro	63	69.8	16.21 (8.06-32.62)
Water consumption			
Tap	428	22.1	Reference
Well	213	25.0	1.38 (0.73-2.61)
Waste water sewage			
Yes	605	22.5	Reference
No	36	47.2	3.09 (1.56-6.10)
Parental* education (n=381)			
University	99	4.0	Reference
Less	282	12.9	3.51 (1.22-10.10)

CI: confidence interval, For children aged < 16 years.

prevalent (28). Consequently, the potential risk of HAV outbreaks in Northern Cyprus exists. The differences in HAV seroprevalence between the lower and higher socioeconomic groups may also increase the potential for outbreaks. Therefore, in addition to improved living conditions, large-scale childhood HAV vaccination as recommended by the WHO (3) in areas of intermediate endemicity seems to be logical in the Turkish Republic of Northern Cyprus.

Acknowledgements

The authors would like to acknowledge the Turkish Republic of Northern Cyprus Hepatitis A Study Team (Dr. Sıdıka Kayımbaşoğlu, Dr. Sonay Özbalıkçı, Dr. Gülten Erçal, Dr. Emine Güllüelli, Dr. Figen Bakkaloğlu, Dr. Ertan Doğan, Dr. Hasan Garabli, Dr. Hüseyin Erçal, Dr. Cemal Mert and Dilek Aslan) for their help and cooperation.

References

- World Health Organization. Hepatitis A. WHO/CDS/CSR/EDC/2000.7. (available on the internet at <http://www.who.int/emc>).
- Melnick JL. History and epidemiology of hepatitis A virus. *J Infect Dis* 1995; 171(Suppl 1): 2-8.
- World Health Organization. Hepatitis A vaccines. WHO position paper. *Weekly Epidemiological Record* 2000; 75: 38-42. (available on the internet at <http://www.who.int/wer/pdf/2000/wer7505.pdf>).
- Lionis C, Frangoulis E, Koulentakis M, Bizziagos E, Kouroumalis E. Prevalence of hepatitis A, B, and C markers in school children of a rural area of Crete, Greece. *Eur J Epidemiol* 1997; 13: 417-20.
- Dubois F, Thevenas C, Caces E, Vol S, Doctoreana A, Ecault JL et al. Seroepidemiology of hepatitis A in six departments in West-Central France in 1991. *Gastroenterol Clin Biol* 1992; 16: 674-9.
- Gil A, Gonzalez A, Dal-Re R, Ortega P, Dominguez V. Prevalence of antibodies against varicella zoster, herpes simplex (types 1 and 2), hepatitis B and hepatitis A viruses among Spanish adolescents. *J Infect* 1998; 36: 53-6.
- Moschen ME, Floreani A, Zamparo E, Baldo V, Majori S, Gasparini V et al. Hepatitis A infection: a seroepidemiological study in young adults in North-East Italy. *Eur J Epidemiol* 1997; 13: 875-8.
- Antunes H, Macedo M, Estrada A. Hepatitis A virus prevalence: Portuguese first results of low endemicity. *Acta Med Port* 2004; 17: 219-24.
- Sacy RG, Haddad M, Baasiri G, Khoriaty A, Gerbaka BJ, Abu-Elyazeed R. Hepatitis a in Lebanon: a changing epidemiological pattern. *Am J Trop Med Hyg* 2005; 73: 453-6.
- 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: 204-10.
- Hadjipanayis A, Hadjichristodoulou C, Kallias M, Sava K, Petsa A, Demetriadou K et al. Prevalence of antibodies to hepatitis A among children and adolescents in Larnaca area, Cyprus. *Eur J Epidemiol* 1999; 15: 903-5.
- Rothenberg RB, Lobanov A, Singh KB, Stroh G Jr. Observations on the application of EPI cluster survey methods for estimating disease incidence. *Bull World Health Organ* 1985; 63: 93-9.
- Henderson RH, Sundaresan T. Cluster sampling to assess immunization coverage: a review of experience with a simplified sampling method. *Bull World Health Organ* 1982; 60: 253-60.
- Sidal M, Unuvar E, Oguz F, Cihan C, Onel D, Badur S. Age-specific seroepidemiology of hepatitis A, B, and E infections among children in Istanbul, Turkey. *Eur J Epidemiol* 2001; 17: 141-4.
- Vançelik S, Güraksın A, Alp H. Hepatitis A seroepidemiology in Eastern Turkey. *East Afr Med J* 2006; 83: 86-90.
- Erdogan MS, Oktun M, Tatman-Oktun M, Akata F, Türe M. The epidemiology of hepatitis a virus infection in children, in Edirne, Turkey. *Eur J Epidemiol* 2004; 19: 267-73.
- Mossong J, Putz L, Patiny S, Schneider F. Seroepidemiology of hepatitis A and hepatitis B virus in Luxembourg. *Epidemiol Infect* 2006; 134: 808-13.
- Beran J, Douda P, Rychly R. Seroprevalence of viral hepatitis A in the Czech Republic. *Eur J Epidemiol* 1999; 15: 805-8.
- Termorshuizen F, Dorigo-Zetsma JW, de Melker HE, van den Hof S, Conyn-Van Spaendonck MA. The prevalence of antibodies to hepatitis A virus and its determinants in The Netherlands: a population-based survey. *Epidemiol Infect* 2000; 124: 459-66.
- Bell BP, Kruszon-Moran D, Shapiro CN, Lambert SB, McQuillan GM, Margolis HS. Hepatitis A virus infection in the United States: serologic results from the Third National Health and Nutrition Examination Survey. *Vaccine* 2005; 23: 5798-806.
- Letaief A, Kaabia N, Gaha R, Bousaadia A, Lazrag F, Trabelsi H et al. Age-specific seroprevalence of hepatitis a among school children in central Tunisia. *Am J Trop Med Hyg* 2005; 73: 40-3.
- de silva KS, Weerasuriya DC, Peelawattage M, Fernando S. Seroprevalence of hepatitis A antibodies in relation to social factors--a preliminary study. *Ceylon Med J* 2005; 50: 54-8.
- Mall ML, Rai RR, Philip M, Naik G, Parekh P, Bhawnani SC et al. Seroepidemiology of hepatitis A infection in India: changing pattern. *Indian J Gastroenterol* 2001; 20: 132-5.
- Mehr AJ, Ardakani MJ, Hedayati M, Shahraz S, Mehr EJ, Zali MR. Age-specific seroprevalence of hepatitis A infection among children visited in pediatric hospitals of Tehran, Iran. *Eur J Epidemiol* 2004; 19: 275-8.
- Lin JB, Lin DB, Chen SC, Chen PS, Chen WK. Seroepidemiology of hepatitis A, B, C, and E viruses infection among preschool children in Taiwan. *J Med Virol* 2006; 78: 18-23.
- Fix AD, Martin OS, Gallicchiol 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: 628-32.
- Tanaka J. Hepatitis A shifting epidemiology in Latin America. *Vaccine* 2000; 18 (Suppl 1): 57-60.
- Anis E, Leventhal A, Roitman M, Slater PE. Introduction of routine hepatitis A immunization in Israel--the first in the world. *Harefuah* 2000; 138: 177-80.